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CONSENSUS STATEMENT

Diagnostic, therapeutic and health-care management protocol in thyroid surgery: a position statement of the Italian Association of Endocrine Surgery Units (U.E.C. CLUB)

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Abstract

Purpose The diagnostic, therapeutic and health-care management protocol (Protocollo Gestionale Diagnostico-Terapeutico-Assistenziale, PDTA) by the Association of the Italian Endocrine Surgery Units (U.E.C. CLUB) aims to help treat the patient in a topical, rational way that can be shared by health-care professionals.

Methods This fourth consensus conference involved: a selected group of experts in the preliminary phase; all members, via e-mail, in the elaboration phase; all the participants of the XI National Congress of the U.E.C. CLUB held in Naples in the final phase. The following were examined: diagnostic pathway and clinical evaluation; mode of admission and waiting time; therapeutic pathway (patient preparation for surgery, surgical treatment, postoperative management, management of major complications); hospital discharge and patient information; outpatient care and follow-up.

Results A clear and concise style was adopted to illustrate the reasons and scientific rationales behind behaviors and to provide health-care professionals with a guide as complete

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as possible on who, when, how and why to act. The protocol is meant to help the surgeon to treat the patient in a topical, rational way that can be shared by health-care professionals, but without influencing in any way the physician–patient relationship, which is based on trust and clinical judgment in each individual case.

Conclusions The PDTA in thyroid surgery approved by the fourth consensus conference (June 2015) is the official PDTA of U.E.C. CLUB.

Keywords Thyroid disease · Thyroidectomy · Preoperative workup · Postoperative management

Introduction

The consensus conference updated the diagnostic, therapeutic and health-care management protocol in thyroid surgery issued by the Italian Association of Endocrine Surgery Units (U.E.C. CLUB), now in its fourth edition.

Members of the U.E.C. CLUB formed the group of experts and compared their clinical experience with the latest scientific literature. In the preliminary phase, the consensus conference involved a selected group of experts; the elaboration phase was conducted via e-mail among all members; the conclusion phase took place during the XI National Congress of the U.E.C. CLUB held in Naples (June 2015).

The objective is to provide the surgeon with protocols that can be of help for treating the patient in a topical, rational way that can be shared by health-care professionals, taking into account important clinical, health-care and therapeutic aspects, as well as potential sequelae and complications. A clear and concise style was adopted to illustrate the reasons and scientific rationales behind behaviors, and to provide health-care professionals with a guide as complete as possible on who, when, how and why to act.

However, it is not within the scope of the authors nor of the U.E.C. CLUB to influence in any way the physician–patient relationship, which is based on trust and clinical judgment in each individual case.

The following were examined:

- clinical evaluation and preoperative workup;
- hospital admission and waiting time;
- therapeutic pathway:

    - patient preparation for surgery,
    - surgical treatment,

    - postoperative management,
    - prevention and management of major complications,
    - hospital discharge and patient information;
- outpatient care and follow-up.

Clinical evaluation and preoperative workup

Proper diagnostic workup of thyroid disease referred to the surgeon encompasses a careful clinical evaluation carried out in endocrinological settings (history and physical examination, laboratory and imaging studies) that, depending on the diagnostic hypothesis, will facilitate the subsequent choice of the most appropriate surgical approach and of the extension of surgical procedure.

The most relevant events in the medical history include: neck or whole body irradiation for bone marrow transplantation or exposure to ionizing radiation during childhood or adolescence, first degree relatives suffering from syndromes that include thyroid cancer (Cowden syndrome, familial polyposis, Carney complex, MEN 2, Werner syndrome, etc.), rapidly growing thyroid nodules and clinical finding of dysphonia [1]. Physical examination should include an accurate assessment of thyroid and cervical lymph nodes.

The diagnostic workup must be essential and targeted not only at the definition of the thyroid disease (laboratory studies), but also at defining the therapeutic strategy and the extension of any potential surgery (instrumental studies).

The correct diagnostic workup for thyroid disease involves first-tier assessments that are necessary for the initial evaluation, and second-tier assessments for further diagnostic evaluation and for defining the therapeutic strategy.

Laboratory studies

First-tier assessments
- At the initial endocrinological evaluation of a patient with a thyroid disease, a serum TSH level should be obtained [1, 2].

Second-tier assessments
- *Calcitonin* Routine measurement of calcitonin in patients with thyroid nodules has the advantage of facilitating the early diagnosis of medullary thyroid carcinoma and, consequently, of being associated with improved 10-year survival of patients with this malignancy [3]. Also in view of these results, some European consensus conferences recommend routine use of calcitonin as screening for medullary thyroid carcinoma [4, 5]. The routine measurement of calcitonin in patients with nodular thyroid disease remains controversial in

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the USA, considering the false-positive results and the resulting low positive predictive value [1]. However, in view of the fact that an early diagnosis of medullary thyroid carcinoma could improve survival and that fine-needle aspiration cytology does not reliably exclude a diagnosis of medullary thyroid carcinoma [3–5], it is advisable to routinely determine calcitonin levels prior to thyroidectomy. In the presence of altered baseline calcitonin levels, it is appropriate to perform a calcium gluconate stimulation test to differentiate between C-cell hyperplasia and medullary thyroid cancer [4]. Stimulated calcitonin levels ≤100 pg/ml do not exclude a diagnosis of medullary thyroid carcinoma, whereas the likelihood of a medullary thyroid carcinoma is high for stimulated calcitonin levels >100 pg/ml. A diagnosis of thyroid medullary carcinoma is almost certain for stimulated calcitonin levels >500 pg/ml [4].

– *Serum calcium* Preoperative measurement of serum calcium is useful for the screening of primary hyperparathyroidism [6].

– *Serum phosphate and parathyroid hormone (PTH)* In case of hypercalcemia [6].

– *Anti-TPO (anti-thyroid peroxidase) and anti-Tg (anti-thyroglobulin) antibodies* If autoimmune disease is suspected.

– *TSH-receptor antibody (TRab)* if Graves' disease is suspected.

Instrumental studies

First-tier assessments

– *Thyroid ultrasound with color flow Doppler scanning* [1, 2, 5, 7].

It must be performed in all patients with a clinical suspicion of thyroid nodule and/or nodular goiter and in all cases of incidental radiological finding of thyroid nodular disease (CT or MRI of the neck, thyroidal uptake on 18FDG-PET scan, etc.) [1, 4, 5]. Ultrasonography allows an accurate morphological evaluation of the thyroid and adjacent regional lymph nodes, and the acquisition of pertinent information:

• location, size (possibly total gland volume) and structure of the lobes;
• the presence, number, size and structure (solid, cystic, mixed) of the thyroid nodules;
• vascular pattern of the nodule on color Doppler;
• status of the contralateral lobe in case of unilateral disease;

• nodular features indicative of malignancy (hypo-echogenicity, micro-calcifications, absence of halo, irregular margins, chaotic intranodular vascularity, round shape);
• condition of the trachea (midline, displaced, compressed);
• status of regional lymph nodes (reactive or suspicious).

