



Preoperative ultrasound mapping of the vagus nerve in thyroid surgery

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Background: Intraoperative neuromonitoring (IONM) in thyroid surgery requires electric stimulation of the vagus nerve to verify correct electrode placement. Classically the nerve is found deep to or in-between the common carotid artery and internal jugular vein, but previous studies have shown that the nerve can sometimes be found superficial to the vessels. Our aim was to determine the incidence of a superficial vagus nerve using ultrasound (US) and study possible clinical factors associated with an anteriorly-located vagus nerve.

Methods: Retrospective study of patients undergoing thyroid surgery (lobectomy or total thyroidectomy) with intermittent IONM. Substernal goiters, locally invasive tumors or bulky lymph nodes were excluded. The vagus nerve was identified at the level of the mid-thyroid lobe on each side on preoperative US performed by two specialized radiologists, and its location according to 6 possible positions in relationship to the common carotid artery was recorded. The anatomic variability of the vagus nerve was analyzed in relationship to patient demographics and thyroid pathology.

Results: Five-hundred twenty-seven patients were included. The right vagus nerve (n=522) was in-between, superficial or deep to the vessels in 92.3%, 6.1% and 1.5% of cases, respectively, and the left vagus (n=517) in 80.2%, 18.6% and 1.2% of cases, respectively, with a statistically significant difference between right and left vagus nerves ($P<0.001$). The type of pathology, size of the dominant nodule or the volume of the thyroid lobe were not correlated to finding a superficial vagus nerve.

Conclusions: The vagus nerve was identified in all cases on US and found to be anterior to common carotid artery at the level of the thyroid lobe in 18.6% of cases on the left and 6.1% of cases on the right. Identifying this anatomic variant preoperatively may facilitate IONM and avoid inadvertent trauma to the vagus nerve during thyroid surgery.

Keywords: Vagus nerve; recurrent nerve; intraoperative nerve monitoring (IONM); thyroid surgery

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Introduction

Recurrent laryngeal nerve injury is a possible complication of thyroid surgery. Permanent paralysis of the recurrent nerve is rare in experienced hands but can significantly impair patients' quality of life. Intraoperative neuromonitoring (IONM) in thyroid surgery is frequently employed as a means to map and test the recurrent nerve and to reduce the rate of recurrent nerve paralysis in some instances (1,2). Localization and stimulation of the vagus nerve is recommended as the first step for accurate IONM. Previous knowledge of the anatomy of the vagus nerve has been based on cadaver studies, with few intraoperative surgical studies of the location of the vagus nerve during thyroidectomy (3). Today, using standard commercially available ultrasound (US) equipment, the vagus nerve can be easily identified and mapped *in vivo* (4,5). Ultrasound has been used to evaluate the vagus nerve in different neurological diseases such as Parkinson's disease and inflammatory polyneuropathy (6-8), and to map the vagus nerve before transcatheter ablation techniques for thyroid nodules (4).

Our previous study showed that the US location of the vagus nerve and intraoperative findings were comparable in 95% of cases (5). This previous study of 82 patients also found that the vagus nerve, instead of being deep to the great vessels at the level of the thyroid lobes, was in a superficial position, anterior to the common carotid artery in 24.4% of cases on the left and in 2.4% of cases on the right. The aim of the present study was to verify these findings in a larger cohort and to identify, if possible, factors associated with this anatomic variation.

We present the following article in accordance with the STROBE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/ggs-21-580/rc>).

Methods

This was a retrospective study of consecutive patients undergoing routine US before thyroid lobectomy or total thyroidectomy with or without central neck dissection or before reoperative surgery for thyroid cancer. Patients with previous external beam radiation therapy to the neck or preoperative laryngeal immobility were excluded, as were patients with substernal goiters, locally invasive cancers or bulky metastatic nodes in the central and/or lateral neck compartments as these factors could impair the visualization of the vagus nerve on US or modify its position. The

location of the vagus nerve was assessed systematically with dynamic US images during preoperative US examination. Preoperative US is routine standard of care for all patients at our institution (9) and the location of the vagus nerve is routinely recorded in a schematic representation in the patients' files since January 2017. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board at Gustave Roussy and individual consent for this retrospective analysis was waived.

