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SFE-AFCE-SFMN 2022 consensus on the management of thyroid nodules

SFE-AFCE-SFMN 2022 consensus on the management of thyroid nodules: Surgical treatment

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ABSTRACT

The SFE-AFCE-SFMN 2022 consensus deals with the management of thyroid nodules, a condition that is a frequent reason for consultation in endocrinology. In more than 90% of cases, patients are euthyroid, with benign non-progressive nodules that do not warrant specific treatment. The clinician's objective is to detect malignant thyroid nodules at risk of recurrence and death, toxic nodules responsible for hyperthyroidism or compressive nodules warranting treatment. The diagnosis and treatment of thyroid nodules requires close collaboration between endocrinologists, nuclear medicine physicians and surgeons, but also involves other specialists. Therefore, this consensus statement was established jointly by 3 societies: the French Society of Endocrinology (SFE), French-speaking Association of Endocrine Surgery (AFCE) and French Society of Nuclear Medicine (SFMN); the various working groups included experts from other specialties (pathologists, radiologists, pediatricians, biologists, etc.). This section deals with the surgical management of thyroid nodules.

1. Introduction

The surgical management of thyroid nodules has been extensively reported in the past decade: extent of thyroid surgery, indication for and extent of neck dissection, prevention of complications, outpatient surgery, and extra-cervical approaches. Thyroid surgery has been shaped by this work, and the present section presents 43 recommendations based on a critical review of the extensive literature now available on the surgical management of thyroid nodules.

These recommendations relate to thyroid nodules for which surgical treatment should be discussed:

- malignant nodules (Bethesda VI);

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- nodules suspected of malignancy (Bethesda III on two successive fine-needle aspiration biopsies (FNAB), Bethesda IV, Bethesda V);
- compressive nodules (any Bethesda grade), with symptomatic tracheal and/or esophageal compression, possibly within a multinodular goiter;
- large thyroid cysts (rapid reproduction after evacuation, failure of alcoholization);
- autonomous nodules with hyperthyroidism for which radioactive iodine (RAI) treatment was not indicated;
- thyroid nodules responsible for esthetic or functional concerns;- autonomous nodules with hyperthyroidism for which radioactive iodine (RAI) treatment was not indicated;
- certain specific situations are also discussed: pregnant women, children, etc. Conversely, medullary thyroid cancers are excluded from these surgical recommendations because of their particularities.

2. Surgeon's checklist before thyroidectomy

Interview and neck examination are essential. Cervical ultrasound is necessary before any thyroid surgery, to determine the appearance of the thyroid, the degree of suspicion of malignancy on EU-TIRADS score [1], and the aspect of the cervical lymph nodes. The report is accompanied by a diagram, specifying the size and distribution of the nodes, which may have been punctured for FNAB, with lymph node mapping in suspected cases. Cytology uses the Bethesda classification, which assesses the risk of malignancy [2]. Cervicothoracic imaging (injected CT or MRI) complements cervical ultrasound in case of mediastinal extension. FDG-PET should not be performed routinely, even in cases of proven malignancy (unless anaplastic or poorly differentiated carcinoma is suspected). Biology is limited to the determination of serum TSH, supplemented by serum calcium and serum calcitonin assays if surgery is indicated.

Recommendation 7.1:
The interview screens for signs of compression or invasion: dyspnea, dysphagia, dysphonia. It specifies the circumstances of discovery of the thyroid pathology (Level of evidence ++ Grade A).

Recommendation 7.2:
The surgeon should be familiar with the EU-TIRADS and Bethesda classifications to assess the risk of malignancy and explain this to the patient. The surgeon should know how to interpret a cervical ultrasound scan to propose the appropriate procedure for the pathology (Level of evidence +++ Grade A).

