

## HEAD AND NECK

# Doppler ultrasonography before thyroidectomy is not useful to prevent cerebrovascular accident

## *L'ecodoppler pre-operatorio non previene il rischio di eventi cerebrovascolari post-tiroidectomia*

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## SUMMARY

Surgical manipulation of the cervical vascular bundle during neck surgery may promote a thromboembolic event. We evaluated if thyroid surgery is associated with any alterations in the carotid artery wall that would imply an augmented risk of cerebrovascular accident (CVA). A prospective evaluation of a consecutive series of patients who underwent total thyroidectomy was performed. High resolution Doppler ultrasonography (HR-DU) was performed the day before and three days after surgery in asymptomatic consenting patients scheduled for total thyroidectomy. Two hundred patients were recruited. Preoperatively, no hemodynamically significant stenosis (> 70%) was observed. Surgery was delayed in one patient because of asymptomatic subclavian steal syndrome. The remaining 199 patients underwent total thyroidectomy. No modification of preoperative findings was observed at the postoperative HR-DU evaluation. No CVA was observed. In the absence of any significant stenosis, thyroid surgery does not affect the presence and extent of arterial wall disease and the consequent risk of CVA. Thus, screening with HR-DU does not seem beneficial in a generally asymptomatic population without significant risk factors.

KEY WORDS: Thyroidectomy • Thyroid surgery • Complications • Postoperative stroke • Doppler ultrasonography

## RIASSUNTO

*La manipolazione del fascio vascolo-nervoso in corso di interventi chirurgici del collo potrebbe facilitare l'instaurarsi di eventi tromboembolici. Abbiamo eseguito una valutazione prospettica di una serie consecutiva di pazienti sottoposti a tiroidectomia totale. Abbiamo valutato se l'intervento chirurgico di tiroidectomia può comportare alterazioni di parete dell'arteria carotide in grado di determinare un rischio aumentato di accidenti cerebro-vascolari. In tutti i pazienti asintomatici per eventi cerebro-vascolari sottoposti a tiroidectomia totale, è stato eseguito un ecodoppler ad alta risoluzione il giorno prima e tre giorni dopo l'intervento chirurgico programmato. Sono stati inclusi 200 pazienti. Alla valutazione preoperatoria non sono state evidenziate stenosi carotidiche emodinamicamente significative (> 70%). L'intervento chirurgico è stato rimandato in un paziente nel quale è stata posta diagnosi di sindrome del furto della succlavia. I rimanenti 199 pazienti sono stati sottoposti a tiroidectomia totale. La valutazione doppler post-operatoria è risultata invariata rispetto a quella pre-operatoria. Nella serie esaminata non sono stati osservati casi di accidenti cerebro-vascolari. In assenza di stenosi carotidiche emodinamicamente significative, l'intervento chirurgico di tiroidectomia non influisce sulla presenza ed estensione della patologia di parete carotidea e sul conseguente rischio di accidenti cerebro-vascolari. In assenza di significativi fattori di rischio, l'esecuzione dell'ecodoppler di screening non sembra indicato nella popolazione generale asintomatica per eventi cerebro-vascolari.*

PAROLE CHIAVE: Tiroidectomia • Chirurgia del collo • Complicanze • Ictus post-operatorio • Ecodoppler

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## Introduction

Carotid artery stenosis (CAS) is the single most important risk factor for cerebrovascular accident (CVA)<sup>1</sup>. Surgery implies an increased risk of CVA in patients with CAS, perhaps because of the thromboembolic risk related to surgery, but also of the surgical and anaesthetic manoeuvres<sup>2</sup>. It is well known that among general surgical patients, those who undergo neck surgeries are at increased risk of CVA compared with those who undergo non-neck

procedures<sup>1-3</sup>. In addition to surgical manoeuvres, this increased risk could be simply related to the fact that neck hyperextension is often required during surgical procedures on the neck, which could lead to intimal tearing of the carotid artery and thrombus formation or plaque ulceration from turbulent blood flow<sup>1-3</sup>.

