

IONM and thyroidectomy in benign thyroid disease. Analysis of adverse events

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SUMMARY: IONM and thyroidectomy in benign thyroid disease. Analysis of adverse events.

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Objectives. *The aim of this study is to identify statistically significant differences in the onset of postoperative complications in patients undergoing thyroid surgery for benign pathology, following the systematic introduction of intraoperative neuromonitoring (IONM) of the laryngeal nerves.*

Materials and methods. *In this study we have retrospectively analysed data of 604 consecutive patients underwent to thyroidectomy in the Unit of General Surgery - University Hospital of Parma between January 2011 and December 2017. All patients were divided in two groups: the first group of patients was operated without the use of IONM (Group A) the second group was operated after the introduction of the systematic use of IONM (Group B). We have compared the incidence of adverse events in these two*

groups, analysing the impact of IONM on the onset of the most frequent complications after thyroid surgery. We have considered the impact of other variables in both groups, such as thyroiditis, hyperfunction and gland sinking in mediastinum.

Results. *No statistically significant differences in the incidence between Group A (patients operated without the use of IONM) and Group B (patients operated with the use of IONM) were detected, though a decreasing trend after the introduction of IONM was observed. No statistically significant differences were reported even analysing the influence of other patient's variables such as thyroiditis, hyperfunction and glandular sinking in mediastinum.*

Conclusion. *Even if the number of patients considered is not sufficient to value statistically significant differences, the decreasing trend of the incidence of postoperative complications after introduction of IONM encourage us. The surgeon expertise is still the most relevant variable influencing the decreasing of postoperative complications, underlining the importance of the centralization of this kind of surgery in the high volume centres.*

KEY WORDS: Thyroidectomy - Goitre - Intraoperative neuromonitoring - IONM - Hypocalcemia - Dysphonia.

Introduction

The surgical option for the treatment of benign thyroid pathology includes thyroidectomy and lobectomy.

The indications for the surgical treatment of the benign thyroid pathology are: large goitre with compressive symptoms, hyperfunction no responding to medical treatment, suspected malignant evolution.

As we have seen in our case studies, the first choice for the treatment of these pathologies in the

majority of cases is total thyroidectomy, in particular in case of bulky goitre, even cervical-mediastinal, or in widespread hyperfunction of the thyroid parenchyma (1).

Many studies have valued the incidence of postoperative complications in thyroid surgery as transient or permanent hypoparathyroidism, postoperative bleeding and transient or permanent lesion of the recurrent laryngeal nerve or superior laryngeal nerve (2-4).

Hypoparathyroidism is one of the more frequent adverse event and manifests with hypocalcemia, clinical or biochemical. It depends on a deficit of PTH caused by an ischemic lesion or an accidental removal of parathyroid glands. We define transient hypocalcemia a calcium serum concentration lower

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than 8.0 mg/dl, which last less than 6 months. In the 80%, hypocalcemia lasts for an average time of 12 months. In literature the incidence of hypoparathyroidism is reported from 6.9 to 49%, while definitive hypoparathyroidism is reported from 0.5 to 9.3% of patients undergone to thyroid surgery (5-10).

In this study we have divided the early and symptomatic hypocalcemia from the biochemical one, without any paresthesia, muscle fasciculation or tetanic contractures.

Postoperative bleeding incidence after thyroid surgery varies from 0.4 to 4.6% in literature, with an average incidence of 1.6% of cases (4, 11).

The majority of studies concerning postoperative bleeding after thyroid surgery focus on the analysis of risk factors, such as operative indication, age and sex of patient and surgeon experience (12). The comprehension of risk factors is essential because it allows reducing the incidence of this complication and this is important especially because bleeding requires a re-surgery which has a risk of developing complications double compared to the first intervention, in particular regarding dysphonia. In fact, the anatomically modified field by the recent operation makes more difficult the recognition of nerve structures (12). Especially in this cases the use of IONM is fundamental. Gland hyperfunction seems to be the most important risk factor for the development of postoperative bleeding (13).

Transient or permanent lesion of the recurrent laryngeal nerve can occur after mobilization of thyroid inferior pole, causing a wide spectrum of voice alterations, involving also difficulty in swallowing.

The lesion is considered permanent if dysphonia lasts more than 6 months after surgery and it could be unilateral or bilateral. Unilateral lesion consists in omolateral vocal cord palsy with dysphonia. In case of bilateral lesion, the patient presents aphonia in association with reduction of respiratory space and dyspnea, up to request a tracheostomy (11).