Recommendation 7.3:
A cervicothoracic CT (or MRI) scan should be ordered if there is suspicion of mediastinal extension of a substernal goiter, either clinically (lower pole of the lobe not palpable behind the clavicle, dyspnea, dysphagia, collateral circulation), or sonographically. It specifies relationships with adjacent organs, assesses extension to the aortic arch and the position of the goiter (anterior, posterior or mixed), in order to plan the appropriate approach (classic cervicotomy, manubriotomy, or sternotomy) (Grade A, ++). Injected cervical CT may also be used in cases of macroscopic lateral lymph-node involvement, for the diagnosis of lymph node metastasis at both ends of the neck (Level of evidence ++ Grade A).

Recommendation 7.4:
FDG-PET is not a routine imaging test, even in case of suspicious nodules. Thyroid scintigraphy should only be used in case of TSH <0.4 μIU/mL (Level of evidence ++ Grade A).

Recommendation 7.5:
Serum TSH, serum calcitonin and serum calcium should be measured prior to thyroid surgery (Level of evidence ++ Grade A).

3. Extent of thyroidectomy

Given the low risk of malignancy of thyroid nodules, the nature of which is sometimes difficult to determine preoperatively, and the excellent prognosis in the majority of thyroid cancers, the question arises as to the appropriateness of surgery and its extent: lobo-isthmectomy (LI) or total thyroidectomy (TT). Various factors are involved in this choice, including the ultrasound and cytological characteristics of the nodule to be operated on, the potential postoperative complications, and the patient's opinion.

The rate of postoperative complications is twice as high after TT as after LI (20.4 vs 10.8% $p < 0.0001$) [3], with an increased risk of compartment hematoma [4,5], definitive recurrent laryngeal nerve (RLN) palsy (1.33 vs 0.59%) [3] and, of course, definitive hypoparathyroidism (1.3 to 10 vs 0%) [4]. LI is also more amenable to outpatient management. In addition, TT requires lifelong hormone replacement in all cases, compared to a 30% risk after LI (for a TSH target < 2 μIU/mL). Predictive factors for hypothyroidism after LI comprise high preoperative TSH, presence of lymphocytic infiltrate, presence of anti-peroxidase antibodies, and low residual thyroid volume [6]. Finally, the few studies comparing quality of life (QoL) after TT vs LI seem to show that, while QoL is better after LI in the short term, the difference decreases with time [7,8].

Preoperative data (ultrasound and cytological features, appearance of the contralateral lobe) and the patient's opinion are also crucial.

Recommendation 7.6:
Frozen section biopsy of the nodule is not recommended in Bethesda II, III and IV because it is not very discriminating between benign and malignant status. It is unnecessary in Bethesda V of ≤ 2 cm and Bethesda VI because the extent of thyroidectomy would not depend on the result [9] (Level of evidence +++ Grade A). Frozen section biopsy of cervical lymph nodes is possible but not routinely recommended, as it is not very informative on macroscopically normal lymph nodes.

Recommendation 7.7:
Lobo-isthmectomy is recommended in the case of a single Bethesda II nodule or Bethesda II nodule limited in a single lobe (compressive, esthetic blemish, patient's wish. . .), Bethesda III (on 2 FNABs) or IV, and ≤ 2 cm Bethesda V or VI without aggressive criteria, without suspicious lymphadenopathy and without large contralateral nodule [10,11] (Level of evidence +++ Grade A).

Recommendation 7.8:
Frozen section biopsy of the nodule may be performed in case of Bethesda V > 2 cm. Total thyroidectomy during the same anesthesia may be proposed if the result is positive [12] (Level of evidence + Grade B). However, this depends on preoperative discussion with the patient, the reliability of the FNAB, the frozen section biopsy and the quality of follow-up in the local health facilities.

