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Original Research Article

# Anatomical Aspects of Thyroid Gland Innervation and their Clinical Significance

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## ABSTRACT

**Background:** The thyroid gland is the largest endocrine gland, and thyroid diseases are common health problems, especially in females. Thyroid disorders like goitre, adenoma and carcinoma can be manipulated mainly through surgical interventions. Nerve fibres provide the innervation of the thyroid gland from two sources: the cervical part of the sympathetic trunk and the vagus nerve, especially from its branches – the superior and inferior laryngeal nerves.

**Material and methods:** 20 human cadavers (17 male, 3 females, age range 30-86 yrs, without any nervous pathology) were dissected in the supine position. The cervical autonomous system was clarified bilaterally through a 'scarf' skin incision made on both sides along the clavicle to its lateral part. Then the vagus nerve, sympathetic trunk, spinal nerves and their branches, and the phrenic nerve were dissected, followed and documented.

**Results:** The number of nerve twigs involved in thyroid innervation is different in each case. In some cases, the branches exiting from the sympathetic trunk dominate over the vagus nerve twigs; on the other hand, vagus nerve branches prevail. If there are additional ganglia in the sympathetic trunk cervical part, the rare cases of its longitudinal distribution were observed. Various situations are drawn in schemes.

**Conclusion:** A thorough and detailed knowledge of thyroid innervation anatomy is essential not only for safe thyroid surgery to minimise postoperative complications, but also for other cervical surgical approaches (like for example, anterior cervical discectomy and fusion).

**KEYWORDS:** Thyroid gland, Innervation, Variability.

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## BACKGROUND

The thyroid gland is the largest endocrine gland, and thyroid diseases are common health problems, especially in females. Thyroid disorders like goitre, adenoma and carcinoma can be manipulated mainly through surgical interventions. Nerve fibres provide the innervation of the thyroid gland from two sources: the cervical part of the sympathetic trunk and the vagus nerve, especially from its branches – the superior and inferior laryngeal nerves [1]. The human thyroid gland receives complex innervation, and its variability is important for both normal function and disease. Variability in thyroid innervation can influence hormone secretion, vascular regulation and may impact disease progression, especially in thyroid cancer.

**Types and patterns of thyroid innervation.** Sympathetic (adrenergic) Innervation: The thyroid is richly supplied with sympathetic nerve fibres, which are found around blood vessels and between thyroid follicles. These fibres can directly influence both blood flow and hormone secretion by acting on smooth muscle cells and follicular cells, respectively [2,3].

**Other nerve types**: In addition to adrenergic fibres, cholinergic and peptidergic nerves are present, contributing to the gland's regulatory complexity [4, 5].

**Innervation in thyroid cancer**. In recent years, tumour innervation has emerged as a significant factor in cancer progression. In papillary thyroid carcinoma (PTC), the density of intratumoral nerves—particularly adrenergic fibres—is significantly increased compared to benign thyroid tissue and follicular thyroid carcinoma (FTC) [4]. This increased nerve density is strongly correlated with extrathyroidal extension and perineural invasion, both indicators of tumour aggressiveness. Multivariate analysis showed that each nerve involved in perineural invasion increased the odds of extrathyroidal invasion by approximately 20% [4].

**Variability and its functional importance**. Inter-individual and interspecies variation: There is significant variability in the density and distribution of sympathetic nerve terminals between individuals and across species. For example, interfollicular sympathetic terminals are more numerous in some species and age groups, suggesting that both genetic and developmental factors shape innervation patterns [3].

**Surgical considerations**. From a surgical perspective, the anatomical complexity of the anterior neck—where the thyroid is located—requires special attention during procedures such as anterior cervical discectomy and fusion (ACDF). Neural structures, such as the recurrent laryngeal nerve (RLN), are at risk during these operations. An enlarged thyroid gland can complicate access to cervical vertebral levels (e.g., C7–T1), necessitating excessive traction that may cause nerve injury [6]. In a documented case, a hemithyroidectomy was intentionally performed before ACDF to minimise risk and enhance surgical exposure, effectively reducing traction-related complications [6]. This example underscores the importance of preoperative evaluation of thyroid morphology and its relationship to surrounding neural structures.

