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REVIEW

Endocrine surgery during and after the COVID-19 epidemic: Expert guidelines from AFCE

G. Baud[a], L. Brunaud[b], J.-C. Lifante[c], C. Tresallet[d], F. Sebag[e], J.-P. Bizard[f], M. Mathonnet[g], F. Menegaux[h], R. Caiazzo[a], E. Mirallié[i], F. Pattou[a,*], AFCE COVID Study Group

[a] *Chirurgie générale et endocrinienne, CHU de Lille, 59000 Lille, France*
[b] *Chirurgie viscérale, métabolique et cancérologique (CVMC), CHRU de Nancy, 54511 Vandœuvre-lès-Nancy, France*
[c] *Chirurgie digestive, oncologique et endocrinienne, CHU de Lyon, 69310 Pierre-Bénite, France*
[d] *Chirurgie viscérale et digestive, AP—HP, hôpital Avicenne, 93000 Bobigny, France*
[e] *Chirurgie générale et endocrinienne, AP—HM, La Conception, 13005 Marseille, France*
[f] *Chirurgie endocrinienne et viscérale, hôpital privé Arras-les-Bonnettes, 62000 Arras, France*
[g] *Chirurgie digestive et endocrinienne, CHU de Limoges, 87000 Limoges, France*
[h] *Chirurgie générale digestive et endocrinienne, AP—HP, hôpital Pitié-Salpêtrière, Sorbonne université, 75013 Paris, France*
[i] *Chirurgie cancérologique, digestive et endocrinienne (CCDE), CHU de Nantes, 44093 Nantes, France*

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Summary The COVID-19 pandemic commands a major reorganisation of the entire French healthcare system. In France, general rules have been issued nationally and implemented by each healthcare centre, both public and private, throughout France. Guidelines drafted by an expert group led by the French-speaking Association of Endocrine Surgery (AFCE) propose specific surgical management principles for thyroid, parathyroid, endocrine pancreas and adrenal surgery during and after the COVID-19 epidemic.

Introduction

The ongoing COVID-19 pandemic commands a major reorganisation of the entire French healthcare system [1]. To respond to the present and expected influx of patients need-

* Corresponding author at: Department of endocrine and metabolic surgery, CHU de Lille, 59000 Lille, France.
E-mail address: fpattou@univ-lille2.fr (F. Pattou).

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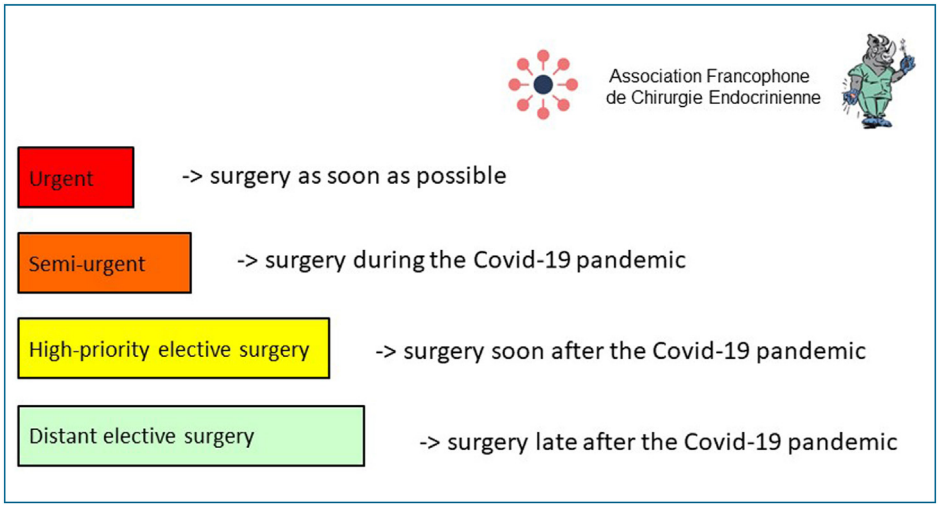

Figure 1. General principles for scheduling endocrine surgery during and after the COVID-19 epidemic.