Recommendation 7.9:
Total thyroidectomy is indicated for nodular lesions in the following situations: bilateral Bethesda II compressive nodules, taking account of surgical risk; Bethesda III or IV with bilateral nodules with at least one > 4 cm suspicious nodule (sonographically, or because of a predisposition to thyroid cancer); > 2 cm Bethesda

V or VI, in classically shaped papillary cancer, in men and women ≥ 55 years of age [10,11], or regardless of size in aggressive variants on FNAB, macroscopic lymph node involvement, or predisposition to thyroid cancer (Level of evidence ++ Grade A).

Recommendation 7.10:
Patients should always be informed, in the initial surgery consultation, that, in case of lobo-isthmectomy, a second procedure may be indicated to complete the thyroidectomy if pathological examination shows thyroid cancer needing RAI treatment.

4. Therapeutic neck dissection

Therapeutic neck dissection consists in removing lymph nodes confirmed to be metastatic (cN1) preoperatively (ultrasound, FNAB) and/or intraoperatively (macroscopic appearance, positive frozen section biopsy) for a malignant thyroid disease. Preoperative cervical ultrasound is fundamental. It must be carried out by a specialized practitioner and should describe not only the thyroid but also the cervical lymph nodes, their appearance and degree of suspected malignancy. FNAB of a lymphadenopathy, possibly associated with in-situ thyroglobulin assay, may complete this examination. Cure requires removal of all malignant tissue [13], including lymph nodes. However, neck dissection is risky (recurrence, hypoparathyroidism, lymphorrhea), and should be carried out in accordance with the indications that optimize tumor prognosis.
In case of proven metastatic lymphadenopathy:

Recommendation 7.11:
When ipsilateral central metastatic lymphadenopathy is demonstrated pre- or intra-operatively (cN1a), ipsilateral central neck dissection should be performed at the same time as thyroidectomy. In case of proven N1a on one side, prophylactic contralateral central neck dissection may be discussed. If there are no suspicious lymphadenopathies on ultrasound in the lateral sector, prophylactic dissection of sectors III and IV is not recommended (Level of evidence + Grade A).

Recommendation 7.12:
It is recommended that neck dissection of the affected compartment be performed in the treatment of thyroid cancers with lymph-node involvement in the ipsilateral lateral compartment (cN1b). This may be limited to sectors III and IV when one or both of these sectors are involved and ultrasound does not show suspicious nodes in the other lateral sectors [14,15] (Level of evidence + Grade B). Associated prophylactic dissection of sectors IIA and IIB is not recommended due to the risk of accessory spinal nerve palsy. Similarly, dissection of sectors V and, exceptionally, sector I is indicated only when there is proven metastatic lymphadenopathy in these sectors [16] (Level of evidence ++ Grade B).

Recommendation 7.13:
Prophylactic neck dissection of sector VB may be discussed in the presence of proven lymphadenopathy in sectors II, III and IV (Level of evidence ++ Grade B).

Recommendation 7.14:
When there is evidence of isolated lateral metastatic lymphadenopathy (cN1b), it is recommended that, in addition to ipsilateral lateral neck dissection, prophylactic dissection of the central compartment (sector VI) should be performed, at least ipsilaterally to the lateral compartment lymph-node metastasis (Level of evidence + Grade B).

Recommendation 7.15:
There is insufficient evidence to recommend contralateral prophylactic neck dissection for unilateral cN1b tumor. It may be discussed for tumors at high risk of recurrence, bilateral tumors, in case of > 3 cm ipsilateral lateral lymphadenopathy or in the presence of > 4 metastatic lymph-node metastasis in the central compartment [17] (Level of evidence ++ Grade B).

5. Prophylactic neck dissection

Prophylactic neck dissection is defined as cervical lymph node dissection in the absence of pre- or intra-operative (clinical or ultrasound) evidence of lymph-node metastasis [13]. The prevalence of occult lymph-node metastasis in the central compartment is high. Several risk factors have been identified in this compartment: young age (< 45 years), male gender, tumor size, and infiltration of perithyroid fat tissue [18]. Currently, there is no evidence that prophylactic central neck dissection improves overall survival, which is similar in N0 and Nx patients [19]. However, prophylactic neck dissection seems to reduce the risk of locoregional recurrence in micro-N1. It also allows the detection of occult metastases and reclassification of the tumor, thus better defining patients at risk of recurrence, to adapt therapeutic strategy and follow-up [20].

