

## Long-term esophageal motility changes after thyroidectomy: associations with aerodigestive disorders

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**SUMMARY: Long-term esophageal motility changes after thyroidectomy: associations with aerodigestive disorders.**

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**Background.** Patients undergoing thyroidectomy often complain aerodigestive disorders. In a previous study we showed the associations between voice impairment and proximal acid reflux, swallowing impairment and Upper Esophageal Sphincter (UES) incoordination and the decrease in UES pressure in thirty-six patients observed before and soon afterwards uncomplicated thyroidectomy. This study investigated the state of post-thyroidectomy esophageal motility changes and its associations with these disorders after 18-24 months.

**Patients and methods.** The thirty-six patients prospectively recruited

according to selection criteria (thyroid volume  $\leq 60$  ml, benign disease, age 18-65 years, previous neck surgery, thyroiditis, pre- or postoperative vocal cord palsy) underwent voice (VIS) and swallowing (SIS) impairment scores, esophageal manometry and pH monitoring once again.

**Results.** After 18-24 months, both VIS and SIS recovered (respectively:  $p=0,022$ ;  $p=0,0001$ ); UES pressure increased ( $p=0,0001$ ) nearing the preoperative values. The persistence of swallowing complaints were associated with the persistence of esophageal incoordination ( $p=0,03$ ); the association between voice impairment and proximal acid reflux was confirmed ( $p<0,001$ ).

**Conclusions.** Our study confirms that aerodigestive disorders after uncomplicated thyroidectomy, largely transient, are strictly connected with upper esophageal motility changes. In this viewpoint, the innervation of upper aerodigestive anatomical structures (larynx, pharynx, upper esophagus) and its variations should be focused.

**KEY WORDS:** Thyroidectomy - Dysphagia - Swallowing impairment - Voice impairment - Aerodigestive symptoms.

## Introduction

Thyroidectomy, that may be performed for benign or malignant nodules as well as autoimmune disorders (Grave's disease or, in selected cases, Hashimoto's thyroiditis), is the most diffused surgical practice for endocrine disorders (1-3). As commonly estimated, a high rate of patients (even the 10%) undergoing thyroid surgery experience a recurrent laryngeal nerve (RLN) palsy, transient or definitive (4-7). Aerodigestive symptoms,

such as dysphonia and dysphagia, commonly affect patients with unilateral RLN damage: respectively, more than 50% and 80% (1, 8-10). The RLN, as well as the external branch of the superior one (EBSLN), are both concerned during thyroidectomy: the first one is associated with the posterior surface of the thyroid lobe, the second one is closely associated with the upper thyroid vascular pedicle, so it can be injured during the manoeuvres of preparation of the upper pole of the gland (1). The EBSLN innervates the cricothyroid muscle, so it allows the stretching of vocal cords; moreover, the internal branch of the superior laryngeal nerve (SLN) provides sensation of the supraglottic space and vocal cords (2-3). The RLN has contingents of motory (abductor and adductor) fibers devoted to vocal cords, as well as sensory branches for the larynx (1-4). The posterior branch of RLN is anastomosed with a contingents of fibers of the SLN: this is the main anastomosis between both systems. Other anastomoses are described at the cricoarytenoid, thyroarytenoid and interarytenoid regions (1, 11). These anatomic assumptions explain the voice and swallowing com-

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plaints that appear as a consequence of a laryngeal nerve (inferior and superior) lesion, but it is well known that, in most cases, the vocal and swallowing disorders appear even after uncomplicated thyroidectomy (3, 8, 12). Symptoms such as hoarseness, sensation of a “lump”, a “too-tightly buttoned shirt collar”, a “foreign body”, “beeing strangled”, “obstacle during swallowing” or cough are frequently described after thyroidectomy, even in absence of evident laryngeal nerve damage (12-15). Several causes have been assumed to explain the association between thyroidectomy and voice and swallowing disorders. In a previous study (3), we specifically examined some functional changes in esophageal motility that were observed after uncomplicated thyroidectomy in a short time of observation (30-45 days after surgical operation). The present long-term study complete the investigation evaluating the same esophageal motility changes in the same sample of patients 18-24 months after the thyroidectomy.