ing a period of intensive care [2], the short-term priority has been directing available material and human resources toward sectors dispensing care for COVID-19 patients [3,4]. This policy has entailed the almost complete descheduling of non-urgent surgery [5]. More than a month now after the start of the epidemic, there is a pressing need to manage other health disorders not linked to COVID-19, but for which deferral of surgery until after the epidemic is over, could worsen prognosis or be life-threatening. It is also important to be thinking now about the conditions under which surgery can be resumed at a normal pace after the epidemic. General rules have been put out nationally and implemented by each healthcare centre, both public and private, throughout France. Specific guidelines have been proposed for visceral surgery [6]. Likewise, to meet their need for specific guidelines, the French-speaking Association of Endocrine Surgery (AFCE) brought together a group of experts to propose principles for the surgical management of thyroid, parathyroid, endocrine pancreas and adrenal pathologies during the COVID-19 epidemic and afterwards, for when surgical activity will be able to return gradually to its normal pattern. These guidelines were drafted in the light of the existing literature. They will be updated as knowledge advances.

General principles for scheduling surgery during and after the COVID-19 epidemic

Four scheduling levels were defined to help prioritise patients (these levels may change according to how the epidemic setting evolves) (Fig. 1):

- urgent surgery that must be carried out as soon as possible because even a short deferral would be life-threatening;
- semi-urgent surgery that can be deferred for a few weeks but not beyond 3 months without threat to life or adverse effects on cancer or functional prognosis;
- high-priority elective surgery that can wait for several months but must be given scheduling priority as soon as the epidemic is over;
- distant elective surgery that can be deferred until well after the epidemic is over, even more than 6 months, without compromising the indication.

For urgent surgery, the ratio of the benefits expected from surgery to the risks incurred by scheduling it during the epidemic must always be evaluated according to how both the national and local contexts are evolving, in particular the resources available: operating room, consumables and hospital capacities, particularly if intensive care may be needed. When surgery is prescribed in the epidemic setting, short hospital stays or outpatient care is recommended [7], provided this does not increase the risk of rehospitalisation. To limit operating time and the risk of postoperative complications, the surgery should also be performed by one or more experienced surgeons. Even if no symptoms of COVID-19 are apparent, the risk of infection should be assessed beforehand as it may be associated with unfavourable prognosis [8,9]. Any surgery on a patient infected or suspected of being infected must be performed according to the rules laid down by the hospital's hygiene teams and infectiologists [10].

Thyroid and parathyroid surgery

Thyroid cancers

Differentiated thyroid cancers most often have an excellent prognosis [11], and there is no high level of proof supporting an optimal surgery deferral time (Fig. 2). During the epidemic, any thyroid tumour suspected of malignancy (Bethesda 5 or 6) must be discussed at a multidisciplinary team (MDT) meeting. When there are clinical or paraclinical signs pointing to an aggressive form of cancer (recurrent nerve palsy, local invasion with esophageal, vascular or tracheal involvement, massive lymph nodes infiltration [12]), surgery must be programmed as semi-urgent. If anaplastic, poor differentiated thyroid carcinoma or lymphoma is suspected, a surgical biopsy must be performed before any surgery is undertaken. If either of these diagnoses is confirmed, an appropriate treatment with corticoids and/or chemotherapy must be proposed as first line therapy [13]. If there is no loco-regional aggressiveness, deferral of surgery for differentiated carcinoma will depend on lymph node and tumour size. A tumour size greater than or equal to 2 cm and/or associated with lymph nodes can be deferred without risk until the epidemic is over but must then be given priority and scheduled within the following 3 months. Tumours smaller than 2 cm in size, with no ganglion metastases, can be deferred until well after the end of the