US was performed with the Toshiba/Canon Aplio 500 and Aplio i900 ultrasound devices using linear probes at 10–18 Mhz in B mode and Doppler (Canon Medical Systems). The location of the vagus nerve on a horizontal axis at approximately the midlevel of the thyroid lobe (or approximately 2 cm below the lower border of the cricoid cartilage) was recorded according to 6 positions (*Figure 1*): positions 1 and 2 were considered as “in-between” the vessels, positions 3 and 4 were considered as “superficial”, and positions 5 and 6 as “deep” to the great vessels. Patient demographics, benign versus malignant pathology, a primary versus a reoperative setting, nodule size and thyroid lobe volume were analyzed from computerized patient files.

Statistical analysis

Statistical analysis with descriptive statistics and nonparametric analysis was performed using the SPSS software (version 26.0.0.1, 2019 SPSS Inc., Chicago, IL, USA).

Results

Five hundred twenty-seven patients were included, with identification of 522 right vagus nerves and 517 left vagus nerves (for a total of 1,039 nerves). In some cases, before thyroid lobectomy, only one vagus nerve was evaluated with US, but both nerves were evaluated in the same patient in 512 patients. These patients included the 82 patients evaluated in our previous study (5). *Table 1* shows demographics and thyroid pathology.

Table 2 shows the US location of the vagus nerve relative to the great vessels. The right vagus nerve (n=522) was in-between, superficial or deep to the vessels in 92.3%, 6.1% and 1.5% of cases, respectively, and the left vagus (n=517) in 80.2%, 18.6% and 1.2% of cases, respectively, with a statistically significant difference between right and left vagus nerves. On the left there was a higher rate of

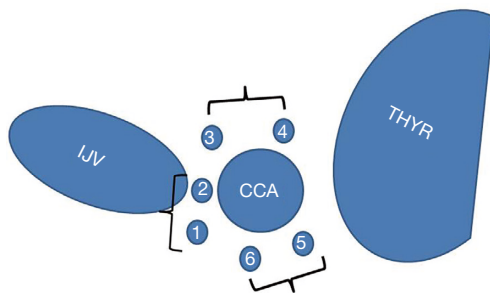


Figure 1 Schematic representation of the location of the vagus nerve on the right side: locations 1 and 2 were “between” the great vessels, locations 3 and 4 were considered “superficial,” or “anterior” and locations 5 and 6 were considered as “deep” to the vessels. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

Table 1 Demographics of the cohort

Demographics	Values
N (female/male)	527 (393/134)
Average age, years (± standard deviation)	48 (±16)
Min–Max	8–87
Median age, years	48
Nerves identified (right/left)	522/517
Cancer	338 (64.1%)
Previous surgery (no/yes)	451 (85.6%)/76 (14.4%)
Nodule side (right/left)	46%/54%
Dominant nodule or cancer size	
Average	28 mm
Standard deviation	±17 mm
Min–Max	2–107 mm
Right lobe volume	
Average	15 cm ³
Standard deviation	±18
Min–Max	1–146 cm ³
Left lobe volume	
Average	17 cm ³
Standard deviation	±23
Min–Max	1–215 cm ³

Table 2 US localization of the vagus nerve as compared to the internal jugular vein and the common carotid artery at the mid-thyroid-lobe level (approximately 2 cm below the inferior border of the cricoid cartilage)

Vagus nerve location	Right vagus (n=522)	Left vagus (n=517)
Between the vessels	482 (92.3%)	415 (80.2%)
Position 1	411 (78.7%)	315 (60.9%)
Position 2	71 (13.6%)	100 (19.3%)
Superficial to vessels	32 (6.1%)	96 (18.6%)
Position 4	13 (2.5%)	66 (12.8%)
Position 3	19 (3.6%)	30 (5.8%)
Deep to vessels	8 (1.5%)	6 (1.2%)
Position 5	0	1 (0.2%)
Position 6	8 (1.5%)	5 (1%)

anteriorly-located vagus nerves: 18.6% versus 6.1% on the right, which was statistically significant (Fisher’s exact test, two-sided P value <0.001). The vagus nerve was anterior to the common carotid artery on both sides in 16/512 patients in whom both nerves were evaluated. Right-left symmetry of the vagus nerve in the same patient (n=512 patients) was observed in 80.7% (413/512), with asymmetry in 19.3% (99/512). Left-right asymmetry was not statistically related to the nodule size or to the diagnosis of cancer. *Figures 2-7* give examples of US images of the vagus nerve and its relationship to the common carotid artery and internal jugular vein (*Figures 2-7*).