Second-tier assessments

Second-tier assessments are aimed at further diagnostic evaluation and at defining the therapeutic strategy, particularly in case of minimally invasive approaches and re-intervention:

• *Contrast-enhanced ultrasound (CEUS)* CEUS represents a non-invasive technique for the differential diagnosis of thyroid nodules. However, due to the operator-dependent evaluation, CEUS has rather variable sensitivity (68–100 %) and specificity (67–94 %) [8].

• *Thyroid scintigraphy with radioactive iodine uptake test* Indications for this investigation have not changed recently and are limited to [9]:

– subclinical or overt hyperthyroidism,
– recurrent goiter,
– suspicion of forgotten or ectopic goiter.

• *Elastography* It measures the degree of distortion of a tissue subjected to an external force, and can therefore determine the elasticity of the tissue being examined. Malignant lesions often associate with changes in tissue mechanical properties; therefore this technique may help refine the diagnosis of the lesion being examined. However, the applicability of elastography in clinical practice is limited by the variable sensitivity (54–69 %) and specificity (60–96 %) described in different reports [10].

• *Fine-needle aspiration cytology (FNAC)* FNAC is the most accurate and cost-effective method for evaluating thyroid nodules [1, 2, 5]. Ultrasound guidance significantly reduces the number of non-diagnostic results and false negatives [1], especially in the case of nodules with a high likelihood of non-diagnostic cytology (>25–50 % cystic component) [11] and/or difficult to palpate or posteriorly located nodules. FNAC is indicated in all clinically or sonographically suspicious nodules with a diameter >1 cm. It is not recommended as a routine procedure for subcentimetric nodules; however, for nodules <1 cm, FNAC is recommended in the following situations [1]:

- pediatric age,
- family history of thyroid cancer,
- the presence of suspicious cervical lymphadenopathy,
- prior radiation therapy to the head, neck and/or mediastinum,
- exposure to ionizing radiation during childhood or adolescence,
- nodule with suspicious sonographic features (hypoechogenicity, microcalcifications, marked vascularity).

The cytology report should be descriptive, but also end with the assignment of the patient to a clearly defined and identifiable diagnostic category. In 2012, the Italian Societies of Endocrinology and the SIAPEC-IAP [12] appointed a working panel of experts to update the former consensus. They present a cytological classification that differs from the previous one in having introduced, in addition to the "Tir 1" category (inadequate sampling, to be repeated), the "Tir 1C" category (cystic nodules; non-diagnostic, but not to be repeated) (Table 1). The new classification subdivides, in addition, the "Tir 3" category into two subcategories (Table 1).

- "Tir 3a" (low-risk indeterminate lesion):

  - scant colloid (mainly at the periphery of the smear), vascular tissue, pigmented histiocytes;
  - medium-sized thyrocytes arranged in microfollicular structures (<60 %), with no nuclear atypia;
  - smears showing cells with regressive changes.

- "Tir 3b" (high-risk indeterminate lesion):

  - scant to absent colloid;
  - microfollicular aggregates of medium-sized thyrocytes (>60 %);

Table 1 The Italian thyroid cytology classification system (2013) [12]

TIR	Diagnostic category	Risk of malignancy (%)
TIR 1	Non-diagnostic	–
TIR 1C	Non-diagnostic cystic	Low
TIR 2	Benign	<3
TIR 3A	Low-risk indeterminate lesion	<10
TIR3B	High-risk indeterminate lesion	15–30
TIR 4	Suspicious for malignancy	60–80
TIR 5	Malignant	>95

- focal polymorphism, in the absence of nuclear atypia suggestive of papillary thyroid carcinoma;
- the same microfollicular or trabecular pattern may be formed by oxyphilic cells (oxyphilic follicular proliferation).

This further subdivision of "Tir3" aims at reducing the percentage of nodules with indeterminate cytology to be submitted to surgery [12]. Immunocytochemical and/or molecular genetic markers can be used to complement cytology: calcitonin, chromogranin A and CEA are used in suspected medullary carcinoma, whereas PTH can detect parathyroid lesions [1, 12].

Thyroglobulin and calcitonin measurement in the wash-out fluid from fine-needle aspiration of thyroid nodules and/or cervical lymph nodes is a valuable complement to conventional cytology for diagnosing primary or metastatic thyroid cancer, especially in doubtful or non-diagnostic cases [1].

- *Core needle biopsy (CNB)* Tissue biopsy is obtained by a cutting needle, usually equipped with a retractable spring-loaded mechanism (18-21 G Trucut needle). This method is carried out only under ultrasound guidance and is currently widely used in routine diagnostics. The sampling of tissue that includes the periphery of the nodule and the surrounding thyroid parenchyma allows examining the architectural characteristics of the thyroid tissue, allowing a microhistological diagnosis. Recently, indications to CNB have been extended to nodules with inadequate (Tir 1) or indeterminate (Tir 3) cytology [13].
- *Laryngeal fibroscopy* Preoperative laryngoscopy is recommended in all candidates to thyroidectomy to assess the morphological and functional integrity of the vocal folds (Table 2).
- *CT/MRI* These alternative imaging modalities may be useful in the assessment of large, rapidly growing, or retrosternal or invasive tumors to assess the involvement of extrathyroidal tissues [1, 2].
- *18F-FDG PET-CT* It can be useful in case of elevated thyroglobulin levels potentially due to local and/or distant recurrence in the setting of suspicious lesions with-

Table 2 Mandatory indications to preoperative laryngoscopy

Patients complaining dysphonia

Re-intervention (to exclude potential pre-existing injury of laryngeal nerves)

Symptomatic large or substernal goiter

Locally invasive thyroid cancer

out 131I uptake. This technique, used for the staging of many cancers, may incidentally reveal areas of increased uptake within the thyroid—"incidentalomas"—that, in 25 % of cases, turn out to be cancer. At present, 18F-FDG PET-CT cannot be considered a routine investigation [1].

Hospital admission and waiting time

- The waiting time for the hospital admission is established on the basis of preoperative diagnosis (Table 3).
- The pre-admission/admission workup includes complete preoperative evaluation (Table 4).
- Recommendations for patients.

  – Patients should continue their current thyroid medications (methimazole, propylthiouracil, thyroxine, beta-blockers taken on a regular basis) until the day prior to surgery, unless otherwise indicated due to medical or anesthesiological reasons [2];
  – As for every surgical procedure, in patients with cardiovascular disease, discontinuation of antiplatelet therapy—which may be substituted with low molecular weight heparins at least 1 week prior to surgery—needs to be balanced against the severity of the comorbidity.
- Admission.
- On the same day of surgery, unless otherwise indicated or required.

Table 3 Priority and waiting time for hospital admission

Preoperative diagnosis	Priority
Confirmed and/or advanced thyroid carcinoma	High (within 1 month)
Thyroid suspicious/ indeterminate nodules	Intermediate (within 3 months)
Hyperthyroidism with poor compliance to medical treatment	
Euthyroid benign disease	Low (within 12 months)
Stabilized hyperthyroid benign disease	

Table 4 Preadmission/Admission workup

Blood chemistry, complete blood count and coagulation tests
ECG
Chest X-ray (where indicated, depending on patient's age and comorbidities)
Anesthesiology consultation
ENT consultation for the assessment of vocal fold mobility (recommended in all patients; mandatory for re-operative surgery, substernal goiter, thyroid malignancy)

Therapeutic pathway

Patient preparation for surgery

- *Antibiotics* Antibiotic prophylaxis is not indicated in thyroidectomy [2, 14], except for particular cases, such as severe diabetes, cardiac valvular disease and immunodeficiency (hemodialysis or transplant patients).
- *Antithrombotic prophylaxis* International guidelines [2, 15] do not make specific recommendations regarding thyroid or neck surgery. Guideline indications for thromboprophylaxis in general surgery are as follows:

  – low molecular weight heparin (LMWH) for surgery lasting >45 min and in patients aged >40 years;
  – use of appropriate graduated compression stockings or intermittent pneumatic compression in the presence of venous thromboembolism risk factors.