Among neck surgical procedures, thyroidectomy is probably the most frequently performed<sup>4</sup>. At present, mortality for this procedure approaches 0% with an overall complication rate that is less than 3% (i.e. compressive

haematoma, recurrent laryngeal nerve palsy and hypoparathyroidism)<sup>5</sup>. Even if CVA following thyroid surgery has been anecdotally reported in the literature<sup>6-7</sup>, perioperative embolic stroke represents the source of malpractice litigation following thyroid surgery in 3% of cases<sup>4</sup>. At least from a theoretical point of view, this operation could imply an increased risk of such a feared complication because of surgical manipulation of the cervical vascular bundle during thyroidectomy. Indeed, retraction of the common carotid artery (CCA) is an important step to expose the trachea-oesophageal groove and safely trace the course of the inferior laryngeal nerve. The risk to reduce vascular flow, with potential ocular or central nervous system damage, is well known and described, as well as the potential to dislodge thrombus or plaque, especially in older patients with a large thyroid gland that requires important retraction and extensive dissection<sup>8</sup>.

However, if this is true for older patients with particular risk factor for CAS, it is not known if surgical manipulation of the cervical neurovascular bundle is a manoeuvre at risk for the general population. This for two main reasons. First, no exact and definitive data concerning the prevalence of the CAS in the general population are available. Secondly, no data concerning the impact of the surgical manipulation during thyroidectomy on the wall of the CCA are available.

We have recently observed a post-thyroidectomy CVA and death in a 45-year-old male patient with an asymptomatic and non-significant carotid stenosis (30-40%). For this reason, we designed this prospective study with the aim to evaluate in a large series of patients aged 40 years or more the prevalence of CAS and the eventual alteration of the carotid wall related to the surgical procedure, in order to define the utility of routine high resolution Doppler ultrasonography (HR-DU) examination to prevent CVA following thyroid surgery.

## Materials and methods

All the patients scheduled for total thyroidectomy (TT) between 1 June 2009 to 30 March 2010 aged 40 years or more were considered eligible. Previous CVA accident, history of CAS or cerebrovascular disease were considered exclusion criteria. Eligible patients provided an informed consent for inclusion in the study. The study protocol was approved by the Ethics Committee of the Università Cattolica del Sacro Cuore, Faculty of Medicine and Surgery in Rome, Italy.

### Study protocol

All recruited patients underwent HR-DU the day before and three days after surgery using the iU22 2D ultrasound system (Philips Electronics, Amsterdam, The Netherlands) with a 7 MHz linear transducer. Patients were examined in the supine position with the neck ro-

tated 45° in the direction opposite the site being examined. To avoid interobserver variability, all measurements were performed by the same operator (A.S.), who was unaware of the subjects' clinical and laboratory findings. The common, internal and external carotid arteries and the vertebral arteries were examined on both sides to exclude stenosis. The intima-media thickness (IMT) of the CCA on each side was assessed. IMT was measured on the far wall at 5, 10 and 15 mm proximal to the carotid bifurcation over both right and left common carotid arteries<sup>9</sup>. The IMT was defined as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line (Fig. 1). Reproducibility of the IMT measurement was acceptable as demonstrated by coefficient of variation (CV) of 3% for the common carotid artery IMT. CV was calculated from two repeated measurements performed in 10 patients and five controls on two different occasions, according to the method described by Bland and Altman<sup>10</sup>. IMT was defined as the mean of the three measurements per side. For the purpose



Fig. 1. Left common carotid artery visualisation (1a) and intima-media thickness (IMT) evaluation (1b) (see text).

of the present study, HR-DU findings of IMT were classified in four different patterns (I to IV). Pattern I included normal wall intima-media thickness (IMT) ( $\leq 0.9$  mm); pattern II wall thickening without plaque (IMT between 0.9 and 1.3 mm); pattern III wall thickening  $> 1.3$  mm atherosclerotic plaque without stenosis ( $< 35\%$ ); pattern IV: wall thickening  $> 1.3$  mm with stenosing atherosclerotic plaque ( $> 35\%$ ). The degree of stenosis was expressed as the percentage of luminal narrowing and the ipsilateral internal/common carotid artery flow velocity ratio was evaluated. Patients were considered to have clinically significant carotid disease if they had stenosis  $\geq 70\%$  in at least one internal carotid artery<sup>11</sup>.

Data were prospectively recorded in a specifically designed database (Microsoft Excel®, Microsoft Corporation, Redmond, WA, USA). The following parameters were collected: age, sex, patient's history and risk factors for CAS if any (hypertension, peripheral vascular disease, diabetes mellitus, smoking habit, atherosclerotic heart disease), preoperative diagnosis, operative time, final histology, complications, and pre- and postoperative HR-DU findings.