## Patients and methods

The patients had been scheduled because of a nodular thyroid disease (solitary nodule, multinodular goiter) for total thyroidectomy from January 2010 to September 2011. The Table 1 summarizes the exclusion criteria, those could be noticed in the preoperative period as well as after thyroidectomy, previously stated. The Table 2 describes the demographic data of the patients enrolled in the study. The thyroid volume had been calculated in the preoperative period by applying the ultrasound measurement:  $ld \times td \times th \times 0,5$  for each lobe ( $ld$  = longitudinal diameter of the lobe;  $td$  = transversal diameter;  $th$  = lobe thickness;  $0,5$  = correction factor for transforming the obtained volume from parallelepiped to an ellipsoid). The autoimmune thyroiditis and the carcinoma had been excluded with conventional clinical, laboratory and pathologic findings. The patients had undergone a preoperative and a postoperative evaluation of vocal fold function. The clinical and laboratory follow-up were started by a referral endocrinologist. All the patients had been operated on by the same surgical team (2 surgeons among G.G., G.S., N.C.P for each procedure) and with the same surgical criteria concerning the dissection and the preservation of the laryngeal nerves and the parathyroid glands, without using a nerve monitoring. The conventional “knoth tie” technique had been applied for larger goiters; according to conventional inclusion criteria (16) in a total of 16 case a “minimally incision” procedure had been performed, 9 of which were MIVATs. In these specific cases, an energy-based surgical instrument had been used (17).

All the patients enrolled in the preliminary study performed at our institution underwent a new comple-

TABLE 1 - EXCLUSION CRITERIA.

- |   |
|---|
| - Total thyroid volume $\geq$ 60 ml   |
| - Nodules in the V or VI category according to Bethesda System                                  |
| - Previous neck surgery   |
| - Severe thyroiditis  |
| - Hyperthyroidism   |
| - Pre- or postoperative vocal cord palsy  |
| - Previous laryngeal disease requiring surgery  |
| - Pulmonary disease   |
| - Smoking habit   |
| - TSH out of the normal range (0.3-3 mU/L) four weeks after surgery                             |
| - Postoperative hematoma  |
| - Hypocalcemia (calcium value $\leq$ 8 mg%) / need for calcium therapy four weeks after surgery |

TABLE 2 - DEMOGRAPHIC DATA.

<i>Age, y</i>	
Range	26 - 65
Mean ( $\pm$ SD)	48,6 (10,6)
<i>Sex, No.</i>	
Male	10
Female	26
<i>Technique, No.</i>	
Conventional	20
Open mini-incision	7
MIVAT	9

te long-term follow-up 18-24 months after the first enrolment.

The voice and the swallowing functions were evaluated with 2 specific questionnaires (Voice Impairment Score, VIS, and Swallowing Impairment Score, SIS) able to evaluate a wide range of symptoms reported by patients (3, 18, 19). The pressures of the esophageal sphincters (lower, LES; and upper, UES) and the esophageal motility were measured with the same precautions for avoiding pharmacological interferences with the esophageal motility and acid gastric secretion (3). The measurements of this long-term study were performed with the same instruments (Narco Bio System MMS 200 manometer, International Biomedical Inc, Austin, Texas; electrodes in connection to an International Biochemical Model 745-0100, International Biochemical Inc, Austin, Texas; multilumen manometric probes, Arndorfer, Greendale, Winsconsin, that were spaced at 5 cm from

TABLE 3 - TRENDS OF AERODIGESTIVE SYMPTOMS.

Symptom	Preoperative	1 month after surgery	Long-term	p-value
SIS = 0 *	22,22%	44,44%	58,33%	< 0,001
VIS = 0 *	44,44%	58,33%	69,44%	= 0,001

\*Note that the higher is the disorder value, the more symptomatic is the patient.

one another; the MicroDigitrapper, Medtronic Functional Diagnostics, Shoreview, Minnesota for pH monitoring). The criteria for classifying the relaxation response to the swallowing of the UES and LES was the same even at long-term evaluation: *complete* if the pressures of the esophageal sphincters decreased to the baseline pressure, *incomplete* if its decrease did not reach the baseline value, *absent* if it did not change. The pH monitoring was analyzed according to standard measurement criteria (DeMeester Score, 20).

During the period between the operation and this control, the patients did not underwent logopedic treatment.