Recommendation 7.16:
Prophylactic neck dissection is only discussed for papillary cancer. It is not indicated for vesicular or oncocytic cancer. Nor should it lead to secondary surgery in the event of incidental discovery of papillary cancer in a thyroidectomy specimen (Level of evidence +++ Grade B).

Recommendation 7.17:
Prophylactic ipsilateral central dissection is warranted for papillary cancer with ≥4 cm diameter on ultrasound and/or intraoperative evidence of macroscopic perithyroid tissue invasion [21]. The benefits and risks of this procedure should be assessed and discussed on a case-by-case basis [22,23] (Level of evidence ++ Grade B).

Recommendation 7.18:
In physiologically healthy elderly patients at low operative risk, prophylactic ipsilateral central neck dissection may be discussed for aggressive types of cancer at high risk of recurrence [24] (Level of evidence ++ Grade B).

Recommendation 7.19:
Only central neck dissection ipsilateral to the tumor is recommended, except for bilateral or isthmic cancers, for which a prophylactic bilateral central dissection may be proposed. This bilateral neck dissection is associated with an increased risk of complications (hypoparathyroidism, RLN injury) (Level of evidence +++ Grade B).

Recommendation 7.20:
Prophylactic lateral neck dissection is not recommended [25] (Level of evidence ++ Grade B)

6. Intraoperative neuromonitoring, place of pre- and/or post-operative flexible endoscopy

RLN injury is one of the classic complications of thyroid surgery. It is also the complication that is most often the cause of litigation after thyroidectomy. Incidence varies, but is generally

underestimated, mainly because of the non-systematic nature of pre- and post-operative laryngoscopy. In a French prospective multicenter study, the incidence of transient RLN injury was between 3.8% and 21.8%, and of definitive RLN injury between 0 and 9.1% [26]. Several mechanisms can cause RLN injury: thermal injury by coagulation, sectioning, or compression of the nerve. However, the mechanism involved in more than 90% of cases is traction. The identification and respect of the recurrent nerves is one of the main principles of thyroid surgery but the morphological integrity does not necessarily imply functional integrity. RLN neuromonitoring is a real intraoperative electromyography and an aid for the surgeon, facilitating location of the nerve and checking its functional integrity in real time. Its objective is to reduce the rate of RLN injury.

6.1. Laryngoscopy

Direct laryngoscopy with flexible endoscopy is the gold standard for visualizing the vocal cords. It can be used to check for asymptomatic RLN injury. According to the International Neuromonitoring Study Group (INMSG), it should be performed routinely, along with recurrent and vagus nerve stimulation, before and after dissection, in the sequence L1, R1, V1, R2, V2, L2. However, its value has been demonstrated only in certain high-risk clinical situations [27].

6.2. Intermittent neuromonitoring

The medical literature on neuromonitoring in thyroid surgery is extensive and the results are contradictory. Several meta-analyses have been published, some showing transient [28] or definitive reduction in RLN injury rates [29], or both [30], while other meta-analyses found no reduction [31,32]. A recent meta-analysis of the 5 randomized prospective trials published to date failed to show a statistically significant difference in RLN injury rate between neuromonitoring and recurrent nerve visualization alone [33].

In total thyroidectomy, loss of signal on one side may lead to discontinuation of surgery and deferral of the contralateral lobe resection, as recommended by the INMSG. This strategy eliminates the risk of bilateral RLN injury, at the cost of unnecessarily shortened cervicotomy in case of false positives [34].

