Modern management of obstructive salivary diseases

L'attuale orientamento terapeutico nelle patologie ostruttive salivari

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SUMMARY

Over the last fifteen years, increasing public demand for minimally-invasive surgery and recent technological advances have led to the development of a number of conservative options for the therapeutic management of obstructive salivary disorders such as calculi and duct stenosis. These include extracorporeal shock-wave lithotripsy, sialoendoscopy, laser intra-corporeal lithotripsy, interventional radiology, the video-assisted conservative surgical removal of parotid and sub-mandibular calculi and botulinum toxin therapy. Each of these techniques may be used as a single therapeutic modality or in combination with one or more of the above-mentioned options, usually in day case or one-day case under local or general anaesthesia. The multi-modal approach is completely successful in about 80% of patients and reduces the need for gland removal in 3%, thus justifying the combination of, albeit, time-consuming and relatively expensive techniques as part of the modern and functional management of salivary calculi. With regard to the management of salivary duct anomalies, such as strictures and kinkings, interventional radiology with fluoroscopically controlled balloon ductoplasty seems to be the most suitable technique despite the use of radiation. Operative sialoendoscopy alone is the best therapeutic option for all mobile intra-luminal causes of obstruction, such as microliths, mucous plugs or foreign bodies, or for the local treatment of inflammatory conditions such as recurrent chronic parotitis or autoimmune salivary disorders. Finally, in the case of failure of one of the above techniques and regardless of the cause of obstruction, botulinum toxin injection into the parenchyma of the salivary glands using colour Doppler ultrasonographic monitoring should be considered before deciding on surgical gland removal.

KEY WORDS: Salivary glands • Salivary calculi • Salivary duct stenosis • Surgical treatment • Extracorporeal lithotripsy • Sialoendoscopy • Botulinum toxin therapy

RIASSUNTO

Negli ultimi quindici anni la sempre maggiore richiesta di terapie minimamente invasive ed i recenti progressi tecnologici hanno favorito l'affermazione di tecniche conservative nel management dei disordini ostruttivi salivari quali la scialolitiasi e le stenosi duttali. Tali nuove opzioni terapeutiche includono la litotrissia extracorporea, l'endoscopia salivare, la litotrissia intra-corporea laser, la radiologia interventistica, la rimozione chirurgica di calcoli parotidei e sottomandibolari video-assistita con preservazione ghiandolare ed il trattamento con tossina botulinica. Le tecniche menzionate possono essere impiegate singolarmente oppure combinate tra loro, generalmente in regime ambulatoriale o di Day Surgery e One-Day Surgery in anestesia locale o generale. L'elevato successo terapeutico, pari a circa l'80%, garantito dall'approccio multimodale e l'abbattimento al 3% dei casi destinati alla scialoadenectomia tradizionale, giustifica l'utilizzo in modo combinato di tali tecniche costose e time-consuming come parte integrante del moderno management della litiasi salivare. La radiologia interventistica, in particolar modo la riabilitazione duttale plastica mediante catetere a palloncino sotto controllo fluoroscopico, appare, nonostante l'impiego di radiazioni, la migliore opzione terapeutica nella gestione delle stenosi e dei kinkings duttali. L'endoscopia salivare operativa, da sola, rappresenta il trattamento di scelta per tutte le ostruzioni endoluminali mobili (microliti, mucous plugs o corpi estranei) e per il trattamento locale di patologie infiammatorie tra cui parotiti ricorrenti croniche o disordini salivari di origine autoimmune. In aggiunta a ciò, in caso di fallimento delle precedenti opzioni terapeutiche, indipendentemente dalla causa dell'ostruzione, l'infiltrazione di tossina botulinica nel parenchima salivare sotto controllo ecocolor Doppler dovrebbe essere considerata prima di optare per l'asportazione chirurgica della ghiandola salivare.

PAROLE CHIAVE: *Ghiandole salivari • Calcoli salivari • Stenosi duttali salivari • Terapia chirurgica • Litotrissia extracorporea • Endoscopia salivare • Terapia botulinica*

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Introduction

Salivary gland diseases are relatively common. The most frequent non-neoplastic salivary disorder is obstructive sialadenitis [1], which may be due to calculi, fibromucinous plugs, duct stenosis, foreign bodies, anatomic variations, or malformations of the duct system leading to a mechanical obstruction associated with stasis [2].

Patients with obstructive sialadenitis present with a history of recurrent painful periprandial swelling of the involved gland, best known as the "meal-time syndrome" [3], which is often complicated by recurrent bacterial infections, with fever and a purulent discharge at the papilla [2 4].

Sialolithiasis

Sialolithiasis is the main cause of obstructive salivary diseases, being involved in 66% of cases [5] and accounting for about 50% of major salivary gland diseases [6]. Post-mortem studies have shown a 1.2% prevalence of salivary calculi in the general population [7], although Escudier and McGurk described the incidence of symptomatic salivary calculi as being about 59 cases per million per annum [8], for a clinical prevalence of 0.45% [9].

Sialolithiasis is more frequent in male patients [10]. Incidence peaks between the age of 30 and 60 years [11], and it is uncommon in children as only 3% of all sialolithiasis cases occur in the paediatric population [12].

Sialolithiasis affects the submandibular gland in 80-90% of cases [13], mainly unilaterally [10] but without a preferred side; this finding is partly explained by recent *post-mortem* morphometric studies which found a symmetry between the right and left gland [14]. In our experience, the mean size of submandibular stones is about 7.3 mm, although giant sialoliths measuring up to 7 cm have occasionally been described [15-19]. The majority of calculi are located in the distal third of the duct or at the hilum of the gland; pure intraparenchymal stones are infrequent [20].