Postoperative dysphonia is not only imputable to nerve lesion but also to other mechanisms that lead to a transient dysphonia with intact nerve, like a laryngeal compression by a large goitre, a vocal cord lesion after tracheal intubation, cervical muscles dissection or nerve compression by an external hematoma.

Related to superior laryngeal nerve, monolateral temporary lesion frequency is about 0.3 - 3,9% (14, 15), even if is probably underestimated because voice changing associated to this type of lesion is frequently subclinical and appears mostly like a marked voice fatigue during long speeches and inability to make high sounds (16). Literature reports permanent monolateral superior laryngeal nerve palsy in 1% of cases after 6-12 months.

Superior laryngeal nerve lesion is particularly symptomatic if is associated to omolateral inferior laryngeal nerve lesion, that can lead to liquids dysphagia (11).

The recurrent laryngeal nerve lesion is still the most fearful complications in thyroid surgery, with significant impact on the patient's quality of life due to the consequent limitations on the social, emotional and physical level.

The different cases available in the current literature show average percentages that stand at 5-8% for transitory paralysis and 1-3% for definitive ones. The intraoperative identification (visualization) of the recurrent laryngeal nerve has been recognized as a standard practice in thyroid surgery, allowing to reduce the risk of iatrogenic lesions, but not to cancel it.

In recent years, intraoperative neuromonitoring (IONM) has been proposed and applied in many centers of thyroid surgery as a further aid, supporting the standard practice of visual identification. The validity of the IONM has been proven in numerous international studies and meta-analyses (17, 18).

The benefits obtained from the use of IONM consist in the identification of the recurrent nerve, in the assistance to the surgical dissection and in the post-operative functional prognostic evaluation.

Nonetheless, this surgical practice is a valid educational support for the trainee, as well as providing, at the end of the procedure, an irrefutable proof of intact nervous function, useful in case of any medical-legal disputes (19, 20).

The intraoperative neuromonitoring device converts muscle activity into acoustic and electromyography signals.

The possible detection techniques are: neurostimulation with intermittent monitoring technique (IIONM), which allows to evaluate the con-

traction of the cricoarytenoid muscle after stimulation of the RLN and/or of the vagus nerve with an electric stimulation probe, and the most recent stimulation with continuous monitoring (CIONM) (21), with persistent electrical stimulation of the vagus, which provides auditory and visual feedback when the recurrent laryngeal nerve is electrically or mechanically stimulated during surgery.

Currently at our Unit, the use of the IIONM technique has been consolidated since 2014 and the CIONM monitoring was introduced in the current year (22).

Patients and methods

In this study we have retrospectively analysed data about 604 patients undergone to thyroid surgery (total thyroidectomy or lobectomy) for benign pathology between January 2011 and December 2017 to verify if the use of IONM technique could influence the onset of adverse events, not only related to recurrent laryngeal nerve function but also to hypocalcemia and postoperative bleeding.

All procedures have been executed by the same team expert in endocrine surgery.

All patients presenting benign thyroid pathology were included while were excluded from the study all patients with neoplastic pathology, suspicious nodule, incomplete clinical relation and patients undergone to thoracotomy.

For each patient involved in the study were analysed preoperative variables (sex, thyroid pathology and gland function), operative variables (surgery extension) and postoperative variables (subclinical or clinical praecox hypocalcemia, dysphonia and postoperative bleeding).

We have divided the patients in two groups considering the use of IONM: the first group comprehends all patients operated from January 2011 to December 2014 without the use of IONM, the second group includes patients undergone to surgery between January 2015 to December 2017 with the routine use of IONM. The data about frequency of postoperative complication have been compared in order to highlight any statistically significant correlations between the period before and after the introduction of intermittent intraoperative neuromonitoring.

The statistically analysis has been executed with SPSS (version 20.0; SPSS Inc. Chicago, IL, USA). Chi-square Pearson chi-squared Test and Fisher Test have been used to compare parametric variables while Student T Test and Mann-Whitney U Test have been used for non-parametric variables. We have considered $p < 0.05$ statistically significant.

Results

We have analysed data about 604 patients undergone to thyroid surgery between January 2011 and December 2017.