6.3. Continuous neuromonitoring

Intermittent neuromonitoring only allows RNL functional integrity to be checked at a single point in time during stimulation of the nerve, and in the segment downstream of the stimulation point. By continuous recording of latency and amplitude, continuous neuromonitoring can compensate for these shortcomings by alerting the surgeon to the imminence of trauma. Compared to intermittent neuromonitoring, continuous neuromonitoring reduces the rate of transient and permanent RLN injury [35], and is not associated with increased morbidity.

Recommendation 7.21:

Preoperative laryngoscopy is mandatory for patients with history of cervical or thoracic surgery, dysphonia, thyroid carcinoma with posterior extension, or significant nodal involvement in the central compartment (Level of evidence ++ Grade B).

Recommendation 7.22:

Postoperative laryngoscopy should be performed for any postoperative dysphonia, swallowing disorder, respiratory symptoms or loss of signal on neuromonitoring of the recurrent and/or pneumogastric nerve (Level of evidence ++ Grade B).

Recommendation 7.23:

Neuromonitoring is useful in thyroid surgery as it reduces the rate of transient RLN palsy, but impact on definitive RLN injury has not been demonstrated. It facilitates identification of the recurrent nerve (Level of evidence ++ Grade B). Continuous neuromonitoring of the vagus nerve may, in some situations, allow early detection of a signal drop during dissection near the recurrent nerve.

7. Prevention of hypoparathyroidism

Hypocalcemia is a common complication after total thyroidectomy, and should be distinguished as transient or definitive. Early postoperative hypocalcemia is common, in the first few days after surgery. It is generally defined by a total or albumin-corrected serum calcium concentration < 2.0 mmol/L on at least one measurement between the 1st and 7th postoperative days, with or without symptoms. It may result from parathyroid insufficiency, but also from other factors, including hemodilution or vitamin D deficiency. Frequency varies between 15% and 25% depending on the definition used in the study.

Permanent postoperative hypoparathyroidism is defined as persistence of impaired parathyroid function preventing sufficient PTH secretion to maintain normal blood calcium levels at a distance in time from surgery. It requires vitamin and calcium replacement to maintain normal blood calcium levels and/or avoid symptoms associated with low or inappropriate PTH, beyond 6 months after surgery. It follows early postoperative hypocalcemia, and results from removal or devascularization of the parathyroid glands. Symptoms significantly impair quality of life [36]. Mean incidence is 4.1% [95% CI, 4.0 - 4.3], variability between studies being partly related to variations in definition.

Screening for early postoperative hypoparathyroidism is performed routinely after total thyroidectomy. The sensitivity of blood calcium measurement alone on the first postoperative day varies between 50% and 94% [37,38] and is therefore not sufficient to rule out postoperative hypoparathyroidism. PTH measurement significantly increases the performance of isolated serum calcium assay on day 1 in predicting postoperative hypocalcemia [39], and early serum assay $\leq$ 6 hours after surgery shows sensitivity of over 80% [40].

Prevention of postoperative hypocalcemia and permanent hypoparathyroidism involves two main components: surgical and medical.

Surgical prevention involves conserving the parathyroids and the parathyroid vascularization by the inferior and superior thyroid arteries: ligation of the terminal branches rather than the vascular trunk significantly reduced the risk of postoperative hypocalcemia in randomized studies [41,42]. Exhaustive search for all four glands, including the lower parathyroids, does not appear to reduce the risk of postoperative hypocalcemia and permanent hypoparathyroidism [43]. When one or more identified parathyroid gland appears ischemic, systematic auto-transplantation is associated with greater postoperative hypocalcemia and permanent hypoparathyroidism [44], while a greater number of glands left in-situ reduces these complications [45] and is also associated with a higher rate of recovery from postoperative hypocalcemia [46].

Drug prevention involves the management of possible preoperative vitamin D deficiency. Preoperative vitamin D deficiency, particularly when less than 10 ng/mL, is thought to increase the likelihood of postoperative hypocalcemia and its severity (symptoms and length of hospital stay) [47]. Correcting preoperative vitamin D deficiency should reduce the risk of postoperative hypocalcemia and length of hospital stay in these patients [48].