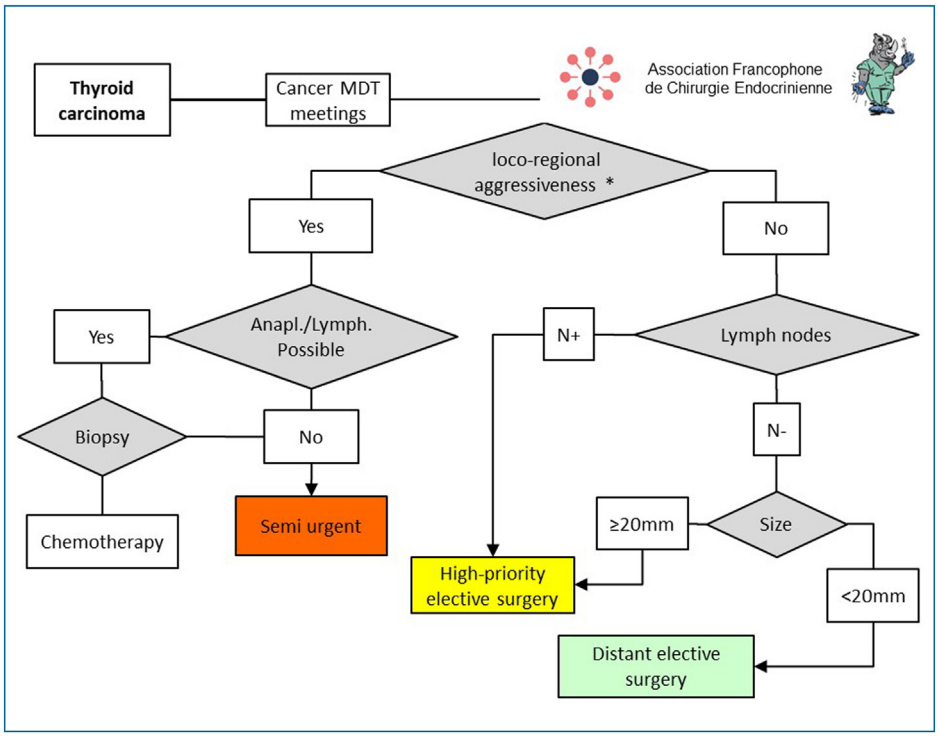

Figure 2. Principles for scheduling thyroid cancers during and after the COVID-19 epidemic. * Loco-regional aggressiveness defined as the presence of recurrent nerve paralysis, local invasion with esophageal, vascular or tracheal involvement, or massive ganglion infiltration. (Anapl = anaplastic, Lymph: lymphoma; MDT: multidisciplinary team).

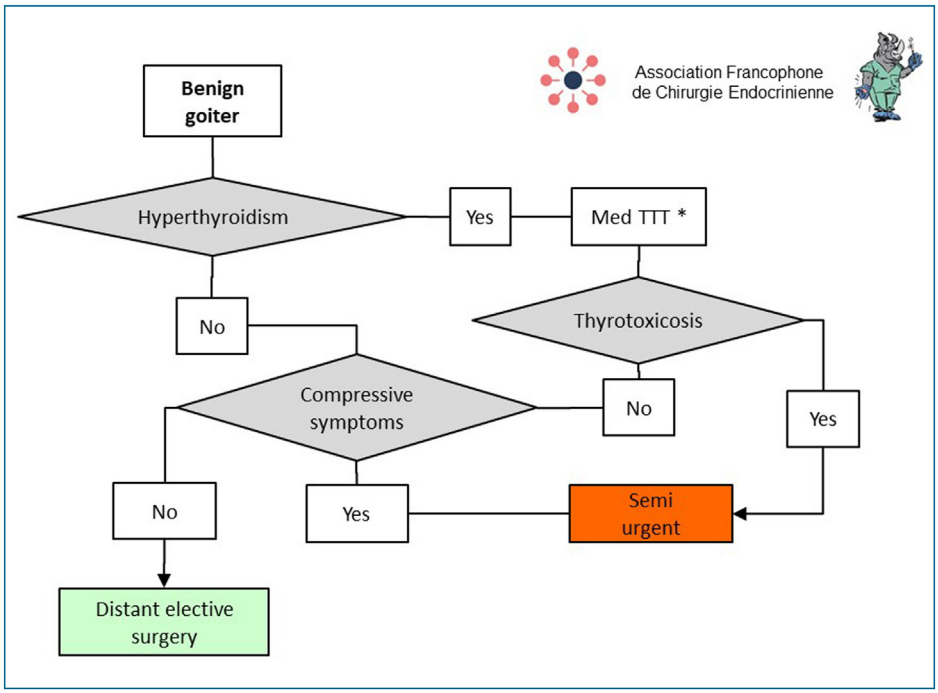

Figure 3. Principles for scheduling surgery for benign thyroid disorders during and after the COVID-19 epidemic. * Synthetic anti-thyroid agents, lithium, potassium perchlorate, plasmapheresis. (Med TTT = medical treatment).

epidemic. Although the prognosis of medullary thyroid carcinoma (MTC) is slightly less favourable than that of follicular differentiated thyroid cancer [14], the care deferral guidelines given above still hold.

