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Review

Human papillomavirus and head and neck carcinomas: focus on evidence in the babel of published data

Papillomavirus umano e carcinomi del tratto aerodigestivo: il punto sulle evidenze nella babele dei dati scientifici

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SUMMARY

Human papillomavirus (HPV)-associated squamous cell carcinoma of the oropharynx is a well-defined entity mostly affecting young to middle-aged male non-smokers. It is generally associated with a favourable outcome, and for this reason a less intensive therapeutic approach has been proposed for this subset of patients. The incidence of HPV-associated oropharyngeal cancers is rapidly increasing in most Western countries, but detailed epidemiological data are not available for the Italian population. Furthermore, among other head and neck regions, a smaller proportion of oral high-grade dysplasia and cancers seems to depend on HPV infection, whereas its role in laryngeal cancer is recognised as less relevant. HPV-dependent neoplastic transformation depends on the expression of viral oncogenes in the infected host cell that can only be directly documented through viral oncogene mRNA identification. The consensus on how to classify these patients from clinical and laboratory diagnostic points of view is still limited, with different approaches based on one or more diagnostic techniques including p16 immunostaining, in situ hybridisation and polymerase chain reation (PCR) amplification of viral DNA. The possibility of early diagnosis relying on the identification of HPV infection in oral and oropharyngeal exfoliated cells has so far provided unsatisfactory results, although viral persistence after treatment has been associated with risk of recurrence. Presently, sufficient data are not available to document the natural history and progression from tonsillar HPV infection to oropharyngeal cancer development, and to clearly define the modality of transmission and risk exposure, among which sexual behaviours appear to play a relevant role. The diffusion of HPV vaccination and its administration to both genders will undoubtedly dramatically modify the epidemiology of HPV-related head and neck cancers in the coming years.

KEY WORDS: HPV • Oropharyngeal cancer • Oral cancer • Diagnosis

RIASSUNTO

I carcinomi squamosi dell'orofaringe associati all'infezione da papillomavirus umano (HPV) costituiscono ormai una entità ben caratterizzata, che interessa prevalentemente maschi, giovani adulti o di mezza età, non fumatori. Essi hanno generalmente una prognosi più favorevole rispetto alla controparte non associate ad infezione, e per questo è stato proposto di dedicare a questo gruppo di pazienti un approccio terapeutico meno aggressivo. L'incidenza dei carcinomi dell'orofaringe associati a HPV è in rapido aumento nella maggior parte dei paesi occidentali, ma per quanto riguarda la popolazione italiana non sono disponibili dati epidemiologici in merito. Per quanto riguarda le altre regioni del distretto testa-collo, una più modesta porzione di lesioni displastiche di alto grado e di neoplasie appare essere correlata all'infezione da HPV, mentre il ruolo del virus nei tumori della laringe è stato parzialmente ridimensionato. HPV determina la trasformazione neoplastica delle cellule infettate tramite l'espressione dei suoi due oncogeni, E6 ed E7, che interagiscono con i meccanismi di apoptosi e regolazione del ciclo cellulare della cellula ospite. L'unica metodica in grado di documentare con certezza l'espressione degli oncogeni virali è attualmente l'amplificazione dell'RNA messaggero trascritto dai due oncogeni. Il consenso riguardo la strategia per l'identificazione dei pazienti affetti da carcinoma dell'orofaringe associato a HPV dal punto di vista clinico e diagnostico è tuttora limitato. Le metodiche diagnostiche più utilizzate, singolarmente o in combinazione, comprendono l'immunocolorazione con anticorpi diretti contro p16, l'ibridazione in situ per genotipi virali ad alto rischio e l'amplificazione del DNA virale mediate PCR. La possibilità di ottenere una diagnosi precoce grazie all'identificazione dell'infezione virale nelle cellule epiteliali esfoliate dal cavo orale o dall'orofaringe non ha finora fornito risultati soddisfacenti, tuttavia la persistenza del virus nel cavo orale in pazienti trattati per carcinoma dell'orofaringe ha dimostrato una significativa associazione con il rischio di recidiva del tumore. Non sono ancora disponibili sufficienti dati che documentino in maniera dettagliata la storia naturale dell'infezione a la sua progressione verso lo sviluppo di una neoplasia, e che definiscano con chiarezza le modalità di trasmissione e i fattori di rischio, comunque è chiaro che i comportamenti sessuali hanno un peso rilevante nel determinare il rischio di sviluppo di neoplasia dell'orofaringe HPV-correlata. La progressive diffusione nelle giovani generazioni del vaccino contro HPV, e soprattutto la sua estensione agli adolescenti di entrambi i generi è sicuramente destinata a modificare in maniera rilevante anche l'epidemiologica dei tumori HPV-correlati nel distretto testa-collo nel prossimo futuro.

PAROLE CHIAVE: *HPV • Carcinoma dell'orofaringe • Carcinoma orale • Diagnosi*

Acta Otorhinolaryngol Ital 2016;36:249-258

Introduction

Head and neck cancers rank as the sixth most common cancer worldwide and represent a serious challenge for the health community. The typical tumour is a squamous cell carcinoma (SCC) with variable grade of differentiation (from well to undifferentiated); it predominantly affects males in their fifth to sixth decade of life and, in Western countries, it is strongly related to tobacco smoke and alcohol abuse. The estimated annual burden of head and neck squamous cell carcinomas (HNSCC) is about 650,000 cases and the rate of death is approximately 50% [1].

The incidence of head and neck (HN) SCC has remained stable or even declined since the late 1980s because of a gradual decrease in typical risk behaviours. Despite this, SCCs occurring in the oropharyngeal (OP) region (particularly in the tonsils and base of the tongue) have increased from 2-3% to 5.5% of all HNSCCs in the USA and other countries [2 3]. Consistently, this increase has been shown to affect young men (30-40 years of age) with limited or no exposure to the typical risk factors. This epidemiological shift first suggested the involvement of a new driver cause for this type of cancer, which has been supported by epidemiologic and molecular evidence showing a causal role of human papillomavirus (HPV) in the subset of HNSCC originating from the oropharynx. The involvement of HPV in oral and oropharyngeal carcinogenesis was first proposed by Syrjanen in 1983 [4] and subsequently confirmed by several studies and recognised by the international scientific community [5]. At present, there is general agreement that clinical and prognostic implications of HPV-related OPSCC differ from those of conventional, tobacco-related SCC, and for this reason its treatment needs to be adapted accordingly [6-8].

Although HPV is unequivocally recognised as a causative agent for a subset of OPSCC, the abundance of published data regarding the biology and natural history of HPV infection, identification methods and best clinical management of patients with HPV-related cancer can be overwhelming for the general medical professional. In this review, the authors will focus on the main implications of HPV biological, diagnostic and prognostic implications in the wealth of published data on HPV investigation and detection in HN cancer.

Definition of HPV-associated carcinoma

General consensus has been reached on the definition of HPV-associated tumours, which requires the expression of viral oncogenic proteins E6 and E7, responsible for the neoplastic transformation of infected cells. Less solid evidence, however, supports the belief that HPV-DNA integration into the host cell genome is an essential step for virus oncogene expression in oropharyngeal cancer, as in the case in cervical carcinomas [9]. Since the first observation by Snijders et al. in 1992 [10], several studies have indeed documented the presence of HPV oncogene transcripts in tumours with prevalent episomal viral genomes [9]. Independently of the process leading to oncogene expression, HPV E6/E7 mRNA identification is considered the gold standard for classification of HPV-related tumours in the head and neck, although for patient stratification and epidemiological purposes more accessible strategies based on DNA or protein expression are generally accepted.

Epidemiological burden of HPV-associated head and neck carcinomas

The prevalence of HPV-associated head and neck carcinomas shows great variation among geographical areas, and is strongly associated with the anatomical site of the tumour. A recent, comprehensive, meta-analysis that considered the methods used to assess HPV tumour status[(11)] provided definite evidence that, among HN compartments, the attributable fraction of E6/E7 mRNA and HPV-DNA positive cases is highest in the oropharynx, close to 40%, whereas it is 16.3% in the oral cavity and less than 10% in the larynx. This result is of great relevance because it provides further confirmation for the current practice of reserving HPV testing to oropharyngeal cancer. Moreover, despite very different prevalences of HPV infection in tumours occurring at subsites such as the larynx [12], no clear prognostic implications have been documented for HPV-positive SCC occurring at these subsites [13].

Despite being so far limited to OPSCC, HPV oncogenesis in the head and neck region appears to be responsible worldwide for an increasingly relevant burden of new cases that are rapidly changing the traditional landscape of HN oncology. In countries where this phenomenon is more relevant, such as the USA and Northern European countries, the incidence of OPSCC among men younger than 60 years of age has been steadily increasing over the last 3 decades, despite the stability or even reduction of oral cancer incidence [14]. Several studies provided evidence for a role of HPV in the shift of HNSCC epidemiology: in Sweden, Ramqvist et al. reported a substantial increase in tonsillar and tongue base SCC during the period 1960-2006, among which the proportion of HPV-related tumours increased from 23% to more than 90% in the most recent years [15]. Studies in the USA have shown a similar trend and projected that, by 2020, HPV-related OPSCC will become the most common HPV-associated tumour, exceeding cervical cancer [2]. The epidemiology of HPV-associated OPSCC in Italy is less well documented. The Cancer Incidence in Five Continents survey [14] reported a moderate parallel reduction of both oral and oropharyngeal cancer incidence over the last 3 decades, but nationwide data on HPV-related cancer incidence have not been collected. By reviewing the scientific literature produced

in Italy, partial data from the north suggests a lower but nonetheless increasing prevalence: two studies published by the Istituto Tumori of Milan with a 6-year interval from each other reported a prevalence increasing from 17% [16] to 50% [17]. Two recent studies reported, respectively, a 32% and 39.8% prevalence of HPV-associated OPSCC in consecutive series of oropharyngeal cancers collected in two different Roman Institutes between 2009-2011 and 2010-2014 [18 19]. Our group could document a similar raising trend: since the beginning of HPV analysis in 1997 until 2010 less than 30% of OPSCC were HPV-positive [20], while the proportion increased to 48% in the years 2011-2013 [21] and has recently reached 50%.

The clinical relevance of the increasing prevalence of HPV-related SCC is not limited to the number of cases, but needs to take into account the specific characteristics of the affected population, which generally differs from the typical HN tumour patient population in younger age, lack of tobacco and alcohol exposure and higher socioeconomic status [22]. This implies a shift towards a therapeutic approach that takes into account the longer expected life span and lower risk of second exposure-related tumours is needed, as well as the need for increased risk awareness for young non-smoker males who have so far been considered at 'low risk' for their lack of exposure to conventional HNSCC carcinogens.

Diagnostic classification of HPV-associated carcinoma

Correctly diagnosing HPV-associated HNSCC now represents one of the major challenges faced by otolaryngologists and HN pathologists. When HPV-associated OPSCC was recognised as an independent subgroup of HNSCC [22], more than of a decade of experience had already been accumulated on the diagnosis of HPV-related cervical cancers, and several diagnostic platforms had been implemented and patented for HPV identification, mostly based on DNA identification and/or amplification. Customary cooperative patterns in pathology units led to the widespread translation of the diagnostic protocols for gynaecological cancer into the HN field. This resulted in a wealth of data that can hardly be comparatively analysed, in part because of the heterogeneity of tests employed, and in part because of the inherent difficulty in precisely defining the subsite of tumour origin. Much evidence supports a correlation between HPV oncogenesis and tumours developing from the epithelium of the tonsillar crypts [23]. However, defining the specific subsite of tumour origin in advanced lesions diffusely extending beyond the limits of the original anatomical structures can be difficult, both with clinical evaluation and imaging, and indeed most studies do not specify the topographic criteria of classification. Although histological evidence of non-keratinising, so-called 'basaloid' morphology is suggestive of a deep tonsillar origin of SCC [24], HPV expression in conventional keratinising SCC is also observed [25]. For this reason, studies aimed at correlating HPV status with precise topographical data and histomorphology are required to further clarify the issue of the specific anatomic site of infection and tumour transformation.

With the above-mentioned limitations, the proportion of HPV-DNA-positive cases in different oropharyngeal subsites ranges from 53.9% (CI 46.4-61.3) to 47.8 (CI 43.1-61.8), respectively, in the tonsil and tongue base [11], However, at variance with cervical tumours, the presence of HPV-DNA in OPSCC cells does not equal HPV-driven oncogenesis [26], being possibly explained by passenger infections facilitated by lowered immune resistance (tumour, therapy, previous smoking), although other explanations, including false-negative mRNA amplification and contaminations, should be taken into account. As previously mentioned, HPV-mediated oncogenesis depends on the expression of the two viral oncogene proteins E6 and E7 that interact with cellular pathways of apoptosis and cell cycle control, and which are also the unequivocal markers of HPV-associated SCC [27]. Although the availability of standardised laboratory methods for mRNA extraction and amplification is increasing, it is not yet easily available for routine diagnosis in general pathology labs, mostly because fresh samples are still required for reliable results. Therefore, we are relying on different diagnostic strategies, whose diagnostic accuracy has to be assessed against the gold standard of HPV-mRNA amplification. Currently used tests that can be applied on routine formalin-fixed, paraffin-embedded samples include DNA amplification, DNA in situ hybridisation (ISH) and immunohistochemical identification of the cell cycle regulator $p16^{ink4a}$. As far as *PCR* amplification is concerned, the vast range of primer sets, most of them patented, targeting either DNA sequences shared by more high-risk (HR) and low-risk (LR) HPV genotypes [28] or specific sequences for a single genotype (esp. HPV16), and the parallel heterogeneity of methods used to analyse and interpret PCR results, make it very difficult to assess overall PCR accuracy with respect to the gold standard of HPV oncogene mRNA expression. The reported sensitivity of various PCR tests is generally high (60-99%), whereas the specificity is low (33-76%) [29-36]. Recently, real-time quantitative (q-) PCR has been applied to the study of HPV-associated OPSCC. Although the use of different experimental approaches (primer sets, target gene, technologies) also impairs comparisons in this setting, this approach can increase test accuracy given that HPV oncogene mRNA expression is strictly correlated with high viral load [32 35]. Commercial qPCR platforms for HPV screening and typing of cervical samples have been released on the market by several companies, but their use in OPSCC is still limited. A recent study analysed the performance of the Roche Cobas™ HPV test on cytological samples of HNSCC, documenting 100% sensitivity and

86% specificity compared with p16 ICH and ISH, but further studies are required to establish the test accuracy with respect to mRNA expression [37].

ISH has acquired a relevant role in HPV identification in OPSCC because of the development of standardised automated protocols using either genotype-specific (HPV16) probes or probes that target several HR genotypes, and the inherent morphological correlations on tissue slides (Fig. 1a). Although the reported sensitivity is ideally 1-2 viral copies per cell 23, ISH sensitivity with respect to mRNA gold standard is generally lower than that of PCR, although its specificity is good (88-100%) [29 30 32 38-40].

p16 immunostaining is the only method showing, albeit indirectly, evidence of HPV transcriptional activity, and contemporarily allowing morphological correlations (Fig. 1b). p16 is a cyclin-dependent kinase inhibitor whose expression is linked via a negative feed-back loop with pRB expression; pRB inactivation by HPV E7 leads to p16 overexpression that can be demonstrated immunohistochemically with specific monoclonal antibodies, while normal expression levels rest below the detection threshold. The prognostic role of p16 expression is sufficiently well documented to support its use in oropharyngeal cancer patient classification even independently of HPV status [41 42], to the point that it was the only selection criterion in multicentre trials aimed at assessing the efficacy of deintensified therapy protocols in HPV-positive patients [43 44]. It is necessary to remark however, that while p16 sensitivity is very high compared to the gold standard of mRNA expression, consistent evidence shows that its specificity is lower (72-80%) [29 30 32 45]. Poor specificity is due to the presence of other regulatory pathways of p16 expression apart from HPV oncogenes [46]. Recent studies have suggested that p16 overexpression in HPV-negative tumour cells may be associated with mechanisms of cell senescence [47]. A further issue that challenges the use of p16 as a surrogate marker of HPV oncogenic infection is its common expression in normal tonsil reticulated cells from which HPV-positive SCC are believed to originate [47]. p16-negative, HPV-mRNA-positive cases have also been reported by some authors [48]. Finally, the optimal cut-off of expression for positivity has not yet been univocally established, although 70% nuclear and cytoplasmic positivity appears to better predict the presence of HPV [49]. Despite these limitations, p16 immunostaining is still considered an acceptable and accessible surrogate marker for the classification of HPV-related OPSCC [31 50 51], provided that the interpretation of staining results follows the reported guidelines and is not translated to non-oropharyngeal sites [52 53].

Diagnostic algorithms

The suboptimal diagnostic accuracy of the above-summarised diagnostic methods can be partially overcome by the use of diagnostic algorithms that pair, either in parallel or sequentially, more than one test. Given a sensitivity approaching 100% and lower cost, there is general agreement on the use of p16 immunostaining as the first diagnostic step, followed by either HPV-DNA amplification or ISH [29 54]. More recently, RNAscope™ (Advanced Cell Diagnostics, Hayward, CA) has been validated as a new ISH method to directly document the presence of HPV mRNA in histological tissue sections [39 55] (Fig. 1c, d). De-

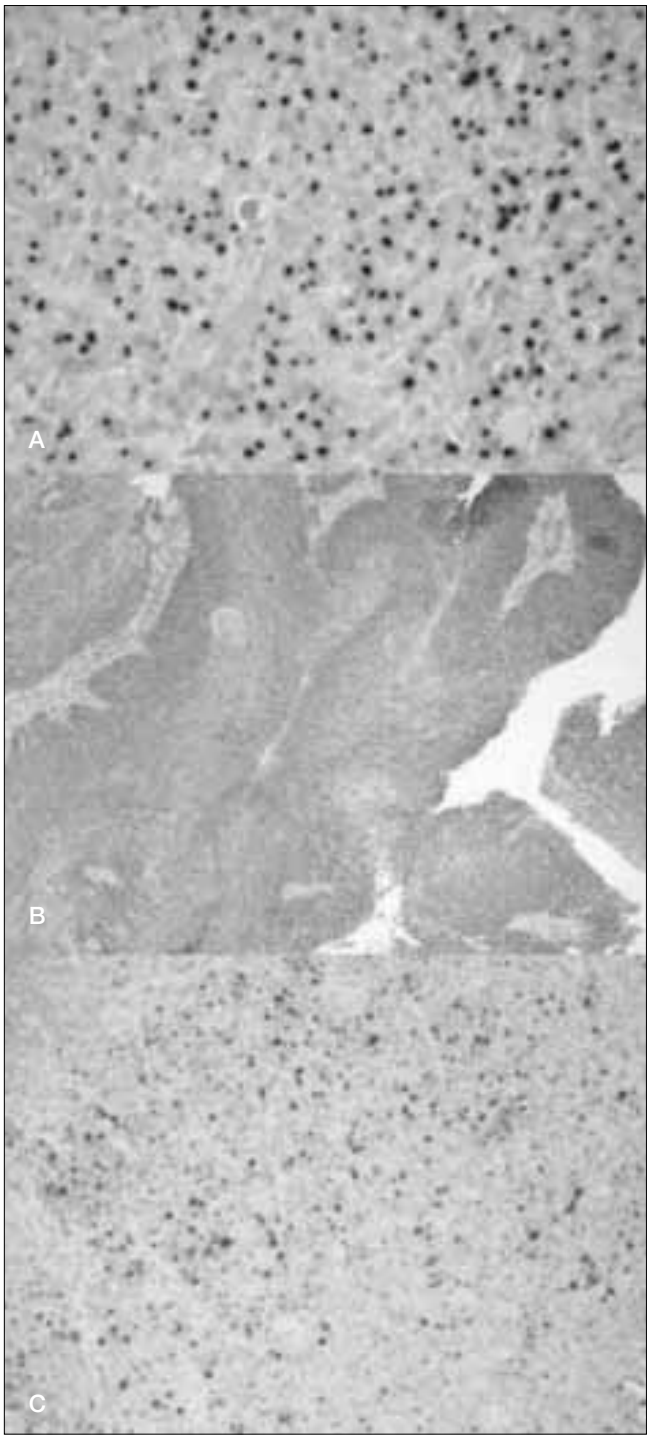

Fig. 1. Light micrographs showing a positive reaction in ISH (a), p16 positive immunostaining (b), and mRNA ISH positive reaction (c) in HPV-positive OPSCC.

spite its excellent diagnostic accuracy [39 56], application of RNAscope in routine diagnosis is probably limited by its high cost and complex protocols. We have demonstrated that a stepwise diagnostic algorithm that includes both ISH and HR-HPV-DNA amplification (Fig. 2) can correctly classify all mRNA ISH-positive cases [21]; however, RNAscope is the only tool for the direct recognition of HPV transcriptional activity in paraffin-embedded samples.

A further issue is whether only HPV16 or all HR genotypes should be investigated in OPSCC, and which viral gene should be amplified. In our experience, we adopted a very sensitive broad-spectrum primer set (SPF10) paired with reverse-line blot genotyping [LiPA, Genotyping Assay Version Extra (Fujirebio Europe, Ghent, Belgium)] that is widely used in genital and head and neck pathology in paraffin samples [2 57] and found non-HPV16 HR infections in 5-10% of cases. When amplifying viral sequences comprised in the L1-L2 region in oropharyngeal SCC, false negative and discordant results can be observed because of possible L1 deletion upon viral integration [20 58 59]. The amplification of the HPV16 E6 gene in a separate reaction can help in resolving ambiguous results (i.e. p16+/ISH+/PCR-).

Topographic correlations. Evidence is accumulating that supports a specific correlation between HPV infection and neoplastic transformation of the reticulated epithelium lining the tonsillar crypts [23], which can in turn explain the typical non-keratinising or 'basaloid' morphology of HPV-associated OPSCC (Fig. 3) [24]. The biological peculiarities of tonsillar structures have been claimed to be responsible for this selective tropism. The deep mucosal crypts may trap HPV viral particles and prolong the contact time between the virus and the mucosa; furthermore, tonsillar reticulated epithelia have intercellular 'gaps' that mimic the microlesions known to allow viral access to the basal cell layers in the cervical epithelium [60]. Another possibility is that the local immune environment of the tonsil is directly involved in malignant transformation. Although HPV-related tumours can by no means arise from superficial tonsillar keratinising epithelium [25], within the oropharyngeal region HPV-related oncogenesis appears to be strongly related to tonsillar structures, whereas other oropharyngeal subsites are rarely involved. Importantly, a clear distinction of the site of origin of the tumour is often not straightforward from a clinical point of view, especially with larger tumours. Therefore, new cases of OPSCC should not be excluded from HPV testing on a purely topographical basis.

Non-oropharyngeal HPV-associated SCC

We have previously mentioned the low impact of HPV infection in non-oropharyngeal oncogenesis. One possible exception can be the oral cavity, where HPV infection has been demonstrated in the periodontal pockets [61], and HPV replication appears to be favoured by the epithelial cell proliferation induced by chronic periodontal inflammation [62]. Recent studies documented HPV association in a morphologically characteristic subset of oral high-grade dysplasia and SCC, mostly originating from the floor of the mouth and mobile tongue [63 64], which accounts for

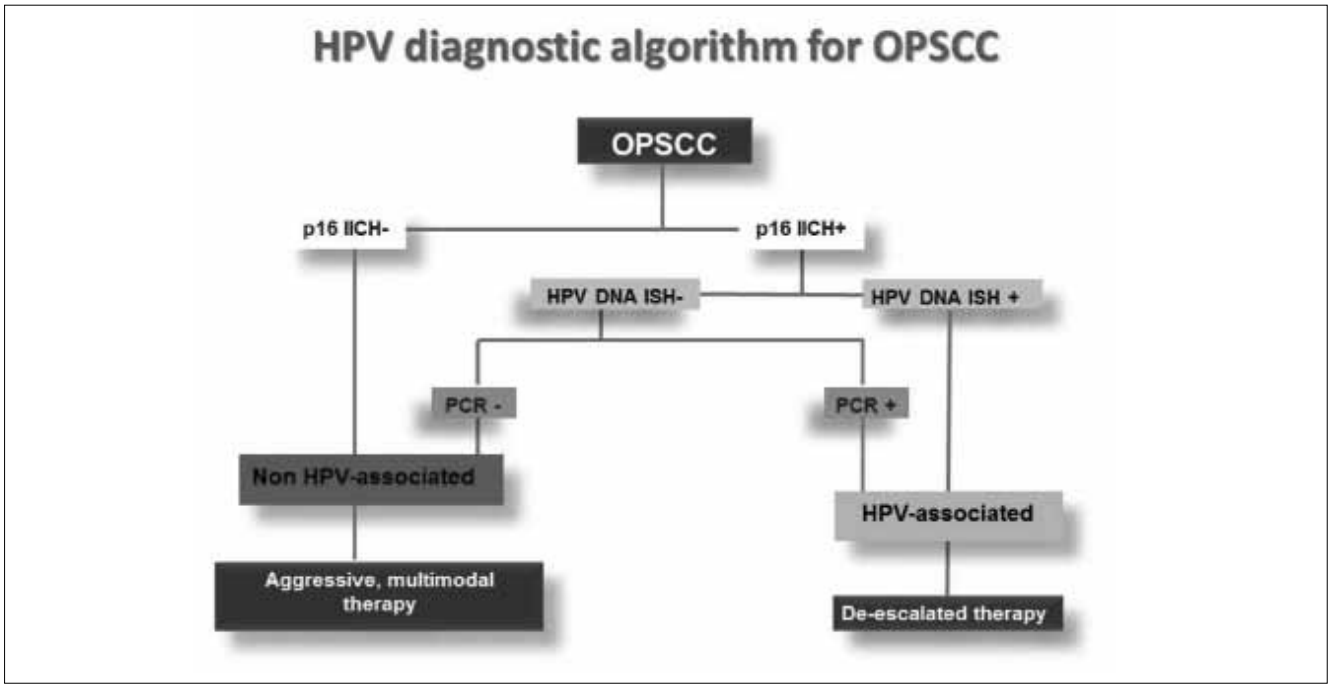

Fig. 2.The diagnostic algorithm currently in use at our centre for the assessment of HPV-status in OPSCC.

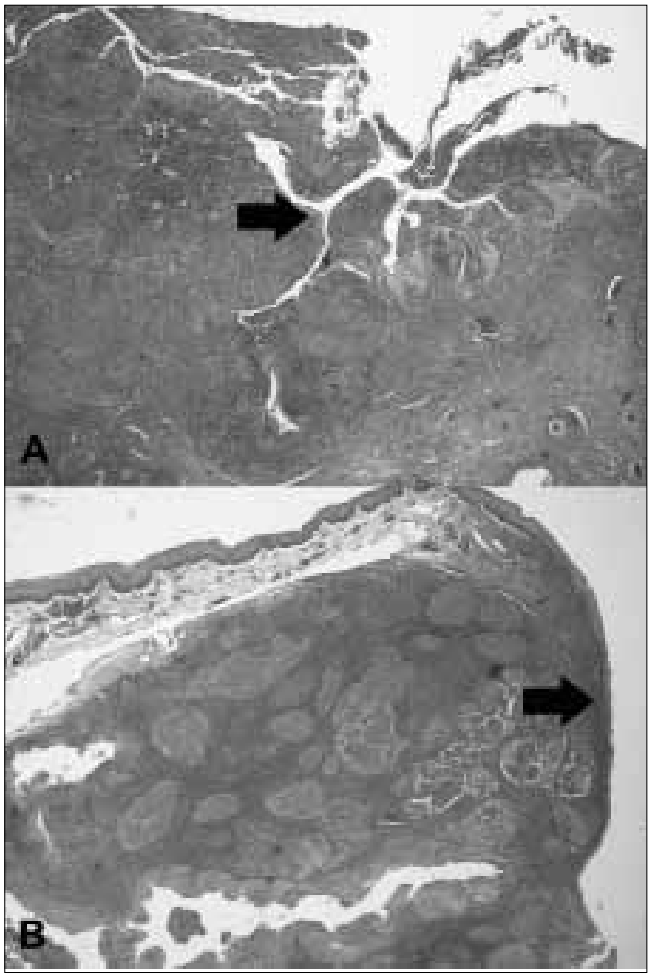

Fig. 3. Different morphological features of HPV-independent (a) and HPV-related OPSCC (b). OPSCC not associated with HPV generally arise from the surface tonsillar epithelium (arrow), have keratinising features and show both superficial and invasive growth. HPV-related OPSCC originate from the tonsillar crypts, do not produce keratin, grow deeply in the tonsil and are covered by intact squamous epithelium (arrow) (a,b, H&E stain).

5.9% of all oral cases [65]. The clinical relevance of these observations must be fully assessed before extending routine HPV characterisation to oral preneoplastic lesions.

Early diagnosis and prevention of HPV-related oropharyngeal SCC

Early identification by Papanicolau smear of HPV-related preneoplastic lesions in the uterine cervix has dramatically changed the epidemiology of female genital tract tumours. Attempts at reproducing the PAP-smear approach in the oral cavity for early diagnosis of OPSCC, however, have not been successful [66]. The failure of this approach can be explained with the anatomical peculiarities of HPV-related tumours: because they most frequently arise from HPV infection and neoplastic transformation of the deep tonsillar crypts, as previously described, the sampling of superficial exfoliated cells, even when specifically targeting the tonsillar surface, will hardly provide transformed cells from the crypts, which are located under the surface [67].

Oropharyngeal cytology and HPV-DNA analysis, on the contrary, represent a valid diagnostic possibility for HPV-status characterisation in patients with clinically-evident oropharyngeal abnormalities. In a recent study, abnormal brush cytology was significantly associated with the risk of HNSCC, whereas HPV positivity in cytobrush samples was strongly associated with a diagnosis of OPSCC [68] and could be used as an alternative to invasive sampling. Furthermore, oral HPV persistence after successful tumour treatment has been shown to be associated with disease recurrence and poor prognosis [69].

More importantly, several studies have been undertaken to define the prevalence and natural history of HPV infection in the oral cavity of healthy subjects to find a possible connection with oropharyngeal tumour development. In the USA, Gillison et al. [70] have shown that the overall incidence of oral HPV infection is 7%, lower than in the genital tract, and is more common in men (10.1% *vs.* 3.6%). Considering HR genotypes, HPV16 has been found in 1% of subjects of both sexes, corresponding to an estimated 2.13 million infected individuals in the USA. Tobacco use appears to be strongly associated with HPV oral infection in healthy subjects in most studies, together with male sex [71]. However, one-time measurement of incident HPV infection does not provide evidence for risk of developing HPV-related cancer, as we know from cervical pathology. The HIM study confirmed that most newly acquired oral infections are cleared within 1 year, similarly to what occurs at genital sites. The median duration of infection was shown to be 6.9 months for any HPV, and 7.3 months for HPV16 [72]. Given that in the female genital tract HPV persistence in the cervical mucosa is the strongest risk factor for high-grade intraepithelial and invasive SCC [73 74], we expect a similar mechanism to take place in tonsillar cancerogenesis. Although persistent oral HR-HPV infection can be found in a proportion of high-risk (HIV-positive) subjects and appears to be associated with tonsillar HPV infection [66], there is as yet no prospective evidence (cytological or epidemiological) that correlates oral or tonsillar HPV infection with risk of OPSC in the general population. Only one study documented a temporal relationship between HPV infection and oropharyngeal cancer development, by showing that seropositivity for anti-HPV16 E6 antibodies in healthy subjects followed longitudinally predated cancer, and was associated with the risk of head and neck SCC and of HPV-associated oropharyngeal SCC [75]. Anti-E6 antibodies were also correlated with risk of tumour recurrence in patients treated for HPV-associated oropharyngeal SCC [76].

The low prevalence of persistent oral HPV infection suggests that the cost-benefit ratio of a large-scale oral

screening programme to identify subjects at risk of oropharyngeal SCC would be extremely low, especially in our population where HPV-associated tumours account for a relatively limited proportion of cases. An alternative strategy could be that of targeting subjects at increased risk of oral HPV infection for screening. In addition to HIV-positive immunosuppressed patients [66], it has been demonstrated that the risk of acquiring oral HPV infection is related to sexual behaviour, both hetero- and homosexual [77 78]. Preliminary evidence suggests that, besides individual sexual habits, the partners of patients with HPV-related squamous epithelial lesions of the genital area are at increased risk for oral HPV infection and oropharyngeal SCC [79-81], so they could represent a potential target for oral HPV infection and oropharyngeal cancer screening protocols.

Future perspectives

Quadrivalent (HPV 6/11/16/18) and bivalent (HPV 16/18) anti-HPV vaccines have been available since 2006 and 2007, respectively. Vaccination policies vary worldwide concerning age of administration, population coverage and gender. Only a few countries have so far introduced gender-neutral vaccination for pre-adolescents, and its introduction was generally delayed by a few years with respect to female vaccinations [82]. Despite this variability, in countries where coverage has been high a dramatic reduction in cervical high-grade squamous intraepithelial lesions as well as warts [83 84] has been observed. It is relevant to note that a significant reduction in cervical but also oral HPV prevalence was demonstrated in the Swedish female population a few years after the introduction of the vaccination [85]. Although the interval between tonsillar HPV infection and SCC diagnosis is unknown, we expect that vaccination benefits in HN cancer epidemiology would be delayed by several years. Notably, a small retrospective study has suggested that previous resection of the palatine tonsils significantly reduces the risk of tonsillar carcinoma, even though it does not affect the risk of HPV-related cancers arising in other oropharyngeal subsites, and opens new interesting opportunities for primary prevention [86].

Conclusions

Five-year survival rates are significantly different for patients with HPV-related OPSCC compared with HPV-negative patients (75-80% *vs.* 45-50%) [6 16 87 88]. Based on the higher survival rates registered among patients with HPV-positive OPSCC, the application of de-intensified protocols has been proposed in this patient group, regardless of the specific treatment strategy (surgery, radiation therapy, concurrent chemoradiotherapy or induction chemotherapy plus concurrent chemoradiation). In addition, the reduced risk of second malignancies in patients with HPV-related OPSCC [89] is also expected to modify the natural history of OPSCC patients, and further supports the need for treatments that do not persistently affect patients' quality of life. Future clinical research will provide further insights, but the combination of tumour HPV status, pack/year amount of tobacco exposure, and cancer stage should already be used routinely to classify patients as having low, intermediate or high risk as proposed by reputed authors [6].

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HEAD AND NECK

Parapharyngeal space tumours: video-assisted minimally invasive transcervical approach

Tumori dello spazio parafaringeo: approccio transcervicale video-assistito mini invasivo

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SUMMARY

The purpose of the present study was to evaluate the advantages of a video-assisted, minimally invasive transcervical approach to benign and malignant parapharyngeal space (PPS) tumours. Ten patients affected by benign and malignant PPS neoplasms underwent a combined transcervical and video-assisted minimally invasive approach, using Hopkins telescopes. We describe the operative technique and perform a review of the literature. Definitive histology revealed 3 pleomorphic adenomas, 2 schwannomas, 2 metastatic papillary thyroid carcinomas, one carcinoma ex pleomorphic adenoma, one cavernous haemangioma and one basal cell adenoma. Mean tumour size was 37.2 mm (range: 19-60). Operation time ranged from 75 min to 185 min (mean: 146.7). One case was converted to transcervical-transparotid approach. Patients were discharged on postoperative day 2-5. One patients presented hypoglossal nerve paresis. The minimally invasive video-assisted transcervical approach is safe and feasible for selected benign and malignant PPS tumours. Furthermore, it offers harmless dissection in a deep and narrow space, accurate haemostasis and continuous control of critical anatomic structures.

KEY WORDS: Parapharyngeal space tumour • Video-assisted • Endoscopic • Pleomorphic adenoma • Papillary thyroid cancer

RIASSUNTO

L'obiettivo dello studio è stato valutare i vantaggi di un approccio transcervicale mini-invasivo video-assistito per l'exeresi di neoformazioni maligne e benigne dello spazio parafaringeo. Sono stati trattati 10 pazienti con approccio trans-cervicale mini-invasivo video-assistito con l'utilizzo di telescopi di Hopkins. Viene descritta la tecnica chirurgica e una revisione della letteratura. L'esame istologico definitivo è stato in 3 casi di adenoma pleomorfo, in 2 casi di schwannoma, 2 metastasi linfonodali da carcinoma tiroideo, un carcinoma ex adenoma pleomorfo, un emangioma cavernoso ed un adenoma a cellule basali. La dimensione massima delle neoformazioni è stata in media di 37,2 mm (da 19 a 60 mm). Il tempo chirurgico è stato dai 75 ai 185 minuti (media 146,7). In un caso è stata necessaria la conversione ad approccio transcervicale-transparotideo. I pazienti sono stati dimessi dalla seconda alla quinta giornata postoperatoria. In un caso è stata osservata paresi definitiva del nervo ipoglosso. L'approccio trans-cervicale mini-invasivo video-assistito è sicuro e offre la possibilità di seguire esattamente il piano di clivaggio, permettendo un'emostasi accurata e avendo sempre il controllo delle strutture anatomiche più critiche.

PAROLE CHIAVE: *Tumori spazio parafaringeo • Video-assistito • Endoscopico • Adenoma pleomorfo • Carcinoma tiroideo*

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Introduction

Parapharyngeal space (PPS) is classically described as an inverted pyramid-like area with the floor at the skull base and apex at the greater horn of the hyoid bone. The tensor-vascular-styloid fascia divides PPS into prestyloid and retrostyloid compartments.

Neoplasms arising in the PPS are rare tumours accounting for 0.5 to 1% of all head and neck masses [1]; 82% are benign and 18% are malignant: pleomorphic adenoma is the most common histotype (29%).

Most PPS lesions need first-line surgical treatment performed with a transoral, transcervical, transparotid, or transmandibular approach, alone or in combination.

Recently, endoscopic and robotic approaches have been widely applied in head and neck surgery to minimise tissue trauma and wound-related complications and improve cosmetic outcomes. Reports on their use in PPS surgery are extremely limited.

Materials and methods

Patients

Ten patients with PPS tumours were treated with transcervical video-assisted surgery at the Department of Otorhinolaryngology – Head and Neck Surgery of the University Vita-Salute San Raffaele, Milan, Italy from July 2012

to March 2015. Mean age was 58.2 years (range: 42-72). The opportunity to opt for a video-assisted approach was mainly evaluated with magnetic resonance imaging (MRI): we enrolled only patients affected by tumours smaller than 6-7 cm in their largest diameter and with a definite cleavage plane from nearby structures.

Only 4 patients were symptomatic (Table I). Diagnostic workup included contrast-enhanced MRI. Computed tomography (CT) was required in 4 cases for better radiological assessment. Preoperative ultrasound-guided fine needle aspiration cytology (FNAC) was performed in 3 patients: directly on the PPS mass in 2 cases and on a cervical node in the other.

Operative technique

All procedures were performed under general anaesthesia by the same surgical team. As previously described [2,3], video-assisted dissection is performed through a minimal cervical incision (depending on the tumour size) made in a natural skin crease, approximately 3 cm below the mandibular angle at the level of the digastric muscle. The aim of this approach is to reach the whole PPS through a small anatomical corridor, wide enough to allow use of an endoscope and some endoscopic instruments. A skin flap is elevated in the subplatysmal plane. The submandibular gland is retracted anteriorly and the tail of the parotid gland posterosuperiorly. The posterior belly of digastric muscle could be divided or cranially retracted. The hypoglossal nerve is then identified and preserved.

The next steps are performed under assistance of 0° and 30° Hopkins telescopes using a high definition camera. During video-assisted surgical steps, the second surgeon keeps the telescope: this allows the first surgeon to use both hands. The third surgeon provides a wider surgical field using retractors. Operative room setup is shown in Figure. 1.

Thereafter, the internal carotid artery is identified. Tumour dissection is performed upwards and circumferentially in an extracapsular plane: nearby vessels and nerves are carefully retracted from the mass. At this point, the suction-dissector becomes a useful tool to maintain a bloodless surgical field. The tumour is then released and removed en bloc. Endoscopic inspection confirms the completeness of the resection. The posterior belly of the digastric muscle is reapproximated if previously divided. A suction drain is placed inside the wound, which is closed in layers. The drain is removed as soon as daily drainage falls below 20 ml: the patient can be discharged the day after.

Results

Gender, age, operating time, tumour size, pathology and postoperative stay are detailed in Table I. Median surgical incision was 67.1 mm (range: 35-140). Tumour size ranged from 19 mm to 60 mm in maximum diameter (mean: 37.2 mm) and markedly affected operation time, which ranged from 75 to 185 minutes (mean: 146.7 min). Definitive histology revealed benign neoplasms in 7 patients and malignant tumours in 3 cases. The drain was removed from postoperative day 2 to 5 and patients were discharged the following day on regular diet.

In particular, patient 6 suffered from a residual, permanent deficit in tongue motility since he was affected by hypoglossal nerve schwannoma. PPS tumour dissection was concomitant to revision thyroidectomy and homolateral selective neck dissection (II-IV, VI levels) in patient 5, as

Table I. Patients and operative features.

Case	Ages	Sex	Presenting symptom	FNAC	Radiological tumour size, mm	Incision Length, mm	Operative time, min	Pathology	LOS, days	Complications
1	53	F	Thyroglobulin elevation	Pap	36x14x19	56	170	Pap	6	None
2	53	F	Dysphagia	NA	46x45x31	48	165	PA	4	None
3	57	F	None (Occasional at MRI)	NA	19x17x15	35	75	Hem	4	None
4	72	F	None (Occasional during clinical examination)	NA	43x40x35	85	105	PA	3	None
5	42	F	Laterocervical swelling	Pap	31x15x16	140*	170*	Pap	4	None
6	60	F	None (Occasional during MRI)	NC	25x22x17	48	130	Schw	4	Hypoglossal paresis
7	70	M	None (Occasional at CT)	NA	20x13x12	44	125	BCA	5	None
8	56	F	Laterocervical swelling	NA	57x50x30	108**	180**	PA	5	None
9	65	F	None (Occasional at MRI)	NA	35x30x25	42	162	Schw	4	None
10	54	F	Left otitis media with effusion	NA	60x59x27	65	185	Ca ex-PA	3	None

**Procedure included selective neck dissection (levels II-IV, VI) and revision thyroidectomy.*

*** Procedure converted to open transcervical-transparotid approach*

LOS = length of stay; Hem = cavernous haemangioma; Pap = papillary thyroid carcinoma; NC: not conclusive; PA = pleomorphic adenoma; Schw: schwannoma; BCA: basal cell adenoma; Ca ex-PA: carcinoma ex pleomorphic adenoma; NA = not available

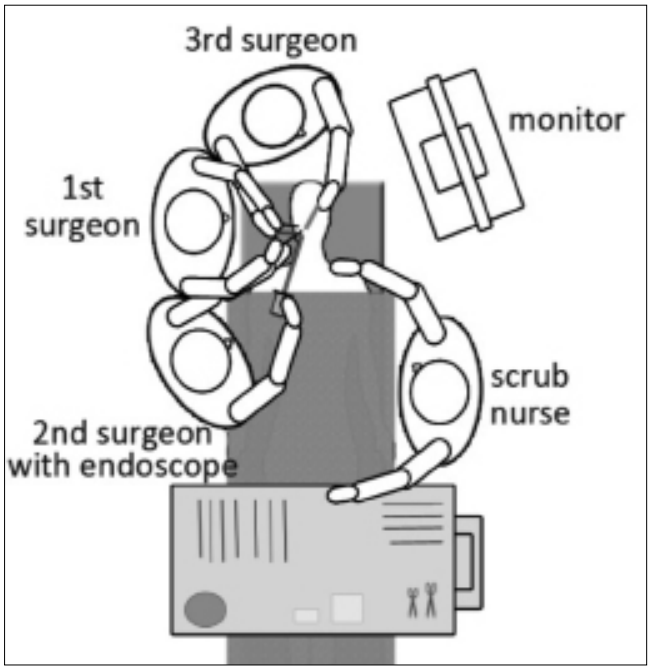

Fig. 1. Operative room setup during video-assisted steps.

he was affected by metastatic papillary thyroid cancer: incision length and operative time were longer. Skull base adhesion of the mass made conversion to transcervical-transparotid approach unavoidable in patient 8. Therefore, excluding cases 5 and 8, median incision length was 52.9 mm (range: 35-85) and mean operative time was 139.6 min (range: 75-185).

