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Transient postsurgical gastroparesis is accompanied by reversible changes of the cervical vagus nerve's morphology after neck dissection – an ultrasound study

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Abstract

Aims: During neck dissection (ND), the vagus nerve (VN) may be exposed to manipulation together with common carotid artery and internal jugular vein. The postsurgical gastroparesis was previous related to the VN injury. The aim of our study was to evaluate by ultrasound the VN changes in patients with unilateral and bilateral ND and to establish if there is a relationship between postoperative findings of VN and postsurgical gastroparesis. **Material and methods:** Seventeen patients in which 30 ND (4 unilateral and 13 bilateral) were performed, were enrolled in the study. The VN's area and diameter were measured preoperative (baseline), one week (T1) and one month (T2) postoperative. Gastrointestinal symptoms were evaluated at T1 and T2 phases using the patient assessment of the upper gastrointestinal symptom severity index (PAGI-SYM). **Results:** There was a statistical difference between area and diameters of VN between T1 and baseline ($p<0.001$), and T1 and T2 phases ($p<0.001$), respectively. No statistical differences were detected at baseline and T2 phases in areas ($p=0.934$) and diameters ($p>0.999$). Gastrointestinal symptoms, found at the T1 phase regressed at T2 phase, were correlated with VN area and diameter changes ($p<0.001$). **Conclusions:** VN ultrasound clearly showed the transient dimensional changes of VN caused by manipulation in ND, which may lead to temporary gastrointestinal symptoms due to reversible dysfunction of VN.

Keywords: neck dissection; ultrasound; gastroparesis; vagus nerve

Introduction

Neck dissection (ND) is an important component of diagnosis and treatment in head and neck cancers. The main goal of ND is to identify suspected lymph nodes and to extirpate pathological lymph nodes [1]. In addition to the lymph nodes, common carotid artery (CCA), internal jugular vein (IJV) and vagus nerve (VN) can be also affected during ND [2].

VN is the major nerve of the brain-gut axis [3]. It is well-known that vagotomy and drugs may cause VN dysfunction [4] but gastroparesis may be related to neurological disorders, such as Parkinson's disease [5].

Postsurgical gastroparesis (PSG) is defined as a syndrome characterized by postprandial nausea and vomiting, postoperative gastric atony, distention and upper gastrointestinal discomfort without mechanical gastric outlet obstruction [6]. PSG is a phenomenon observed in upper abdominal surgery, especially in vagotomy and vagus injury [7].

VN is particularly exposed to manipulation during ND, upper gastrointestinal changes being observed in patients in the first month after ND [8]. PSG like symptoms after ND might depend on VN manipulation.

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The aim of this study was to evaluate the possible morphological changes of VN using ultrasound examination in patients undergoing ND and to evaluate the relationship between these changes and potential PSG symptoms.

Materials and methods

Study design and population selection

The study was approved by the local Ethics Committee. Seventeen patients with head and neck malign tumors who underwent ND between August 2018 and April 2019 in Otorhinolaryngology clinic were enrolled. Sign informed consent was obtained from all patients. The criteria for inclusion were age over 18 years and the presence of a malignant mass in the head and neck with indication for ND. Exclusion criteria were diabetes mellitus, Parkinson's disease, VN mass and previous radiotherapy (RT) to the neck. All patients underwent modified radical neck dissection which included lymph node levels I, II, III and IV. The carotid sheath fascia was incised at III and IV level in the neck region. Once VN was identified, the fascia overlying the IJV was peeled off (fig 1).

Vagus nerve ultrasound protocol

VN ultrasound was performed by the same examiner using Toshiba™ Aplio ™ XG ultrasound device with a 6-12 MHz linear probe. At the level of the thyroid gland on the axial ultrasound image, CCA and IJV were found. At neck level III and IV, lower cervical VN was observed between these anatomic structures in the vagina carotica as a hypoechogenic round image and its continuity was depicted according to the literature [9,10]. After that, the probe was rotated with 90º and the VN was examined in longitudinal axis. The VN area was measured in the axial plane and its diameter in longitudinal axis (fig 2).

The VNs were evaluated before ND (baseline), 1 week (T1) and 1 month postoperative (T2). Changes of diameter, area and echogenicity in VN were noted.