Systematic calcium and/or active vitamin D replacement after total thyroidectomy appears to reduce the risk of biological and/or

symptomatic postoperative hypocalcemia [49]. However, it does not alter the risk of permanent hypoparathyroidism, and may even lead to its diagnosis being overlooked.

Recommendation 7.24:
Prior to total thyroidectomy, routine vitamin D replacement has been suggested, but there is no clear evidence of its effectiveness (Level of evidence: Expert opinion, Grade B).

Recommendation 7.25:
Ligation of the terminal branches rather than the trunks of the inferior and superior thyroid arteries is recommended, as it reduces the risk of postoperative hypocalcemia and permanent hypoparathyroidism (Level of evidence +++ Grade A).

Recommendation 7.26:
Identification of the upper parathyroid glands and conservation of their vascularity is recommended (Level of evidence: Expert opinion, Grade A). Auto-transplantation of devascularized glands, particularly when identified in the thyroidectomy specimen, is recommended (Level of evidence: Expert opinion, Grade A). In contrast, resection and auto-transplantation of parathyroid glands due to an ischemic aspect is not recommended (Level of evidence +++ Grade A).

Recommendation 7.27:
The combination of PTH and blood calcium assay within 24 hours of total thyroidectomy can detect hypoparathyroidism. The combination of PTH >15 ng/L and serum calcium >2.00 mmol/L has a negative predictive value of close to 100% (Level of evidence +++ Grade A).

Recommendation 7.28:
Early serum PTH measurement ($\leq$ 6 hours after surgery) accelerates diagnosis of hypoparathyroidism and optimizes management by guiding vitamin and calcium replacement therapy. The optimal time between thyroid resection and serum PTH assay, assay method and diagnostic thresholds are still under discussion (Level of evidence +++ Grade C).

8. Prevention of compressive cervical hematoma

Postoperative cervical hematoma (POCH) requiring reoperation is rare, occurring in about 1% of cases, but is serious, with risk of death or severe neurological sequelae. The risk is greatest in the first 6 hours after surgery and then gradually decreases [50].

Recommendation 7.29:
Thyroid surgery involves intermediate risk of bleeding according to the French Society of Anesthesia and Intensive Care Medicine (*Société Française d'Anesthésie-Réanimation* [SFAR]); it is therefore feasible without interruption of acetylsalicylic acid. Perioperative management of other antiplatelet and anticoagulant drugs should follow the recommendations for surgery at intermediate risk of bleeding [51] (Level of evidence +++ Grade A).

Recommendation 7.30:
New mechanical coagulation devices have not been shown to be effective in preventing hematoma [52], nor have inactive (cellulose) or active (fibrin) hemostatic agents [53] (Level of evidence + Grade C).

Recommendation 7.31:
Routine drainage of the surgical site is not recommended. It does not reduce the risk of hematoma, and increases hospital stay, pain and risk of local infection [54] (Level of evidence +++ Grade A).

Recommendation 7.32:
Prevention of compressive cervical hematoma requires protocols for intraoperative and immediate postoperative blood pressure monitoring, as well as effective control of pain, nausea and vomiting [5] (Level of evidence ++ Grade A). The recognition and emergency management of compressive cervical hematoma should be the subject of written protocols and specific training of medical and paramedical teams [55] (Level of evidence +++ Grade B).

9. Outpatient surgery

Outpatient surgery is developing rapidly. It reduces the risk of iatrogenic complications, and particularly nosocomial infection. Thyroidectomy is theoretically an excellent candidate for this type of management because it is rarely a source of complications [56]. It is rapid, with little pain or bleeding. However, outpatient management is not widely implemented because of the potential seriousness of one particular surgical complication: compressive neck hematoma. The French Endocrine Surgery Association (AFCE) published cautious recommendations in 2013 [57], advocating overnight stay in hospital after any thyroid surgery. The situation has, however, since progressed: outpatient surgery pathways are better organized, surgical techniques (hemostasis) and anesthesia have improved, and patients have understood that this is a beneficial trend in surgery, provided that appropriate information is given and rules of caution are respected in a well-defined care pathway.