After a mean follow-up period of 22 months (from 2 to 37 months), neither radiologically nor clinically relapse was detected into the PPS.

Discussion

Surgery is the mainstay of treatment of most PPS tumours. The anatomic complexity (Fig. 2) of the PPS had led to the development of several surgical approaches. Tumour size, proximity to cervical neurovascular structures and histotype should guide the surgeon in tailoring the strategy for treatment.

The transcervical approach is commonly used for most PPS neoplasms [4]: it provides good local disease control with minimal risk of facial nerve injury and good cosmetic results. However, it is not considered safe for masses with significant vertical extension or radiological suspicion of invasion of cranial foramina [5].

The transparotid approach is used for tumours of the deep lobe of parotid gland [6]. It offers a wide access to PPS, but the risk of facial nerve injury is higher due to its unavoidable extensive dissection and retraction during the procedure [2 7].

Many authors [8-10] have addressed the need for additional approaches to obtain oncologically safe results, such as mandibulotomy. In particular, Malone et al. [10] described 40% of combined techniques. The transmandibular ap-

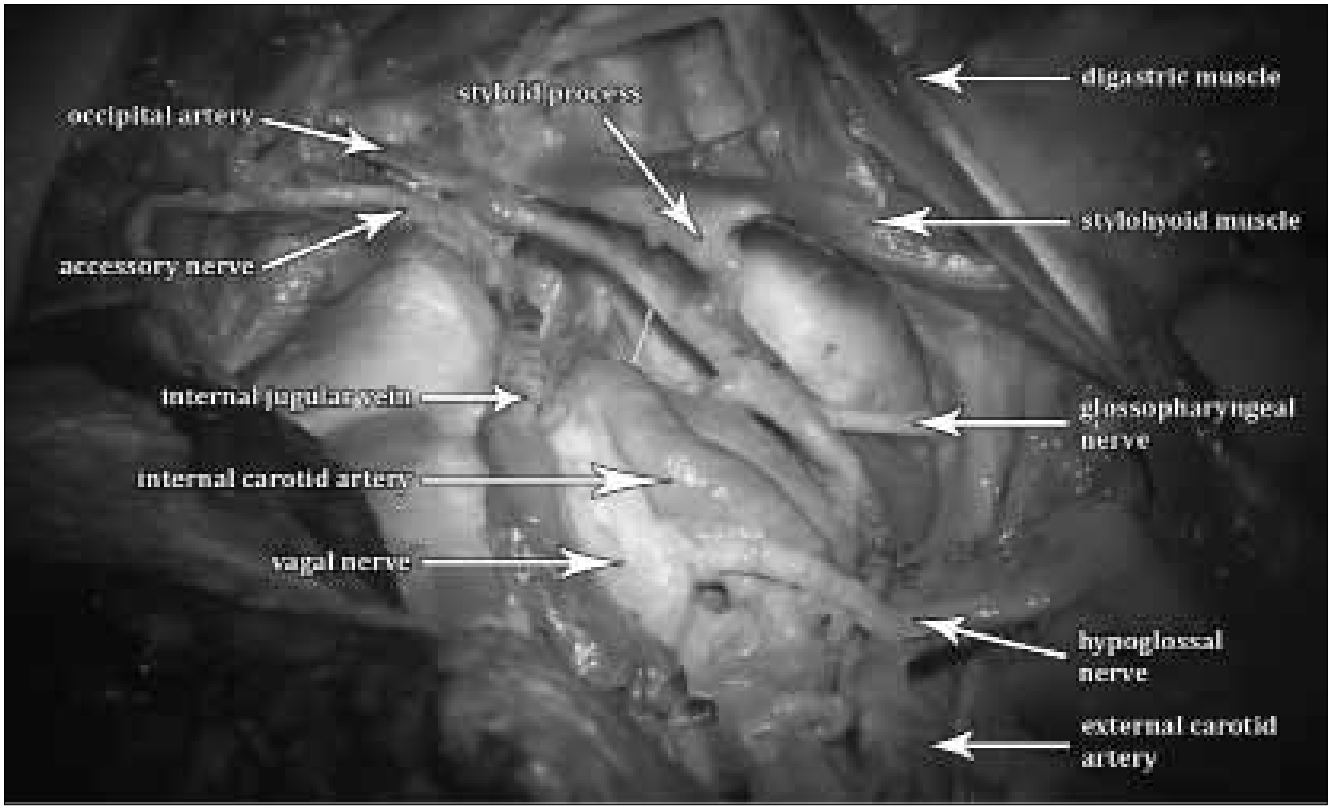

Fig. 2. Anatomy of the PPS.

proach ensures very wide exposure of the PPS and should be considered for highly vascularised neoplasms, recurrent tumours, malignant masses and lesions invading the skull base. However, it should be kept in mind that this technique often results in important nerve injuries, malocclusion and malunion [2].

The orbitozygomatic-middle fossa approach is another technique reported in literature, although it has been described for a restricted number of extremely large tumours involving the skull base [11].

The transoral approach is the most controversial. It provides limited, direct access to the PPS and makes identification of neurovascular structures more difficult. Moreover, it is linked to a higher risk of intra-surgical tumour rupture, incomplete removal of the mass, uncontrollable haemorrhage and facial nerve injury [4].

Some authors [12] suggested robotic transoral resection for large benign masses that are accessible from the oropharynx and involving the poststyloid space. This approach offers a high rate of disease control and a low risk of post-operative complications, such as lockjaw or cranial nerve injuries.

Endoscopic visualisation has been introduced relatively recently in order to obtain better neoplasm control and improve wound cosmetic outcomes. Dallan et al. [13] identified some critical surgical landmarks in endoscopic transoral PPS dissection of six fresh human cadaver heads. Another anatomic study was conducted by Taniguchi et al. to assess the feasibility of an endoscopic transnasal route [14]. The first endoscopic PPS approach on a living person was published in 2010 for paediatric transnasal abscess drainage [15]. Subsequent reports were published with transvestibular [16], transoral [17] and transcervical [2] approaches for benign PPS tumours.

The traditional transcervical approach provides very limited surgical exposure to the PPS: in fact, it is 5-6 cm deep from the cutaneous surface (Fig. 3d). Surgeons are forced to work in a long, dark and narrow tunnel. Digital exploration and digitoclasia are certainly helpful, but direct visual control is not possible during these operations.

The goal of this early experience was to appreciate the advantages of an endoscopic approach, especially from the surgeon's perspective. Using 0° and angled telescopes it is possible to constantly check relationships between the mass and nearby vessels or cranial nerves. The close visual control and magnification of the image allow the surgeon to follow the tumour surface, easing the recogni-

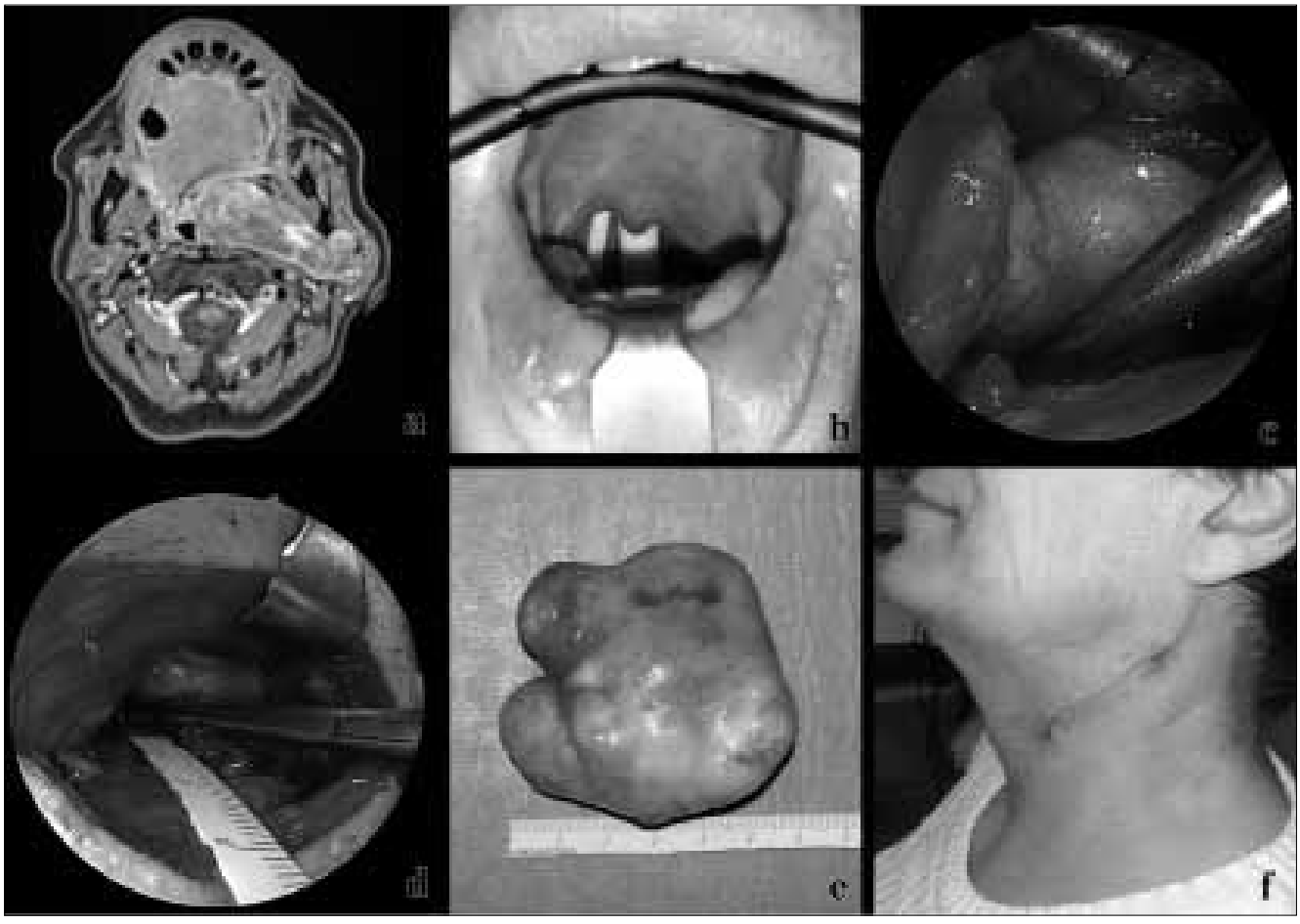

Fig. 3. Case 10: A, pre-operative RMN; B, medialisation of the left pharyngeal wall; C, video-assisted dissection of PPS tumour using suction-dissector; D, demonstration of the deep and narrow surgical tunnel for PPS tumours dissection; E, surgical specimen; F, aesthetic result on postoperative day 11.

tion of cleavage planes, even in lobulated neoplasms. This latter feature reduces the risk of tissue spillage that could have dramatic consequences even for benign lesions.
The video-assisted technique simplifies the identification of small vessels, allowing accurate haemostasis. Furthermore, using the suction-dissector (Fig. 4) it is possible to work in a near-bloodless surgical field due to one-hand simultaneous or alternate dissection and aspiration.
In our series, the nature and the dimensions of the masses markedly influenced operation time. Average surgical time (146.7 min) was similar to that reported by Beswick et al. [2] (133 min) in the only video-assisted PPS tumour dissection previously reported in the literature.
Hospitalisation time was similar to our non-video-assisted approaches, but was higher than that reported by Beswick et al. [2], perhaps due to our prudential attitude in removal of drains.
In summary, a minimally invasive video-assisted transcervical approach should be considered for PPS tumours smaller than 7 cm in their largest diameter. In our opinion, histotype is not an indication itself: even selected malignant neoplasms could be excised with this technique if a definite cleavage plane is recognisable and if the histotype does not require removal of marginal healthy tissues around the mass. We effectively treated three malignant tumours: 2 expected nodal metastases of thyroid papillary carcinomas and an occasional carcinoma ex pleomorphic adenoma. In all these cases surgery was definitive. Nonetheless, after our preliminary experience we would not recommended this technique for malignant masses invading adjacent tissues: a video-assisted minimally invasive transcervical approach cannot offer sufficient access to PPS. Furthermore, we consider it dangerous to use a video-assisted approach for hypervascular tumours (e.g., paragangliomas).

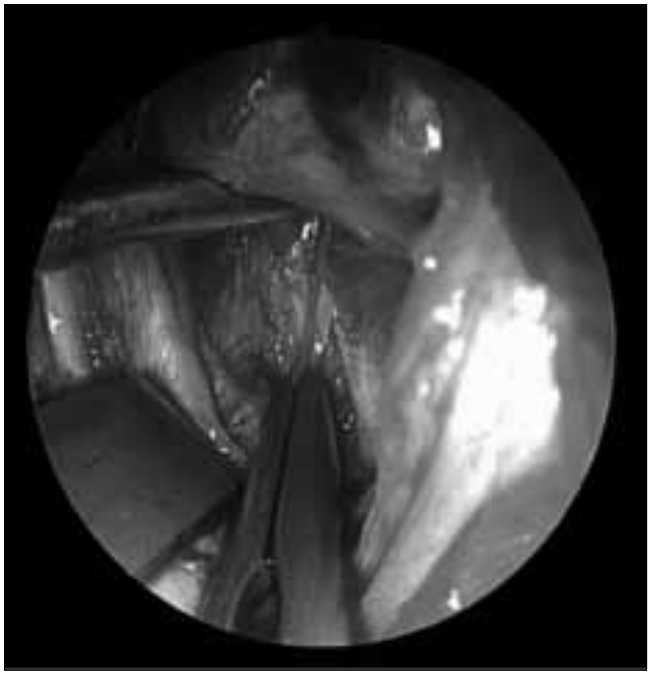

Fig. 4. Video-assisted dissection of PPS tumour (patient 2) from pre-vertebral fascia using suction-dissector.

Conclusions

A minimally invasive video-assisted transcervical approach is a new technique for excision of sizable benign and selected malignant PPS tumours. It allows clear identification of critical surgical landmarks and guides the dissection through the right cleavage plane, offering the chance for accurate hemostasis while decreasing surgical complications.

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HEAD AND NECK

Surgical complications in orbital decompression for Graves' orbitopathy

Complicanze chirurgiche in pazienti sottoposti a decompressione orbitaria per oftalmopatia di Graves

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SUMMARY

The objective of this study is to analyse the complications of orbital decompression in Graves' orbitopathy. The clinical records of 946 patients who had been operated on with orbital decompression for Graves' orbitopathy were reviewed and the intra- and post-operative complications with minimum follow-up of six months were analysed. An extensive review of the literature was carried out to compare results. In the case-series reported here the most frequent complications were: wasting of the temporal region (100%) in patients operated on using a coronal approach; permanent hypoesthesia of V2 (13%) and V1 (8%) in patients operated on with an upper eyelid incision. In only one patient was a total monolateral lesion of V2 reported. The most severe complications consisted in reduction of visual acuity in 5 patients, and CSF leak with cerebral complications in 2 patients, who were operated on with a non-endoscopic endonasal approach. Three patients had intra-operative haemorrhages and 3 patients had post-operative haemorrhages requiring further surgical intervention. The incidence of symptomatic sinusitis/mucoceles was 0.75%. In conclusion, orbital decompression carried out with endoscopic endonasal technique and via transpalpebral accesses appears to be associated with a low incidence of complications. Knowledge of the causes of the possible complications in the different surgical approaches can definitely help to reduce their incidence.

KEY WORDS: Graves' orbitopathy • Orbital decompression • Different approaches • Complications

RIASSUNTO

L'obiettivo di questo studio è analizzare le complicanze della decompressione orbitaria in pazienti affetti da oftalmopatia Basedowiana. Abbiamo analizzato 946 pazienti sottoposti a decompressione orbitaria per orbitopatia di Graves e le complicanze intra- e post-operatorie con un follow-up minimo di 6 mesi. Abbiamo eseguito inoltre un'estesa revisione della letteratura per comparare i risultati. Nel nostro studio le più frequenti complicanze sono state: atrofia della regione temporale (100%) nei pazienti sottoposti a decompressione con approccio coronale; ipoestesia permanente di V2 (13%) e V1 (8%) in pazienti sottoposti a decompressione con approccio transpalpebrale superiore. Un solo paziente ha avuto una lesione totale monolaterale di V2. Le complicanze più gravi sono state la riduzione dell'acuità visiva, che si è verificata in 5 pazienti, e la perdita di liquido cerebrospinale con complicanze cerebrali, verificatesi in 2 pazienti, entrambi operati con approccio endonasale non endoscopico. 3 pazienti hanno avuto un'emorragia intraoperatoria mentre 3 pazienti un'emorragia postoperatoria che ha richiesto un secondo intervento chirurgico. L'incidenza delle sinusiti/mucoceli sintomatici è stata dello 0,75%. In conclusione abbiamo evidenziato come la decompressione orbitaria eseguita con tecnica endoscopica endonasale e con accessi transpalpebrali sia una procedura chirurgica con una bassa incidenza di complicanze. La conoscenza delle cause delle possibili complicanze nei differenti approcci chirurgici può sicuramente aiutare a ridurre la loro incidenza.

PAROLE CHIAVE: *Orbitopatia di Graves • Decompressione orbitaria • Approcci differenti • Complicanze*

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Introduction

Graves' Orbitopathy (GO) is an auto-immune inflammatory disease that causes an increase in the volume of orbital adipose tissue and the extrinsic muscles of the eye. Proportionally to the prevalence of oedema or fibrosis, clinical manifestations of GO are extremely variable. The surgical indication for orbital decompression can thus be attributed to mild aesthetic problems, but also to severe proptosis, subluxation of the ocular globe, corneal exposure, in the presence or absence of diplopia and/or strabismus. Most of the publications available on orbital decompression of GO describe case-studies focusing on patients with differing pathological situations, operated on with different techniques [1]. To further complicate the

situation, surgical techniques are generally not described in detail, and chosen by the surgeon on the basis of his specialisation [2]. In fact, this makes evaluation of surgical complications very difficult.

To our knowledge, few publications have reported the rate of complications adequately [3-12]. Leong et al. [12] reported that the global incidence of complications was 9.3%, while the rate of severe complications with long-term sequelae was estimated to be 0.12%. The authors underline that many studies do not mention complications, although this does not necessarily mean that no complications arose. Moreover, Boboridis and Bunce [1] mentioned that it is difficult to reach any safe conclusions regarding the efficacy and possible complications of various techniques. However, it is of fundamental importance to investigate more in depth possible complications, and above all their causes, to further improve surgical techniques and achieve better results.

In this work, the complications that occurred in the case-histories of 946 patients with the use of different surgical techniques are collected and analysed. Furthermore, the causes are critically evaluated and the techniques implemented to reduce the incidence. A careful comparison with data from literature is presented.

Materials and methods

Clinical records of 946 (1762 orbits) of 957 consecutive patients (11 patients lost to follow-up) operated on by a single surgeon from December 1992 to December 2014 were collected. Post-operative data refer to a minimum follow-up period of 6 months. The local research ethics committee approved the study.

The first surgical technique used was the trans-antral infero-medial decompression (TA) according to Walsh and Ogura [13], (21 patients, 39 orbits). Next, the three-wall decompression with coronal approach (C) according to Mourits et al. [14] (21 patients, 38 orbits) was used. Our variation on this technique was the infero-medial approach performed with non-endoscopic trans-nasal access. The combination of the two techniques (TA + C) was carried out in 30 patients (54 orbits).

Since 2000 orbital decompression has been performed on the three walls (lateral, medial and inferior) with or without removal of adipose tissue, adapting the technique to the severity of the proptosis and/or the presence of optic neuropathy and eyes imbalance. Lateral (L) and medial (M) orbital wall surgery was performed as described previously [15 16]. The orbital floor was approached with trans-inferior eyelid access or with the "swinging eyelid" technique [17]. Due to the fact that every complication is correlated to the surgical approach, it is important to know the exact number of each surgical procedures to understand the incidence rate. The lateral orbital wall approach was used 1489 times, medial orbital wall approach 1200 times and infero orbital approach 278 times.

Adipose tissue was removed, but only in combination with decompression of one or more bony walls and almost always with external approaches. In the bilateral forms, both eyes were decompressed during the same operation to better balance the level of decompression between the two sides.

The following were all considered as major complications: death, loss or reduction of visual acuity, cerebrospinal fluid leaks (CSF), central nervous system pathologies, significant bleeding that significantly prolonged the duration of the operation or which rendered a second surgical intervention necessary, permanent impairment of the supraorbital nerve (V1) or the infraorbital nerve (V2) and total palpebral ptosis. Minor complications included injury of the dura mater of the medial and/or anterior cranial fossae, easily controlled bleeding, transient hypo-aesthesia of the forehead (V1) and of the cheek and upper lip (V2), sinusitis, mucocele, corneal lesions, cutaneous palpebral lesions, mild ptosis, wasting of the temporal region, oscillopsia and subcutaneous emphysema.

Possible causes and technical tips are analysed in order to reduce the incidence of single complications.

The problem of post-operative diplopia, considered by some authors to be a common sequela of the decompression operation [18 19], and certainly closely linked to the disease of the extrinsic muscles of the eye [20], was not taken into account.

A systematic review of the literature was performed using large biomedical databases (PubMed and Cochrane) and combining the key words "orbital decompression", "complications", "Graves' disease", "Graves' orbitopathy", "ophthalmopathy" and "thyroid eye disease". We critically analysed and selected 40 of 189 articles that reported the following complications: loss of visual acuity, cerebral complications, haemorrhages and haematomas, hypesthesia and dysesthesia in areas of innervation of the first (V1) and second (V2) branches of the trigeminal nerves, symptomatic sinusitis and mucoceles.

Results

The rates of complications in our patients with the surgical techniques used are shown in Table I.

Death

No death was correlated with the intervention of orbital decompression during the entire period examined.

Loss of visual acuity

We had five patients with mono-lateral loss of visual acuity, three following an endonasal approach, though not

Table I. Surgical complications.

Complications	Number of patients (Surgical technique)	Rate of complications (Surgical technique)
Death	0	0%
Loss of visual acuity	3 (TA); 2 (L+M)	3.23% (TA); 0.13% (L+M)
CSF leaks	8 (M); 38 (L)	0.67% (M); 2.55% (L)
Pneumocephalus	1 (M)	0.08%(M)
Meningitis	1 (M)	0.08% (M)
Cavernous sinus bleeding	1 (M)	0.08% (M)
Major bleeding	2 (L)	0.13% (L)
Haematoma of the temporal muscle	1 (C)	1.09% (C)
Intraorbital bleeding	3 (M)	0.25% (M)
Epistaxis	1 (M)	0.08% (M)
Hypoesthesia of V1	118 (L)	8% (L)
Hypoesthesia of V2	196 (S); 9 (TA)	13% (S); 9.68% (TA)
Anaesthesia of V2	1 (I)	0.36% (I)
Symptomatic chronic sinusitis	5 (M)	0.42% (M)
Mucocele	4 (M)	0.33% (M)
Corneal ulcers	8 (L)	0.54% (L)
Section of the levator muscle	7 (L)	0.47% (L)
Small areas of burn on the upper eyelid	30 (L)	2.01% (L)
Wasting of the temporal region	51 (C)	100% (C)
Oscillopsia	2 (L)	0.13% (L)
Hyposmia	4 (M)	0.33% (M)
Subcutaneous emphysema	6 (M)	0.5% (M)

TA: transantral. C: coronal. L: lateral wall. M: medial wall. I: inferior wall.

endoscopic, during the first years of our experience. The other two patients had a balanced decompression. One developed ocular keratitis and the other remained without a certain cause. Only partial recovery of visual acuity was seen during follow-up.

Cerebral complications and CSF leaks

We observed one case of meningitis after a CSF leakage not identified and not treated intra-operatively and one case of pneumocephalus. Another eight CSF leaks were identified and managed intra-operatively, without complications. One patient presented a cavernous sinus bleeding and haematoma that was managed post-operatively in a conservative fashion.

We observed 38 cases of mono-lateral lesion of the meninges of the middle or anterior cranial fossa, during lateral approaches with removal of the greater wing of the sphenoid bone. All cases were managed conservatively in 2-3 days, with compressive packing of the eye.

Haemorrhages/haematomas

We had 2 intra-operative major bleedings, during a lateral approach, which complicated the intervention, but both patients recovered without sequelae.

In the postoperative period we had a haematoma of the temporal muscle, after a coronal approach, which required intervention with general anaesthesia. Similarly, three patients were taken back into surgery within 24 hours after first surgery for intraorbital lateral bleeding.

Hypo/anaesthesia of V1, V2 innervation areas

We had 260 cases of mono-lateral hypesthesia of V1 (17.5%) one month after surgery; 118 (8%) continued to report permanent hypesthesia 6 months after surgery.

419 cases operated on externally had mono-lateral hypesthesia of V2 (28%) at one month after surgery; 196 (13%) continued to report permanent hypesthesia 6 months after surgery. We had 9 cases (9.7%) of hypesthesia of V2 in patients operated on with the TA technique. One patient (0.36%) reported the section of V2, with total deficit, during a revision procedure performed on the orbital floor with an inferior eyelid approach.

Symptomatic sinusitis/mucocele

We had 5 patients with persistent post-operative sinusitis (two frontal and three maxillary sinusitis), that were managed successfully with medical therapy. Furthermore, other four patients were operated on for mucocele (two posterior-ethmoidal and two frontal-ethmoidal) 5-8 years after orbital decompression. All these patients were operated on with endoscopic transnasal access.

Palpebral lesions

In 7 patients (0.47%) section of the levator muscle of the upper eyelid occurred with access through the upper eyelid. Six patients had no sequelae because the levator muscle was sutured with absorbable stitches at the end of the surgery. In 1 patient the lesion was not recognised during the intervention, but the patient refused corrective surgery. In 30 patients (2.01%) operated on with a lateral approach, small areas of burn on the skin of the upper eyelid, caused by the drill, occurred.

Corneal ulcers

We had some cases of corneal de-epithelisation and 8 cases (0.54%) of corneal ulcer caused by intra-operative manoeuvres, all during an external approach; all these resolved successfully with medical treatment.

Wasting of the temporal region

21 patients (100%) operated on with a coronal approach manifested hollowing, of various degrees, of the temporal region. These patients complained of mild disorders with mastication, but no aesthetic damage.

Oscillopsia

2 patients (0.13%) operated on with lateral approach, including complete removal of the greater wing of the sphenoid bone, manifested oscillopsia during mastication. The disorder was well tolerated and the patients refused corrective surgery.

Hyposmia

4 patients (0.33%) operated on with an endonasal approach complained of hyposmia.

Subcutaneous emphysema

6 patients (0.5%) operated on with endo-nasal approach presented inferior palpebral emphysema in the post-operative period, after having violently blown their noses. All these cases resolved spontaneously.

Discussion

Many works reporting the results of decompression intervention are available in the literature, although in general these describe small groups of patients often presenting varying clinical situations. Moreover, orbital decompression is performed with different techniques, depending more on the specialisation and experience of the surgeon than on ocular muscle impairment. Since the typology of complications is closely associated with the technique utilised, we wished to carry out an accurate analysis of the complications arising in our patients, in view of the fact that we used all the approaches described with the exception of Olivari's technique [21], despite the removal of adipose tissue being an integral part of many of our interventions. Leong et al. [12] reported that of 4176 decompressed orbits, the incidence of complications was 9.3%. We feel that, rather than making a simple evaluation, it is important to distinguish between major and minor complications and to try to understand the causes. Leong refers that no death occurred as a consequence of orbital decompression, but in the medical literature 2 deaths have been described following post-operative complications with the TA and infero-medial transpalpebral technique [8 22].

The worst ocular complication is total or partial loss of visual acuity. In our case-series, there were had 5 cases. Three were at the beginning of our experience with a non-endoscopic endonasal approaches. In the first case (TA technique), it was most likely that traction maneuvers on adipose tissue, which was very fibrotic, were performed to increase decompression, causing severe damage, more probably on a vascular basis, of the optic nerve. In the other 2 patients, bone fragments (anterior section of the lateral wall of the sphenoid sinus in one case and a small fragment of lamina papyracea in the other) directly or indirectly compressed the nerve: with endoscopic techniques, this complication may easily be avoided. Another patient developed ocular keratitis after balanced decompression. The last patient had total loss of visual acuity after balanced decompression partially recovered after steroid therapy. The cause of the visual loss was not identified because postoperative MRI and CT scan were negative. In the literature, 2 cases of monolateral blindness [23] and 2 cases of visual loss [3] have been reported, all of whom were operated on with infero-medial decompression. Warren et al. [24] reported 5 patients who developed postoperative panophthalmitis and progressed to blindness. Jernfors et al.[10] reported one bilateral and one monolateral postoperative blindness in patients operated on due to progressive optic neuropathy.

We report 1 case of meningitis and 1 of pneumocephalus due to incorrect closure of CSF leaks in patients operated on with a non-endoscopic endonasal approach. Subsequently, 8 other CSF leaks were closed with a middle turbinate mucoperiosteal flap. There are 28 other cases reported in the literature of CSF leaks and other major cerebral complications (Table II). Although in some cases spontaneous closure of the fistulas is described, we strongly recommend performing skull base reconstruction. On the opposite side, small lesions of the meninges of the anterior and middle cranial fossa with CSF tears (through lateral access) usually represent a minor concern which does not require any skull base reconstruction. We found 5 similar cases in the literature [7 25 26]. In our experience, in the case of lesions of less than 2-3 mm, maintenance of drainage without suction and moderate compressive eye-packing resolve the leaks in a few days.

We had 2 major bleedings, during lateral approaches, which were managed intra-operatively. One patient who was operated on with a coronal approach presented bleed-

Table II. Cerebral complications and treatment after orbital decompression reported in literature.

Authors	Surgical technique	Number of patients	Number of orbits	Cerebral complications	Treatment
Bailey et al. [28]	3-walls	55	97	2 CSF leaks	1 nasal packing; 1 neurosurg op
De Santo [23]	TA	200	399	4 CSF leaks	No treatment for the leak
Garrity et al. [3]	TA	428	851	15 CSF leaks (4 meningitis, 1 patient died); 1 frontal lobe haematoma	4 second operations
Kashkouli et al. [9]	Transconjunctival approach	1 (case report)		1 subarachnoid haemorrhage and frontal lobe ischemia	No treatment for the leak
Kasperbauer et al. [33]	Medial wall and floor (endoscopic approach)	59	88	2 CSF leaks	2 closed intraop
McCormick et al. [8]	Medial wall and floor (inferomedial approach)	2 (case report)		2 CSF leaks (1 died)	No treatment for the leak
Murchison et al. [34]	Medial wall and floor (transconjunctival approach)	1 (case report)	1	Meningoencephalocele	Resection of the herniated brain tissue and skull-base reconstruction
Nadeau et al. [35]	1 orbit: medial wall 16 orbits: medial and lateral walls 6 orbits: medial wall and floor 50 orbits: medial, lateral and floor	40	73	1 CSF leak	No treatment for the leak
Schaefer et al. [36]	Inferomedial approach	41	72	1 CSF leak	No treatment for the leak
Warren et al. [24]	TA	305	610	1 CSF leak with meningitis	No treatment for the leak

TA: transantral. CSF: cerebrospinal fluid.

Table III. Haemorrhages and haematomas after orbital decompression reported in the literature.

Authors	Surgical technique	Number of patients	Number of orbits	Bleeding
Antisdel et al. [37]	3-walls	50	86	1 epistaxis (second operation)
Eloy et al. [38]	Endoscopic approach	16	27	1 epistaxis
Garrity et al. [3]	TA	428	851	1 frontal lobe haematoma 11 blood transfusions
Jernfors et al. [10]	TA / Transnasal endoscopic approach	78	144	2 epistaxis
Kashkouli et al. [9]	Transconjunctival approach	1 (case report)		1 subarachnoid haemorrhage and frontal lobe ischaemia
Kikkawa et al. [39]	3-walls		9	1 haemorrhage (second operation)
Lund et al. [40]	59 orbits: inferomedial approach	33	59	3 moderate haemorrhages
McCormick et al. [8]	Medial wall and floor (transconjunctival approach)	2 (case report)		1 epistaxis
Metson et al. [19]	8 orbits: lateral wall 33 orbits: medial and lateral walls	26	41	1 epistaxis
Nadeau et al. [35]	1 orbit: medial wall 16 orbits: medial and lateral wall 6 orbits: medial wall and floor 50 orbits: medial, lateral and floor	40	73	1 epistaxis
Olivari [21]	Fat removal	57	108	1 haematoma
Pezato et al. [41]	3-walls	15	17	1 haematoma
Ulualp et al. [30]	Medial wall (endo) and floor (transconjunctival approach)	15	28	1 haematoma
White et al. [42]	Medial (endo) and lateral walls	34	64	2 epistaxis

TA: transantral.

ing in the area of the temporalis muscle (which was sectioned and sutured with this technique). This patient required a revision procedure. Two other patients presented bleeding in the lateral orbit compartment, starting from the adipose tissue. Currently, our strategy is to carefully check bleeding of the adipose tissue that has been re-arranged laterally at the end of the intervention, and we use drainage with suction for 24 hours. More or less severe bleedings have been reported in the literature, described in all surgical approaches, although they are more prevalent in the endonasal approaches (Table III).

In 9 patients operated on with the TA technique, hypoesthesia of V2 occurred. Subsequently, with both endoscopic and non-endoscopic endonasal approaches, we had no more sensitivity disorders of V2 while hypoesthesia of limited areas of the forehead (8%), of the cheek, lip and wing of the nose (13%) were frequent with external access. The cause of impairment of the nerve is associated with drilling of the lower tract of the greater wing of the sphenoid bone, near the inferior orbital fissure, prior to the entrance of V2 in the bony canal of the maxillary bone. Only 1 patient had a monolateral section of V2: this happened during a revision procedure of the orbital floor. In the literature, this complication has been reported to ranges from 0.7% to 32% for V2 and around 5% for V1 (Table IV).

The incidence of symptomatic sinusitis is quite low, considering that some patients already present signs of chronic sinusitis at the moment of the orbital decompression. We have had only 4 mucoceles treated surgically. This incidence, however, is likely to be underestimated insomuch as small mucoceles can remain asymptomatic for years and some patients may not refer to our hospital for postoperative sinusitis. Our data is in agreement with those in the medical literature. The incidence of symptomatic sinusitis and mucoceles was low (Table V).

We had 1 case of complete unilateral lesion of the levator palpebrae muscle, not identified during surgery. We advise performing the superior eyelid approach carefully in order to reduce the risk of damaging the levator palpebrae muscle: in the event of partial or complete cut, immediate suturing of the muscle should resolve the problem [15].

Table IV. Hypesthesia and dysesthesia in areas of innervation of V1/V2 after orbital decompression reported in the literature.

Authors	Surgical technique	Number of patients	Number of orbits	Number of transient V1 hypoesthesia	Number of permanent V1 hypoesthesia	Number of transient V2 hypoesthesia	Number of permanent V2 hypoesthesia
Bailey et al. [28]	3-walls	55	97			5 (5%)	
Barkhuysen et al. [43]	3-walls (transconjunctival approach)	7	14			2 (14.3%)	1 (7.1%)
Carrasco et al. [44]	63 orbits: TA 65 orbits: transconjunctival approach	75	128			29 (46%) WO 4 (6.1%) transconj	
De Santo [23]	TA	200	399			200 (50%)	10 (2.5%)
Garrity et al. [3]	TA	428	851			Frequent	23 (2.7%)
Goh et al. [45]	10 orbits: lateral wall 65 orbits: medial and lateral wall 5 orbits: medial wall and floor 2 orbits: lateral wall and floor 69 orbits: medial, lateral and floor	88	151			15 (9.9%)	1 (0.7%)
Jernfors et al. [10]	TA / Transnasal endoscopic approach	78	144				25 (32%)
Kalmann et al. [4]	3-walls (coronal approach)	125	250	Almost all	1 (0.4%)	6 (2.4%)	1 (0.4%)
Kingdom et al. [46]	3-walls	77	114				1 (0.9%)
Liao et al. [47]	Transforniceal	35	62			2 (3.2%)	1 (1.6%)
Lund et al. [40]	35 orbits: Patterson's approach 24 orbits: endoscopic approach	33	59				4 (6.8%)
Maroon et al. [26]	4-walls (ext)	4	7				1 (14.3%)
Michel et al. [48]	Endoscopic approach	78	145				4 (2.8%)
Olivari [21]	Fat removal	57	108	2 (1.9%)	5 (4.6%)		
Sasim et al. [27]	92 orbits: coronal approach 47 orbits: swinging eyelid approach	74	139		5% of the coronal approach		25% of the swinging eyelid approach
Tjon et al. [49]	TA	75					3 (4%)
Warren et al. [24]	TA	305	610			20%	5%

TA: transantral.

Table V. Symptomatic sinusitis and mucoceles after orbital decompression reported in literature.

Authors	Surgical technique	Number of patients	Number of orbits	Number of frontal sinusitis	Number of maxillary sinusitis	Number of sinus surgery
Antisdel et al. [37]	3-walls	50	86	1	2	3
Bough et al. [50]	TA	1 (case report)	2		2	2
Cansiz et al. [51]	18 orbits: TA + medial wall (endoscopic approach) 8 orbits: TA + medial wall (endoscopic approach) + lateral wall	19	26		1	1
Carrasco et al. [44]	63 orbits: TA 65 orbits: transconjunctival approach	75	128		10 (6 TA, 4 transconjunctival)	
Eloy et al. [38]	Endoscopic approach	16	27	1		1
Garrity et al. [3]	TA	428	851		18 (not specified what kind of sinusitis)	0
Goh et al. [45]	10 orbits: lateral wall 65 orbits: medial and lateral wall 5 orbits: medial wall and floor 2 orbits: lateral wall and floor 69 orbits: medial, lateral and floor	88	151		3	1
Hanabury et al. [52]	TA	28			4	1
Jernfors et al. [10]	TA / Transnasal endoscopic approach	78	144		14	3
Kasperbauer et al. [33]	Medial wall and floor (endo)	59	88		3 (2 maxillary sinusitis, 1 ethmoid mucocele)	3
Lee [53]	External ethmoidectomy	1 (case report)	1	1		1
Leung et al. [11]	Endoscopic approach	20	29	4	1	3
Lund et al. [40]	35 orbits: Patterson's approach 24 orbits: endoscopic approach	33	59	1	2	2
Mensink et al. [54]	3-walls	1 (case report)	1	1		
Michel et al. [48]	Endoscopic approach	78	145	1	1	
Nadeau et al. [35]	1 orbit: medial wall 16 orbits: medial and lateral wall 6 orbits: medial wall and floor 50 orbits: medial, lateral and floor	40	73		8 (20%, not specified what kind of sinusitis)	4
Remulla et al. [5]	Endoscopic approach	3 (case report)		3		
Rizk et al. [55]	18 orbits: TA + medial wall (endoscopic approach) 2 orbits: medial wall (endoscopic approach)	10	20		1 ethmoid sinusitis	0
Rose et al. [56]	3-walls	6	6		6 Silent Sinus Syndrome	6

TA: transantral

All patients we operated with coronal approach presented hollowing of various degrees in the temporal regions, and temporary disorders of mastication. These complications are also described in coronal approaches and lateral orbitotomies [25 27-29].

With lateral approaches we had some cases of lesions of the cornea. Currently, our strategy is to temporarily close the eyelids during intervention with two 5-0 nylon stitches [15].

With the combined technique of swinging and endonasal endoscopy, a case of entrapment of the medial rectus muscle has also been described. This problem required a secondary procedure [30].

Olivari [31] described several possible complications of transpalpebral lipectomy, but in his vast experience (697 patients) he reported only 3 retro-orbital haematomas which were operated on immediately, 16 cases of paresis

of V1, in some other cases temporary paresis of the supratrochlear nerve, and 2 intra-orbital infections.
With the same technique, Kazim et al. [32] described only 2 cases of myogenic impairment of inferior oblique muscle function.

Conclusions

The incidence of 9.3% of complications reported by Leong et al. [12] is likely to be underestimated since many publications do not report any complications. Furthermore, many surgeons utilise the same surgical technique in all patients and often report data relating to small case-series: this makes it difficult to understand which method is associated with minor complications [1].
From the analysis of our data and of those present in literature, we conclude that the most severe complications, such as diminishing/loss of visual acuity and CSF leaks, are more frequent during trans-maxillary and non-endoscopic endonasal approaches. Certainly, correct closure of accidental CSF leaks has significantly reduced the incidence of severe complications. We do not consider small meningeal lesions caused during external approaches as major complications as the use of drainage without suction and moderate eye-packing for a few days are usually sufficient to resolve this problem. Lesions of V1 and V2 were much more frequent with external access, and therefore maximum attention is required to not traumatise these nerves during surgery. The incidence is likely to be underestimated also for this complication because patients tend not to refer minor complaints unless specifically asked.
Generally speaking, bleedings have a low incidence. For lateral approaches, the use of drainage with suction for 24 hours seems to be very useful in managing mild to moderate bleeding.
Symptomatic sinusitis was not frequently reported, but in the endoscopic approach it is important to perform extensive antrostomy involving the natural ostium, remove the lower two thirds of the middle turbinate and carry out a complete anterior sphenoidotomy to allow adequate ventilation of the sinuses. We advise keeping the anterior one third of the lamina papyracea in place to avoid the risk of frontal sinus dysventilation.
It is also advisable to protect the cornea and conjunctiva during surgery, especially during external approaches, by closing the eyelids with stitches. The introduction of endoscopic endonasal techniques through the medial wall and with superior and inferior eyelid incisions, as used in blepharoplasty, have made this intervention less invasive and have reduced the incidence of complications [15].
It should be noted that most complications represent a minor problem for the patient compared to a pathology with important functional and psychological impairments.

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Otology

The audiological and take results of perichondrium attached cartilage island graft in tympanoplasty: PACIT

Risultati audiologici e rate di attecchimento dell'innesto di cartilagine con pericondrio nella timpanoplastica: PACIT

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SUMMARY

Cartilage is one of the most preferable grafts for tympanoplasty (TPL). The anatomical and audiological results and take rates of perichondrium attached cartilage island graft in tympanoplasty (PACIT) are presented herein. One hundred ninety four ears of 191 patients (108 male, 83 female) were evaluated retrospectively in terms of the type of surgery, graft take rate and hearing results. Type I, II, and III TPL were performed in 127 (65.46%), 45 (23.20%), and 22 (11.34%) ears, respectively. The overall mean preoperative pure tone average-air bone gaps (PTA-ABGs) for TPL types were 33.74 ± 9.60, 52.58 ± 9.07, and 56.58 ± 10.27 dB HL, respectively; postoperative mean values for TPL groups were 18.55 ± 9.25, 31.21 ± 4.36, and 44.84 ± 12.45 dB HL. Postoperative hearing results showed an improvement (≥ 10 dB) in 76.81% of ears with a mean gain of 20 dB HL (range 10-40 dB). However, 19.07% of ears showed no change (< 10, ≥ 0 dB) in hearing, and hearing worsened in 4.12% of ears (< 0 dB) postoperatively. Overall, graft take was 91.24% at least 13 months (mean 68.64) after surgery with a graft failure rate of 8.76%. Graft take was successful in TPL groups. Postoperative PTA-ABG results demonstrated significant improvement. The long-term eligibility of perichondrium attached cartilage island graft in TPL is emphasised with this study.

