INTRODUCTION

Thyroid gland represents the largest endocrine organ which has an important role in the regulation of almost all vital functions. Thyroid gland disorders are present in a considerable amount of the world population and thyroidectomy represents the most commonly performed endocrine surgical procedure worldwide. Medical teams involved in surgical treatment of these patients can face a series of complications, out of which some might be life-threatening.

MATERIALS AND METHODS

The paper analyzes the most difficult complications that can arise during and after thyroidectomy, presents risk factors for their development and contemporary literature concepts regarding this topic.

RESULTS

Understanding the mechanisms which lead to their occurrence and methods of their prevention, along with adequate and timely application of therapeutic measures represent basic strategies that should be employed in order to reduce the rate of these complications.

CONCLUSION

Adequate preoperative preparation of patients, experienced surgical team and the meticulous technique, early recognition and urgent treatment of complications by the anaesthesiologist, along with multidisciplinary approach, are the basic preconditions for successful treatment in thyroid surgery.

KEYWORDS: anaesthesia, surgery, complications, thyroid gland.

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Introduction

Thyroid gland represents the largest endocrine organ which has an important role in the regulation of almost all vital functions. Thyroid gland disorders are present in a considerable amount of the world population and are the most common endocrine system disorders. According to the American Thyroid Association approximately 20 million Americans have some form of thyroid disease, up to 60% of them are not aware of the disorder and more than 12% of the total population of the United States during a lifetime will develop some form of this organ’s disorder.

Thyroidectomy represents the most commonly performed endocrine surgical procedure worldwide. The main indications for thyroidectomy include hyperthyroidism resistant to the conservative treatment, tumors, compressive and mechanical disturbances and esthetic reasons. As in other surgical branches, various complications (out of which some may be even life-threatening) may be encountered in thyroid gland surgery, so surgical treatment of thyroid gland should be applied only if medically indicated and justified, or if there is no other form of treatment that would give equally good results as surgery.
The aim was to analyze the most difficult complications that can arise during and after thyroidectomy, to present risk factors for their development and contemporary literature concepts regarding this topic.

**Recurrent laryngeal nerve injury in thyroid surgery**

The lesion of recurrent laryngeal nerve (RLN) is well known and potentially disastrous complications of thyroid gland surgical treatment. RLN injury can occur in different ways: by cutting the nerve, by clip or ligature placement on the nerve, by thermal injury, by stripping (traction), by stripping the nerve and by compression due to edema or hematoma\(^{(5)}\). Even if the incidence of RLN injuries in thyroid gland surgery is relatively low, precisely this complication is the main reason for the majority of lawsuits against surgeons specialized for this branch of surgery. This fact emphasizes the significance of this problem\(^{(5)}\). Permanent post-operative RLN lesions occur with an incidence of 0.3 to 4.8% of the cases\(^{(6,9})\), while the incidence of transient RLN injuries varies in the range of from 3 to 6%\(^{(6,9,10})\). Still, not all vocal cord dysfunction should be considered as consequences of surgical RLN injuries. In 0.4 to 3% of cases, they may develop due to trauma during the (difficult) intubation, mucosal erosions, edema or even subluxation of arytenoid cartilage\(^{(11})\).

Intraoperative RLN injuries may appear in the form of paresis and rarely as paralysis of the nerve. Furthermore, injuries may occur on a motor or sensory nerve branch: sensory branches injury is manifested as swallowing disorders (particularly liquids), and injury of the motor branch is accompanied by ipsilateral vocal cord immobility\(^{(12})\).