There is no consensus among endocrine surgeons on the indications for thromboprophylaxis with LMWH, because of the high risk associated with the development of a postoperative cervical hematoma.

- *Blood units* autologous predeposit blood donation or preparation of blood units for thyroidectomy is not justified.
- *Position on the operating table* (joint responsibility of the surgeon and anesthesiologist).

  – patient in the supine position with a small wedge beneath the shoulders, at the scapular level, to allow a mild hyperextension of the neck;
  – the neck is slightly hyperextended and arms adducted and secured next to the patient's body to avoid rare, but severe and sometimes irreversible, brachial plexus paralyses due to stretch injury [16];
  – elbows should be adequately padded to avoid ulnar nerve paralysis secondary to compression;
  – eye protection to avoid corneal ulceration and ocular trauma.
- *Informed consent*
  Patients should be adequately informed by the surgeon of the indications for surgery, possible alternative treatments, advantages expected from surgery, general and specific complications, rehabilitation therapy, if needed, and the clinical consequences of potential permanent postoperative injuries.
  The information provided should be clearly and completely explained. After providing the most complete information, the physician will seek the patient's consent to perform surgery, taking into full consideration

any expression of dissent, even on individual aspects of the procedure or its potential consequences.

Transmission of information and the informed consent should preliminarily take place during the first visit and be renewed upon admission, before surgery, especially if enough time has passed, such that the initial conditions may have changed. In fact, the patient must be given the opportunity to discuss in depth with his/her physician (or other trusted persons) the information received and, if desired, to get information on the health facility where he or she will be treated and/or on the team that will perform the surgery.

Given the peculiarity of the therapeutic intervention (partial or total removal of the thyroid gland) and its potential consequences on the physical integrity of the subject [17], it is necessary that written documentation of the informed and conscious consent be retained, and that the informed consent process be documented in a specific chart note.

With this aim, a specific consent form is adopted that should be personalized and signed off both by the patient and the physician each time (see additional material).

- *Indications*

Surgical thyroid disease mainly includes thyroid malignancies and dysplastic–hyperplastic focal or diffuse thyroid disease, hyperthyroidism and, marginally, thyroiditis.

Thyroid malignancy encompasses a diverse group of cancers characterized by a considerable diversity regarding biology and prognosis. Most malignant thyroid neoplasms arise from follicular cells: papillary carcinoma, follicular carcinoma, and poorly differentiated and undifferentiated (anaplastic) carcinoma. Other neoplasms arise from thyroid parafollicular cells or C cells (medullary carcinoma) and, finally, a minority of thyroid neoplasms arise from thyroid mesenchymal cells (malignant lymphoma, sarcoma, etc.).

Benign surgical thyroid conditions include all conditions characterized by alterations in the morphology and/or function of the gland. In this context, diagnostic procedures are aimed at clarifying the nature of the thyroid disease and at defining all the morphological and functional alterations of the gland, taking into account the different treatment options available. An indication for surgery should take into account the results of diagnostic testing and localization studies, possible conservative treatment options and potential complications of surgery.

Specific diagnostic procedures may be required to better plan the surgical intervention, such as preoperative ultrasonography performed by the surgeon, which can

Table 5 Main surgical indications for thyroid disease

Suspected or confirmed malignancy
Severe compressive disease (dysphagia, dysphonia, dyspnoea)
Rapidly growing lesions
Substernal goiter
Trachea and/or esophagus deviation and/or compression
Toxic goiter (uni-/multinodular)
Graves' disease resistant to medical therapy and/or with severe ophthalmopathy [20]
RET gene mutation

be useful in assessing the extent of surgery needed [18, 19]. Careful postoperative follow-up should be planned for prompt detection of any complications or sequelae. The main surgical indications for thyroid disease are reported in Table 5.

Surgical treatment

Of all the procedures that have been proposed for thyroid surgery, the following can be considered to be in current use:

- *Lobectomy plus isthmusectomy* [1].
- *Total thyroidectomy* (considered as synonym for near-total thyroidectomy, as the presence of remnants, although minimal, is pretty much constant, without affecting the radicality of the intervention) [1, 21];
- *Subtotal thyroidectomy with unilateral remnant* Its use is limited in clinical practice, due to the increased incidence of relapses. Given these disadvantages, it is controversial whether there is a benefit in terms of postoperative complications compared to total thyroidectomy [22, 23].

The surgical report must be accurate and provide a description of the thyroid gland and the macroscopic characteristics of the most relevant nodules.

The surgeon should also report on the identification and preservation of the external branch of the superior laryngeal nerve [24]; the identification and preservation of the inferior laryngeal nerves, mentioning dissection difficulties, if any; the parathyroid glands, specifying their location, morphology and preservation of anatomical integrity and blood supply.

A decision to leave macroscopic thyroid remnants in situ should be substantiated, and the location and size of the remnants should be specified.

- *Minimally invasive techniques*

In the last few years, several techniques have been developed for minimally invasive thyroidectomy [25]. Minimally invasive approaches for thyroidectomy can be classified into techniques with and without the use of an endoscope. The latter (MIT; minimal incision thyroidectomy) differ from conventional thyroidectomy by a shorter skin incision and involve the use of optical aids (magnifying glasses 2.5–3.5×) [25]. Techniques that involve using an endoscope can be divided into pure endoscopic techniques and video-assisted techniques.

An important limitation of endoscopic techniques is the difficulty of purely endoscopic dissection, especially when using accesses that are completely different from those used in conventional surgery (axillary, breast, chest access), which limited their use to the authors who have proposed them [25, 26].

Minimally invasive video-assisted thyroidectomy (MIVAT) is a totally gasless technique that involves a 1.5–2.0 cm central horizontal incision, use of a 5 mm 30 degree endoscope and dedicated dissection tools [27, 28]. This technique has large consensus and is safe and reproducible, with similar complications as compared to conventional surgery and significant advantages in terms of postoperative pain and discomfort, as well as of the esthetic outcome [29, 30].

Indications and contraindications to MIVAT [27–33] are reported in Table 6.

- *Robotic thyroidectomy*
  Use of robotic technology in the head and neck area allows several indirect approaches for thyroidectomy: gasless transaxillary (the most used) [34], transoral [35], retroauricular [36] and axillo-breast [37] approach.
  Indications and contraindications to robotic thyroidectomy [34, 38] are reported in Table 7.