KEY WORDS: Chronic otitis media • Cartilage tympanoplasty • Cholesteatoma • Mastoidectomy • Graft take rate • Pure tone audiogram • Air bone gap • PACIT

RIASSUNTO

La cartilagine rappresenta una delle opzioni più interessanti per il confezionamento dell'innesto nella timpanoplastica (TPL). Col presente studio presentiamo i nostri risultati audiologici e il rate di attecchimento nei casi di TPL trattati con innesto di cartilagine con pericondrio (PACIT). Sono stati analizzati, in termini di tipo di chirurgia effettuata, attecchimento dell'innesto e risultati audiologici, 194 orecchi di 191 pazienti (108 maschi, 83 donne). Sono state effettuate 127 (65,46%) TPL tipo I, 45 (23,20%) tipo II e 22 (11,34%) tipo III. Il gap medio fra via aerea e via ossea all'audiometria tonale preoperatoria è stato rispettivamente 33,74 ± 9,60, 52,58 ± 9,07, e 56,58 ± 10,27 dB HL; i valori nel postoperatorio sono stai invece 18,55 ± 9,25, 31,21 ± 4,36, and 44,84 ± 12,45 dB HL. Nel postoperatorio di è registrato un miglioramento della soglia (≥ 10dB) nel 76,81% degli orecchi valutati, con un recupero medio di 20 dB HL (range 10-40 dB). Tuttavia il 19,07% degli orecchi valutati non ha mostrato un miglioramento della soglia uditiva, e il 4,12% ha manifestato un peggioramento della soglia. L'innesto ha attecchito correttamente nel 91,24% dei casi con follow-up di almeno 13 mesi con una media di 68,64 mesi, mentre si è registrato un fallimento nel 8,76% dei casi. In considerazione dei livelli postoperatori della soglia uditiva e dell'elevato rate di attecchimenti registrato, il presente studio ha evidenziato l'efficacia a lungo termine dell'innesto di cartilagine con pericondrio.

PAROLE CHIAVE: *Otite media cronica • Timpanoplastica con innesto di cartilagine • Colesteatoma • Mastoidectomia • Attecchimento dell'innesto • Audiometria tonale • Gap ossea-aerea • PACIT*

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Introduction

Tympanoplasty (TPL) and tympano-mastoidectomy operations have been performed in the treatment of chronic otitis media (COM) since 1774 [1]. Temporalis fascia and perichondrium can be used as a graft material to repair tympanic membrane with high success rates, up to 95%. These materials may not be appropriate to use in cases with severe tubal dysfunction, total tympanic membrane perforation, fibro-adhesive processes and revision operations. In such situations, a cartilage graft is a good choice because of its stability, and there is no need for extra instruments dur-

ing the operation [2]. Cartilage grafts are also used in revision surgery, in which the tympanic membrane was previously reconstructed with fascia, and in recurrent cholesteatoma cases [3]. Cartilage grafts may be used in different ways, such as perichondrium cartilage island, palisade or shield graft and cartilage reinforcement technique [4 5].

The aim of this study was to establish the long term results of type I-II-III cartilage TPL achieved with a cartilage island graft with its perichondrium attached to one side, defined as *perichondrium attached cartilage island tympanoplasty (PACIT).* Patients were evaluated for extent of disease, surgical procedures, take rates and hearing results. An overview of the literature on the cartilage TPL is also presented.

Materials and methods

The study was approved by the Ethics Committee of Bursa Sevket Yilmaz Training and Research Hospital. The study included 194 ears in 191 patients (83 females, 108 males) with a mean age of 42.64 years who underwent PACIT. The operations were classified as originally described by Wullstein in 1956 [6]. The patients who underwent type I, II and III TPL were included in the study. Operations which were performed along with partial or total ossicular replacement prosthesis were excluded from the study.

All operations were performed by two senior surgeons (FS, DA) between 2002 and 2012 at Department of Otolaryngology. In the cases of bilateral TPL, the second operation was performed with an interval of at least 6 months. Surgical records and patient charts were reviewed retrospectively.

Data on background variables (gender, age, side, TM perforation and middle ear pathology), surgical approach, complications and anatomical and functional outcome were collected from the patient charts. Each patient had a pure tone audiogram (PTA) at 0.5, 1, 2 and 4 KHz frequencies preoperatively and at least 6 weeks postoperatively. The failure of middle ear surgery was accepted when there was a re-perforation, lateralisation or retraction of the tympanic membrane, graft failure, sensorineural hearing loss, facial nerve injury and residual cholesteatoma. All patients included in the study were regularly monitored for at least one year following surgery.

All operations were performed under general anaesthesia. Four quadrants of the external ear canal and both sides of tragus were infiltrated using 1% lidocaine with epinephrine 1:100,000 before the operation. The surgery was performed in a post auricular or endaural approach. After the edges of the tympanic membrane perforation were denuded and tympanic membrane remnants with tympanosclerosis were removed, a tympanomeatal flap (vascular strip) was elevated from 12 to 6 o'clock. Then the middle ear was explored, the status of the ossicular chain was checked, and any pathology in this area was removed. If there was a fixation or defect on the ossicular chain, mobilisation and reconstruction of the chain was performed. Continuity of the ossicular chain was restored with a strut (reshaped incus or cortical bone) in type II tympanoplasty (Fig. 1b,c,d). In the cases of type III tympanoplasty, the graft was placed directly on the capitulum of stapes as myringo-stapediopexy (Fig. 1e,f). Primary type II and III tympanoplasty operations were performed with intact canal wall (ICW) and canal wall down (CWD) procedures. We did not use partial or total ossicular replacement prosthesis in any of cases included in this study.

The cartilage graft with bilateral perichondrium was harvested from the tragus without thinning out. To prepare a perichondrium attached cartilage graft (PACG), the perichondrium on one side of cartilage was elevated and left attached to spread on the external ear canal and adhere to the tympanomeatal flap subsequently (Fig. 1a). Next, the cartilage was sized to the tympanic annulus and a V-shaped piece of cartilage was excised to accommodate the graft to the manubrium of malleus in type I TPL (Fig. 2).

The PACG was placed with the underlay technique. The attached perichondrium part of graft was spread on the posterior quadrant of external auditory canal or mastoid cavity. The middle ear was packed with gelfoam, and gelfoam pledgets impregnated with antibiotic ointment (Furacin®, Zentiva, Istanbul, Turkey) were placed lateral to the graft for stabilisation and to secure proper positioning of the tympanomeatal flap. Skin and subcutaneous incisions were closed in two layers. A rolled gauze pack impregnated with antibiotic ointment was placed in the external ear canal, and a mastoid dressing was applied for 3 days.

Skin sutures were removed 1 week after surgery. Absorbable gelatine sponges were partially suctioned from the external ear canal in CWD and ICW cases at 1 and 2 weeks after the surgery, respectively. Ear drops with steroid (Onadron®, IE Ulagay-Menarini Group, Istanbul, Turkey) and antibiotic (Siprogut®, Bilim Pharmaceuticals, Istanbul, Turkey) were prescribed for 2 weeks. The take of tympanic membrane was examined and audiometry was carried out at least 6 weeks after surgery. The patients were followed up postoperatively by serial audiometries at 1.5, 6, and 12 months and yearly thereafter.

Ears were evaluated for the closure of tympanic membrane (take rates) at least 6 weeks after the operation. Long term take rates with respect to tympanoplasty types were evaluated on the basis of last visit after surgery. Preoperative and postoperative pure tone average-air bone gaps (PTA-ABG) regarding to TPL types were compared with Student's t test. A p value less than *0.05* was considered significant.

The improvements in air conduction levels were also evaluated. Ears were rated with respect to the difference between preoperative and postoperative air conduction lev-

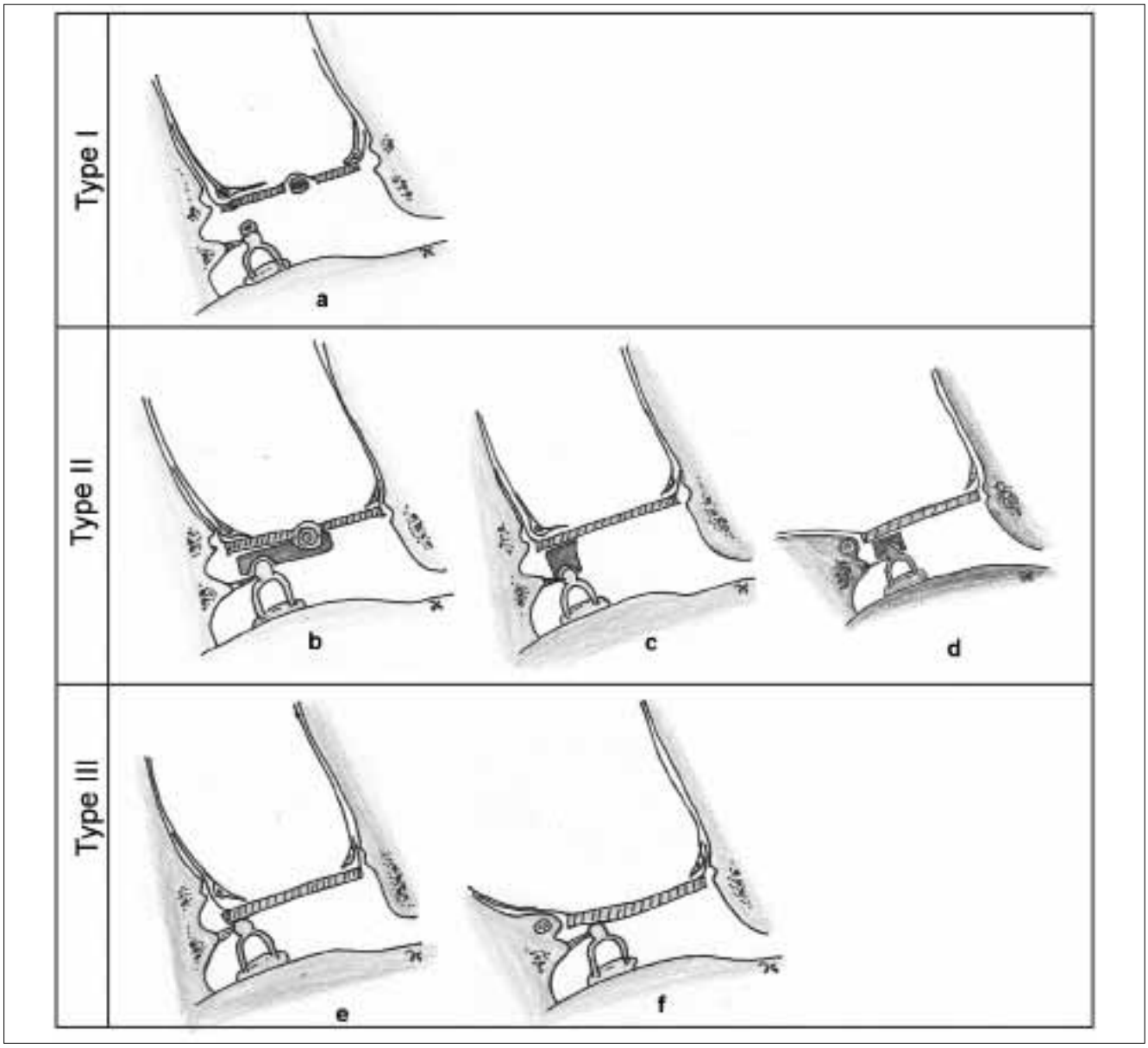

Fig. 1. Schematic drawings of PACIT types. Type I (a), type II; partial ossicular reconstruction, cartilage graft plus interposition with reshaped incus or cortical bone on stapedial capitulum in intact canal wall and canal wall down tympanoplasty (b,c,d), type III; intact canal wall with myringostapediopexy (e) and canal wall down tympanoplasty with myringostapediopexy (f).

els (dB) as improved (≥ 10 dB), no change (< 10, 0 ≥ dB) and worsened (< 0 dB).

Results

The study included 191 patients (194 ears) who underwent PACIT. Eighty-three (85 ears) (43.81%) were female and 108 (109 ears) (56.19%) were male. The age of patients ranged from 18 to 59, with a mean age of 42.64 ± 8.8 years. The mean follow-up time was 68.64 ± 8.0 months (range 13 to 110). Three patients (3 female, 1 male) had underwent bilateral TPL. Of the remaining 188 ears, 86 had right (45.87%) TPL and 102 had left (54.12%) TPL.
All patients required total tympanic membrane reconstruction for the following causes: 120 ears (61.85%) had central perforation, 33 (17.01%) ears had large -total/subtotal- perforation and 41 (21.14%) had perforation with cholesteatoma. The distribution of preoperative middle ear disease and tympanic membrane perforations is shown in Table I.
Type I TPL without mastoidectomy was performed in 127 (65.46%) ears, type II tympanoplasty in 45 (23.20%) (ICW = 33, CWD = 13) and 22 (11.34%) ears underwent type III TPL (ICW = 5, CWD = 16). Of the 41 ears with cholesteatoma, 29 had CWD and 12 had ICW procedures. There were no complications such as haematoma, facial nerve injury, wound infection, fistula, or sensorineural hearing loss. During the follow-up period, recurrent cholesteatoma occurred in 2 patients (4.88%) at 11 and 18 months

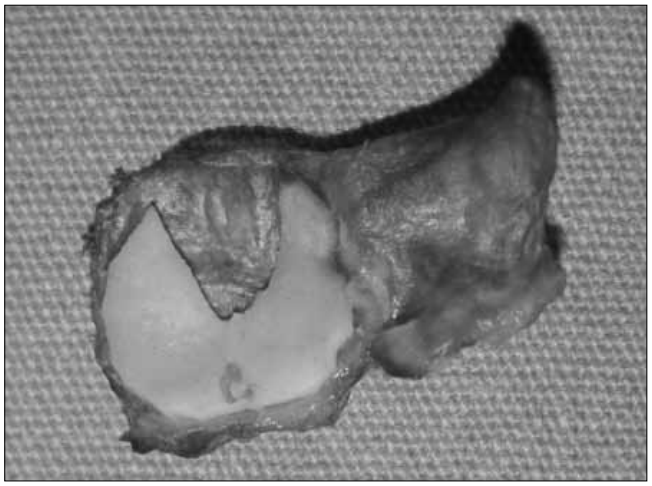

Fig. 2. The cartilage graft harvested from the tragus. The perichondrium on one side is elevated and left attached; a V-shaped wedge of cartilage is excised to accommodate the manubrium of the malleus for type I tympanoplasty.

after primary ICW procedures. The diseases were treated successfully with CWD. Only the audiological results of primary operations were evaluated in the study. There were 3 cases of graft medialisation in the type II TPL group. No complications such as stenosis of the external auditory canal were reported after harvesting the tragal cartilage.

Patients were followed postoperatively by serial PTA-ABG at 1.5, 6 and 12 months and yearly thereafter. The follow-up periods that were more than 12 months in 194 ears were considered adequate to interpret the stability of postoperative graft take.

Overall, graft take was successful in 177 ears (91.24%) of all procedures at least 13 months after the surgery. Two (0.98%) grafts failed due to the recurrence of cholesteatoma. No new perforations occurred during follow-up period. Moreover, there was no lateralisation or medial retraction of the graft. Overall, failure rates according to the groups are shown in Table II.

The overall mean pre-operative PTA-ABGs for type I, II and III TPL were 33.74 ± 9.60, 52.58 ± 9.07 and 56.58 ± 10.27 dB HL, respectively, whereas postoperative PTA-ABG values were 18.55 ± 9.25, 31.21 ± 4.36 and 44.84 ± 12.45 dB HL for the same groups. When preoperative and postoperative PTA-ABG were compared, there

Table I. Preoperative middle ear/TM status of operated ears.

Middle ear and TM disease	Type I (N = 127) n/%	Type II (N = 45) n/%	Type III (N = 22) n/%	Total n/%
Central TM perforation	120/61.85	0/0	0/0	120/61.85
Large-total/subtotal-TM perforation	07/03.61	26/13.40	0/0	33/17.01
Cholesteatoma	0/0	19/09.80	22/11.34	41/21.14
Total	127/65.46	45/23.20	22/11.34	194/100.00

n: number of ears, TM: tympanic membrane

Table II. Overall failure and recurrence of cholesteatoma rates.

Overall failure	Type I (N = 127) n/%	Type II (N = 45) n/%	Type III (N = 22) n/%	Total n/%
Overall graft failure	10/05.15	4/02.06	3/01.55	17/08.76
Medialisation	0	3/01.55	0	3/01.55
Recurrence of cholesteatoma π	0	1/00.515	1/00.515	2/01.03
Total graft failure for each group	10/07.88	4/08.89	3/13.64	

π: assessed in terms of cause of failure
n: number of ears

Table III. Overall pre- and post-operative Pure Tone Averages – Air Bone Gap (dB HL).

Pure Tone Averages – Air Bone Gap (dB HL)	Type I (N = 127) PTA ± SD	Type II (N = 45) PTA ± SD	Type III (N = 22) PTA ± SD
Preoperative	33.74 ± 9.60	52.58 ± 9.07	56.58 ± 10.27
Postoperative	18.55 ± 9.25	31.21 ± 4.36	44.84 ± 12.45
p*	< 0.0001	< 0.0001	0.0012

**: Student's t test used, $p < 0.05$*
PTA: pure tone averages

Table IV. Hearing improvement after the operations in tympanoplasty groups.

Audiological change**(dB HL)	Type I (N = 127) n/%	Type II (N = 45) n/%	Type III (N = 22) n/%	Overall n/%
Improved (≥ 10 dB	106/83.46	29/64.45	13/59.09	148/76.29
No Change (< 10, 0 ≥ dB)	21/16.54	10/22.22	04/18.18	35/18.04
Worsened (< 0 dB)	00/00.00	06/13.33	05/22.73	11/05.67
Total	127/100.00	45/100.00	22/100.00	194/100.00

***: The difference = preoperative air conductive level – postoperative air conduction level (dB HL)*
n: number of ears

was a statistically significant improvement in PTA-ABG for all three TPL types ($p < 0.05$) (Table III).

Evaluation of the difference between pre- and post-operative air conduction levels revealed that the latter decreased in 8 (4.12%) ears; the early postoperative hearing results (at 1.5 and 3 months after surgery) remained stable in all patients. Postoperative hearing results in our study showed an improvement (≥ 10 dB) in 149 ears (76.81%) with a mean gain of 20 dB (range 10-40 dB). The difference between pre- and post-operative air conduction levels was unchanged (< 10, 0 ≥ dB) in 37 (19.07%) ears. The improvements in postoperative hearing levels regarding tympanoplasty types are summarized in Table IV.

Discussion

Tympanoplasty is performed to repair the tympanic membrane. With this surgical procedure there are two main targets. The first aim is to close the tympanic membrane and to have a closed middle ear, which will prevent the ear from subsequent infection and drainage. The second is to provide free movement of ossicles, which will result in better sound transmission and hearing. Skin, fascia lata, vein, temporalis fascia, perichondrium and dura mater have been used in the literature [7]. Today, temporalis fascia is the most commonly employed material for tympanic membrane reconstruction [8].

The use of cartilage is proposed in middle ear surgery, since it offers a reliable technique in cases of advanced middle ear pathology and eustachian tube dysfunction [9]. In 1963, Salen [10] and Jansen [11] first reported the use of cartilage composite grafts for tympanic membrane reconstruction. The interest for this material has risen in last decade. Clinical and experimental studies show that the cartilage is well tolerated in tympanoplastic surgery [12 13].

Despite the thickness of cartilage, various authors pointed out equal or better hearing results for the cartilage comparing to temporalis fascia in tympanoplasty [9 14]. Shield cartilage TPL using sliced tragal cartilage-perichondrium composite graft in terms of functional and anatomic results has been studied. The perforation closure and air bone gap closure was reported to be successful [15]. In a systematic review on 1,475 patients comparing cartilage and fascia graft in TPL, no statistically significant difference between cartilage and temporalis fascia regarding function and hearing outcome was reported. In addition, TPL using cartilage with or without perichondrium was reported to have better morphological outcomes than TPL using temporalis fascia [16].

Cartilage grafts may be used in different ways, such as perichondrium cartilage island graft, palisade or shield graft and cartilage reinforcement techniques [4 5]. The use of cartilage as shield graft in tympanic membrane reconstruction is an easily applied technique, and is recommend by many authors [17]. The reconstructed membrane

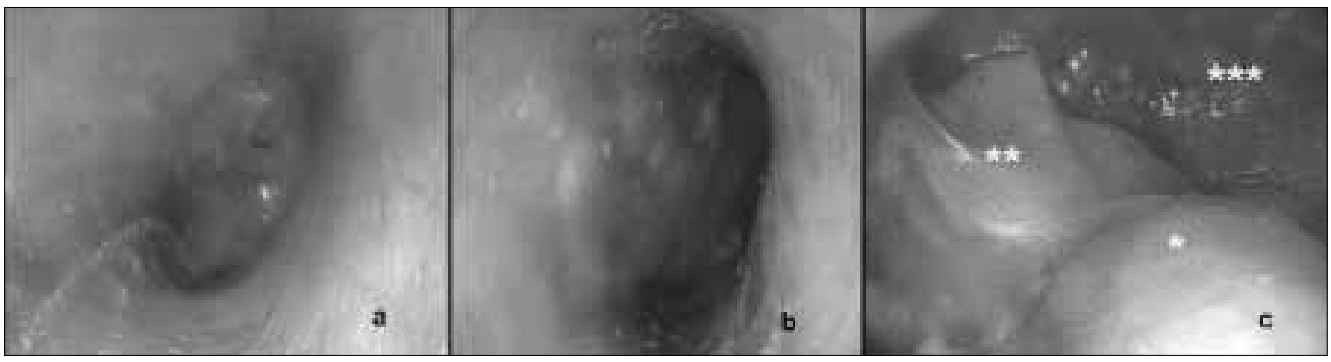

Fig. 3. Postoperative appearance of cartilage graft in type I, II and III tympanoplasty. Type I in a right ear at postoperative 15th month (a); type II-intact canal wall in a right ear at postoperative 13th month (b); type III-canal wall down at 18th month postoperatively. Facial ridge (single asterisk), cartilage graft (double asterisk), mastoid cavity (three asterisks) (c).

will have resistance against the negative middle ear pressure, and long term integrity will be provided. Cartilage graft is mostly preferred in the posterosuperior retraction pockets of TM, since recurrent retractions are observed with the use of fascia graft over time [18].

The cartilage graft may be harvested from tragus or concha. We prefer the tragal cartilage, because of its flat surface, ideal thickness and sufficient size. It was used as cartilage island graft with the perichondrium attached to one side, since its thickness is less than 1 mm.[17]

Guneri et al. [3] reported a mean gain of 20 dB (64%) in a retrospective clinical study presenting their experience with cartilage grafts in ear surgery; postoperative hearing levels were improved in all type III tympanoplasties with ossicular reconstruction without mastoidectomies (100%), followed by CWD tympanomastoidectomy with ossicular reconstruction (66%), type I TPL (62%), and ICW tympanomastoidectomy with ossicular reconstruction (25%).

Cavaliere et al. [7] reported their personal experience with "tragal cartilage shield" graft in TPL with 306 adult patients. Graft take was achieved in 304 patients (99.35%) and there was no immediate post-operative complication. The overall preoperative PTA-ABG was 43.79 ± 7.07 dB, whereas it was 10.43 ± 5.25 dB at one year after the surgery. Conchal cartilage, shaped as a shield, was used to replace the entire tympanic membrane and reconstruct the ossicular chain in patients with an absent incus as type III cartilage "shield" TPL. It was reported as an effective technique for hearing improvement in selected patients with chronic otitis media [19].

Ozbek et al. [20] studied the long-term efficacy of cartilage palisades in TPL for atelectatic ears. The mean follow-up time was 44.5 months. The closure of tympanic membrane perforation was achieved in 91% of ears. Postoperative PTA-ABG was less than 20 dB in 71% of ears. The average preoperative and postoperative ABG values, including all types of tympanoplasty operations (type I, II and III), were 28.4 ± 5.8 and 16.9 ± 6.7 dB, respectively ($p < 0.001$). They concluded that palisade cartilage tympanoplasty was an effective technique for tympanic membrane closure and hearing improvement in atelectatic ears. They also indicated that the mastoidectomy did not affect anatomic or audiological outcomes.

The reported follow-up rates in the current literature are between 19.9 months and 12 years according to our search [3 7 20-22]. Mean follow-up time was 68.64 months in the present study. It is a relatively long time period, compared with many studies in the literature.

Of the 41 ears with cholesteatoma, recurrent disease emerged in 2 patients after ICW procedures, which were managed successfully with CWD. The overall take rate was 91.24% for all patients; in type I, II, III TPL take rates were 92.12%, 91.11% and 86.36% respectively. No new reperforations occurred during follow-up period. The postoperative hearing results in our series showed an improvement in 76.29%, no change in 18.04% and a worsening in 5.67% of ears. Of the 11 ears whose hearing levels worsened postoperatively, 6 had primary CWD + Type II TPL and 5 had primary CWD + Type III TPL. Decreasing hearing levels may be due to the structural changes of middle ear during surgery.

Conclusions

Our study represents the results of PACG in type I, II and III primary TPL for treatment of COM with or without cholesteatoma. A limitation of study is the heterogeneity of the middle ear pathologies: we did not evaluate the effect of atelectasis, cholesteatoma and revision on the success rate of TPL. The inherent disadvantages of a retrospective study prevent formation of a true control group, and there may also be bias in selection of techniques. The overall graft take rate for PACIT was 91.24% at least 13 months after surgery. Postoperative PTA-ABG results demonstrated a significant improvement in our study for all types of TPL. The worsening hearing results were observed in the ears that underwent CWD due to cholesteatoma. This situation may depend on the structural changes of middle ear during surgery, rather than the type of graft used for tympanic membrane reconstruction. A cartilage island graft with the perichondrium attached to one side harvested from tragus may be useful in type I, II and III TPL due to high stability and good hearing results.

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Otology

Role of Kabat rehabilitation in facial nerve palsy: a randomised study on severe cases of Bell's palsy

Ruolo della riabilitazione Kabat nella paralisi del nervo facciale: studio randomizzato su casi severi di paralisi di Bell

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SUMMARY

The treatment of Bell's palsy (BP), based on steroids and/or antiviral drugs, may still leave a certain percentage of affected subjects with disfiguring sequelae due to incomplete recovery. The different procedures of physical rehabilitation have not been demonstrated to play a favourable role in this disorder. The aim of the present study was to compare functional outcomes in severe cases of Bell's palsy when treated by steroids alone or by steroids accompanied by Kabat physical rehabilitation. This prospective study included 94 subjects who showed sudden facial nerve (FN) palsy with House-Brackmann grade IV or V and who were divided into two groups on the basis of the therapeutic approach: one group (a) was treated by steroids, and the other (b) received steroids in combination with physical rehabilitation. Medical treatment consisted in administration of steroids at a dosage of 60 mg per day for 15 days; physical rehabilitative treatment consisted in proprioceptive neuromuscular facilitation according to Kabat, and was administered to one of the two groups of subjects. Recovery rate, degree of recovery and time for recovery were compared between the two groups using the Mann-Whitney and univariate logistic regression statistical tests (Ward test). Kabat patients (group b) had about 20 times the odds of improving by three HB grades or more (OR = 17.73, 95% CI = 5.72 to 54.98, $p < 0.001$) than patients who did not receive physical treatment (group a). The mean speed of recovery in group b was the half of that recorded for group a (non-Kabat subjects). No difference was observed in the incidence of synkineses between the two groups. Steroid treatment appears to provide better and faster recovery in severe cases (HB IV and V) of BP when complemented with Kabat physical rehabilitation.

KEY WORDS: Bell's palsy • Physical rehabilitation • Kabat • House-Brackmann grading system • Steroid treatment

RIASSUNTO

La terapia della paralisi di Bell, incentrata su farmaci steroidei e/o antivirali, può ancora far esitare nei soggetti affetti sequele disfiguranti per un recupero incompleto. Le diverse procedure riabilitative non si sono dimostrate al giorno d'oggi in grado di giocare un ruolo favorevole in questo senso. Scopo di questo lavoro è stato quello di mettere a confronto i risultati funzionali di pazienti affetti da forme severe di paralisi di Bell, quando trattati con solo cortisone con quelli nei quali al cortisone è stata affiancata una terapia riabilitativa secondo Kabat. Lo studio prospettico ha incluso 94 soggetti con paralisi di Bell di grado IV e V secondo House-Brackmann (HB) a loro volta suddivisi in due gruppi: (a) trattato con terapia steroidea; (b) trattato con terapia steroidea e riabilitazione Kabat. Il trattamento medico è consistito di 60 mg di prednisolone al giorno per 15 giorni; la terapia riabilitativa è consistita nel trattamento di facilitazione neuromuscolare propiocettiva secondo Kabat. Percentuale, grado e tempi di recupero sono stati comparati utilizzando l'analisi statistica Mann-Whitney e il test di regressione logistica multivariata (Ward test). I pazienti Kabat (gruppo b) hanno avuto 20 volte di più la possibilità di migliorare di 3 o più gradi HB (OR = 17,73, 95% IC = 5,72 a 54,98, $p < 0,001$) rispetto a quelli di gruppo a. La velocità media di recupero nel gruppo b è risultata la metà di quella registrata nel gruppo a. Nessuna differenza è stata invece riscontrata sull'incidenza di sincinesie. Si può dunque concludere che la terapia steroidea permette un migliore e più rapido recupero dei casi severi di paralisi di Bell, quando associata a terapia riabilitativa Kabat.

PAROLE CHIAVE: *Paralisi di Bell • Terapia riabilitativa • Kabat • Classificazione House-Brackmann • Terapia steroidea*

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Introduction

Bell's palsy (BP) is an acute, sudden unilateral peripheral paralysis of the facial nerve (FN) that accounts for almost 75% of all acute facial palsies (FP). The annual incidence varies between 11 and 40 cases per 100,000 subjects [1 2] or even higher, as indicated by a recent survey [3].

The aetiology of BP is still unknown, but reactivation of a latent Herpes simplex virus would seem to play a major

role [4]. Inflammation and entrapment of the nerve in the narrow bony labyrinthine segment of the Fallopian canal have specifically been proposed as possible mechanisms for inducing nerve sufferance [4 5].

The therapeutic options are not universally accepted in terms of priority. Medical treatment is based on administration of corticosteroids, and several studies have shown that they may be able to reduce the time of recovery and occurrence of sequelae [6 7], while no evidence has been gathered on the adjunctive role of antiviral drugs [7].

Surgical decompression of the FN has also been proposed in the past, with the rationale to release the edematous nerve from its bony canal, but its efficacy has been recently debated [8] and, in recent years, the number of these procedures has drastically reduced.

Several procedures of FN rehabilitation have also been applied in combination with medical treatment, mostly in the post-surgical FP setting, although a recent Cochrane review was unable to identify any significant benefit or harm by any type of rehabilitative procedure [9]. When analysing physical rehabilitative procedures, the recent scientific contributions have examined the application of manual therapies [10-12], electrical stimulation [13], exercises and ago-puncture [14 15] and laser [16]. Barbara et al. compared clinical outcomes and ENoG values of patients affected by BP and rehabilitated with the Kabat method [17], showing that the better and faster recovery of an early rehabilitative protocol was independent of the nerve condition as assessed by ENoG findings [18].

The purpose of the present study was to shed light on the favourable role played by Kabat physical rehabilitation in the outcomes of subjects affected by severe BP. Clinical outcomes were compared between two different protocols: pharmacological treatment associated with physical rehabilitation and pharmacological treatment alone.

Materials and methods

A series of consecutive subjects admitted to the Emergency Department (ED) of a tertiary University Hospital with diagnosis of BP during the years 2005-2012 were considered. In all, FN palsy was graded according to the House-Brackmann (HB) system [19]. From a total of 390 patients, only those staged HB IV or higher were taken into consideration. Pregnant women and individuals with involvement of other cranial nerves were also excluded from the study. Ninety-six patients, hence composing the study group, were enrolled: HB IV (66 subjects) and HB V (28 subjects).

Randomisation of these patients was performed by the personnel working at the ED that, on the basis of individual judgment on the FN severity, sent 66 BP patients home and 28 to our FN Center for consultation. In this way, two separate groups were identified:

- s*tudy group a,* formed by 66 patients, aged 16-90 years (mean = 57.1), 30 females and 36 males, 58 with HB IV and 8 with HB V. All these subjects were sent home by the ED with medical steroid protocol treatment, eye drops for eye protection and paracetamol in case of pain;
- *study group b*, formed by 28 patients, aged 32-74 years (mean = 55.7), 13 males, 15 females, 10 with HB IV and 18 with HB V. All these patients were sent for consultations to our FN Centre by ED staff. At our Centre, standard facial movements (brow lift, gentle eye closure, forced eye closure, snarling, smiling and lip pucking) were documented in each patient by video-recording with a mobile phone, and reviewed by a senior ENT to assign the appropriate HB grade. The Kabat physical rehabilitation was started within 7 days from BP onset, and was associated for two weeks with medical treatment, consisting of daily prednisolone (2 mg/kg), for 10 days and tapered off within 2 weeks.

G*roup b* subjects were evaluated at our Centre twice a week, during the rehabilitation sessions and at the end of the cycle, defined with the maximum improvement of FN function that remained stable for a least 1 month of follow-up. Once a week from FP onset, *group b* patients were re-evaluated, so as to define the progression or eventual recovery in days via direct clinical observation.

At day 7 from FP onset, *group a* subjects received a telephone contact and were classified according to the capability of eye closure, so as to distinguish grade III or better from grade IV or worse. Next, they were asked to self-assess and report in a diary, from that day on, facial features such as:

1. symmetry of the face at rest: if the right and left sides of the face appeared similar at rest (without any movement);
2. facial motion through different facial movements (brow lift, gentle eye closure, forced eye closure, snarling, smiling and lip picking).

Kabat rehabilitation consists in the facilitation of the voluntary response of an impaired muscle through the global pattern of an entire muscular section that undergoes resistance. This method appears to be extremely rational for facial muscles, since most of the face muscular fibers run diagonally, with easy irradiation to the upper facial region due to the cross-FN innervations. Three regional fulcra were taken into consideration: upper, intermediate and lower fulcrum. The first (forehead and eyes) is connected via a vertical axis to the intermediate one (nose), while the lower mimic-chewing-articulatory fulcrum lies along the horizontal axis. Hence, action on the upper fulcrum also involves the other two fulcra. The manipulation of these three fulcra is carried out by utilising both contralateral contractions and basic propioceptive stimulation, including stretching, maximal resistance, manual contact and verbal input. In the upper fulcrum, the activation of the

frontal, corrugators and orbicularis muscles is carried out by their upwards or downwards traction, which is always in a vertical plane depending on the specific function that needs to be activated. In the intermediate fulcrum, activation of the common elevator muscle of the ala nasi and the upper lip is also carried out using traction movements, in this case contrary to the normal direction, following a vertical line. For the lower fulcrum, the maneuvers are carried out on the risorium and orbicularis oris muscles in a horizontal plane, and on the mental muscle in a vertical plane.

For statistical purposes, the time of recovery has been expressed in days. The time of recovery and the final HB degree of palsy were compared between groups.

Statistical analysis

The dataset was cleaned before analysis with respect to inconsistent and missing values, duplicates, outliers, digit preference and normality of continuous variables. The non-parametric Mann-Whitney-Wilcoxon (MWW) U test was used to verify the null hypothesis that the two study groups are the same against an alternative hypothesis, namely that one group would tend to have better recovery values than the other. Univariate logistic regression (Ward test) was used to compare all rehabilitated (group b) and non-rehabilitated (group a) patients for the final grade of improvement, degree of improvement (1-grade, 2 grades, 3 grades and 4-grades) and timing of recovery. The effect of treatment was evaluated by three different approaches, adjusted for age and gender: i) multiple linear regression to model the paired change of HB grade between before and after treatment (at the end of follow-up); ii) multiple logistic regression to model the chances of having a paired decrease in disease status by three HB grades or more, before and after treatment (at the end of follow-up); iii) multiple Cox proportional hazards regression for time of improvement (speed of recovery), with follow-up time in days (information about patient status was retrieved daily). Statistical assumptions underlying the tests were systematically checked.

Results

Grade IV at baseline was recorded in 87.9% of group a and in 35.7% of group b. Grade V at baseline was present in 12.1% of group a and 64.3% of group b. Group b subjects with grade V at baseline underwent Kabat treatment and showed better improvement after treatment with a faster recovery time in comparison with group a (64.6 days in respect to 117.1 days in group a). Moreover, at the end of follow-up, in group b there was no case of one-grade improvement, while an improvement by four grades was found in 25.0% of subjects; in group a, one-grade improvement was observed in 16.7% of patients, and none showed a four-grade improvement (Table I).

When comparing (MWW) the rehabilitated (*group b*) versus non-rehabilitated (*group a*) groups, independently of the initial FP grade, significant differences were found ($p = 0.009546$) and shown in Figure 1. With respect to the entire study group, a greater significance between the two modalities of treatment was identified when taking into account individually grade IV ($p = 0.0001349$) and grade V subjects ($p = 0.009025$) (Fig. 2 and 3).

The multiple linear regression model for the change in HB grade after treatment is reported in Table II. With respect to group a, in the rehabilitated group (b) the HB grade decreased by one further point (coefficient = -0.99%, 95% CI = -1.27/1.71, $p < 0.001$), in HB IV (coefficient = 0.86,

Table I. Sample description by categories of treatment strategy.

	Non-Kabat (n = 66)				Kabat (n = 28)				
Variable	Mean or proportion	SD	Min	Max	Mean or proportion	SD	Min	Max	p*
Age	56.8	17.9	16	90	55.8	12.7	32	74	0.778
Male	54.5%				57.1%				0.817
HB V at onset	12.1%				64.3%				< 0.001
Synkineses after treatment	12.1%				7.1%				0.479
Time to first improvement (days)	117.1	90.3	34	365	64.6	50.7	12	194	
Grade improvement † at the end of follow-up	2.0	0.6	1	3	3.0	0.7	2	4	<0.001
1-grade improvement	16.7				0.0				
2-grades improvement	69.7				28.6				
3-grades improvement	13.6				46.4				
4-grades improvement	0.0				25.0				

** P values were computed using univariate logistic regression (Wald test) with Kabat as outcome.*
** Negative values indicate improvement, i.e. decrease in grade.*
† Improvement means decrease in grade after treatment.

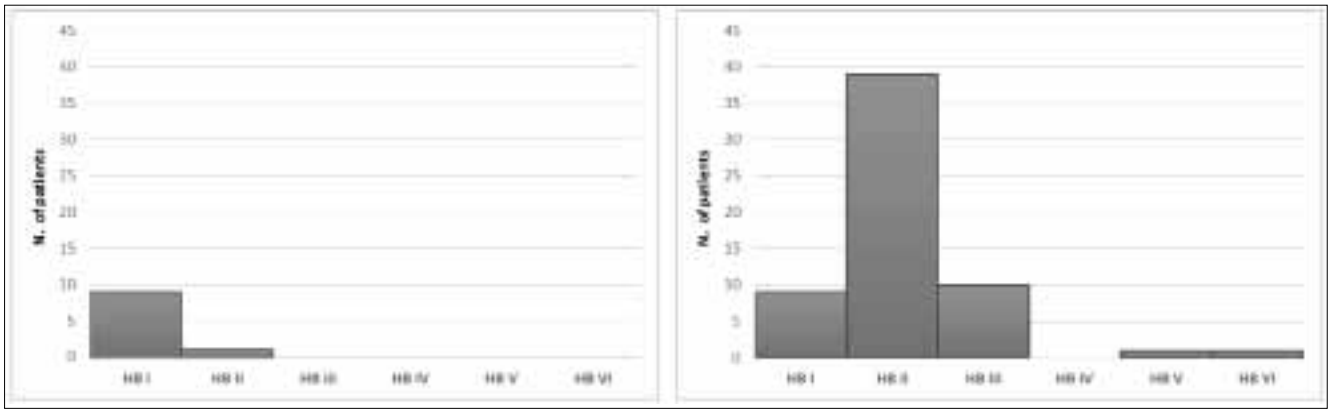

Fig. 1. Comparison between rehabilitated and non-rehabilitated groups (Mann-Whitney (U-test), HB IV and V together, independently of the severity of facial palsy at onset. A significant difference in the outcome was found between groups (p = 0.009546).

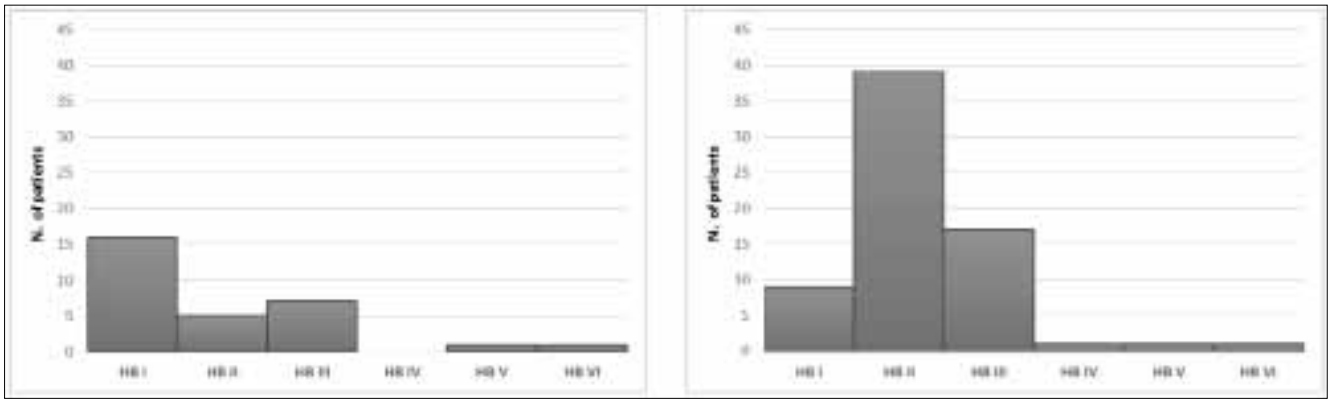

Fig. 2. Comparison between rehabilitated and non-rehabilitated groups (Mann-Whitney (U-test) in HB IV subjects, independently of the severity of facial palsy at onset. A significant difference in the outcome was found between groups (p = 0.0001349).

