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Review

Endocrine Surgery during the COVID-19 Pandemic: Recommendations from the Turkish Association of Endocrine Surgery

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Abstract

The 2019 novel coronavirus disease (COVID-19) was initially seen in Wuhan, China, in December 2019. World Health Organization classified COVID-19 as a pandemic after its rapid spread worldwide in a few months. With the pandemic, all elective surgeries and non-emergency procedures have been postponed in our country, as in others. Most of the endocrine operations can be postponed for a certain period. However, it must be kept in mind that these patients also need surgical treatment, and the delay time should not cause a negative effect on the surgical outcome or disease process. It has recently been suggested that elective surgical interventions can be described as medically necessary, time-sensitive (MeNTS) procedures.

Some guidelines have been published on proper and safe surgery for both the healthcare providers and the patients after the immediate onset of the COVID-19 pandemic. We should know that these guidelines and recommendations are not meant to constitute a position statement, the standard of care, or evidence-based/best practice. However, these are mostly the opinions of a selected group of surgeons. Generally, only life-threatening emergency operations should be performed in the stage where the epidemic exceeds the capacity of the hospitals (first stage), cancer and transplantation surgery should be initiated when the outbreak begins to be controlled (second stage), and surgery for elective cases should be performed in a controlled manner with suppression of the outbreak (third stage).

In this rapidly developing pandemic period, the plans and recommendations to be made on this subject are based on expert opinions by considering factors, such as the course and biology of the disease, rather than being evidence-based. In the recent reports of many endocrine surgery associations and in various reviews, it has been stated that most of the cases can be postponed to the third stage of the epidemic.

We aimed to evaluate the risk reduction strategies and recommendations that can help plan the surgery, prepare for surgery, protect both patients and healthcare workers during the operation and care for the patients in the postoperative period in endocrine surgery.

Keywords: COVID-19; endocrine surgery; pandemic.

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The new coronavirus (Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)) causing 2019 novel coronavirus disease (COVID-19) first appeared in Wuhan, China, in December 2019. It quickly spread and became a public health problem worldwide and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. On May 28, the total number of cases in the world in 216 countries reached 5.596.550 and the number of deaths reached 353.373.[1] The rapid spread of the disease and high hospitalization rates forced healthcare professionals to drastically change their practice and quickly organize hospitals. With the pandemic, all elective surgeries and non-emergency procedures have been postponed in our country, as in others. Most of the endocrine operations can be postponed for a certain period. However, it must be kept in mind that those patients also need surgical treatment and that the waiting time should not cause delays that may have a negative effect on the surgical outcome or disease process. It has recently been suggested that elective surgical interventions can be described as medically necessary, time-sensitive (MeNTS) procedures.[2]

When planning the surgery during and after the peak period of the COVID-19 pandemic, in addition to the factors related to the patient and hospital conditions considered to date, the risk of contamination to patients and healthcare workers who are COVID 19 negative, hospital facilities, especially the conditions related to the operating room and postoperative care should be considered.[2]

Some guidelines have been published on proper and safe surgery for both the healthcare providers and the patients after the immediate onset of the COVID-19 pandemic.[3–5] These guidelines are gradually increasing. We should know that these guidelines and recommendations are not meant to constitute a position statement, the standard of care, or evidence-based/best practice. However, these are mostly the opinions of a selected group of surgeons. Each institution and the surgeon must consider their individual patient within the context of their organization for decision making about the timing of surgery. The major surgical societies have issued specific guidelines addressing the place of minimal invasive surgery in these challenging times.[6–14]

We aimed to evaluate the risk reduction strategies and recommendations that can be helpful for the planning of the surgery, preparing for surgery, protecting both patients and healthcare workers during the operation and caring for the patients in the postoperative period in endocrine surgery.

Planning and Prioritization in Endocrine Operations during COVID-19 Pandemic

Generally, only life-threatening emergency operations should be performed in the stage where the epidemic exceeds the capacity of the hospitals (first stage), cancer and transplantation surgery should be initiated when the outbreak begins to be controlled (second stage), and surgery for elective cases should be performed in a controlled manner with suppression of the outbreak (third stage).[15]

When planning for surgery during and after the peak period of the COVID-19 pandemic, in addition to the factors related to the patient and hospital conditions considered to date; the risk of contamination to COVID-19 negative patients and healthcare workers, hospital facilities, especially the conditions regarding the operating room and postoperative care should be considered.[2] In this rapidly developing pandemic period, the plans and recommendations to be made on this subject are based on expert opinions by considering factors, such as the course and biology of the disease, rather than being evidence-based. The proposal by the British Association of Endocrine and Thyroid Surgeons (BAETS) for the timing of the surgery, related to the urgency and priority of endocrine surgeries during the pandemic seems practical and feasible.[16]

Endocrine surgeries are divided into four priority levels. These are;

Level 1a: Life-threatening situations that need to be operated within 24 hours to save the patient

Level 1b: Conditions that need to be operated between 24-72 hours for life-threatening conditions that may cause, such as obstruction, bleeding, local or regional infection, permanent injury/clinical harm from the progression of conditions, such as spinal cord compression

Level 2: Conditions requiring elective surgical intervention and where surgery can be postponed safely for up to four weeks before a negative condition develops

Level 3: Conditions in which elective surgical intervention can be postponed for up to three months without a predicted negative outcome

Level 4: Conditions in which elective surgical intervention can be postponed more than three months without a predicted negative outcome

Especially after the peak period of the COVID-19 pandemic, not only endocrine surgical interventions but also other elective surgeries have to be planned as well. For this, all operations must be arranged in a certain order according to the hospital's facilities and the number of operating rooms activated according to its conditions. Thus, it is recommended to classify and prioritize all postponed cases according to their specificities, such as cancer and transplantation, arranging all other surgeries according to an objective scoring system, and create an appointment plan according to this scoring.[15, 17]