Between 5% and 10% of cases occur in the parotid gland [13]. The striking difference between parotid and submandibular stones is partially related to the ascendent and sharper angled duct system of the submandibular gland and the type of (mainly mucous) secretion [3]. The sublingual and other minor salivary glands are rarely affected (about 0-5% of cases) [13].

The traditional aetiopathogenetic factors associated with stone formation are obstruction, reduced salivary flow rate, dehydration, change in salivary pH associated with oropharyngeal sepsis and impaired crystalloid solubility [3]; physiologically, microliths may be detected following precipitation in a supersaturated solution of mucous plugs [3] or membrane phospholipids within redundant secretory vesicles [21 22], which become symptomatic and act as a *nidus* in which successive layers of inorganic and organic substances are deposited.

In addition to these classic hypotheses, Marchal et al. [4] have recently suggested a retrograde theory in lithogenesis, according to which a retrograde migration of foods, bacteria or foreign bodies from the oral cavity to the duct system may lead to stone formation, being facilitated by variations in the sphincter-like mechanism reported in 90% of cases [23]. This hypothesis has been supported by Teymoortash et al. [24], who used polymerase chain reaction (PCR) to extract gene fragments belonging to oral bacteria from salivary calculi, most of which related to *Streptococcus* species (the same as those found in gingival bacterial plaque).

The traditional diagnostic approach consists of standard radiography, which does not reveal radiolucent [25], intraglandular or small stones in about 20% of cases [7 26], and computed tomography (CT), which is limited by the fact that the stone can be occulted by thick radiological slices and that scans do not provide the precise localisation of a sialolith within the duct system [27]. Colour Doppler sonography has also been considered useful in patients with sialolithiasis [28]. Ultrasonography currently represents an excellent first-level diagnostic technique [29] insofar as, in experienced hands, it reveals ductal and highly mineralised stones with a diameter of at least 1.5 mm with a accuracy of 99% [30].

Recent advances in optical technology have led to the development of sialoendoscopy, a new diagnostic means of directly visualising intra-ductal stones that has bridged the diagnostic gap between the clinical suspicion of salivary obstruction and the limitations of conventional radiology. Appropriately miniaturised instruments for the mean diameters of the excretory ducts of the major salivary glands (0.5-1.4 mm for Stensen's duct and 0.5-1.5 mm for Wharton's duct, as suggested by histological studies [31]), allow an almost complete exploration of the duct system in most patients.

Duct anomalies

Strictures and kinks are the second most frequent cause of obstructive sialadenitis [32] and, unlike sialolithiasis, frequently involve the parotid ductal system (75.3% [33]) and mainly affect females [33].

Sialographic findings indicate that salivary duct stenosis accounts for about 23-30% of recurrent parotid swellings [34 35] and 3% of recurrent submandibular swellings [34]. Other anatomic variations have been described in the case of salivary gland obstructions; these include accessory ducts [27], sphincter-like mechanisms located near the papilla in Wharton's duct or posteriorly in Stensen's duct [36 37], pelvis-like formations which are basin-like structures at the hilum instead of a bifurcation or trifurcation [1 38 39], and intraductal evaginations [1 38].

Strictures are usually a result of epithelial duct injuries following recurrent infections or traumas caused by sialoliths or surgical procedures, although congenital strictures have also been described [2 34 40]. In this context, bilateral parotid duct sialectasia in patients with parotid obstruction but no signs of chronic parotitis may be considered a congenital anomaly.

Concerning the origin of kinks, Nahlieli et al. [41] have described the involvement of the sharp bend in Wharton's duct above the lingual nerve and the mylohyoid muscle in the region known as the "knee area", in addition to herniation of the surrounding tissue through the mylohyoid muscle or the loosening of the same [41 42].

The traditional diagnostic approach to duct stenosis includes sialography, which is still considered the diagnostic gold standard, and also plays a therapeutic role by stretching duct walls as a result of contrast medium injection [43]. Sialo-CT has also been proposed for the diagnosis of abnormalities in the duct system. However, these imaging modalities visualise the salivary duct system indirectly [27], expose patients to radiation, and may be complicated by infections or iatrogenic lesions of the duct wall [44].

Magnetic resonance (MR) sialography has more recently been introduced as a new diagnostic tool for visualising the duct system up to the tertiary branches and the parenchymal tissue [45 46]. It has the advantages that it does not require contrast medium, there is no radiation and no need for ductal cannulation, it can also be performed during acute gland infection and, finally, the use of citric acid to stimulate salivary secretion (dynamic sialo-MR) allows a functional evaluation of the affected gland [47] (Fig. 1).

Fig. 1. Sialo-MR image of parotid duct stenosis of distal third.

MR sialographic 3-dimensional reconstruction imaging and MR virtual endoscopy for salivary gland ducts have recently been proposed on the basis of experiences using MR virtual endoscopy in other systems such as the gastrointestinal, urinary and biliary tracts, and vascular structures [48-51]. This new diagnostic modality has been proposed as a non-invasive pre-surgical procedure in order to fit conventional surgical endoscopy to the patient's individual anatomy on the basis of the endoluminal views provided [52].

Sialoendoscopy is useful in detecting ductal anomalies that may not be detected by means of either traditional or new imaging techniques.