Evaluation of gastrointestinal system

All patients were examined by an experienced specialist in gastrointestinal motility disorders using a detailed medical history, physical examination and comprehensive metabolic panel to exclude a pre-existing gastrointestinal system disorder and possible non-PSG gastroparesis. The patients were evaluated with the "patient assessment of upper gastrointestinal symptom severity index" (PAGI-SYM) test to evaluate the gastrointestinal system at 1 week (T1) and 1 month (T2) postoperative phases. During the PAGI-SYM evaluation, day heartburn, regurgitation or reflux, nausea, upper abdominal pain, stomach fullness, bloating, heartburn (lying down), retching, vomiting and upper abdominal discomfort symptoms were investigated as described in the literature at T1 and T2 phases and were scored from 0 to 5 according to symptom severity [11,12] .

Statistical analysis

Data were analyzed using IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). The Shapiro-Wilk test was used to determine whether the distribution of continuous numerical variables was close to normal. In the descriptive statistics, continuous numerical variables were expressed as the mean±standard deviation, while categorical variables were shown as the number of cases and percentages (%).

The statistical relationship of the mean vagus area and vagus diameter between the evaluation periods was

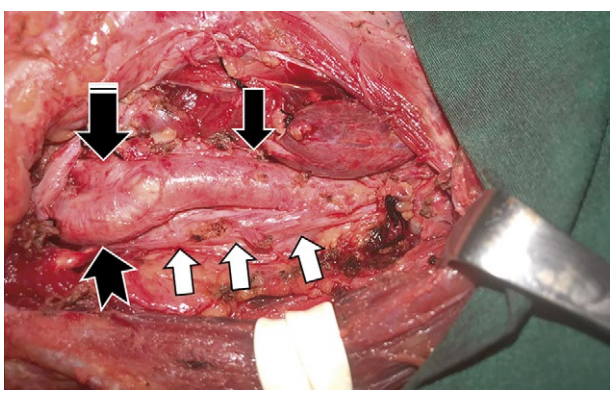

Fig 1. Appearance of neck dissection following removal of the IJV. VN (white arrows) can clearly be seen behind the CCA (black arrow), ECA (black stripe arrow) and ICA (black tailed arrow). IJV, Internal Jugulary Vein; VN, Vagus Nerve; CCA, Common Carotid Artery; ECA, External Carotid Artery; ICA, Internal Carotid Artery.

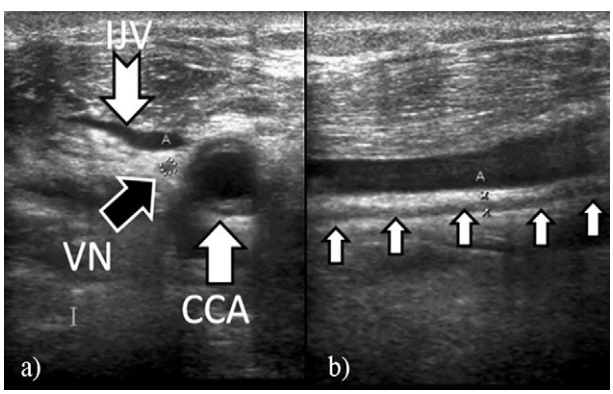

Fig 2. a) Axial neck ultrasound shows the VN (black arrow) as a hypoechoic round image between CCA (white arrow) and IJV (white tailed arrow); b) Longitudinal neck ultrasound shows the longitudinal trace of VN (white arrows) behind the IJV. VN, Vagus Nerve; CCA, Common Carotid Artery; IJV, Internal Jugulary Vein.

evaluated using the Lambda test of Wilks with a Variance Analysis in repeated measurements. For unilateral dissection cases, the dependent t-test was used to determine whether there was a statistically significant difference between the dissected and the non-dissected sides of the neck in terms of the mean vagus area and the vagus diameter. The statistical significance between PAGI-SYM values at T1 and T2 phases was determined by the Wilcoxon signed rank test. A p value of <0.05 was accepted to be statistically significant.

Results

The mean age of the 17 patients was 59.0±13.6 (range: 36-86 years) and 14 patients (82.4%) were men. Four (23.5%) of the patients underwent unilateral ND and 13 (76.5%) bilateral ND. There were statistically significant differences in the mean VN areas and diameters between the baseline and T1 phases (p<0.001) and between T1 and T2 phases (p<0.001), respectively. There were no statistically significant differences between mean VN areas (p=0.934) and diameters (p>0.999) at the baseline and T2 phases (Table I) (fig 3). In patient with unilateral ND, areas and diameters of VN modified only in the dissected side (Table II). All the gastrointestinal symptoms scored from 0 to 5 in PAGI-SYM evaluation had higher scores in T1 comparing with T2 phase (p<0.001) (Table III).

