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## **Complications in total thyroidectomy:** **our experience and some considerations.**

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## **Abstract**

The authors discuss 1,636 cases of total thyroidectomy with reference to specific complications, classifying them under the headings: major and minor, early and tardy, temporary and definitive.

They report nineteen cases of post-surgical haemorrhage, all within 12 hours after the operation, 31 transitory and 15 definitive cases of recurrent laryngeal nerve paralysis, 14 cases of definitive hypoparathyroidism.

As far as minor complications are concerned there was a greater incidence of seroma following the use of harmonic scalpel.

The risk factors and the physio-pathological mechanisms connected with each type of complication are analysed here, above all those responsible for the major and definitive complications. The need for routine preparation of the recurrent nerve, in order to prevent occurrence of post-surgical paralysis is underlined, as well as the efficacy of vitamin D in preventing symptomatic post-surgical hypocalcaemia.

Key words: total thyroidectomy, complications.

## **Riassunto**

### Scopo dello studio

Gli Autori riportano la propria casistica di 1636 tiroidectomie totali, allo scopo di analizzarne le complicanze specifiche, classificandole in maggiori e minori, precoci e tardive, temporanee e definitive.

### Materiali e metodi

Sono state analizzate solo le tiroidectomie totali senza procedure di linfectomia associate. Tra le complicanze minori sono state rilevate il numero di suppurazioni della ferita, il numero di sieromi postoperatori e la percentuale di inestetismi a distanza. Tra quelle maggiori l'emorragia postoperatoria, le paralisi ricorrenti e l'ipoparatiroidismo postoperatorio con e senza l'utilizzo della profilassi con vitamina D e sali di calcio per os.

### Risultati

Per quanto riguarda le complicanze minori si evidenzia la maggior incidenza di sieromi dopo utilizzo del bisturi armonico ad ultrasuoni.

Vengono riportati 19 casi (1.16%) di emorragia postoperatoria, sempre insorta entro le prime 12 ore dall'intervento, 31 paralisi ricorrenti transitorie (1.89%) e 15 definitive (0.91%), 14 ipoparatiroidismi definitivi (0.85%). Vengono analizzati i fattori di rischio connessi con ogni tipo di complicanza ed i meccanismi fisiopatologici, soprattutto quelli responsabili delle complicanze maggiori e definitive.

### Conclusioni

Viene sottolineata la necessità della preparazione routinaria del nervo ricorrente per ridurre l'incidenza di paralisi postoperatorie e l'utilità del trattamento con vitamina D nella prevenzione dell'ipocalcemia postoperatoria sintomatica.

Parole chiave: tiroidectomia totale, complicanze.

## **Introduction**

Total thyroidectomy complications may be classified as **early and tardy**, according to the time of their onset, **temporary and definitive**, depending on the duration of their effect and as **major and minor**, in relation to their gravity. (Table I)

Complications which occur during the period of hospitalisation are considered early, while those defined as definitive fail to recede within six months following surgery and /or those which require further, often emergency, surgery. Major complications are those which place the patient's life at risk or cause the loss of important physiological functions.

The various classes are not rigidly watertight, as a complication may belong simultaneously to more than one category within the same class, besides belonging to various classes. For example, if post-surgical vomiting is always minor, early and transitory, recurrent laryngeal nerve palsy may be early or tardy, temporary or definitive, while remaining a major phenomenon.

As can be seen in Table I, the minor complications are prevalently early and temporary and consist in: 1) pain stemming from posture assumed on the operating table; 2) post-surgical nausea and vomiting; 3) seromas and infection of the surgical wound (these may also be tardy).

The only definitive minor complications which emerge late are those connected with the cosmetic aspect of the surgical wound due to hypertrophic scarring or to cheloide, or osteoporosis.

The major complications are, essentially, those which place the patient's life at risk, like post-surgical bleeding or bilateral injury of the lower larynx nerves, and those which, while not representing a threat on life, cause the loss of important physiological functions, such as monolateral paralysis of the lower larynx nerves, mono and bilateral paralysis of the upper larynx nerves and definitive hypoparathyroidism.

## **Patients and methods**

We carried out 1,947 operations between January 1987 and May 2002 at the Eighth Surgical Pathology Division of University of Rome “La Sapienza”.

The operations involving neoplastic pathologies totalled 361 (Table II) and, of these, 87 also involved lymphadenectomy associated with total thyroidectomy (Table III).

The operations associated with benign pathologies numbered 1,586 (Table IV). Of these, 188 patients underwent lobectomy plus hystmusectomy. These cases, however, belong to the earlier phase of our experience, seeing that for the past 5 years we have carried out total thyroidectomies only.