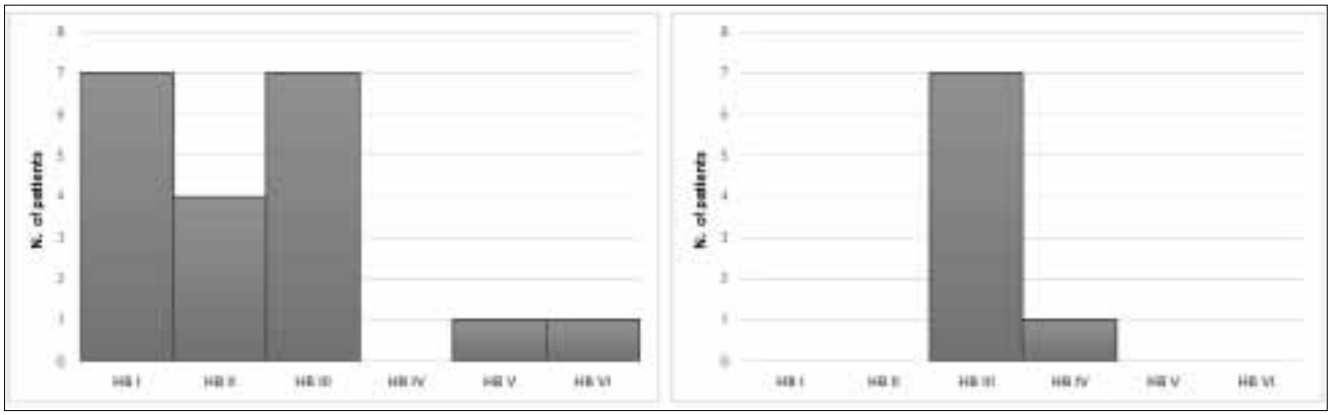

Fig. 3. Comparison between rehabilitated and non-rehabilitated groups (Mann-Whitney (U-test), in HB V subjects, independently of the severity of facial palsy at onset. A significant difference in the outcome was found between groups (p = 0.009025).

95% CI = -1.23/0.49, p < 0.001) and in HB V ((coefficient = -1.10, 95% CI = -1.82/0.38, p < 0.005).

Group b patients showed about 20 times the odds of improving by three HB grades or more (OR = 17.73, 95% CI = 5.72 to 54.98, p < 0.001) than group a (Table III). *Group b* HB IV patients had 65 times the odds of a three-grade improvement than those in group a (non rehabilitated), while a three-grade improvement was only observed in HB V patients in *group b*. The mean speed of recovery in group b was half of that recorded in group a (HR = 2.19, 95% CI = 1.37 to 3.51, p = 0.001). *Group b* HB IV patients had seven times shorter times of recovery than similar grades of *group a*

Table II. Multiple linear regression model for the change in disease grade after treatment.

	Study group (n = 94)			Grade IV at onset (n = 68)			Grade V at onset (n = 26)		
Variable	Change difference*	95% CI	p	Change difference*	95% CI	p	Change difference*	95% CI	p
Kabat	-0.99	-1.27, -0.71	< 0.001	-0.86	-1.23, -0.49	< 0.001	-1.10	-1.82, -0.38	0.005
10-years increase in age	0.05	-0.03, 0.13	0.206	57.1%	0.01, 0.17	0.029	-0.06	-0.29, 0.16	0.56
Male	-0.02		0.888	64.3%	-0.32, 0.21	0.698	0.08	-0.58, 0.74	0.80

**Negative values indicate improvement, i.e. decrease in grade*
** All patients who had an improvement by three grades or more were treated with Kabat.*

Table III. Multiple logistic regression model for the chances of having a decrease by three grades or more after treatment.

	Study group (n = 94)			Grade IV at onset (n = 68)			Grade V at onset (n = 26)		
Variable	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Kabat	17.73	5.72, 54.98	< 0.001	64.25	0.65, 660.41	< 0.001	N/A*		
10-years increase in age	0.76	0.54, 1.08	0.122	0.65	0.42, 1.01	53	1.37	0.55, 3.38	0.500
Male	0.64	0.21, 1.93	0.443	0.48	0.11, 2.03	319	0.62	0.09, 4.31	0.631

** All patients who had an improvement by three grades or more were treated with Kabat.*

(HR = 7.92, 95% CI = 3.68 to 17.04, p < 0.001). *Group b* HB V patients showed nearly half shorter time of recovery than the same grade in *group a* (HR = 1.80, 95% CI = 0.65 to 5.01, p = 0.26) (Table IV). The incidence of synkineses after treatment was 7.1% in *group b* and 12.1% in *group a*, no statistical difference (p = 0.479).

Discussion

Evaluation of the actual efficacy of the different treatments of BP is generally biased by several factors, such as the high likelihood of complete spontaneous recovery, the initial time of treatment and steroid administration that is generally given in all cases. Although steroid treatment is considered the gold standard of medical therapy, the observation that a not insignificant number of BP subjects may retain some important sequelae has promoted the adoption of additional forms of treatment and several types of rehabilitative procedures have also been taken into consideration. Each rehabilitative procedure would theoretically work with specific targets and is tailored to the patient's need and time from FP onset. For instance, the exercises based on gross movements determine a massive and spread contraction of the muscular components of the face, but a high likelihood of synkineses may develop even in the presence of improvement in facial stiffness [11]. Laser and biofeedback techniques are usually performed only when signs of recovery of face movements are observed [16 18]. Moreover, neuromuscular retraining therapy, which focuses on motor control of facial movements triggered by different feedback stimulation and which is particularly indicated to prevent or treat synkineses, is not advised before three months of paresis [19]. Likewise, mime therapy, which consists of massage, relaxation, inhibition of synkinesis, and co-ordination and emotional expression exercises, has been proposed only at a late stage of paresis, with no reports on its potential role when applied at an early stage [20].

After having positively experienced the role of physical Kabat rehabilitation in the jatrogenic or post-surgical forms of FP, when applied at an early stage [21], it seemed reasonable to perform a study in order to assess whether this type of protocol, which involves an early approach to the affected patient, could also work in BP patients

Table IV. Multiple Cox proportional hazards model for time to first improvement (speed of recovery).

	Study group (n = 94)			Grade IV at onset (n = 68)			Grade V at onset (n = 26)		
Variable	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Kabat	2.19	1.37, 3.51	1	7.92	3.68, 17.04	< 0.001	1.80	0.65, 5.01	0.260
10-years increase in age	0.85	0.74, 0.97	0.013	0.81	0.69, 0.94	6	0.93	0.67, 1.28	0.642
Male	1.61	1.06, 2.47	0.027	1.44	0.86, 2.40	0.167	1.49	0.65, 3.40	0.346

presenting with a HB grade IV or worse. In fact, to our knowledge, studies comparing the effect of physical treatment to that of exclusive steroid treatment in BP are scanty. In the present study, the composition of the study groups was not achieved by randomisation, but by the individual attitude of the ED staff to either send patients home or to our attention for consultation, although the former protocol mostly included less severe cases. In both instances, all patients received steroid treatment, while the Kabat rehabilitation was only performed on subjects that were sent and followed directly at our Clinic and that formed study *group b*.

In the present study, only the most severe cases, i.e. HB IV and V subjects, were taken into account for the final evaluation. Through this methodology, it was possible to have comparable patients in the study groups, as well as in HB IV or V subjects separately, for assessment of the primary outcomes of the study, i.e. recovery time, final HB grade and probability to achieve a 3-grade HB improvement.

Although *group a* (steroids only) patients were numerically greater than those of *group b*, this latter included only the most severe HB grades and therefore all were addressed to rehabilitative treatment. The use of such physical rehabilitation led to a faster recovery time in group b, nearly half of that recorded in *group a* subjects, while for HB IV subjects it was reduced by seven times less than in group a. After physical rehabilitation, the degree of improvement (grade reduction at the HB) at the time of definitive clinical outcome was significant in comparison to the final condition of patients treated only with steroids, since patients treated simultaneously with pharmacological and rehabilitative therapy recovered in a significant number to normality (HB I), while in most of the patients who received only steroids, the maximum recovery was HB II.

When considering HB IV only, the significance value of difference between rehabilitated and non-rehabilitated cases was ten times less than that observed in the entire group (HB IV and V); the same finding was observed in HB V, with less significance than HB IV, due to a marked intersection of values at the HB III level. This is why in the most severe subjects (HBV), there was a prevalence of recovery to HB III in non-rehabilitated cases and to HBI in rehabilitated subjects.

Moreover, group b patients recovered by three grades two times more frequently than those in *group a*, and in group b the degree decreased, i.e. improved, by one further point, in total and single grades, compared to *group a*. In *group b*, moreover, a 20 fold higher probability of improvement by three HB grades was seen, and the most severe cases had similar improvement only when rehabilitated.

Most of the severe (HB V), non-rehabilitated patients reached as maximum result of HB III, while similar cases when undergoing Kabat rehabilitation could even obtain a normal facial function (HB I).

Conclusions

It is possible to conclude that, when Kabat rehabilitation is associated with standard steroid treatment in the case of severe BP, affected subjects may be likely to have a faster and better recovery than those in whom only medical treatment is applied. It would therefore be worthwhile to always include this type of physical rehabilitation in patients with BP, especially in the most severe cases which may carry the risk of disfiguring facial sequelae.

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LARYNGOLOGY

Malignant salivary gland tumours of the larynx: a single institution review

Tumori maligni delle ghiandole salivari della laringe: un'unica review istituzionale

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SUMMARY

Malignant salivary gland tumours of the larynx are very rare, with limited reports of clinical outcomes. We present the decade-long experience of a single institution. A 10-year retrospective chart review of a tertiary head and neck cancer centre was performed. Index patients were identified from a review of a pathology database, and reviewed by a head and neck pathologist. Patient demographics, presenting signs and symptoms, treatment modalities and clinical outcomes were extracted from electronic medical records. Six patients were included, with an age range of 44 to 69. All six had malignant laryngeal salivary gland tumours. Pathologies included: three adenoid cystic carcinoma (2 supraglottic, 1 subglottic), one mucoepidermoid carcinoma (supraglottic), one epithelial-myoepithelial carcinoma (supraglottic) and one adenocarcinoma (transglottic). All were treated with surgery (2 endolaryngeal, 4 open) and five of six with the addition of adjuvant therapy (4 radiotherapy, 1 concurrent chemoradiation). One patient had smoking history; no patients had significant alcohol history. With 4.5 years of median follow-up, none of the patients has had recurrence or local/distant metastasis. Salivary gland tumours of the larynx present in mid to late-age, and can be successfully managed with a multi-modality approach, resulting in excellent local and regional control rates.

KEY WORDS: Larynx • Cancer • Salivary • Chemotherapy • Surgery • Partial laryngectomy

RIASSUNTO

I tumori a istotipo salivare della laringe sono molto rari, con pochi report in letteratura in merito al loro andamento clinico. Nel presente manoscritto discutiamo un'esperienza di 10 anni presso una singola struttura. Abbiamo condotto una review retrospettiva della casistica di un centro di oncologia della testa e del collo di terzo livello. I pazienti sono stati individuati mediante analisi di un database e sono stati revisionati da un Anatomo Patologo testa collo. I dati inerenti la clinica, le modalità di trattamento e gli esiti sono stati prelevati da archivi elettronici. Sono stati inclusi sei pazienti nello studio, con un range di età dai 44 ai 69 anni. Tutti e sei erano affetti da neoplasie maligne a istotipo salivare della laringe. Gli istotipi includevano: tre carcinomi adenoido-cistici (2 sopraglottico, 1 sottoglottico), un carcinoma mucoepidermoidale (sopraglottico), un carcinoma epiteliale-mioepiteliale (sopraglottico), e un adenocarcinoma (transglottico). Tutti sono stati sottoposti a trattamento chirurgico (2 chirurgie laser, 4 open) e 5 dei 6 pazienti sono stati successivamente sottoposti a terapia adjuvante (4 a radioterapia, 1 a radio-chemioterapia concomitante). Un paziente era fumatore; nessun paziente aveva storia di abuso di alcolici. A un follow-up con mediana di 4,5 anni nessuno dei pazienti ha presentato recidiva o metastasi locali o a distanza. I tumori a istotipo salivare della laringe si presentano solitamente in pazienti della seconda/terza età, e possono essere trattati con successo mediante approcci multimodali, con un ottimo controllo locoregionale di malattia.

PAROLE CHIAVE: *Laringe • Cancro • Salivare • Chemioterapia • Chirurgia • Laringectomia parziale*

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Introduction

Malignant salivary gland tumours of the larynx are very rare neoplasms, which account for < 1% of all laryngeal malignancies [1]. The most common malignant minor salivary gland tumours are adenoid cystic (32-69%) and mucoepidermoid carcinomas (15-35%) [2]; adenocarcinomas are less frequent, and epithelial-myoepithelial carcinomas are even more rare [3]. Unlike squamous cell carcinoma, which is strongly associated with inhaled tobacco use, malignant salivary tumours in the larynx have no strong association with smoking and appear to occur equally in both sexes. These tumours arise from subepithelial mucous glands in the larynx, which are found most commonly in the subglottis and supraglottis [4]. In the true glottis, the possible areas of origin are floor of the ventricle and below the anterior commissure in the subglottis. Because these tumours do not arise on the free edge of the true vocal folds which are covered with thin squamous epithelium, there is often no voice change to detect these tumours at an early stage. They typically present in a subepithelial

fashion, and can grow to a large size before they present with dysphonia or airway symptoms.

The aim of this study is to present our experience over the last decade with these rare tumours to provide insight into the multimodality treatment that is typically required for long-term oncologic success.

Materials and methods

In an IRB-approval protocol, the pathology archives of the Johns Hopkins Hospital and clinical records of patients with laryngeal cancer were reviewed to identify patients with malignant salivary gland laryngeal lesions between January 2004 and December 2013. Age, gender, presenting symptoms, location of the tumour, pathology, TNM classifications, treatment modality (surgery and/or chemo radiotherapy) and disease status was extracted from patient charts.

Results

Six patients (3M, 3F) were included, with an age at diagnosis range of 44 to 69 (mean: 56 years). Pathologic classifications are summarised in Table I and included: three adenoid cystic carcinomas, one mucoepidermoid carcinoma, one epithelial-myoepithelial carcinoma and one adenocarcinoma, not otherwise specified. The most common presenting symptom was dysphonia. Half of patients presented with advanced stage disease, but all except the adenocarcinoma presented without regional or distant metastases. Only one patient was a smoker (T4 subglottic adenoid cystic carcinoma).

Treatment modalities and oncologic results are summarised in Table I. All patients were treated primarily with surgery, and negative surgical margins were obtained in all cases. The type of surgical approach varied with each case, but two were successfully managed with endolaryngeal surgery, while four required an open surgical approach. All but one patient underwent additional adjuvant therapy regardless of pathologic type or surgical margins (4 radiotherapy, 1 concurrent chemoradiation). After 4.5 years of median follow-up, none of the patients has had recurrence or local/distant metastasis. To highlight the unique presentation and management of these cases, three case studies with pathologic images are presented below.

Representative cases

Case two: A 44-year-old male professor presented with dysphonia lasting two years. He denied any difficulty swallowing; however, he had a significant amount of coughing while eating. On fiberoptic laryngoscopy a laryngeal mass on the epiglottis was identified with normal vocal fold mobility (Fig. 1), and a staging CT scan demonstrated a large bulky supraglottic lesion on the laryngeal surface of the epiglottis from the tip to the petiole, extending into the preepiglottic space, with fat planes preserved along the hyoid bone. Direct laryngoscopy and biopsy was performed. The lesion was consistent with adenoid cystic carcinoma with both tubular and cribriform histology (Fig. 2).

With these findings, he underwent an open supraglottic laryngectomy. The final pathology demonstrated adenoid cystic carcinoma with perineural invasion and no definitive venous/lymphatic invasion and extensive involvement of the paraglottic space, staging the tumour as T3. Surgery was followed by post-operative adjuvant radiation therapy. At latest follow-up, 1.5 years after surgery, he was free of disease.

Table I. Patient demographics and tumour characteristics, treatments and uutcomes.

Case	Age	Gender	Histology	Primary Site	Stage	Tobacco	Clinical presentation
1	61	F	Adenoid cystic carcinoma	Supraglottis İnfrahyoid epiglottis	T1N0M0	N	Dysphagia
2	44	M	Adenoid cystic carcinoma	Supraglottis İnfrahyoid epiglottis	T3N0M0	N	Dysphonia
3	57	F	Adenoid cystic carcinoma	Subglottis	T4N0M0	Y	Hemoptysis
4	69	M	Muco epidermoid carcinoma	Supraglottis İntra-arytenoid	T1N0M0	N	Dysphonia
5	58	F	Epithelial-myoepitheial carcinoma	Supraglottis suprahyoid-epiglottis	T1N0M0	N	Cough
6	47	M	Adenocarcinoma	Transglottic	T4N2cM0	N	Dysphonia

TL-Total laryngectomy; ND- Neck dissection; RT- Radiation therapy; CT- Chemotherapy; ANED- Alive with no evidence of disease

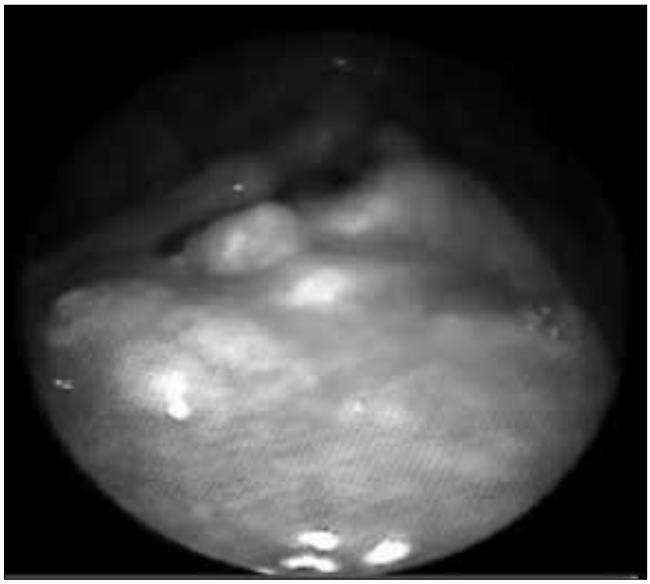

Fig. 1. Flexible laryngoscopy showing a large mass of the epiglottis that did not impair vocal fold mobility, but did cause dysphonia through a mass effect on the supraglottic.

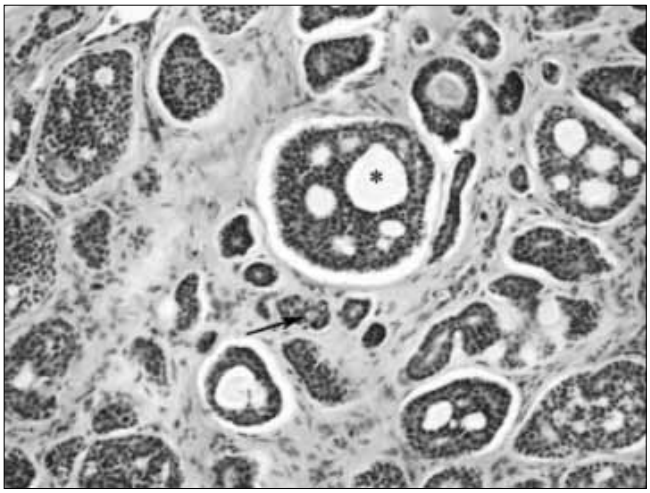

Fig. 2. This case of adenoid cystic carcinoma consists of tubules and cribriform collections of cells with minimal cytoplasm and hyperchromatic, angulated nuclei. Prominent false ducts (asterisk) and subtle true ducts (arrow) are present, as is classic for this tumour type.

Case four: A 69-year-old man presented with hoarseness and a history of slow and progressive voice change in the last 2 months. He denied pain, bleeding, cough, dysphagia, or otalgia. He was a non-smoker but had persistent gastro-oesophageal reflux. A suspicious mass was noted in the posterior commissure of the larynx on flexible laryngoscopy, and biopsy revealed a mucoepidermoid carcinoma in the larynx. He was then referred to our centre for management.

The lesion was centred in the posterior commissure, directly between the arytenoids, approximately 1 cm in maximum diameter. A preoperative MRI of the neck revealed a fullness of the posterior commissure with no well-defined mass, and no pathological cervical lymphadenopathy. The lesion was therefore completely excised endoscopically, using sharp instrumentation and a tissue shaver. Final pathology demonstrated 'intermediate grade mucoepidermoid carcinoma' (Fig. 3). All surgical margins were negative and post-operative radiation was used as adjuvant treatment. On last follow-up, 8 years after treatment, there was no evidence of disease.

Case five: A 55-year-old woman complained of persistent cough of one year duration. She had presented one year prior for the same complaint and was noted at that time to have a small, benign appearing lesion of the epiglottis, which was diagnosed as presumptive epiglottic cyst. A chest x- ray performed as part of her work-up revealed

Surgical management	Approach	Surgical margins	Adjuvant therapy	Laryngeal preservation	Follow-up period	Outcome
Supraglottic Laryngectomy	Open	-	RT	Y	3 y	ANED
Supraglottic Laryngectomy	Open	-	RT	Y	13 m	ANED
TL + İpsilateral ND	Open	-	RT	N	14 y	ANED
Partial Laryngectomy	Laser Endoscopic	-	RT	Y	4.5 y	ANED
Supraglottic Laryngectomy	Laser Endoscopic	-	None	Y	6 y	ANED
TL + Bilateral Selective ND, Levels 1-5	Open	-	RT / CT	N	11.5 y	ANED

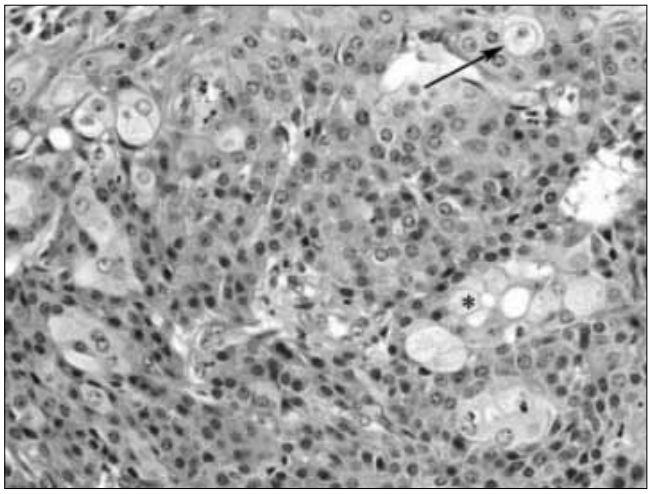

Fig. 3. Mucoepidermoid carcinoma consists of variable numbers of squamoid cells, mucous cells and intermediate cells. This laryngeal intermediate-grade mucoepidermoid carcinoma consists primarily of uniform intermediate cells with abundant eosinophilic cytoplasm, with focal mucous cells (asterisk) and squamoid cells (arrow).

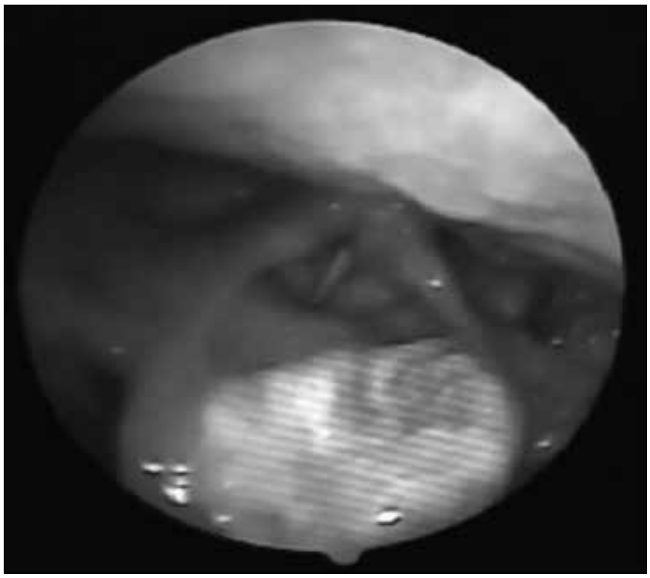

Fig. 4. Flexible laryngoscopy demonstrating an ulcerative mass on the laryngeal surface of the epiglottis with normal vocal fold mobility.

non-small cell lung carcinoma, for which she received chemotherapy with etoposide and cisplatin, radiation, and left lobectomy with mediastinal and hilar lymph node dissection. Despite treatment for lung cancer, her cough and throat irritation persisted and she therefore represented to clinic. She was a life-long non-smoker.

On flexible examination, the mass on the epiglottis was demonstrated again and was larger in size (Fig. 4). Therefore, endoscopic biopsy and excision of the mass was performed with CO^2 laser. The lesion was centred on the laryngeal surface of the epiglottis and completely excised to normal-appearing margins. The pathology of the lesion returned as epithelial-myoepithelial carcinoma of the epiglottis (Fig. 5), with tumour extending to multiple cauterised specimen edges. Therefore, two months later, she underwent a repeat suspension microlaryngoscopy and CO^2 laser excision of epiglottis with all final margins negative for tumour. She has been regularly followed up for 6 years, and has no evidence of disease.

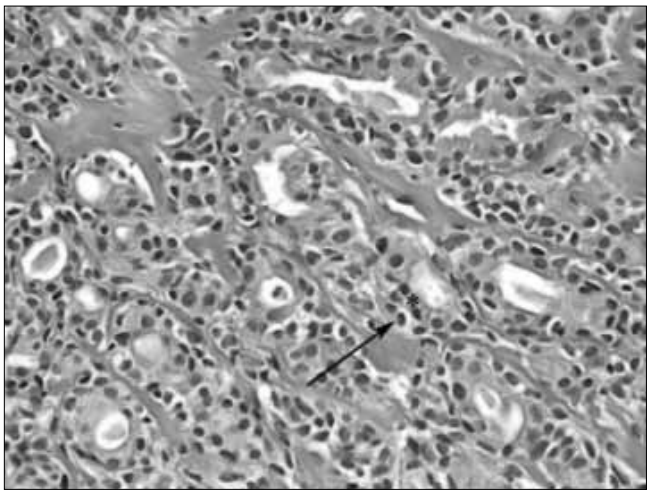

Fig. 5. This case of laryngeal epithelial-myoepithelial carcinoma was biphasic, with an inner layer of ductal cells (asterisk) tightly coupled with an outer layer of myoepithelial cells with clear cytoplasm (arrow).

Discussion

In the larynx, salivary glands have a distinct anatomic distribution [4], and occur mainly in the subglottis and supraglottis. Relative rates of salivary malignancies for these subsites differ by series [2 5], but true vocal cord involvement is rarely reported. This is in contradistinction to squamous cell carcinoma, which most commonly originates in the squamous epithelium covering the true vocal folds, and explains the difference in presenting symptoms and stage [6]. Most of our cases (67%) had supraglottic tumours and therefore the most common presenting symptom was hoarseness, dysphagia and cough. It is interesting to note that the supraglottic tumours in our series mimic the patterns of spread seen in traditional squamous cell carcinoma – invasion in the preepiglottic but not to the true vocal cord, allowing for laryngeal preservation surgery. This suggests that the barriers to tumour spread within the larynx, such as the quadrangular membrane and conus elasticus, are resistant to tumours of all histologies. As in most other series, we report a male to female ratio of 1:1 [1 2 7 8], with a minority of patients having a history of smoking [2].

The predominant pathologic diagnosis in the literature is adenoid cystic carcinoma, consistent with the 50% rate reported in our series [2 5]. In the early stages, salivary gland tumours may not present with any symptoms due to slow submucosal spread. Two of three adenoid cystic carcinoma cases were diagnosed as T3 and T4 tumours. One of

these patients had perineural invasion. There are no standardised therapeutic decisions with prospective studies due to the rarity and different histopathological types. Tumour type, grade, location and symptoms should be taken into consideration while choosing treatment options. Postoperative radiotherapy is widely accepted as adjuvant modality, especially in cases with a high-grade tumour, unclear or positive margins, and perineural spread [8-12]. All three patients in our series with adenoid cystic carcinomas had adjuvant radiotherapy and none had recurrence. Nodal disease was not present in any patient in our study, and a low rate of nodal disease is consistent with previously published reports [1].

One of our patients had supraglottic mucoepidermoid carcinoma. About 60% of patients with mucoepidermoid carcinomas of the larynx are localised in the supraglottic area [13]. In patients with high-grade mucoepidermoid carcinomas, neck dissections have been suggested regardless of clinical nodal status [13]; others conclude that neck dissections are not indicated in salivary gland tumours of the larynx unless nodal metastasis is clinically apparent [1 2 7 8]. Radiotherapy is also recommended in high-grade cases because of the high incidence of local recurrence [14]. Our patient underwent endoscopic excision, and given the patient's intermediate grade pathology he also underwent adjuvant radiation therapy.

The most common site of epithelial-myoepithelial carcinoma (EMC) is the parotid gland or submandibular gland. EMC of the larynx is very rare. Only four cases have been previously reported in the literature to date [3 15-17]; one of them being the present case [15]. Information about demographics, treatment and prognosis of EMC in the larynx is scarce because of its rarity and there is no consensus for management. In our case, long-term disease control was achieved with surgical excision, but as highlighted in the case presentation, submucosal spread and an unusual pathology has the potential to create diagnostic uncertainty and inadequate initial resection if the surgeon is anticipating a benign pathology. Therefore, our case required re-resection to achieve negative margins after final pathology from the surgical specimen revealed EMC and positive margins.

Finally, one patient in the current series presented with advanced adenocarcinoma, not otherwise specified (NOS) with significant local and nodal disease. Only 0.35% to 0.5% of all laryngeal malignancies are adenocarcinomas NOS, and are mostly seen in males [18], as in our case. Adenocarcinomas NOS of the larynx tend to metastasise to both regional and distant site [19-21] and therefore require aggressive surgical management and adjuvant therapy. Our patient did not have any recurrence or metastasis after total laryngectomy and adjuvant chemoradiotherapy after a follow-up of 11.5 years.

Careful long-term follow-up for laryngeal salivary tumours is critical. Distant metastases to the lung is a hallmark of adenoid cystic carcinoma and long-term follow up is mandatory, since recurrences may occur after more than 10 years after primary treatment [2 8 12 22]. Nevertheless, adjuvant therapy may have a role in achieving long-term disease control, as the majority of our patients received adjuvant treatment and none had recurrences and/or local or distal metastasis after a median follow-up of 4.5 years.

Conclusions

Salivary gland malignancies are rare tumours of the larynx that present in mid- to late-age, and can be successfully managed with a multi-modality approach, resulting in excellent local and regional control rates.

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Laryngology

Evaluation of pharyngeal muscle activity through nasopharyngeal surface electromyography in a cohort of dysphagic patients with acute ischaemic stroke

Valutazione dell'attività muscolare faringea attraverso elettromiografia di superficie nasofaringea in pazienti disfagici affetti da ictus ischemico acuto

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SUMMARY

Oro-pharyngeal dysphagia is frequently present during the acute phase of stroke. The aim of the present study was to evaluate whether the recording of surface EMG using a nasopharyngeal (NP) electrode could be applied to evaluation of pharyngeal muscle activity in acute stroke patients and if this neurophysiological measure is related with clinical assessment of swallowing. Patients were examined and clinical severity was assessed with the National Institute of Health Stroke Scale (NIHSS) score; dysphagia was evaluated through bedside screening test using the Gugging Swallowing Scale (GUSS). Extension of the ischaemic lesion was measured by quantitative score, based on CT scan [Alberta Stroke Programme Early CT Score (ASPECTS)]. We analysed 70 patients; 50 were classified as dysphagic (Dys+), and 20 as non-dysphagic (Dys–). Each participant underwent a surface NP EMG recording performed with a NP electrode, made of a Teflon isolated steel catheter, with a length of 16 cm and a tip diameter of 1.5 mm. The electrode was inserted through the nasal cavity, rotated and positioned approximately 3 mm antero-inferior to the salpingo-palatine fold. At least four consecutive swallowing-induced EMG bursts were recorded and analysed for each participant. Swallowing always induced a repetitive, polyphasic burst of activation of the EMG, lasting around 0.25 to 1 sec, with an amplitude of around 100-600mV. Two parameters of the EMG potentials recorded with the NP electrode were analyzed: duration and amplitude. The duration of the EMG burst was increased in Dys+ patients with a statistically significant difference compared to Dys- patients ($p < 0.001$). The amplitude was slightly reduced in the Dys+ group, but statistically significant differences were not observed ($p = 0,775$). Nevertheless, the burst amplitude showed a significant inverse correlation with NIHSS [$r(48) = –0.31$; $p < 0.05$] and ASPECTS scores [$r(48) = –0.27$; $p < 0.05$], meaning that the burst amplitude progressively reduced with an increase of clinical severity (NIHSS) and topographic extension of brain lesions in CT (ASPECTS). These results suggest that NP recordings can give a semi-quantitative measure of swallowing difficulties originating from pharyngeal dysfunction, in fact, electromyographic findings suggest reduced pharyngeal motility.

KEY WORDS: Dysphagia • Acute stroke • Nasopharyngeal electrode • Surface EMG • GUSS

RIASSUNTO

La disfagia orofaringea è spesso presente durante la fase acuta di un ictus. Lo scopo di questo lavoro è stato quello di valutare se la registrazione elettromiografica di superficie tramite un elettrodo nasofaringeo può essere impiegata per testare l'attività muscolare del faringe nei pazienti con ictus acuto e se queste misurazioni elettrofisiologiche possono essere correlate con la valutazione clinica della deglutizione. Dal punto di vista clinico la severità del quadro è stata valutata mediante l'utilizzo della scala del National Institute of Health Stroke (NIHSS); la disfagia è stata valutata mediante il test di screening Gugging Swallowing Scale (GUSS); l'estensione della lesione ischemica alla TAC è stata misurata attraverso l'Alberta Stroke Programme Early CT Score (ASPECTS). Abbiamo valutato 70 pazienti di cui 50 disfagici (Dys+), e 20 non disfagici (Dys–). Ciascun partecipante è stato sottoposto a un'elettromiografia di superficie registrata mediante un elettrodo NP costituito da un catetere di Teflon isolato in acciaio (lungo 16 cm e con un diametro in punta di 1,5 mm). L'elettrodo è stato inserito attraverso la cavità nasale, ruotato e posizionato approssimativamente 3 mm antero-inferiormente rispetto alla volta salpingo-palatina. Per ogni partecipante sono state registrate ed analizzate le risposte elettromiografiche di almeno quattro deglutizioni volontarie ripetute. La deglutizione induce sempre all'elettromiografia burst ripetitivi e polifasici di durata compresa fra 0,25 e 1 secondo, con un'ampiezza intorno ai 100-600mV. I disfagici hanno mostrano una maggiore durata del burst rilevato all'elettromiografia rispetto ai non disfagici, con una differenza statisticamente significativa ($p < 0,001$), ma non hanno mostrano differenze in termini di ampiezza del burst stesso ($p = 0,775$); quest'ultima invece era inversamente correlata con lo NIHSS score [$r(48) = –0,31$; $p < 0,05$)] e con lo ASPECTS score [$r(48) = –0,27$; $p < 0,05$]. Questi risultati suggeriscono che le registrazioni nasofaringee possono rappresentare un indice semi-quantitativo delle difficoltà deglutitorie secondarie a disfunzione faringea ed in particolare, i risultati dell'elettromiografia sarebbero indicativi di una ridotta motilità faringea durante la fase acuta di un ictus.

PAROLE CHIAVE: *Disfagia • Ictus acuto • Elettrodo nasofaringeo • EMG di superficie • GUSS*

Introduction

Dysphagia is a common consequence of ischaemic stroke. Oropharyngeal dysphagia is frequently present during the acute phase of stroke: clinically evident dysphagia, evaluated through bedside screening techniques, is reported in 37-45% of patients in the first three days after stroke onset, largely varying depending on the diagnostic method applied and the dimension and site of stroke lesion [1]. The presence of dysphagia increases the risk of aspiration pneumonia, malnutrition and dehydration, and can therefore be potentially life-threatening deserving rapid identification and treatment [2]. Dysphagia has generally a favourable course, and its prevalence declines significantly within the first week after stroke [3-5]. At three months, most patients recover completely [4 6].

Methods for detecting dysphagia include non-instrumental bedside screening and instrumental methods such as videofluoroscopic study of swallowing or flexible endoscopic evaluation with sensory testing, which are regarded as the gold standard for evaluation of swallowing, although not always feasible in the acute setting. Even though bedside screenings are not as sensitive and standardised as instrumental methods, they are commonly used in daily clinical practice for their ease and repeatability [7].

In a previous paper [8] we used a nasopharyngeal (NP), surface electrode, applied trans-nasally, to record the electromyographic (EMG) activity of pharyngeal muscles during swallowing (Fig. 1). We observed that the NP electrode was able to record polyphasic reproducible EMG potentials during swallowing, with duration of approximately 0.5-1.5 sec and average amplitude of 100-600 mV. The polyphasic response recorded by the NP electrode is characterised by an initial downward deflection (when the potential wave travels towards the recording electrode) followed by an upward deflection (when the potential moves away from the electrode) (Fig. 2); thus, it reflects a wave of muscular activation travelling in the pharynx.

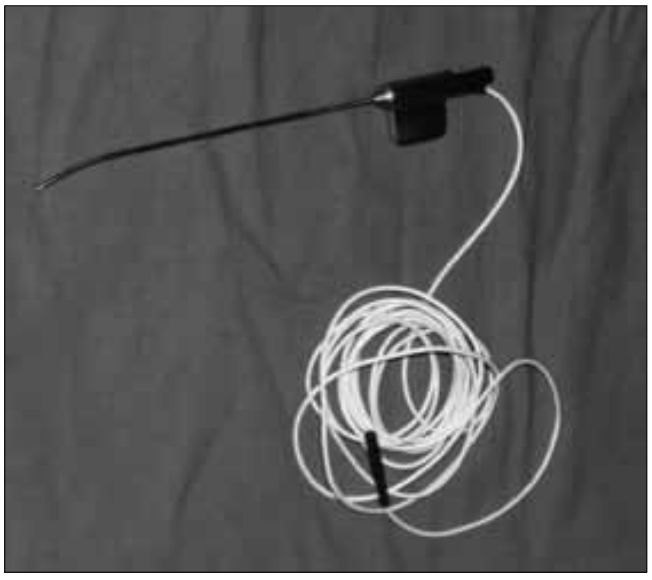

Fig. 1. The naso-pharyngeal electrode.

In the present study, our aim was to evaluate whether this recording technique may be applied to the evaluation of pharyngeal muscle activity in acute stroke patients and if this neurophysiological measure is related with clinical assessment of swallowing.

Materials and methods

A cohort of acute ischaemic stroke patients was prospectively enrolled in this study. All patients were evaluated within 48 hours of stroke onset. The diagnosis of stroke was always confirmed by both computed tomography (CT) and magnetic resonance imaging (MRI). Extension of the ischaemic lesion was measured by quantitative score based on CT scan [Alberta Stroke Programme Early CT Score (ASPECTS) [9]]. Clinical evaluation included neurological examination and bedside clinical assessment for dysphagia. Clinical severity was assessed with the National Institute of Health Stroke Scale (NIHSS) [10]. As the neurophysiological method used in this study was based on the EMG measure of voluntary swallowing, patients unable to produce a voluntary pharyngeal contraction (i.e. patients comatose, or patients with severe aphasia, unable to understand the request) were excluded from the study. Patients with a history of head and neck damage, neurologic disease other than cerebrovascular disorders or current dysphagia were also excluded from the study. The ethical committee of the hospital approved the study, and patients gave their consent to participate.

Clinical and neurophysiological measure of pharyngeal muscle activity

Clinical evaluation of dysphagia and neurophysiologic recording were performed in the same session, in the first 48 hours following stroke presentation. For the evaluation of dysphagia, the Gugging Swallowing Score (GUSS) [11] was applied. The GUSS is a validated clinical bedside test for dysphagia, which includes a preliminary indirect four step assessment of swallowing followed by a direct swallowing test that consists of three sequentially performed subtests, starting with semisolid, liquid and finally solid textures. The GUSS score ranges from 0 to 20; patients with GUSS = 20 were classified as non dysphagic (Dys–), patients with a GUSS equal or below 19 were considered dysphagic (Dys+) [11].

Each participant underwent a surface NP EMG recording performed with a NP electrode, made of a Teflon isolated steel catheter, with a length of 16 cm, tip diameter 1.5 mm (Fig. 1). The electrode was inserted through the nasal cavity, rotated, and positioned approximately 3 mm anteroinferior to the salpingo-palatine fold, as described by Su et al. [12] In this way, it was placed in a site that allowed record-

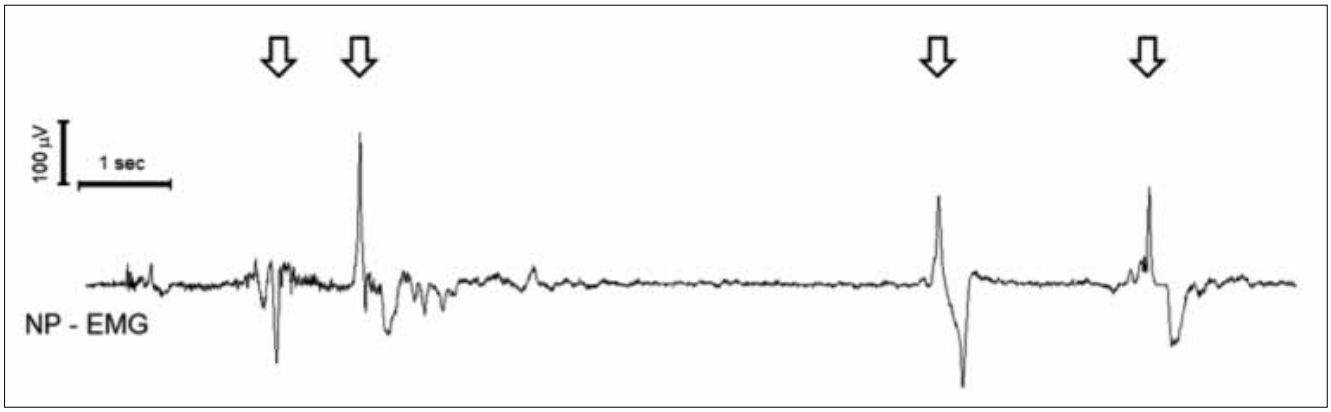

Fig. 2. Naso-pharyngeal EMG recording. The arrows indicate swallowing-induced EMG bursts. Time scale and amplitude calibration are in the upper left corner.

ing the activity of the posterior oropharyngeal muscles. The outer part of the electrode was fixed with a tape to the nostril to reduce movement artifacts. A reference electrode was placed on the mastoid bone. The EMG signal was acquired witha Micromed® SystemPlus digital polygraph; sampling rate was 1024 Hz, high pass filter was 10 Hz, low pass filter was 500 Hz and gain was 5 mV/mm. Patients were lying in a supine position during the recording. After electrode placement, subjects were invited to swallow repeatedly, and the position of the electrode was slightly moved, until the maximum amplitude of the swallowing-related potentials was obtained. Then, the patients were asked to swallow repeatedly, at least four times per recording. The parameters measured were the duration of the recorded potential (Fig. 2, from the initial deflection from baseline to the return to baseline) and the peak-to-peak amplitude. For each patient, we measured the average duration and amplitude of the four best responses.

Statistical analysis

The following variables were analysed: age, gender, NIHSS, ASPECTS and GUSS score, amplitude (Amp) and duration of the EMG potential (T_{dur}). Statistical analysis was performed in multiple steps. In a first step, we evaluated the normality of the distribution of the Amp and T_{dur} of the EMG potentials, using the Shapiro-Wilk test, with a significance level of $p < 0.05$. When the distribution was normal in both the samples (Dys+ groupand Dys– group) comparison was made using a Student's t-test. When the distribution was not normal, a non-parametric test was applied (Mann-Whitney U-test). Significance level was set at $p < 0.05$. Categorical variables were compared with Fisher's exact test. Within the Dys+ group, correlations were tested between Amp and T_{dur} of the EMG potentials versus age, NIHSS, ASPECTS and GUSS score, using Pearson's correlation coefficient. The critical value of Pearson's correlation coefficient was set to $r(48) = 0.28$, corresponding to a significance level of $p < 0.05$.