The endpoints of the present study were to evaluate the long-term trend of the variables that have had a significant change in the early postoperative period in comparison with the preoperative one. Then, the patients underwent once again the questionnaires investigating the voice and the swallowing impairment (VIS and SIS); moreover, they underwent a pH esophageal monitoring and an esophageal manometry for investigating the changes associated with these symptoms. Finally, the changes in UES pressure were also investigated.

Institutional Ethical Board (Comitato Bioetico A.O.U.P.) approved the present updating study.

### Statistical analysis

The non-parametric Freedman test was applied for the comparison between multiple groups (preoperative, early postoperative and long-term) concerning the medians of UES values, VIS and SIS scores. The Cochran test was applied for verifying the association between voice and swallowing impairment, esophageal incoordination and acid reflux. The data were collected in a dedicated database (Microsoft Excel®, Microsoft Corporation, Redmond, WA, USA) and analyzed by a professional statistician. The IDE RStudio (version: 0.98.945), with the software R, version 3.1.0. (2014.04.10) was used for the statistical analysis.

## Results

The results of VIS, SIS and UES pressure (preoperative; 30-45 days after operation; 18-24 months after

operation) were recorded in three box plot graphics. A Freedmann non-parametric test was used with the aim to identify the significance in the changes of the results of each class of measurements. Concerning the SIS evaluation, the difference of results before, 1 month and 18-24 months after thyroidectomy was significant ( $p=0,0001 < 0,05$ ). Moreover, the average of patients complaining aerodigestive symptoms decreased during the time (Table 3), concerning the voice (Figure 1) as well as the swallowing (Figure 2).

UES pressure showed a long-term increasing ( $p<0,0005$ ) and neared the preoperative values (Figure 3).

Moreover, at the long-term control, 20 patients improved the SIS, but 16 had not a variation of this score. All the three patients who showed a persistence of UES incoordination were included in this group. This association should be considered statistical significant ( $p=0,03$ ).

The correlation between the 23 patients that complained a persistence or impairment of voice symptoms and the 13 who had an esophageal acid proximal reflux an was confirmed ( $p<0,001$ ).

Finally, it should noted that the 11 patients in which the VIS increased (worsened) at the long-term control, had at least one between reflux or UES pressure decrease.

## Discussion

The aerodigestive disorders associated with uncomplicated thyroidectomy are reported in several studies (2, 12-14). As commonly observed, they can also precede the surgery, and, in some cases, they can be explained as a consequence of the thyroid disease (3). These complaints, together with other, may affect the quality of life (21-23). Both symptoms are very frequent even in non-thyroidectomized patients (24, 25). In our previous study we investigated these symptoms in both clinical and functional views. The causes previously appealed were orotracheal intubation, changes in laryngeal vascular net, cricothyroid dysfunction, denervation of neck muscles, neck pain or anxiety. The role of the type of endocrine neck disease, the technique used and the extent of surgery play an unclear role in the origin of these symptoms; neither the possible advantages of minimally-invasive techniques have been clarified (5, 15, 26-33). Another possible risk factor for aerodigestive complaints is the intraoperative bleeding (34). The hemostatic tools are usually used at our Institution with the aim of reducing the incidence of this event this as well as possible (35-37), but we have not investigated yet the possible advantages of this practice in reducing these symptoms. A recent study carried out with ultrasonic analysis of laryngeal movements,