Of the total 527 patients, 451 (85.6%) underwent primary surgery and 76 (14.4%) were reoperative cases. For the position of the right vagus nerve, there was no difference between primary and reoperative patients: the rate of a superficial right vagus nerve was 6% in primary surgery patients and 6.6% for reoperative patients (P=0.25). For the left vagus nerve, a superficial location was observed in 18.8% of primary surgery patients versus 14.5% of reoperative surgery patients (P=0.07). Age, gender, nodule pathology, and nodule size did not statistically influence the position of the vagus nerve on the left or on the right (P>0.5 in all instances). The volume of the right lobe did not influence the position of the vagus nerve on the right or the rate of an anteriorly-located vagus nerve on the right (P=0.19

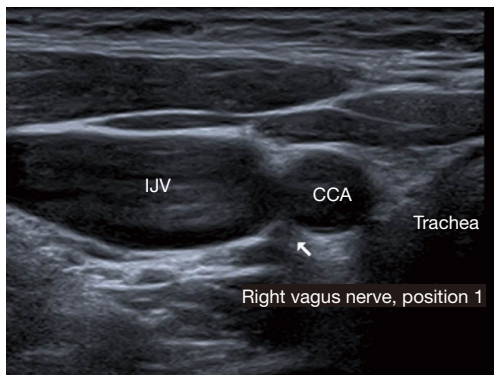


Figure 2 Ultrasound aspect of the right vagus nerve (white arrow) in position 1. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

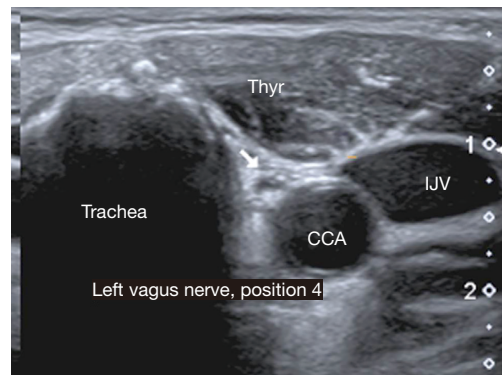


Figure 5 Ultrasound aspect of the left vagus nerve (white arrow) in position 4. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

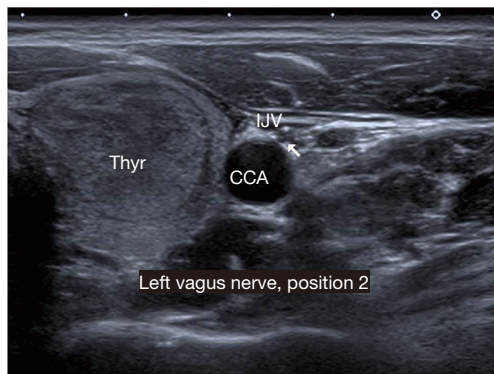


Figure 3 Ultrasound aspect of the left vagus nerve (white arrow) in position 2. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

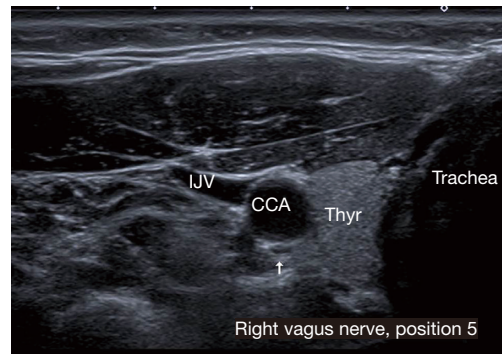


Figure 6 Ultrasound aspect of the right vagus nerve (white arrow) in position 5. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

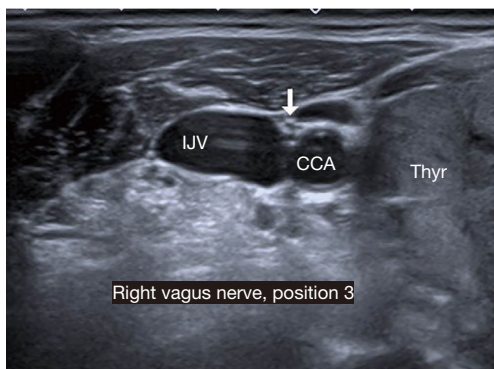


Figure 4 Ultrasound aspect of the right vagus nerve (white arrow) in position 3. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