On the whole the total thyroidectomies numbered 1,723, including 1,636 *tout court* total thyroidectomies and 87 total thyroidectomies associated with lymphadenectomies.

The relapses numbered 153 (151 for benign pathologies, all associated with plurinodular/hypofunctional goitre, and 2 for neoplastic pathologies).

The assessment of the post-surgical complications concerned only the 1,636 patients who underwent total thyroidectomy without associated lymphadenectomy.

The minor complications were calculated on the basis of the number of suppurations of the surgical wound and the post-surgical seromas as well as on the long-term anti-aestheticisms which arose due hypertrophy of the scar.

Some of the major complications were calculated according to the number of post-surgical haemorrhages against the number of hours after the operation, to the percentage of temporary and definitive mono and bilateral paralyse of the recurrent laryngeal nerves, as well as to post-surgical hypocalcaemia and definitive hypoparathyroidism within six months of the operation.

In order to reduce the percentage of post-surgical cases of hypocalcaemia and eliminate tetanic crises altogether, 215 consecutive patients, belonging to the latest phase of our case study, who underwent total thyroidectomy, were treated orally, from the day of the operation itself, with calcitriol and

calcium salts. 104 of these were given a dose of 0.5 mcg of calcitriol twice a day, the other 111, twice that amount. In the case of both groups the calcium salt dose was 500 mg per day. 202 previously-operated patients who had been orally treated with the same dose of calcium salts only acted as the control group. The treatment lasted an average of 15 days following surgery, and the drug doses were gradually reduced until total suspension, with calcaemia and phosphoremia level tests at very change of dosage. Assessment of post-surgical iPTH and CT levels (during and after treatment) compared with pre-surgical levels completed the patients' follow-up screening.

## **Results**

As to the minor complications, no lesions due to bad posture on the operating table were registered. 5.75% (94 patients) complained of post-surgical pain which was never intense and was always appeased by use of ordinary pain-killers; in any case it never lasted beyond 24 hours after surgery.

Post-surgical nausea and vomiting involved 191 out of 1,636 patients (11.67%) and receded in all cases within 24 hours of surgery with the help of common anti-emetic drugs.

We registered 3 (0.18%) suppurations of the residual cavity after total thyroidectomy for the removal of cervicomediastinal goitres and in all cases the insertion of a laminar drain, alongside appropriate antibiotic treatment, cured the infection. In one case monolateral recurrent laryngeal nerve palsy occurred.

Post-operative seromas numbered 98 (5.99%) and were solved by recourse to prompt simple transcutaneous aspiration with a needle. Of these 98 patients, 22 were operated on availing of harmonic ultra-sound scalpel for the dissection and in 11 of these cases drainage was not applied.

Aesthetic complication of the surgical wound occurred in 3.36% (55 patients) cases where the patients witnessed the onset of hypertrophic scars on all or part of the cervicotomy while no case of cheloide was observed.

Bleeding occurred in 19 out of 1,636 total thyroidectomies (1.16%) and in all these cases it occurred within 12 hours of surgery.\*

In all of these cases the wound was treated surgically. In one patient the bleeding was caused by continuous leaking from the wall of the right anterior jugular vein due, by all appearances, to suture of the pre-thyroid muscles ; another patient presented a leakage of the ligature of the right middle

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\* A curious instance is that of a patient, not included in this study, who having undergone total thyroidectomy, experienced a haemorrhage 7 days after surgery, due to a violent sneeze which, by suddenly increasing the venous pressure of the neck, was responsible for the leakage of the right central thyroid vein ligature. A prompt second operation solved the problem.

thyroid vein; in another case bleeding was due to loss of the ligature of the anterior branch of the upper right thyroid artery; in two patients the source of the haemorrhage was the posterior branch of the lower right thyroid artery. In the other fourteen cases it was impossible to discover the exact origin of the bleeding, as it took the form of a rexis from the entire surgical area.

As to the external branch of the upper larynx nerve, we came across no instrumentally proven lesions ; this we believe is the result of the care with which we separately normally tie the branches of the upper thyroid artery.

However, although we pay just as much attention to dissection of the recurrent laryngeal nerve , we have registered, nonetheless, a minimal incidence of paralysis of the lower larynx nerve.

In 31 out of 1,636 total thyroidectomised patients (1.89%) there were cases of transitory paralysis of the recurrent laryngeal nerve which in five cases was bilateral, obliging us to perform a tracheostomy.

All 31 patients underwent phoniatic therapy and all recovered mobility of the vocal chords, including the five tracheostomised patients , permitting closure of the tracheostomy 90 days after surgery.