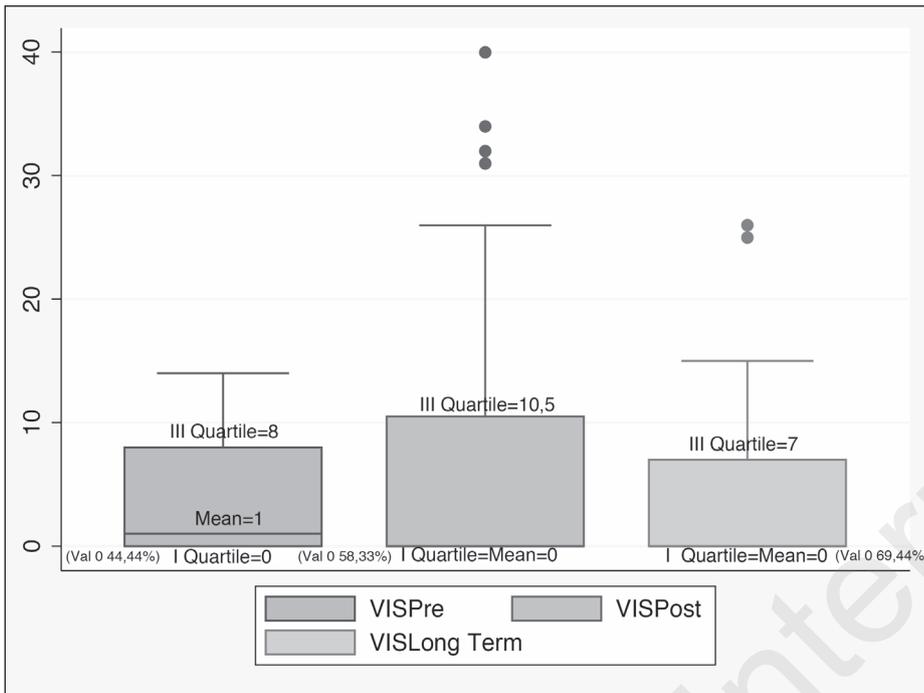


Figure 1 - This box-plot graphic shows that the VIS (Voice Impairment Score) score concerning the immediate postoperative period is lower compared to the pre-operative and the long-term evaluation. All these differences are significant.

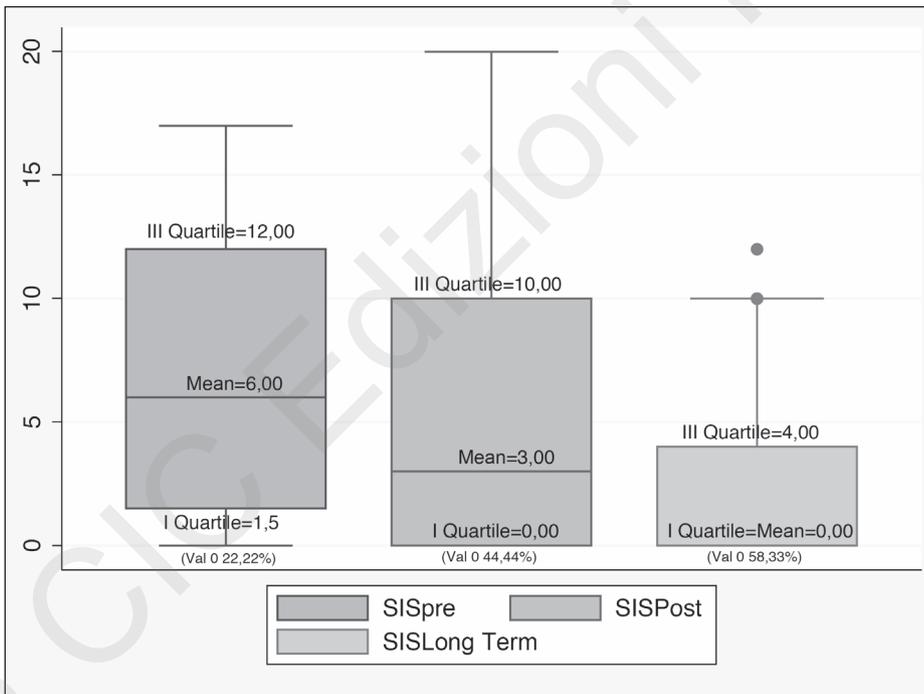


Figure 2 - This box-plot graphic shows that the SIS significantly improved in both immediate and long-term postoperative periods. Legend: SIS pre = preoperative Swallowing Impairment Score; SIS post = Swallowing Impairment Score evaluated 30 – 45 days after thyroidectomy; SIS long-term = Swallowing Impairment Score evaluated 18-24 months after thyroidectomy.

showed a significant impairment of laryngeal mobility in the early post-thyroidectomy period in a selected group of patients, a partial recovery of these instrumental findings in a long-term control (6 months) (38).

Although these evidences confirm an involvement of several laryngeal, pharyngeal and esophageal functional

changes in the post-thyroidectomy aerodigestive symptoms, we would underline that some of these could be present before the thyroidectomy (3); these symptoms are acceptable indications for thyroidectomy, but an association with laryngopharyngeal reflux has also been found (39).