Recommendation 7.33:
The surgeon should inform the patient and their family of the normal postoperative course after thyroidectomy, the potential complications (compressive hematoma requiring urgent revision surgery, recurrent nerve damage and hypocalcemia due to hypoparathyroidism), and the specificities of outpatient management. The information collected from the patient on the conditions of discharge home (family environment, organization of the journeys) and that given to them during the preoperative consultation (postoperative consequences, specificities of outpatient management) must be recorded in the file [58,59] (Level of evidence +++ Grade A).

Recommendation 7.34:
Ambulatory thyroidectomy should only be performed by an experienced surgeon within a trained medical and paramedical team. The healthcare facility should be fully resourced for outpatient management, with 24-hour, 7-days-a-week care for emergency readmission. In all cases, contact between the facility and the patient the day after surgery is crucial (Level of evidence ++ Grade A).

Recommendation 7.35:
Ambulatory management can be proposed for lobo-isthmectomy or isthmectomy (unless contraindicated: anticoagulants at effective dose, absence of escort on discharge and at home the night following surgery, poor comprehension), even with associated neck dissection. It is also feasible for secondary totalization of thyroidectomy (after lobectomy). On the other hand, the indications for one-stage total thyroidectomy should be

limited, giving priority to the proximity of the place of residence to a care facility with an appropriate technical platform, and to the pathology operated on (euthyroid goiter without substernal extension) [60,61] (Level of evidence ++ Grade B).

Recommendation 7.36:

A precise clinical pathway must be established with formalized pre-, intra- and post-operative protocols for both surgery (hemostasis procedures) and anesthesia (prevention of pain, vomiting and hypertensive episodes). We recommend a minimum 6 hours' postoperative monitoring in the ambulatory facility [62,63] (Level of evidence +++ Grade B).

Recommendation 7.37:

Where outpatient management is not possible or not recommended, hospital stay after thyroidectomy may be limited to 24 hours, with some exceptions (effective-dose anticoagulant therapy, postoperative complication) (Level of evidence ++ Grade B).

10. Extracervical approaches: robotic thyroidectomy

Extracervical approaches were reported in Asia in the 1990s, with the aim of resecting the thyroid endoscopically, without visible anterior cervical scar [64]. The initial motivation was esthetic and associated with improved postoperative quality of life and body image. Several extra-cervical procedures have been proposed: uni- or bi-lateral transaxillary, uni- or bi-lateral axillo-areolar (BABA), retroauricular using a cervicofacial lift and, more recently, the transoral route [65]. Most of these procedures are still under evaluation; only transaxillary robotic thyroidectomy and, to a lesser degree, the transoral route have become widespread. Like all surgical innovations, these new techniques are initially the object of enthusiasm, until the test of time allows a clearer perception of the risk-benefit ratio [66].

The transaxillary route has been the subject of numerous studies, mostly retrospective with low levels of evidence. There are only a few randomized studies comparing the robotic approach and cervicotomy, with esthetic scores favoring the robot, at the cost of longer surgery and rare specific complications (brachial plexus injury, seroma, neuropathic pain) [67,68]. No studies have clearly shown an advantage of the robot over cervicotomy in terms of quality (reduction in complications or improvement in resection quality) [69]. A meta-analysis including 30 studies and 6622 patients even concluded that the robotic approach was associated with longer operating time and fewer resected nodes in neck dissection [70].