Patients were 478 (79.1%) females and 126 (28.9%) males; 56 (9.3%) patients presented Basedow disease, 539 (89.1%) goitre and 9 (1.5%) Plummer adenoma (Figure 1).

Within the considered population, 539 (89.1%) patients underwent to total thyroidectomy and 65 (10.8%) lobeistmectomy.

In the 55.8% ($n=337$) the operation was executed without the use of IONM (Group A) while in the 44.2% ($n=267$) IONM was used during the procedure (group B) (Table 1). Group A includes all patients operated for benign thyroid pathologies from January 2011 to December 2014, the second group includes patients undergone to surgery between January 2015 to December 2017 after the introduction of the routine use of IONM.

We have then analysed the incidence of individual complications within the two groups trying to highlight statistically significant differences that could indicate a modifying effect of IONM on the development of postoperative complications (Tables 1, 2).

In group A we recorded 8 cases of dysphonia in 337 patients (2.4%) and in group B 2 cases in 267 (0.7%). Despite the decreasing trend, there were no statistically significant differences between the two groups ($p=n.s.$).

We recorded 4 cases of postoperative bleeding in group A (1.2%) and in group B 3 cases (1.1%). Despite of the decreasing trend, no statistically significant difference was noticed ($p=n.s.$).

About early clinical hypocalcemia in group A we recorded 6 cases of symptomatic hypocalcemia (1.8%) and in group B 14 cases (5.2%). In these cas-

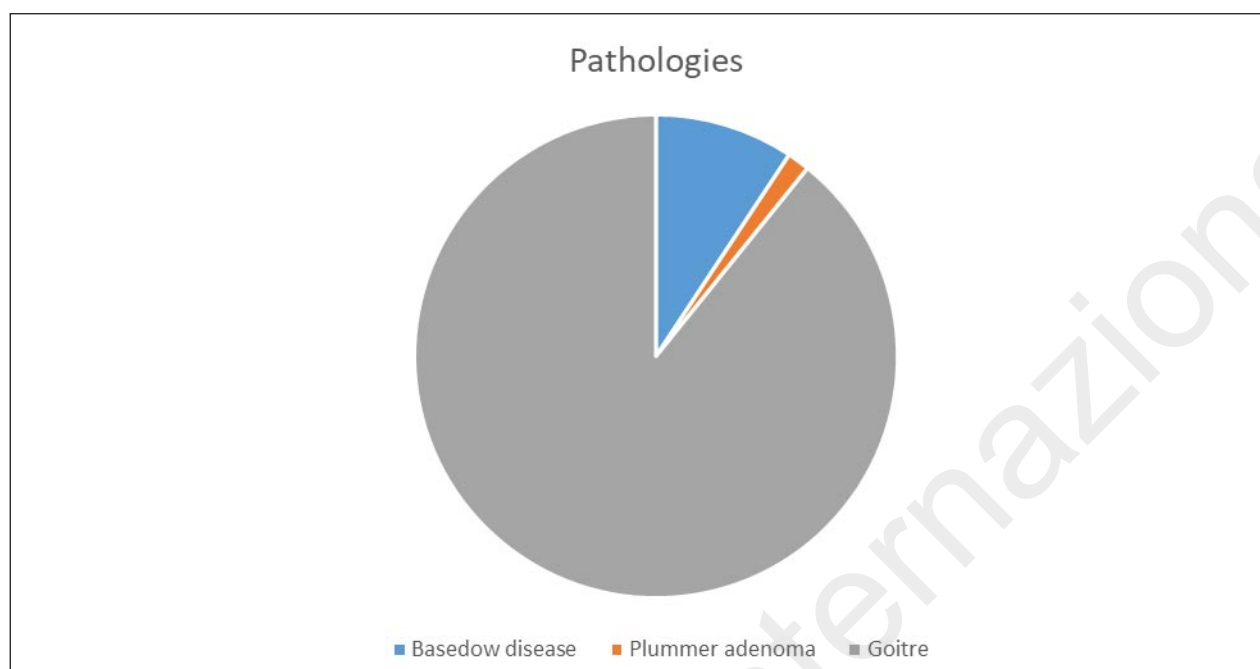


Figure 1 - Pathologies distribution.

TABLE 1 - GROUP DISTRIBUTION BASED ON NIM USE.