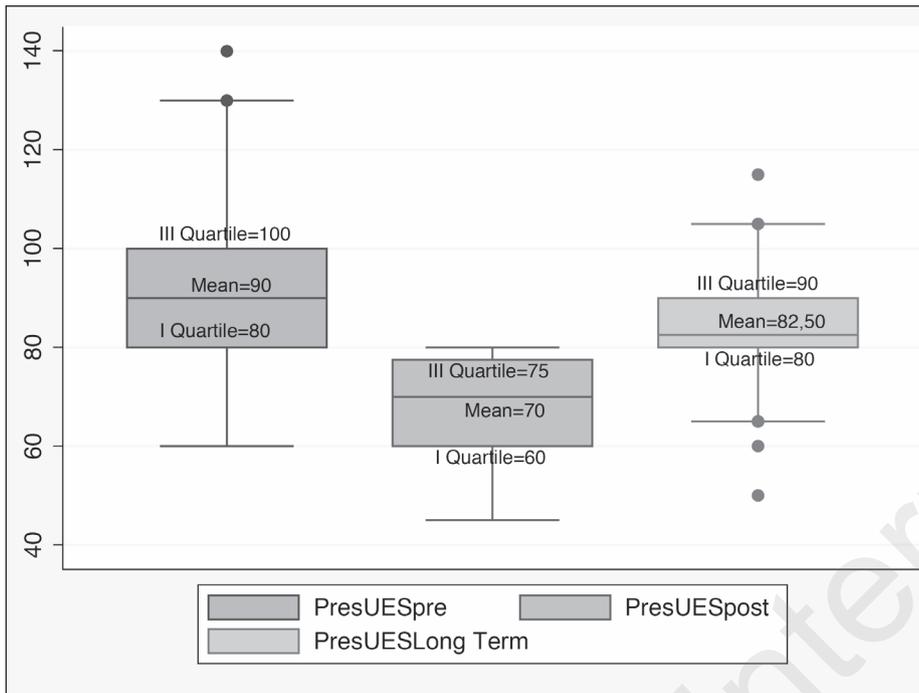


Figure 3 - This box-plot graphic shows that the UES pressure values decrease significantly in the immediate postoperative period and recover in the long-term control. Legend: pres UES pre = preoperative UES pressure; pres ES post = UES pressure evaluated 30-45 days after thyroidectomy; pres UES long term = UES pressure evaluated 18-24 months after thyroidectomy.

The role of the damage of terminal nervous branches and anastomoses of the laryngeal superior and inferior nerves, concerning the somatic and the autonomous system, have been already discussed (3, 14). Further interesting results of the previous study were:

- the variable but unchanging decrease in UES pressure;
- the possible correlation between *wide* decrease in UES pressure and appearance of its incoordination;
- the association between UES incoordination and swallowing alterations;
- the association between acid *proximal* reflux and voice impairment.

These results led us to hypothesize a likely role of UES pressure decrease in promoting on one hand its own incoordination and, as a consequence, the post-thyroidectomy swallowing impairment. On the other hand, this pressure decrease could make itself less effective towards proximal acid reflux, that could explain why the patients that underwent thyroidectomy complained voice impairment in the contemporaneous presence of proximal acid reflux.

The present long-term study confirmed that the clinical aerodigestive symptoms and the esophageal motility changes after uncomplicated thyroidectomy are related each other and showed that they are largely, but not invariably (40, 41), transient. In our study, the VIS and SIS improved 18-24 months after the thyroidectomy in comparison with the results of the immediate po-

stoperative period. Moreover, the trend in postoperative UES pressure allows us to confirm and strengthen the hypothesis of the crucial role of the UES in determining the physiology of the upper aerodigestive tract. In fact, in the present study its basal pressure tend to recovery in the same way with the voice and swallowing disorders. In the patients in which the voice complaints worsened, the unchanging presence of acid reflux *or* UES pressure decrease, an action of acid, direct or secondary to the UES failure should be invoked as a cause of voice impairment. Likewise, the swallowing complaints persist in association with the UES incoordination; this one is a physiological change strongly associated to a persistent full decrease of its pressure, then the UES could be concerned once again.