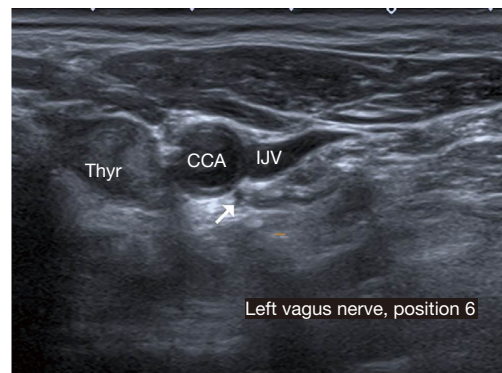


Figure 7 Ultrasound aspect of the left vagus nerve (white arrow) in position 6. THYR, thyroid lobe; IJV, internal jugular vein; CCA, common carotid artery.

and $P=0.3$, respectively). However, on the left, an anterior vagus nerve was significantly related to a lower lobe volume. The lobe volume for cases with an anteriorly-located vagus nerve was 13 ± 19 versus 18 ± 24 cm³ for cases with a vagus nerve deep to or in-between the great vessels ($P=0.036$).

Discussion

The term “vagus” means “wandering”. The vagus, or the tenth cranial nerve, is the longest cranial nerve, coursing from the nucleus ambiguus in the brainstem through the jugular foramen then to the neck and thorax all the way to the abdomen (10). It carries both somatic and visceral afferents and efferents with motor, sensory and autonomic parasympathetic nerve fibers. Its complex functions include regulation of breathing, digestion, heart rate and blood pressure, inflammatory response and symptoms of stress or anxiety, as well as motor functions ensuring pharyngeal and vocal fold mobility, in particular.

In a report dating back to 1915, A. Gibson cites several anatomical studies from the 19th century describing an “abnormal relationship” of the cervical vagus in its relationship to the common carotid artery (11). Gibson described a rare finding in a 59-year-old male subject of both vagus nerves running anteriorly to the common carotid arteries. According to his literature search at that time, only three cases of an anteriorly-located vagus nerve had been described in the literature on the right side, whereas a much larger proportion of anteriorly-located vagus nerves on the left had been observed. In one cited study of 50 cases, “the majority” of the left vagus nerves were anterior to the common carotid artery starting from the level of the upper border of the thyroid cartilage all the way down to the thoracic inlet. In a second study, 11/30 cases had a left anterior vagus nerve. The theory of the day was that the anterior location was related to age. The 8 fetal and infant subjects in a study published by Casali in 1911 and cited by Gibson all had a left vagus nerve coursing anteriorly to the common carotid artery. Of the 24 fetuses studied by Gibson himself, however, none had an anterior vagus nerve on either side. Today, there is still no satisfactory explanation for this “abnormal” anterior location of the vagus nerve. Some have hypothesized that the relationship between the vagus nerve and the cervical plexus may alter the location of the vagus nerve, but the most plausible explanation would seem to be embryological due to variations in the fusion of the carotid sheath with other fascial planes during development. This does not explain, however, the left-sided

predominance of this phenomenon (5,12).

Today’s US technology allows precise visualization of peripheral nerves. The diameter of the vagus nerve in the neck has been widely studied in healthy adults and children and in various diseases (13). The vagus nerve on the right in the mid-neck has been shown to have a larger diameter than the left vagus nerve (14,15). US measurements of the diameter of the vagus nerve have been studied in Parkinson’s disease (6,16), bulbar atrophy (17), inflammatory polyneuropathies (7,18), and neurosarcoidosis (19). US guidance has been largely employed for neurostimulator placement in epilepsy (10,20) and has also recently been employed for microelectrode insertion into the vagus nerve for electrophysiologic microneurography (21).

The trajectory and anatomic relationships of the vagus nerve, particularly pertaining to IONM for thyroid surgery, have not been widely studied. Identification of the vagus nerve is necessary for intra-operative neuromonitoring during thyroid surgery. Dissection of the carotid sheath may put medially- or anteriorly-positioned vagus nerves at risk of inadvertent injury from dissection or from energy devices. Heat diffusion during radiofrequency ablation of thyroid nodules may also put an anteriorly- or medially-positioned vagus at risk, and US localization of the vagus may be useful before thermoablation particularly of large nodules (4). Identification and dissection of the vagus nerve at the level of the thyroid lobes is also required for electrode placement for continuous intra-operative nerve monitoring (CIONM) (22-24). With this technique, the vagus nerve is electrically stimulated at regular intervals during the entire surgical procedure. A decrease in the amplitude and/or an increase in the latency of the electromyographic signal detected by the surface electrodes of the endotracheal tube on the vocal folds is an early sign of nerve trauma. This early “warning” during CIONM may enable the surgeon to avoid further, irreversible injury to the nerve by modifying the surgical maneuvers (25-27).