GROUPS	IONM	N° PATIENTS	%
GROUP A	No	337	55.8 %
GROUP B	Yes	267	44.2 %

es the trend seems to be increasing but at statistical analysis no statistically significant difference was noticed ($p=n.s.$). Analyzing the early biochemical hypocalcemia ($Ca < 8.0$ mg/dl) in group A we recorded 79 cases (23.4%) and in group B 78 cases (29.2%). Statistical analysis showed no significant difference was noticed ($p=n.s.$).

TABLE 2 - POSTOPERATIVE COMPLICATIONS COMPARING IN THE TWO GROUPS.

Postoperative complications	Group A	Group B	P value
Dysphonia	8 (2.4%)	2 (0.7%)	0.198
Bleeding	4 (1.2%)	3 (1.1%)	1.000
Symptomatic hypocalcemia	6 (1.8%)	14 (5.2%)	0.220
Biochemical hypocalcemia	79 (23.4%)	78 (29.2%)	0.113

Subsequently, we have valued the possible influence of further factors on the development of postoperative complications in the two groups. In particular, we analysed the presence of cervicomediastinal goitre, histological thyroiditis and preoperative gland hyperfunction (Figures 2, 3, 4); no statistically significant differences were found even considering these variables.

Discussion

The percentages of incidence of postoperative complications following the thyroid surgery for benign pathology reported in our study are comparable to those described by literature (2-4, 11).

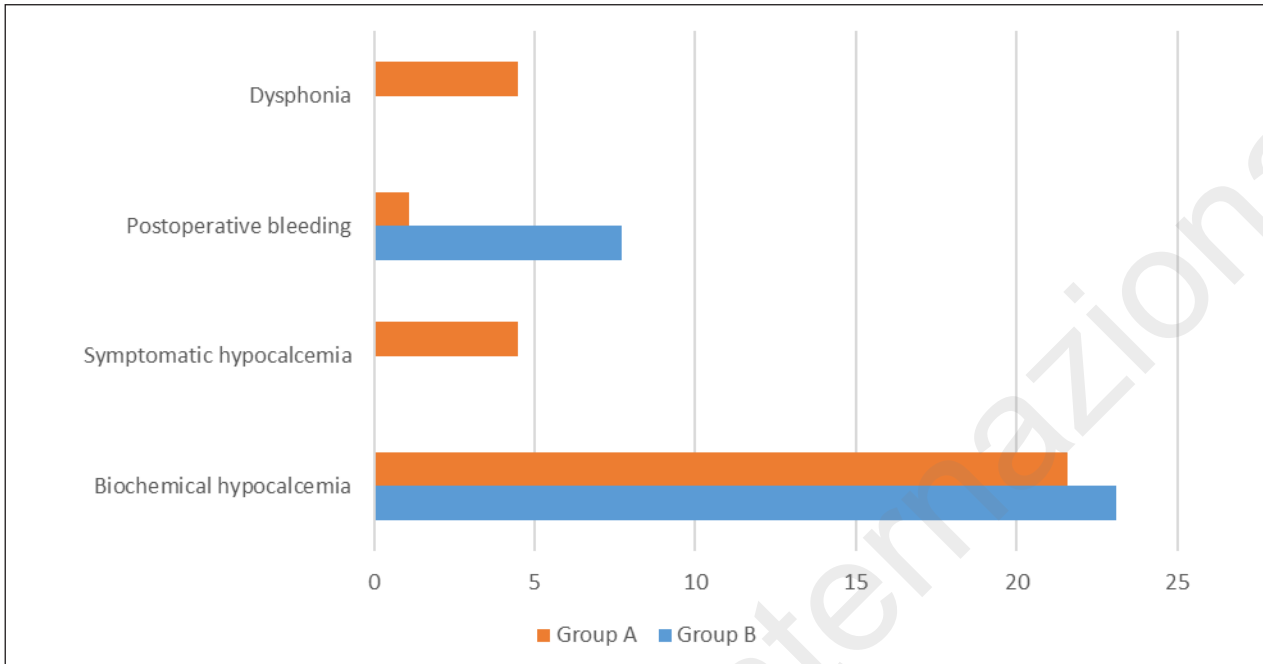


Figure 2 - Influence of thyroiditis on development of complications.