The limitations of our studies are the small size of the sample of patients involved and the absence of comparison with a comparable group of non-operated individuals, but we think that they are useful because these functional points of view have not been evaluated elsewhere.

## Conclusions

The present study confirms the results previously obtained at our Institution and enhance the role of the upper aerodigestive motility and, for some aspects, of the proximal esophageal acid reflux in supporting the post-thyroidectomy voice and swallowing complaints. The-

se changes usually come down or disappear, but they can continue during the time and become chronic.

The complexity of mechanisms involved do not allow, at the moment, a clear and complete pathogenetic hypothesis.

Our findings put the UES pressure decrease on the centre of attention in leading aerodigestive disorders, but we are conscious that other studies enhance different mechanisms in determining these disorders. All in all, our study showed some correlation between this specific change and the trends of these disorders.

## References

- Chandrasekhar SS, Randolph GW, Seidman MD, Rosenfeld RM, Angelos P, Barkmeier-Kraemer J, Benninger MS, Blumin JH, Dennis G, Hanks J, Haymart MR, Kloos RT, Seals B, Schreibstein JM, Thomas MA, Waddington C, Warren B, Robertson PJ. Clinical practice guideline: Improving voice outcomes after thyroid surgery. *Otolaryngol Head Neck Surg.* 2013;148 (Suppl. 6):1-37.
- Wassermann JM, Sundaram K, Alfonso AE, Rosenfeld RM, Har-EL G. Determination of the function of the internal branch of the superior laryngeal nerve after thyroidectomy. *Head Neck.* 2008;30:21-7.
- Scerrino G, Inviati A, Di Giovanni S, Paladino NC, Di Paola V, Lo Re G, Almasio PL, Cupido F, Gulotta G, Bonventre S. Esophageal motility changes after thyroidectomy; possible associations with postoperative voice and swallowing disorders: preliminary results. *Otolaryngol Head Neck Surg.* 2013;148(6):926-32.
- Lo CYm, Kwok KF, Yuen PW. A prospective evaluation of recurrent laryngeal nerve paralysis during thyroidectomy. *Arch Surg.* 2000;135:204-7.
- Scerrino G, Romano G, Salamone G, Farulla MA, Salamone S, Gambino G, Pompei G, Buscemi G. Our trend in conservative surgery in differentiated carcinoma of the thyroid. *Ann Ital Chir.* 2002;73(1):17-22.
- Shindo M, Chheda NN. Incidence of vocal cord paralysis with and without recurrent laryngeal nerve monitoring during thyroidectomy. *Arch Otolaryngol Head Neck Surg.* 2007;133(5):481-5.
- Jeannon JP, Orabi AA, Bruch GA, Abdalsalam HA, Simo R. Diagnosis of recurrent laryngeal nerve palsy after thyroidectomy: a systematic review. *Int J Clin Pract.* 2009;63(4):624-9.
- Stojadinovic A, Shaha AR, Orlikoff RF, Nissan A, Kornak MF, Singh B, Boyle JO, Shah JP, Brennan MF, Kraus DH. Prospective functional voice assessment in patients undergoing thyroid surgery. *Ann Surg.* 2002;236(6):823-32.
- Leder SB, Ross DA. Incidence of vocal fold immobility in patients with dysphagia. *Dysphagia.* 2005;20(2):163-7.