American College of Surgeons recommends the scoring system made by Prachand et al. in this period. This system proposed a detailed scoring system for all elective surgical interventions, including a total of 21 factors, scored with points ranging from 1 to 5 points, with 7 factors related to surgery (operating room time, estimated hospital stay, possibility of requiring postoperative intensive care, expected blood loss, probability of intubation, surgical region), six factors related to the disease (effectiveness rate of nonoperative treatment option, risks of nonoperative treatment, effect of two weeks delay on disease outcomes, effects of two weeks delay on the difficulty and risks of surgery, effects of four weeks delay on disease outcomes, effects of four weeks delay on the difficulty and risks of surgery), eight factors related to the patient (age, presence of lung disease, presence of obstructive sleep apnea, presence of cardiovascular disease, presence of a condition related to immune system suppression, influenza-like symptoms, contact with a person known to be COVID-19 positive in the past 14 days). The high total score, ranging from 21 to 105, is associated with worse perioperative patient outcomes, increased risk of transmission of COVID-19 to the healthcare team, and/or increased hospital resource utilization. It is recommended that after reserving an adequate number of operating rooms for emergency surgeries according to the instant dynamic situation, a value of threshold point for the elective operations can be determined, and operations exceeding that threshold can be postponed depending on the hospital's facilities.

The researchers stated that this scoring system could also be used to facilitate planning in the prioritization of elective cases waiting for surgery in the plateau period, while the pandemic begins to decrease. This scoring system can enable the evaluation and planning of not only endocrine surgery but all surgeries together, especially in centers where operating room conditions are limited.[2]

It is suggested in the early stages of discussions on planning the post-pandemic period. New systems may also be proposed according to the requirements over time. However, after the pandemic, institutions can create a similar triage strategy according to their operating room and bed facilities, patient and disease conditions, features of the operation and the risk for COVID-19.

Thyroid Surgery during the COVID-19 Pandemic

Firstly, the patients should be examined for the presence of the COVID-19 symptoms. The diagnosed COVID-19 patients should be administered COVID-19 treatment primarily if they do not have an airway failure due to thyroid disease. In case of the individuals having no COVID-19 symptoms and findings, but being under the risk of viral transmission, actions should be taken in compliance with the recommendations of the relevant units if they do not have an acute airway failure due to thyroid disease. Although there are no clear guidelines in the management of patients applying for thyroid diseases, it would be appropriate to manage these patients based on the analysis of risk groups. The first approach should be determining if there is airway distress due to thyroid disease or not, while the second approach should be distinguishing benign and malignant cases. The following section, during the COVID-19 pandemic, can give clues regarding the approach to the thyroid diseases that may require surgical intervention.

Benign Conditions

A- Large Goiters: In case of long-term huge goiter (nodular or diffuse), causing a tracheal deviation and mild compressive symptoms, it would be appropriate to avoid surgery.[18, 19] This situation should be explained to the patient in an appropriate manner without stressing the patient. On the other hand, surgery should be considered in a short while in case of goiter showing a rapid growth or causing acute airway distress. Mostly, removing out the lobe, causing compression on the airway, with the isthmus (hemithyroidectomy) would be sufficient, in the absence of intraoperative suspicion of malignancy.

B- Fine Needle Aspiration Biopsy (FNAB) Proven Benign Thyroid Nodules and Graves' Disease: They can be managed in the same way as they were before the pandemic. However, if any severe complication, such as recurrent neutropenia/agranulocytosis or liver failure, occurs in a patient receiving anti-thyroid therapy for Graves' disease, surgical intervention may be considered after managing these complications. British Thyroid Association (BTA) states that the operation is safe and acceptable in most cases19 because patients with uncontrolled thyrotoxicosis may have a higher risk of thyroid storm due to COVID-19. These patients can be operated after 5-7 days of preoperative rapid preparation (with a beta-blocker, iodine solution and dexamethasone).

C- Asymptomatic Incidentally Discovered Thyroid Nodules (with Physical Exam or Ultrasound (US)): The guidelines recommended by various associations, such as the American Thyroid Association (ATA), American College of Radiology (ACR) or BTA for FNABs of incidental thyroid nodules, should be applied vigorously.[18, 20, 21] While ATA divides nodules into benign, very low, low, medium and high suspicion patterns, ACR and BTA use the TIRADS classification consisting of five groups. In fact, both classifications, which are based on the ultrasonographic pattern, are quite similar. According to these recommendations, FNAB should be considered in TIRADS 3, 4, 5 or ATA's low, intermediate, high

suspicious nodules; if the maximal dimension is greater than 2-2.5 cm, 1.5 cm, 1 cm, respectively. Nodules that do not meet these criteria can be re-evaluated with the US after 6-12 months.[22]

Similarly, a triage model proposed by Jenn Kuo, and James Lee (from Columbia University) can also be helpful:

- An enlarging neck mass with concern for anaplastic thyroid carcinoma (ATC) or lymphoma should be biopsied as soon as possible.
- A nodule with concern for medullary thyroid carcinoma (MTC), lymph node disease that will direct surgical treatment, suspicious nodules of >4 cm and new-onset hoarseness require FNAB in less than one month.
- FNAB can be delayed for more than three months with suspicious nodules of 1-4 cm in size (ATA risk classification: moderate or high risk/TIRADS classification: 4 or 5) and incidental positron emission tomography-computed tomography (PET-CT) avid nodules.[23]

Although serum calcitonin measurements are still controversial for patients with thyroid nodules, the measurement of calcitonin level may be helpful in deciding for FNAB, especially patients with a family history of MTC or nodules located in the posterior upper third of lateral lobes. If calcitonin level is higher than 10 pg/ml, FNAB should be offered as early as possible. Moreover, if calcitonin level is higher than 100 pg/ml, this should be considered an indication for surgery without FNAB.[22]

Management after FNAB Results

A- Indeterminate Nodules (Bethesda III and IV categories)

These patients can be followed up. Furthermore, it is suggested that the positivity of the molecular markers, such as BRAF or TERT, is not a determinant for immediate surgical intervention.[18, 21]

B- Malignant Nodules (Bethesda V and VI categories): Differentiated Thyroid Carcinoma (DTC), MTC and ATC

Despite a major health crisis like COVID-19, patients are concerned about their own problems, such as proven or suspected thyroid cancer. Some thyroid cancers are life-threatening and will require urgent attention while other tumors may be monitored or treated lately. In most cases, postoperative radioiodine (RAI) therapy is not urgent and can be safely delayed.