- *Intraoperative nerve monitoring (IONM)*
  Inferior laryngeal nerve injury is one of the most feared complications after thyroidectomy, and medical litigation is increasingly frequent [2, 39, 40]. Further, it is known that anatomical nerve integrity does not necessarily imply functional integrity and, therefore, not all nerve injuries are recognized intraoperatively [41, 42].
  Several techniques have been proposed for intraoperative monitoring of the recurrent nerve (intraoperative nerve monitoring: IONM), but the most widespread and standardized method involves using endotracheal tube surface electrodes that are placed in contact with the mucosa of the vocal cords [43].

The use of IONM may be associated with a benefit in terms of transient recurrent laryngeal nerve injury [44]. However, despite a sensitivity >90 % [43], the specificity varies widely (30–80 %) [43–45] and the rate of false positives is high. Selective use of IONM has been proposed for high-risk patients (reinterventions, malignancy, and substernal goiter) based on improvements in postoperative outcomes [39], but this result has not been confirmed in other reports [39].

Thus, intraoperative use of IONM can be regarded as an adjunct in selected cases, but cannot replace meticulous surgical techniques based on the knowledge of the anatomy of the nerve and its variants.

More promising results are expected from the continuous intraoperative nerve monitoring (C-IONM), which allows real-time evaluation of the inferior laryngeal nerves function during surgical maneuvers and, therefore, could allow to prevent intraoperative injuries [46].

- Surgical treatment of hyperthyroidism

  - Isolated toxic adenoma: lobectomy plus isthmusectomy, especially for nodules ≥3 cm, compressive symptoms and poor patient compliance to radioiodine therapy [20].
  - Toxic multinodular goiter: total thyroidectomy [20].
  - Flajani–Basedow–Graves' disease: total thyroidectomy (indicated in case of intolerance, ineffectiveness or recurrence after thyrostatic treatment or when radioiodine therapy is contraindicated due to large thyroid size, compressive symptoms, young patient age and/or thyroid nodular disease). The presence of severe ophthalmopathy is another indication for surgery [20].

- Surgical treatment of euthyroidism

  - Unilateral nodular disease (negative cytology; normal contralateral lobe): lobectomy plus isthmusectomy [1].
  - Multinodular goiter: total thyroidectomy [22, 23, 31].

- Surgical treatment of substernal goiter

By definition, a substernal goiter extends into the mediastinum by at least 50 % of its volume. The incidence is reported to be between 1 and 30 %. Being influenced by the anatomical situation due to intrathoracic extension of the goiter, surgical procedures are burdened with a greater incidence of complications

Table 6 Indications and contraindications to MIVAT [27–33]

Indications	Contraindications	Relative contraindications
Thyroid nodules ≤35 mm	Prior neck surgery (except for completion thyroidectomy)	Prior neck irradiation
Thyroid volume ≤30 ml	Locally advanced thyroid carcinoma	Thyroiditis or Graves' disease
Low- and intermediate-risk papillary thyroid carcinoma [31–33]	Preoperative evidence of lymph node metastases	
Patients with RET gene mutation		

Table 7 Indications and contraindications to robotic thyroidectomy [34, 38]

Indications	Contraindications	Relative contraindications
Benign disease: nodules ≤5 cm, indeterminate nodules, Graves' disease	Previous thyroid or breast surgery	Arthrosis or previous surgery of the shoulder joint
Small differentiated thyroid carcinomas	Previous head and neck irradiation	Thyroiditis or Graves' disease
	Electronic medical devices (pacemakers, defibrillators) in the pectoral region	Body mass index (BMI) >30
		Distance from the axilla to the sternal notch >15 cm

[47, 48]. Substernal goiter is classified as primary (very rare, originating from ectopic mediastinal thyroid tissue, with no connection to the cervical thyroid gland, and blood supply from branches of the aorta, the innominate artery or the internal mammary artery) or secondary (originating from the thyroid, with preserved vascular, parenchymal or fibrous connection to the gland). Substernal goiter should be treated by total thyroidectomy through cervical access, which is possible in 90 % of cases [47–49]. Additional sternotomy and/or thoracotomy is necessary for malignancies with local infiltration of the mediastinum, for rare cases of primary substernal goiter [47, 48] or when the mediastinal and/or retrovascular component of the goiter is such that to make removal through the cervical incision dangerous or impossible.

• Surgical treatment of thyroid malignancy

– *Differentiated carcinoma* Surgery should ensure radicality, with removal of all tumor foci and minimal incidence of postoperative complications.
The extent of thyroidectomy (hemithyroidectomy versus total thyroidectomy) for differentiated thyroid carcinoma is subject to debate, as high-level evidence favoring a more aggressive surgical approach in terms of recurrence risk reduction and absolute survival is lacking [1, 50, 51]. A well-performed total thyroidectomy is associated with a relatively low incidence of complications, ensures good local control of cancer by removing even microscopic tumor foci (that are frequent and often bilateral), facilitates subsequent radiometabolic treatment and allows using serum thyroglobulin monitoring for follow-up. On the other hand, hemithyroidectomy may be proposed because of the relatively low risk of recurrence in exchange for half the postoperative complications of total thyroidectomy [50].
For lymphadenectomy, please refer to the appropriate section.

– *Medullary carcinoma* For the treatment of the tumor (T), total thyroidectomy is the only potentially curative treatment [2, 4, 52], for both sporadic (70 %) and hereditary (30 %) forms, either isolated or as part of a multiple endocrine neoplasia: MEN 2A or Sipple's syndrome (in association with pheochromocytoma and hyperparathyroidism); MEN 2B or Gorlin–Steinert syndrome (in association with pheochromocytoma, ganglioneuromatosis and marfanoid habitus). If medullary carcinoma is associated with pheochromocytoma, adrenalectomy must be planned and performed prior to or at the same time as thyroidectomy, after appropriate pharmacological preparation of the patient. If present, parathyroid disease will be treated during thyroidectomy. For lymphadenectomy, please refer to the appropriate section.

– *Undifferentiated or anaplastic carcinoma* Due to high aggressiveness, this cancer has an unfavora-

ble prognosis in most cases (median survival of approximately 5 months). However, a reduction in its incidence has been reported in recent years, partly related to early diagnosis that allows treatment of the differentiated histological types in the initial stages. When anaplastic carcinoma is suspected, clinical and instrumental assessment of disease by a multidisciplinary team (surgeon, pathologist, oncologist, radiation oncologist, radiologist) is pivotal for the evaluation of treatment options and advantages/disadvantages of the proposed treatments. The clinical onset is generally characterized by extensive local infiltration and/or distant metastases, although incidental findings on final pathology report are not rare. All anaplastic thyroid cancers are considered as stage IV (AJCC/UICC): stage IVa and IVb patients may be potential candidates for a multimodal treatment including a more or less radical surgical resection associated with radio- and chemotherapy, which, in some cases, allows subsequent surgical re-exploration for local disease control. In patients with stage IVc, treatment options remain limited and controversial. Treatment is mostly palliative (tracheostomy or tracheal esophageal stent), with the intent of improving patient quality of life as much as possible [53]. For lymphadenectomy, please refer to the appropriate section.