#### *Surgical technique*

All procedures were performed by an experienced endocrine surgeon or by a resident operating under supervision. Total thyroidectomy was performed in all cases. The surgical technique has been described elsewhere<sup>12,13</sup>. The neck of the patients is hyperextended on the operating table. During any procedure, minimal lateral retraction of the carotid artery is obtained by means of Farabeuf retractors, in order to expose the tracheo-oesophageal groove and to have a good exposition of the inferior laryngeal nerve, which is usually identified where it crosses the inferior thyroid artery and then followed until its entrance into the larynx.

#### *Surgical outcomes*

Laryngoscopy was performed postoperatively to check vocal cord motility in all patients. Postoperative PTH, calcium and phosphorus levels were measured in all cases. Hypocalcaemia was defined as a serum calcium level below 8.0 mg/dl, even if only in a single measurement. Hypocalcaemic patients received supplementation therapy even if asymptomatic. Supplementation therapy always included oral calcium and vitamin D (calcitriol). Recurrent laryngeal nerve palsy and hypoparathyroidism were considered definitive if they did not recover within 12 months after intervention.

Follow-up evaluation was obtained by outpatient consultations or telephone contacts with patients or their referring physicians. Patients with hypoparathyroidism were followed by periodical serum measurements of calcium, phosphorus and PTH, and on the basis of these findings supplementation therapy was subsequently tapered. Pa-

tients with vocal cord palsy were followed with periodical laryngoscopy and underwent speech therapy when necessary.

## Results

Two hundred consecutive patients were recruited for this study. There were 155 females and 45 males with a mean age of  $54.1 \pm 10.5$  years (range: 40-84). Demographic, clinical, surgical and pathological characteristics of patients are reported in Table I. Overall risk factors for carotid atherosclerotic disease were found in 93 patients (48.2%): smoking in 37, hypertension in 31, diabetes in 9 and combined risk factors in 16 patients.

One hundred and ninety-nine patients underwent total thyroidectomy. In the remaining patient, surgery was delayed because of HR-DU evidence of asymptomatic subclavian steal syndrome, that was referred to vascular surgeons.

Postoperative complications included: 3 transient recurrent laryngeal nerve palsy (1.5%), 54 transient hypocalcaemia (27.1%) and 2 definitive hypoparathyroidism (1.0%). No other complications occurred. Moreover, no postoperative bleeding and/or haematoma requiring reoperation was observed. No perioperative or postoperative CVA was seen.

#### *HR-DU findings*

No preoperative evidence of clinically significant stenosis of internal and external carotid arteries and of the vertebral artery was observed. Preoperative mean IMT was  $1.01 \pm 0.18$  mm (range: 0.9-1.3) on the right side and  $0.98 \pm 0.22$  mm (range: 0.9-1.3) on the left side. On the right side, IMT pattern was type I in 125 patients (62.5%),

**Table I.** Demographic, clinical, surgical and pathological characteristics of patients.

N	200
<b>Age</b> mean $\pm$ SD (years) (range)	$54.1 \pm 10.5$ (40-84)
<b>Sex</b> Males/Females	45/155
<b>Risk factors for atherosclerosis</b> <sup>§</sup>	
Diabetes/smoking/hypertension	13/52/46
<b>Pre-operative diagnosis</b>	
Euthyroid multinodular goitre	97
Toxic multinodular goitre	25
Graves' disease	12
Indeterminate or suspicious nodule	49
Papillary thyroid carcinoma	17
<b>Final histology</b>	
Benign disease	133
Papillary thyroid carcinoma	62
<b>Operative time</b> mean $\pm$ SD (min) (range)	$61.1 \pm 23.5$ (27-140)
<b>Complications</b>	
Transient recurrent laryngeal nerve palsy	3
Transient hypocalcaemia	54
Definitive hypoparathyroidism	2

SD: Standard deviation; <sup>§</sup> 16 patients had a combination of risk factors.

type II in 50 (25.0%), type III in 15 (7.5%) and type IV in the remaining 10 cases (5.0%). Patients with a pattern IV had a mean stenosis of  $41.3 \pm 6.7\%$  (range: 35-55%). On the left side, IMT pattern was type I in 106 patients (53.0%), type I in 55 (27.5%), type III in 27 (13.5%) and type IV in the remaining 12 cases (6.0%). Patients with pattern IV had a mean stenosis of  $41.2 \pm 6.0\%$  (range: 35-50%). Overall, preoperatively no haemodynamically significant stenosis ( $> 70\%$ ) was observed. Postoperative HR-DU showed no modification of pre-operative findings. In particular, postoperative HR-DU patterns were the same as in the preoperative evaluation in all 199 patients. No intimal tearing, thrombus formation, plaque ulceration, or turbulent flow was observed postoperatively.