B1- DTC (ATA Low and Intermediate Risk): These patients (without compressive symptoms and signs, no apparent nodal metastasis, no voice changes) may wait 3-6 months for surgery. During this time, COVID-19 can be controlled and may pose less risk for health care workers. If an extended observation period is needed, imaging with the US once again after three months may encourage patients to delay surgery further.

Intrathyroidal Papillary Microcarcinomas (PTMC) can definitely be observed. Moreover, some of these patients can be encouraged to remain under active surveillance.[24] It should be kept in mind that US examination should be repeated with certain intervals.[24]

B2- DTC (ATA High risk): Large compressive or Locoregional aggressive DTC (Evidence of aero-digestive tract compression, recurrent laryngeal nerve palsy due to malignancy, the rapid growth of tumor) require surgical intervention. Appropriate cross-sectional imaging (CT, Magnetic resonance imaging (MRI)) can be very helpful in determining the extension of surgery.[19]

B3- MTC: The extent of the disease should be determined using cross-sectional imaging, calcitonin and CEA levels; that can be important for the timing of the surgery. In this context, if the disease appears to be limited to the thyroid region and calcitonin levels are not high (under 400), patients can be monitored for a few months hoping for COVID-19 to be taken under control.[19] This situation should be discussed between the surgeon and patients to make them feel more confident. On the other hand, according to BTA, MTC should be managed similarly with the usual practice.

Prophylactic surgery should not be postponed if possible in pediatric MEN2 patients having a high risk of malignancy. If the surgery is deferred, the patient should be carefully monitored with calcitonin levels and US.[18]

B4-ATC

B4a. Proven Anaplastic Thyroid Cancer with FNAB or Core Biopsy: Patients with rapidly growing thyroid tumors require emergent management. The extent of the disease should be evaluated with cross-sectional imaging.[19] If the tumor appears to be unresectable, and the patient has acute airway distress, tracheostomy or cricothyrotomy may be necessary. Otherwise, appropriate targeted therapies, such as multikinase inhibitors and external radiation therapy, should be considered.[18]

B4b. Rapidly Growing Thyroid Tumors without Histological Diagnosis. The definitive diagnosis can be made easily using US-guided core biopsy. The patient should be approached as in B4a if the result is reported as ATC. If the result indicates a systemic disease, such as lymphoma, the patient should be transferred to the relevant unit for systemic chemotherapy, and the airway should be monitored closely.

Parathyroid Surgery during the COVID-19 Pandemic

Parathyroid surgery is one of the surgical procedures that are mostly evaluated in the elective operation group. Consider-

ing that the majority of patients with hyperparathyroidism consist of asymptomatic or normocalcemic patients, it is recommended to perform surgery only for such a group of patients summarized below under appropriate elective conditions and to use focused surgical approaches if possible.[16, 25]

For Primary Hyperparathyroidism:

Cancer suspicion (severe hypercalcemia, imaging-clinical findings)

Serum calcium level is above 3 mmol/L (12 mg/dl) and does not fall below this level with medical treatment (hydration, furosemide, cinacalcet)

Pregnant patients (should be decided together with the endocrinologist, and, if possible, operated on the second trimester)

For secondary Hyperparathyroidism:

Life-threatening calciphylaxis (necrosis and sepsis due to soft tissue calcifications)

Development of the pathological bone fracture

For Tertiary Hyperparathyroidism:

Hypercalcemia that impairs renal function in the post-transplantation period.

Adrenal Surgery during the COVID-19 Pandemic

The two endocrine surgery societies, BAETS and American Association of Endocrine Surgeons (AAES) published their recommendations about adrenal surgery in pandemic.[9, 14]

BAETS classified adrenal surgery into urgent and semi-urgent adrenalectomy. Since the adrenal cancers are usually very aggressive and surgical resection of the tumor is the only effective treatment, BAETS recommended urgent adrenalectomy (priority 1) for confirmed adrenal cancer diagnosis or highly suspicious masses (also including malignant pheochromocytoma). Indeterminate masses of >6 cm, especially increasing in size or hot (and nonfunctional) on PET-CT scan was classified as 'priority 2' and urgent adrenalectomy is recommended. BAETS also recommended urgent adrenalectomy for benign pathologies, such as refractory Cushing's syndrome and pheochromocytoma presenting with heart failure.[14]

BAETS classified adrenal metastases, pheochromocytoma, indeterminate masses of <6 cm and Cushing's syndrome with comorbidities as semi-urgent. The recommendation for adrenal metastases is to rescan after three months and re-prioritize in case of progression. BAETS recommendation for pheochromocytoma is to block the highest degree that a patient can tolerate. PET scan was recommended for indeterminate masses of <6 cm and medical treatment via metyrapone was recommended for Cushing's disease with co-morbidities.[14]

The AAES classified adrenal lesions in four categories. They recommend urgent adrenalectomy for adrenocortical cancer, adrenal incidentaloma of >6 cm or suspicious for malignancy, medically refractory endocrine disorders (e.g., medically refractory pheochromocytoma), endocrine disorders jeopardizing the lives of the mother and fetus in pregnant patients that cannot be controlled medically (Category 1). In this statement, pheochromocytoma/paraganglioma, Cushing's and adrenal metastases have been classified as Category 2. Primary hyperaldosteronism, adrenal incidentaloma of <6 cm have been classified as Category 3. Rest of the other adrenal lesions have been classified as Category 4.9 However, endoscopic surgery (Laparoscopic, Retroperitoneoscopic or Robotic) for adrenal masses is another topic to discuss in COVID-19 pandemic because the creation of an artificial pneumoperitoneum may increase the risk of aerosol exposure to the whole operating team in endoscopic surgery. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and The European Association for Endoscopic Surgeons (EAES) published a guideline including recommendations for minimally invasive surgery (MIS).[13]

The major recommendation of this guideline is to postpone all elective and endoscopic surgeries at the current time. However, they recommend that these decisions should be made locally, based on COVID-19 burden and in the context of medical, logistical, and organizational considerations. The guideline recommends that the surgical care of patients should be limited to those whose needs are imminently life-threatening, including patients with malignancy that could progress or with active symptoms.