However, from the anesthesiological and surgical aspect of crucial importance is the fact that whether the injury is unilateral or bilateral. Unilateral RLN lesion results in a modification of voice tone (usually hoarseness) with mild upper airway dysphonia that represents a consequence of laryngeal paralysis with unilateral vocal fold immobility. It is often associated with swallowing disorders problems, but the patient can breathe. After the application of corticosteroid therapy, vitamin B and phoniatic exercises, these problems are improving in a few weeks or months. On the other hand, bilateral RLN injury is a medical emergency, which is, when it comes to thyroid surgery, often much heavier problem than the underlying disease for which the patient underwent surgical treatment. It results in dramatic symptoms of acute dyspnea, which manifests as severe stridor and is caused by a complete adduction of vocal cords. The incidence of this condition is very low - bilateral RLN injury occurs in one of 1,000 patients, in specialized centers\(^{(13})\). Therefore, bilateral lesions of RLN in the form of paralysis, represents an acute and life-threatening condition, since it leads to a lethal outcome in a short period of time if urgent tracheal intubation in order to ensure the airway is not performed promptly. The second step involves the use of high-dose regimen of corticosteroid therapy over the next 48 hours, in order to reduce laryngeal edema, which should be accompanied by broad-spectrum antibiotics\(^{(14})\). Extubation of the patient should be tried after 24-48 hours. If the situation is not improved and bilateral vocal cord paralysis is confirmed by otolaryngology examination, the next step is tracheotomy.

Although RLN injury can be observed during the operation, in most cases it is noticed postoperatively. During the last 15 years neuromonitoring was introduced in thyroid gland surgery practice, for intraoperative RLN identification. However, despite the introduction of this advanced technology, the risk of RLN injuries is decreased, but not completely disappeared. Intraoperative RLN neuromonitoring represents safe technique and has high sensitivity and specificity. However, the results of some studies dispute the fact that the use of neuromonitoring reduces the incidence of RLN injuries compared with standard intraoperative visualization and identification of nerve\(^{(13,16})\).

On the other hand, the results of meta-analysis conducted by Zheng and colleagues showed a marked decrease in the incidence of transitory, but not permanent RLN injury by the use of neuromonitoring, in relation to the identification of the nerve\(^{(17})\). Therefore, RLN neuromonitoring still represents a matter of debates, but most studies agree that it should be used in terms of additional and ancillary technique for the identification and preservation of RLN, especially in patients who are at increased risk for the occurrence of this complication. According to findings from the literature, this group includes patients who undergo re-operation in thyroid surgery, patients who are operated due to thyroid malignancies\(^{(5})\), and total thyroidectomy or re-intervention due to postoperative bleeding\(^{(18})\).

If RLN injury occurs, a cautious, thorough monitoring of such patient is advised, since some of
these injuries represent medical life-threatening emergencies that require immediate treatment and a multi-disciplinary approach.

**Hematoma following thyroidectomy**

Hematoma which occurs following thyroidectomy implies acute bleeding in the area of the surgical wound. It represents medical urgency and absolutely life-threatening condition, and thereby the most difficult surgical complication in this branch of surgery. Fortunately, the hematoma is a rare phenomenon - contemporary literature data indicate that the incidence ranges from 0.19 to 2.1%.[19-21] The physical examination might reveal the hematoma primarily due to presence of swelling in the area of the surgical wound and increased solid mass. Patients might experience symptoms such as feeling of suffocation and breathing difficulties, especially during the neck flexion, along with dysphagia and difficulties in phonation.

In addition, the early signs and symptoms of hypoxia can be present: tachycardia, sweating, agitation and confusion. These might indicate the formation of a hematoma before visible swelling of the neck. Given that the presence of these signs and symptoms is sufficient for the clinical diagnosis and that post-thyroidectomy hematoma is a medical emergency that can quickly lead to a fatal outcome, any further evaluation, in terms of radiographic and ultrasound diagnostics is unnecessary and leads to delay surgery.[22]

The arterial bleeding under infrahyoid muscles can quickly lead to compression of the membranous part of the trachea and consequential asphyxia. On the other hand, due to pressure increase in a tight compartment below the neck muscles disruption venous and lymphatic drainage and laryngo-pharyngeal edema may occur. Securing the airway in such cases represents an imperative. In the case of severe respiratory distress due to airway obstruction, the patient should be immediately intubated. In order to provide relief from hypoxia, onsite decompression by removal of surgical stitches should be done.[23, 24] The persistence of laryngeal edema after the evacuation of hematoma may prolong time to extubation. Sometimes, urgent tracheotomy might be necessary, in order to avoid life-threatening asphyxia.