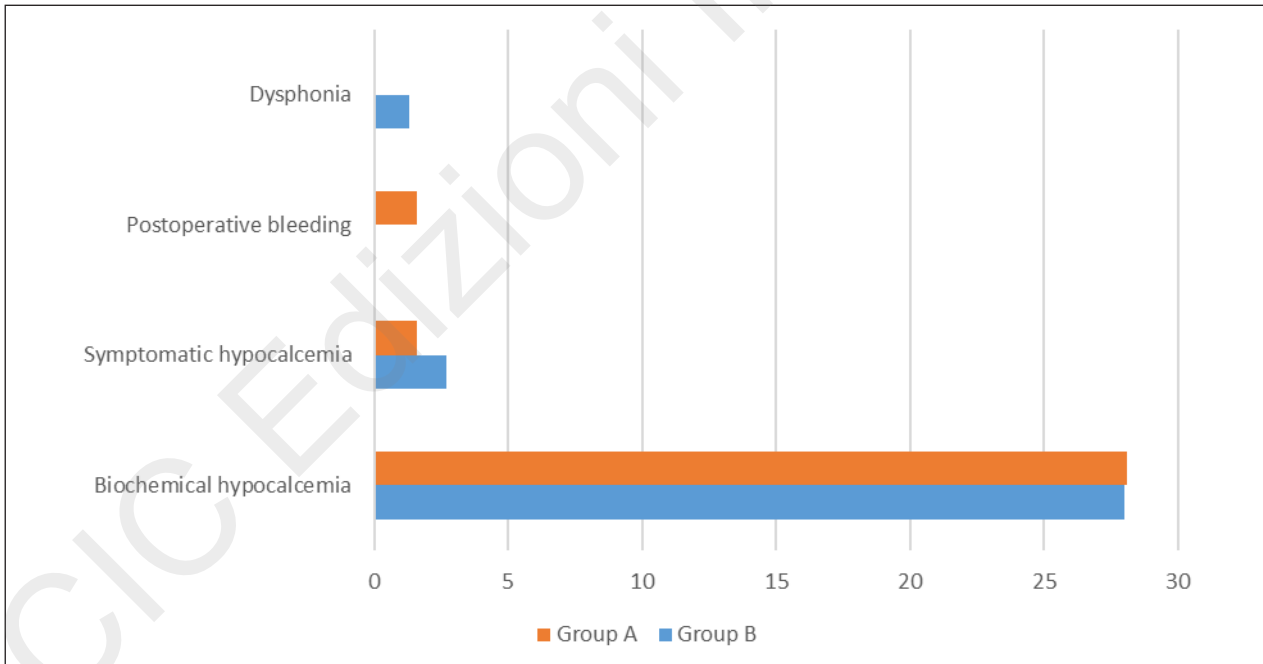


Figure 3 - Postoperative complications in cervicomedial goitre.

In our protocol we compared two groups including respectively 337 patients operated between 2011 and 2014, before the introduction of IONM, and 267 patients operated with the use of IONM in the period 2015-2017, searching a statistically significant correlation between its use and postoperative

complications incidence. The results did not highlight any statistically significant difference, probably due to an insufficient number of patients in the study sample.

The early hypocalcemia, both clinical and biochemical, resulted to be the most frequent complica-