SAGES and EAES strongly recommend that the possibility of viral contamination to staff during open, laparoscopic, or robotic surgery should be considered. Protective measures that have been recommended by national or international organizations, including the WHO or Centers for Disease Control (CDC), have to be strictly employed to maintain the safety of the operating room (OR) staff and a functioning workforce.[13] The personal protective equipment should include at least the N95 masks and face shields.[26, 27] Although there are some published data showing that laparoscopy may lead to aerosolization of blood-borne viruses,[28–30] this guideline reports that neither there is evidence to indicate that this effect is seen with COVID-19, or that it would be isolated to MIS procedures. Nevertheless, for MIS procedures, the use of devices to filter released CO_2 for aerosolized particles should be strongly considered. Besides the proven benefits of MIS, guideline mentions that the ultrafiltration of aerosolized particles may be more difficult during open surgery.[31, 32]

SAGES and EAES guideline also offer to set electrosurgery units to the lowest degree as much as possible for the desired effect and minimize the use of monopolar electrosurgery, ultrasonic dissectors, and advanced bipolar devices which can lead to particle aerosolization,[33–39] and if available, monopolar diathermy pencils with attached smoke evacuators should be used.[31] Surgical equipment used during procedures with COVID-19 positive or suspicious patients should be cleaned separately.

SAGES and EAES practical recommendations for laparoscopy;

1. Incisions for ports should be as small as possible not to allow for leakage around ports.
2. CO_2 insufflation pressure should be minimized as much as possible and an ultrafiltration (smoke evacuation system or filtration) should be used, if available.
3. At the end of surgery or before converting to open surgery or removal of trocars, the pneumoperitoneum should be carefully released[40] and safely evacuated via a filtration system in case of aerosol formed during the operation.[13, 32, 41, 42]

On behalf of the Endocrine Surgery Society of Turkey, we recommend urgent adrenalectomy for all patients with confirmed adrenocortical carcinoma and suspicious adrenal tumors, including malign pheochromocytoma during Covid-19 pandemic. We also recommend urgent surgery for patients with medically uncontrollable pheochromocytoma/paraganglioma and pregnant patients with endocrine disorders jeopardizing the lives of the mother and fetus that cannot be controlled medically. However, every patient should be considered within the context of the institution and the current situation of the disease for decision making about the timing and the technique of the surgical (open or endoscopic) procedure. For endoscopic procedures (laparoscopic, retroperitoneoscopic or robotic), the OR staff should be strictly employed with personal protective equipment and safe evacuation and filtration systems should be used if available. The indications can be extended in the period of the plateau and indeterminate masses of >6 cm, refractory Cushing's syndrome and pheochromocytoma with cardiac complications can be treated surgically.

Neuro-Endocrine Tumors

To our knowledge, there is only one updated guideline for neuro-endocrine tumors (NETs) during the pandemic period.[43] They recommend only life-saving surgery and mention that surgery may be considered for high-grade patients with NETs. We recommend that all elective procedures should be postponed. However, life-threatening high-grade tumors and patients with hormone-active NETs whose symptoms cannot be controlled (e.g., medically refractory insulinoma) medically should undergo surgical treatment. Nevertheless, every surgeon and institution should consider their individual patient within the context of their organization for decision making about the timing and the technique of the surgical (open or endoscopic) procedure.

Preoperative Planning and Preparation in COVID-19 Period

During the COVID-19 pandemic, the preoperative planning of the patients is different from routine surgical planning. The most important factor in this planning is to determine whether the patient has an infection due to SARS-CoV-2 or not. This evaluation includes taking an anamnesis and physical examination of the patient, biochemical tests, microbiological and radiological examinations.

The patient's tests regarding his presurgical disease should be examined in advance to minimize contact. During the interview with the patient, both the patient and doctor should use a surgical medical mask. The patient's travelling history and contact history with cases of suspected/confirmed infection with COVID-19 in the last 14 days should be questioned. After symptomatic interrogation, physical examination should be started by measuring fever and pulse. The informed consent, prepared exclusively for COVID-19, should be taken except the standard surgical consent form and also it is very important to inform the patient about COVID-19. Preoperative routine biochemistry tests are not used for the diagnosis of COVID-19 but may contain suspicious values for possible disease. Decreased albumin level, increased alanine aminotransferase, aspartate aminotransferase, and total bilirubin levels, hyponatremia, hypokalemia, hypocalcemia, increased blood urea nitrogen, creatinine, and glucose levels can be seen in patients who are infected with COVID-19.[44] Lactate dehydrogenase and d-dimer which are not included in the routine preoperative examinations may increase. In complete blood count, an increase in the number of leucocytes and neutrophils can be seen, while the number of lymphocytes and platelets may decrease. However, none of these tests and findings is specific to COVID-19.