Benign thyroid disorders

Most thyroidectomies for benign lesions can be deferred without risk (Fig. 3). However, specific situations can require semi-urgent scheduling, e.g. thyrotoxicosis (Graves's disease, toxic nodules, toxic goiters, iatrogenic hyperthyroidism) resistant to or poorly controlled by synthetic anti-thyroid (SAT) agents [15]. In this situation, lithium, potassium perchlorate, and if this fails, plasmapheresis may be useful to normalise levels of triiodothyronine (T3) and control those of thyroxine (T4) at the time of surgery. Non-suspect goiters responsible for severe compressive symptoms (inspiratory dyspnea due to tracheal compres-

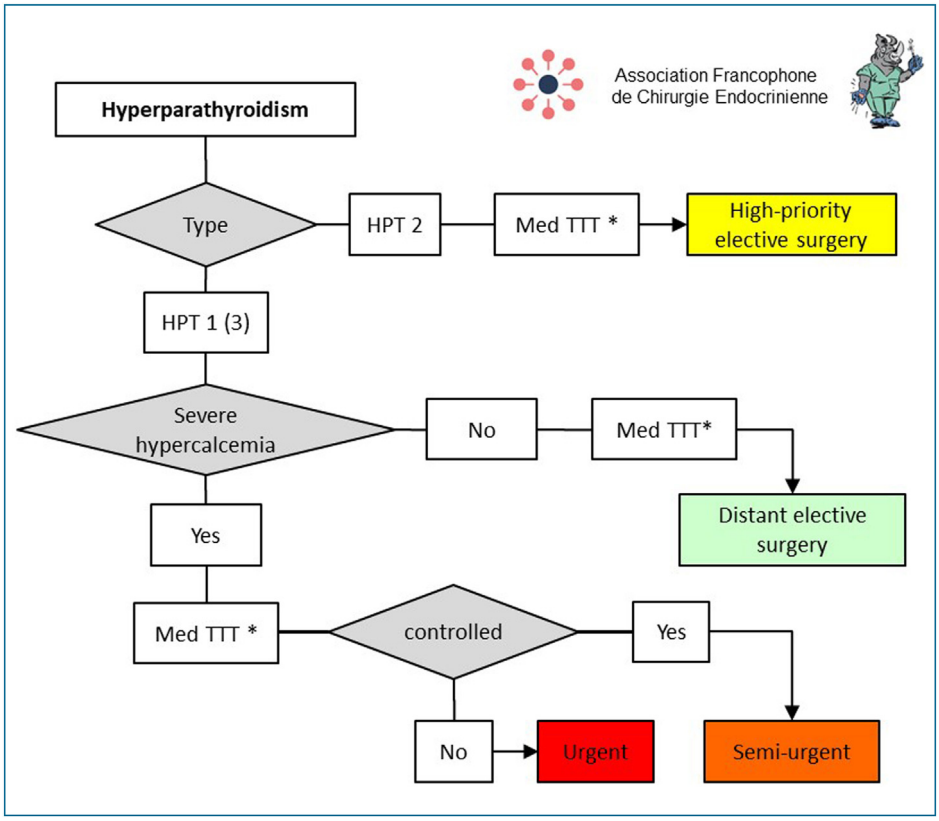

Figure 4. Principles for scheduling parathyroid surgery during and after the COVID-19 epidemic. Blood calcium > 3.5 mmol/L and/or presence of clinical complications (acute pancreatitis secondary to HPT, brown tumour, calciphylaxis fracture osteopenia, cardiac rhythm disorder with heart failure). * Hydration, calcimimetic (Med TTT = medical treatment).

sion, dysphagia due to esophageal compression, superior vena cava syndrome due to deep vein compression) must also be scheduled for semi-urgent surgery before the epidemic ends.