Results

Seventy patients were enrolled, 46 men and 24 women. Mean age was 67.30 ± 13.1 years; mean scores of NIHSS, ASPECTS and GUSS was 7.44 ± 6.86, 2.90 ± 2.26 and 12.51 ± 7.14, respectively; 50 patients were classified as Dys+ and 20 as Dys–. Mean and SD of NIHSS, ASPECTS and GUSS in the two groups are reported in Table I.

Each recording session lasted 5 to 15 min. At least four consecutive swallowing-induced EMG bursts were recorded and analysed for each participant. Swallowing always induced a repetitive polyphasic burst of activation of the EMG, lasting around 0.25 to 1 sec, with amplitude around 100-600mV (Fig. 2).

The Shapiro-Wilk test showed a normal distribution for Amp and T_{dur} of the EMG potentials in the Dys– group, whereas the distribution was not normal in the Dys+ group either for the duration ($p < 0.001$) or for the amplitude ($p = 0.040$). Consequently, comparison between Dys+ and Dys– group was performed with a non-parametric test (Mann-Whitney U-test). Compared to Dys– patients, Dys+ patients showed older age (Dys+ = 70.1 ± 11.8 years; Dys– = 60.3 ± 14.0 years; U-test = 293.0; $p = 0.007$), while no difference was observed in gender composition (Fisher's exact test $p = 0.782$). Dys+ patients showed a greater NIH score (Dys+ = 9.2 ± 7.3; Dys– = 3.1 ± 2.3; U-test = 182.0; $p < 0.001$), while no difference was observed in the ASPECTS score (Dys+ = 3.2 ± 2.5; Dys– = 2.1 ± 1.1; U-test = 423.5; $p = 0.307$). Regarding EMG data, the Dys+ group showed longer EMG burst duration (Dys+ = 809 ± 505 msec; Dys– = 338 ± 107 msec; U-test = 127.0; $p < 0.001$), but no differences in amplitude (Dys+ = 424 ± 190 mV; Dys– = 405 ± 75 msec; U-test = 522.0; $p = 0.775$). Finally, in the correlation analysis the EMG burst amplitude was inversely correlated with NIHSS [$r(48) = –0.31$; $p < 0.05$] and the ASPECTS score [$r(48) = –0.27$; $p < 0.05$].

Table I. Clinical features of the study population, Dys+ and Dys- groups, and results of statistical comparison.

Condition		Age	Gender	NIHSS	ASPECTS	GUSS	Amp	Tdur
		years	n	n	n	n	mV	msec
All	Mean	67.30	46M 24W	7.44	2.89	12.51	418.80	674.40
	SD	13.14		6..87	2.27	7.14	165.20	479.90
Dys+ (n = 50)	Mean	70.10	32M 18W	9.20	3.20	9.52	424.2	809.0
	SD	11.79		7.31	2.54	6.31	190.1	505.1
Dys- (n = 20)	Mean	60.30	14M 6W	3.05	2.10	20.00	405.3	337.9
	SD	14.00		2.28	1.07	0.00	75.4	107.3
Mann Whitney	U-test	293.0		182.0	423.5		522.0	127.0
	p	0.007		< 0.001	0.307		0.775	< 0.001
Fisher			0.78					

Discussion

We studied a population of acute ischaemic stroke patients in which surface EMG evaluation of pharyngeal muscles was performed using a surface nasopharyngeal electrode. In our sample, stroke-related dysphagia was present in 71% of patients, and was associated with older age, greater clinical severity (higher NIHSS score) and larger brain lesions (higher ASPECT score). These findings are in agreement with data from the literature, which suggest that swallowing impairment in stroke is more frequent and severe in patients with extensive brain damage and severe clinical deficits [4 13 14].

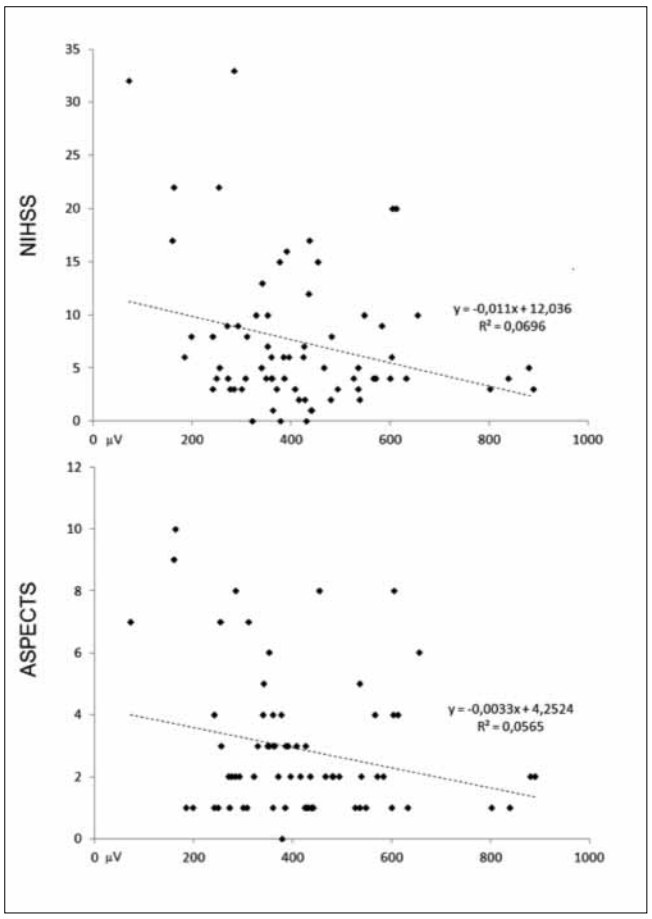

Fig. 3. Correlation plots between EMG mean burst amplitude and NIHSS (upper panel) and ASPECT score (lower panel).

The NP recording results suggest that the EMG nasopharyngeal burst recorded in dysphagic patients are different from those observed in non-dysphagic ones. Two parameters of the EMG potentials recorded with the NP electrode were analysed: duration and amplitude. The duration of the EMG burst was increased in Dys+ patients with a statistically significant difference compared to Dys- patients. The amplitude was slightly reduced in the Dys+ group, but statistically significant differences were not observed. When we analysed correlations between clinical parameters and EMG data, the burst amplitude showed a significant inverse correlation with NIHSS and ASPECTS scores, meaning that the burst amplitude progressively reduced with the increase of clinical severity (NIHSS) and topographic extension of brain lesions by CT scan (ASPECTS). The increased duration of the EMG burst with a slightly reduced amplitude suggests a temporal dispersion of neuromuscular inputs and a loss of synchrony between muscle cells, which results in less efficient muscular activation.

Swallowing difficulties in stroke patients may be due to several mechanisms. Physiologically, the swallowing sequence is triggered by sensory inputs and completed by a complex bilateral reflex muscular response, organised by a brain stem central pattern generator and modulated by various peripheral and supranuclear controls [14-18]. Epidemiological studies in stroke populations have outlined three major mechanism at the basis of neurogenic dysphagia: 1) impaired pharyngeal motility due to hypoactivation of the tongue, incomplete closure of the laryngeal sphincter and/or delayed opening of upper oesophagus sphincter; 2) sensory pharyngeal and laryngeal impairment; 3) altered tongue coordination [19 20]. The surface EMG recordings described in the present study, which estimate oropharyngeal muscle activity, can only give information concerning pharyngeal motility. With these limitations,

we suggest that NP recordings can give a semi-quantitative measure of swallowing difficulties originating from pharyngeal dysfunction. In particular, increased duration of the EMG burst suggests reduced pharyngeal motility, and burst amplitude is related with the extension and clinical severity of the stroke. If confirmed, these data suggest that surface NP-EMG recording can be helpful in bedside, non-invasive assessment of stroke patients with swallowing impairment.

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Rhinology

Monolateral sinonasal complications of dental disease or treatment: when does endoscopic endonasal surgery require an intraoral approach?

Complicanze sinusali monolaterali da patologia o trattamenti dentali: quando la chirurgia endoscopica endonasale necessita un approccio intraorale?

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SUMMARY

The widespread use of dental implants and reconstructive procedures for their positioning has led to an increase in sinonasal complications of dental disease and treatment (SCDDT). Diagnosis requires accurate dental and rhinological evaluation, including computed tomography (CT). The aim of this study is to investigate a multidisciplinary approach for the treatment of SCDDT by combining endoscopic endonasal surgery (EES) and an intraoral approach on the basis of a preliminary classification system already proposed by other authors. Moreover, we analysed the percentage of odontogenic maxillary sinusitis extending to the anterior ethmoidal sinuses and bacteria involved in the pathogenesis of SCDDT. Between January 2012 and August 2015, in our series of 31 patients, 16/31 patients (51.6%) were treated with EES, 3/31 patients (9.7%) with an intraoral approach and 12/31 patients (38.7%) with a combined approach. All patients reported improvement in sinusitis symptoms confirmed by clinical examinations and CT scan. No significant complications were recorded and revision surgery was not required. Finally, the results of this preliminary study suggest that a multidisciplinary approach to SCDDT from diagnosis to therapy allows more precise diagnosis and comprehensive therapy to achieve a rapid recovery and minimise the risk of recurrence.

KEY WORDS: Odontogenic maxillary sinusitis • Chronic rhinosinusitis • FESS • Sinus floor elevation • Oral implant

RIASSUNTO

L'utilizzo diffuso degli impianti dentali e delle procedure ricostruttive per il loro posizionamento ha portato un aumento delle complicanze sinusali da patologia o trattamenti dentali (SCDDT). La diagnosi richiede una valutazione dentale e rinologica accurata, compresa la tomografia computerizzata (TC). Lo scopo di questo studio è stato quello di considerare un approccio multidisciplinare per il trattamento delle SCDDT, combinando la chirurgia endoscopica endonasale (EES) e l'approccio intraorale sulla base di un sistema di classificazione preliminare già proposto da altri autori. Inoltre, gli autori hanno analizzato la percentuale di sinusite mascellare a eziologica odontogena che si estende a interessare i seni etmoidali anteriori come anche i batteri coinvolti nella patogenesi delle SCDDT. Tra il gennaio 2012 e agosto 2015, nella nostra casistica di 31 pazienti, 16/31 pazienti (51,6%) sono stati trattati con approccio EES, 3/31 pazienti (9,7%) con approccio intraorale, e 12/31 pazienti (38,7%) con approccio combinato. Tutti i pazienti hanno riferito un miglioramento dei sintomi della rinosinusite, confermato attraverso i risultati degli esami clinici e della TC di controllo. Non è stata osservata nessuna complicanza significativa, né si è ricorsi a una revisione chirurgica. Infine, i risultati di questo studio preliminare suggeriscono che un approccio multidisciplinare delle SCDDT dalla diagnosi alla terapia permette una diagnosi più precisa e una terapia più esauriente, così da ottenere un rapido recupero, riducendo al minimo il rischio di recidiva.

PAROLE CHIAVE: *Sinusite mascellare odontogena • Rinosinusite cronica • Chirurgia endoscopica funzionale sinusale • Rialzo del pavimento del seno mascellare • Impianti orali*

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Introduction

Sinonasal complications of dental disease and treatment (SCDDT) are a significant disorder of the paranasal sinuses [1-4] accounting for 10-12% of all cases of chronic maxillary sinusitis (CMS) [5-12]. In recent publications, it has been reported that 30-40% of CMS cases are of a dental origin [12-14] and 8% of all EES are due to odontogenic aetiologies [14].

SCDDT occurs when the Schneiderian membrane is violated by conditions such as: a) oroantral fistulae (OAF) [8 9 15 16]; b) chronic periapical odontogenic infections of the maxillary posterior teeth; c) odontogenic cystitis; d) iatrogenic factors including intraoral foreign bodies (dental fillings, tooth roots in traumatic extraction and parts of broken instruments); e) penetration of dental implants

into the maxillary sinus; f) elevation of the sinus floor followed by dislocation of the grafting material and/or dental implant into the sinusal cavity [6 10 11 1-21]; g) maxillary osteomyelitis or maxillary medication related osteonecrosis of the jaw (MRONJ) [15 22].

SCDDT deserves special consideration because it differs from other forms of rhinogenous sinusitis in terms of pathophysiology, microbiology, diagnosis and management [6 10 17]. A close collaboration between ENT, oral and maxillofacial specialists is essential for accurate diagnosis and optimal treatment of both sinusitis and the odontogenic source.

Our study included 31 patients with SCDDT who underwent surgery between January 2012 and August 2015. Despite its limited nature, the aims of this preliminary study were: a) to apply a classification system proposed by Felisati et al. [1], partially modified by us (Table I), for surgical treatment of SCDDT combining endoscopic endonasal surgery (EES) and an intraoral approach where necessary; b) to analyse the percentage of odontogenic maxillary sinusitis extending to the anterior ethmoid sinuses and investigate the presence of anatomical variations from maxillofacial computed tomography (CT) scans; and c) to investigate the bacteria and fungi involved in the pathogenesis of SCDDT (Table II).

Materials and methods

Between January 2012 and August 2015, 31 patients underwent surgery for SCDDT at the ENT Department in San Luigi Gonzaga Hospital, Turin, Italy (Table I). Eighteen patients were women (58.1%) and 13 were men (41.9%), aged from 30 to 75 years, with an average age of 51.3 (SD: 13.28), which is similar to that found by other authors [7 8 23]. The male to female ratio was 1:1.4, similar to that reported in previous studies [7 10 12]. Three patients underwent urgent surgery (# 18, 19, 22). The guidelines from the Helsinki Declaration were followed in this study, and informed consent was obtained from all patients.

All patients had a history of dental treatment and did not respond to medical therapy. Patients with a history of bilateral chronic rhinosinusitis, allergic rhinitis, or asthma, or OAF after tooth extraction without sinusitis, or those treated with only antibiotics after dental treatment were not included. We decided to limit fungal forms to only fungus balls by excluding invasive forms because these conditions are usually not of odontogenic origin. The interval from the dental procedure to first visit for symptoms was less 1 month in 3 patients (# 18,19,22) and 8-12 months for the remaining patients.

The suspected diagnosis of SCDDT was based on the presence of unilateral signs and symptoms of sinusitis, nasal endoscopy and oral examination. The definitive diagnosis was made by axial and coronal contiguous 1 mm CT scans, with post-processing sagittal CT scans [24] showing inflammation of the maxillary sinus, OAF, periapical lesions, dental roots, dental materials, implants, materials for sinus augmentation, or parts of broken instruments in the maxillary sinus. The diagnosis of anterior ethmoid sinusitis and/or the presence of anatomical variations was obtained from coronal CT scans. Recently, we have started using cone beam computed tomography (CBCT) to evaluate the dental cause of sinusitis, particularly in patients with peri-implant disease.

In the presence of peri-implant osteitis with sinusitis or other kinds of maxillary dentoalveolar infection associated with sinusitis or in presence of OAF, endoscopic endonasal surgery (EES) has been used along with an intraoral approach for the removal of infected bone or dental implants and the closure of oroantral communication. Therefore, by analysing the results of the literature, we have done is in accordance with what proposed by Felisati's classification.

Since August 2013, we implemented a standardised expert-team composed of ENT specialists and oral surgeons to resolve these pathologies with either EES alone, or a combination of EES and an intraoral approach.

Endoscopic endonasal surgery (EES)

With regards to these pathologies, EES not only has the objective of eliminating *infection in the involved paranasal sinuses and removing infected grafting material from the maxillary sinus, but also removing any obstacle to correct sinus drainage and ventilation.*

EES was performed under general anaesthesia with a local anaesthetic solution containing epinephrine to minimise bleeding. A rigid 0°, 4.0-mm endoscope (Karl Storz, Germany) was used to perform turbinoplasty of the middle turbinate, concha bullosa, or paradoxical middle turbinate. Then, an inferior uncinectomy was made and the natural ostium was identified. The ostium was enlarged in a postero-inferior direction to a size sufficient for clear visualisation of the maxillary sinus and for effective drainage after healing. SCDDT treatment generally requires a type II or III maxillary sinusotomy [25]. Rigid 45° and 70°, 4.0-mm endoscopes (Karl Storz) were used for inspection and treatment of the inferior maxillary recess of the maxillary sinus and to allow the use of angled and curved instruments inside the sinus. In a type II sinusotomy, it is opened further posteriorly and inferiorly (< 2 cm diameter). In type III sinusotomy, the antrostomy is extended close to the level of the posterior wall of the maxillary antrum, anterior to the lacrimal sac, and inferior to the base of the inferior turbinate [25]. In patients whose maxillary sinus infections were associated with ethmoidal cells, an anterior ethmoidectomy was performed with total removal of the uncinate process. Moreover, concomitant anatomical variations (significant septal deviation, concha bullosa, paradoxical middle turbinate, Haller's cell, hypertrophy

of the uncinate process) were corrected to eliminate every possible obstacle to the recovery of sinus functionality, if present.

Intraoral surgery

The objective of the intraoral approach was to remove grafting material in the inferior portion and anterior recess of the maxillary sinus not reachable with endoscopy, remove necrotic bone, perform periapical endodontic surgery, and where necessary, close the oroantral communication by removing fistulae and performing a closure with local flaps.

When the EES had been completed, a full thickness buccal mucoperiosteal flap was prepared in the lateral-posterior maxilla according to the position of the OAF or infected implant allowing easy access to the alveolar process. In the case of maxillary osteitis or peri-implantitis, a meticulous revision of the alveolar process was performed using a diamond bur. In all cases, bone revision or implant removal led to an oroantral communication, and a local flap was used to close the communication with the maxillary sinus. Before suturing the flaps, an additional endoscopic control was performed and the maxillary sinus mucosa was washed with antibiotic solution (rifamycin). When the communication was very narrow (0.5-0.8 mm), a simple mucoperiosteal flap was used to close the communication and sutures were applied after careful flap mobilisation by periosteal incisions.

In the case of larger oroantral communication, a pedicled buccal fat pad flap (PBFPF) was used [22]. The approach to the buccal fat pad was made by periosteal incision in the posterolateral region of the maxilla, and the fat pad was transferred onto the defect; after that, two or three holes were made in the lateral maxillary wall to secure the flap in the correct position without tension using a resorbable 3/0 suture. A trans-mucosal suture was then made to fix the flap on the palatal aspect. Finally, a mucosal flap was prepared to form a vestibular flap to cover the fat pad flap. A horizontal counter incision was made through the periosteum to release the mucosal flap and it was sutured over the PBFPF without tension. From the fifth postoperative day onward, physical therapy consisting of active mouth-opening exercises is strongly recommended.

The hospitalisation period after surgery was 24 hours and nasal packaging was removed 48 h after surgery. All patients were instructed to: (i) follow antibiotic therapy (amoxicillin-clavulanic acid 2 g/day or levofloxacin 500 mg/day) before and after surgery, for 14 days total; (ii) administer saline nasal sprays and nasal wash with saline; (iii) apply nasal unguent for 60-90 days after surgery; (iv) optimise oral hygiene with chlorhexidine for 10-12 days until oral suture removal; (v) carry out physical therapy consisting of active mouth-opening exercises from the fifth postoperative day onward.

Results

The results of the study are shown in Tables I and II, and some clinical cases are presented in Figures 1-7.

Conventional dental treatment (class 3b) was the most common cause of SCDDT, found in nine patients (35.5%). Sinus floor elevation and grafting procedures with OAF (class 1) were present in five patients (16.1%), and without OAF (class 1a) in two patients (6.5%); peri-implant osteitis with sinusitis (class 2a) in six patients (19.4%); a odontogenic cyst (DCY) in five patients (16.2%) of which 3/5 with OAF (class 3a) while 2/5 without OAF (class 3b); implant dislocation with sinusitis and without OAF (class 2c) in three patients (9.7%); and a supernumerary tooth (ST) was present in one patient (3.1%).

Unilateral purulent rhinorrhoea was the most common presenting sign and symptom in 20 patients (64.5%), followed by nasal obstruction in 19 patients (61.3%), postnasal drip in 18 patients (58.1%), bad smell in 17 patients (54.9%), facial pain in 14 patients (45.2%) and swollen cheek in 12 patients (38.7%).

A paranasal sinus CT scan was carried out in all cases. In 16 of 31patients (51.6%), maxillary sinusitis was associated with anterior ethmoid sinusitis, in 4 of 31 patients (12.9%) maxillary sinusitis was associated with anterior ethmoid and frontal sinusitis, and in 16 of 31 patients (51.6%) concomitant anatomic variations were observed. Twenty-six of 31 patients (83.9%) presented obstruction of the ostiomeatal complex (OMC); in nine of 26 patients (35%), concomitant anatomic variations were observed. Saibene Am et al. [26] retrospectively evaluated 315 surgically treated SCDDT patients and in 18.7% have found bilateral involvement.

Sixteen of 31 patients (51.6%) were treated with EES; in 12 of 31 patients (38.7%), EES was combined with an intraoral approach, while the remaining 3 of 31 patients (9.7%) were only treated with an intraoral approach for removal of a large dentigerous cyst in two patients and a supernumerary tooth in the third patient. Anterior ethmoidectomy was performed in 16/31 (51.6%) patients whose maxillary sinus infection was associated with anterior ethmoidal cells. Cases affected by concomitant anatomical variations (16/31 patients) were treated to eliminate every possible obstacle to recovery of sinus functionality.

Follow-up was performed with nasal endoscopy (rigid optic 0-45°, 3 mm) and scheduled at 1-3-5-8-12-16-24 weeks, and then after 1 year. No major intraoperative or immediate postoperative complications were observed in any patient, and no recurrences were observed during the follow-up period. A minor complication, nasal synechia, was seen in one case (# 14). Twenty-nine of 31 patients had CT scans about 4-5 months after surgery, which showed a significant improvement in line with clinical and radiological findings.

Preoperative bacterial culture, endoscopically obtained

Table I. Patient demographics. Preoperative symptoms, signs and radiological characteristics. The classification of Felisati et al. [12] has been used, modified by us for aetiologic factors and surgical treatment of SCOD (No. of patients = 31).

ID	Name	Sex	Age	Preoperative symptoms and signs	Radiological characteristics	Aetiologic factors and class	Surgical Treatment
1	MG	M	55	FP + NO	MS + OMC	3a (DCY)	Intraoral approach
2	CG	M	69	PR	MS + OMC + ES	3b	EES
3	SG	F	47	FP	MS + OMC	ST	Intraoral approach
4	MA	M	45	FP + SC	MS + OMC + SD	3b (DCY)	EES
5	SS	M	70	PR + BS + NO + PD	MS + OMC + ES + SD	3b	EES
6	CR	M	40	FP + NO + SC	MS + OMC	3a (DCY)	Intraoral approach
7	CL	F	61	BS + PD	MS + OMC + ES + FS	2c	EES + implant removal
8	DF	F	51	PR + NO + PD	MS + OMC + PMT	3b	EES
9	CC	M	44	FP + NO + SC	MS + MSS	3b (DCY)	EES
10	BV	M	50	PR + BS + NO + PD	MS + OMC + ES + SD	2c	EES + implant removal
11	BL	F	45	BS + NO + PD	MS + OMC + BE	2c	EES + implant removal
12	BV	M	60	FP + SC	MS + CB	2a	Combined: EES + implant removal + OAF repair
13	PM	F	42	FP + SC	MS + OMC + UP	2a	Combined: EES + implant removal + OAF repair
14	CC	M	73	PR + BS + NO + PD	MS + OMC + ES	2a	Combined: EES + implant removal + OAF repair
15	MR	F	42	PR + BS + NO + PD	MS + OMC + ES	3b	EES
16	PM	F	56	FP + SC	MS + CB	2a	Combined: EES + implant removal + OAF repair
17	VR	F	35	FP + SC	MS + OMC	3a (DCY)	Combined: EES + Canine fossa approach with endoscopic aid
18	FL	M	36	PR+FP+BS+NO+PD+SC	MS + OMC + ES + FS	3b	Combined: EES + tooths removal
19	CP	F	39	PR+FP+BS+NO+PD+SC	MS + OMC + ES	1	Combined: EES + infected material removal + OAF repair
20	GM	F	36	PR+BS+PD	MS+ES+CB+AEA	3b	EES
21	FA	F	37	PR+BS+NO+PD	MS+OMC+ES+FS+AEA	3b	EES
22	NS	M	33	PR+FP+BS+NO+PD+SC	MS + OMC + ES + MSS	3b	EES
23	PR	F	56	PR + BS + NO + PD	MS + CB + BE + UP	3b	EES
24	GR	F	51	PR + BS + NO + PD	MS + OMC + ES + CB	1	Combined: EES + infected material removal + OAF repair
25	AF	F	72	PR + FP	MS + OMC + PMT	2a	Combined: EES + implant removal + OAF repair
26	PG	F	59	FP + SC	MS + OMC + SSS	1	EES + infected material removal
27	MM	F	57	PR + BS + NO + PD	MS + OMC + ES + FS	1a	EES + infected material removal
28	OM	M	74	PR + BS + NO + PD	MS + OMC + ES	2a	Combined: EES + implant removal + OAF repair
29	CLA	M	30	BS + NO + PD	MS + OMC	1	Combined: EES + infected material removal + OAF repair
30	PS	F	51	PR + BS + NO + PD	MS + OMC + ES+FS	1a	EES+ infected material removal
31	OI	F	75	PR + FP + SC	MS+OMC+ES+FS+CB+MSS+SSS	1	Combined: EES + infected material removal + OAF repair

Symptoms and signs: FP = facial pain; NO = nasal obstruction; PR = purulent rhinorrhea; SC = swollen cheek; BS = bad smell; PD = post-nasal drip. Radiological characteristics: MS = maxillary sinusitis; ES = ethmoidal sinusitis; FS = frontal sinusitis; OMC = obstruction of the ostiomeatal complex; SD = significant septum deviation; PMT = paradoxical middle turbinate; MSS = septated maxillary sinus; BE = hypertrophic ethmoidal bulla; CB= concha bullosa; SSS = silent sinus syndrome; PU = hypertrophic uncinate process; AEA = anterior ethmoidal artery. Etiologic factors and class: DCY = dentigerous cyst; ST = supernumerary tooth; 1 = sinusitis after maxillary sinus (MS) lift with oroantral fistulae (OAF) (+/– dislocation of grafting material in MS); 1a = sinusitis after MS lift without OAF (+/– dislocation of grafting material in MS); 2a = peri-implant osteitis with sinusitis; 2c = implant dislocation with sinusitis and without OAF; 3a = Bacterial or fungal sinusitis with OAF resulting from conventional dental treatment complications 3b = bacterial or fungal sinusitis resulting from conventional dental treatment complications. Surgical treatment: EES = endoscopic endonasal surgery; OAF = oroantral fistulae.
Note: # 6, 10, 18, 21, 24, 26 and 27 are reported in Figs 1–7.

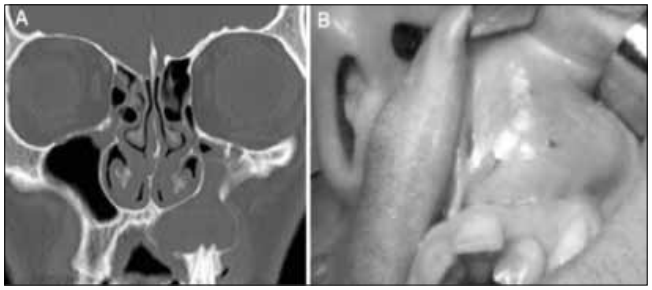

Fig. 1. Patient 6. SCDDT resulting from odontogenic cyst (Class 3a). A) Coronal maxillofacial CT, and B) clinical examination showing a bulging of the upper gingiva caused by the cyst.

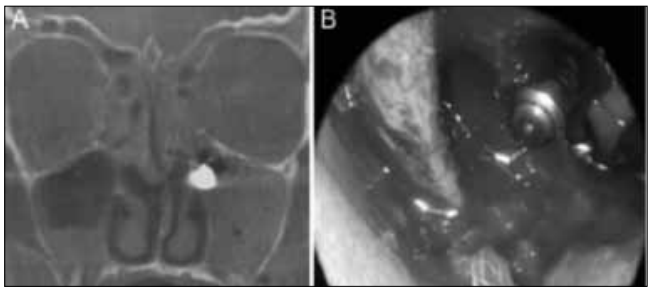

Fig. 2. Patient 10. SCDDT resulting from implant dislocation (Class 2c). A) Coronal CT scan showing the implant inside the maxillary sinus, near the natural ostium but unable to be dragged in the ostiomeatal complex due to the small size of the natural ostium itself; B) Endoscopic endonasal surgery and implant removal.

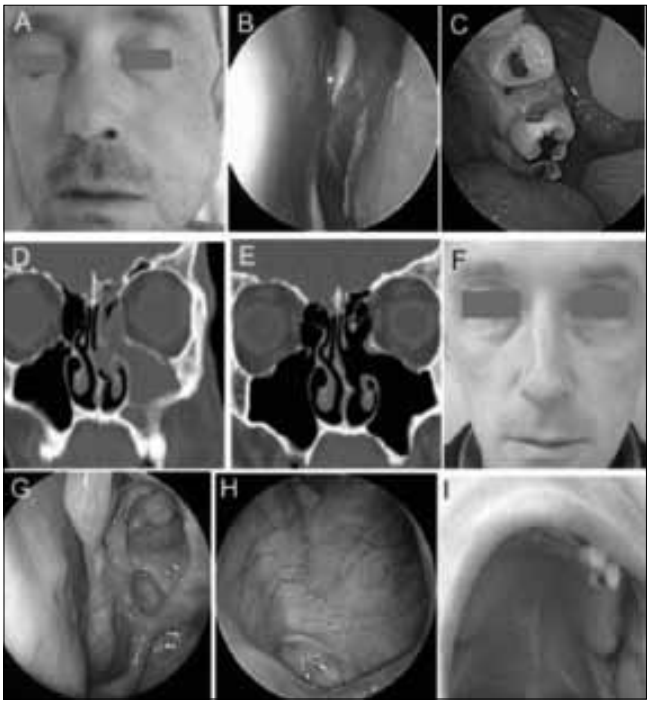

Fig. 3. Patient 18. SCDDT resulting from dental treatment complicated by bacterial sinusitis (Class 3b). A) Swelling on the left cheek and B) relevant purulent secretion in the middle meatal and olfactory cleft of the left side with a fetid purulent discharge, in a patient with C) dental caries and presence of dental pathology; D) Coronal CT scan showing complete obliteration of the left maxillary sinus and the anterior ethmoid cells as well as the obstruction of the frontal recess. Note the asymmetrical skull base; E) Nine-month postoperative coronal CT scan showing complete aeration of all paranasal sinuses; F) as well as the complete absence of swelling on the cheek. G, H) The postoperative endoscopic view 9 months after endoscopic endonasal surgery showing the appearance of the anterior ethmoidectomy, turbinoplasty of the middle turbinate and maxillary sinusotomy. I) Intraoral appearance of healing after teeth extraction.

from the middle meatus with nasal swab, was performed on 20/31 patients with unilateral purulent rhinorrhoea. Bacteriological examination was positive in 8/20 patients (Table II), while it was negative on the remaining 12/20 patients.

Positive intraoperative cultures were obtained in eight patients, and new specific antibiotic therapies guided by antibiograms were prescribed. The predominant organisms identified using classic biochemical methods were Gram-positive aerobes (Table II). No anaerobes were observed in our cases, while Saibene AM et al. reported the presence of anaerobes in 14% of cases [27].

Drago L et al. [28] recently described the identification of Dialister pneumosintes in a case of chronic maxillary sinusitis of odontogenic origin. D. pneumosintes is a known endodontic and periodontal pathogen found in necrotic pulp, subgingival plaque and deep periodontal pockets.

In agreement with other authors [23 29], the removed extramucosal material of fungal aspect was sent for histopathological analysis as well as a biopsy of the mucosal sinus wall (Table II). The biopsy of the mucosal sinus was done when a fungal infection was suspected in advance.

On the basis of histopathological results, the presence of extramucosal non-invasive fungal hyphae forms were found in five cases (# 2,3,5,21,23). In 3/5 cases, the causative agent was Aspergillus (Table II). Furthermore, other dental-related microbes caused by *Actinomyces spp.* can be found in histopathological examination [30]. In no case was the biopsy of the mucosal sinus positive for fungal hyphae, but they were all non-invasive extramucosal fungal forms. Therefore, no local or general antifungal treatment was administered, as reported by other authors [27 31].

Discussion

The incidence of SCDDT is very low despite the high frequency of dental pathologies [8]. In a meta-analysis by Arias-Irimia et al. [7], the most common cause of SCDDT was iatrogenic effects (55.97%) – extrusion of endodontic obturation materials in the maxillary sinus, amalgama remaining after apicoectomy, elevation of the sinus floor with poorly positioned dental implants or those which had migrated to the maxillary sinus with OAF – followed by periodontitis (40.38%) and dentigerous cysts (6.66%). In a retrospective study of 27 patients with SCDDT, Lee and Lee reported that implant related causes were the most common (37%), followed by dental extraction-related

Table II. Comparison between preoperative and intraoperative positive bacterial cultures and histological examination. Note: # 6, 18, 21, 24, 26 and 27 are reported in Figs 1-7.

ID	Name	Preoperative bacterial culture	Intraoperative bacterial culture	Histological examination
1	MG			Odontogenic cyst
2	CG			Fungal Hyphae
3	SG			Aspergillus
5	SS	Staphylococcus aureus (g+)		Sinonasal aspergillosis
6	CR			Odontogenic cyst
8	DF		Streptococcus constellatus (g+)	Chronic rhinosinusitis
9	CC			Mucocele
14	CC		Streptococcus intermedius (g+)	Chronic rhinosinusitis
18	FL	Staphylococcus aureus (g+)	Streptococcus constellatus (g+)	Chronic rhinosinusitis
21	FA	Aspergillus		Fungal hyphae
23	PR	Aspergillus		Aspergillus
24	GR		Streptococcus parasanguinis (g+)	Heterologous bone
2 6	PG	Strepto coccus intermedius (g+)		Chronic rhinosinusitis
27	MM	Staphylococcus epidermidis (g+)	Streptococcus constellatus (g+) and Staphylococcus epidermidis (g+)	Heterologous bone
28	OM	Staphylococcus aureus (g+)	Streptococcus intermedius (g+)	Chronic rhinosinusitis with nasal polyps
29	CLA			Osteoma
30	PS	Stenotrophomonas maltophilia (g-)	Streptococcus anginousus (g+)	Chronic rhinosinusitis with nasal polyps
31	OI		Staphylococcus epidermidis (g+)	Chronic rhinosinusitis with nasal polyps + heterologous bone

complications (29.6%) and dentigerous cysts (11.1%); radicular cyst, dental caries and a supernumerary tooth accounted for 7.4% of cases [8]. In our study, the most common cause of SCDDT was conventional dental treatment in 29% of patients.

Classic symptoms of SCDDT can include unilateral purulent rhinorrhoea and nasal obstruction, bad smell and taste, hyposmia, headache, post-nasal drip and ipsilateral cheek pain [6 8 12]. In a series of 21 patients with SCDDT, Longhini and Ferguson reported dental pain in only 29% of patients [13]. In our study, 70.1% of patients complained of unilateral purulent rhinorrhoea as the main symptom.

The diagnostic work-up requires evaluation of symptoms, history of dental treatment, dental examination and nasal endoscopy. In addition, in the presence of unilateral purulent rhinorrhoea, we recommend preoperative and/or intraoperative bacterial culture from the middle meatus under endoscopic guidance, so as to prescribe antibiotics guided by an antibiogram.

CT is the gold standard in the diagnosis of SCDDT due to its high resolution and ability to discern bone and soft tissue [17]. It can show the relationship between the odontogenic origin and the maxillary sinus, foreign bodies within the maxillary sinus, opacification of the maxillary sinus and OMC, OAF, periapical lesions defined as a rounded lucency adjacent to the roots of a tooth, dental roots, dental materials, dental implants, material for sinus elevation, or parts of broken instruments in the maxillary sinus as well as the spread of inflammation into the other paranasal sinuses and anatomical variations [5 32 33]. In the presence of suspected fungal balls on CT scans, magnetic resonance imaging (MRI) with gadolinium can also be useful (Fig. 4).

Previous studies have identified anterior ethmoid involvement during SCDDT without determining its prevalence [34 35]. In our series, although limited, 16/31 patients (51.6%) also presented unilateral anterior ethmoid sinusitis, while 16/31 patients (51.6%) had anatomical variations so as to cause obstruction of the OMC.

However, Saibene AM et al. found in a retrospective study of 315 patients surgically treated for SCDDT that 18.7% of cases were affected by bilateral sinonasal involvement [26]. Di Pasquale D et al. reported a case of bilateral odontogenic sinusitis after a bilateral maxillary sinus augmentation [36] similar to other authors [37].

Recently, cone beam computed tomography (CBCT) has been introduced in dental and maxillofacial imaging. It has several advantages over traditional CT including utilising approximately 10% of the radiation dose of conventional CT, higher resolution and is a chairside process [38]. The technique is gaining popularity in the field of implant dentistry as there is frequently a need to assess the thickness of the floor of the maxillary sinus and to eliminate the presence of concurrent sinus disease before implantation.

However, at the moment, because of its high costs, CBCT,

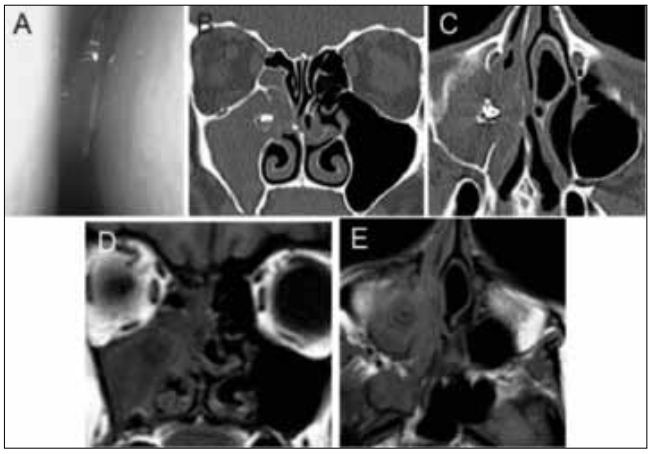

Fig. 4. Patient 21. SCDDT resulting from dental treatment complicated by fungal ball sinusitis (Class 3b). A) Preoperative endoscopic view of purulent secretions in the right middle meatus; B, C) Coronal and axial maxillofacial CT scans showing radiodense material and erosion of bone in the right maxillary sinus indicative of aspergillosis with obstruction of the ostiomeatal complex; D, E) Coronal and axial T1 magnetic resonance image in the same patient showing iso- or hypointensity on T1-weighted images in the right maxillary sinus.

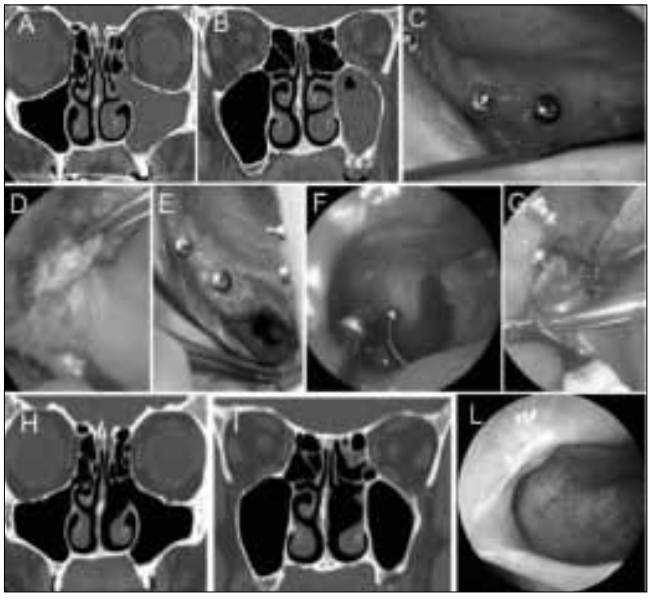

Fig. 5. Patient 24. SCDDT resulting from maxillary sinus lift with OAF (Class 1). Preoperative coronal CT scans showing A) unilateral left maxillary sinusitis and obstruction of the ostiomeatal complex, and B) maxillary osteitis after bone graft in the posterior maxillary alveolar process; C) Preoperative intraoral view: no clinical evidence of infection; D) Intraoral approach with trapezoidal flap, and E) after bone graft removal and bone debridement; F) Intraoperative view showing a probe, inserted through the oroantral communication, visible from maxillary sinusotomy (45° endoscope); G) Buccal fat pad flap preparation, then Rehrmann buccal flap was used for pedicled buccal fat pad flap (PBFPF) covering; H, I) Control coronal CT scans, 6 months after surgery showing complete aeration of the maxillary and ethmoid sinuses on the left side as well as removal of the bone graft and its repair; L) Nasal endoscopy showing the maintenance of the maxillary sinusotomy and the absence of mucosal degeneration (45° endoscope).

even if it allows examination of all paranasal sinuses and alveolar processes, is only complementary to traditional CT.

A combination of medical and surgical approaches is generally required for the treatment of SCOD. The Caldwell-Luc technique was the first to be described and used for SCDDT, while EES is a recent addition [9 21 39]. Moreover, the Caldwell-Luc technique can induce sinusal sclerosis, atelectasis and hypoplasia of the maxillary sinus [40] as well as silent sinus syndrome (Fig. 6), infraorbital nerve damage, facial swelling, facial and teeth paraesthesia, OAF and recurrent sinusitis [40 41]. In addition, the Caldwell-Luc operation is an absolute contraindication to performing sinus elevation [42].

Furthermore, the maxillary sinus has an effective mucociliary clearance to the natural ostium; this remains after EES through middle meatal antrostomy, but not after the Caldwell-Luc technique, because the artificial antrostomy is made in the inferior meatus [43]. EES can be considered to be a relevant improvement for several reasons: (i) it is less invasive with low morbidity [34 40]; (ii) it allows recovery of normal sinus function through spontaneous drainage from the natural ostium; (iii) it eliminates the need for total sinus mucosa removal, as originally proposed by Caldwell and Luc; (iv) it is possible to surgically manage the other paranasal cavities involved in the infection as well as that of widening the ostium and to treat anatomic variations that might contribute to normal ventilation of the OMC [44-46]. Lopatin et al. [9] were the first to report 70 cases of SCDDT treated with EES, and since then, EES has been the surgical technique indicated in the treatment of this disease. In our series, 28/31 (90.3%) of patients were treated with EES or EES combined with oral surgery and none experienced any complications.

In accordance with the literature we wish to stress the importance of close collaboration between the implantologist, maxillofacial/oral and ENT specialists to treat complex cases of SCDDT, to distinguish osteitis or osteomyelitis of the alveolar process and to prevent recurrence and complications [47 48]. In this regard, the surgical treatment for SCDDT as already reported in Felisati et al. classification [1] is represented in most cases by a mul-

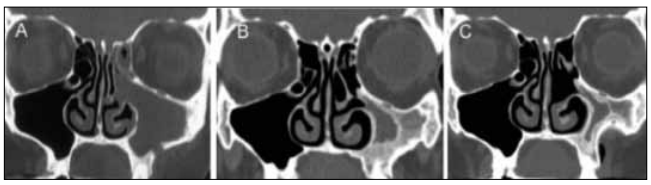

Fig. 6. Patient 26. SCDDT resulting from possible complications in the Caldwell-Luc technique. A) Coronal CT scan after Caldwell-Luc technique and inferior meatotomy for left odontogenic sinusitis; B) Coronal CT scan 7 years after Caldwell-Luc technique showing atelectasis and sclerosis of the left maxillary sinus, hypoplasia and progressive enophthalmos in silent sinus syndrome.