- Ollivier B, Duce K, Rowlands G, Harrison P, O'Reilly BJ. Swallowing dysfunction in patients with unilateral vocal fold paralysis: aetiology and outcomes. *J Laryngol Otol.* 2006;120(1):38-41.
- Randolph GW. *Surgery of the Thyroid and Parathyroid Glands.* Philadelphia, P.A.: Saunders-Elsevier Science, 2003.
- Mihai R, Randolph GW. Thyroid surgery, voice and the laryngeal examination-time for increased awareness and accurate evaluation. *World J Endocr Surg.* 2009;1:1-5.
- Tedla M, Chakrabarti S, Suchankova M, Weickert MO. Voice outcomes after thyroidectomy without superior and recurrent laryngeal nerve injury: VoiSS questionnaire and GRBAS tool assessment. *Eur Arch Otorhinolaryngol.* 2016. DOI 10.1007/s00405-016-4163-6.
- Pereira JA, Girvent M, Sancho JJ, Parada C, Sitges-Serra A. Prevalence of long-term upper aerodigestive symptoms after uncomplicated bilateral thyroidectomy. *Surgery.* 2003;133:318-22.
- Musholt TJ, Musholt PB, Garm J, Napiontek U, Keilman A. Changes of the speaking and singing voice after thyroid or parathyroid surgery. *Surgery.* 2006;140(6):978-88.
- Scerrino G, Paladino NC, Di Paola V, Morfino G, Inviati A, Amodio E, Gulotta G, Bonventre S. Minimally invasive video-assisted thyroidectomy: four-year experience of a single team in a General Surgery Unit. *Minerva Chir.* 2013;68(3):307-14.
- Scerrino G, Paladino NC, Di Paola V, Morfino G, Matranga D, Gulotta G, Bonventre S. Total thyroidectomy performed with the Starion vessel sealing system versus the conventional technique: a prospective randomized trial. *Surg Innov.* 2010;17(3):242-7.
- Lombardi CP, Raffaelli M, D'Alatri L, Marchese MR, Rigante M, Paludetti G, Bellantone R. Voice and swallowing changes after thyroidectomy in patients without inferior laryngeal nerve injuries. *Surgery.* 2006;140(6):1026-32; discussion 1032-4.
- Lombardi CP, Raffaelli M, De Crea C, D'Alatri L, Maccora D, Marchese MR, Paludetti G, Bellantone R. Long-term outcome of functional post-thyroidectomy voice and swallowing symptoms. *Surgery.* 2009;146(6):1174-81.
- Streets CG, DeMeester TR. Ambulatory 24-hour esophageal pH monitoring: why, when and what to do. *J Clin Gastroenterol.* 2003;37:14-22.
- Scerrino G, Morfino G, Paladino NC, Di Paola V, Amodio E, Gulotta G, Bonventre S. Does thyroid surgery for Graves' disease improve health-related quality of life? *Surg Today.* 2013;43(12):1398-405.
- Massolt ET, van der Windt M, Korevaar T, Kam BL, Burger JW, Franssen GJ, Lehmpul I, Köhrle J, Visser WE, Peeters RP. Thyroid Hormone and its Metabolites in Relation to Quality of Life in Patients Treated for Differentiated Thyroid Cancer. *Clin Endocrinol (Oxf).* 2016 May 13. Doi: 10.1111/cen.13101.
- Rosato L, Pacini F, Panier Suffat L, Mondini G, Ginardi A, Maggio M, Bosco MC, Della Pepa C. Post-thyroidectomy chronic asthenia: self-deception or disease? *Endocrine.* 2015;48(2):615-20.
- Gullo R, Inviati A, Almasio PL, Di Paola V, Di Giovanni S, Scer-