Fifteen of the 1,636 patients (0.91%) presented a permanent monolateral recurrent laryngeal nerve deficit. In one case this was the outcome of voluntary resection because of infiltration of the nerve by a medullar carcinoma ; in four cases the lesions were accidental, once in the presence of a fourth De Quervain thyroiditis relapse, once in a chronic thyroiditis patient and twice in the presence of large cervicomediastinal goitres. In the case of these latter four patients, as the lesion was recognised immediately, in three of the cases direct reconstruction of the nerve was undertaken availing of termino-terminal anastomosis of the two stumps and in the fourth anastomosis using the hypoglossal ansa availing of micro-surgical techniques. In one case paralysis of the recurrent laryngeal nerve, which occurred a few days after surgery, was due to suppuration of the residual cavity left after total thyroidectomy because of cervicomediastinal goitre.



In 9 further cases although the anatomical integrity of the recurrent laryngeal nerve had been safeguarded it was not possible to detect any other plausible cause of post-surgical paralysis.

Despite phoniatric treatment, none of these patients, including those who underwent microsurgical reconstruction recovered mobility of the vocal chords, while all improved their voice tone by compensational use of the contra-lateral chord.

As to hypoparathyroidism, we decided to consider as hypocalcaemic all those patients with a calcaemia value lower than 8.0 mg/dl, even when this level resulted from one only of the tests carried out during hospitalisation. Availing of this parameter, which is undoubtedly very narrow, the patients with a hypocalcaemic condition after total thyroidectomy numbered 54.8% (897 out of 1,636).

Of these, 357 patients (21.82% of the total number and 39.79% of the hypocalcaemics) presented various symptomatic levels, from simple silent perioral paresthesias to evident tetanic crises in 85 cases (5.19% of the overall total and 9.47% of the hypocalcaemic patients).

The treatment of the patients with symptoms consisted in administering calcium salts orally in less severe cases and associating them with vitamin D in more severe cases; the tetanic crises were treated with intravenous doses of gluconated calcium administered until the symptoms receded completely.

Definitive hypoparathyroidism emerged in only 0.85% (14 out of 1,636 patients) of the cases.

Preventive oral treatment with calcitriol and calcium salts led to the disappearance of tetanic crises in the groups given the highest doses of vitamin D and to a significant drop in the percentage of symptomatic patients (from 28.71% to 17.1% -  $p < 0.05$ ) and, in the latter, of the intensity of the symptoms which took the form of very slight paresthesias of the extremities, often without any evident clinical signs (negative Chwosteck).

Furthermore, rapid “weaning” from the therapy avoided the onset of possible inhibitory effects on the parathyroid function of calcitriol with a return to pre-surgical values of calcium, phosphorous levels and to intact parathormone and calcitonin values.

## **Discussion**

Analysing the minor complications registered in our case history, we came across no instances of lesions due to stretching of the cervical plexus and arm radices resulting from bad posture on the operating table. To avoid discomfort due to posture, it is good practice when positioning the patient to place both the upper limbs along the side of the trunk, and make sure that the head be fixed in such a manner as to avoid lateral turning and guarantee that the scapular cingula are adequately supported avoiding forced hyperextension of the rachis, especially in the presence of large cervicomediastinal goitres where hyperextension of the cervical rachis tends to occur to favour extrinsication of the goitre.

Notwithstanding the precautions taken during the immediate post-surgical phase it is possible that more or less intense pain of the neck muscles may occur, although this may recede during the following 24 hours thanks to early mobility and/or the use of bland orally-administered pain-killers.

The post-operational after-effects of anaesthetic like nausea and vomiting (PONV), rarely continue after twenty-four hours following surgery and these symptoms may usually be controlled by administration of anti-emetic drugs. More than the drugs used to induce, those used to prolong general anaesthesia seem to be the cause of this kind of complication [1].

In order to reduce the dose of anaesthetic drugs and thus diminish the incidence of post-surgical complications connected with them, some authors have suggested using, in the place of general anaesthetic, hypno-sedative methodologies, which exploit hypnosis as a coadjutant to conscious intravenous sedation. The results obtained by the University of Liege surgical group on 300 patients, while encouraging, still appear insufficient to permit routine employment of the method [2;3]

In our experience we have witnessed slightly more than 11% post-surgical cases of nausea and vomiting, all of which, regressed within 24 hours either spontaneously or following treatment with common anti-emetic drugs.

Of the 98 patients suffering from seromas in the surgical wound , 22 were operated on using harmonic ultra-sound scalpel, while 76 underwent traditional methodologies.

As 120 of our patients were treated with harmonic scalpel, the percentage of seroma cases was 18.33% (22 out of 120) against 5.01% (76 out of 1,516) for those treated with traditional dissection.