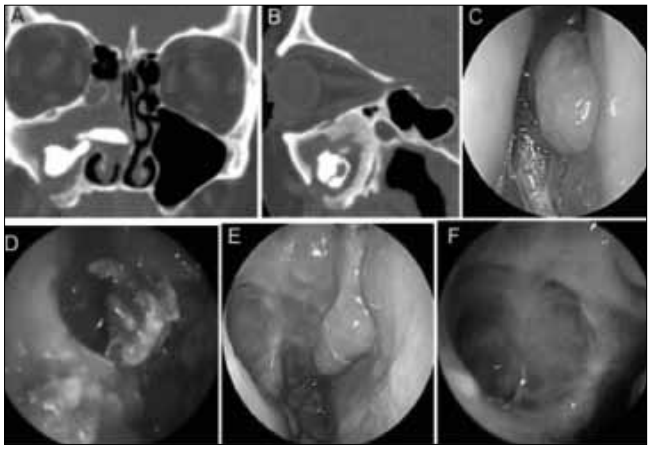

Fig. 7. Patient 27. SCDDT as a result of elevation of the maxillary sinus floor with dislocation of grafting material (Class 1a). The patient was treated in 1990 for the elevation of the maxillary sinus floor. In 2007, three dental implants were added to the patient, which later were removed because of infection. The patient referred to us for a swollen cheek and unilateral purulent rhinorrhoea, without symptoms of OAF. She refused any oral procedures, and underwent EES. A, B) Coronal and sagittal CT scans showing filling material within the right maxillary sinus (MS), erosion of the inferior wall of the MS determined by the sinus floor lifting procedure and complete obliteration of both MS and the ostiomeatal complex; C) Purulent secretions in the middle meatal of the right nasal cavity; D) Removal of the grafting material used for sinus floor elevation and ethmoidectomy; E, F) Postoperative nasal endoscopy 5 months after surgery showing the restitutio ad integrum of the MS and the anterior ethmoid. Note the turbinoplasty of the middle turbinate.

tidisciplinary approach combining EES with an intraoral approach (Classes 1, 2, 3a). We have added subclass "1a" to include patients suffering from sinusitis after maxillary sinus lift without OAF, who request only EES.

In the combined approach, the intraoral approach, allows treatment of pathologies that are impossible to treat with EES only [1], such as: (i) removal of infected dental implants [49] with apical portions penetrating into the maxillary sinus or any other migrated material [50]; (ii) foreign bodies or odontogenic cyst [51]; (iii) removal of infected grafting material which can be more difficult to eliminate with endoscopy; (iv) maxillary osteitis or osteomyelitis; (v) periapical odontogenic infections of the teeth; (vi) dentigerous cysts; (vii) dental extraction-related complications; and (viii) the closure of OAF. In addition, OAF must be quickly closed as its persistence intensifies the possibility of inflammation of the sinus by infection from the oral cavity. Concerning the EES approach: (i) it is possible to surgically manage the paranasal cavities eventually involved in the infection, which are not reachable via an intraoral approach while preserving physiological sinonasal cavity function; (ii) it is possible to eliminate the anatomical variations that might contribute as co-factors to infection or obstruction of OMC; (iii) it is also possible to treat a foreign body, implant or grafting material dislocated into the sinusal cavity, fungus ball, or persistent maxillary sinus problems dependent on dental pathology under the control of rigid 4 mm, 45° and 70° angled endoscopes and a microdebrider with 40° curved blade, which are useful to treat the deepest regions of the maxillary sinus such as the alveolar recess. Furthermore, a one-step surgical procedure including simultaneously EES and a sinus floor elevation procedure through an intra-oral approach can be performed in selected cases. Thus, treatment of local contraindications to sinus augmentation can help prevent a second surgical procedure and a reduce the waiting period before final prosthetic rehabilitation [52-55].

Finally, a review of the current literature indicates that the results of treatment of SCDDT, where the most common causes are iatrogenic effects and periodontitis, have a high success rate in terms of healing (80-100%) with low complication rates (trigeminal neuralgia, orbital haematoma, visual disturbance, cerebrospinal fluid leak, nasal synechiae), recurrence (OAF, sinusitis) and revision surgery (< 10%) as well as a reduction in the time required for rehabilitation [9 18 21 34 39].

Conclusions

The possibility of SCDDT should always be considered when a patient has unilateral nasal symptoms that do not respond to medical treatment. Despite the limited number of cases treated on the basis of these preliminary satisfactory results, implantologist, maxillofacial/oral specialists and rhinological consultations are mandatory. The same is needed for an accurate diagnosis of infections of dental origin and associated sinusitis in SCDDT to resolve the odontogenic source and sinus infection in the shortest possible time without risking relapse.

The results of our study seem to be in accordance with the classification system proposed by Felisati, to which we referred. This could be useful in the standardisation of surgical treatment protocols, according to pathological conditions, to better harmonise cases reported by different authors. Nonetheless, we think that the number of the subgroups could be increased, especially for the pathological conditions included in Class 3.

Lastly, in our experience we can assert that EES must be associated with an intraoral approach whenever the maxillary alveolar process is affected by an infectious disease such as osteitis, osteomyelitis, peri-implant pathology, teeth periapical lesions, maxillary sinus lift complications, oroantral fistulae, or oroantral communication.

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AUDIOLOGY

Possibility of differentiation of cochlear electrodes in radiological measurements of the intracochlear and chorda-facial angle position

Possibilità di differenziazione degli elettrodi cocleari nelle misurazioni radiologiche della posizione intracocleare e dell'angolo cordo-facciale

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SUMMARY

Due to an increasing number of cochlear implantations, quality control has become more important. In addition to intraoperative biophysical measurements, radiological imaging is another possibility. An upcoming technique regarding this is Cone Beam CT (CBCT). Sixty-five data sets (35 Nucleus Contour Advance–Cochlear; 30 Flex Soft–MedEl) of postoperative imaging by CBCT (Accu-I-tomo F17, Morita, Kyoto, Japan) underwent further evaluation. Insertion angle, height of the cochlea, distance of the electrode to the medial or lateral wall, angle between chorda tympani and facial nerve and the precise position of the electrode cable in the facial-chordal angle were determined. The typical difference between the perimodiolar and lateral course of the electrodes could also be shown in radiological measurements. This demonstrates the accuracy and advantage of CBCT in visualisation of small structures with fewer metal artifacts. Furthermore, in 75% of patients, the angle of the chorda and facial nerve could be visualised. Significant differences in dependence of the electrode type for the relation of them to the facial nerve could be seen. In conclusion, CBCT achieves reliable visualisation and detailed imaging-based measurements of the intracochlear position of different cochlea electrodes. Additionally, clinically known differences can be reproduced. Even visualisation of the position of the electrode in the chorda-facial angle is possible. Therefore, CBCT is a useful tool in intra- and postoperative control of cochlear implants.

KEY WORDS: Cochlear implant • Cone beam computed tomography • Visualisation of cochlea • Measurement of cochlea • Facial nerve

RIASSUNTO

Con l'incremento del numero di impianti cocleari effettuati, il controllo di qualità è divenuto sempre più importante. Oltre alle misurazioni biofisiche intraoperatorie ci si può avvalere dell'imaging radiologico. Una nuova tecnica utilizzata in questo campo è il Cone Beam CT (CBCT). Nel presente studio sono stati valutati 65 casi (35 Nucleus Contour Advance–Cochlear; 30 Flex Soft–MedEl) studiati mediante CBCT (Accu-I-tomo F17, Morita, Kyoto, Japan). Nello specifico sono stati rilevati: l'angolo di inserzione, l'altezza dell'impianto, la distanza dell'elettrodo dalla parete mediale o laterale, l'angolo tra la corda del timpano e il nervo facciale e la posizione precisa del filo dell'elettrodo nell'angolo cordo-facciale. È stato inoltre possibile valutare la differenza tra il decorso peri-modiolare e laterale degli elettrodi. I dati presentati dimostrano l'accuratezza e il vantaggio della CBCT nella visualizzazione di piccole strutture grazie al ridotto numero di artefatti da indurimento del fascio. Inoltre nel 75% dei pazienti è stato possibile visualizzare l'angolo tra la corda del timpano e il nervo facciale. È stato possibile notare differenze significative fra i vari tipi di elettrodo in funzione del tipo di rapporto con il nervo facciale. In conclusione mediante la CBCT è possibile ottenere una visualizzazione precisa e dettagliate misurazioni della posizione intracocleare dei diversi elettrodi. È persino possibile la corretta valutazione della posizione dell'elettrodo rispetto all'angolo cordo- facciale. La CBCT è quindi, dal nostro punto di vista, un utile strumento per il controllo intra e post-operatorio degli impianti cocleari.

PAROLE CHIAVE: *Impianto cocleare • Cone beam computed tomography • Visualizzazione della coclea • Misurazioni della coclea • Nervo facciale*

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Introduction

Cochlear implantation is currently the standard in rehabilitation of hereditary or acquired high grade inner ear hearing loss. This results in increasing standardisation and improvement of surgical techniques and technical development of newly dedicated implants. To achieve this and to prevent complications, intra- or postoperative evaluation of the implanted situation is necessary. In addition to biophysical measurements, radiological imaging is the only way to get information about the intracochlear position and the relation of the electrode to anatomic important structures. In the beginning, conventional radiography was used. Today, more information is needed, and

thus computed tomography (CT) and cone beam computed tomography (CBCT) are used and recommended by current guidelines [1 2]. Regarding the irradiation, naturally conventional plain radiography has the lowest dose, but in almost the same manner the lowest grade of information. Considering CBCT and CT, the former has about the half to a third of the radiation dose of CT, which is a main advantage particularly in children [3-5].

Imaging methods methods with fewer artifacts are needed, not only to visualise that the electrode is inside the cochlea, but also to present an impression of the detailed intracochlear position and distances to the modiolus or lateral wall. Therefore, CBCT has been introduced into ENT imaging with a special focus on visualisation of middle and inner ear implants [6-8]. Despite some studies that have focused on possibilities [9-12] and limitations [13 14] of this method in comparison to CT, some questions still remain. Can different types of electrodes (modiolar vs. lateral position) also be differentiated not only by impression of the observer, but also reproduced by measurements based on CBCT images? Is it possible to visualise the angle between the chorda tympani and facial nerve and the relation of the electrode/cable to these structures [15]? The current paper aims to answer some of these questions.

Methods

All of our data on patients with a cochlear implant and imaging of their implant by CBCT two typical groups (N = 82) were analysed. Inclusion criteria were: one of the following implant types, existing row data for detailed radiological measurement, low enough artifacts for precise intracochlear measurements and full insertion of the electrode. The first group consisted of patients with a perimodiolar positioned electrode of the cochlea (Contour Advance 512; N = 35). The second group consisted of patients with the lateral wall electrode of MedEl (Flex soft standard electrode; N = 30). All electrodes were inserted through the regular or enlarged round window.

Of the 65 patients, 52% (N = 33) were female and 48% (N = 32%) were male. The mean age at the time of imaging was 51.6 years (range 5 to 88 years). Forty-five percent (N = 29) of the data sets concerned the left ear, whereas 55% (N = 36) were right ears. In three patients, both ears were analysed.

All images were performed on the day of operation or the day after using a CBCT device from Morita (Accu-I-tomo, F17, Kyoto, Japan). The tube current ranged between 84.0 and 90.0 kV. The tube voltage was between 3.0 mA and 8.0 mA. The primary size of the acquired voxels was at 0.08 mm. Imaging analyses and measurements were performed using One Volume Viewer (I-Dixel 2.0, Morita, Kyoto, Japan).

According to a consensus paper, the insertion angle of each single electrode was measured in relation to the entrance of the cochlea (Fig. 1) [16]. In the background of the known difficulties of evaluation in the middle and apical turn and to compare both electrode types, only the first 360° of the cochlea was analyzed.

Based on this reconstructed image, for each single electrode the following parameters were measured. First, the diameter of the cochlea was determined on a line orthogonal to the lateral and medial wall through the electrode. Second, along the same line, the diameter of the electrode, and third the distance of the electrode to the lateral wall (in the case of group 1) or the distance of the electrode to the medial wall (in the case of group 2) were measured (Fig. 2).

Due to the relationship of the electrode and its cable and the facial nerve with the chorda tympani, all 82 patients were reviewed for visibility. Four patients were excluded due to a field of view that was too small. Fourteen pa-

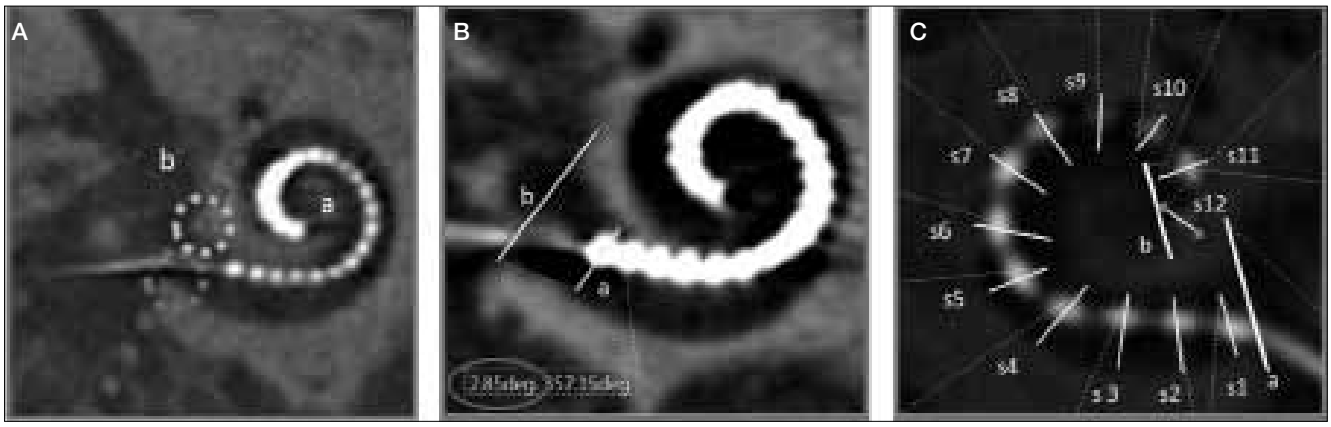

Fig. 1. Visualisation of the way of measurement the insertion angle (in accordance to [16]). The baseline is defined by round window edge and turning point of cochlea to vestibule (A). The angle is measured with a standard tool between the baseline and a line through the single electrode orthogonal to the lateral and medial wall of the cochlea (B). Angle measurements were performed for each single electrode (C).

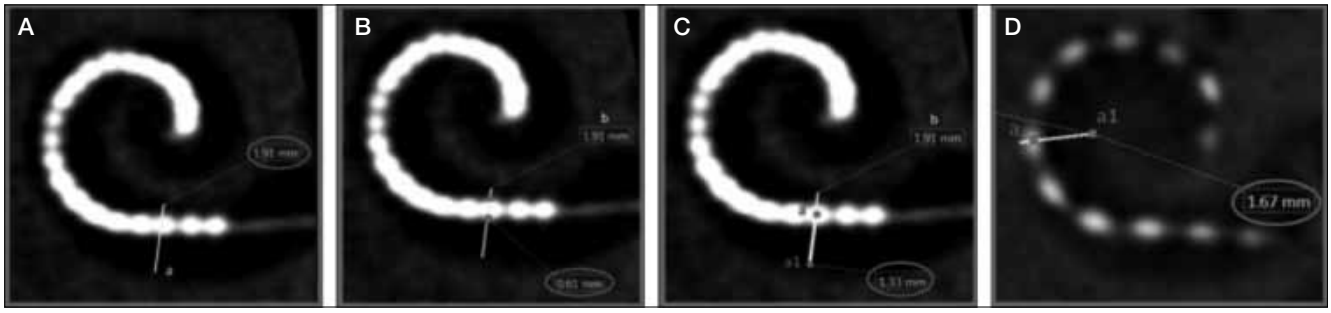

Fig. 2. The diameter of the cochlea (A) and the electrode (B) were measured. In case of perimodiolar electrodes, the distance from lateral wall to electrode (C) and in case of lateral wall electrodes, the distance from medial wall to electrode (D) were determined.

tients had to be excluded due to missing visibility of the chorda tympani, and two more due to too many artifacts. In all, 62 of the 82 (75%) underwent further analysis. A standardised multiplanar reconstruction resulted in a view showing the chorda tympani, facial nerve, horizontal semicircular canal and the cable of the electrode. The angle between the chorda tympani and facial nerve was determined by a standard angle measurement option (Fig. 3). The following measurements were performed on a parallel horizontal line to the semicircular canal at the point of the electrode in the chorda-facial-angle. The diameter of the facial nerve, thickness of the bony coverage in direction to the electrode and distance of the electrode to the bony canal of facial nerve were determined at this point (Fig. 4).

Results

Regarding the group of the Contour Advance electrode, in 9 of 35 patients (26%) all 22 electrodes were in the first 360° of the cochlea. In all patients, the first 18 electrodes could be detected in the first 360°. In the Flex-soft group, the first seven electrodes were within the first 360° in all patients. In all patients of this group, electrodes 10 to 12 were deeper than 360°.

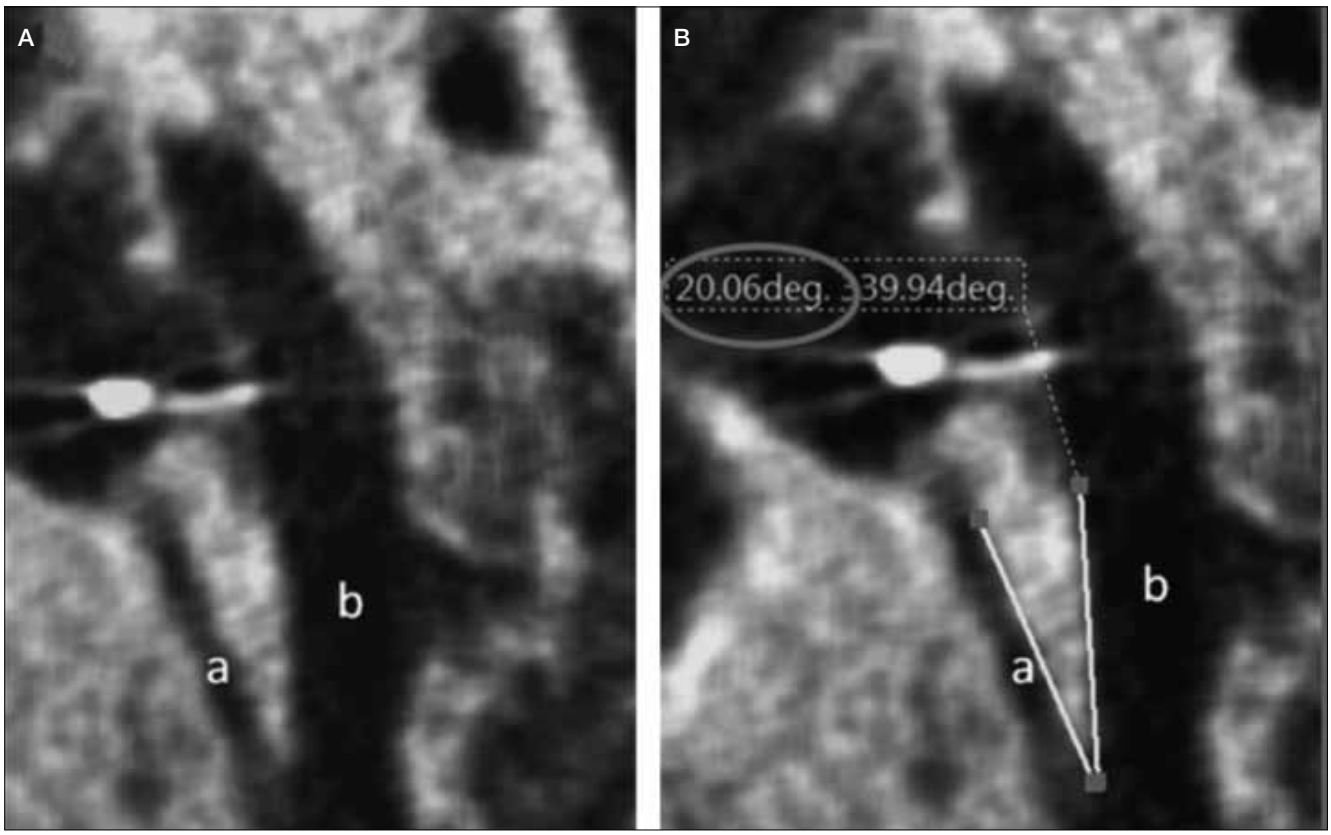

Fig. 3. Typical image of the chorda tympani (a) and the angle to the facial nerve (b) is presented (A). The angle between both structures was measured in each case (B).

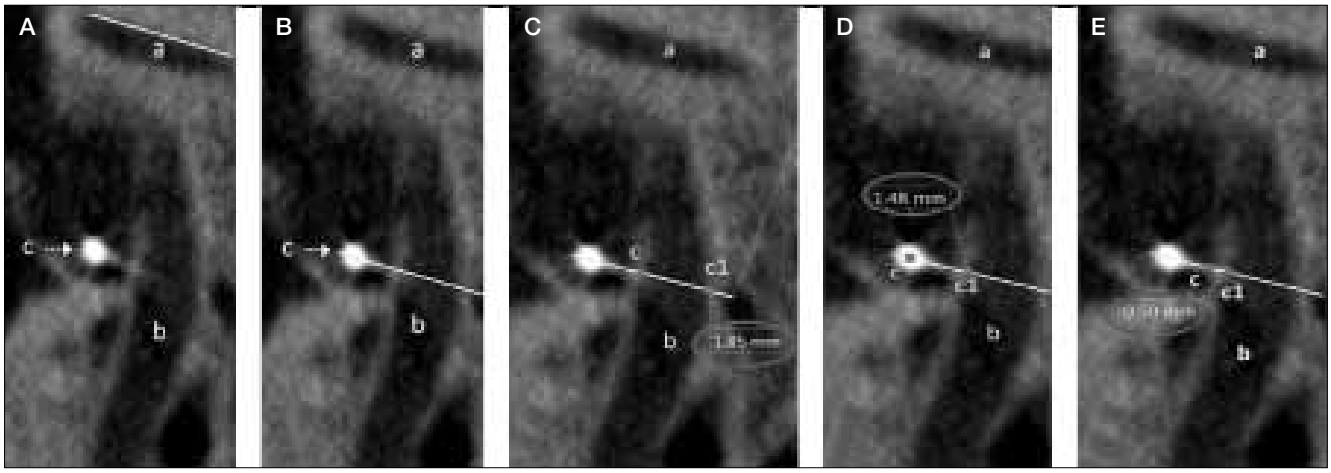

Fig. 4. The distances were measured based on a reference line parallel through the horizontal semicircular canal (A) at the point of the electrode cable (B). The diameter of the facial nerve (C), the distance of the electrode cable to the nerve canal (D) and the bony thickness over the nerve (D) were determined.

The diameter of the cochlea showed a continuously decrease from beginning in direction of apex, whereas a maximum of 2.1 ± 0.43 mm could be seen at the insertion angle between 106° and 120° and a minimum of 1.58 ± 0.3 mm could be detected at the insertion angle between 346° and 360°. No significant differences between groups could be seen (Fig. 5, A). Also, the measurements of the electrode diameter showed the expected decrease from basal to apical (Fig. 5, B).

In the group of Contour Advance electrodes, the mean

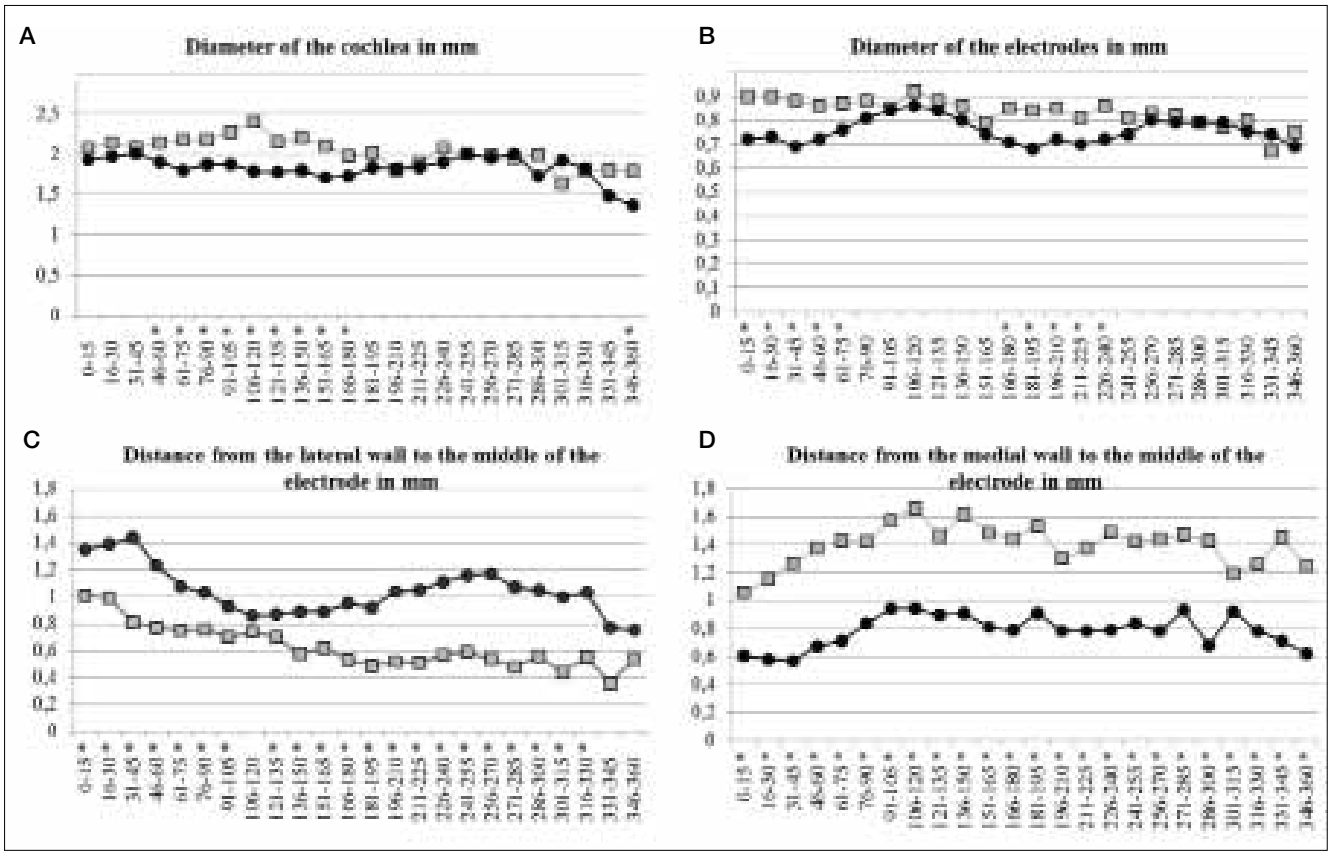

Fig. 5. All graphs show the results for the different measurements and different types of electrodes (grey - Standard flex electrode; black - Contour Advance electrode) in relation to the insertion angle (in 15° groups). All *-marked regions of insertion angle are significant different between both groups ($p < 0.05$). A) Diameter of the cochlea. B) Diameter of the electrode. C) Distance from medial wall to middle of the electrode. D) Distance from the lateral wall to the middle of the electrode.

distance from the electrode to the medial cochlea wall was 0.78 ± 0.12 mm whereas in the Flex-soft group, the mean was at 1.4 ± 0.15 mm. The opposite could be seen in the mean distance of the electrode to the lateral wall (Contour advance group: 1.0 ± 0.18 mm vs. Flex soft group: 0.63 ± 0.16 mm). All differences were significant for the mean and each value of the separate 15°-angle-group ($p < 0.01$). In both measurement curves, a decrease from basal to apical could again be detected (Fig. 5, C and D).

Measurements at the point of chorda-facial-angle are summarised in Table I. The mean angle for all patients between the chorda tympani and facial nerve was 22.6 ± 9.5°. No significant difference could be seen between the groups (group 1: 23.7 ± 9° vs. group 2: 21.2 ±10°; $p = 0.61$). The diameter of the bony facial nerve canal was 1.8 ± 0.4 mm. Interestingly, a significant difference was found between groups (group 1: 1.7 ± 0.4 mm vs. group 2: 2.0 ± 0.4 mm; $p = 0.001$). The mean distance from the electrode to the facial nerve was 1.8 ± 0.7 mm. No difference between groups was detected (group 1: 1.7 ± 0.6 mm vs. groups 2: 1.8 ± 0.7 mm; $p = 0.41$). The mean bony coverage of the facial nerve was 0.8 ± 0.4 mm. Again, no significant difference was seen (group 1: 0.78 ± 0.36 mm vs. group 2: 0.84 ± 0.37 mm; $p = 0.35$).

Discussion

The number of cochlear implantations has been increasing for many years. This is because of consequent newborn hearing screening programmes and implantation of patients with single sided deafness and residual hearing [17]. For further development of electrodes and improvement of surgical techniques, sufficient postoperative visualisation of the implanted electrode is necessary. Conventional radiography only shows implantation into the cochlea or not, and gives no information about the detailed anatomy and specific intracochlear position. CT is much better, but due to the high range of metal artifacts, the potential of specific analyses is still low [18-20]. CBCT is upcoming technique with high potential for visualisation of bony anatomy and implants due to fewer artifacts in comparison to CT[3]. Several publications have shown its potential in visualisation of cochlear electrodes and its accuracy in comparison to histological examination [11 21-23]. Even in CBCT, metal artifacts exist and result in reduced power of determination in medial and apical turn of the cochlear [13 14]. The next steps of development will be automatic analyses of the images and imaging fusion of pre- and postoperative data [6]. Therefore, precise measurements of the electrode and its intracochlear position are needed. Additionally, measurement-based differentiation of different electrode types is necessary. The current study focused on this topic.

As expected, a decreasing diameter of the cochlea could be detected. This is in accordance with the knowledge based on anatomic studies and shows the accuracy of the performed measurements [24 25]. A relevant inter-individual range of the size of the cochlea exists and leaves open the question of the sense of standardised length of electrodes [24 26]. Variability could be seen in the number of implanted electrodes into the individual cochlea. In the group of Contour Advance electrodes, only 26% (9/35) of all 22 electrodes were within in the basal turn (first 360°) of the cochlea. Based on the different design, all patients with the Flex Soft electrode were inserted deeper than the basal turn. The impact of implantation depth on speech understanding and hearing quality of music is still controversial [27 28]. Particularly with this background, and the focus of inner ear trauma, visualisation of the inner structure of the cochlea before and after implantation remains a focus of research. The current study demonstrates that it is possible to measure the visible and well known differences of the different implant types. Thus, a significant difference in the distances of the electrode to the medial and lateral cochlea wall was found for both groups. A second indicator of accuracy was the determined diameter of the electrode itself, which was in concordance with the information from the manufacturers.

Another frequent problem in cochlear implantation surgery is the relationship to the facial nerve, the chorda tympani and the risk of unexpected postoperative facial nerve stimulation [29]. This might be caused, for example, by extracochlear electrodes, thin bony coverage of facial nerve or direct electric stimulation of the middle ear- or vestibular part of the facial nerve [29]. Because of this problem, the second part of this study analysed the potential of CBCT in visualisation of the chorda-facial angle and relationship to the electrode. Preclinical examinations of temporal bones showed the principal possibility of visualisation of the chorda tympani in CT and CBCT [15 30]. No clinical data based on daily routine imaging data were found in the literature. Therefore, astonishingly, in a fairly high number of patients – 75% (64/82) – the chorda-facial angle could

Table I. Results of measurements at the point of the chorda-facial angle.

	All implants together	Cochlear	MedEl	p-Wert
Chorda-facial angle (°)	22.6 ± 9.5	23.7 ± 9	21.2 ± 10	0.61
Diameter of bony facial nerve canal (mm)	1.8 ± 0.4	1.7 ± 0.4	2.0 ± 0.4	0.001
Distance from electrode to facial nerve canal (mm)	1.8 ± 0.7	1.7 ± 0.7	1.8 ± 0.7	0.41
Thickness of bone above facial nerve (mm)	0.8 ± 0.4	0.78 ± 0.36	0.84 ± 0.37	0.35

be visualised and analysed. The mean angle was 22.6 ± 10° and the distance of the electrode to the bony canal of the facial nerve was about 1.8 mm with a thickness of the bony coverage of about 0.8 mm. The diameter of the facial nerve canal was determined at 1.8 mm and is in principal accordance with other studies [31]. Interestingly, a significant difference in the diameter of facial nerve canal could be detected between groups. We interpret this as a result of different insertion angles of the different types of implants. This might lead to a slightly different position regarding the height of the electrode in the chorda-facial angle, and in conclusion, to a different diameter of the facial nerve canal at the corresponding position. However, this problem should be addressed for detailed analyses in further studies.

Conclusions

CBCT has high potential for visualisation of different types of cochlear implants and achieves a reliable measurement-based analysis of the detailed intracochlear position of the electrode. Furthermore, visualisation and analyses of the chorda-facial angle and its relation to the electrode cable are frequently possible. Therefore, CBCT should be regarded as a useful tool for further radiological/audiological studies.

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CLINICAL TECHNIQUES AND TECHNOLOGY

Prevention of bisphosphonate-related mandibular fractures

Prevenzione delle fratture mandibolari conseguenti alla necrosi ossea da difosfonati

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SUMMARY

Mandibular fracture is usually the clinical end of bisphosphonate-related osteonecrosis of the jaw. This is a painful complication and patients cannot feed as usual, with a worsening of their quality of life. The goal of treatment in bisphosphonate related osteonecrosis of jaw (BRONJ) patients is to slow progression of bone necrosis. We present a novel technique for treatment of severe mandibular BRONJ in stage 3 patients that present with a high risk to develop fracture, since they have a residual unaffected mandibular bone height less than 6 mm. We treated 10 patients in this clinical situation with an extra-oral application of a reconstructive plate superficial to the platysma, to keep the plate separated from the infected site to avoid contamination and consequent need of removal, followed by an intraoral approach for active curettage of mandibular necrosis. The preservation of blood supply to the mandible and avoidance of direct contact of the infected site with the reconstructive plate are some advantages of this technique. This plate allows enhancement of mandibular strength, allowing proper treatment of the BRONJ site on the oral side without fear of causing a mandibular fracture when the residual mandible is thin. This technical solution guarantees these patients an extended disease-free period since it is effective in preventing mandibular fractures in patients with low mandibular residual height left after the BRONJ onset.

KEY WORDS: Bisphosphonate jaw fracture • Pathologic mandibular fracture • Extra-platysma stabilization • BRONJ Treatment

RIASSUNTO

La frattura della mandibola rappresenta solitamente l'evento finale nei pazienti che presentano una progressione della necrosi ossea derivante dall'impiego dei difosfonati. Si tratta di una grave complicanza molto dolorosa che impedisce ai pazienti di alimentarsi correttamente, essendo pertanto un fattore che peggiora notevolmente la loro qualità di vita. L'obiettivo del trattamento dei pazienti che presentano la necrosi ossea legata ai difosfonati (BRONJ) dovrebbe essere rallentare la progressione della malattia. Presentiamo una soluzione tecnica per il trattamento dei pazienti che presentano necrosi mandibolare in stadio 3 ad alto rischio di sviluppare una frattura, avendo un'altezza mandibolare residua di osso sano inferiore a 6 mm. Il trattamento consiste nel posizionamento di una placca ricostruttiva mandibolare per via extra-orale in un piano superficiale al muscolo platisma per tenere i mezzi di sintesi separati dal sito infettivo e non farli contaminare con conseguente necessità di doverli rimuovere, seguito dal courettage per via endorale della necrosi mandibolare. Il rispetto della vascolarizzazione mandibolare e l'assenza di contatto diretto tra il sito di osteonecrosi e la placca ricostruttiva rappresentano alcuni dei vantaggi di questa metodica. La placca ricostruttiva rinforza la mandibola e consente di aggredire energicamente l'area di necrosi mandibolare, senza esporre il paziente a rischio di frattura iatrogena. Questo garantisce al paziente un rallentamento della progressione della malattia e impedisce la frattura patologica della mandibola, inevitabile epilogo delle necrosi ossee mandibolari.

PAROLE CHIAVE: *Frattura mandibolare da difosfonati • Frattura patologica della mandibola • Stabilizzazione extra-platismatica • Trattamento delle necrosi ossee da difosfonati*

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Introduction

Mandibular fracture is usually the clinical end of bisphosphonate-related osteonecrosis of the jaw (BRONJ). This situation is associated with a sudden worsening of patients' quality of life, since they start experiencing pain and cannot eat in a normal fashion. Since at present there is no evidence of an effective medical or surgical therapy to produce complete healing of the necrotic bone, the goal of treatment in BRONJ patients is to slow the progression of bone necrosis. Worsening of the pathology includes further fistulae formation and mandibular pathologic fracture due to osteolysis extending to the inferior border.

We decided to apply a reconstructive mandibular plate generally used to stabilise BRONJ-related mandibular fractures in patients who have not developed a mandibular fracture, but who are at a high risk of its development. Since there is no literature on this topic, we arbitrarily selected a minimal residual thickness of unaffected mandibular bone of 6 mm (Fig. 1) to apply the plate on an extra-platysmatic dissection plane [1]. When the residual height of normal mandibular bone is more than 6 mm, we

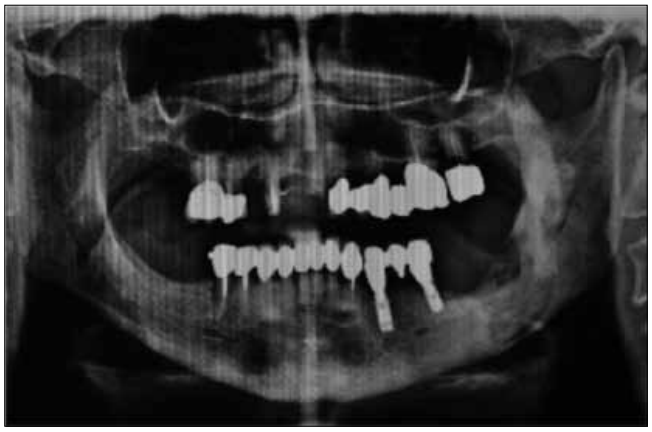

Fig. 1. Panoramic radiograph reveals wide bone destruction in the left mandibular angle, with residual height less than 6 mm.

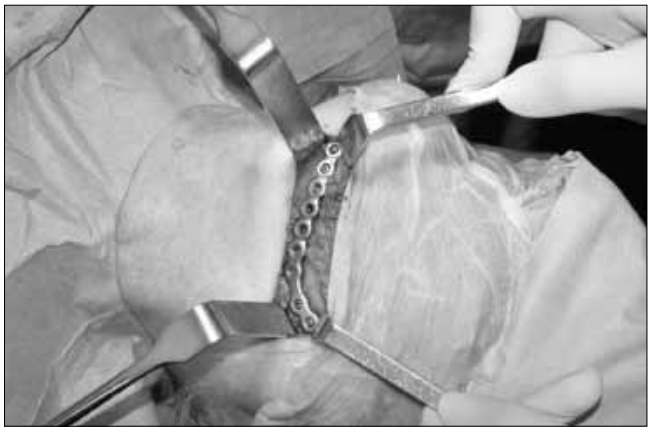

Fig. 2. Intraoperative view: the position of the 2.5 mm plate in the extra-platysmatic plane.

treat patients by simple curettage of the bone necrosis and possible removal of the sequestrum.

The proposed technique consists of the application of a reconstructive plate in a plane superficial to the platysma with an extraoral surgical access followed by an intraoral approach for active curettage of mandibular necrosis and rinsing of the surgical site. The main advantages of this technique are related to the maintenance of the blood supply to the mandible and avoidance of direct contact of the infected site with the reconstructive plate.

The position of this stable plate on a plane superficial to the platysma also allows the proper treatment of the BRONJ site on the oral side, without fear of causing a mandibular fracture due to the surgical curettage, and can allow mandibular resection when clinically needed without loss of occlusion.

Description of clinical technique

A sterile drape is placed over the mouth and face to avoid any direct contamination of the cervical field by the infected bone. After inducing vasoconstriction with 1:200,000 epinephrine into the submandibular region, a 10-cm skin incision is made ~2 cm inferior to the mandibular border, following its profile. The dissection plane is immediately over the platysma muscle, 5 cm in front of and 5 cm behind the site of BRONJ. A 2.5-mm reconstructive locking plate is modelled with the help of a template and then placed superficial to the platysma. Stabilisation is obtained through mono-cortical locking screws placed a few cm from the BRONJ site, under plentiful rinsing solution (Fig. 2). Meticulous haemostasis and the application of an aesthetic suture completes the extra-oral surgical procedure.

The cervical suture is covered by a sterile-drape dressing, and the BRONJ site is accessed through an intraoral approach with minimal to no dissection of the periosteum. Surgery is limited to curettage and rinsing of the residual bone. Rotating burs are avoided, while piezosurgical instrumentation is preferred. Bony sequestrum is removed when present.

Between 2013 and 2015 we operated on 10 patients affected by BRONJ of the mandible who were at risk to develop a mandibular fracture. Clinical data are shown in Table I.

All patients were discharged after 2 days, with prompt relief of pain and allowance of feeding. We observed no facial nerve lesions. After a mean follow up time of 22.2 months, we saw no infection of plates and all means of fixation are stable at the time of writing. In one patient, after 12 months we observed local progression of disease that was treated by intra-oral courettage without need for plate removal.

Discussion

BRONJ is a clinical situation first reported in the modern era by Marx in 2003 [2]. Other authors have observed that a similar disease was described 100 years earlier, in 1899 by Dearden in the *British Medical Journal* in workers in the white phosphorus mines and in match factories; this was known as "Phossy Jaw". It is possible that long-term exposure to phosphorus in these workers induced the precipitation of bisphosphonates in bone leading to a clinical condition similar to the well-known BRONJ.

The aetiopathological hypothesis of this disease is that bisphosphonates are powerful osteoclast inhibitors, and long-term use can result in suppression of bone turnover with increased trabecular bone density, inducing vascular insufficiency and causing bone necrosis. Moreover, the impaired bone turnover leads to failed removal of old osteocytes. Osteocytes are not immortal cells; thus, when these cells die bone necrosis occurs [3].

BRONJ is a clinical situation that is observed increasingly frequently. The effectiveness of bisphosphonates in preventing bone pain and reabsorption in osteoporosis and control-

Table I. Clinical data of patients.

Patient name/gender/age	Residual unaffected mandibular height (mm)	Bisphosphonate means of administration	Disease	Follow-up time (months)
M.E./F/ 65	2	IV	Multiple myeloma	36
B.M./F/56	1	IV	Breast cancer metastasis	26
M.P./M/70	4	IM	Paget	24
L.S./F/72	6	Oral	Osteoporosis	18
G.V./F/78	6	Oral	Osteoporosis	30
A.F./M/72	1	IM	Melanoma metastasis	20
T.A./F/74	3	IM	Breast cancer metastasis	20
L.V./M/77	5	IM	Multiple Myeloma	26
A.P./F/82	4	Oral	Osteoporosis	14
S.S./F/75	3	IM	Osteoporosis	8

ling bone metastasis in the oncologic population leads to the increased use of this therapy. BRONJ is related to both IV and oral administration, the latter being less risky [1].