The real-time polymerase chain reaction (PCR) test studied from the nasal and pharyngeal swab, which is the gold standard in the diagnosis of new coronavirus SARS-CoV-2, should be performed in the preoperative period. The sensitivity of this test in clinical practice is between 37% and 71%.[45] The most important factors affecting false-negative results are the sample, including inadequate material, type and transportation of the sample, and taking the sample in too early or late periods of infection. The health worker who takes the swab should have the appropriate personal protective equipment. If the test result is positive, it is recommended to repeat the test for confirmation. In cases with suspected in-

fection whose test results were negative, repeating samples with an interval of 24-48 hours is recommended.[46]

The use of direct radiography and CT in diagnosis is increased due to the PCR test's sensitivity being not high enough and difficulties in reaching the test. The sensitivity of direct radiography is low in the early stage of the disease or mild disease. Thus, direct radiography should not be used in patients who are considered to have elective surgery and have no symptoms since its diagnostic value is low. Thorax CT has a high specificity of 93-100% and moderate sensitivity of 72-94%.[46, 47] Thorax CT has diagnosed existing pneumonia in 67% of COVID-19 negative cases and 94% of COVID-19 positive patients according to the PCR test result. Thorax CT which is going to be used in the preoperative evaluation should be taken in the last 24 hours before surgery.[46]

Endoscopic vocal cord examination, which is normally recommended for preoperative evaluation before thyroid or parathyroid surgery, should not be routinely performed.48 Vocal cord examination should be performed only in selected cases with hoarseness and appropriate personal protective equipment should be used during the examination. In the postoperative period, the laryngeal examination should only be performed on patients with recurrent laryngeal nerve injury or loss of signal during intraoperative neuromonitoring or if further contralateral surgery is planned in the near future.

Although the resulting time of these tests applied for the diagnosis of COVID-19 differs according to the centers, it takes an average time of 4-8 hours. It is a rare condition in endocrine surgery to confront such a severe acute respiratory distress that cannot wait for this time. Thus, routine biochemistry tests, PCR test and thorax CT are recommended before all the surgical procedures49,50 It should be kept in mind that although all these tests are normal, the disease may be present.

Preoperative Preparation of the Operation Room

Although it is strongly advised to defer surgeries during the COVID-19 pandemic period, the need for surgery not only arises for COVID-19 positive or suspected patients but also for asymptomatic and PCR negative patients in emergent or semi-emergent conditions. There are extra measures to be taken except for the routine practices for surgeries during the COVID-19 pandemic period. Hospitals should be prepared and organized to perform non-deferrable surgical procedures particularly for the infected patients in a way to save the patient and the healthcare workers from the infection and to prevent the contamination of the hospital environment from saving other patients and hospital staff.[51]

In the period of COVID-19 pandemic, all patients should be considered suspicious, so disease and infection control measures should be taken. Suspicious or confirmed COVID-19 cases should be scheduled at the end of the list if possible.[52] This organization should be planned meticulously beginning with the transfer of the patient from the surgical ward to the OR. The patient should be transferred with a surgical mask.

It is important that this transfer is carried out as quickly as possible and with minimal contact with the hospital environment and other people. An elevator reserved for the transfer of COVID-19 positive patients should be used if needed and immediate disinfection is performed after the transfer.[51]

An OR located away and isolated from the general operating complex must be reserved for infected patients. The room's location is planned as the shortest way to the transfer gate of the operating complex, which is advised to be a separate gate to minimize contamination. The OR reserved for patients with COVID-19 should be marked visibly for everyone and should not be used for any other purpose.

It is obvious that intubation for general anesthesia bears the aerosol effects. Designing the OR for infected patients as negative pressure rooms is important to prevent the halls and other parts of the operating complex from contamination.[53] Still, most of the ORs are equipped with positive pressure. It is advised to convert at least one OR to a negative pressure room. Positive pressurization and air conditioners must be closed if a negative pressure room is not possible. Maintaining the OR gate closed except for mandatory needs, especially strictly after intubation and extubation for 10 minutes, will help protection of viral spread outside the OR. Providing at least 25 times/hour circulation of OR air, HEPA filters will remove more than 99% of the viral load.[53] Discontinuation of positive pressure for at least 20 minutes after the deport of the patient from the room is beneficial. Adding checklist specific to COVID-19 to the routinely used checklist before surgery is recommended because it minimizes the risk of errors or adverse events.[49]

All the equipment and surgical items are prepared in the room before the patient is accepted to the OR. The trolleys for anesthesia are kept outside the room and all the drugs, medications and equipment that are needed by anesthesia are kept in the OR in a disposable tray. This provides prevention of contamination of all the trolley and material transfer during surgery. All the unnecessary equipment and devices must be taken out of the OR. Surgery of COVID-19 infected patients must be planned to be performed as quickly as possible with the least number of surgical staff. The surgical staff who will be in charge during the surgery should be predetermined, recorded and allowed to enter the room.

Unless there is an emergency, the team should never be changed during the surgery. Unnecessary mobility should be restricted. The adequacy of laminar flow and function of high-efficiency filters are periodically controlled by technicians. Consultations and planning of the operation between the surgery and anesthesia departments should be made in advance to ensure minimal time consumed with the patient. The surgical team should use suitable, tested personal protective equipment (PPE) during the surgery of confirmed or suspected COVID-19 patients.[46] PPE should be available outside the OR and worn before entering the OR. Personal protective equipment consists of the mask-N95, sterile surgical gown, disposable sterile gloves, goggles/face protector, disposable surgical cap, disposable foot protector/overshoe and waterproof surgical overalls, alcohol-based hand antiseptic.

Personal accessories (e.g., necklaces, earrings) should be removed before entering the OR, and items such as keys, purses, phones should be left out of the OR. Those with long hair should collect their hair in a way that it is totally covered with the surgical cap. Disposable caps should be preferred-personal surgical caps should not be used; if used, they should be washed and disinfected after the case.[54]

Disposable foot protector/overshoe and waterproof surgical overalls should be worn, especially in cases where fluid contamination is thought to be high. Then, the hands should be washed, and at least an N95 mask should be put on. An additional surgical should be worn over the N95 mask to limit the risk of splash contamination in case the mask replacement is needed during surgery. Those with beards should make sure that the mask fits the face properly. Goggles or face protectors should be used to prevent the conjunctival mucosa from virus contamination. Face shields, in particular, can limit the use of a surgical microscope, DaVinci console or surgical loupes. Surgeons should test the use of these devices before surgery.[55]

All the PPE required must be ready in the operation complex and the surgical team must wear and get ready before the patient arrives the OR. It is important not allowing anyone from the surgical team and any equipment or waste to go out of the OR unless emergent. Intubation should be done in the OR and the surgical team should not be in the OR until the preoperative anesthesia preparation and intubation are completed.[46] Communication between the OR and the team outside the OR is provided with phones or similar communication devices that must be provided and checked before surgery.[46]

Instruments and devices that cannot be taken out of the room is better covered with disposable plastic covers and eliminated properly after surgery. All the medical wastes and disposable instruments must be packed and eliminated according to the hospital's infection control committee rules. The ORs should be disinfected with hydrogen peroxide or other proven methods just after the end of the surgery.[56]

Although rare, COVID-19 PCR negative patients undergoing surgery may develop symptoms and become test positive in the postoperative period. Therefore, except for a negative pressure OR, other rules are advised to be applied as much as possible.