Other causes of obstruction

Salivary duct obstruction may be caused by mucous plugs, foreign bodies, sialodochitis, *ab estrinseco* compression due to a neoplasm or reactive intraparenchymal parotid lymph nodes, intraductal polyps, or the granulation tissue sometimes associated with immunological disorders such as Sjögren's syndrome [1 27 38].

Obstructive symptoms can also follow dose- and time-dependent damage to salivary glands exposed to radioiodine therapy administered to patients with thyroid carcinoma, because the salivary glands, and especially the serous parotid cells, selectively concentrate iodine [53].

Salivary duct obstruction of the parotid gland due to a lack of neuromuscular masseteric coordination has also been described [54], as well as obstruction due to traumatic erupting teeth [34] or denture-induced compression of the salivary duct orifice.

In most of such cases in which traditional and modern imaging techniques cannot visualise the cause of the obstruction, sialoendoscopy provides immediate and direct information.

Traditional management

The traditional approach to obstructive salivary disorders suggests duct dilatation, incision and dissection in the case of distal stones (sometimes followed by marsupialisation,

with the risk of post-operative stenosis), and sialadenectomy in the case of proximal, hylar or intraparenchymal sialoliths. Sialolithiasis is still the main indication for sialadenectomy [55], although common post-operative complications include nerve injury, recrudescent symptoms due to stones retained in the remaining duct [55 56], and unsatisfactory aesthetic outcomes. With regard to parotid stones, total conservative parotidectomy has been considered better than superficial parotidectomy in order to avoid recurrences [57]. The main complication reported after superficial parotidectomy for obstructive salivary disorders is facial nerve palsy (temporary nerve weakness in 16-38% of cases, permanent in up to 9% [58-60]); Frey's syndrome is rare [61 62]. After sub-mandibular gland excision, there is a 1-8% risk of permanent marginal mandibular nerve palsy [63-66] and a 1-5% risk of lingual nerve injury [63-65]. Sialocele, salivary fistulas or cyst formation, neurinomas, infections and haematomas are rarely encountered after sialoadectomy for obstructive disease [67].

In the case of ductal anomalies, traditional management suggests surgical derivation of salivary flow or by-pass with the creation of a new excretory duct proximal to the stenosis, or ductal sialodochoplasty [68-70].

Current management

Although sialolithiasis has been associated with a high incidence of chronic inflammation suggesting that the obstruction of the duct of the salivary glands led to irreversible parenchymal damage, recent scintigraphic [71 72] and histopathological studies [73] have shown that recovery of secretory function after stone removal is guaranteed in most cases. For example, on the basis of scintigraphic examination, Yoshimura et al. [72] assessed functional restoration in 78% of salivary glands after sialolithotomy, and Marchal et al. [73] found that at least half of his patients who underwent sialoadenectomy showed a normal histological pattern.

Herewith, a review is presented of the main minimally invasive gland-preserving techniques currently used in the management of obstructive salivary disease, including shockwave lithotripsy, sialoendoscopy, interventional radiology, endoscopically video-assisted trans-oral and cervical surgical retrieval of stones, and botulinum toxin therapy.

Shock-wave lithotripsy

In 1989, Iro et al. [74] introduced the application of extracorporeal shock-wave lithotripsy (ESWL) (previously used in the urological and gastroenterological fields) for the management of sialolithiasis. Sialolithotripsy is a non-invasive method of fragmenting salivary stones into smaller portions in order to favour their possible flushing out from the salivary duct system spontaneously or after salivation induced by citric acid or other sialogogues. Exploiting the change in impedance at the stone/water interface, lithotripsy leads to stone fracture by producing a compressive wave that spreads through the calculus and an expansive wave that pits it and induces its cavitation [75]. The shock-waves may be generated extra-corporeally using piezoelectric [76] and electromagnetic techniques [77-79], or intra-corporeally using electro-hydraulic [80], pneumatic [81 82] or laser endoscopic devices [83 84].

Extra-corporeal shock-wave lithotripsy

Extra-corporeal electromagnetic shock-wave lithotripsy
Dedicated lithotripters with a mobile arm (Minilith SL-1, Storz Medical, Kreutzlingen, Switzerland) are currently used for the treatment of salivary calculi (Fig. 2). The ultrasound-guided shock-wave generated by a small-diameter, cylindric, electromagnetic source focuses on the salivary stones by means of a parabolic reflector within the cushion, while the patients remain supine in a semi-reclined position in a dentist's chair [85]. The 2.4 mm size of the shock-wave focus permits the treatment of stones with diameters of ≥ 2.4 mm [85]. The pulse frequency of the wave may vary from 0.5 to 2 Hz and no more than 4000 shock-waves may be administered per session. Continuous sonographic monitoring allows direct visualisation of the degree of fragmentation during treatment and avoids lesions to the surrounding tissues [9 85].

Fig. 2. Dedicated miniaturised extracorporeal lithotripter for fragmentation of salivary stones.