- Regional neck nodes dissection

  – *Differentiated carcinoma* Regional lymph node metastases at diagnosis are reported in 30–60 % of patients [54, 55]. The prognostic significance of lymph node involvement and, consequently, indications for and the extent of lymphadenectomy are still subject to debate [1, 54, 55]. Lymph node metastases are associated with increased risk of disease recurrence and reduced survival [55]. For this reason, when lymph node metastases are found pre- or intraoperatively, therapeutic lymphadenectomy extended to the levels involved is indicated [1]: level VI neck dissection if lymph nodes of the central compartment are involved; lateral cervical lymphadenectomy if lateral cervical lymph node levels are involved (ipsi- and/or bilaterally).
  The role and extent of prophylactic lymphadenectomy in differentiated thyroid carcinoma, in the absence of pre- and intraoperative evidence of lymph node involvement (cN0) is still debated [1, 50].
  It is known that prophylactic central neck dissection may be associated with an increased risk of postoperative complications (hypoparathyroidism and recurrent nerve injury), with no high-level scientific

evidence confirming its benefits. However, it has potential benefits: reduction of disease recurrence and postoperative serum thyroglobulin levels, more accurate disease staging and selection of patients in whom radioiodine treatment is indicated [50]. Although tumor size is considered as one of the risk factors for occult lymph node metastases to the central compartment, it has been shown that microcarcinomas behave like larger tumors with regard to biological aggressiveness and risk of local (lymph node) and/or distant metastases [56]. In conclusion, there are no preoperative parameters (age, gender, tumor size) to reliable identify an "at-risk" population who could benefit from a prophylactic central neck dissection [57].
Prophylactic ipsilateral central neck dissection with or without intraoperative pathology consultation on the nodes removed has been proposed for clinically unifocal and cN0 tumors, to reduce the risk of complications associated with prophylactic central neck dissection [54, 58–60].
Prophylactic lateral neck dissection in patients with differentiated thyroid carcinoma is not indicated. Ipsilateral or bilateral therapeutic functional lateral neck dissection (level II–III–IV–V lymph nodes) should be performed, if node metastases have been documented (ultrasonography, cytology, Tg measurement in washout fluid from fine-needle aspiration, intraoperative pathology consultation) [1]. Lateral neck dissection must be complete (level II, III, IV and V lymph nodes), compartment oriented and non-selective, i.e., not limited to macroscopically involved levels [1, 4].

  – *Medullary carcinoma* Medullary carcinoma is characterized by early and variable metastatic spread to lymph nodes in the central (50–81 %) and lateral (34–81 %) compartment [61]. Clearly, a careful neck dissection, where indicated, is crucial in the treatment of this cancer. Minimum treatment for tumors >5 mm is total thyroidectomy associated with central neck dissection (level VI) [61]. However, indications for and extent of lateral neck dissection remain controversial [4, 52]. In fact, there is no consensus on recommending bilateral prophylactic dissection of lymph nodes in the lateral compartments in the recent guidelines by the American Thyroid Association (ATA) (recommendation 25) [52]. The proposed approaches include: prophylactic bilateral neck dissection in the case of palpable tumors and/or node metastases in the ipsilateral lateral neck and/or high calcitonin levels (>200 pg/ml) [4, 52]; prophylactic ipsilateral lateral neck dissection in the case of palpable tumors and/or moderately increased calcitonin

levels (between 20 and 200 pg/ml) [4, 52]; therapeutic ipsilateral lateral neck dissection, in the case of preoperative and/or intraoperative evidence of lymph node metastases in the lateral compartment [4, 52, 61].

– *Anaplastic carcinoma* For patients being treated with radical intent, neck dissection should be considered if nodes are involved [53].

• *Drainage* The use of wound drains after thyroid surgery is widely practiced, despite several studies showing no real benefit in controlling postoperative bleeding [62]. Nevertheless, a potential benefit of drains—suction drains would be preferable—should be assessed in relation to the clinical situation.

• *Histological examination* Definitive histology of the gland after surgical removal is mandatory. Orienting the specimen with a surgical suture placed at the upper pole of the right lobe is always recommended to facilitate the histological description. The surgeon should not dissect the specimen to avoid affecting macroscopic examination by the pathologist.

Intraoperative consultation could be useful to confirm suspicious nodules ("Tir 4" on cytology, according to SIAPEC 2013 classification) [12] or node metastases. It is not useful for nodules with indeterminate follicular cytology (SIAPEC 2013 classification) [12], because it is generally non-diagnostic [63].

Postoperative management

Postoperative management should be provided by qualified medical and nursing staff trained to promptly recognize and treat possible complications, such as dyspnea, bleeding and hypocalcemic crisis. The recommended post-thyroidectomy nursing and medical care is summarized, respectively, in Tables 8 and 9.

Prevention and management of major complications

• Compressive hematoma

Post-thyroidectomy hematoma is a serious complication that can lead to severe consequences such as hypoxia, neurological disorders and death [2, 39]. The term "compressive hematoma" is well known in the medical literature and indicates possible airway compromise. Risk factors may be related to the patient, the thyroid disease and the surgeon [39]. Risk factors related to the patient essentially include a history of coagulopathy (hemophilia, von Willebrand disease, chronic renal

Table 8 Recommended post-thyroidectomy nursing care

Check of the surgical dressing and of the neck (exclude neck swelling)

Monitoring of drains, if any, for patency and proper functioning

Blood pressure monitoring

Notification of the on-call physician in case of:

  Exceeding blood loss from drains

  Progressive cervical swelling

  Onset of agitation, dyspnea, feeling of tightness around neck

  Clinical signs of hypocalcemia (paresthesia, Trousseau's signs)

Monitoring of serum calcium and/or PTH after total thyroidectomy

Table 9 Recommended post-thyroidectomy medical care

In case of "compressive hematoma" decompression of the neck removing cutaneous, subcutaneous and muscle sutures at the bedside, if the patient's conditions warrant it

Wound check and drain removal prior to discharge

Appropriate calcium and vitamin D supplementation therapy according the serum calcium and PTH level

If symptomatic hypocalcaemia (paresthesia, tetanic crisis) develops despite oral therapy, urgent serum calcium measurement should be ordered and calcium gluconate infused i.v.

Levothyroxine replacement therapy with adequate dosage based on weight, age and extent of thyroidectomy (lobectomy plus isthmusectomy versus total thyroidectomy)

failure and hemodialysis, liver diseases, etc.) and use of anticoagulants or antiplatelet agents. With regard to the risk associated with thyroid disease, toxic goiter and Graves' disease are presumed risk factors for postoperative bleeding. Substernal, intrathoracic or recurrent goiters are also at risk of postoperative bleeding [39, 64].

Surgeon-related risks are associated with correct performance of the surgical technique [39]. Even the surgical access may be a source of bleeding, due to a section of strap muscles and partial resection of thyroid tissue, as well as to injury to the anterior jugular veins [64]. Simulation of Valsalva maneuver by the anesthesiologist during the hemostasis phase can be useful, as it may reveal potential sources of venous bleeding. Incomplete closure of the strap muscles, leaving a marginal "hole", is a measure that allows spontaneous decompression of the hematoma in case of bleeding [2, 39]. If symptomatic hematoma develops, early diagnosis, immediate reopening of the wound and surgical revision are necessary. Clot removal and optimization of hemostasis are the definitive treatment for this potentially lethal complication and are to be preferred to prolonged observation. Conservative treatment should only be considered for asymptomatic and self-limiting hematomas.