Differences in Anesthesia and Preoperative Preparation (COVID (+) Patient /COVID (-) Patient)

Anesthetic management in patients with surgical need during outbreaks depends on certain factors. The most important of these are the severity of the condition requiring surgery, the stage of the epidemic, and the conditions and status of the hospital.[15] However, in infections with high risk of contamination with aerosol release such as COVID-19, intubation and extubation phases have an extremely high risk for anesthesia.[57] Therefore, since most of the cases will be operated under emergency conditions until the epidemic is taken under control, anesthesia management requires all patients to be considered as if they were diagnosed with COVID-19 or suspicious.[58, 59]

In the recent reports of many endocrine surgery associations and in various reviews, it has been stated that most of the cases can be postponed to the third stage of the epidemic. However, since the conditions leading to airway obstruction require urgent surgery and may result in a very high-risk intervention for aerosol propagation, such as tracheostomy, the highest protection measures should be taken in anesthesia management in such cases.[9, 16, 48, 60]

The main goal to be considered in the perioperative anesthetic management of the patient, who is diagnosed or suspected of COVID-19, is to keep the risk of contamination of the entire OR team and medical devices to a minimum without compromising patient safety.[51, 57]

Pre-operative Preparation: High level (Level 3) PPE is considered as the most important barrier to protect the anesthesia team during intubation and extubation stages when they are exposed to the highest level of aerosol contamination. Therefore, physician and technician who will perform anesthesia should use PPE.[46, 61] One of the precautions to be taken before bringing the patient to the designated COVID-19 OR is the covering of devices, such as anesthesia device, monitor, infusion pump and defibrillator, with disposable transparent covers. These covers should be replaced after each operation and disinfection of the devices should be provided.[59, 62, 63] A separate breathing circuit should be used for each patient and a filter should be placed in the inspiratory and expiratory

connections of these circuits.[59, 62]

Anesthesia Induction and Intubation: Except in special circumstances, general anesthesia is recommended[46, 51, 62] in patients diagnosed with COVID-19 or suspected diagnosis to reduce the risk of transmission. Administration of high-flow oxygen should be avoided during the preoxygenation phase, and it is recommended to cover the nose and mouth area with 2 layers of wet gauze or a transparent cover to evade secretions.[59, 62] Rapid induction by avoiding mask ventilation is necessary to minimize contamination.[57, 59, 62] Proper muscle relaxation should be provided to prevent coughing during intubation, and an endotracheal tube clamped distally should be placed at the ideal depth at once and the cuff inflated immediately to prevent leakage, without bending over the patient's face.[59, 62] If available, intubation is recommended with the assistance of video-laryngoscope or bronchoscope.[59, 62] During induction, short-acting medications should be used at a minimum dose, deep anesthesia and excessive muscle relaxation should be avoided.[62] Positive pressure ventilation should be avoided after the induction phase.[62] If possible intubation cabins are strongly advised.

The integrity of the breathing circuit should be checked during the surgery, and if the line should be separated for any reason, the tube should be clamped from the farthest part to the heat and moisture exchanger (HME). Closed suction systems should be used to avoid viral aerosol release, if not available, excessive suction should not be applied.[49, 56]

Extubation and Recovery of the Patient: Coughing or forced sputum removal after endotracheal extubation when patient is awakening, poses a significant risk for all staff. Thus, all staff other than the anesthesia team should leave the OR before extubation.[64]

The patient should be extubated in the designated COVID-19 OR with a closed suction system. Intratracheal or intravenous lidocaine can be used to minimize aerosolization that arises from cough during airway manipulation.[64] All materials that have been in contact with the patient must be disposed in a separate waste bag.[51, 58, 59] During extubation, mouth and nose area can be covered with wet gauze or a transparent cover to minimize exposure to viral aerosole. Extubation can be performed so that the mask remains under the transparent cover by passing the connector part through the cover.[59] The patient with COVID-19 should be taken to the isolated ward or isolation intensive care unit, after he/she is woken up and recovered in the OR without going to the recovery room.[46, 51, 59] Therefore, the patients should not be kept in the OR and the operative team should not remove the protective equipment before the verification of safe extubation of the patient without any complications.[57, 65] After the patient leaves the OR and the proper cleaning of the reusable materials is ensured, the PPE can be removed and if necessary, preparations for the next patient can be started.[59]

When resuming elective surgery in the third stage of COVID-19 pandemic, careful distinction of COVID-19 positive and negative cases is mandatory. According to Turkish Society of Anesthesia and Reanimation's Suggestions for Resuming Elective Surgery[66] in normalization period of COVID-19 Pandemic, the pre-operative assessment of patient should include:

1. A checklist specific to COVID-19 including symptoms and suspicious contact with any COVID-19 patient,
2. A Chest CT in suspicious conditions such as fever, cough, dyspnea for further evaluation,
3. Two negative RT PCR results in last 5 days.

Chest CT is not recommended for the assessment of asymptomatic patients. For patients with positive RT PCR test but no clinical and radiological findings other than anosmia, gastroentistinal system symptoms, and myalgia, elective surgery should be planned at the earliest 28 days later after 2 negative RT PCR results. There is not yet enough information in the literature about the healing process of patients who have had COVID-19 pneumonia (with RT PCR (+), respiratory symptoms and CT findings). In this group, individual factors (age, comorbid diseases, etc.), respiratory status and type of surgery are important parameters for the timing of elective surgery and involvement of chest physician is required for decision making. The weekly scheduling of operation room for elective cases (with substitute cases) may allow a better planning in this transition time.[66]

On the other hand, due to the high rate of false negativity in PCR tests, negative[67] CT findings at the early stage of COVID-19 infection are up to 56%, and that the period when the epidemic is just being controlled has not yet been completed, personal protection measures for anesthesia management are kept at the third level. Because most hospitals in our country are still in the status of Pandemic Hospital is another factor that causes the precautions taken in anesthesia management of elective cases to be kept at a high level.