The exclusion criteria for ESWL are stones with a diameter of < 2 mm or which cannot be identified using an ultrasound probe, and the presence of complete distal duct stenosis; the procedure is contra-indicated in patients with acute sialadenitis or acute inflammation in the head and neck region, as well as in patients with cardiac pacemakers [85 86].
The main limitation of ESWL is that it does not always completely clear the calculus but leaves stone fragments inside the duct system that may subsequently become the *nidus* of recurrent sialolithiasis [73]. In fact, ESWL completely eliminates 34-69% of parotid calculi [9 78 79 85 87] and 32-42% of sub-mandibular calculi [78 79 85 87 98]. Capaccio et al. [87] analysed a series of 322 patients, and found statistically significant associations between favourable outcomes and parotid stones and intraductal sub-mandibular stones, calculi < 7 mm, age < 46 years, and fewer than 2000 shock-waves. On the basis of these experiences, ESWL is currently considered the treatment of choice for all parotid calculi and submandibular perihilar or intraparenchymal stones < 7 mm [9 88].
The reported untoward effects are skin pain over the treated area (in 79.5% of cases [87]), glandular swelling (35.2% [87]), duct haemorrhage (36.8% [87]), and cutaneous petechiae (22.7% [87]).

Extra-corporeal piezoelectric shock-wave lithotripsy
The piezoelectric technique exploits the pressure wave produced in water by the expansion of crystals due to the application of voltage. The crystals are placed on a concave disk that converges the wave on a 3 mm area to a depth of 11 mm [75]. Iro et al. [76 89-92] have documented results of 50-58% of stone-free cases, and 76-100% of patients experiencing symptom relief.

Intra-corporeal shock-wave lithotripsy
In intra-corporeal lithotripsy, the shock-waves reach the stone surface through a lithotripsy probe placed inside the salivary duct system under endoscopic guidance [93]. The energy needed to fracture the stone is usually provided by means of a laser beam, pneumatic devices, or electro-hydraulic probes.

Endoscopically guided intra-corporeal laser lithotripsy
In 1990, Gundlach et al. [94] reported the first successful application of endoscopically guided intra-corporeal lithotripsy for salivary stones using a laser beam, achieving 92% of stone clearance. Intra-corporeal laser lithotripsy using Holmium YAG (yttrium-aluminum-garnet) or pulsed dye lasers has also been reported in limited series of patients [43 84]: the former, the efficacy of which, for urolithiasis, is well known [95 96], is associated with a high risk of soft tissue damage, and their difficulty of use is attributable both to their thermal effects and absorption by the surrounding tissues [5 43]; the latter are harmless, but extremely expensive [43 97].
Raif et al. [98] recently proposed the development of an erbium (Er) fibre delivery system for endoscopic lithotripsy of salivary stones: hollow metal wave guides optimised for an Er: YAG laser were end-sealed with a polished sapphire rod of 0.63 mm, designed to adapt to the laser and the sialoendoscope. Complete stone fracture was achieved in 5/21 calculi treated.

Endoscopically controlled intra-corporeal electro-hydraulic lithotripsy
In 1993, Konigsberger et al. [80] used endoscopically controlled intra-corporeal electro-hydraulic lithotripsy by placing a flexible fibroscope with an additional probe inside the ductal system: the shock wave was generated by a sparkover at the tip of the probe electrode placed 1 mm in front of the stone. The clinical trial led to complete stone fragmentation in 20/29 patients with sub-mandibular sialolithiasis [80]. On the basis of the results of *in vitro* and experimental animal studies, Iro et al. [99] criticised this procedure as having a high risk of ductal iatrogenic injuries and being scarcely efficacious at low voltage, and it has now been abandoned on account of possible tissue damage.

Endoscopically controlled intra-corporeal pneumatic lithotripsy
In 1996, Arzoz et al. [82] introduced a rigid 2.1 mm urethroscope with a 1 mm working channel in order to perform intraductal stone fracture using both a pneumoblastic lithotriptor and a laser device under endoscopic control in 12 patients. Pneumatic lithotriptors work by means of ballistic energy and can be likened to a biological "pneumatic hammer" [100]. However, despite the encouraging results achieved in the urological field, the use of pneumoballistic devices in the treatment of human sialolithiasis is considered unjustified because the results in *in vitro* studies suggest a high risk of ductal perforation [100].

Sialoendoscopy

Initially used for diagnostic purposes, sialoendoscopy is now scheduled interventionally in the case of obstructive salivary gland disease [23].

Sialoendoscopy was first described, in 1991, by Katz [101], who used a 0.7 mm flexible endoscope to remove salivary stones with Dormia baskets. Since then, various rigid [82 102 103], semi-rigid and moderately flexible [104] devices, with different diameters, and equipped with working channels and irrigation ports have been developed, and a new more flexible semi-rigid instrument in nitinol has recently been described [105]. According to anatomic studies, 1.2 mm should be the upper limit of the diameter of a sialoendoscope in order to avoid iatrogenic lesions [31]. As the main problem with sialoendoscopy is entering the ductal ostium, various techniques have been proposed to overcome the ostium, including dilatation with lacrimal probes or bougies on guide wires, papillotomy using a CO_2 laser, a sialolithotomy opening, or microsurgical dissection of the anterior ductal portion (the "ductal cutdown" technique) [38 106 107]. The mean duration of diagnostic and operative sialoendoscopy is, respectively, 26 ± 14 and 73 ± 43 minutes [5]; the ductal lumen is irrigated with isotonic saline fluid through the irrigation port during the procedure in order to permit advancement of the endoscopic device and free movement of the operative instruments.

The only absolute contraindication to the procedure is complete distal obliteration of the duct that is impenetrable by the endoscope. The most frequent side-effect is a transient glandular swelling due to the irrigation with physiological solution in 80-100% of cases [1 37 39 104 107], but ductal strictures (2-4% [39 104]) or lacerations (1-8% [5 27]), basket block (6% [5]), infections (2-3% [37 39 104 107]), temporary lingual nerve paresthesia (0.4-0.6% [37 39 104 107]), ranula formation (0.6-0.9% [37 39 104 107]) and bleeding (0.5% [37]) have also been described.