It must be pointed out that 11 of the 22 patients operated on availing of harmonic scalpel did not undergo drainage because of the absolute precision of the haemostasis. While attributing a greater incidence of post-surgical seromas to the group operated on using this technique, if we exclude the 11 patients who did not undergo drainage, 8.17% who underwent normal draining procedure presented post-surgical seromas in the surgical wound, almost double the rate for patients operated on with traditional dissection.

We believe that the reason for this undeniable increase in post-surgical seromas is to be found in the fact that the harmonic scalpel, though less so than in the case of electric scalpel, disperse heat in the tissues treated and in those surrounding them, to such a degree as to create a vaster than average serum-producing surface, with subsequent increase of the amount of serum excreted and, in particular, of the duration of this normal post-surgical phenomenon.

Notwithstanding this, transcutaneous needle aspiration solves this complication, providing it is carried out promptly and before the deposit becomes organised, the which occurs more frequently when the haematic content is larger. This makes aspiration impossible to perform and may cause a permanent aesthetic deficit.

Of the major complications, haemorrhage is the most easily solved.

Immediate re-operation solves this complication in all cases and does not affect post-surgical hospitalisation except that it postpones, by about 48 hours, removal of the metal staples from the wound and may cause subcutaneous spread of blood in the neck and the upper thorax, which represents a transitory aesthetic complication which normally disappears within 30 days after discharge from hospital.

The cause of the haemorrhage is not always detectable and in 5 out of 19 cases (26.31%) treated for haemorrhage by us, we were unable to establish the source of the bleeding. In most of the cases the bleeding took the form of a rexis involving the entire area operated on, and was probably due to post-surgical hypertension. All our haemorrhagic patients were, in fact, in a state of hypertension and, for this reason, we recommend very close monitoring of pressure during the first twenty-four hours after surgery (even in the case of patients whose pre-surgical diagnoses exclude hypertension) and prompt treatment of all manifestations of hypertension with appropriate drugs.

It is good practice, in our opinion, to leave the pre-thyroid muscles completely open along the median line, with only one or two stitches on the upper third to draw them together. By doing this, in the case of a sudden haemorrhage, the pressure caused by the nascent haematoma may find an outlet in the subcutaneous compartment instead of along the laryngo-tracheal axis, avoiding possible asphyxia or, in any case, retarding it.

As to damage to the external branch of the upper larynx nerve, we have come across no such case in our experience. This does not mean that, with absolute certainty, such events did not occur within our case history. It means that this type of lesion is objectively difficult to detect and often leads to a slight "fatigue" of voice tone, which may overlap normal post-surgical symptoms. Furthermore, lesions of the external branch of the upper larynx nerve are associated with damage to the recurrent laryngeal nerves which are obviously considered the only causes of the symptoms.

As to the latter, one must distinguish between definitive and temporary lesions. We report 31 patients with temporary recurrent laryngeal nerve lesions of whom 5 with a bilateral lesion following tracheostomy. All these patients recovered mobility of the chords within 90 days of the operation, after phoniatic therapy, including the 5 with bilateral deficit who were able to close the tracheostomy.

The definitive recurrent monolateral lesions numbered fifteen. In six of these cases it was possible to pinpoint the cause of the damage. For the other nine no evident cause was detected, given the anatomic integrity of the nerve. To this regard, it is opportune to make a number of considerations.

The risks leading to recurrent laryngeal nerve palsy are numerous: failure to prepare the nerve, relapse surgery, the presence of inflammatory infiltration in the thyroid parenchyma as occurs in instances of thyroiditis, cervicomedial goitre, recurrent laryngeal nerve course anomalies, neoplastic disease, but also lack of surgical experience.

With regard to these universally recognised risk factors, we feel we can say that the preparation of the recurrent laryngeal nerve must be seen as a vital aspect of the dissection and should invest the entire cervical tract up to the entry into the larynx; in cases of relapse, thyroiditis and cervicomedial goitres are, undoubtedly, the chief risk factor and it is no coincidence that damage occurs in these very circumstances. As regards cervicomedial goitre in particular, the problem occurs principally on the right side. On the right, in fact, the recurrent laryngeal nerve runs along the subclavian artery, separate from the tracheo-oesophageal axis which it approaches gradually before becoming attached to it four or five centimetres before entry into the larynx. The goitre during its descent into the mediastine may, in most cases, as occurs also on the left, bring pressure to bear the nerve on the tracheo-oesophageal axis; it may also insinuate itself between the trachea and the lower larynx nerve which is thus pushed forward towards the thyroid parenchyma which may assume an "hour-glass" contour having a smaller cervical portion and a larger mediastinal one, separated by an isthmus along which the lower larynx nerve runs. In this case the recurrent laryngeal nerve may be cut without being recognised or in any case stretched and broken during dislocation of the goitre. One should be aware of this possibility which must be suspected in all cases of cervico-mediastinal goitres, especially those which emerge in retro-vascular fashion; certainly in these, as in cases of post-surgical anomaly, the experience of the surgeon plays a fundamental role. It may be very useful to carry out the procedure recommended by Prove [4] where the recurrent laryngeal nerve is traced downward from its point of entry into the larynx.