- Hypoparathyroidism

  – If inadvertent devascularization or accidental removal of a parathyroid occurs during surgery, the gland could be reimplanted into a pocket in the ipsilateral sterno-cleidomastoid muscle previous its fragmentation in 0.5–1 mm slices (one for frozen section) [2, 65].
  – An incision in the parathyroid capsule may be useful in the case of venous congestion for decompression.
  – The onset of symptomatic hypocalcemia despite oral calcium carbonate and vitamin D supplementation mandates, after measuring serum calcium, intravenous administration of two 10 ml vials (2 g) of calcium gluconate diluted in 250 ml of normal saline, until symptoms have resolved.
  – Based on recent evidence [66, 67], combined assessment of postoperative PTH and serum calcium levels may be useful to modulate the treatment of patients with postoperative hypocalcemia (≤8 mg/dl). In the presence of normal PTH levels, hypocalcemia is usually controlled with oral calcium carbonate (2–6 g) given in at least three daily administrations. When hypocalcemia is associated with low PTH levels, calcium carbonate supplementation should be associated with calcitriol (0.50–1.5 mcg/day); treatment can be taken at home with weekly monitoring of serum calcium and progressive reduction of dosages, where possible. Calcium supplements with added sodium should be avoided in the elderly and hypertensive patients.

- Transient or permanent injury to the recurrent laryngeal nerve [2, 39]

  – Sections of the recurrent laryngeal nerve that are recognized intraoperatively can be repaired using microsurgical reconstruction techniques. Nerve reconstruction can be done using end-to-end or fascicular neurorrhaphy, or using a graft. The anastomosis between the inferior laryngeal nerve and the loop of the hypoglossal nerve, and in particular the terminal branch to the sternothyroid muscle, has also been described. These techniques, however, do not restore vocal cord motility; they can help improve tone and muscle trophism of the vocal cords, sometimes with positive effects on the phonatory and ventilatory function [68].
  – In the event of respiratory distress due to bilateral vocal cord paralysis at the time of extubation, immediate tracheotomy should be avoided and the patient should be kept intubated for the following 24 h. After 24 h extubation will be attempted, with fiber-optic assistance to check vocal folds motility.

  – Persistence of bilateral paralysis mandates maintaining intubation for an additional 24 h.
  – Tracheotomy is recommended if bilateral paralysis in adduction and respiratory distress further persists.
  – Tracheotomy is not necessary for phonatory bilateral paralysis with an adequate airway (vocal folds in the paramedian position).
  – Unilateral vocal cord paralysis usually only needs to be treated with speech therapy, according to indications by the ENT surgeon/phoniatrist.
  – Concomitant dysphagia to liquids, which is often associated with inhaling disturbances, mandates adding thickening agents to liquids, which are easier to swallow when turned into jelly.
  – In all instances, clinical observations and proposed and/or administered treatments must be accurately recorded on the patient's chart.

Hospital discharge and patient information

Patients are informed of their expected date of discharge one day in advance. On the appointed day, following medical examination, wound care and measurement of serum calcium in case of total thyroidectomy, discharge is confirmed and the patient is provided with relevant clinical documentation.

Timing

One-day surgery is possible only for patients undergoing thyroid lobectomy plus isthmusectomy, provided that patient history, clinical and family situation as well as logistics allow it [69].

Some authors have proposed one-day surgery also for patients undergoing total thyroidectomy for benign disease [69]. Day surgery and, even more so, outpatient surgery, is discouraged.

In this type of surgery, in addition to immediate complications, postoperative hypocalcemia should be taken into account. Calcium supplementation in all patients, who have undergone total thyroidectomy, regardless of serum calcium levels, may be an overtreatment and represent an additional cost [66]; further, it could cause iatrogenic hypercalcemia.

Patient information

Hospital discharge summary

Upon discharge, the patient should be provided with a comprehensive clinical report (a copy should be included

in the patient's chart) addressed to the primary care physician, signed off by the attending physician who discharges the patient, and containing the following essential information:

– date of admission and admit diagnosis;
– main diagnostic (laboratory and instrumental) investigations performed during the hospital stay, with particular emphasis on those with altered results;
– date and description of the surgical procedure, with reporting of any intraoperative difficulties encountered and reimplantation of parathyroid tissue, if performed;
– description of the postoperative course, with accurate highlighting of any complications (hemorrhage, dyspnea, dysphagia, dysphonia, hypocalcemia, etc.);
– pharmacological treatments administered to the patient;
– discharge diagnosis (final pathology report, if available);
– medications on discharge, clearly indicating posology and administration way;
– patient education on how to manage the surgical wound and promptly recognize symptoms of hypocalcemia;
– recommended and/or scheduled clinical and/or diagnostic follow-up;
– follow-up ENT/phoniatrics follow-up visit in the case of dysphonia and rehabilitation program if altered vocal fold mobility is documented;
– direct phone number of the hospital/clinic.

After discharge, the patient is attended by the primary care physician. For individuals who reside in a different region, discussing possible issues related to means of transport, length and type of travel with the patient or her/his family could be useful to establish the most appropriate timing for discharge and to give proper advice.

Practical advice upon discharge It may be useful to provide the patient with a leaflet containing practical information on self-management of recovery and contact information for use in case of need for advice.

The form proposed and adopted by the U.E.C. CLUB is enclosed and available in the section additional materials.

Outpatient care and follow-up

The following take place at the Endocrine Surgery outpatient service:

• Initial visits of patients referred by their primary care physician, endocrinologist or the anatomic pathology service. Patients considered for admission should be promptly provided with adequate information on:

– indications for surgery;
– possible alternative treatments;
– advantages that surgery may offer and possible risks associated with the surgical procedure to be performed;
– detailed description of transient and permanent postoperative complications.

The patient is provided with a short clinical report that includes:

– medical history, with particular reference to health conditions that may require special consideration;
– physical examination;
– diagnosis;
– proposed treatment;
– diagnostic testing/investigations recommended, if any;
– agreement or disagreement with other consultants' reports provided by the patient;
– if surgery is proposed, the information provided to the patient should be clearly noted on the report, to obtain a preliminary consent to the recommended treatment;
– application for hospital admission, including priority for admission.
– Follow-up visits, if surgical dressings are needed. Otherwise, the patient will be referred to the outpatient endocrinology clinic for follow-up.
– ENT consultation for follow-up, with fiberoptic laryngoscopy to assess vocal fold mobility in case of symptoms (dysphonia), and speech therapy, if needed, based on recommendations by the ENT surgeon and/or the phoniatrist.

Patient with differentiated thyroid carcinoma

Support of the endocrinologist, nuclear medicine physician, pathologist and radiologist should be ensured at all stages of the diagnostic–therapeutic pathway, particularly in patients with thyroid carcinoma, and the most appropriate management of challenging cases should be determined collegially.

For patients with differentiated carcinoma, indication for postoperative radioiodine therapy should be based on risk factors for recurrence [1].

Risk stratification is essential not only to determine the most appropriate postoperative radioiodine therapy regimen, but also to establish appropriate thyrosuppressive therapy and determine the intensity and frequency of follow-up.