Hyperparathyroidism

Surgical treatment of primary hyperparathyroidism (HPT) is generally not urgent (Fig. 4) [16]. In the COVID-19 epidemic setting, its scheduling depends on the presence or absence of severe hypercalcemia, defined by a very high level of blood calcium > 3.5 mmol/L (140 mg/L) [17], and/or the presence of clinical complications—acute pancreatitis secondary to HPT, brown tumour, calciphylaxis, fracture osteopenia, heart rhythm disorders (QT shortening on ECG, bradycardia with risk of asystole) with cardiac insufficiency [17—20]. In all cases, hypocalcemic treatment must first be given. In the epidemic setting, the use of cinacalcet is recommended [21]. In cases of severe hypercalcemia, surgery must be scheduled as semi-urgent, without waiting for the epidemic to end, or as urgent when it escapes control by the medical treatment. If there is no severe hypercalcemia, surgery can be deferred without risk until the epidemic is over. These guidelines are valid for cases of genetically determined primary HPT. For tertiary HPT, the blood calcium threshold defining severe hypercalcemia must be lowered to 2.8 mmol/L to protect renal grafts (nephrocalcinosis, acute tubular necrosis, lithiasis) and bone and vascular impact [22,23]. For secondary HPT, surgical treatment is not recommended during the epidemic because of the higher risk of COVID-19 infection in dialysed patients [24]. When indicated, surgery must be scheduled as a priority in the three months following the epidemic in cases of disabling bone pain, brown tumour or temporary contraindication for renal transplant [25].

Technical aspects of neck surgery

Uni- or bilateral cervicotomy is the approach recommended for the surgical treatment of thyroid or parathyroid pathologies in the epidemic setting, so as to limit operating time and complication risk [26]. Surgery requiring a thoracic or mediastinal approach and/or postoperative intensive care [27] must be deferred whenever possible until after the epidemic is over. Endoscopic surgical approaches, with or without robotic assistance, are not recommended [28]. If there is no dysphonia, laryngoscopy before or after surgery is not recommended [29] because of the high risk of airborne SARS-CoV-2 transmission during such examination [30]. Neuromonitoring of the inferior laryngeal nerve is recommended:

- to make sure the neuromuscular apparatus of the larynx is functioning before and after surgery [31];
- to reduce the risk of bilateral recurrent nerve palsy that can require intensive care and interruption of surgery if the signal is lost during the dissection of the first side [32].

Peroperative PTH assay is possible but must not increase time spent in the operating room. The usual guidelines for the prevention and/or management of postoperative hypocalcemia remain unchanged during the epidemic [33].