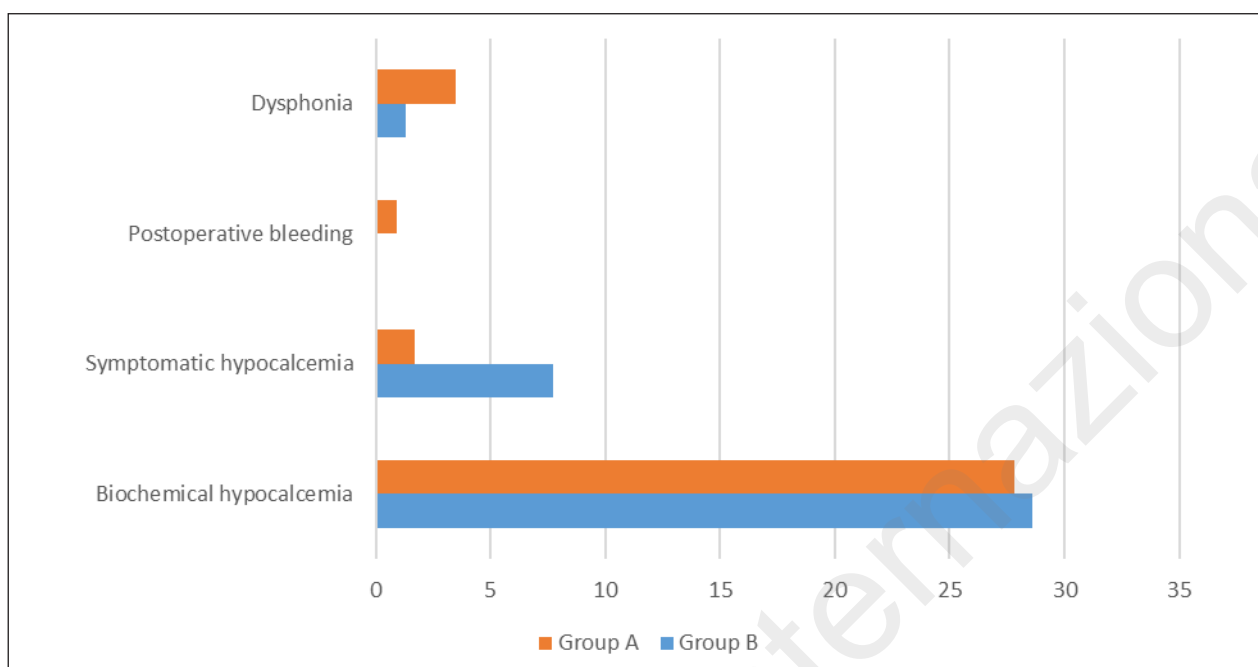


Figure 4 - Postoperative complications in patients with thyroiditis.

tion after thyroidectomy as in literature (5-8, 10), with an incidence of 26% for biochemical hypocalcemia and 3.3% for clinical. Comparing the two groups, appears a slight increase of incidence in group B, but at statistical analysis there were no statistically significant difference between the two groups.

The analysis of postoperative bleeding has revealed reduction of incidence after the introduction of IONM, although remains a non-statistically significant difference due to low incidence of this complication (2, 4).

Neuromonitoring would seem to have greatly improved the dissection modalities, providing a better understanding of the anatomical structures so as to allow a safer dissection and a greater use of energy devices, associated with a greater haemostatic control also in mini-invasive procedures (22, 23).

Its use in operative management has therefore led to a decrease in the frequency of bleeding in the postoperative period, and consequently also in the following re-operations, burdened by a greater number of postoperative complications.

Analysis of the data collected did not reveal any statistically significant differences even analysing the impact of IONM on postoperative bleeding in the presence or absence of further variables such as thy-

roiditis and glandular hyperfunction.

Analysing the incidence of dysphonia conflicting data are highlighted. In literature there are controversial data on the decrease in the frequency of dysphonic patients following total thyroidectomy and lobeistmectomy for benign thyroid pathology with the aid of IONM (24).

Our data do not allow highlighting statistically significant differences in this regard, however it can be noted that dysphonia is one of the parameters most subject to variations both in relation to the use of the IONM and in relation to its use associated with other analysed conditions such as thyroiditis, hyperfunction, sinking and type of intervention.

As reported in Table 2, the percentage of postoperative dysphonia in operation executed without the use of IONM is 2.4% against 0.7% in group B, the difference is not statistically significant, the decrease seems to suggest an initial protective impact of IONM on this type of complication.

Comparing data and considering additional variables, in particular thyroiditis and hyperfunction, does not confirm a uniform decreasing trend, but even in this case no statistically significant difference.

Finally, considering the influence of a cervico-mediastinal development of the thyroid goitre,

found in 139 of 604 cases, on the occurrence of postoperative complications, we found no statistically significant differences either considering all the patients or considering the two separate groups, confirming literature results about the non-protective role of IONM on the onset of complications.

Conclusion

Ultimately, the systematic use of IONM in thyroid surgery in our centre showed a decreasing trend in the development of postoperative complications, although no statistically significant differences emerged. The smallness of the sample and the low

complication rate could not give statistical confirmation to our data which show an improvement in the absolute numbers of the postoperative outcome in our patients with a picture that seems encouraging. Further studies with larger sample are necessary.

It is interesting to note that a clear and decisive role in lowering the frequency of the complications always results in the expertise and experience of the surgeon (24). It is therefore essential to perform this type of surgery in high-volume reference centres with expert multidisciplinary team and appropriate tools.

Conflict of interest

The Authors have no conflict of interest.

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