- rino G, Gulotta G, Bonventre S. A functional study of the esophagus in patients with non-cardiac chest pain and dysphagia. *Turk J Gastroenterol.* 2015;26(2):99-103.
25. Misono S, Marmor S, Roy N, Mau T, Cohen SM. Multi-institutional Study of Voice Disorders and Voice Therapy Referral: Report from the CHEER Network. *Otolaryngol Head Neck Surg.* 2016;155(1):33-41.
  26. Scerrino G, Salamone G, Farulla MA, Romano G, Salamone S, Pompei G, Buscemi G. Non-toxic multinodular goitre: which surgery? *Ann Ital Chir.* 2001;72(6):647-51.
  27. Scerrino G, Cocorullo G, Paladino NC, Salamone G, Gulotta G. Quantification of the risk of relapses after thyroid lobectomy for benign thyroid nodules. *Ann Ital Chir.* 2005;76(4):321-8.
  28. Lombardi CP, Bellantone R, De Crea C, Paladino NC, Fadda G, Salvatori M, Raffaelli M. Papillary thyroid microcarcinoma: extrathyroidal extension, lymph node metastases, and risk factors for recurrence in a high prevalence of goiter area. *World J Surg.* 2010 Jun;34(6):1214-21.
  29. Scerrino G, Di Giovanni S, Salamone G, Melfa GI, Inviati A, Raspanti C, Gulotta G. Surgical complications in prophylactic central neck dissection: preliminary findings from a retrospective cohort study. *Minerva Chir.* 2014;69 (Suppl. 1 to n. 2):131-134.
  30. Paladino NC, Guérin C, Slotema E, Franco IF, Henry JF, Sebag F. Endoscopic parathyroidectomy. In: *Minimally invasive therapies for endocrine neck diseases.* (Lombardi C.P., Bellantone R.), Eds. Springer International Publishing, 2016:167-80.
  31. Scerrino G, Attard A, Melfa GI, Raspanti C, Di Giovanni S, Attard M, Inviati A, Mazzola S, Modica G, Gulotta G, Bonventre S. Role of prophylactic central neck dissection in cN0-papillary thyroid carcinoma: results from a high-prevalence area. *Minerva Chir.* 2016;71(3):159-67.
  32. Romano G, Scerrino G, Profita G, Amato G, Salamone G, Di Buono G, Lo Piccolo C, Sorce V, Agrusa A, Gulotta G. Terminal or truncal ligation of the inferior thyroid artery during thyroidectomy? A prospective randomized trial. *Int J Surg.* 2016;28 Suppl 1:S13-6.
  33. Melfa GI, Raspanti C, Attard M, Cocorullo G, Attard A, Mazzola S, Salamone G, Gulotta G, Scerrino G. Comparison of minimally invasive parathyroidectomy under local anaesthesia and minimally invasive video-assisted parathyroidectomy for primary hyperparathyroidism: a cost analysis. *G Chir.* 2016 Mar-Apr;37(2):61-7.
  34. Silva IC, Netto Ide P, Vartanian JG, Kowalski LP, Carrara-De Angelis E. Prevalence of upper aerodigestive symptoms in patients who underwent thyroidectomy with and without the use of intraoperative laryngeal nerve monitoring. *Thyroid.* 2012;22(8):814-9.
  35. Scerrino G, Paladino NC, Di Paola V, Morfino G, Amodio E, Gulotta G, Bonventre S. The use of haemostatic agents in thyroid surgery: efficacy and further advantages. Collagen-Fibrinogen-Thrombin patch (CFTP) versus cellulose gauze. *Ann Ital Chir.* 2013;84:545-50.
  36. Fingerhut A, Uranues S, Ettorre GM, Felli E, Colasanti M, Scerrino G, Melfa GI, Raspanti C, Gulotta G, Meyer A, Oberhofer M, Schmoekel M, Weltert LP, Vignolini G, Salvi M, Masieri L, Vittori G, Siena G, Minervini A, Serni S, Carini M. European initial hands-on experience with HEMOPATCH, a novel sealing hemostatic patch: application in general, gastrointestinal, biliopancreatic, cardiac, and urologic surgery. *Surg Technol Intern.* 2014;25:30-5.
  37. Docimo G, Tolone S, Conzo G, Limongelli P, Del Genio G, Parmeggiani D, De Palma M, Lupone G, Avenia N, Lucchini R, Monacelli M, Gulotta G, Scerrino G, Pasquali D, Bellastella G, Esposito K, De Bellis A, Pezzolla A, Ruggiero R, Docimo L. A gelatin-thrombin matrix topical hemostatic agent (Floseal) in combination with harmonic scalpel is effective in patients undergoing total thyroidectomy: a prospective, multicenter, single-blind, randomized controlled trial. *Surg Innov.* 2016;23(1):23-9.
  38. Gohrbandt AE, Aschoff A, Gohrbandt B, Keilmann A, Lang H, Musholt TJ. Changes of Laryngeal mobility and symptoms following thyroid surgery: 6-month follow-up. *World J Surg.* 2016;40(3):636-43.
  39. Holler T, Anderson J. Prevalence of voice and swallowing complaints in pre-operative thyroidectomy patients: a prospective cohort study. *J Otolaryngol Head Neck Surg.* 2014;43:28.
  40. Grover G, Sadler Gm, Mihai R. Morbidity after thyroid surgery: patients perspective. *The Laryngoscope.* 2013;123:2319-23.
  41. Romano G, Luna E, Cocchiara G, Calderone F, Zumbino C, Muzio M, Lo Nigro MC, Lo Monte AI, Buscemi G, Di Bernardo C, Napoli N. The surgical treatment of nodular thyroid lesions: our experience. Analysis of 462 cases. *G Chir.* 2004 Jan-Feb;25(1-2):23-6.