The clinical presentation of BRONJ patients can differ. Attempting to standardise the management of these patients, the American Association of Oral and Maxillofacial Surgeons guidelines proposed a modified staging system in 2009 [4]:

- At-risk category. Includes asymptomatic patients previously treated with either oral or IV bisphosphonates;
- Stage 0. No clinical evidence of necrotic bone, but nonspecific clinical findings and symptoms;
- Stage 1. Exposed necrotic bone, asymptomatic, and with no evidence of infection;
- Stage 2. Exposed and necrotic bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent drainage;
- Stage 3. Exposed and necrotic bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone, resulting in pathologic fracture, extraoral fistula, oroantral/oro-nasal communication, or osteolysis extending to the inferior border of the mandible or the sinus floor.

In the early stages conservative treatment is usually advised, while in approaching more complex clinical situations, as with stage 2-3 patients, the correct choice is challenging since management is not yet standardised. Surgical debridement/resection, in combination with antibiotic therapy, may offer a long-term palliative and valid solution, but progression to a more complex situation is more likely to occur with time.

In fact, usually the last stage is clinically characterised by pain, swelling, fistulae and finally mandibular fracture. In this situation patients cannot properly eat and, even if the fracture is reduced and stabilised with surgery, the fracture is not likely to heal. On the contrary, the presence of osteosynthesis material over the fracture may sustain a chronic infection.

Kuijpers et al. in 2011 [5] described a unique case of spontaneous healing of a BRONJ-related mandibular fracture in a 74-year-old woman, thus showing the persistent healing potential of bisphosphonate-treated bone, but of course this is not a rule.

Deciding not to treat patients often means sentencing them to a quick decline of their quality of life because of the high degree of pain. In selected cases they can even be treated with free flap reconstruction after mandible resection [6], but most of these patients are old and in poor general condition, thus their clinical situation cannot be addressed with complex surgical procedures.

Therefore, we decided to stabilise the mandibular bone affected by BRONJ before fracture in those cases in which this clinical evolution is highly predictable, leading to a better clinical situation and preventing painful complications.

We arbitrarily decided to apply a mandibular reconstructive plate using the previously described extra-platysma technique [1] when the residual height of the unaffected mandible is no more than 6 mm (Fig. 3). The skin incision in the neck is set 2 cm inferior to the lower mandibular border to improve the aesthetic result. The presence of osteosynthesis material over the platysma and placement of the screws distant from the infected surgical site reduce the risks of maintenance of chronic infection and worsening of osteonecrosis.

This plate is fixed in a plane superficial to the platysma muscle so that surgical dissection is not dangerous for the facial nerve since the marginalis mandibulae branch lies deeper inside. However, placing the screws without direct vision of the nerve branch could lead to nerve injuries. This is rare, and has never occurred in our patients.

This technique is an application of well-known concepts of stabilisation of atrophic jaws, without removal of the periosteal support to the residual stumps; consequently, blood supply to the affected mandible is maintained [7]. That is likely important for spontaneous healing of the necrotic bone and preventing expansion of the osteitis.

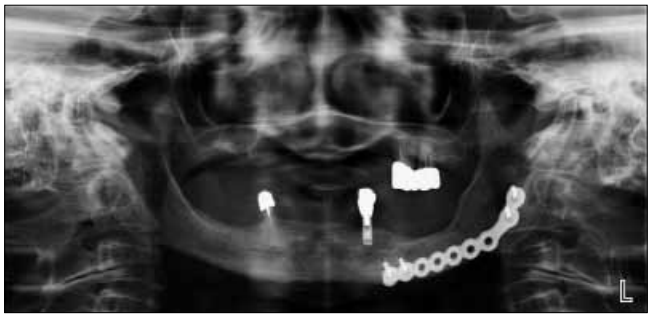

Fig. 3. Postoperative panoramic radiograph (at 24 months) showing the stable position of the reconstructive plate and extraordinary regrowth of mandibular bone.

Use of copious rinsing solution when drilling the screws is also advised to reduce the risk of BRONJ progression. The use of a locking instead of a compressive plate is important to avoid forcing of the weakened mandibular bone, which could lead to a mandibular fracture. The use of monocortical screws is intended to avoid excessive mechanical stress on the bone; the use of bicortical screws could lead to overloading. The oral approach stage of the operation is limited to curettage and rinsing of the surgical site. This is usually performed trying to avoid round burs and using ultrasound surgical devices such as a piezoelectric drill.

The presence of cutaneous fistulae does not represent a barrier to the application of this technique. In fact, in three cases we removed the fistula at the time of neck skin incision, and then closed it with a lower platysma pedicled flap to separate the necrotic site from the dissection plane where the reconstructive plate was going to be positioned. Rapid relief and preservation of normal masticatory function are achieved, and patients usually recover promptly.

The technique is painless, and patients can easily eat and be discharged after a few days, and thus this surgical solution can also be used in patients in poor general clinical conditions.

The suggested technique is easy to apply and in our patients was effective in preventing mandibular fractures in patients with low mandibular residual height after BRONJ onset.

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CLINICAL TECHNIQUES AND TECHNOLOGY

Vastus lateralis myofascial free flap in tongue reconstruction

Lembo miofasciale di vasto laterale nella ricostruzione della lingua

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SUMMARY

In the last decade, the antero-lateral thigh free flap (ALT) has become the most popular free flap for tongue reconstruction because of less donor site morbidity and better cosmetic outcomes. However, fascio-cutaneous ALT may be insufficient to reconstruct major tongue defects, while its muscular-cutaneous variant (using the vastus lateralis muscle) may be too bulky. The present study describes our preliminary experience of tongue reconstruction with vastus lateralis myofascial flap, which could potentially offer unique advantages in head and neck reconstruction including adequate bulk when needed, optimal functional results and obliteration of dead space thus preventing fistulas and infections with minimal morbidity.

KEY WORDS: Free flap • Glossectomy • Rectus femoris • Tongue reconstruction • Vastus lateralis

RIASSUNTO

Nell'ultimo decennio il lembo antero-laterale di coscia (ALT) è diventato il lembo libero più utilizzato nella ricostruzione della lingua, dal momento che esso è caratterizzato da bassa morbidità a livello del sito donatore e da migliori risultati estetici. Tuttavia, l'ALT fascio-cutaneo può essere insufficiente nella ricostruzione nei difetti maggiori (es. glossectomia totale) mentre la sua variante muscolo-cutanea (che include il muscolo vasto laterale)' può essere troppo voluminosa. Scopo dello studio è quello di descrivere la nostra esperienza preliminare nella ricostruzione della lingua utilizzando il lembo libero mio-fasciale di vasto laterale che potrebbe a nostro parere offrire notevoli vantaggi nella ricostruzione testa-collo come: possibilità di confezionare un lembo voluminoso quando necessario, ottimi risultati funzionali, obliterazione di spazi morti con prevenzione dello sviluppo di fistola e infezione con minima morbidità a livello del sito donatore.

PAROLE CHIAVE: *Lembo libero • Glossectomia • Retto femorale • Ricostruzione della lingua • Vasto laterale*

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Introduction

Nowadays many free flaps have been described and successfully used in oral cavity reconstruction [1 2]. In the last decade, the antero-lateral thigh free flap (ALT) become the most popular because of less donor site morbidity and better cosmetic outcomes [2]. However, fascio-cutaneous ALT may be insufficient to reconstruct major tongue defects, while its muscular-cutaneous variant (using the vastus lateralis muscle) may be too bulky, especially in patients with a high body mass index (BMI).

The aim of our study was to describe surgical technique and analyze the feasibility of vastus lateralis myofascial free flap (VLMFF) in tongue reconstruction, which to our knowledge has not been reported in the current literature.

Clinical technique

The National Cancer Institute 'Regina Elena' of Rome Ethics Committee approved the pilot study. Three patients affected by tongue squamous cell carcinoma (SCC) were treated from July to October 2015. All patients were staged with biopsy of the tumor, head and neck contrast MRI/CT and PET-CT. All patients underwent a temporary tracheostomy and nasogastric feeding tube placement. In Table I we summarised the patients' clinical data. Reconstructions were performed by VLMFF.

VLMFF harvesting and insetting

A line was drawn from the anterior superior iliac spine to the lateral border of the patella (Fig. 1a). The incision was made along the aforementioned line between the inferior and superior third. A suprafascial dissection was extended at least 5 cm medially and laterally ligating the skin perforators (Fig. 1b). The intermuscular septum between the vastus lateralis and rectus femoris was visualised and the curved line with lateral concavity, medial to the intermus-

Table I. Clinical data.

Case	Gender/ age	pTNM	Surgery	Complications	Decannulation/ NG tube removal	Adjuvant therapy
1	F/70	yT2N0M0	Subtotal glossectomy + bilateral ND (I-IV)	None	5/13 days	No
2	M/59	T4N2cM0	Subtotal glossectomy + bilateral ND (I-V;I-IV)	None	8/16 days	Chemoradiation
3	F/69	pT2N0M0	Hemiglossectomy + ipsilateral ND (I-III)	None	4/9 days	No

ND: neck dissection

cular septum, was marked with a surgical pen and incised (Fig. 1c). Fascia was elevated medial-to-lateral to identify the intermuscular septum between the vastus lateralis and rectus femoris (Fig. 1d). The intermuscular septum was then gently dissected and the descending branch of the lateral circumflex femoral artery (DLCF) was identified along with the vastus lateralis motor nerve (Fig. 2a). A fascia paddle was then included over the vastus lateralis exceeding 20% of the desired muscle flap size in all directions (Fig. 2b). VLMFF was raised in a caudal-cephalic direction using a harmonic ultrasonic scalpel (Harmonic Focus, Ethicon Endo-Surgery, Cincinnati, USA) according to the desired shape and respecting the neurovascular pedicle (Fig. 2c). Pedicle dissection continued until adequate neuro-vascular pedicle length was reached (Fig. 2d). Harvesting times were 40, 42 and 47 min, respectively.

In cases 1 and 3, the DLCF artery was anastomised with the superior thyroid artery, while in case 2 with the facial artery. Venous anastomoses were performed in all cases end to side to the internal jugular vein. Nerve anastomo-

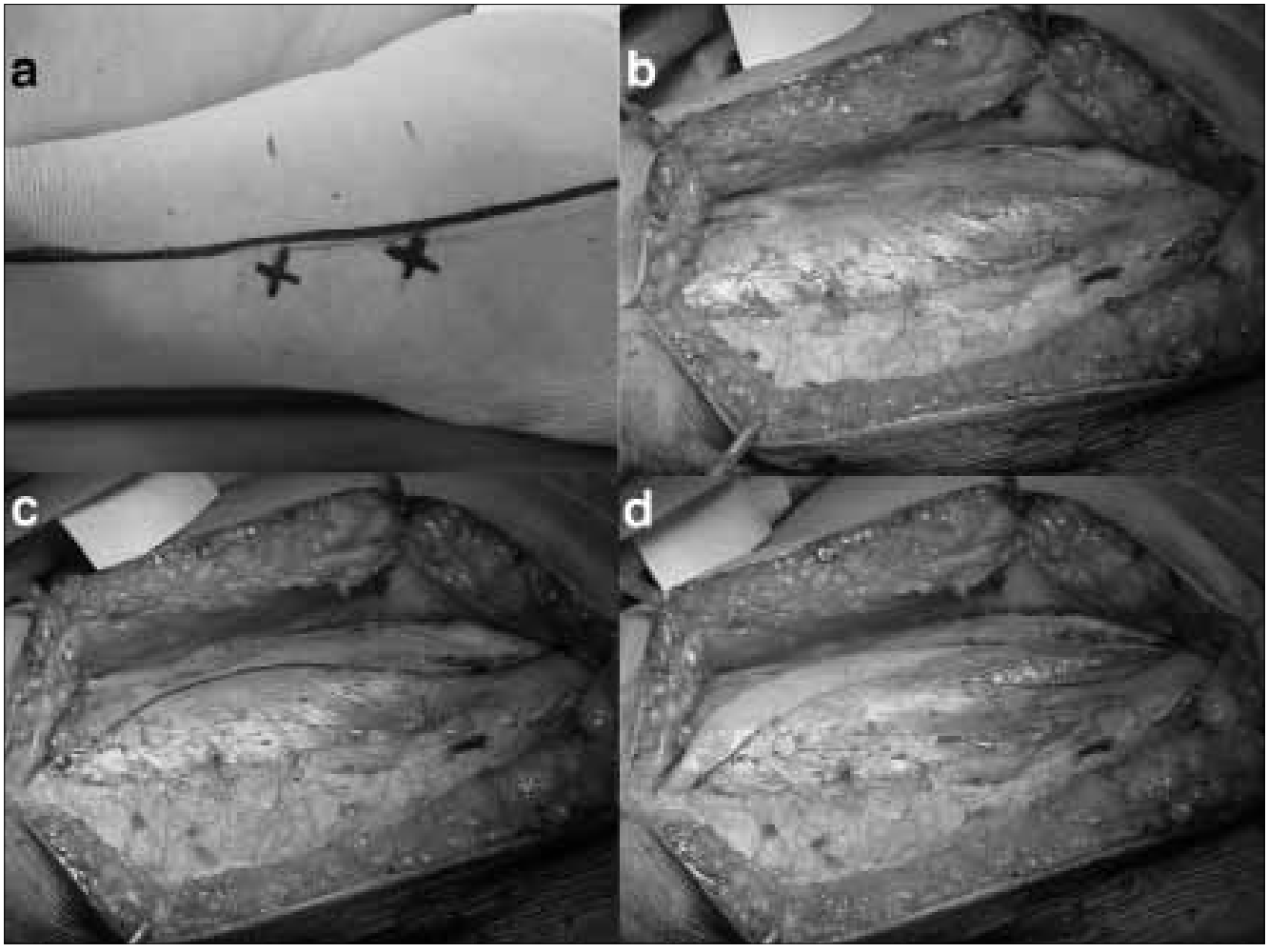

Fig. 1. VLMFF harvesting: a) incision line; b) suprafascial dissection; c) a curved line with lateral concavity is marked with a surgical pen; and d) elevated medial-to-lateral.

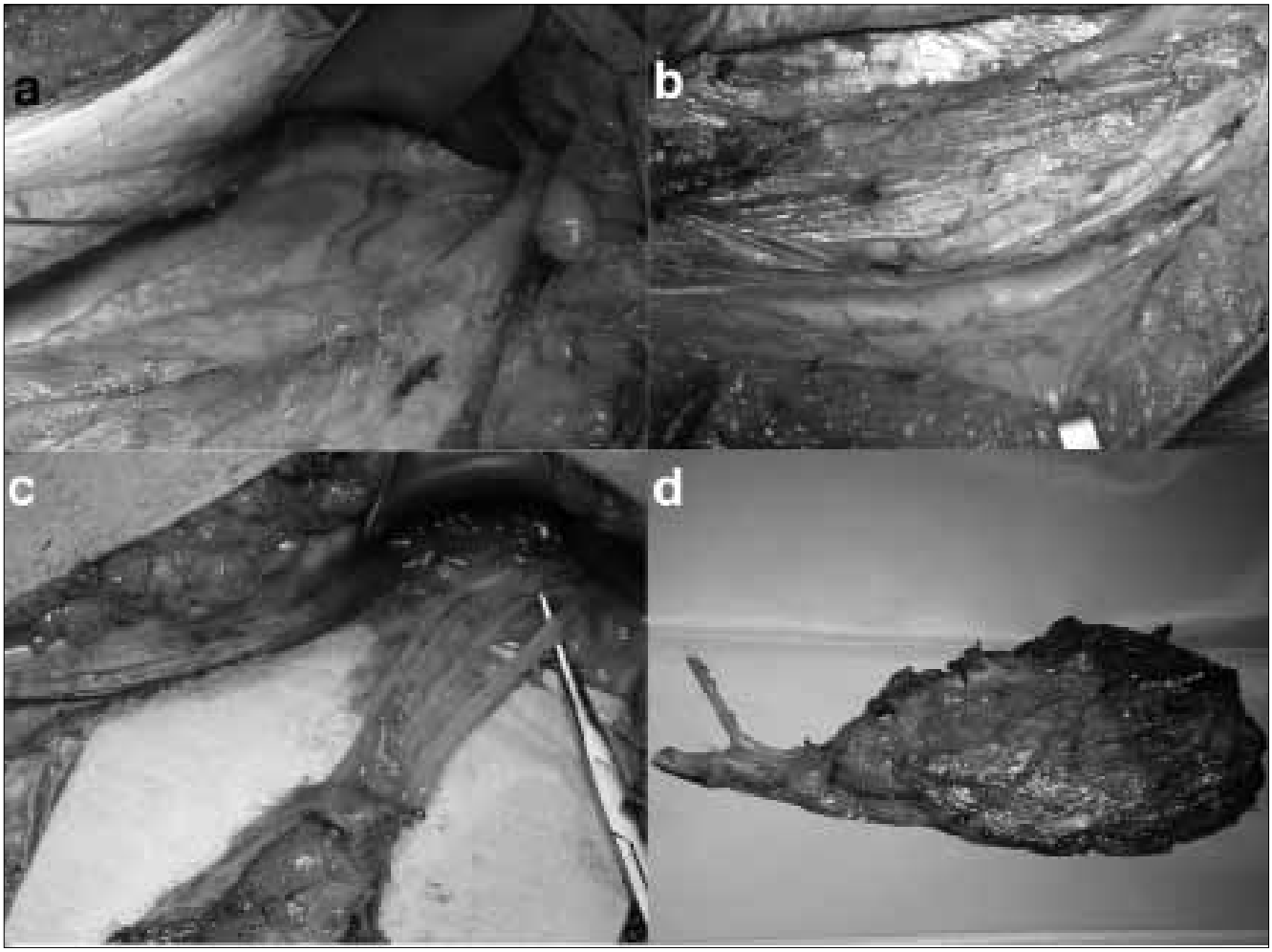

Fig. 2. VLMFF harvesting: a) the descending branch of the lateral circumflex femoral artery is identified; b) a fascia paddle is included over the vastus lateralis; c) VLMFF is raised including an adequate neuro-vascular pedicle; d) VLMFF completed harvesting.

ses between the hypoglossal nerve and vastus lateralis motor nerve was performed in all cases. In Figure 3 we show VLMFF insetting and 30-day post-operative results.

Discussion

The present study describes our preliminary experience of tongue reconstruction with VLMFF. VLMFF seems feasible, not technically demanding and safe. In our first three cases, we did not experience major complications such as necrosis, local infection or donor site impairment. VLMFF it is not time or budget consuming compared to the fascio-cutaneous and myocutaneous ALT variants since it does not imply further surgical steps and does not require adjunctive preoperative studies [3]. Harvesting of VLMFF required on average of 43 minutes.

VLMFF does not require harvesting of a skin island and consequently does not require preoperative study of vascular anatomy. This results in less closure tension and possibly in less donor site complications and better scar healing. Due to its rich vascular supply, VLMFF does not require any perforator branch dissection either supra/sub fascial or intramuscular. This represents an important advantage since the aforementioned surgical steps imply a higher incidence of flap vascular supply impairment.

VLMFF has also some recipient site advantages. Thanks to the high number of muscular perforators, when the main vascular pedicle is preserved VLMFF could theoretically be shaped freely basing on the reconstruction necessity. However, we should point out that a 20-30% flap mass reduction due to muscular shrinkage should be expected.

Another advantage is represented by the satisfactory cosmetic results. ALT flap classically includes a skin island that is responsible for a certain degree of color mismatch. In VLMFF, the use of muscle implies a better cosmetic result in tongue reconstruction. Moreover, thigh fascia protection adequately prevented fistula development in our 3 patients.

A criticism to our technique could be in terms of donor site postoperative morbidity since the vastus lateralis muscle is sacrificed. However, as reported by Hanasono et al. [4] in a series of 220 ALT free flap and later by Bi-

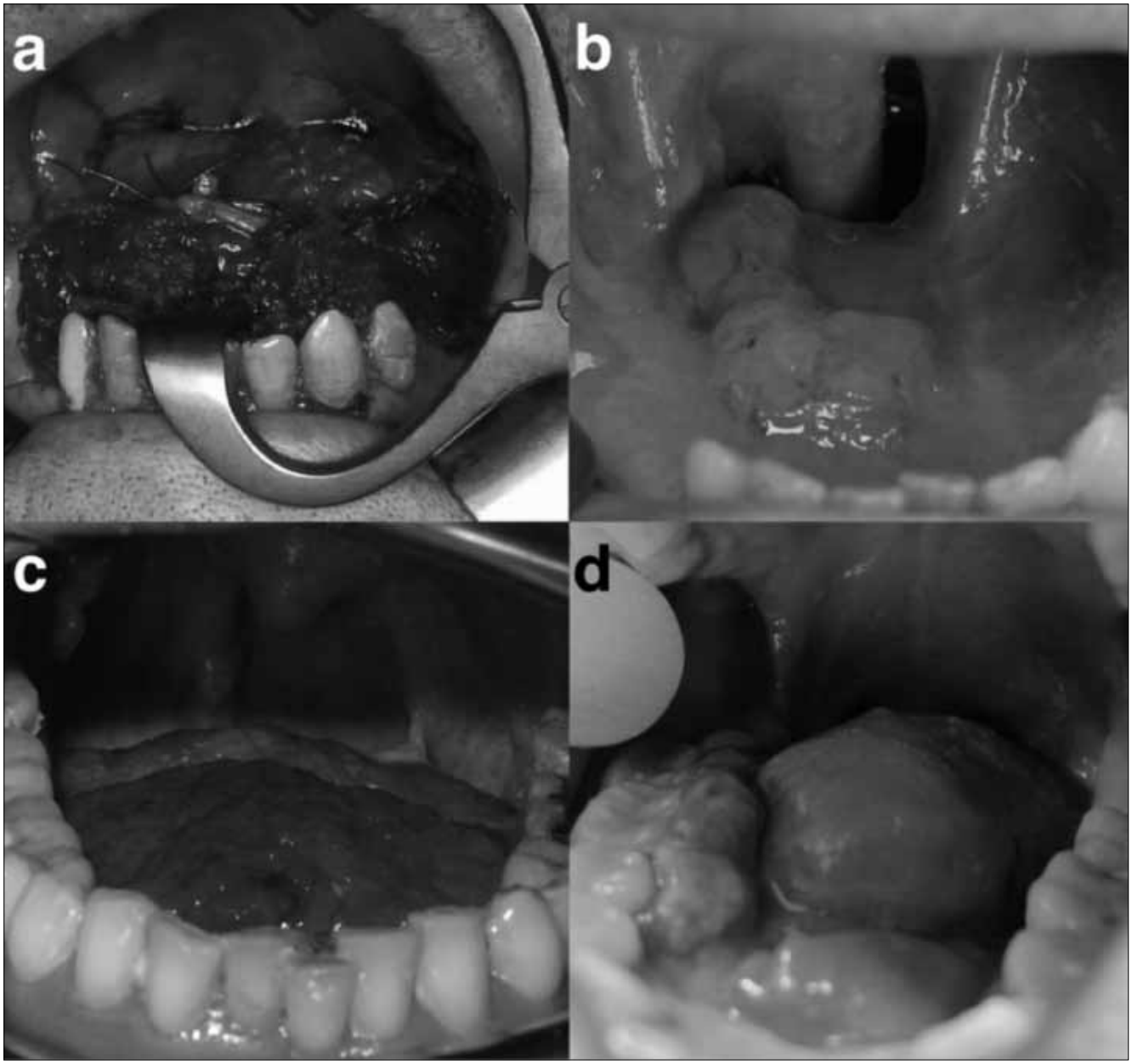

Fig. 3. Post-operative results: a) VLMFF insetting in patient 2. Tongue reconstruction with VLMFF in patient 2 (b) and 1 (c), 30 days after surgery; d) tongue reconstruction with VLMFF in patient 3, 30 days after surgery.

anchi et al. [5] in a series of 98 musculo-cutaneous ALT free flap, the harvesting of the muscular component does not seem to significantly increase donor-site morbidity. Hanasono et al. [5] reported only an 8% of thigh weakness after muscle harvesting that was not associated with the amount of muscle harvested or motor nerve transection. Our 3 patients did not report thigh weakness and did not complain of any limitations in daily physical activity at 30 days after surgery.

Conclusions

The free VLMF flap could potentially offer unique advantages in head and neck reconstruction, including adequate bulk when needed, optimal functional results and obliteration of dead space, thus preventing fistulas and infections with minimal morbidity.

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Letter to the Editor

The relevance of counseling in patients with nasal polyps

L'importanza del counseling nei pazienti affetti da poliposi nasale

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To the Editor,

Management of nasal polyps (NP) is based on medical and surgical strategies [1-3]. At present, medical therapy might be preferable, but it may not be long-lasting. In fact, NP patients have frequent relapses after medical and/or surgical treatment, and thus there is the need for adequate follow-up. In this regard, we previously proposed a clinical-cytological grading to calculate a prognostic index of relapse [4]. Consequently, NP patients must be carefully assessed and followed over time, using appropriate exams. Therefore, it is fundamental to approach NP patients by giving appropriate counseling, such as adequate information and communication, to manage their expectations [5]. In this regard, Oscarsson and colleagues performed a long-term prospective study enrolling 33 patients with untreated NP to investigate the natural history [6]. These authors concluded that occasional NP are frequently part of a chronic disorder that do not necessarily evolve into a more relevant condition over time. Thus, treatment should be decided considering both the presence of NP and severity of symptoms. This issue highlights the relevance of paying careful attention to NP patients and performing appropriate follow-up. Accordingly, we performed a multicentre survey with the aim to evaluate the grade of medical communication in 375 NP patients (206 males, mean age 46.8 years). Table I reports the questions and answers. This investigation underlines that patients were often misinformed, and consequently overall patient satisfaction grade is rather low. Accordingly, surgeons should do a better job in explaining the natural history of NP. This issue is particularly relevant as active and shared participation of the patient is fundamental to achieve optimal management. We firmly believe that medical communication is very relevant in NP management. Thus, a precise and thorough counseling is mandatory in all NP patients.

Table I. Questions and answers about NP management.

Questions	Yes	No
Did the doctor inform you that NP is a chronic disorder and that long-term follow-up is needed?	68%	32%
Did you know that NP have a high probability of relapse?	64%	36%
Did the doctor inform you that another operation might be needed because of relapse?	71%	29%
Did the doctor point out that operation is not curative and will not improve smell or taste?	70%	30%
Did you have periodical check-ups after surgery?	83%	17%
Did the doctor perform anterior rhinoscopy after surgery?	67%	33%
Did the doctor perform nasal fiber-endoscopy after surgery?	33%	67%
Did the doctor prescribe medications to prevent relapse?	83%	17%
Did you take medications to prevent relapse?	75%	25%
Is your overall satisfaction good?	26%	74%

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CASE SERIES AND REPORTS

Effects of simultaneous palatal expansion and mandibular advancement in a child suffering from OSA

Effetti di simultanei espansione palatale e avanzamento mandibolare in un paziente pediatrico con apnee ostruttive notturne

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SUMMARY

This clinical report describes a child suffering from obstructive sleep apnoea (OSA) and class II skeletal malocclusion with maxillary contraction and anterior open bite. He presented moderate obstructive sleep apnoea with large impact on quality of life of patient and parents. He was treated using an innovative orthodontic device (Sleep Apnea Twin Expander) to simultaneously carry out palatal expansion and mandibular advancement. After orthodontic therapy, the OSA-18 questionnaire demonstrated an improvement of the main respiratory symptoms, while cardiorespiratory sleep study revealed a reduction in obstructive sleep apnoea events. Post-treatment, clinical assessment and cephalometric analysis showed a reduction of sagittal maxillary discrepancy and an extension of upper airway space. In conclusion, this case report suggests that orthodontic treatment might be a valuable alternative treatment in children with obstructive sleep apnoea related to craniofacial anomalies.

KEY WORDS: Obstructive sleep apnea • Palatal expansion • Mandibular advancement appliances

RIASSUNTO

Questo caso clinico illustra il trattamento di un bambino affetto da apnee ostruttive nel sonno (OSA) che presenta una malocclusione di classe II scheletrica da retrusione mandibolare con contrazione del mascellare superiore e morso aperto anteriore. Il paziente presenta apnee ostruttive del sonno di grado moderato con un alto impatto sulla qualità della vita del paziente e dei genitori. Il paziente è stato trattato utilizzando un dispositivo ortodontico innovativo (Sleep Apnea Twin Expander), al fine di realizzare l'espansione del palato e l'avanzamento mandibolare contemporaneamente. Dopo la terapia ortodontica, il questionario sulla qualità della vita ha evidenziato un miglioramento dei principali sintomi respiratori e lo studio cardiorespiratorio del sonno ha rivelato una riduzione degli eventi di apnee ostruttive. Al termine della terapia, la valutazione clinica e l'analisi cefalometrica hanno evidenziato una riduzione della discrepanza sagittale e verticale tra il mascellare superiore e la mandibola e un ampliamento dello spazio delle vie aeree superiori. In conclusione, questo case report suggerisce che il trattamento ortodontico può essere una valida terapia alternativa nei bambini con apnea ostruttiva del sonno associata ad anomalie cranio-facciali.

PAROLE CHIAVE: *Apnee ostruttive notturne • Espansione palatale • Apparecchi di avanzamento mandibolare*

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Introduction

Obstructive sleep apnoea (OSA) in children is a "sleep breathing disorder characterised by prolonged partial airway obstruction and/or intermittent complete obstruction that interrupts normal ventilation and normal sleep patterns" [1]. OSA in children is associated with a series of daytime and night time symptoms, such as daytime sleepiness, morning headache, snoring, laboured breathing, restless sleep and nocturnal enuresis [2]. Untreated OSA can result in serious cardiovascular, neurocognitive, behavioural and metabolic problems [2]. The "gold standard" for the diagnosis of OSA is polysomnography even if nocturnal cardiorespiratory sleep study (CRSS) represents a good alternative as an abbreviated diagnostic tool [3]. The main risk factors of OSA in children include adenotonsillar hypertrophy, obesity, neuromuscular disorders and craniofacial anomalies [3]. The first line therapy for children with OSA is adenotonsillectomy, but it is not universally effective due to multifactorial aetiology of the disease [4]. Some authors have suggested the presence of a strong association between sleep breathing disorders and mouth breathing, abnormal placement of the tongue and anomalies in orofacial anatomy [5]. The most common craniofacial anomalies reported are retrognathism, maxillary con-

traction usually associated with unilateral or bilateral cross bite and open bite [6]. The potential benefit of an orthodontic approach in patients with OSA and malocclusion was previously described by several authors [7-9]. We report our experience on treatment of paediatric OSA with an innovative oral device that we called the "Sleep Apnea Twin Expander".

Clinical case

Patient: A 5-year-old boy D.S. referred to "Bambino Gesù" Children's Research Hospital for sleep apnoeas since the age of 30 months. The patient underwent a baseline home nocturnal cardiorespiratory sleep study (CRSS) which revealed moderate OSA with apnoea/hypopnoea index (AHI) of 6 events per hour of sleep and no alteration in oxygen saturation (mean of 98%, minimal 92%). Clinical history revealed poor appetite, no allergies, diurnal and nocturnal mouth breathing, loud snoring and repeated apnoeas during sleep. On physical and ear nose and throat (ENT) examination the patient showed good general conditions, pectus excavatum and patological tonsillar hypertrophy grade III) with no signs of inflammation. The initial extraoral and intraoral photographs are shown in Figure 1. The lateral cephalogram (Fig. 1) showed adenoidal hypertrophy (75% of obstruction) confirmed by fiberoptic evaluation. The cephalometric analysis (Table I) showed a class II skeletal malocclusion, increased maxillary-mandibular divergence, reduced rhinopharyngeal and oropharyngeal airway dimension. The quality of life (QOL) of the patient was measured with a questionnaire (OSA-18) [10]. The score reported in our patient was 81 which suggested a large impact on QOL for both the patient and parents.

Table I. Cephalometric analysis. Maxillary and mandibular skeletal assessment: maxillary position in relation to cranial base (SNA angle), mandibular position in relation to cranial base (SNB angle), maxillomandibular sagittal differential (ANB angle). Vertical skeletal assessment: maxillo-mandibular divergence (ANS-PNS/GO-GN angle). Airway dimensions: rhinopharyngeal airway dimension (AD1-PNS), oropharyngeal airway dimension (PAS-PPAS).

	Pre-treatment	Post-treatment	Normal value
SNA	73.5	73.4	81.4 ± 1.7
SNB	66.1	67.1	76.4 ± 1.4
ANB	7.4	6.3	5.0 ± 1.5
PNS-ANS/GO-GN	39.8	34.4	29 ± 5.0
AD1-PNS	7.3	7.9	18.9 ± 5.2
PAS-PPAS	3.1	4.8	12.0 ± 3.2

Treatment: after multidisciplinary assessment, the child was prescribed a conservative treatment including orthodontic treatment and medical therapy. In order to correct malocclusion, we developed an innovative custom-made device, that we called "Sleep Apnea Twin Expander". For development of the device, anatomical impressions and a wax bite registration in maximal intercuspation position

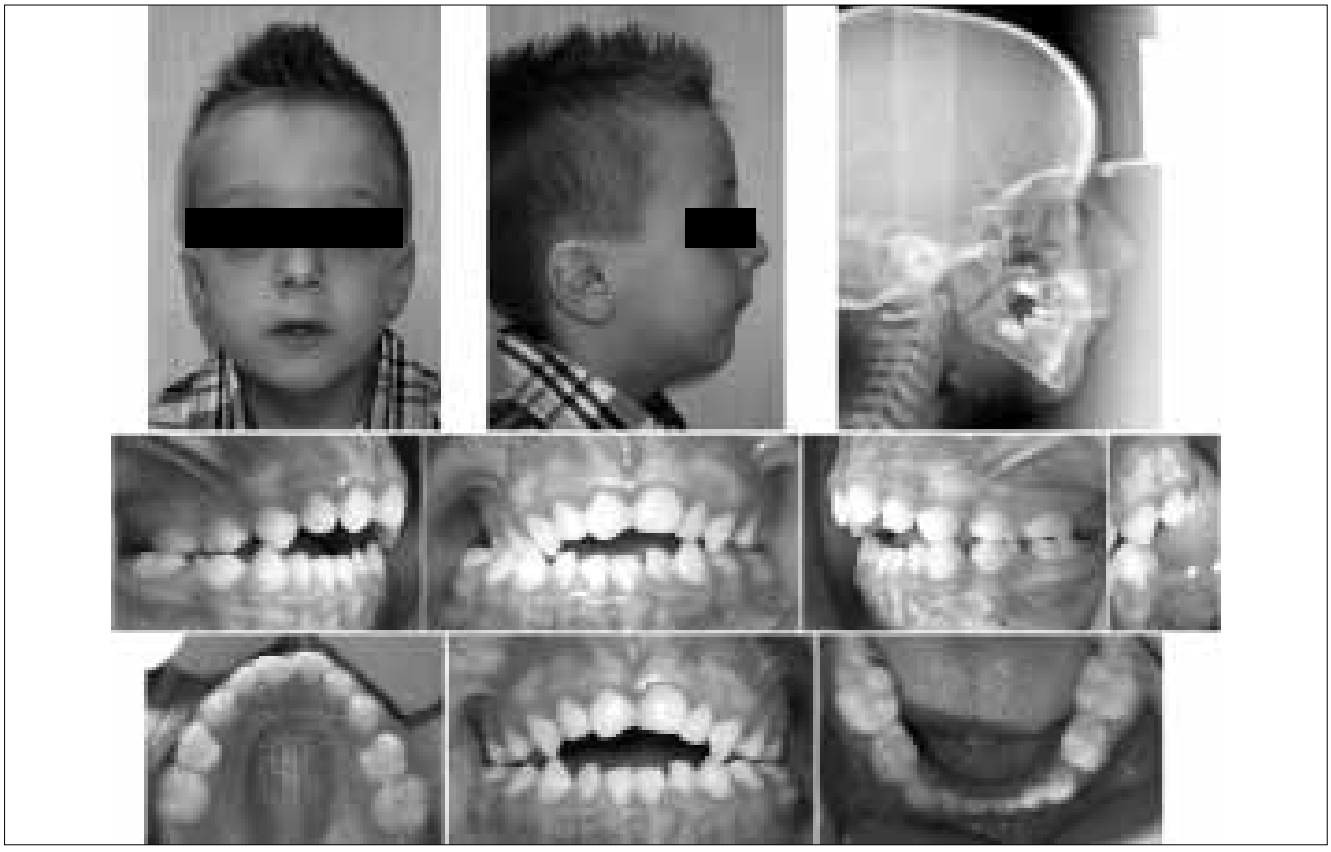

Fig. 1. Pre-treatment extraoral, intraoral photographs, lateral cephalogram.

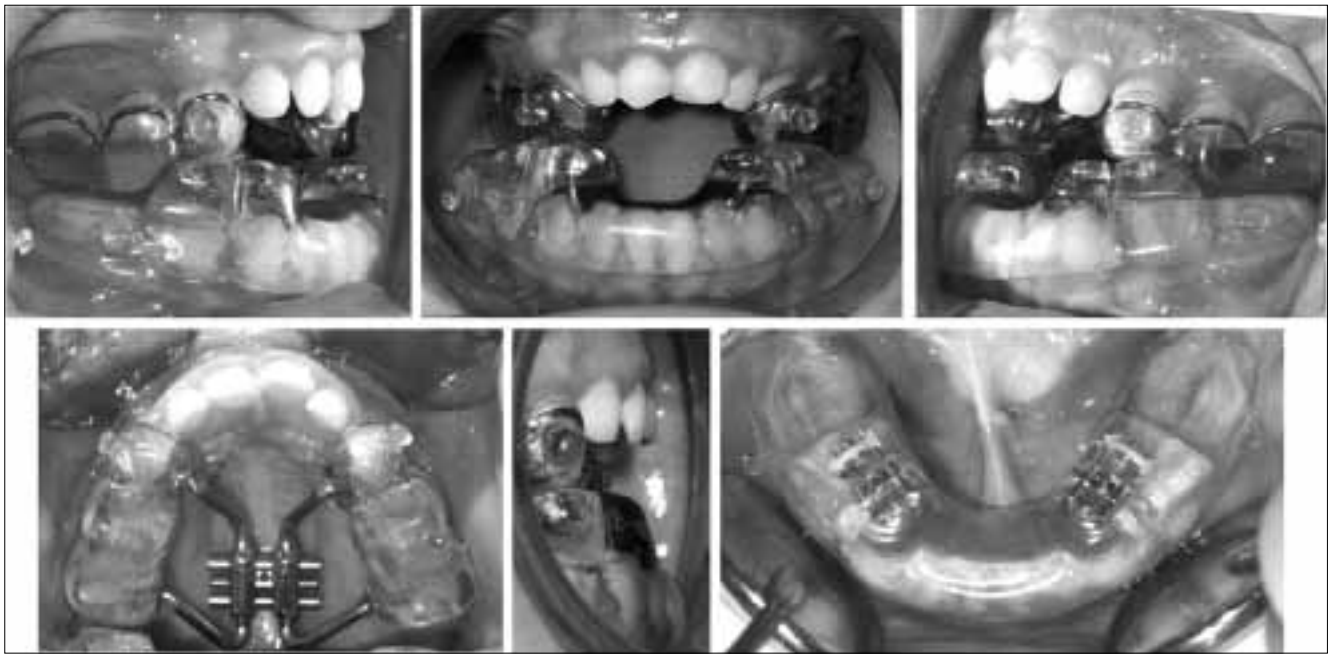

Fig. 2. Sleep Apnea Twin Expander in situ.

and in maximum mandibular protrusion were taken. The device (Fig. 2) is a double plate consisting of two separate elements, an upper fixed and a lower removable. It is a combination between the bite block expander by McNamara [11] and twin block appliance by Clark [12]. The upper part is a modified bite block palatal expander, consisting of a Hyrax-type screw 10 mm (Philoshopy 1, Lancer) secured to the maxillary arch with a 0.045-inch wire framework imbedded in acrylic covering the buccal, lingual and occlusal surfaces of the deciduous canine and first and second deciduous molars. The acrylic was 2 mm thick at the canines and 7 mm thick at the first and second deciduous molars creating steep inclined planes interlocked at about 70° to the occlusal plane. The lower appliance consisted of removable bite plane of acrylic retained with 0.9-mm ball clasps placed in the mandibular interproximal areas of first and second deciduous molars. The mandible was guided to protrude forward by the inclined planes in acrylic. Reactivation of the advancement was carried out with an adjustable screw mechanism on the lower splint to achieve movement of inclined planes for gradual advancement of the mandible. This appliance allows to carry out palatal expansion and mandibular advancement simultaneously in order to obtain an extension of upper airway area and a possibile improvement of OSA symptoms in a short period. The upper bite block expander was bonded to the maxillary arch with resin reinforced glass ionomer cement (Fuji Ortho, GC America). The mother of the patient was instructed to advance the screw once a day for 30 days. In addition, after one week the patient was instructed to wear the lower device during the night. The otorhinolaringologist prescribed intranasal corticosteroids. The advancement screw on the lower appliance was initially activated at 50% of the maximum mandibular protrusion. Thirty days after the oral device placement, the patient's mother referred a reduction of snoring and disappearance of apnoea events. Intraoral examination revealed an expansion of the transverse diameter of the upper jaw and an upper interincisal diastema. The screw of the lower plate was reactivated to increase mandibular advancement until 60% of maximal protrusion, the patient was instructed to wear it 14 hours per day, to stop activations in upper expander and was instructed about nasal breathing exercises. The patient was seen at 4-week intervals for an average of 10 additional months. After four months of orthodontic therapy the patient performed a second home nocturnal CRSS with device in situ in order to evaluate the effectiveness of the occlusal device in reducing

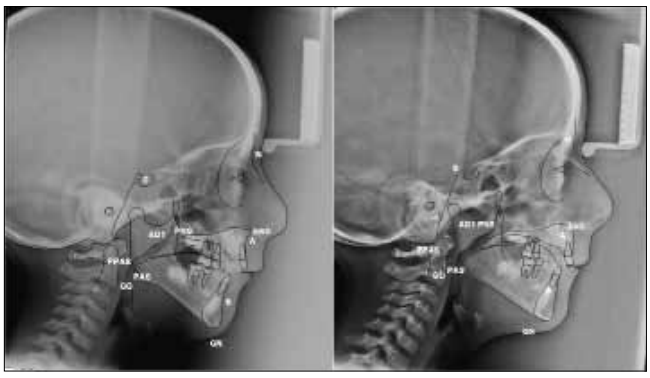

Fig. 3a-b. Lateral cephalogram pre- and post-treatment. Cephalometric points used in the analysis of the child. Points: A, A-point; ANS: anterior nasal spine; B: B-point; Gn: gnathion; Go: gonion; N: nasion; PNS: posterior nasal spine; AD1: adenoid inferior; S: sella; PPAS: posterior pharyngeal wall; PAS: anterior pharyngeal wall around gonial angle

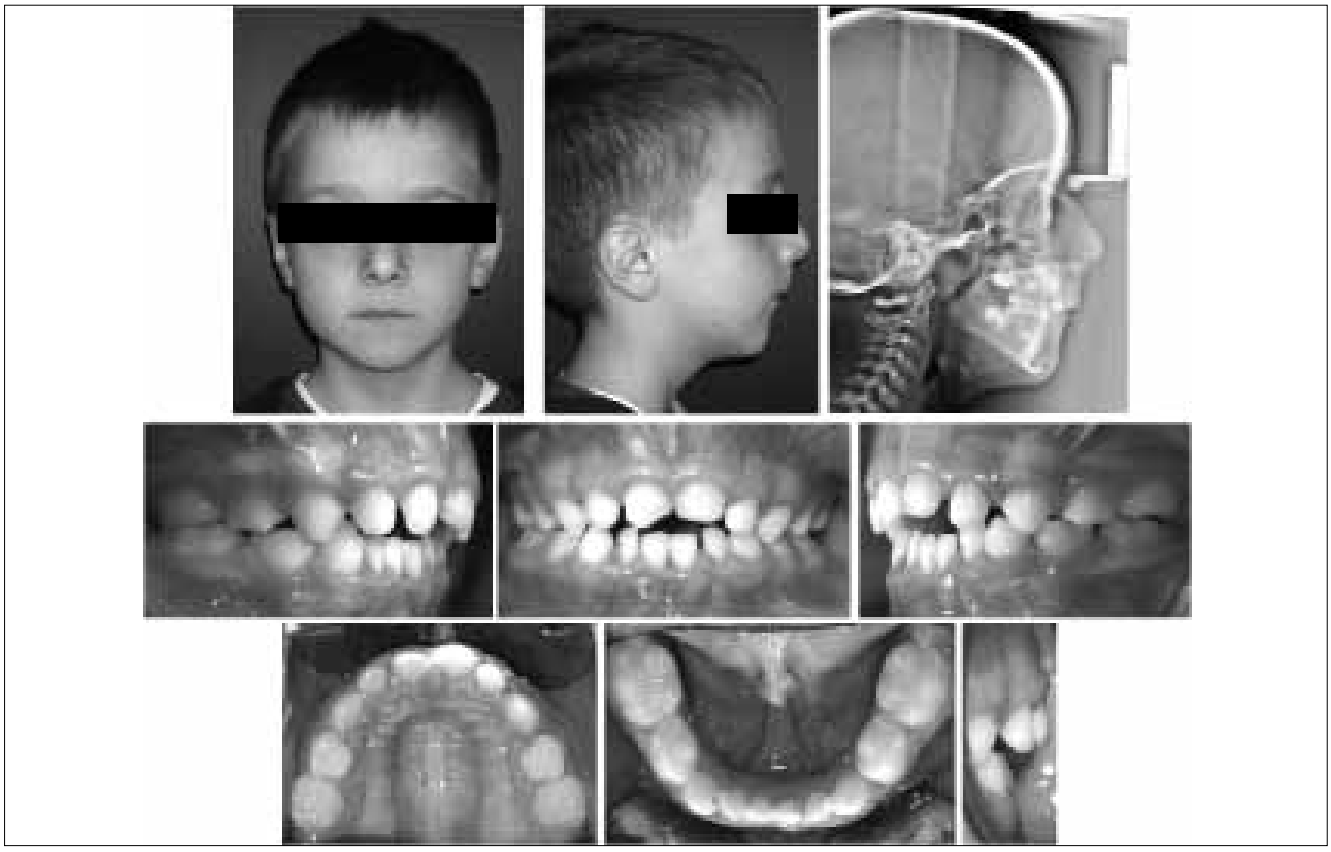

Fig. 4. Post-treatment extraoral, intraoral photographs, lateral cephalogram.

apnoea events at night. The CRSS showed the absence of significant apnoeas with oxygen saturation within normal limits (AHI = 0.6; oxygen saturation mean of 98.2%, minimal 94%). After eight months of retention, the upper appliance was removed, and lateral cephalogram was performed. The patient was prescribed to use the device as removable during the night. The comparison between cephalometric analysis pre- and post-orthodontic treatment (Fig. 3, Table I) showed an increase in the rhinopharyngeal and oropharyngeal space and a reduction in maxillo-mandibular sagittal and vertical discrepancy. The examination of the patient after orthodontic treatment showed an improvement in face appearance, lip competence and dry lips, and the intraoral view showed a class I malocclusion and reduction of the overjet and open bite (Fig. 4). The OSA-18 QOL questionnaire administrated to the parents at the end of orthodontic treatment showed that the score was reduced to 20, suggesting a large improvement. ENT assessment at the end of the treatment showed reduction in hypertrophy of palatal tonsils and adenoids to grade II, and with no indication for surgical treatment.