Depending on the clinical course of disease and response to therapy, the risk of recurrence and mortality may vary over time. Reclassification of risk based on the information obtained during follow-up may be useful, and it is essential to ensure proper management [1, 70].

Availability of a database that can be searched and updated at any time by any member of the multidisciplinary team and containing information essential to build and implement an individualized plan for each patient (risk stratification, adjuvant treatment, follow-up) is desirable [71].

Compliance with ethical standards

Conflict of interest   The authors declare that they have no conflict of interest.

Ethical approval   This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent   For this type of study formal consent is not required.

References

1. Haugen BR, Alexander EK, Bible KC et al (2016) 2015 American Thyroid Association Management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 26:1–133

2. Rosato L, De Toma G, Bellantone R et al (2012) Diagnostic, therapeutic and healthcare management protocols in thyroid surgery: 3rd consensus conference of the Italian association of endocrine surgery units (U.E.C. CLUB). Minerva Chir 67:365–379

3. Elisei R, Bottici V, Luchetti F et al (2004) Impact of routine measurement of serum calcitonin on the diagnosis and outcome of medullary thyroid cancer: experience in 10,864 patients with nodular thyroid disorders. J Clin Endocrinol Metab 89:163–168

4. Dralle H, Musholt TJ, Schabram J et al (2013) German Association of Endocrine Surgeons practice guideline for the surgical management of malignant thyroid tumors. Langenbecks Arch Surg 398:347–375

5. Gharib H, Papini E, Paschke R et al (2010) American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocrinol Pract 16(Suppl 1):1–43

6. Rosato L, Raffaelli M, Bellantone R et al (2014) Diagnostic, therapeutic and healthcare management protocols in parathyroid surgery: II consensus conference of the Italian Association of Endocrine Surgery Units (UEC CLU). J Endocrinol Invest 37:149–165

7. Yeh MW, Bauer AJ, Bernet VA et al (2015) American Thyroid Association statement on preoperative imaging for thyroid cancer surgery. Thyroid 25:3–14

8. Yu D, Han Y, Chen T (2014) Contrast-enhanced ultrasound for differentiation of benign and malignant thyroid lesions: meta-analysis. Otolaryngol Head Neck Surg 151:909–915

9. Kahaly GJ, Bartalena L, Hegedus L (2011) The American Thyroid Association/American Association of Clinical Endocrinologists guidelines for hyperthyroidism and other causes of thyrotoxicosis: a European perspective. Thyroid 21:585–591

10. Dudea SM, Botar-Jid C (2015) Ultrasound elastography in thyroid disease. Med Ultrason 17:74–96

11. Bellantone R, Lombardi CP, Raffaelli M et al (2004) Management of cystic or predominantly cystic thyroid nodules: the role of ultrasound-guided fine-needle aspiration biopsy. Thyroid 14:43–47

12. Nardi F, Basolo F, Crescenzi A et al (2014) Italian consensus for the classification and reporting of thyroid cytology. J Endocrinol Invest 37:593–599

13. Chen BT, Jain AB, Dagis A et al (2015) Comparison of the efficacy and safety of ultrasound-guided core needle biopsy versus fine-needle aspiration for evaluating thyroid nodules. Endocr Pract 21:128–135

14. Gentile I, Rosato L, Avenia N et al (2014) Do Italian surgeons use antibiotic prophylaxis in thyroid surgery? Results from a national study (UEC–Italian Endocrine Surgery Units Association). Ann Ital Chir 85:33–37

15. Gould MK, Garcia DA, Wren SM et al (2012) Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 141:e227S–e277S

16. Delfrate R, Lampugnani R, Rosato L (2008) Complicanze da posizione sul letto operatorio e lesioni del plesso brachiale. In: Rosato L (ed) Trattato Italiano di Endocrinochirurgia. CLUB delle U.E.C., Grafica Santhiatese, vol I, pp 403–404

17. Federazione Nazionale degli Ordini dei Medici Chirurghi e degli Odontoiatri (2014) Codice di Deontologia Medica 2014, capo IV° Informazione e Comunicazione Consenso e Dissenso, artt., pp 33–39

18. Carneiro-Pla D, Amin S (2014) Comparison between preconsultation ultrasonography and office surgeon-performed ultrasound in patients with thyroid cancer. World J Surg 38:622–627

19. Oltmann SC, Schneider DF, Chen H et al (2015) All thyroid ultrasound evaluations are not equal: sonographers specialized in thyroid cancer correctly label clinical N0 disease in well differentiated thyroid cancer. Ann Surg Oncol 22:422–428

20. Bahn Chair RS, Burch HB, Cooper DS et al (2011) Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid 21:593–646

21. Kebebew E, Clark OH (2000) Differentiated thyroid cancer: "complete" rational approach. World J Surg 24:942–951

22. Agarwal G, Aggarwal V (2008) Is total thyroidectomy the surgical procedure of choice for benign multinodular goiter? An evidence-based review. World J Surg 32:1313–1324

23. Moalem J, Suh I, Duh QY (2008) Treatment and prevention of recurrence of multinodular goiter: an evidence-based review of the literature. World J Surg 32:1301–1312

24. Bellantone R, Boscherini M, Lombardi CP et al (2001) Is the identification of the external branch of the superior laryngeal nerve mandatory in thyroid operation? Results of a prospective randomized study. Surgery 130:1055–1059

25. Linos D (2011) Minimally invasive thyroidectomy: a comprehensive appraisal of existing techniques. Surgery 150:17–24

26. Slotema ET, Sebag F, Henry JF (2008) What is the evidence for endoscopic thyroidectomy in the management of benign thyroid disease? World J Surg 32:1325–1332

27. Bellantone R, Lombardi C, Raffaelli M (2004) Tiroidectomia video-assistita. Enciclopédie Médico-Chirurgicale—Tecniche Chirurgiche—Chirurgia Generale, I–46–460-A. Elsevier SAS, Paris, pp 1–14

28. Miccoli P, Berti P, Raffaelli M et al (2001) Minimally invasive video-assisted thyroidectomy. Am J Surg 181:567–570

29. Lombardi CP, Raffaelli M, D'Alatri L et al (2008) Video-assisted thyroidectomy significantly reduces the risk of early postthyroidectomy voice and swallowing symptoms. World J Surg 32:693–700

30. Miccoli P, Minuto MN, Ugolini C et al (2008) Minimally invasive video-assisted thyroidectomy for benign thyroid disease: an evidence-based review. World J Surg 32:1333–1340

31. Lombardi CP, Raffaelli M, de Crea C et al (2007) Report on 8 years of experience with video-assisted thyroidectomy for papillary thyroid carcinoma. Surgery 142:944–951

32. Lombardi CP, Raffaelli M, De Crea C et al (2012) Video-assisted versus conventional total thyroidectomy and central compartment neck dissection for papillary thyroid carcinoma. World J Surg 36:1225–1230

33. Miccoli P, Pinchera A, Materazzi G et al (2009) Surgical treatment of low- and intermediate-risk papillary thyroid cancer with minimally invasive video-assisted thyroidectomy. J Clin Endocrinol Metab 94:1618–1622

34. Lee J, Kang SW, Jung JJ et al (2011) Multicenter study of robotic thyroidectomy: short-term postoperative outcomes and surgeon ergonomic considerations. Ann Surg Oncol 18:2538–2547