The patients should be transferred to isolated negative pressure rooms postoperatively, to minimize the risk of air-borne transmission.[57, 68] All of the staff should follow the general principals and use protective equipment.[69] The patients without a verified diagnosis of COVID-19 should be accepted as asymptomatic carriers and isolation protocols should be applied. The patients with suspected or confirmed COVID-19 should be treated in negative pressure rooms and preferably with multidisciplinary approach specialized for pandemia.[69]

Protection of the Patient and the Team during the Surgery

Electromedical devices (e.g., US) and surfaces should be used with adequate protective covers and adequately sterilized at the end of the operation.[46] After standard surgical hand washing, sterile surgical gowns and gloves are worn in the OR. Using double pair of gloves is recommended. The surgical procedure should preferably be performed by an experienced surgeon. This will shorten operation time and reduce the complication rate and the risk of need for re-operation. It is highly recommended to avoid using such situations for teaching purposes. As in any surgery, including this case, verbal communication of the surgical team is important. Verbal orders should be used in tool exchange if possible, instead of handling the cutting tools directly from hand to hand, the tool tray should be used for the transition. In the end, all cutting tools should be collected in a container in accordance with surgical procedures.[54, 55]

Many devices used during operations create a "smoke" by burning tissue microparticles, creating combustion products, and carbon dioxide suspension with the risk of aerosolizing infectious diseases. These devices include electrocautery, ultrasonic harmonic devices and lasers used for tissue ablation. There is limited evidence for the choice of energy device. The use of bipolar electrocautery can produce less smoke than monopolar cautery or harmonic devices. Although devices, such as harmonic scalpel, can add efficiency and speed to the procedures performed, more vivid cells have been detected in the smoke from this device. While case reports of actual transmission infections are rare, there is a major concern, particularly concerning the respiratory transmission of SARS-CoV-2. Care should be taken to collect and evacuate smoke properly. The Association of Operating Room Nurses and the National Institute of Occupational Safety and Health recommend the use of smoke evacuation devices and filtration systems when working on a patient with a disease that is potentially or truly airborne transmitted. Ultra-low particle air (ULPA) filters are depth filters that filter matter in different ways depending on the particle size and can hold 99.9% percent of the particles of 0.1 µm size.[70] This makes them ideal for removing particles created in electrosurgery and laser procedures.

There are also other benefits of using smoke evacuation devices like keeping the surgical field clean, preventing equipment corrosion due to the released chemicals and reducing odor. In the absence of such smoke evacuation devices, it is recommended to use alternative techniques instead of using electrocautery.

To remove PPE, there should be a hand hygiene station and special medical waste boxes at the exit of the OR. If there is no such area, removal of the PPE should be carried out in the area closest to the OR door. While removing PPE, the following order should be respected: shoe covers, first layer of gloves and surgical overalls.

The second layer of gloves are either removed in the end and after removing the mask, or they are removed without leaving the OR, and the hands are disinfected after each step of removal of remaining PPE. Goggles and face protectors are removed outside the OR. If there is no visible contamination, this equipment is placed in the appropriate area for re-sterilization.

Afterwards, surgical cap and mask are removed. A clean mask is worn again after hand hygiene. In the dressing room, the surgical form is removed and the shower is taken.

While there are no data on COVID-19 viral load in body fluids or tissue samples, efforts should be made to minimize the risk of contamination associated with samples sent to the pathology department. Medical records, surgery report and postoperative treatment follow-up records of the patient should be written outside the OR.[46]

In endocrine surgery, endoscopic procedures for thyroid and parathyroid gland diseases and laparoscopic interventions for the adrenal gland and neuroendocrine tumors can be applied. Although laparoscopy has been shown to lead to aerosolization of blood-borne viruses, there is no evidence that this effect is seen with COVID-19. There are different opinions regarding the use of laparoscopy. Additional measures are available to protect the surgical team during laparoscopic procedures. A closed smoke aspiration system should be used during laparoscopic applications. There are HEPA or ULPA filtered systems special for laparoscopic interventions.[70] Unnecessary incisions should be avoided. In the Hasson technique applied for the first trocar's placement, it is recommended that the first entry is made with a Veress needle or laparoscope placement with the aim to decrease-large fascia and skin opening. Thus, there is a tighter fascia defect around the port and the risk of gas leakage is reduced. Trocars that prevent gas leakage, such as balloon trocars, should be used. During the surgery, smoke should not be evacuated from trocars. The entire pneumoperitoneum should be aspirated before removing the trocars and specimen.[50, 64, 70]

Postoperative Follow-up in Endocrine Surgery

There is a lack of studies investigating whether hormonal dysfunctions or complications related to endocrine surgery affect the clinical course of COVID-19 infection. The main principle after surgery should be an early and safe discharge of the patient and manage necessary replacement treatments considering difficulties in reaching medical facilities during the pandemic.

Thyroidectomy

The management and follow-up of the patients at risk for hypocalcemia after thyroidectomy should be undertaken in a safe outpatient environment. Patients with severe symptomatic hypocalcemia should be treated in the hospital until safe to discharge to avoid emergency re-admission. Thyroid function tests may be difficult to access and thyroid hormone (levothyroxine) treatment at a dose of 1.8 µgr/kg is recommended after total thyroidectomy until thyroid hormone testing is available.[71]

In low-risk differentiated thyroid cancer patients, RAI treatment can be delayed up to six months postoperatively.[72] However, the risk-benefit assessment and timing of RAI treatment in high risk metastatic patients are difficult.[72]

Adrenalectomy

There are not available data yet on cortisol dynamics in patients with COVID-19.[73] Adrenal insufficiency may cause dysfunction of natural killer cells and lead to increased risk of respiratory viral infections due to impaired immune system.[74] In collaboration with the endocrinology department, hydrocortisone replacement doses should be optimized to reduce hospital stay.[75] Further monitoring of diabetes and blood pressure is recommended to be managed by local primary care providers to reduce face to face follow-up.[75] Rapid clinical evaluation should be performed if symptoms, such as cough and fever, develop after discharge from the hospital.