Even after location and preparation of the nerve, dislocation of the "hour-glass" goitre remains, nonetheless, a difficult and dangerous manoeuvre.

Finally, neoplastic disease represents an increasingly less significant risk factor, given the greater accuracy and precocity of recent diagnostic methods which mean fewer direct infiltrations of the nerve (1 out of 361 of our patients equal to 0.27%).

As to recurrent laryngeal nerve paralysees without apparent cause, a number of acceptable hypotheses have been formulated. One possibility is *viral pathogenesis* of the recurrent lesions which may occur even in absence of surgery [5], facilitated by infections of the primary respiratory tract [6], often of a herpetic nature [7,8,9,10,11,12,] or due to the Epstein-Barr virus [13]. Some hold, besides, the possibility that dormant neurotropic viruses localised in the recurrent laryngeal nerve following previous pharyngeal-laryngeal infections reawaken stimulated by surgical or anaesthetic intervention [8,14] causing post-surgical paralysis.

Some authors explain transitory paralysis of the recurrent laryngeal nerve recalling that the upper larynx nerve may innervate the lateral and posterior cricoarytenoid and thyroarythenoid muscles, and associate these deficits to misinterpreted lesions of these muscles [15].

Other authors believe that *extra-laryngeal causes*, possibly associated to malfunction of the pre-thyroid muscles and to larynx nerve injury, lead to post-surgical dysphonia [16].

In some instances cases of recurrent paralysis have been attributed to traction. This pathogenetic mechanism may be triggered off by the upward and lateral dislocation of the laryngeal-tracheal axis while attempting to extend the recurrent laryngeal nerve in order to make it more easily palpable, or more frequently during dislocation of large cervicomediastinal goitres, especially those requiring median sternotomy. It is probable that repeated attempts to use traction before recourse to sternotomy may be responsible for lesions to the recurrent laryngeal nerve [17].

Chronic gastro-oesophagic reflux, which causes “acidic” laryngitis, is also considered a capable of paving the way for post-surgical paralysis [18].

So-called *difficult intubation*, often due to deviation of the trachea, according to some authors, may be responsible for lesions of the recurrent laryngeal nerve due to pressure and traction on its terminal branches. [19] Laursen suggests mechanical and neurogenetic causes. The former consist in

dislocation and subluxation of the cricoarytenoid with consequent stretching of the recurrent laryngeal nerve during traumatic insertion or removal of tubes. The neurogenetic causes are principally connected with the cuffing of the endotracheal tube at sub-glottal larynx level instead of within the trachea, with compression of the recurrent laryngeal nerve between the cuff and thyroid cartilage [20]. Raeder also attributes responsibility to the gas with which the cuff of the endotracheal tube is inflated : a mix of O<sub>2</sub> and N<sub>2</sub>O would guarantee fixed pressure within the cuff, while insufflation of air into the cuff causes a considerable increase of pressure over time causing relative traumatic compression [21].

Lesions due to use of laryngeal masks [22, 23, 24], also in cases not involving pathology of the neck, have been described. One cause may be the bad positioning of the distal end of the mask between the false chords causing direct trauma of the vocal chords with possible paresis; another cause arises due to compression of a part of the mask's cuff, the pressure of which, exceeding the critical pressure of the capillary perfusion of the pharyngeal mucous, thrusts it against portions of the pharynx which are crushed against surrounding structures such as the hyoid bone or the cervical vertebrae.

The recurrent endolaryngeal nerves may, according to us, suffer as a result of heat, especially if intense and prolonged, when this is applied to the exterior of the thyroidal cartilage by a diathermocoagulator but also when produced by harmonic ultra sound scalpel during removal of long and voluminous Lalouette pyramids. In these cases, we recommend, therefore, the use of bipolar coagulators which produce minimal energy-transfer effects upon the surrounding tissue.

Hypoparathyroidism is a complication which generally appears precociously, although 4 cases of late hypoparathyroidism emerging at a distance between 5 and 23 years after total thyroidectomy have been reported [25]. It may be transitory or definitive and is, without any doubt, the most frequent complication arising after thyroid surgery, especially following total thyroidectomy. Hypoparathyroidism is considered definitive when it still requires pharmacological treatment six months after surgery, even if some authors place this time limit at one year [26].