## Discussion

The incidence of perioperative stroke depends on the type and complexity of the surgical procedure<sup>2</sup>. Perioperative strokes are predominantly ischaemic and embolic<sup>14,15</sup>. The timing of embolic postoperative strokes has a bimodal distribution. Approximately 45% of perioperative strokes are identified within the first day after surgery, while the remaining 55% occur from the second postoperative day onward<sup>2</sup>. Cardiac and vascular surgeries, in particular combined cardiac procedures, are associated with higher risks<sup>2</sup>.

Despite the relative infrequency of stroke complicating general surgical procedures, the incidence of stroke in surgical patients exceeds what would be expected in similar populations not undergoing intervention<sup>16-19</sup>. The incidence of perioperative stroke following general surgical procedures is between 0.08 and 0.7% in patients without a previous history of cerebrovascular disease<sup>2,18,20</sup> and appears to be confined to those with a cardioembolic source or to patients with CAS<sup>15,19,21</sup>.

It is well known that CAS, especially if symptomatic, is a risk factor for postoperative CVA<sup>2</sup>. The estimated prevalence of CAS in the general population over the age of 65 is about 1%<sup>22</sup>. Studies have found that carotid artery stenosis is more prevalent in older adults, smokers, and in those with hypertension and/or heart disease<sup>22</sup>. Research has not found any individual risk factor or clinically useful risk stratification tool that can reliably and accurately identify people with clinically important CAS.

Moreover, asymptomatic CAS has been proposed to be a special risk factor for increased morbidity for patients undergoing unrelated surgery<sup>19</sup>. However, there are currently no definitive data to assess the contribution of CAS to complications in general surgical procedures<sup>23</sup>. In a general surgical population, carotid stenosis of at least 50% has been associated with ischaemic stroke in approximately 3.6% of patients<sup>24</sup>. Indeed, this risk markedly exceeds the risk reported for the general population and patients with bruits<sup>16-18,25</sup> and approximates the 1-year risk

for stroke in patients with asymptomatic high grade carotid lesions<sup>26</sup>. However, a greater degree of stenosis did not result in an increased risk<sup>24</sup>. Moreover, in a retrospective study of 38 patients with a history of vertebrobasilar ischaemia undergoing general surgical operations under general anaesthesia, the risk of perioperative stroke was 6.0% in the vertebrobasilar territory, which is notably higher than the risk for patients with other patterns of cerebrovascular disease<sup>27</sup>.

Similarly, the type and nature of the surgical procedure influence the risk of CVA. Perioperative stroke may result from extracranial carotid or vertebral artery dissections resulting from neck manipulation and hyperextension during anaesthesia and neck surgery or from dislodgement of arterial atherosclerotic plaques from manipulation of extracranial internal carotid or vertebral arteries during neck surgeries<sup>2</sup>.

Among patients who undergo non-cardiovascular procedures, those undergoing head and neck surgery are considered at higher risk of postoperative stroke<sup>2,20</sup>. Nonetheless, only a few studies have addressed the incidence of CVA in patients undergoing head and neck surgery<sup>1,3,28,29</sup>. The higher incidence of postoperative CVA in patients undergoing neck dissection for head and neck surgery is usually attributed to concomitant significant risk factors for CAS (i.e. hypertension, diabetes, peripheral vascular disease, smoking, age, external irradiation), to exposure and manipulation of vascular and neurologic structures and to neck hyperextension and rotation<sup>1,3,28</sup>. In addition, neck dissection may involve haemodynamic instability, blood loss, exposure and manipulation of vascular and neurologic structures of the neck, all of which may increase the risk<sup>1</sup>.

Perioperative stroke in patients undergoing head and neck surgery has been reported in 0.2-4.8% of cases<sup>1-3</sup>. This wide spectrum of incidences could be related to variations in surgical technique, with consequent differences in neck hyperextension and rotation and in different amounts of carotid artery retraction<sup>28</sup>.