On US, the vagus nerve in the lower portion of the neck is recognized as a “thin band” in the posterior angle formed between the common carotid artery and the internal jugular vein (28). Already in 1998, Knappertz *et al.* used US to visualize the vagus nerve in 100 normal subjects, and then in 2001 Giovagnorio *et al.* used US to analyze the vagus nerve in 144 normal subjects (28,29). Neither author reported a variation with regards to the classic, posterior position.

Chen *et al.* reported a study of 314 patients (628 vagus nerves) evaluated using US between 2015 and 2016 (30). The efficacy of visualization of the lower vagus nerve was

99.6% (626/628 nerves were seen). At the upper level of the neck in 551 cases, however, they found that 89.8% of the vagus nerves were in a lateral position as compared to the internal carotid artery, 3% were located medially, 1.6% were located anteriorly and 5.4% of nerves were posterior to the internal carotid artery. The left vagus nerve had significantly more anatomic variation in the upper neck than the right vagus which was more often lateral to the artery (92.8% on the right versus 86.8% on the left).

In the study by Park *et al.* identifying the vagus nerve at the level of the thyroid using US, the anterior variation of the vagus nerve was observed in 4.3% of cases (14/326) with a predominance on the left side (10 cases on the left, versus 4 cases on the right) (31). The medial variation was seen in only 1.2% of cases, 3 on the right and 1 on the left.

Dionigi *et al.* studied the surgical anatomy of the vagus nerve in the context of IONM identifying the vagus nerve using electric neurostimulation (3). In 140 consecutive patients (280 vagus nerves) they found that 96% of the vagus nerves were deep to the common carotid artery and internal jugular vein. They noted an “in-between and deep” position in 77% of vagus nerves on the right side and 73% on the left. In only 4% of cases were the vagus nerves superficial to the carotid-jugular axis and no apparent difference between the right and left sides for this configuration was noted. The difference in the rate of anteriorly-located vagus nerves between our study and that of Dionigi *et al.* may be related to the use of an electric stimulation to locate the nerve without performing an anatomic dissection. In the study by Dionigi *et al.* the nerve stimulator was set at 1–3 mA to electrically locate the nerve along the carotid sheath. If the nerve was not easily located at 1 mA, the stimulation was increased to 2 or 3 mA. At this level of stimulation, some diffusion of the electricity may be expected, so the nerve may be a few millimeters away and still be stimulated. This may have introduced some inaccuracy in the exact location of the vagus nerve in this electrical study.

Ha *et al.* defined 4 types of vagus nerves on US mapping: a usual type, in-between the great vessels; an anterior type, superficial to the common carotid artery; a medial type, medial to the common carotid artery; and a posterior type, behind the carotid artery (4). Out of 607 vagus nerves, they found that the in-between type occurred in 91.7% of cases on the right, with the anterior type occurring in 6.9% of cases and the other locations in only 1.3% of cases. On the left, however, they found that the in-between type occurred in only 62.2% of cases and that the anterior type occurred in 35.2% of cases. On the left, the other two types (medial

and posterior) were only observed in 2.6% of cases.

Preoperative knowledge of the location of the vagus nerve can save precious time when stimulating the vagus nerve at the beginning of the thyroid operation (V1, in the guidelines) (1). Preoperative Us may enable the surgeon to avoid unnecessary dissection of the carotid sheath in the case of anteriorly-located nerves and limit the dissection between the carotid artery and the internal jugular vein if the vagus nerve lies medially to the carotid artery. Finding the vagus nerve for electrode placement for CIONM can be faster with the knowledge from preoperative US, as well. Knowing that there is an anteriorly-located vagus nerve may also warn the surgeon, avoiding inadvertent traction, coagulation or blind dissection in the region of the carotid sheath at the beginning of the operation.

Knowing where the vagus nerve is located may also be helpful in remote-access endoscopic and robot-assisted techniques such as the axillary, retroauricular, transoral or bilateral axillary breast approach (BABA). IONM in remote-access surgery seems to be more difficult and less reliable than for open surgery, and CIONM is not frequently reported in these remote-access techniques. A review by Dionigi *et al.* published in 2017 found only 9 studies reporting the use of IONM during robot-assisted or endoscopic thyroidectomy (32). Vagus nerve stimulation according to the IONM guidelines was performed in only 30% of the reported cases. For robot-assisted retroauricular (facelift) and transoral approaches, the standard procedure for IONM with stimulation of the vagus nerve as well as the recurrent nerve was only applied in 76% of facelift robotic cases and 17% of transoral cases in the study by Ji *et al.* (33). Knowing exactly where to dissect and stimulate the carotid sheath at the beginning of the operation or where to dissect to place the electrode for CIONM could facilitate IONM and possibly increase the use of the standardized, recommended procedure. In addition, in the axillary approach, in particular, the robotic arms are placed between the two heads of the sterno-mastoid muscle and may come into close contact with the carotid artery. Knowing that the vagus nerve is superficially located along the carotid sheath may make the surgeon more careful during the dissection and robotic arm placement.