Surgical relevance of laryngeal nerve anatomy. The recurrent laryngeal nerve (RLN) and the external branch of the superior laryngeal nerve (EBSLN) are vital for voice and airway function. Injury to these nerves during thyroidectomy can result in temporary or permanent vocal cord paralysis, hoarseness, and airway compromise. Papachristos et al. (2022) [7] emphasised the evolution of surgical techniques to minimise such risks, including the use of intraoperative nerve monitoring (IONM) and retrograde dissection of the RLN to avoid traction injuries at the ligament of Berry. Their data from over 21,000 thyroidectomies showed that routine IONM significantly reduced the rates of permanent RLN injury (0.3%) and bilateral palsy (0.02%), while also improving identification of the EBSLN, which is often overlooked but crucial for preserving voice quality [7].

**Anatomical considerations in thyroid surgery**. Understanding the detailed anatomy of the thyroid gland and its innervation is essential for safe surgical practice. Singh (2020) [8] provided a comprehensive review of the thyroid's neurovascular relationships, highlighting the variability in the course of the RLN and EBSLN. The RLN may pass anterior, posterior, or between branches of the inferior thyroid artery, making it susceptible to injury during vessel ligation. Similarly, the EBSLN's proximity to the superior thyroid artery necessitates careful dissection to prevent voice-related complications [8]. The review also discussed the importance of identifying anatomical variants such as the Zuckerkandl tubercle and pyramidal lobe, which can obscure nerve pathways and complicate surgery if not properly accounted for.

With all the above-mentioned bearing in mind, the goal of our study was the examination of the variability of thyroid gland innervation morphology.

## MATERIALS AND METHODS

20 human cadavers (17 male, 3 females, age range 30-86 yrs, without any nervous pathology) were dissected in the supine position. The cervical autonomous system was clarified bilaterally through a 'scarf' skin incision on both sides along the clavicle to its lateral part. First, we prepared the vagus nerve (n. vagus), sympathetic trunk (truncus sympathicus), spinal nerves (nn. spinales) and their branches, and the phrenic nerve (n. phrenicus). In older cadavers, the elasticity of the nerves and their strength were significantly reduced. The position of the ganglia and nerves was documented photographically. Tissues identified as ganglia were excised for both histological examination and immunohistochemical analysis and verification. Histological techniques were used to reliably identify ganglia obtained during dissections to determine if the identified structures contained neurons and cell bodies. Ganglia removed during dissections were immediately fixed in 10% formalin solution for 24 hours and then embedded in paraffin. The samples were cut to a thickness of 5 µm and examined under a microscope. All ganglia obtained were stained with haematoxylin-eosin (H&E).

## RESULTS AND DISCUSSION

**A. In some cases** (Figure 1, Figure 2 and Scheme 1) the branches exiting from the sympathetic trunk dominate over the nerve twigs exiting from the vagus nerve. Sympathetic nerve twigs withdraw either directly from the ganglia of the sympathetic trunk, especially from the upper ganglia, or from interganglionic branches. The majority of these fibres lead to the thyroid gland near the upper and lower thyroid arteries (a. thyroidea superior et inferior), along with the periarterial sympathetic plexuses, the branches of which enter the parenchyma of the gland. The second, smaller part of the branches from the sympathetic trunk to the thyroid gland does not accompany the arterial vessels.

**B)** Branches of the sympathetic trunk enter the thyroid gland along the posterior part of the outer surface and spread evenly along it. In other cases (Figure 2, Figure 3 and Scheme 2), among the nerves involved in the innervation of the thyroid gland, the vagus nerve dominates above the branches of the sympathetic trunk. High participation of branches of the vagus nerve to the thyroid gland recedes from n. laryngeus sup. and n. laryngeus inf. The number of branches from the sympathetic trunk to the thyroid gland is small in these cases, entering the thyroid gland either in the assembly of the vagus nerve (Figure 3 and Scheme 2 – right side) or together with the branches of the arteries of the thyroid gland (Figure 4 and Scheme 2 – left side).