Operative sialoendoscopy in the case of salivary stones

Graspers, miniforceps, Dormia baskets and balloons are mainly used for the endoscopically-controlled retrieval of stones or their fracture into smaller pieces through the working channel or by pushing them forward in parallel to the endoscopic device (Fig. 3). Intra-corporeal laser lithotripsy may be alternatively adopted to fragment the stone before using the graspers or baskets [38].

Fig. 3. Sialoendoscopic removal of submandibular stone by basket.

Endoscopic stone removal is not indicated in the case of deep intra-glandular sialoliths [108] or stones embedded in the ductal wall. The published success rates are 89% for sub-mandibular stones [37 107] and 83-86% for parotid sialoliths [37 107]. Sialoendoscopy is also effective in removing mucus plugs, foreign bodies, polyps, and granulation tissue.

Operative sialoendoscopy in the case of ductal anomalies

Use of saline pressure irrigation, during sialoendoscopy, is usually enough to stretch strictures that are less than half of the duct diameter [41] up to the hilar area [32]. In the case of severe strictures, a sialoballoon with a diameter of < 1 mm (2.5-3 Fr) is inserted through the diagnostic unit [32 38 41]: it is usually inflated to 18 Bar for 90 sec. up to a maximum of 3 mm, then deflated and re-inflated [38 41]. Miniature grasping forceps can also be used in a retrograde fashion along the inner wall towards the stricture [32 38]. An intraductal injection of hydrocortisone and the insertion of a sialostent to avoid recurrences are recommended [38 41].

Nahlieli et al. [38 41] have described an "anti-kink procedure" in which the kink is envelopped by means of a balloon before performing an advancement ductoplasty: the duct is stripped, some millimetres are removed from the anterior portion, and then a stent is positioned, with its anterior edge being sutured to the mucosa and the periostium in order to extend the angle [38 41].

According to Nahlieli et al. [37 41], the endoscopic treatment of strictures has a success rate of 80-81%; with regard to kinks, they documented the complete remission of symptoms in all nine patients submitted to the anti-kink procedure in 2001 [41].

Interventional radiology

Interventional radiology in the case of salivary stones

Interventional radiology was first reported by Kelly et al. [109], who removed a sub-mandibular duct stone using Dormia baskets under fluoroscopic control in 1991. Since then, various techniques have been proposed for the removal both of parotid and sub-mandibular stones, including the use of a coronary angioplasty balloon, a wire loop vascular snare, or an embolectomy catheter under fluoroscopic control.

Fluoroscopically guided stone retrieval is currently the best therapeutic option in interventional radiology, and is indicated for mobile stones located in the middle and proximal portion of the sub-mandibular ductal system [9 110] and parotid duct stones [110]. The reported success rates range from 40% to 100% [9 110-115], and failures are related to unsuccessful stone identification and the presence of fixed or unreachable stones [93 110 113]. The main complications described after radiological stone retrieval include gland swelling (100% [110]), infections (8% [110]), and a gland-impacted basket requiring surgical intervention [110]. The main limitation of the procedure is the administration of ionising radiation.

Interventional radiology for stricture dilatation

In 1992, Buckenham et al. [116] pioneered the use of a coronary angioplasty balloon catheter to dilate parotid strictures using digital subtraction imaging; subsequently, sub-mandibular duct dilatations were also performed [2 111 117].

In 2006, Brown [118] completely eliminated duct stricture in 71.5% of a series of 125 patients by means of balloon ductoplasty, under fluoroscopic control; 9.6% of this group showed residual stenosis at post-operative sialography.

Conservative trans-oral surgical removal of sub-mandibular stones

Seward [119 120] first attempted trans-oral sub-mandibular stone removal from the anterior floor of the mouth in 1968, but

it is only recently that conservative trans-oral release has been judged feasible enough to replace traditional sialoadenectomy in the management of sialoliths located inside the proximal duct or at the hilum [9] [16] [88] [121] [122]. Trans-oral surgical stone removal is currently considered the treatment of choice for deeply sited hilar sub-mandibular stones fixed to the ductal wall that are bimanually palpable and have a diameter of at least 8 mm [9] [16] [122]. The only contra-indication is limited mouth opening.

Stones can be retrieved trans-orally using various techniques: Zenk et al. [88] have proposed an expanding duct excision from the papilla until the stone is visible and then a hilar marsupialisation of the duct after stone release, whereas McGurk et al. [9] [121] [122] and Capaccio et al. [16] preserve the entire Wharton's duct until the hilum and make an incision directly over the palpated stone [9] [16] [121] [122] (Fig. 4); the ductal opening can be sutured with stitches or using a net of Surgicel in order to cover the incision area.
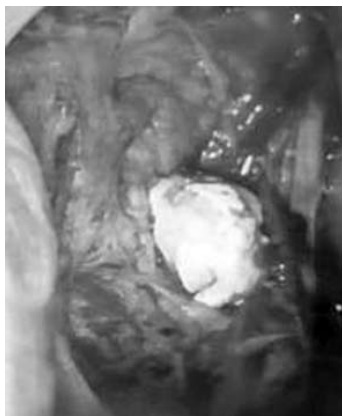

Fig. 4. Delivery of hylar submandibular stone during transoral conservative approach.