Discussion

In this case report we describe the successful treatment of moderate OSA with a new oral device in a 5-year-old boy. Although adenotonsillectomy represents the first choice for treatment of OSA in children, we decided to treat him with an orthodontic approach based on the moderate degree of OSA with a normal oxygen saturation index and the possibility of a conservative therapeutic strategy. The Sleep Apnea Twin Expander device was suitable for the patient described because it combined maxillary expansion and mandibular advancement. Orthodontic treatment resulted in an improvement of OSA symptoms through modification of the facial skeletal components. The positive effects of maxillary expansion and mandibular anterior repositioning have been previously described in children [7-9]. The rapid maxillary expansion can produce significant increment of the total nasal volume [13] and mandibular advancement enlarges the retrolingual space and at the same time promotes lingual advancement during the night [7]. These aspects, however, have not been confirmed by literature review because of the limited number of studies and further studies are necessary to examine the effect of orthodontic device in a large sample of paediatric patients [14 15].

In our patient, breathing pattern and skeletal improvements were documented: the post-treatment lateral cephalogram showed an increase of rhinopharyngeal and oropharyngeal space, a reduction of maxillo-mandibular sagittal and vertical discrepancy, AHI passed from 6 to 0.6 events/night and the OSA-18 score decreased from 81

to 20. Moreover, a reduction of the adenoidal and tonsillar hypertrophy degree was demonstrated, similar to data reported in a previous study [7]. We hypothese that this effect may be related to the enlargement of the upper airway and retropharyngeal spaces that produce a relative reduction of the hypertrophy. The successful therapy of this case confirms the importance of a multidisciplinary approach in diagnosis and therapy of paediatric OSA. The early orthodontic approach, aimed to obtain simultameus palatal expansion of the upper maxillary and the mandibular advancement at the first phase of the treatment, associated with medical and breathing exercises, may modify the skeletal maxillo-mandibular anatomy by preventing obstruction of the upper airway. Considering the results of this case, further studies are warranted to examine the effects of orthodontic treatment with the Sleep Apnea Twin Expander in a large number of paediatric OSA patients with similar craniofacial anomalies.

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The authors thank to Dr. Vincenzo D'Antò for ideation of "Sleep Apnea Twin Expander". The authors acknowledge Professor Ambrosina Michelotti, Dr. Renato Cutrera, Dr. Emanuela Sitzia and Dr. Valeria Viarani for their contribution to this case report.

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CASE SERIES AND REPORTS

Arterio-venous malformation of the mandible. Case report and review of literature

Malformazione arterovenosa della mandibola. Caso clinico e revisione della letteratura

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SUMMARY

Arteriovenous malformation (AVM) of the head and neck is a rare and potentially life threatening entity due to massive haemorrhage. There are several indications for treatment, including age of the patient and location, extent and type of vascular malformation. Endovascular therapy can effectively cure most lesions with limited tissue involvement. Surgery can be used in selected cases in combination with embolization. Here we report the case of a young woman affected by a massive AVM on the left side of the mandible and submandibular region, and also review the literature on AVM with special attention to treatment strategies.

KEY WORDS: Arterio-venous malformation • Mandible • Submandibular region • Treatment

RIASSUNTO

Le malformazioni arterovenose (MAV) del distretto cervico-facciale sono patologie rare e potenzialmente letali a causa delle imponenti emorragie che possono determinare. Il trattamento dipende dall'età del paziente, dalla sede, dall'estensione e dalla tipologia della malformazione. La terapia endovascolare è efficace nella maggior parte dei casi che presentano un'estensione limitata. In casi selezionati, e sempre in associazione con l'embolizzazione, si può ricorrere alla chirurgia. Nel presente articolo riportiamo il caso di una giovane donna affetta da un'estesa MAV dell'emimandibola e della regione sottomandibolare sinistra. Viene inoltre effettuata una revisione della letteratura prodotta su questo argomento con particolare attenzione alla strategia di trattamento.

PAROLE CHIAVE: *Malformazione artero-venosa • Mandibola • Regione sottomandibolare • Trattamento*

Acta Otorhinolaryngol Ital 2016;36:333-336

Introduction

According to Mulliken and Young, two types of vascular lesions can be recognized, which depend on the intrinsic properties of endovascular cells, namely haemangiomas and vascular malformations [1]. Haemangiomas demonstrate endothelial hyperplasia and enlarge by cellular proliferation. Clinically, haemangiomas usually appear in early infancy, grow rapidly during the first months of life, then slowly involuting over 5 or 6 years [2 3].

Arteriovenous malformations (AVMs) in contrast to the abnormal proliferation of endothelial cells of a haemangioma, display progressive ectasia of abnormal vessels, lined by flat endothelium. AVMs occur as a result of errors in embryogenesis, are always present at birth, may manifest at any time during life and grow proportionately with the child [3 4]. AVMs can be subdivided based on the rate of blood flow: "slow flow" (capillary, venous, lymphatic or mixed) and "fast flow" (arterial, arteriovenous, fistulae or shunt) subtypes [5]. Vascular malformations are frequently seen in the skin, but rarely affect the visceral organs or bones; approximately 51% occur in the head and neck, with a male-female ratio of 1 to 1.5. About 50% of all bone involvement occur in the skull and the maxillo-facial area [6 7].

Lesions of the mandible are rare and potentially life-threatening entities that can present as innocuous episodes of gingival bleeding, slow-growing expansile masses, or severe haemorrhage. A biopsy or even a simple tooth extraction can cause a catastrophic bleeding that may even lead to death [8-12]. However, the clinical course of malformations involving the mandible and the maxilla remains unclear and unpredictable. Treatment may be surgical or non-surgical. The latter includes intravascular embolization with coil and/or sclerosing solutions. Surgical resection is reserved for lesions that are extensive and/or refractory to endovascular therapy. Cure is defined as the complete eradication of disease or permanent resolution of symptoms with complete devascularization [8-16].

Herein, we report the case of a 23-year-old woman with an AVM of the mandible and submandibular region, and review the relevant literature, focusing on the best options for treatment.

Case report

In December 2009, a 23-year-old woman, after tooth extraction, presented at our ENT division with a massive haemorrhage from the left side of the mandible.

The bleeding was initially controlled by packing the mandible, and blood transfusions were required. The patient reported no malocclusion and no history of infection, and family history was also unremarkable. She was affected by insulin dependent diabetes mellitus. The only extraoral finding was a slight left facial swelling.

Retrospective analysis of the radiograms used for dental cure revealed the following. By panoramic radiograph, an extensive radiolucency in the left mandible involving the molar area (Fig. 1) was evident, while by dental scan, an abnormal enlargement of the left alveolar canal with integral cortical bone (Fig. 2) was present.

In the subsequent, urgent surgical intervention, a temporary ligation of the external carotid artery was ineffectively attempted because of a large anastomotic blood supply. The haemorrhage was then controlled by filling the mandibular cavity with sheets of oxidized cellulose, taking advantage of the natural pathway created by the previous tooth extraction. A haemostatic suture of the alveolar mucosa was finally done.

In the strong suspicion of a vascular malformation, the patient underwent head and neck magnetic resonance imaging (MRI) and magnetic resonance with angiography (MRA). The examination showed an extensive highly vascularized lesion involving the left side of the mandible and left submandibular region (Fig. 3).

Ten days later, after the correction of severe diabetic decompensation, an angiography was performed. This study confirmed the diagnosis of arteriovenous malformation in the sites mentioned before, and associated with feeding vessels from the external carotid artery. Superselective coil embolization was performed of the facial artery, lingual artery and internal maxillary artery.

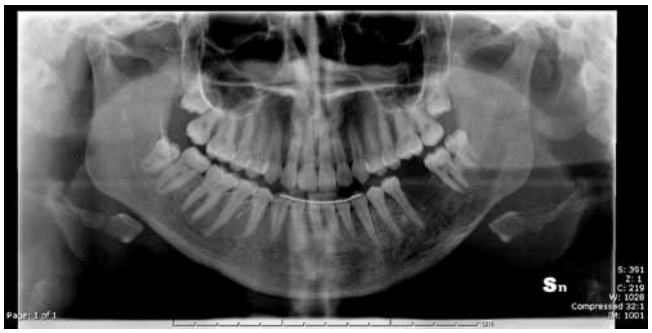

Fig. 1. Extensive radiolucency in the left mandible by panoramic radiograph.

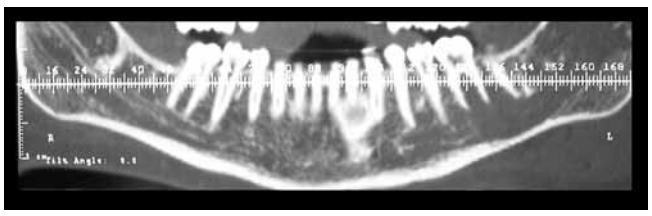

Fig. 2. Abnormal enlargement of the left alveolar canal with integral cortical bone by dental scan.

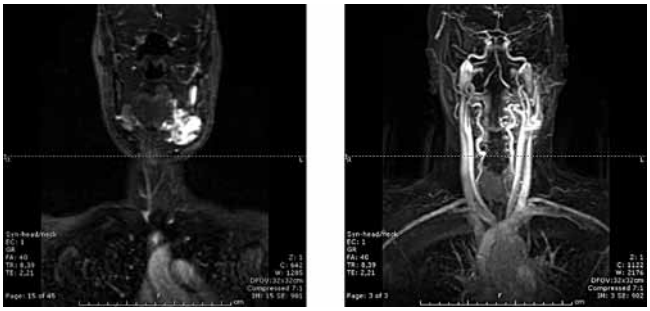

Fig. 3. MRI and MRA scans showing an extensive highly vascularized lesion involving the left side of the mandible and left submandibular region.

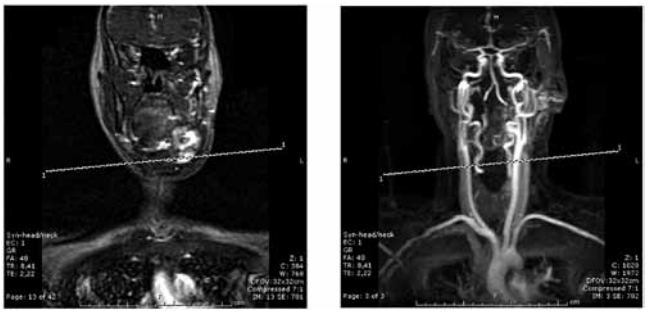

Fig. 4. Subtotal closure of the AVM on MRI and MRA performed the day after embolization.

The day after, follow-up MRI and MRA revealed a subtotal closure of the AVM (Fig. 4).

Two days later, the patient underwent surgical intervention. Passing through the incision of the previous carotid ligation, we removed a large highly vascularized lesion occupying the left submandibular region and substituting the submandibular gland itself. From the empty alveolar ridge, the intraosseous component of the AVM was injected with sodium tetradecyl sulphate (3%). There was no damage to the mandibular branch of the facial nerve. There were no intraoperative complications, and the es-

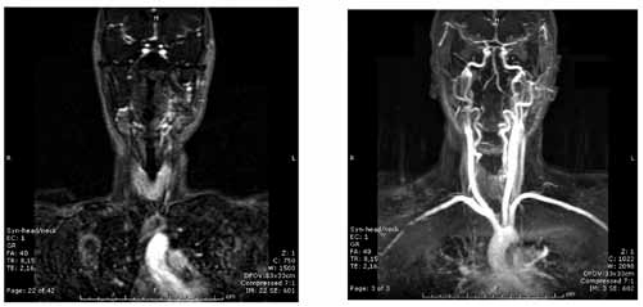

Fig. 5. Two months after intervention, post-surgical MRI and MRA showed an empty submandibular triangle and almost complete reabsorption of the AVM in the mandible.

timated blood loss was 500 ml. The postoperative period was uneventful, and the patient was discharged on the fifth postoperative day. The final histopatological diagnosis was arterio-venous malformation.

At the time of writing, after six months of follow-up, the patient has not experienced symptoms of trigeminal neuralgia. A minor bleeding episode was controlled with intraosseous injection of methylprednisolone acetate. Subsequently, no further episodes of bleeding were observed. Two months after the operation, post-surgical MRI and MRA showed an empty submandibular triangle and almost complete reabsorption of the AVM in the mandible (Fig. 5). Bone fractures and tissue necrosis or infection have not occurred.

Discussion

AVMs are extremely rare entities that can be life threatening if left untreated due to massive blood loss during tooth extraction or biopsy. Although rare, 50% of all intraosseous AVMs occur in the maxillo-facial region and are extremely infrequent in the mandible [17]. Very few cases of extraosseous submandibular AVMs have been reported, with 6 cases cited in the literature (5 females and 1 male) [18-20]. Our study confirms this trend. To our knowledge, this is the first documented case of a combined AVM involving both the mandible and the submandibular region. AVMs usually present with non-specific symptoms including bruit, dental loosening, swelling of soft tissues, change in skin and mucosal colour and dysesthesia of the lower lip or chin. Although CT, MRI and MRA may localize the arterio-venous shunt lesion, superselective arteriography remains an essential tool for diagnosis and planning of treatment [8-10 13 14]. Management of AVMs is usually complex and requires a multidisciplinary team for successful outcome. Observation may be used as a temporary measure in special situations, such as extreme age, pregnancy or refusal of therapy. No spontaneous regressions have been documented. On the other hand, it has been reported that the volume of the lesion may gradually increase [9].

Arterial ligature was used in the past as a purely symptomatic treatment or before surgery. At present, it is well known that ligation of external carotid artery should not be performed, firstly as many anastomoses promote the rapid appearance of a collateral circulation, and secondly because future embolization would be impossible [9 10 13]. In addition, in our experience, emergency ligation of the external carotid artery is insufficient to stop the haemorrhage because of a large and already developed network of anastomotic blood vessels.

At present, superselective angiographic embolization is considered first line treatment, alone or in combination with surgical approach to reduce intraoperative bleeding. Occlusion of the lesion is obtained using movable balloon, coils or liquid glue. Endovascular therapy as definitive treatment for the AVMs of the mandible has been reported to have a success rate of 70%. This avoids mutilating surgery and related sequelae, especially if AVMs occur before adolescence [8-10 13-16].

However, serious complications after embolization (e.g., occlusion of pulmonary or cerebral vessels) or recurrence of AVMs should be considered. In some cases, the procedure has to be carried out in several sessions such as previous history of arterial ligation or high flow characteristics of the lesion or microshunts, which are invisible during hyperselective catheterization and therefore inaccessible to treatment [9 11 13].

Therefore, intraosseous injection of sclerosing agents should be used to achieve further obliteration of the AVMs [16]. In this case, we used sodium tetradecyl sulphate 3% which in our division is regularly employed to treat many different vascular lesions of the head and neck with a high cure rate and very low incidence of side effects.

Surgery is not the treatment of choice for AVMs of the mandible. Block resection of the affected area has been suggested, and temporary reconstruction with alloplastic bone plate or with the patient's own free, previously curetted mandibular segment has been reported. More definite bony reconstruction is recommended as soon as possible with a free fibular graft or iliac crest to avoid facial deformities and allow dental implantation [8-10 11 12 21].

In the past years, some authors have commented that radical surgical resection as in threating cancer [22 23]. This has been tempered by acknowledgement that radical resection and reconstruction of an extensive benign vascular lesion of the maxillo-facial and mandibular area typically causes severe disfigurement with considerable morbidity. Furthermore, recurrences may occur even after radical resection, and relapses are reported to be even more difficult to treat [8].

On the other hand, surgical excision of AVMs involving soft tissues such as the submandibular space can be achieved without severe sequelae [18]. No data on relapse have been reported for this very rare condition. According to the literature, we tailored treatment of the present case by performing superselective arterial embolization, leaving the intraosseous part of the AVM in situ and resecting only the part located in submandibular region. Surgery should always be performed after embolization, with a short interval between the procedures, based on the general recommendation that surgery should take place within 48 hours to 2 weeks to avoid revascularization of the lesion. In this period, we recommend MRI and MRA angiography studies to evaluate the effective devascularization of AVMs.

In conclusion, considering the present case and literature data, we can define the following general principles of treatment.

Arterial ligation should not be performed, even in emergency settings. Superselective arterial embolization is the

treatment of choice and can be repeated in the case of relapse. Intraosseous injection of sclerosing agents can be used in the attempt to reduce the number of arterial embolizations. In AVMs of the mandible, surgery should be reserved only for cases that are refractory to endovascular therapy and/or for therapeutic complications that are not otherwise treatable (bone fractures and/or necrosis). In AVMs of the soft tissue, surgery could be used if there are no significant side effects. Lastly, the interval between embolization and surgery should be as short as possible, and MRI and MRA should be repeated before surgery.

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In Memoriam of Pietro Ferrara (1934-2015)

We were all deeply saddened by the loss of Professor Piero Ferrara, Director of the Clinic of Otorhinolaryngology of the University of Palermo, from 1980 to 2004.
Prof. Pietro Ferrara was born at San Giuseppe Jato (Palermo) January 4th 1934.
Graduated in Medicine and Surgery on 19 July 1958. Otorhinolaryngology professional qualification on 12 December 1961.
Anesthesiology professional qualification in 1963.
Academic career in University of Palermo: he was Voluntary Assistant from 1960 to 1962. He had entrusted assistant from 1962 to 1964 and Ordinary Assistant in 1964.
He was Lecturer in Otorhinolaryngology from 1969.
From 1974 to 1980 he had entrusted of the teaching of Otorhinolaryngology.
From the 1980 Ordinary Professor professional qualification in Otorhinolaryngology.
He was Chief Medical Executive of the Complex Unity of Otorhinolaryngology and Manager of the Department of the Special Surgeries in Azienda Ospedaliera Universitaria Policlinico of Palermo.
His teacher was Professor Ettore Borghesan, who was internationally known for his research on the internal ear. Professor Ferrara inherited a passion for research and a deep-felt attachment to the Institution from his teacher and dedicated himself to the study of Histopathology and Histochemistry in the field of Otorhinolaryngology
After brilliantly completing his specialization in Otorhinolaryngology in 1961, he progressively and successfully scaled all the steps of his academic career .
Director of Otorhinolaryngology clinic, Director of the School of Specialization, and finally, Director of the Department of Otorhinolaryngology.
His scientific research in various fields of Otology, Vestibology and Otosurgery, and clinical and experimental Oncology, were published in many highly regarded journals. Professor Ferrara was also a Speaker and Chairman at many national and international congresses, an Organizer of courses and meetings.
He was Member of numerous Italian and international Scientific Societies: Italian Society of Otorhinolaryngology, Italian Society of Audiology, Italian Society of Phoniatry , Italian Society of Pediatric Otorhinolaryngology, Sicilian Society of Otorhinolaryngology, International Association of Physicians in Audiology (IAPA), Prosper Ménière Society, Fondation Portmann, Politzer Society, European Academy of Otology & Neuro-Otology, European Skull Base Society.
He was also President of the Sicilian Board of Otorhinolaryngology, Audiology, and Phoniatry.
He was a brilliant otosurgeon and a passionate researcher who was always open to innovation. He published more than 200 articles (indexed/Peer reviewed Journals) 1 book chapters and more than 100 abstracts presented as oral presentation or posters at national and international scientific congress).
Main topics of his activity were: otology, neurotology, middle ear surgery, neuroradiology, audiology.
My memories go back to those first years in which I was student and attended the Department of Otorhinolaryngology of the University of Palermo. In those years, I assisted Professor Ferrara both in clinical research projects and in the wards and surgery rooms.
His pupils will remember always his great sense of duty, dedication to the work, and his teaching.

Riccardo Speciale

Notiziario SIO

CONSIGLIO DIRETTIVO SIO (2016/2017)

Leone C.A.	Presidente SIO	(Scad. Maggio 2017)
Cassandro E.	Vice-Presidente	(Scad. Maggio 2017)
Vicini C.	Vice-Presidente	(Scad. Maggio 2018)
Scasso F.	Segretario	(Scad. Maggio 2017)
Gallo A.	Tesoriere	(Scad. Maggio 2017)
Ralli G.	Bibliotecario	(Scad. Maggio 2018)
Capasso P.	Segretario del Presidente	(Scad. Maggio 2017)
Barillari U.	Consigliere	(Scad. Maggio 2018)
Benazzo M.	Consigliere	(Scad. Maggio 2018)
Croce A.	Consigliere	(Scad. Maggio 2018)
Cuda D.	Consigliere	(Scad. Maggio 2018)
Gianformaggio C.	Consigliere	(Scad. Maggio 2018)
Greco A.	Consigliere	(Scad. Maggio 2018)
Pisani P.	Consigliere	(Scad. Maggio 2018)
Santandrea L.	Consigliere	(Scad. Maggio 2018)
Tortoriello G.	Consigliere	(Scad. Maggio 2018)
Tirelli G.	Consigliere	(Scad. Maggio 2018)
Filipo R.	Past president	(Scad. Maggio 2017)
Paiano M.T.	Consigliere agg. LP	(Scad. Maggio 2018)

Comitato permanente per l'aggiornamento dello statuto e del regolamento

Leone C.A.	Presidente SIO	(Scad. Maggio 2017)
Lauriello M.	Segretario dell'AUORL	(Scad. Maggio 2018)
Rugiu M.G.	Segretario dell'AOOI	(Scad. Maggio 2018)
Scasso F.	Segretario SIO	(Scad. Maggio 2017)
Maiolino L., Motta S., Passali GC.	Colleghi nominati dall'AUORL	(Scad. Maggio 2017)
Della Vecchia L., Iemma M., Piemonte M..	Colleghi nominati dall'AOOI	(Scad. Maggio 2018)

Revisori dei conti SIO

Fiorella M.L.	(Scad. Maggio 2020)
Sessa M.	(Scad. Maggio 2020)

Collegio dei Proibiviri SIO

Chiesa F.	(Scad. Maggio 2018)
Conticello S.	(Scad. Maggio 2018)
De Benedetto M.	(Scad. Maggio 2018)
Fiorella R.	(Scad. Maggio 2018)
Passali D.	(Scad. Maggio 2018)

Coordinatore del Controllo di Qualità

Della Vecchia L.	(Scad. Maggio 2019)

Organo di consulenza SIO

Bussi M., Camaioni A., Casolino D., Conticello S., Coppo L., Danesi G., De Benedetto M., De Campora E., De Campora L., De Vincentiis I., Felisati D., Fiorella R., Laudadio P., Marcucci L., Miani P., Motta G., Ottaviani A., Passali D., Paludetti G., Piemonte M., Puxeddu P., Rinaldi Ceroni A., Sartoris A., Serra A., Sperati G., Spriano G., Zaoli G.

Delegati

EUFOS	Cuda D.	(Scad. Maggio 2018)
	Fiorella M.L.	(Scad. Maggio 2017)
IFOS	Piemonte M.	(Scad. Maggio 2018)
	Galli J.	(Scad. Maggio 2017)
UEMS	Cuda D.	(Scad. Maggio 2018)
	Motta G.	(Scad. Maggio 2017)
EHNS	Spriano G.	(Scad. Maggio 2018)
	Motta G.	(Scad. Maggio 2017)

CONSIGLIO DIRETTIVO AOOI

Danesi G.	Presidente	(Scad. Maggio 2018)
Barbara M.	Vice-Presidente	(Scad. Maggio 2018)
Della Vecchia L.	Vice-Presidente	(Scad. Maggio 2018)
Radici M.	Vice-Presidente	(Scad. Maggio 2018)
Rugiu M.G.	Segretario-tesoriere	(Scad. Maggio 2018)
Achilli V.	Consigliere	(Scad. Maggio 2018)
Boccuzzi S.	Consigliere	(Scad. Maggio 2018)
Campanini A.	Consigliere	(Scad. Maggio 2018)
De Campora L.	Consigliere	(Scad. Maggio 2018)
Miani C.	Consigliere	(Scad. Maggio 2018)
Napolitano A.	Consigliere	(Scad. Maggio 2018)
Panetti G.	Consigliere	(Scad. Maggio 2018)
Panu F.	Consigliere	(Scad. Maggio 2018)
Raso F.	Consigliere	(Scad. Maggio 2018)

Collegio dei probiviri AOOI

Barbieri F.	(Scad. Maggio 2020)
De Benedetto M.	(Scad. Maggio 2020)
Laudadio P.	(Scad. Maggio 2020)
Richichi M.	(Scad. Maggio 2020)
Villari G.	(Scad. Maggio 2020)

Delegati

IFOS	Piemonte M.	(Scad. Maggio 2018)
UEMS EUFOS	Cuda D.	(Scad. Maggio 2018)
EHNS	Spriano G.	(Scad. Maggio 2018)

CONSIGLIO DIRETTIVO AUORL

Bussi M.	Presidente	(Scad. Maggio 2017)
Paludetti G.	Vice-Presidente	(Scad. Maggio 2017)
Nicolai P.	Vice-Presidente	(Scad. Maggio 2017)
Lauriello M.	Segretario-tesoriere	(Scad. Maggio 2018)
Aluffi Valletti P.	Consigliere	(Scad. Maggio 2017)
Maiolino L.	Consigliere	(Scad. Maggio 2017)
Martini A.	Consigliere	(Scad. Maggio 2017)
Motta G.	Consigliere	(Scad. Maggio 2017)
Passali F.M.	Consigliere	(Scad. Maggio 2017)
Quaranta N.	Consigliere	(Scad. Maggio 2017)
Sellari Franceschini S.	Consigliere	(Scad. Maggio 2017)
Cassandro E.	Past-President	(Scad. Maggio 2017)

Collegio dei probiviri

Barillari U.	(Scad. Maggio 2017)
Fusetti M.	(Scad. Maggio 2017)
Marchiori C.	(Scad. Maggio 2017)
Rinaldi Ceroni A.	(Scad. Maggio 2017)
Staffieri A.	(Scad. Maggio 2017)

Revisori dei conti

Bussi M.	(Scad. Maggio 2017)
Mancini P.	(Scad. Maggio 2017)

Comitato permanente per l'aggiornamento dello statuto e del regolamento

Bellussi L.	(Scad. Maggio 2017)
Chiarella G.	(Scad. Maggio 2017)
Ralli G.	(Scad. Maggio 2017)

Delegati

UEMS	Motta G.	(Scad. Maggio 2017)
EUFOS	Fiorella M.L.	(Scad. Maggio 2017)
IFOS	Galli J.	(Scad. Maggio 2017)
EHNS	Motta G.	(Scad. Maggio 2017)

Congresso Nazionale S.I.O. Sorrento 2017

Relazione Ufficiale
Cianfrone G.: Controversie diagnostico-terapeutiche in otorinolaringoiatria

Temi di Comunicazione
Temi liberi

Tavola Rotonda
Ricci Maccarini A.: Insidie e strategie nella gestione della patologia della voce

Relazione Ufficiale 2018
Scasso F., Ferrari G., De Vincentiis G.C.: Patologia infettiva emergente e riemergente in otorinolaringoiatria.

Calendar of events – Italian and International Meetings and Courses

Acta Otorhinolaryngol Ital 2016;36:341-343

Information, following the style of the present list, should be submitted to the Editorial Secretariat of Acta Otorhinolaryngologica Italica (actaitalicaorl@rm.unicatt.it).
In accordance with the Regulations of S.I.O. and Ch.C.-F. (Art. 8) Members of the Society organising Courses, Congresses or other scientific events should inform the Secretary of the Association (A.U.O.R.L., A.O.O.I.) within the deadlines set down in the respective Statutes and Regulations.

AUGUST-DECEMBER 2016

12th OTOLOGICAL MICROSURGERY COURSE • ***August 29-31, 2016 • Bern – Switzerland***

E-mail: otology@swiss-meeting.org – Website: http://otology.swiss-meeting.org

4th INTERNATIONAL SYMPOSIUM ON OTOSCLEROSIS, DIAGNOSIS AND TREATMENT
August 31- September 2, 2016 • Utrecht – The Netherlands

E-mail: info@otosclerosis.com – Website: http://www.otosclerosis2016.com/

ENDOSCOPIC COURSE FOR PARANASAL SINUS AND SKULL BASE SURGERY
September 1-3, 2016 • Bern – Switzerland

E-mail: paranasal@swiss-meeting.org – Website: http://paranasal.swiss-meeting.org

INTERNATIONAL MEETING OF RHINOPLASTY SOCIETIES
September 8-10, 2016 • Versailles (Paris) – France

Chairmen: Wolfgang Gubisch, Bahman Guyuron – E-mail: contact@imrhis2016.com – Website: www.imrhis2016.com/en/

EUROSAS SURGERY • ***September 15-17, 2016 • Rimini – Italy***

Organising Secretariat: Filippo Montevecchi, Andrea De Vito – E-mail: filippomontevecchi72@gmail.com; dr.andrea.devito@gmail.com – Website: www.eurosas2016.com/

I WORKSHOP NAZIONALE – DAY SURGERY IN OTORINOLARINGOIATRIA
September 16-17, 2016 • Rome – Italy

Presidenti: Fabrizio Ottaviani, Gianluca Bellocchi. Website: www.daysurgeryitalia.it

OTOLOGY 3.0: L'OTOLOGIA NEL TERZO MILLENNIO • ***September 22-24, 2016 • Padova – Italy***

Director: Alessandro Martini – E-mail: meet@meetandwork.com

LA CHIRURGIA ENDSCOPICA RINOSINUSALE DALLA TEORIA ALLA PRATICA
September 26-28, 2016 • Pavia – Italy

Responsabile Scientifico: F. Pagella, U.O.C di Otorinolaringoiatria, Fondazione IRCCS, Policlinico San Matteo, Pavia, Italy – Website: www.nadirex.com. Organizing Secretariat: Nadirex Internetional Srl – E-mail: info@nadirex.com

INSTRUCTIONAL WORKSHOP EUROPEAN ACADEMY OF OTOLOGY AND NEURO-OTOLOGY
September 28 - October 1, 2016 • İzmir – Turkey

President: O. Nuri Ozgirgin – Website: www.eaono.org

28th CONGRESS OF UNION OF EUROPEAN PHONIATERS: PHONIATRICS AND COMMUNICATION
September 29 - October 1, 2016 • Bilbao – Spain

Website: http://phoniatrics-bilbaocongress.com

SIMPOSIO ITALO FRANCESE DI VESTIBOLOGIA • ***September 30 - October 1, 2016 • Matera – Italy***

Responsabili Scientifici: G.A. Libonati, B.Cohen, Hotel Del Campo, Matera, Italy. Organizing Secretariat: Prisco Provider Srl – E-mail: info@priscoprovider.it – Website: www.priscoprovider.it

CORSO PRATICO DI ANATOMIA CHIRURGICA E DISSEZIONE SPERIMENTALE OTOLOGICA 2° LIVELLO - XX EDIZIONE • *October 3-7, 2016 • Sanremo (IM) – Italy*

President: S. Nosengo – E-mail: franco.cocchini@studiumorl.com – A cura di: A. Tombolini, F. Baricalla – Co-ordinato da: A. Tombolini – Website: www.studiumorl.com

IFHNOS 2016 • *October 5-7, 2016 • Praha – Czech Republic*

E-mail: ifhnos2016@guarant.cz – Website: www.ifhnosprague2016.org/

RHINOLOGY & RHYNOALLERGOLOGY INTERNATIONAL CONFERENCE 5th BULGARIAN ITALIAN RHINOLOGY MEETING • *October 13-15, 2016 • Senigallia – Italy*

Directors: Dilyana Vitcheva, Alessandro Varini, Giuseppe Frau, Alessandro Bucci. Scientific Secretariat: A. Bucci, Finis Africae Country House S.P. Sant' Angelo 155 Senigallia (AN), Italy – Website: www.rhinology.eu. Organizing Secretariat: Events Congress & Communication – Website: wwww.rhinology.eu

SWISS ENDOSCOPIC EAR SURGERY COURSE (SEES) • *October 14-15, 2016 • Bern – Switzerland*

E-mail: anschuetz.lukas@gmail.com – Website: http://sees.swiss-meeting.org

6th INTERNATIONAL COURSE ON FUNCTIONAL AND AESTHETIC SURGERY OF THE NOSE – LIVE SURGERY • *October 16-19, 2016 • Imola (BO) – Italy*

Course Director: Ignazio Tasca – Scientific Secretariat, E.N.T. Department, Imola Hospital, Italy – Tel. +39 0542 662101/293 – Fax +39 0542 662284 – E-mail: i.tasca@ausl.imola.bo.it – Executive Secretariat: A & R Eventi sas di Verlicchi Clara e C., via R. Benassi 28, 40068 San Lazzaro di Savena (BO), Italy – Tel. +39 051 474238 – Fax +39 051 4839525 – E-mail: clara@areventi.it – Website: www.imolarhinoplasty2016.com

4° MASTER DI LARINGOLOGIA ONCOLOGICA • *October 17-20, 2016 • Vittorio Veneto – Italy*

Scientific Secretriat: A. Bertolin, Ospedale Civile di Vittorio Veneto, Vittorio Veneto, Italy. Organizing Secretariat: Nord Est Congressi – E-mail: mail@nordestcongressi.it – Website: www.nordestcongressi.it

ANZHNCS ANNUAL SCIENTIFIC MEETING AND THE IFHNOS 2016 WORLD TOUR *October 25-27, 2016 • The Langham Auckland – New Zealand*

E-mail: anzhncs.asm@surgeons.org – Website: www.ifhnosauckland2016.org

15th INTERNATIONAL CONGRESS OF IRANIAN SOCIETY OF OTOLARYNGOLOGY, HEAD AND NECK SURGERY • *November 8-11, 2016 • Tehran – Iran*

E-mail: mahtab_rabbani@yahoo.com – Website: www.iranent.org/congress/

APPROCCIO PRATICO ALLA VPPB LEZIONI TEORICHE E PRATICHE *November 10-12, 2016 • Matera – Italy*

Scientific Secretariat: G.A. Liberati, Hotel Del Campo, Matera, Italy. Organizing Secretariat: Prisco Provider Srl – E-mail: info@priscoprovider.it – Website: www.priscoprovider.it

4° CONGRESSO AGGIORNAMENTI IN ORL "ENDORL" • *November 12, 2016 • Montegranaro (Fermo) – Italy*

President: Luigi Fasanella – Scientific Secretariat: Cesare Carlucci – Tel. +39 0733 823030 – E-mail: carlucci7@tin.it

HANDS-ON COURSE ON NEW ENDOSCOPIC APPROACHES TO LATERAL SKUL BASE, INNER EAR AND CEREBELLO-PONTINE ANGLE *November 12-13, 2016 • Verona – Italy and November 14, 2016 • Modena – Italy*

Scientific Secretariat: L. Presutti, D. Marchionni, AOU di Modena Policlinico. Organizing Secretariat: ICLO Srl – E-mail: info@iclo.eu – Website: www.iclo.eu

CORSO DI ANATOMIA CHIRURGICA ENDOSCOPICA DEI SENI PARANASALI E DELLA BASE CRANICA *November 13-15, 2016 • Verona – Italy*

Scientific Secretariat: F. Pagella, E. Emanuelli, ICLO San Francesco di Sales Teaching and Research Center di Arezzo (Via A. Einstein, 12). Organizing Secretariat: ICLO Srl – E-mail: info@iclo.eu – Website: www.iclo.eu

MASTER DI DISSEZIONE E CHIRURGIA ENDOSCOPICA DEI SENI PARANASALI E DEL BASICRANIO *November 14-18, 2016 • Milan – Italy*

Director: Alberto Dragonetti – E-mail: a.dragonetti@fastwebnet.it

9th INTERNATIONAL SYMPOSIUM ON RECENT ADVANCES IN RHINOSINUSITIS AND NASAL POLYPOSIS (ISRNP 2016) • *November 21-23, 2016 • Kuala Lumpur – Malaysia*

E-mail: sympo@isrnp2016.net – Website: http://www.isrnp2016.net/

CORSO MICROSCOPICO E VIDEOENDOSCOPICO DI DISSEZIONE SU CADAVERE PROPEDEUTICO ALLA CHIRURGIA OTOLOGICA • *November 24-25, 2016 • Milan – Italy*

Presidents: Raffaele Pugliese, Alberto Dragonetti – E-mail: corsieconvegni@eurocompany.mi.it

RHINOFORUM 2016 • *December 1-3, 2016 • Warsaw – Poland*

E-mail: info@forumrynologiczne.pl – Website: http://rhinoforum.pl/en

JANUARY-DECEMBER 2017

CORSO DI DISSEZIONE OTOLOGICA, OTONEUROLOGICA E IMPLANTOLOGIA UDITIVA, DISSEZIONE ENDOSCOPICA DELL'ORECCHIO MEDIO E INTERNO • *January 10-12, 2017 • Paris – France*

Directors: Olivier Sterkers and Daniele Bernardeschi

12th SURGICAL ANATOMY IN HEAD&NECK CANCERS PROCEDURES • *March 1-3, 2017 • Arezzo – Italy*

Scientific Secretariat: M. Benazzo, F.G. Chiesa, ICLO San Francesco di Sales Teaching and Research Center di Arezzo (Via A. Einstein, 12). Organizing Secretariat: ICLO Srl – E-mail: info@iclo.eu – Website: www.iclo.eu

9th MILANO MASTERCLASS • *March 24-28, 2017 • Milan – Italy*

Charimen: Paolo Castelnuovo and Pietro Palma – Website: www.milanomasterclass.it

2nd WORLD CONGRESS ON ENDOSCOPIC EAR SURGERY • *April 27-29, 2017 • Bologna – Italy*

Chairmen: Livio Presutti, Muaaz Tarabichi, Daniele Marchioni

104° CONGRESSO NAZIONALE SIO – SOCIETA ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE • *May 24-27, 2017 • Sorrento – Italy*

President: Carlo Antonio Leone – Website: www.sioechcf.it

9th INTERNATIONAL BIENNALE MILANO MASTERCLASS – THE NOSE INSIDE OUT
March 24-28, 2017 • Milan – Italy

Scientific Secretariat: P. Castelnuovo, P. Palma – Website: www.milanomasterclass.it. Auditorium "IL SOLE 24 ORE" Via Monte Rosa, 91 - 20149 Milano. Organizing Secretariat: MZ Congressi Srl – E-mail: mima@mzcongressi.com

IFOS PARIS 2017 - ENT WORLD CONGRESS • *June 24-28, 2017 • Paris – France*

Tel. +33 (0)1 44 64 15 15 – E-mail: contact@ifosparis2017.org – Website: www.ifosparis2017.org

4th CONGRESS OF THE EUROPEAN ORL-HNS • *October 19-22, 2017 • Antalya – Turkey*

E-mail: dburkaya@topkon.com – Website: www.ceorlhns2017.com

CORSI PRATICI DI VIDEOCHIRURGIA ENDOSCOPICA NASO-SINUALE E DEL BASICRANIO
November 13-17, 2017 • Milan – Italy

Scientific Secretariat: A. Dragonetti, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy. Organizing Secretariat: Eurocompany Srl – E-mail: corsieconvegni@eurocompany.mi.it

17th ASEAN ORL HNS CONGRESS • *November 16-18, 2017 • Myanmar*

E-mail: phillip.samual27@gmail.com

JANUARY-DECEMBER 2018

15th INTERNATIONAL CONFERENCE ON COCHLEAR IMPLANTS AND OTHER IMPLANTABLE AUDITORY TECHNOLOGIES • *June 13-16, 2018 • Antwerp – Belgium*

Chairman: Paul Van de Heyning – E-mail: vincent.van.rompaey@uza.be – Website: www.ci2018.org

6th WORLD CONGRESS OF THE INTERNATIONAL FEDERATION OF HEAD AND NECK ONCOLOGIC SOCIETIES • *September 1-5, 2018 • Buenos Aires – Argentina*

Website: http://ifhnos2018.org/

JANUARY-DECEMBER 2019

14th ASIA-OCEANIA ORL-HNS CONGRESS 2019 • *January 9-13, 2019 • Hyderabad – India*

E-mail: secretariat@14asiaoceania.com – Website: http://14asiaoceania.com/