Table I. Vagus nerve area and diameter according to follow-up time

	VN area (mm^2)	VN diameter (mm)
Baseline	2.09±0.62[a]	1.70±0.25[a]
T1 phase	4.35±1.41[a,b]	2.36±0.38[a,b]
T2 phase	2.23±0.77[b]	1.76±0.34[b]
p-value †	**<0.001**	**<0.001**

Data shown as mean±standard deviation. † Analysis of variance in repeated measures, Lambda test of Wilks; a: The difference between baseline and T1 phase was statistically significant (p <0.001); b: The difference between T1 phase and T2 phase was statistically significant (p <0.001). VN: Vagus Nerve.

Table II. Vagus nerve areas and diameters of dissection side and contralateral side in unilateral ND cases

	Dissection side	Non-dissected side	p-value †
VN area			
Baseline	3.25±0.50	2.50±1.29	0.319
T1 phase	6.50±2.08	2.75±0.96	**0.036**
T2 phase	3.25±0.96	2.75±0.96	0.604
VN diameter			
Baseline	2.20±0.22	1.77±0.17	0.099
T1 phase	3.00±0.29	2.02±0.39	**0.029**
T2 phase	2.05±0.19	2.02±0.40	0.934

Data shown as mean±standard deviation. †Dependent t test. VN: Vagus Nerve, ND: Neck dissection

Discussion

Previous published studies have focused on VN injuries in ND but the transient nerve dysfunction due to manipulation without nerve injury was not discussed [13]. We clearly demonstrated that in patients undergoing ND, the VN increases in diameter and cross sectional area in the first postoperative week due to accompanying edema. In these cases, without injury in the VN, the pathologic

Table III. Patient assessment of upper gastrointestinal symptom severity index (PAGI-SYM) scores of the post-operative first week (T1) and postoperative first month (T2) phases of cases

		p-value †
Heartburn (during day)		**<0.001**
T1 phase	3.29±0.69 (2-5)	
T2 phase	0.76±0.56 (0-2)	
Regurgitation or reflux		**0.004**
T1 phase	3.00±0.94 (1-5)	
T2 phase	1.53±0.87 (0-3)	
Nausea		**0.002**
T1 phase	2.76±0.97 (1-4)	
T2 phase	1.35±0.86 (0-3)	
Upper abdominal pain		**0.003**
T1 phase	2.06±1.14 (0-4)	
T2 phase	0.88±0.78 (0-2)	
Stomach fullness		**0.003**
T1 phase	2.24±0.83 (1-3)	
T2 phase	1.18±0.95 (0-3)	
Bloating		**0.010**
T1 phase	2.35±1.11 (0-4)	
T2 phase	1.35±0.79 (0-3)	
Heartburn (lying down)		**<0.001**
T1 phase	3.53±1.01 (2-5)	
T2 phase	1.12±0.49 (0-2)	
Retching		**0.007**
T1 phase	2.53±0.80 (1-4)	
T2 phase	1.53±0.72 (0-3)	
Vomiting		**0.002**
T1 phase	3.12±1.22 (1-5)	
T2 phase	1.47±0.62 (1-3)	
Upper abdominal discomfort		**<0.001**
T1 phase	3.65±0.79 (2-5)	
T2 phase	0.41±0.51 (0-1)	

Data shown as mean±standard deviation (minimum-maximum). † Wilcoxon signed rank test