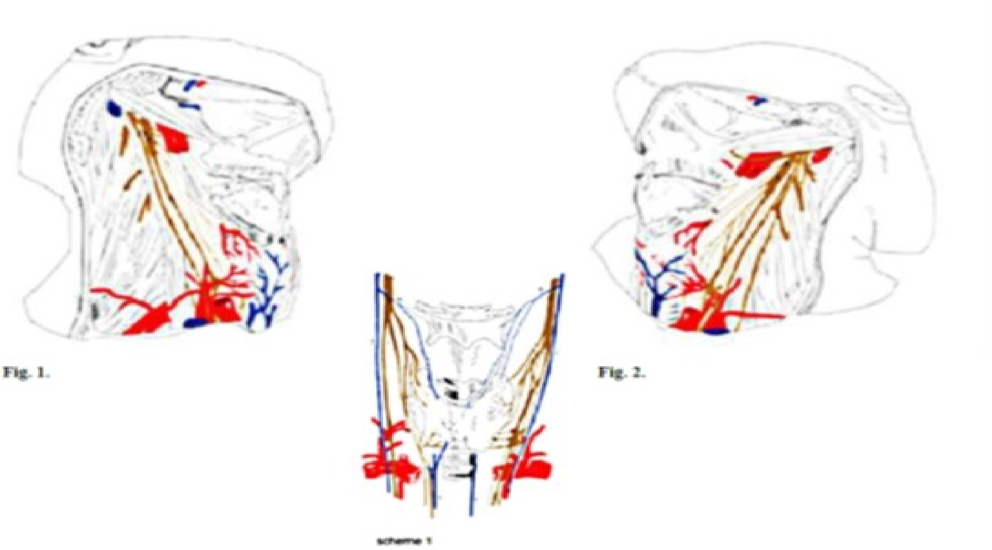
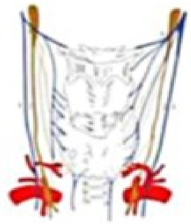



**Figure 1, Figure 2, Scheme 1:** Sympathetic nerve fibres dominance in the thyroid innervation.

The branches exiting from the sympathetic trunk (1) dominate over the nerve twigs exiting from the vagus nerve (2), sympathetic trunk – brown, vagus nerve – blue, upper ganglia (3), the upper (4) and lower (5) thyroid arteries (a. thyroidea superior et inferior).

Fig. 3.



scheme 2

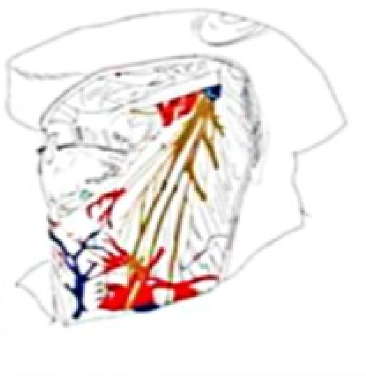


Fig. 4.

**Figure 3, Figure 4, scheme 2:** Vagus nerve fibres dominance in the thyroid innervation. Figure 3 and Scheme 2: Among the nerves involved in thyroid innervation, the vagus nerve (1) prevails over the branches of the sympathetic trunk. Figure 4: Ganglia can be located as paired (1 – middle cervical ganglion) or partially split (2 – superior cervical ganglion).

**C)** If there are additional ganglia in the cervical part of the sympathetic trunk (besides the superior, middle and inferior ones), some peculiarities are observed, especially in rare cases of its longitudinal distribution (Figure 5, Figure 6 and Scheme 3). Ganglia can be placed either evenly (1 – ganglion medium) or partially split (2 – ganglion superior), while doubled interganglionic rami are present. Sympathetic branches to the thyroid gland in these cases usually exit only from the medially distributed ganglia. A large part of them is near the rami thyreoidae superiores et inferiores branches. Some branches also exit from the vagus nerve for the thyroid gland.

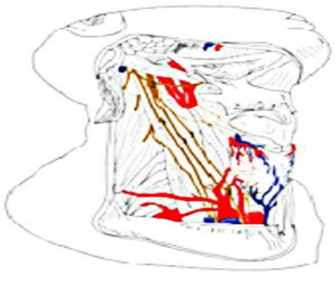
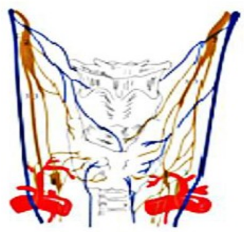


Fig. 5.



scheme 3

Fig. 6.

**Figure 5, Figure 6, scheme 3:** Presence of additional cervical ganglia in the thyroid innervation**.**

Figure 5.: Rare longitudinal distribution of the cervical sympathetic trunk ganglia (sympathetic trunk – brown, vagus nerve – blue). Scheme 3 and Figure 6.: Rare longitudinal distribution of the cervical sympathetic trunk ganglia. (1) ganglion medium; (2) ganglion superior, doubled interganglionic rami; (3) rami thyreoidae superiores (4) et inferiores (5); (6) vagus nerve.