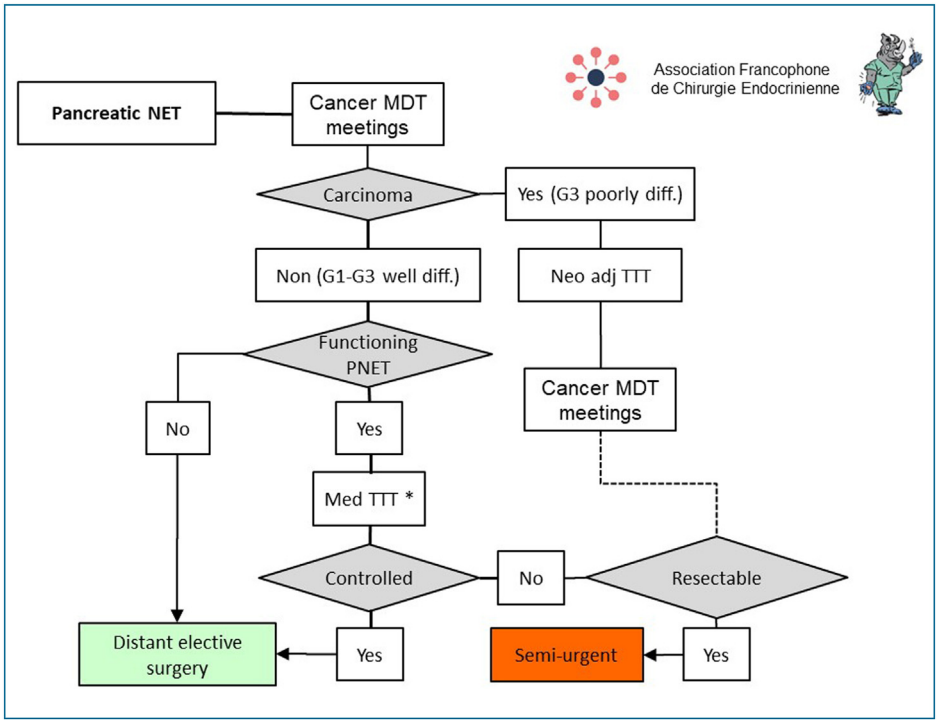

Figure 5. Principles for scheduling surgery for neuroendocrine tumours of the pancreas during and after the COVID-19 epidemic. * Diazoxide, proton pump inhibitor, somatostatin analogues, (TTT med: medical treatment; MDT: multidisciplinary team).

Neuroendocrine tumours of the pancreas

In the epidemic setting, the indication for the surgical treatment of a neuroendocrine tumour of the pancreas must be discussed in an MDT meeting to assess the balance between the risks of surgery and its oncological and/or secretory benefits (Fig. 5) [34]. The management of Grade 3 carcinomas (poorly differentiated) has already been the subject of guidelines as part of the French National Digestive Oncology Thesaurus [35], and the COVID-19 epidemic does not change the usual guidelines favouring chemotherapy or neoadjuvant radio-chemotherapy [36]. A pancreatectomy may be indicated when a curative resection can be considered after clinical and morphological reassessment [37], in which case surgery is scheduled as semi-urgent before the epidemic has ended. Patients with a well-differentiated neuroendocrine tumour of the pancreas (Grades G1, G2 or G3), that is non-secretory, can be deferred until well after the epidemic is over. If there is an associated secretory syndrome, a medical treatment should first be given [38]. If this treatment fails to control the secretory syndrome satisfactorily, pancreatectomy must be scheduled as semi-urgent before the end of the epidemic. If the medical treatment is effective, surgery can be deferred until well after the epidemic has ended. When technically possible, laparoscopy is recommended for left pancreatectomies and enucleations to minimise postoperative impact on respiratory function and hospital length of stay [6,10,19].

Adrenal lesions

In the epidemic setting, the indication for the surgical treatment of an adrenal lesion must be discussed at an MDT meeting to assess the balance of risk and its oncological and/or secretory benefits (Fig. 6).

Lesions suspected to be malignant (adrenal cortical carcinoma, metastases) must undergo surgery when they are considered resectable [39,40]. In cases of secretory syndrome, prior management by a medical treatment is recommended (metyrapone, ketoconazole). Surgery must be scheduled as semi-urgent, before the end of the epidemic, in an expert centre [41]. Chromaffin lesions (pheochromocytoma and/or paraganglioma) must first receive an appropriate anti-hypertension treatment (alpha-blocking agents, beta-blocking agents, calcium inhibitors), and be monitored by an experienced care team [42]. If this treatment controls the secretory syndrome, close monitoring can be continued until the adrenalectomy, which will be scheduled as a priority when the epidemic ends. If this treatment fails to control the secretory syndrome satisfactorily, surgery can be scheduled as semi-urgent, before the epidemic ends, in an experienced centre.

For other secretory adrenal lesions (in particular, hypercorticism and hyperaldosteronism), an appropriate medical treatment (steroidogenesis inhibitors, anti-aldosterone) must first be implemented. If the secretory syndrome is not controlled or if impact is marked, adrenalectomy can be scheduled as semi-urgent during the epidemic. In other cases, adrenalectomy can be scheduled well after the epidemic has ended. During the epidemic, laparoscopy remains the preferred approach for adrenalectomy. Conversely, for suspect lesions and/or those larger than 10 cm, laparotomy is recommended [43].