About half of post-thyroidectomy hematoma occurs approximately 6 hours after surgery.[20] Due to the low incidence of reporting, there are no sufficiently precisely defined risk factors for the development of hematoma after thyroidectomy, although a large number of studies have examined this issue. Thus, the study Weiss and associates that included over 150,000 thyroidectomy patients, showed that the black race, male sex, age over 45 years, inflammatory disease of the thyroid gland, partial thyroidectomy, coagulation disorders and chronic renal failure represent risk factors for the hematoma development[25].

In 2013, Campbell and colleagues conducted a multicenter study, which included 15 medical centers in three countries, and has allocated a total of 207 patients who have developed post-thyroidectomy hematoma. The authors have shown that older patients, male gender, smokers, patients taking antiplatelet/anticoagulant therapy, patients with Graves’ disease, patients who underwent bilateral thyroidectomy and patients who underwent simultaneous parathyroidectomy are at higher risk for hematoma formation. As independent predictors for the development of hematoma after surgery of the thyroid gland, the authors indicated Graves’ disease, benign thyroid pathology, antiplatelet and/or anticoagulant therapy and the increased weight of the thyroid gland[26]. When it comes to the type of surgery of the thyroid gland, opinions are opposed - some studies have showed that the incidence of hematoma is higher after total or near-total thyroidectomy[27], while other studies did not support these results[28, 29].

Similarly, there is a disagreement regarding the usage of antiplatelet/anticoagulant therapy: some studies associate the usage of these medications with the formation of a hematoma[25, 26] while the results of other studies state that as long as the intraoperative hemostasis is meticulously done, the use of these drugs is not relevant[21, 30].

The post-thyroidectomy hematoma occurrence should be precluded. Preventive measures should be started preoperatively, continued during the surgical procedure and in the postoperative period. Preoperatively, patients which are at potentially higher risk should be identified and such patients should be carefully evaluated. Further, the crucial moment should certainly represent the establishment and verification of intraoperative hemostasis, at the end of surgery. In this manner in the thyroid gland surgery the Valsava maneuver is applied. However, although this maneuver helps in detection of venous bleeding, it may represent a double-edged sword: it leads to a significant systemic hypotension, which conceals possible arterial
bleedings, which are much less common, but far more dangerous. Postoperatively, it is necessary to carefully monitor the patient’s vital parameters, along with rigorous control of blood pressure and timely application of antihypertensive therapy, given that postoperative hypertension represents an independent predictor in the occurrence of postoperative hematoma \[^{29, 31}\]. Also, a timely application of antiemetic and analgetic therapy is crucial, since pain and postoperative nausea and vomiting might contribute to the postoperative hematoma development.

It is necessary to apply all preventive measures in order to minimize the risk of hematoma, but a key position should be occupied by a careful and thorough surgical hemostasis. If hematoma develops, early recognition and urgent surgical treatment are essential.

**Difficult airway in thyroid surgery**

The airway management is one of the basic tasks, but also responsibility for the anesthesiologist. On the other hand, difficult airway and/or difficult tracheal intubation (DI) represent the biggest challenges for the anesthesiologist. Failed tracheal intubation entails many medico-legal issues, although the frequency of complications and fatal outcome in securing the airway is quite low: it is estimated that inability to manage the airway results in one severe complication in 22,000 general anaesthesias, or with one fatal outcome per 150,000 general anaesthesias \[^{32}\]. However, approximately 30 to 40% of all anaesthesia-related deaths may be attributed to the inability to resolve the difficult airway \[^{33}\].

The most commonly cited definition of the difficult airway is the one suggested by American Society of Anesthesiologists: “difficult airway represents the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with face mask ventilation of the upper airway, difficulty with tracheal intubation, or both” \[^{34}\]. Since no standard definition of the difficult airway can be identified in the available literature, the incidence of difficult airway varies widely, and depends of branch of surgery and patients characteristics. In a population with no predisposing factors, in general surgery the incidence of difficult airway is approximately 1% \[^{35, 36}\]. In thyroid surgery, numerous studies indicated that the incidence of DI is even several times higher and that is in the range of 5.3 to 16.5% \[^{37-39}\].

The reasons for the increased incidence of DI in surgery of the thyroid gland are numerous, but the crucial place takes thyroid gland disease \[^{40}\], since it is associated with the development of thyromegaly, in a large percentage of patients.