It is not always possible to compare case histories concerning this type of complication by simply matching numerical data, because it often occurs that these refer to varieties of diseases and surgical types thus preventing homologation of the results; furthermore, the data related to hypocalcaemia include at times all patients with values below a certain laboratory threshold, at times they refer to symptomatic patients and those in need of pharmacological treatment.

In reality hypocalcaemia is the diagnostic element of greatest clinical importance. The diminution of calcium serum levels is not always directly proportional to the gravity of the symptomatic picture; furthermore, it has been established that calcaemia often drops below conventional parametrical reference-levels even after surgery on other organs or apparati [27]. It is ionized calcium (that is the physiological form of greatest relevance and that responsible for various biological functions) which should be measured in order to obtain a trustworthy and constant reference parameter. This measurement is not carried out in the vast majority of cases.

Without ionized calcium level data symptomatic hypocalcaemia is the only significant marker available for assessment and this varies considerably from case to case.

The incidence of symptomatic manifestations is closely related to the "risk factors" which make certain patients particularly prone to post-surgical hypoparathyroidism. These factors include female gender, lengthy operations, considerable blood loss, low pre-surgical calcium levels, smaller residual thyroid weight, greater goitre volume, larger areas of thyroid tissue removed, youthfulness of patients, high levels of TBII (TSH-binding immunoglobulin)[28], relapse surgery, previous treatment with radio iodine, lymphadenectomy-associated procedure, sternal split, visualisation of one parathyroid only, self-transplant of more than one parathyroid [26], low parathormone values immediately after surgery [29].

Other factors which make subjects prone to hypoparathyroidism are hypomagnesaemia [30, 31, 32], possible early post-surgical calcitonin peak due, maybe, to pressure brought to bear on the gland during the operation [33, 34], high pre-surgical alkaline phosphate levels [35], late return to euthyroidism status [36, 37]. This last factor is, according to us, a very important determinant. In



fact, hypothyroidism determines a diminution of renal alpha-1-hydroxylase with consequent lack of conversion of active form vitamin D and diminution of calcium absorption notwithstanding regular parathormone levels [38], or even the presence of hyperparathyroidism due to hypocalcaemia. This is why some authors, including us, recommend early treatment with thyroid substitute and use of vitamin D as a preventive measure against early post-surgical hypocalcaemia, until reestablishment of correct TSH values occurs [37].

We are convinced, in fact, supported by the results of our research, that, unless all the parathyroids are removed, full doses of vitamin D must be administered for a number of days to avoid post-surgical tetanic crises, to be suspended gradually, but rapidly enough to avoid inhibition of the residual parathyroids.

Administration of vitamin D has always led to heated debates concerning the opportunity and the timing of the treatment. Up until recently many have held, as we did, that substitution treatment should be reserved only to patients suffering from severe hypocalcaemia and evident tetanic crises, rightly persuaded that the best stimulus for recovery of parathyroid functionality was the low plasmatic level of calcium. An intake of vitamin D caused inhibition of the post-surgical residual parathyroids to the point of making transitory hypocalcaemias permanent [26, 29].

In reality a recent study carried out by us has revealed the absence of permanent inhibitory effects of vitamin D on the production of parathormones which, following a curve specular to the calcaemic one, and after an initial phase of suppression, gradually returns to normal levels parallel to the diminution of calcitriol dosages, providing that the “weaning” occurs rapidly within a period of 2-3 weeks after the operation (table V). Besides, even patients who, according to the usual procedure, required vitamin D treatment were not necessarily destined to suffer from definitive hypoparathyroidism, but recovered earlier or later, depending on the time and quantity of the doses administered.

We too, in agreement with other authors, until quite recently, did not provide substitution to our symptomatic patient suffering from various degrees of paresthesia but administered only calcium

salts orally. This meant that these patients had to bear with hypocalcaemic symptoms for several days before reestablishment of calcium levels, in some cases to the point of a tetanic crisis. While easily handled in hospital, this complication is badly tolerated by patients and may cause a certain degree of alarm, in some cases even an anxiety neurosis for fear the crisis occurs again. Besides, having to wait for reestablishment of correct calcium homeostasis levels means longer hospitalisation, especially in cases of patients operated for hyper-functional pathologies.