Adrenergic innervation (sympathetic nervous system) plays a modulatory role in thyroid gland (TG) function, although its direct influence is weaker than hormonal control via TSH. Stimulation of sympathetic nerves or administration of adrenergic substances can increase thyroid hormone production (T3 and T4), even though it reduces blood flow to the gland. Norepinephrine, released from sympathetic nerve endings, may influence thyroid function both via blood vessels and directly on thyrocytes. In hypothyroidism, adrenergic fibres and their varicosities (catecholamine storage sites) remain present but show diffuse distribution, suggesting altered neurotransmitter release patterns. Adrenergic innervation is also found in cervical lymphatic vessels and lymph nodes, which are closely connected to the thyroid. This innervation may affect lymph flow and node contractility [9].

Adrenergic innervation is essential for proper thyroid function. It modulates hormone secretion and vascular regulation through catecholaminergic signalling. In experimental models of hypothyroidism, although the structural integrity of adrenergic nerve plexuses and varicosities remains intact, catecholamines tend to diffuse out of these structures, leading to decreased nerve activity and compromised regulatory function [10].

In our study we have identified 3 morphological patterns of thyroid innervation:

**1. type A –** Sympathetic dominance: where the nerve branches from the sympathetic trunk (especially from upper ganglia) are more numerous than those from the vagus nerve. These fibres typically follow the superior and inferior thyroid arteries (a. thyroidea superior et inferior) and form periarterial plexuses that enter the thyroid parenchyma. some sympathetic fibres reach the gland independently of blood vessels.

**2. type B –** Vagal dominance: vagus nerve branches (notably from the superior and inferior laryngeal nerves) predominate. Sympathetic fibres are fewer and often accompany vagal branches or thyroid arteries.

**3. type C –** Additional cervical ganglia: rare anatomical variants with extra or split ganglia in the cervical sympathetic trunk. Sympathetic fibres to the thyroid arise mainly from these medial ganglia and follow the thyroid arteries. Some vagal fibres also contribute to thyroid innervation.

Such differences in the morphological pattern of the thyroid innervation were not yet followed by the researchers.

**Age-related changes**: According to Melander et al. (1975) [3], the number of interfollicular sympathetic terminals can change with age, being higher in young animals and decreasing in older ones, which may affect thyroid hormone secretion dynamics. In our study, we didn´t follow the exact number of nerves (nerve fibres) entering the thyroid gland. And also, we have just focused on the human thyroid gland innervation patterns; we didn´t follow other species (as was done by Melander et al., 1975 [3]). We just observed that the elasticity of the nerves and their strength were significantly reduced in older cadavers.

**Clinical implications**: Our findings are more useful, probably due to the surgical considerations of the approach around the thyroid gland (for thyroid gland pathology itself, or the anterior cervical discectomy and fusion). Rowe et al. (2020) [4] concentrated on the thyroid pathology innervation pattern. Increased nerve density in papillary thyroid cancer is associated with more aggressive disease and extrathyroidal invasion, highlighting the potential role of innervation variability in cancer progression [4].

## CONCLUSION

Variability in thyroid gland innervation is functionally significant, influencing hormone secretion, vascular control, and disease outcomes. Understanding this variability is crucial for both basic thyroid physiology and the management of thyroid diseases, including cancer.

A thorough and detailed knowledge of thyroid innervation anatomy is essential not only for safe thyroid surgery to minimise postoperative complications, but also for other cervical surgical approaches (like for example, anterior cervical discectomy and fusion).

## Abbreviations

**ACDF-** Anterior Cervical Discectomy And Fusion
**EBSLN-** External Branch Of The Superior Laryngeal Nerve
**FTC-** Follicular Thyroid Carcinoma
**H&E-** Haematoxylin-Eosin
**IONM-** Intraoperative Nerve Monitoring
**PTC-** Papillary Thyroid Carcinoma
**RLN-** Recurrent Laryngeal Nerve

## Author Contributions

**Zora Haviarová-** drafting the manuscript, analysis and interpretation of data, **Roman Kuruc-** acquisition of data, critical revising of the study, **Štefan Durdík-** analysis and interpretation of data, **Viktor Matejcík-** conception, design and acquisition of data of the study, critical revising of the manuscript.

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## Conflicts of Interests: None

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