Enlarged thyroid gland (Fig. 1) can lead to the occurrence of DI, since thyroid size affects visualization of the glottis during laryngoscopy \[^{41, 42}\] and enlarged thyroid represents risk factor for DI \[^{43}\]. Also, enlarged thyroid can lead to DI indirectly, by increasing the circumference of the neck. This parameter is an independent predictor of DI occurrence \[^{44, 45}\] in obese and in lean patients \[^{46}\]. Further on, enlarged thyroid gland might lead to tracheal deviation (tracheal shift from the median line for more than 1 cm) \[^{37}\], stenosis or concurrent tracheal deviation and stenosis, (Fig. 2, 3) which, based on results of some studies contribute to the occurrence of DI \[^{41, 47, 48}\].

Severe tracheal stenosis in large, retrosternal goiters might lead to total airway obstruction and to difficult or impossible tracheal intubation \[^{49, 50}\]. Thyroid malign neoplasms by its growth or infiltration of the airway, may lead to airway deformations and thereby to contribute to the occurrence of DI. Also, since they appear nearby laryngeal and pharyngeal structures, they lead to the limited neck
mobility, which is a well-known predictor of DI\(^{(51-53)}\). Excess body weight may be associated with almost all diseases of the thyroid gland\(^{(54)}\) (Fig.4). Obesity is a significant predictor of DI: excess body weight leads to difficulties in securing the airway by reducing the space behind the base of the tongue that is required for good visualization during laryngoscopy\(^{(55,56)}\).

Although tracheal intubation is considered as a relatively safe and the best way for securing the airway, it also carries certain risks of complications, ranging in the spectrum from minor soft tissue injuries, to life-threatening conditions\(^{(59)}\). Since the incidence of airway injuries that occur as a result of intubation ranges from 0.5 to 7%\(^{(60)}\) since 8% of lawsuits against anesthesiologists are exactly complications of the airway management\(^{(61)}\) and since airway injuries that occur as a result of tracheal intubation represent a significant financial burden\(^{(62)}\), the potential complications of tracheal intubation should be prevented. For that purpose it is necessary to timely identify patients who are candidates for DI\(^{(32)}\). Today there are many screening tests and scales to predict DI, out of which the most commonly used, are Mallampati score, upper lip bite test, TMD measurement, inter-incisors gap, and Wilson’s scale. By including many tests in preoperative screening for DI, a higher specificity is gained, but, unfortunately, not enough high sensitivity. However, DI is not easy to predict, for a simple reason - no scale (test) for predicting DI, created to date is ideal.

Disruption of gas exchange in a period of just a few minutes can lead to catastrophic consequences, so DI remains a significant source of morbidity and mortality in every-day anesthesia practice. Detailed and careful preoperative evaluation by the anesthesiologist is essential in preventing these complications.

**Thyroid storm**

Thyroid storm represents an urgent condition which is defined as acute, rapid deterioration (decompensation) of hyperthyroidism. Most often this hypermetabolic state results as a consequence of undiagnosed thyrotoxicosis under the conditions of another illness or after surgery. A few available literature data do not provide precise information on the epidemiological characteristics of this condition, since there are only individual series. Thus, a study conducted in Japan in 2012 showed the annual incidence of thyroid storm of 0.20 per 100,000 hospitalized patients and mortality rate of approximately 10%\(^{(63)}\). In undiagnosed or in untimely diagnosed cases the mortality is 100%.
Severe underlying illness and patients’ unpreparedness for surgery are stated as two main reasons for the occurrence of thyroid storm.

This life-threatening condition occurs either as a consequence of excessive release of thyroid hormones, which leads to adrenergic hyperreactivity, or as a result of altered peripheral tissue response to the effects of thyroid hormone, all due to the existence of precipitating factors, such as infection, stress, myocardial infarction or trauma. Although the incidence of thyroid storm is drastically reduced in thyroid gland surgery, due to the advances in diagnostic and therapeutic procedures, this condition can occur in patients with unregulated hyperthyroidism when undergoing surgical procedures in other surgical branches.