Recently we altered our attitude towards post-surgical hypocalcaemia, focussing our attention on attempts to reduce symptomatic hypocalcaemia completely and, in particular, to eliminate incidences of post-surgical tetanic crises, independently of numerical plasmatic calcium counts. For this, we began routine vitamin D treatment of all patients undergoing total thyroidectomy, rapidly reducing the post-surgical doses until total suspension. The results of this experience have met with our complete satisfaction, because post-surgical tetanic crises have been eliminated totally in the cases treated by us, while cases of symptomatic patients have been reduced significantly.

Besides the various and proven pathogenetic justifications mentioned above, the causes of post-surgical hypoparathyroidism are to be sought, in our opinion, above all in the fortuitous ablation of one or more parathyroids or to the damage caused to their anatomical and/or vascular integrity by dissection. Perhaps high percentages of intra-thyroid parathyroids may be responsible for non-intentional avulsion of more than one gland, to the extent that Lo CY recommends searching the surgically removed parts scrupulously for sub-capsular parathyroids accidentally removed and self-transplanting them immediately [39].

This is certainly a useful procedure in cases of accidental avulsion, with a 75%-100% success level, even if transitory hypoparathyroidism occurs with greater frequency in patients who undergo parathyroid re-implants (21.4% as against 8.1%) [40] while symptomatic cases number 18%. There is no instance of definitive hypoparathyroidism after self-transplant. This seems to testify in favour of the true correlation existing between anatomical parathyroid damage and transitory hypothyroidism, besides confirming the efficacy of self-transplant in time, even if three cases of

hypoparathyroidism after 6 years following thyroidectomy with self-transplant have been reported [41].

In any case, there are reports of recovery of pre-surgical iPTH values one year after the operation in 83% of the patients who did not undergo self-transplant, 43% in the case of those who did [42].

In the case of self-transplanted patients, post-surgical administration of vitamin D may not be advisable, as it may prevent the transplanted parathyroids from re-acquiring their functionality [43].

Besides accident removal, an important role in the generation of parathyroid damage has been attributed to possible devascularisation of the parathyroids due to the surgical dissection. The recommendation which suggests tying the lower thyroid artery to the branches of the distal division instead of the trunk is based on the intention to safeguard the integrity of the parathyroid vascular stems.

Furthermore, some specific studies report the absence of statistically significant differences between patients whose lower thyroid artery was tied to the trunk, which certainly shortens surgery time and keeps the operating zone more blood-free, and therefore “safer” against risks of dissecting the recurrent laryngeal nerve, and those whose arteries were tied to the branches of the distal division [44,45].

We did not notice any statistically significant differences between patients with branch ligatures and those (over 200) with trunk ligatures on whom we have operated bilaterally for about two years.

Finally, as far as definitive hypothyroidism is concerned, this affects our patients for 0.85% (14 out of 1,636 patients) and we have reason to suspect that the reason why at least five of these remained hypoparathyroidal in time is to be sought in their post-surgical therapeutical conduct at home : assumption of vitamin D for too long or in excessive doses, which inhibited their residual parathyroids.

It is, therefore, preferable to prevent severe hypocalcaemia through post-surgical administration of calcitriol for a brief period rather than be obliged to treat it for an excessively long period and risk iatrogenic hypoparathyroidism.

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	<u>TEMPORARY</u>	<u>DEFINITIVE</u>
<u>EARLY</u>	<ul style="list-style-type: none"> <li>- <i>Postoperative pain</i></li> <li>- <i>Nausea e vomiting</i></li> <li>- <i>Seromas and infections</i></li> <li>- <b>Unilateral or bilateral superior laryngeal nerve palsy</b></li> <li>- <b>Unilateral or bilateral inferior laryngeal nerve palsy</b></li> <li>- <b>Hypoparathyroidism</b></li> </ul>	<ul style="list-style-type: none"> <li>- <b>Postoperative bleeding</b></li> <li>- <b>Unilateral or bilateral superior laryngeal nerve palsy</b></li> <li>- <b>Unilateral or bilateral inferior laryngeal nerve palsy</b></li> <li>- <b>Cervical – mediastinal lesions (thoracic duct, pleura, cervical sympathetic plexus)</b></li> <li>- <b>Hypoparathyroidism</b></li> </ul>
<u>TARDY</u>	<ul style="list-style-type: none"> <li>- <i>Seromas and infections</i></li> </ul>	<ul style="list-style-type: none"> <li>- <i>Hypertrophic and keloid scars</i></li> <li>- <i>Osteoporosis</i></li> <li>- <b>Unilateral inferior laryngeal nerve palsy</b></li> <li>- <b>Hypoparathyroidism ?</b></li> </ul>