Thyroidectomy is the most frequently performed head and neck surgical procedure<sup>4</sup>. Even if CVA following thyroid surgery has been anecdotally described<sup>6,7</sup>, it has been recently reported that embolic stroke represents the source of malpractice claims litigation following thyroidectomy in 3% of case<sup>4</sup>. This rate is the same as for hypoparathyroidism<sup>4</sup>. Obviously, this implies that post-thyroidectomy CVA following thyroidectomy is rare, but not exceptional. The risk of stroke related to retraction of the cervical neurovascular bundle is well known and described, especially in older patients with large goiters<sup>8</sup>. It has also been reported that voluminous cervico-thoracic goitres may determine compression of the common carotid artery with subsequent cerebral ischaemia<sup>30</sup>. Moreover, as already seen, the neck hyperextension required for thyroidectomy may determine extra-cranial carotid or vertebral-artery



dissections or dislodgements of arterial atherosclerotic plaques<sup>27 31</sup>.

Unfortunately, we recently observed a post-thyroidectomy stroke that evolved into the death of a 45-year-old patient with no significant CAS or risk factors. Following this serious complication, we designed the present study with the primary aim of evaluating if surgical manipulation during thyroidectomy is associated any alteration of the CCA wall, which implies a potential increased risk of postoperative stroke. As a secondary aim, we determined the prevalence of CAS in an asymptomatic consecutive series of patients scheduled for thyroidectomy.

Morphological abnormalities of arterial walls can be imaged by B-mode ultrasonography. This high-resolution, non-invasive technique is one of the best methods for detection of early stages of atherosclerotic disease, because it is easily applicable, readily available and demonstrates wall structure with better resolution than magnetic resonance angiography or conventional angiography<sup>32</sup>. Accordingly, ultrasound has been used to monitor the IMT of carotid arteries, which is associated with risk factors for cardiovascular accidents<sup>32</sup>. IMT reflects not only atherosclerosis, but also non-atherosclerotic intimal reaction such intimal hyperplasia and intimal fibrocellular hypertrophy<sup>32</sup>. This differentiation is important because epidemiological studies have shown that wall thickening as depicted by ultrasonographic measurement of IMT is different from atherosclerotic plaque regarding localisation, risk factors and predictive value of cardiovascular events<sup>32</sup>. Standard use of IMT measurement was recently recommended in all epidemiological and interventional trials dealing with cardiovascular disease<sup>32</sup>. All of these reasons lead us to include IMT measurement in the present study.

The results of this study demonstrated that in a general asymptomatic population aged  $\geq 40$  years the prevalence of CAS is very low, even in the presence of at least one risk factor (47% of cases). Indeed, a plaque with stenosis  $> 35\%$  was observed only in a minority of patients (5% on the right and 6% on the left side). Moreover, no significant stenosis ( $> 70\%$ ) was observed. Obviously these findings, even if based on a relatively small patient series, confirmed, in a prospective study design, that screening for asymptomatic CAS does not seem to be beneficial in a general asymptomatic population. This is in agreement with the recommendations of the U.S. Preventive Services Task Force, which recently expressed against screening for asymptomatic CAS in the general adult population<sup>22</sup>. However, the most important finding of this study is that surgical manoeuvres during thyroidectomy do not determine any alterations in the carotid artery wall, at least in the absence of significant stenosis. This is of utmost importance since we strongly demonstrated for the first time with HR-UD examination that neck hyperextension and surgical manipulation during thyroid procedure<sup>33</sup> do not

appear to be associated with an increased risk of CVA. Obviously, manipulation of the cervical vascular bundle during thyroidectomy is minimal and not comparable to that of neck dissection and the operative time is relatively short. Further studies should be performed to verify if longer duration of surgery or more extensive manipulation of vascular neck structures in other kinds of head and neck procedures (i.e. lateral neck dissection) might determine alteration of the carotid artery wall and consequent increased risk of CVA, as suggested by previously published studies on this topic.

## Conclusions

In the absence of significant CCA stenosis, thyroid surgery does not affect the presence and extent of arterial wall disease and the consequent risk of cerebrovascular accidents. Screening with HR-DU does not seem to be beneficial in a general asymptomatic population without significant risk factors.

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