The clinical presentation of thyroid storm includes sudden tachycardia, hyperthermia, consciousness disorders, agitation and other symptoms by the gastrointestinal and cardiovascular system. When surgical procedures are concerned, thyrotoxic storms occur most often 6-24 h following surgery, but can also occur intraoperatively. In those cases, which rarely can be seen mostly in insufficiently prepared patients with hyperthyroidism in thyroid surgery, a significant problem in terms of diagnosis occurs: in patients under general anesthesia, out of large number of symptoms and signs which characterize this state, only tachycardia and hyperthermia are apparent.

This fact might partially explain high mortality rates in intraoperative thyroid storm. Therapy of this condition should be promptly initiated - as soon as diagnosis is suspected and most commonly requires multidisciplinary approach in an intensive care setting. Treatment implies urgent application of β-blockers, administration of antithyroid drugs (methimazole and propylthiouracil) and corticosteroids, along with adequate hyperthermia management and supportive and resuscitative measures. Identification of the underlying precipitating factors and its management also play a crucial role in complex therapy of thyroid storm. Still, prevention of this condition by thorough preoperative evaluation and preparation of patients with thyroid gland disorders represents significant step in reduction of mortality rates. Since thyroid storm may occur in patients who have survived it, these patients should receive definite therapy for their underlying hyperthyroidism.

**Chyle leak**

Chyle leak following neck surgery is uncommon complication of total thyroidectomy with, most frequently, lateral neck dissection. The incidence rates vary widely in a range from 1 to 8.3% and depend on the extent and type of the procedure. This complication results as main thoracic duct injury or as injury of smaller lymphatic channels. The severity of leakage determines clinical presentation and severity of this complication. Due to chyle accumulation in surgical wound, severe electrolyte and metabolic disturbances, protein depletion, malnutrition and even impaired immunity might develop. Also, chronic lymphatic fistula might arise.

Early diagnose is crucial, since if diagnosed intraoperatively, the leakage site can be immediately ligated. Postoperatively, the majority of leaks can be successfully conservatively managed, but if complicated with lymphatic fistula or cyst reoperation is most often needed. Although unusual, this complication should be considered in the differential diagnosis in patients with neck swelling following thyroidectomy.

**Complications in different techniques of thyroidectomy**

Due to significant technical development and the development of surgical techniques during recent decades, minimally invasive video-assisted and techniques of robotic surgery for thyroidectomy have been introduced for surgical treatment of thyroid gland diseases. These approaches are less invasive, reduce the size of incisions and according to some studies can be used equally safely as methods of conventional thyroid surgery. Also, these techniques are characterized as safe, less painful and carry along significantly higher grades regarding patients’ satisfaction.

Still, some authors state that minimally invasive video-assisted techniques imply more traumatic manipulation of the thyroid and the extraction of the thyroid lobe through a small skin incision might result in rupture of thyroid capsule with spillage of thyroid cells. This is highly significant in malignant thyroid diseases and explains why some authors entitle this technique as “minimally invasive.”

On the other hand, no major differences regarding the most difficult complications between open approach and minimally invasive video-assisted thyroidectomy techniques can be identified.
Similarly, due to trauma of the tissue along the route to the thyroid, robotic thyroidectomy might be accompanied by the complications which are not encountered in conventional thyroid surgery, such as conversion to an open procedure and injury to the carotid artery, jugular vein, brachial plexus, vagus nerve, esophagus and skin flap perforation. Rates of permanent RLN injuries are comparable with rates of this complication in conventional thyroid surgery, but the incidence of postoperative hematoma is lower in robotic surgery.

Based on the available literature data it seems that recently developed surgical techniques can be equally safely performed as conventional thyroidectomy, since rates of complications are similar. Still, since this issue represents a matter of debates, further high quality randomized clinical trials are needed in order to resolve this dilemma.

**Conclusion**

Thyroid gland surgery is highly-specific and specialized surgical branch. As for other surgical procedures, the same rule is applied in thyroid surgery: complications are possible, and sometimes even inevitable. Fortunately, in thyroid surgery, severe and life-threatening complications occur rarely. Still, some of those complications might lead to a fatal outcome in a short period of time.

Experienced surgical team, early recognition and prompt treatment of complications by the anesthesiologist, along with multi-disciplinary approach represent the basic preconditions for the successful treatment in thyroid surgery.

**References**

The most difficult complications in thyroid surgery


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