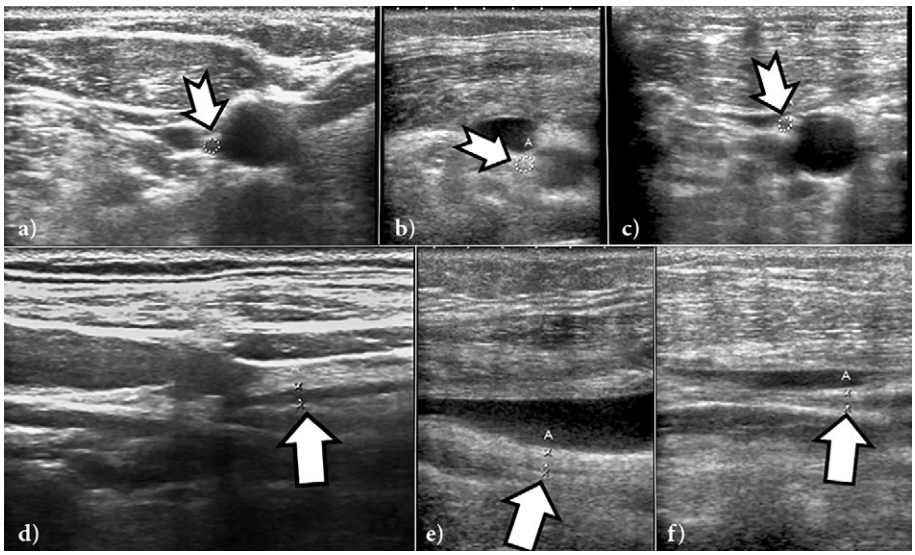

Fig 3. Axial ultrasound shows the area of the VN at a) baseline (2 mm^2), b) T1 (6 mm^2) and c) T2 (2 mm^2) phases (white tailed arrows). Ultrasound also shows the increase of echogenicity of VN due to edema at T1 phase. Longitudinal ultrasound shows the diameter of the VN at d) baseline (1.6 mm), e) T1 (3.1 mm) and f) T2 (1.8 mm) phases (white arrows). VN, Vagus Nerve.

findings resolved in the first month after operation. Our study also depicted that there were no changes of VN dimensions on the non-dissecting side, and significant changes on the dissection side due to VN manipulation at unilateral neck dissection.

We demonstrated that this reversible increase in VN dimensions correlated with the gastrointestinal symptoms associated with reversible PSG and the symptoms regressed due to the resolution of VN edema. The manipulation of the VN during ND is the main cause for the reversible edema, as we established in patients with unilateral ND.

ND is increasingly performed as an important component of head and neck surgery [14]. Following neck surgery, VN injuries can be viewed as surgical complications. VN injuries usually manifest due to IJV ligations [15]. The evaluation of VN in an anterior triangle is especially important for VN injuries [16]. Polistena et al [17] reported that in 1765 patients who underwent thyroidectomy and neck dissection, only one patient (0.14%) had VN injury. Depending on the level of VN injury, vocal cord paralysis, dysphagia and aspirations can appear [1,18].

In the literature, the effects of ND on CCA and IJV have been discussed [19-21]. There are also studies about the patency of IJV in ND [22,23]. In these studies, the lumen, flow velocity, and thrombus presence of IJV after ND were evaluated. There are also studies about morphological changes and function of VN. Grimm et al showed the enlargement of VN in the acute phase of the Guillain-Barré syndrome [24] and Pelz et al depicted the relationship between heart rate variabilities and VN area using ultrasound [25].

Gastroparesis, an entity that develops due to VN dysfunction, can occur after surgery (PSG) or in patients with diabetes mellitus, Parkinson's disease, multiple sclerosis or connective tissue diseases [26,27]. PSG is the third most common type of gastroparesis and accounts for approximately 3-17% of all gastroparesis cases. Gastrectomies, vagotomies and thoracic surgery are the most frequent situation associated with PSG [6]. Particularly after lung transplantation, PSG may become manifest and due to gastroesophageal reflux, microaspirations to the lung and consequently bronchiolitis may occur [28]. The "vagal nerve integrity test" can be used to determine whether gastroparesis is secondary to VN injury or dysfunction [29]. We found that PSG-like upper gastrointestinal system symptoms occurred in the postoperative first week and regressed in the fourth week. The coincidence of these symptoms with edema due to the manipulation of VN and consequently with the increase in VN diameter and area measured confirmed the initial hypothesis.

In this study, the small number of cases was the main limitation. Further studies with more patients would provide a broader understanding of VN dysfunction and related gastrointestinal symptoms in ND. The lack of intra and interobserver reliability, absence of comparison with other imaging techniques and comparison with the level of dissection are other limitations of the study.

In **conclusion**, ultrasound is a useful diagnostic imaging technique for the postsurgical screening of neuronal and vascular structures after ND. The reversible edema in VN producing a temporary increase in the dimensions of VN is responsible for reversible upper gastrointestinal symptoms.

Conflict of interest: None

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