The success rate of trans-oral surgery in removing sub-mandibular stones is 82-98% [9] [16] [88] [122]. Post-operative complications include tingling at the tip of the tongue [16] [122], swelling of the floor of the mouth (5% [88]) and lingual nerve injury (1% [88]), and ranulas (2% [88] [122]), strictures (2-5% [88] [122]) and infections (5% [122]) may develop during follow-up. Recurrences have been reported in about 1-10% of cases [88] [123].

Endoscopically assisted removal of parotid and sub-mandibular stones

Baurmarsh and Dechiara [124] were the first to retrieve a parotid stone extra-orally in 1991 and, a few years later, Nahlieli et al. [125] proposed an endoscopically assisted parotid stone retrieval technique. Since then, a number of new endoscopically assisted procedures have been proposed for extra-ductal sialolithotomies, including both intra- and extra-oral techniques: intra-oral sialolithotomy (the so-called "ductal stretching technique" [38]) can be used for both parotid and sub-mandibular stones, and consists of conservative trans-oral stone release by means of an extended dissection under endoscopic control [38]; the extra-oral technique is reserved for impacted or intraparenchymal parotid stones or sialoliths posteriorly situated in the parotid duct system with proximal duct obstruction [38].

It is contra-indicated for severe stenoses or stones located deeper than 6 mm from the outer skin surface [38] [126]. Once the stone has been visualised through the endoscope, trans-illumination is used as a guide to mark its exact location on the outer skin before the stone is exposed and delivered through a 1 cm incision above it or through the creation of a pre-auricular skin flap which preserves the buccal branch of the facial nerve [38] [126].

This combined technique has led to high success rates according to McGurk et al. [126] [127] and Marchal [128], who documented symptomatic relief in 92% of 37 patients with parotid stones [128]. The post-operative complications have been described as: swelling and paresthesia of the peri-auricular skin, infections, post-operative strictures, and damage to the ductal system, sometimes requiring duct ligation [126] [127].

Botulinum toxin therapy

Botulinum toxin therapy, which is already used in the neurological field, has recently been introduced in the management of otorhinolaryngological disorders clinically characterised by an increased salivary flow rate such as drooling, sialorrhea [129-131], and salivary fistulas [132-134]; the rationale underlying the use of botulinum toxin is the selective chemical denervation obtained by blocking neurotransmitter release at the cholinergic parasympathetic nerve terminals of the salivary glands [135]. An injection of botulinum toxin reduces the secretory capacity of the gland while avoiding xerostomia as basal secretory activity is maintained through the adrenergic pathway. Botulinum toxin therapy has also been successfully used to treat sialoceles [136-138], and chronic and recurrent parotitis [131], responsible for obstructive salivary symptoms.

The most frequently used botulinum toxin type A can be injected under electromyographic [134] or colour Doppler US control [131] [138], the latter being preferred since it is thus possible to avoid intra-vessel toxin penetration.

The rare complications reported in the literature are transient paresis of the upper lip, loss of the naso-labial fold, and numbness of the upper cheek [139]. The major limitation of the treatment is the relatively brief duration of its effect (3-4 months, in most cases), which is why patients require a second injection 4-7 months after the first [131].

Conclusions

Over the last fifteen years, increasing public demand for minimally invasive treatment together with the rapid development in medical technology have led to various minimally invasive and conservative methods becoming available for the management of obstructive salivary disease with preservation of the salivary glands.

The use of ESWL under ultrasonographic monitoring began in 1989, and the long-term experience since acquired in centres throughout the world show that it has become the preferred minimally invasive treatment for all parotid stones and may also be used as a primary treatment modality for intraductal and intraparenchymal sub-mandibular stones < 7 mm.

Since its introduction in 1990, considerable progress has been made in diagnostic and operative sialoendoscopy as

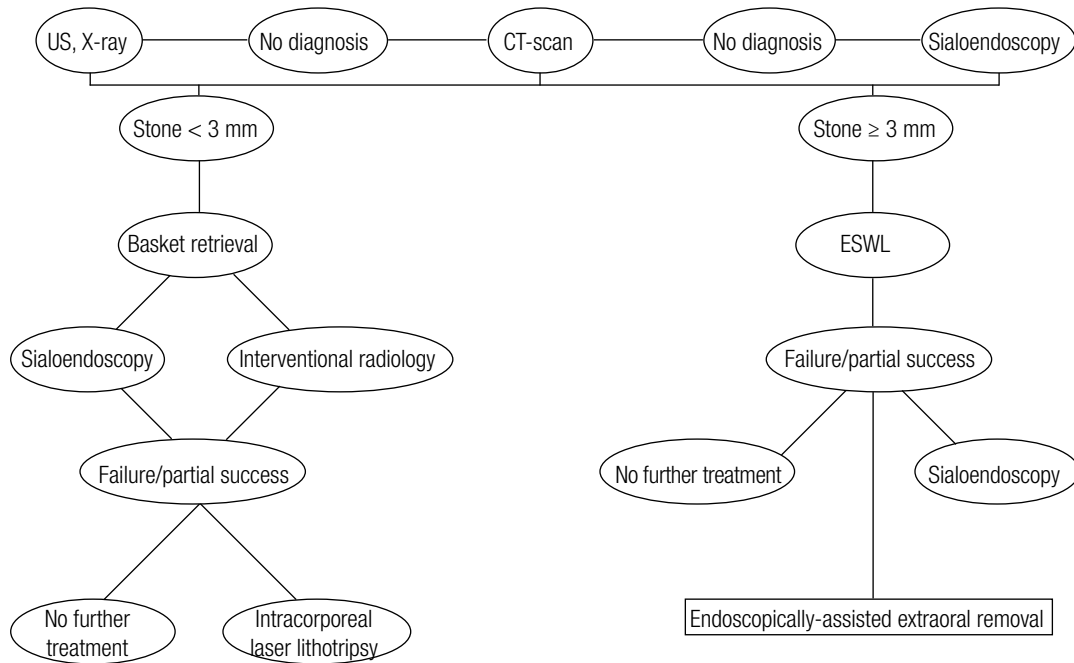**Table I.** Management of parotid obstruction caused by calculi.

```
US, X-ray ── No diagnosis ── CT-scan ── No diagnosis ── Sialoendoscopy
     │                                                        │
  Stone < 3 mm                                          Stone ≥ 3 mm
     │                                                        │
  Basket retrieval                                         ESWL
     │                                                        │
Sialoendoscopy   Interventional radiology          Failure/partial success
     │                                              │                  │
  Failure/partial success              No further treatment    Sialoendoscopy
     │                                                        │
No further treatment   Intracorporeal laser lithotripsy   Endoscopically-assisted extraoral removal
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Table II. Management of submandibular obstruction caused by calculi.