Postoperative follow-up in the epidemic setting

Postoperative follow-up consultations must be maintained during the epidemic. Tele-consultation is recommended to ensure continuity of care while limiting the risks of coronavirus propagation in healthcare centres. For a consultation

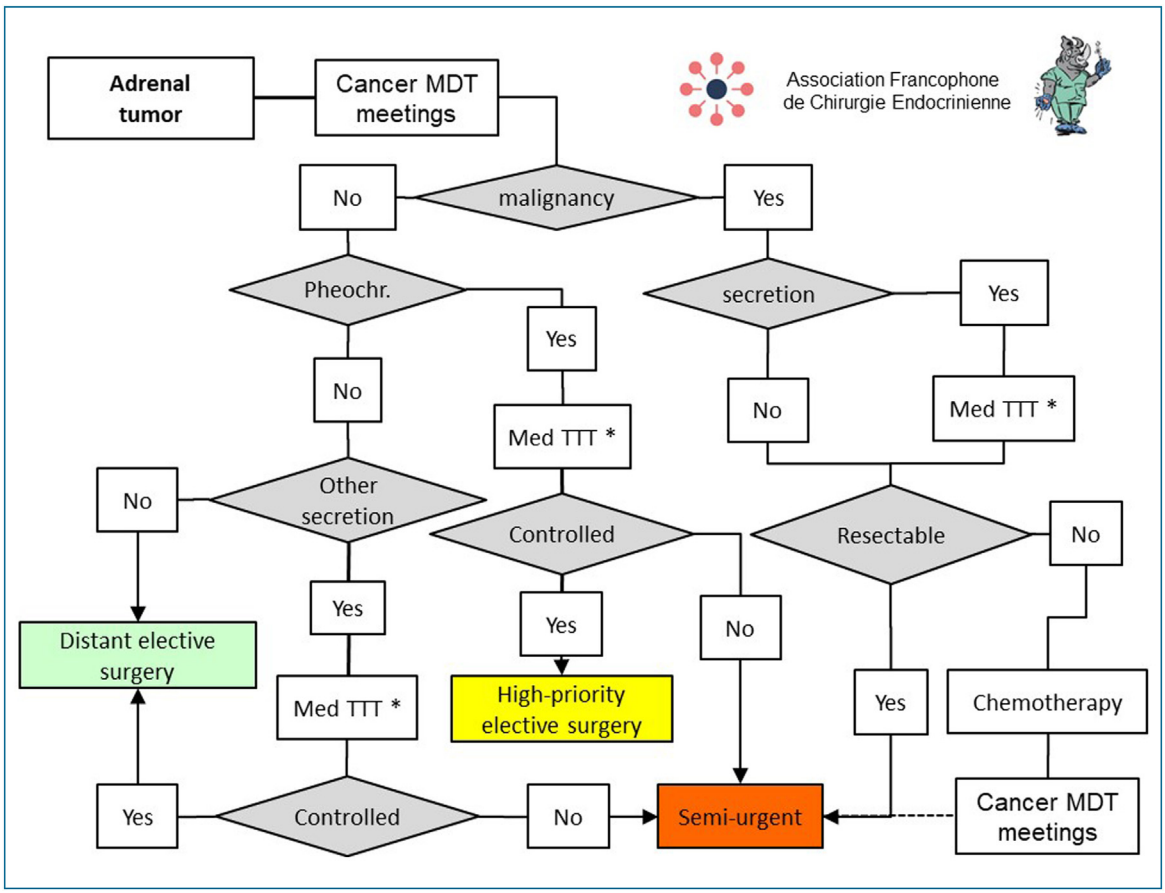

Figure 6. Principles for scheduling surgery for adrenal tumours during and after the COVID-19 epidemic. * Steroidogenesis inhibitors (metyrapone, ketoconazole), anti-hypertensive agents (alpha-blocking drugs, beta-blocking drugs, calcium inhibitors), anti-aldosterone diuretics, (Med TTT:medical treatment, pheochr: pheochromocytoma; MDT: multidisciplinary team).

in which a diagnosis of cancer or a therapeutic strategy is to be announced, some form of video exchange is recommended. Whenever possible, blood tests and imaging must be performed outside hospitals.

In a situation where medical drugs of major therapeutic importance may be in short supply, patients, who are dependent on a hormone substitution treatment, should be reminded never to interrupt their treatment longer than 24 h for corticoids [44], longer than 48 h for calcium [45], and longer than one week for thyroid hormones [46].

Disclosure of interest

The authors declare that they have no competing interest.

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