Extracervical robotic approaches are marginal in Europe and the USA, at less than 1% for the treatment of thyroid cancer [65]. They have never been in a position to replace cervicotomy in Europe or the USA, especially as use of robots for thyroidectomy was disputed by Intuitive Surgical Inc. in 2011 in the USA due to medico-legal risks, slowing down the spread of the technique. This obstacle compounded the difficulties of learning, even within a team trained in thyroid surgery (between 40 to 75 procedures are necessary before considering oneself autonomous in this technique) [71], and of significant additional cost [72].

Recommendation 7.38:

Transaxillary robotic thyroidectomy is not the gold-standard approach. It is sometimes proposed for highly selected patients with a small (2 cm) unilateral nodule, exclusively cervical and without lymph-node involvement, within a thyroid lobe not exceeding 6 cm, in a slim subject wishing to avoid a cervical scar. Patients should be informed of the specific risks of the technique and the lack of evidence that it is equivalent to cervicotomy in terms of quality of life and satisfaction (Level of evidence ++ Grade B).

Recommendation 7.39:

Patients with malignant nodules or suspected malignancies >2 cm, cancers with gross lymph-node metastasis, plunging goiters, history of cervical surgery or active thyroid disease should be excluded from robotic surgery (Level of evidence ++ Grade B).

Recommendation 7.40:

Robotic thyroidectomy should be performed in centers with expertise in both thyroid surgery and robotic surgery (Level of evidence: expert opinion, Grade B).

11. Extracervical routes: transoral thyroidectomy

The main advantages of the transoral endoscopic thyroidectomy vestibular approach (TOETVA), which has gained in popularity in recent years, are the ability to perform thyroidectomy without a skin incision, and its minimally invasive nature compared with other endoscopic and/or robotic approaches. It also enables bilateral surgery, with good visibility of the recurrent nerves and parathyroids (or at least the superior parathyroid) on a 30° HD camera [73]. Evaluation of this innovative technique is still incomplete and has been based on retrospective studies, often from the same (Asian) teams, depending on the experience of the surgeons and the particular morphological criteria of the patients included. According to one study, half of the patients requiring thyroid surgery could be eligible for a transoral approach [74]. The best evaluated procedures are lobectomy and isthmectomy. Bilateral nodular pathologies have been operated on using this approach, including Graves' disease, but in the latter case there was a non-negligible risk of recurrence of hyperthyroidism due to residual thyroid tissue often left in place along the recurrent nerve. The technique is perfectly feasible in obese patients, unlike the transaxillary approach, which is more complex in this situation [73,75].

The transoral approach requires specific perioperative and intraoperative care, but data are sparse. However, it is recommended that antibiotic therapy be started intraoperatively by intravenous injection and continued orally for 5 to 7 days postoperatively [76], that oral hygiene measures be taken, and that analgesia be adapted. Transient postoperative neck and chin pain was reported, and the patient should be informed of this [73,77]. The rate of postoperative complications (recurrent nerve palsy, hypocalcemia, hematoma of the lodge) is identical to that in cervicotomy [78,79], as is length of hospital stay, with the possibility of performing this procedure on an outpatient basis for unilateral surgery with a dedicated care pathway.

Recommendation 7. 41:

Transoral thyroidectomy can be proposed in selected patients with a thyroid < 45 ml and/or a nodule < 4 cm in case of Bethesda II, III or IV lesion, or < 2 cm in case of Bethesda V or VI lesion, without suspicion of lateral lymph-node involvement or mediastinal extension, wishing to avoid a cervical scar, with satisfactory dental status, and who have been informed of the specific risks of the transoral route and the need for perioperative oral care, as well as the lack of evidence of its effectiveness in terms of quality of life and patient satisfaction (Level of evidence ++ Grade B).

Recommendation 7.42:

Patients should be informed of the possibility of postoperative neck and chin pain that may persist for days to weeks after surgery (Level of evidence + Grade A).

Recommendation 7.43:

Transoral thyroidectomy should be performed in centers with expertise in thyroid surgery (Level of evidence +++ Grade A).

Disclosure of interest

The authors declare that they have no competing interest.

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