Parathyroidectomy

The necessity for calcium infusion due to symptomatic hypocalcemia and longer hospital stay are more frequent after subtotal parathyroidectomy in renal hyperparathyroidism compared to single adenoma excision.[76] Multidisciplinary team approach with endocrinology and nephrology is recommended to reduce hospital stay. Face to face follow-up should be minimized and further laboratory assays can be carried out on an outpatient basis by local primary care providers.[77] An adequate supply of calcium and vitamin D supplements is recommended in case of difficulties in calcium testing until testing is available.[77]

There are many guidelines to determine COVID-19 positive patients in the preoperative period.[78, 79] However, there are not sufficient studies yet to identify the asymptomatic/pre-symptomatic patients who underwent surgery and became positive in the course of hospitalization.[76] The PCR positive stool test was found in 23% to 82% of the patients with confirmed COVID-19 infection 11±9 days after the surgery, even though the respiratory samples turned negative.[81] Respiratory PCR test and fecal test have been recommended 12-14 days after discharge to identify asymptomatic/pre-symptomatic positive patients after hospitalization.[82]

In conclusion, the main principles of postoperative management following endocrine surgery can be summarized as follows:

1. A multidisciplinary approach for safe and early discharge of the patient
2. Arrangement of replacement or supplement treatments to reduce hospital visits
3. Collaboration with the family practitioners or local health providers to enable further testing and treatments on an outpatient basis
4. Use of tools, such as phone and mail, to contact the patient and guide follow-up
5. Screening, if possible, after discharge to identify asymptomatic/pre-symptomatic patients who became positive in the course of hospitalization

Telemedicine in Endocrine Surgery

As COVID-19 cases increased, hospitals in each country have been required to be organized quickly.[83] Following these developments, Disease Control and Protection Centers suggested cancelling all the elective surgeries in all facilities with inpatient clinics.[84] Also, many hospitals cancelled face-to-face outpatient visits of the patients requiring prolonged care. Endocrine surgeon likewise, other surgeons were deeply affected by these drastic measures. At the same time, these measures made it necessary for doctors to find ways to proceed with the follow-up and treatment of their patients.

Popularity and prevalence of telemedicine have rapidly increased during this pandemic since many physicians sought ways for continuity of patient care.[83, 85] These initiatives have been shown to lead to reduce costs and visit time and increase patient satisfaction in surgical fields previously.[86, 87] Telehealth provides health-related services and information through electronic information and telecommunication technologies. It also provides long-distance contact, care, advice, reminders, training, intervention, monitoring and remote patient care for clinicians and patients.[88, 89] Telemedicine used synonymously with "remote medical care" refers to providing clinical healthcare through electronic communication technologies rather than interpersonal meetings between patients and physicians.[90, 91] The use of video calls and other telecommunication applications has recently improved healthcare services.[92]

The current standard of care in surgical practice includes preoperative consultation, postoperative visit and ongoing visits for certain conditions at risk of recurrence. With this model, the burden placed on both the patient and the

outpatient clinic increased. The patient endures travel time, work hour loss, loss of salary and travel expenses. The clinic undertakes the cost of hosting potentially new patients, as well as staff costs. Telemedicine is a rapidly developing tool to provide care that does not require face-to-face visits. It is associated with improvements in attaining care and operational efficiency.[93, 94] However, before implementing the telemedicine program, issues regarding patient privacy, financial reimbursement and technological platforms' reliability should be considered.[95]

Previous studies have demonstrated the applicability of telemedicine in a wide range of applications, from diabetic retinopathy screening to postoperative visits for pediatric urology. Surgical procedures, such as inguinal or umbilical hernia repair, have been found to be particularly suitable for telemedicine encounters since these operations are associated with relatively lower complications that require face-to-face evaluation or intervention.[96] Similarly, patients who underwent thyroid and parathyroid surgery may represent an ideal population for telemedicine because postoperative care involves wound examination, wound care, discussion of pathology results and voice evaluation.[95–97]

Serious postoperative complication rates for thyroidectomy and parathyroidectomy are low and it makes these patients ideal candidates for telemedicine.[95] Zheng et al. showed that after telemedicine encounters with low face-to-face appointment rates, a single telemedicine visit was sufficient for postoperative care and eliminated the need for face-to-face visits.[95] In thyroid and parathyroid surgery, it is important to evaluate voice quality, as well as incision. Therefore, it requires the integration of the video or audio components of telemedicine.

The applicability, ease and cost-effectiveness of telemedicine are supported by various publications.[94–96] Still, most physicians are skeptical about providing the traditional patient-physician relationship with telemedicine. Both the patients and healthcare professionals are not convinced that telemedicine will replace face-to-face clinical visits. However, the repression enforcing health system due to COVID-19 pandemic has brought telemedicine to the forefront more than ever before. When database screening throughout Turkey was done, it is remarkable that this application is put into practice nearly in all private hospitals. Consultations between patients and relevant physicians through media channels, such as phone, FaceTime and e-mail can help the issue of the patients whether to apply to a health center or not in areas where COVID-19 is common.

Our personal experience is that by providing necessary precautions, the initial patient visit should be done face-to-face during the pandemic period in compulsory situations. The comfort or stress of the patient and physical examination are essential for the evaluation of clinical status and such evaluations, it is challenging to make interferences through video calls remotely. At the same time, it is also required to establish a legal infrastructure for this system to be a safe practice.

As a result, an unprecedented pandemic has brought telemedicine to the forefront of the healthcare system. Further studies are needed to further adopt telemedicine and to evaluate the efficacy of telemedicine practice between specialties.

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