35. Richmon JD, Pattani KM, Benhidjeb T et al (2011) Transoral robotic-assisted thyroidectomy: a preclinical feasibility study in 2 cadavers. Head Neck 33:330–333

36. Terris DJ, Singer MC, Seybt MW (2011) Robotic facelift thyroidectomy patient selection and technical considerations. Surg Laparosc Endosc Percutan Tech 21:237–242

37. Lee KE, Koo do H, Im HJ et al (2011) Surgical completeness of bilateral axillo-breast approach robotic thyroidectomy: comparison with conventional open thyroidectomy after propensity score matching. Surgery 150:1266–1274

38. Piccoli M, Mullineris B, Gozzo D et al (2015) Trans-axillary thyroidectomy and parathyroidectomy. In: Spinoglio G (ed) Robotic surgery—current application and new trends. Springer-Verlag, pp 15–22

39. Lombardi CP, Raffaelli M, De Crea C et al (2007) Complications in thyroid surgery. Minerva Chir 62:395–408

40. Rosato L, Avenia N, Bernante P et al (2004) Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. World J Surg 28:271–276

41. Bergenfelz A, Jansson S, Kristoffersson A et al (2008) Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. Langenbecks Arch Surg 393:667–673

42. Woodson G (2003) Pathophysiology of recurrent laryngeal nerve. In: Randolph GW (ed) Surgery of the thyroid and parathyroid glands. Saunders, Philadelphia, pp 366–373

43. Randolph GW, Dralle H, International Intraoperative Monitoring Study Group et al (2011) Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. Laryngoscope 121(Suppl 1):S1–S16

44. Barczynski M, Konturek A, Cichon S (2009) Randomized clinical trial of visualization versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy. Br J Surg 96:240–246

45. Sitges-Serra A, Fontane J, Duenas JP et al (2013) Prospective study on loss of signal on the first side during neuromonitoring of the recurrent laryngeal nerve in total thyroidectomy. Br J Surg 100:662–666

46. Phelan E, Schneider R, Lorenz K et al (2014) Continuous vagal IONM prevents recurrent laryngeal nerve paralysis by revealing initial EMG changes of impending neuropraxic injury: a prospective, multicenter study. Laryngoscope 124:1498–1505

47. Raffaelli M, De Crea C, Ronti S et al (2011) Substernal goiters: incidence, surgical approach, and complications in a tertiary care referral center. Head Neck 33:1420–1425

48. Testini M, Gurrado A, Avenia N et al (2011) Does mediastinal extension of the goiter increase morbidity of total thyroidectomy? A multicenter study of 19,662 patients. Ann Surg Oncol 18:2251–2259

49. White ML, Doherty GM, Gauger PG (2008) Evidence-based surgical management of substernal goiter. World J Surg 32:1285–1300

50. McLeod DS, Sawka AM, Cooper DS (2013) Controversies in primary treatment of low-risk papillary thyroid cancer. Lancet 381:1046–1057

51. Pacini F (2015) Observation for newly diagnosed micro-papillary thyroid cancer: is now the time? J Endocrinol Invest 38:101

52. Wells SA Jr, Asa SL, Dralle H et al (2015) Revised american thyroid association guidelines for the management of medullary thyroid carcinoma. Thyroid 25:567–610

53. Smallridge RC, Ain KB, Asa SL et al (2012) American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid 22:1104–1139

54. Raffaelli M, De Crea C, Sessa L et al (2012) Prospective evaluation of total thyroidectomy versus ipsilateral versus bilateral central neck dissection in patients with clinically node-negative papillary thyroid carcinoma. Surgery 152:957–964

55. Sancho JJ, Lennard TW, Paunovic I et al (2014) Prophylactic central neck dissection in papillary thyroid cancer: a consensus report of the European Society of Endocrine Surgeons (ESES). Langenbecks Arch Surg 399:155–163

56. Lombardi CP, Bellantone R, De Crea C et al (2010) Papillary thyroid microcarcinoma: extrathyroidal extension, lymph node metastases, and risk factors for recurrence in a high prevalence of goiter area. World J Surg 34:1214–1221

57. Giordano D, Valcavi R, Thompson GB et al (2012) Complications of central neck dissection in patients with papillary thyroid carcinoma: results of a study on 1087 patients and review of the literature. Thyroid 22:911–917

58. Moo TA, Umunna B, Kato M et al (2009) Ipsilateral versus bilateral central neck lymph node dissection in papillary thyroid carcinoma. Ann Surg 250:403–408

59. Raffaelli M, De Crea C, Sessa L et al (2015) ipsilateral central neck dissection plus frozen section examination versus prophylactic bilateral central neck dissection in cN0 papillary thyroid carcinoma. Ann Surg Oncol 22:2302–2308

60. Raffaelli M, De Crea C, Sessa L et al (2013) Can intraoperative frozen section influence the extension of central neck dissection in cN0 papillary thyroid carcinoma? Langenbecks Arch Surg 398:383–388

61. Dralle H, Machens A (2013) Surgical management of the lateral neck compartment for metastatic thyroid cancer. Curr Opin Oncol 25:20–26

62. Woods RS, Woods JF, Duignan ES et al (2014) Systematic review and meta-analysis of wound drains after thyroid surgery. Br J Surg 101:446–456

63. Udelsman R, Westra WH, Donovan PI et al (2001) Randomized prospective evaluation of frozen-section analysis for follicular neoplasms of the thyroid. Ann Surg 233:716–722

64. Harding J, Sebag F, Sierra M et al (2006) Thyroid surgery: postoperative hematoma—prevention and treatment. Langenbecks Arch Surg 391:169–173

65. Testini M, Rosato L, Avenia N et al (2007) The impact of single parathyroid gland autotransplantation during thyroid surgery on postoperative hypoparathyroidism: a multicenter study. Transplant Proc 39:225–230

66. De Pasquale L, Sartori PV, Vicentini L et al (2015) Necessity of therapy for post-thyroidectomy hypocalcaemia: a multi-centre experience. Langenbecks Arch Surg 400:319–324

67. Raffaelli M, De Crea C, Carrozza C et al (2012) Combining early postoperative parathyroid hormone and serum calcium levels allows for an efficacious selective post-thyroidectomy supplementation treatment. World J Surg 36:1307–1313

68. Hong JW, Roh TS, Yoo HS et al (2014) Outcome with immediate direct anastomosis of recurrent laryngeal nerves injured during thyroidectomy. Laryngoscope 124:1402–1408

69. Materazzi G, Dionigi G, Berti P et al (2007) One-day thyroid surgery: retrospective analysis of safety and patient satisfaction on a consecutive series of 1,571 cases over a three-year period. Eur Surg Res 39:182–188

70. Rosario PW, Mourao GF, Siman TL et al (2014) A low postoperative nonstimulated serum thyroglobulin level excludes the presence of persistent disease in low-risk papillary thyroid cancer patients: implication for radioiodine indication. Clin Endocrinol (Oxf)

71. Carty SE, Doherty GM, Inabnet WB 3rd et al (2012) American Thyroid Association statement on the essential elements of interdisciplinary communication of perioperative information for patients undergoing thyroid cancer surgery. Thyroid 22:395–399