```
US, X-ray ── No diagnosis
                  │
            Sialoendoscopy
                  │
Palpable distal   Mobile ductal   Proximal and hilar    Hilar stone   Intraparenchymal
intraductal       stone ≤ 3 mm    stones > 3 mm         > 7 mm        stone
stone                             and ≤ 7 mm
     │                │                │                   │               │
Endoral          Basket            ESWL              Transoral         ESWL
sialolithectomy  retrieval                           removal
                    │                │              │         │          │
         Sialoendoscopy  Interventional   Failure/partial  Partial   Failure   Failure/partial
                         radiology        success          success             success
                    │                      │              │         │          │
         Failure/partial success      Sialoendoscopy  ESWL and/or       Sialoadenectomy
                    │                      │          sialoendoscopy
Intracorporeal   No further            Failure/
laser lithotripsy treatment            partial success
                                           │
                                   Endoscopically-
                                   assisted transoral
                                   removal
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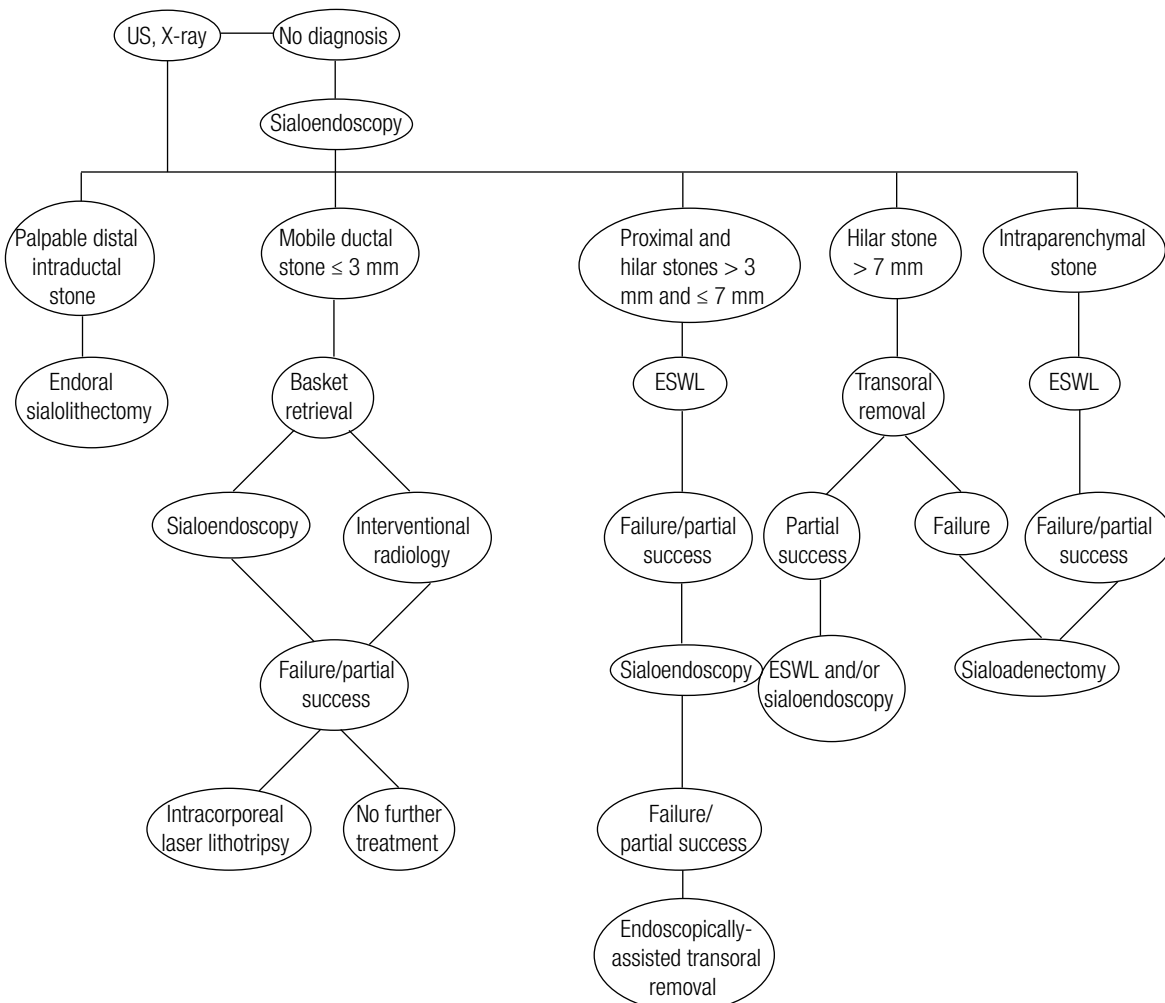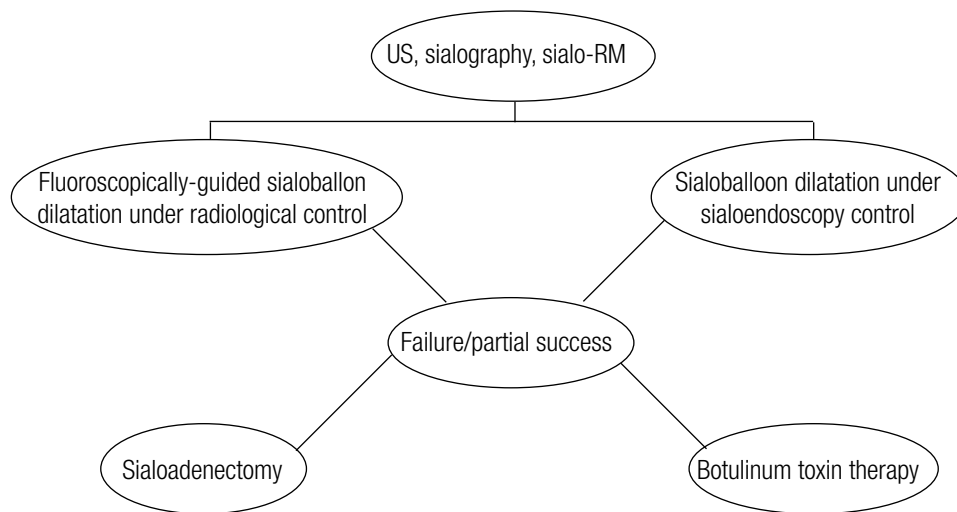
Table III. Management of salivary ductal stenosis.