The anteriorly located vagus nerve seems more vulnerable in open surgery due to the fact that the carotid sheath is approached from its anterior aspect through the neck incision. During thermal ablation of thyroid nodules with radiofrequency, laser, microwave or ethanol ablation, the heat (or ethanol) applied to the nodule may in rare instances

go beyond the thyroid capsule and endanger other anatomic structures (34). In these cases, a medially-positioned vagus nerve may be more vulnerable to injury (4). Knowledge of the location of the vagus nerve can be very valuable to physicians performing these techniques, to inform patients and to attempt to avoid spread of heat or ethanol in the presence of a vulnerable nerve.

Our previous study and this current study more closely resemble that of Ha *et al.* In our previous study, the correlation between US localization of the vagus nerve and in-vivo surgical anatomy was exact in 96% cases for the right vagus nerves and in 95% of cases for the left vagus nerves (5). Most interestingly, we found that on US, the anterior position on the left occurred in 24.4% of cases while on the right it was seen in 2.4% of cases. This tendency has been confirmed in the present study with 18.6% of anteriorly-located vagus nerves on the left and 6.1% on the right. The deep variant was seen on US in our first study in 3.6% of cases on the left and on the right, but in the present study this variant was seen in 1.5% of cases on the right and 1.2% of cases on the left.

The discrepancy between our 2 cohorts with 26% anteriorly-located left nerves in our previous study versus 18.6% in the present study may possibly be related to the inclusion of reoperative cases in the present study which had a slightly lower rate of anterior left vagus nerves (14.5%), possibly due to previous dissection of the carotid sheath and shifting of the nerve due to scarring. The other source of discrepancy between our two studies is in the average size of the left lobe. In the present study, on the left, an anterior vagus nerve was significantly related to a lower lobe volume. The lobe volume for cases with an anteriorly-located vagus nerve was 13 ± 19 versus 18 ± 24 cm³ for cases with a vagus nerve deep to or in-between the great vessels ($P=0.036$). In our previous study, the average left lobe volume was 13 ± 18 cm³, so relatively smaller than the average left lobe volume in the present study. A large lobe may possibly displace the vagus nerve more posteriorly or laterally. This finding, however, contradicts the study by Ha *et al.* who found a very high rate of left anteriorly-located vagus nerves (35%) in their cohort of patients undergoing thyroid US for evaluation before radiofrequency ablation. They found that the presence of a bulging nodule was a risk factor for a vulnerable nerve, that is, susceptible to be close to the radiofrequency probe tip, and therefore anterior or medial (4).

Finally, discrepancies among published studies may also be related to the subjective nature of the interpretation of

US images. We did not study the inter- or intra-operator consistency on repeated US exams describing the location of the vagus nerve, so that reports even from the same radiologist may have a certain amount of variability. The location of the vagus nerve actually seems to be a continuum from medial to medial-anterior then to lateral-anterior, lateral, lateral-posterior, etc. so that categorizing the exact location for reproducibility, even into 6 groups as we did, contributes to some variability and subjectivity.

Conclusions

The vagus nerve can be reliably located on US performed before thyroid surgery. The nerve was superficial to the great vessels on the left in 18.6% of cases and in 6.1% of cases on the right, confirming previous US studies. These findings may be useful for surgeons performing IONM and particularly continuous nerve monitoring, to preoperatively map the vagus nerves and avoid trauma to anteriorly-located nerves. Further studies are needed in normal and abnormal thyroids to better understand normal anatomy and the modifications that large lobes and nodules can induce in the anatomy of the vagus nerve and to elaborate a standardized description of the anatomic variations of the vagus nerve for US reporting.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gS-21-580/rc>

Data Sharing Statement: Available at <https://gs.amegroups.com/article/view/10.21037/gS-21-580/dss>

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commercializes a device for intraoperative neuromonitoring. This disclosure did not influence, however, the findings of the study or its' clinical implications. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board at Gustave Roussy and individual consent for this retrospective analysis was waived.

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