**Tab. I:** Minor complications: *in italics* - Major complications: **in bold.**

<b>OPERATION</b>	<b>DISEASE</b>	<b>N.</b>	<b>TOTAL</b>
<b>TOTAL THYROIDECTOMIES</b>	Papillar carcinoma	220	<b>325</b>
	Follicular carcinoma	65	
	Hurtle cells carcinoma	9	
	Medullar carcinoma	12	
	Insular carcinoma	6	
	Anaplastic carcinoma	5	
	Papillar carcinoma + Medullar carcinoma	3	
	Papillar carcinoma + Hashimoto thyroiditis	2	
	Lymphoma	3	
<b>PALLIATIVE RESECTIONS + TRACHEOSTOMY</b>		13	<b>13</b>
<b>CERVICAL -MEDIASTINAL LYMPHADENECTOMIES NOT CONTEMPORARY TO TOTAL THYROIDECTOMY</b>	Papillar carcinoma	16	<b>23</b>
	Insular carcinoma	3	
	Follicular carcinoma	2	
	Medullar carcinoma	2	
<b>TOTAL</b>			<b>361</b>

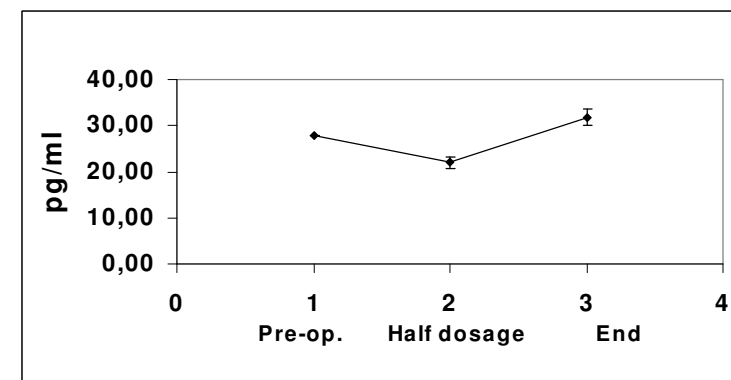
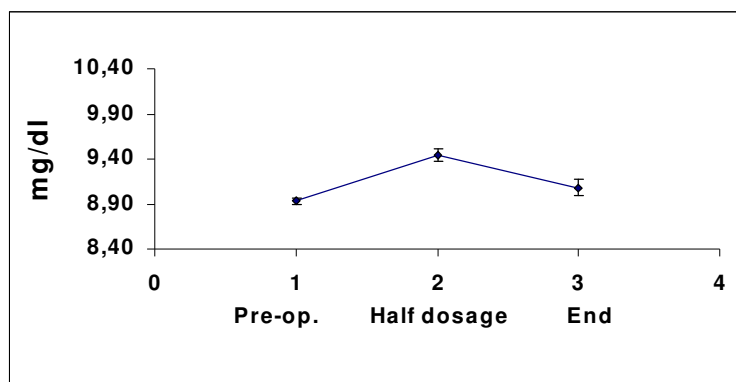
**Tab. II: Operations for neoplastic disease.**

<b>OPERATION</b>	<b>DISEASE</b>	<b>N.</b>	<b>TOTAL</b>
<b>CENTRAL LYMPHADENECTOMIES</b>	Papillar carcinoma	45	<b>50</b>
	Medullar carcinoma	1	
	Insular carcinoma	3	
	Papillar carcinoma + Hashimoto thyroiditis	1	
<b>UNILATERAL CERVICAL - MEDIASTINAL LYMPHADENECTOMIES</b>	Papillar carcinoma	2	<b>4</b>
	Medullar carcinoma + Papillar carcinoma	2	
<b>BILATERAL CERVICAL - MEDIASTINAL LYMPHADENECTOMIES</b>	Papillar carcinoma	24	<b>33</b>
	Anaplastic carcinoma	1	
	Hurtle cells carcinoma	1	
	Medullar carcinoma	7	
<b>TOTAL</b>			<b>87</b>

**Tab. III: Total thyroidectomy plus lymphadenectomies for neoplastic disease.**

OPERATION	DISEASE	N.	TOTAL	
<b>TOTAL THYROIDECTOMY</b>	Normal/hypo-functioning plurinodular goitre	1216	<b>1398</b>	
	Toxic multinodular goitre	107		
	Graves' disease	59		
	Thyroiditis	Hashimoto		13
		De Quervain		2
Riedel		1		
<b>LOBECTOMY + ISTMUSECTOMY</b>	Normal/hypo-functioning uninodular goitre	157	<b>188</b>	
	Toxic uninodular goitre	31		
<b>TOTAL</b>			<b>1586</b>	

**Tab. IV: Operations for non-neoplastic disease.**



**Tab. V: Behaviour of calcium and iPTH serum levels in relation to vitamin D dosage**