a result of the development of improved optical systems and endoscopic units. Flexible, rigid, and semi-rigid endoscopes have been used with outer diameters ranging from 0.8 to 2.7 mm, and the latest highly flexible semi-rigid sialoendoscopes appear to be able to adjust to the anatomical landmarks of the salivary duct system. All of these sialoendoscopes have a working channel that allows the introduction of microforceps, a basket or a balloon catheter for the operative removal of single or multiple stones; however, on the basis of published results and personal experience, the major limitation of sialoendoscopy alone is the difficulty in removing stones with a diameter > 4 mm, or located in a secondary branch of the ductal system or after an acute bend in the main duct. Future progress in the field of endoscopic laser lithotripsy, such as the use of erbium laser, will probably soon bridge this therapeutic gap.

Interventional radiology with the basket retrieval of stones under fluoroscopic imaging is currently used (especially in the UK) and has a complete success rate of 71.5%. The long-term experience acquired by the main European and Middle Eastern centres has shown that up to 30% of patients undergoing ESWL (particularly those with large hilo-parenchymal stones) have not had successful results with this therapeutic approach, which has prompted clinicians to investigate new conservative and gland-preserving surgical approaches.

The recently proposed trans-oral removal of palpable hilar sub-mandibular stones by means of extended duct dissection or direct hilar incision (possibly under endoscopic control) now represents one of the main therapeutic options for sub-mandibular stones. Finally, the video-assisted surgical removal of palpable and ultrasonographically superficial stones of the parotid gland has recently been described.

All these minimally invasive procedures are carried out mainly under local anaesthesia and general anaesthesia in Day Surgery or One-Day Surgery and it is likely that further improvement in this field will definitely shift the treatment of salivary stones from an in-patient to an outpatient setting.

The multimodal approach to salivary calculi based on lithotripsy, sialoendoscopy and gland-preserving surgical techniques (Tables I, II) leads to a high overall success rate (about 80%) in terms of stone elimination, and only 3% of patients require gland excision; this justifies combining these time-consuming and relatively expensive techniques as part of the modern and functional management of salivary calculi.

With regard to the management of salivary duct anomalies such as strictures and kinkings (Table III), interventional radiology with balloon ductoplasty under fluoroscopic control seems to be the most adequate technique notwithstanding the use of radiation; in this regard, the use of sialoendoscopy for the rehabilitation of the ductal system is to be preferred, especially in paediatric patients.

Finally, sialoendoscopy alone is to be considered the best therapeutic option for all mobile intraluminal causes of obstruction, such as microliths, mucous plugs, foreign bodies, or polyps. Moreover, sialoendoscopy is useful in the management of inflammatory conditions, such as recurrent chronic parotitis [32] or autoimmune salivary disorders (e.g. the presence of intraluminal granulation tissue in Sjögren's syndrome), by means of ductal lavage and irrigation with steroids and antibiotics.

In the case of failure of any one of the above techniques, and regardless of the cause of obstruction, botulinum toxin injection into the parenchyma of salivary glands using colour Doppler US monitoring should also be considered before deciding on surgical removal of the affected gland.

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