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Review

Surgical Treatment of Substernal Goiter Part 1: Surgical Indications, Pre-Operative, and Peroperative Preparation

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Abstract

Surgery is one of the most appropriate treatment options for many patients with substernal goiter (SG). However, SG surgery has some technical difficulties and a higher risk of complications compared to normal cervical thyroid surgery. Due to these technical difficulties and complication risks, which we also mentioned in our study, SG surgery should be performed by experienced and high-volume endocrine surgeons in centers with a large team and technical equipment. Pre-operative clinical and radiological evaluation and definitions in SG were evaluated in detail in our previous study. Detailed pre-operative evaluation, pre-operative risk assessment, surgical anatomy, anesthesia, appropriate surgical planning and estimation of surgical width are extremely important in SG surgery, where surgical technical difficulties and increased complication risks compared to cervical thyroid surgery come to the fore. In this study, we aimed to evaluate these preoperative and peroperative preparations in detail.

Keywords: Peroperative preparation, preoperative evaluation, substernal goiter, surgical indications

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Surgery is one of the most appropriate treatment options for many patients with substernal goiter (SG). However, surgery for SG has some specific technical difficulties and higher complication risk compared to cervical thyroid surgery. Therefore, it should be performed by experienced and high-volume endocrine surgeons and in centers with extensive team and technical equipment to get the most optimal result.[1]

Pre-operative clinical and radiological assessment and definitions in SG were evaluated in detail in our previous study.[2]

In these patients, detailed pre-operative evaluation, pre-operative risk assessment, surgical anatomy, anesthesia, appropriate surgical planning, and prediction of surgical width are as important as surgical technique. In this study, we aimed to evaluate these preoperative and peroperative preparations in detail.

Indications for Surgery in SG

Surgery is the most effective and gold standart treatment for SG patients. The presence of symptoms is the main factor in determining the need for surgery.

In the literature, there has been consensus on the indication for surgery in symptomatic patients due to compression of the enlarged SG on adjacent organs, patients with hyperthyroidism, patients with suspected or diagnosed malignancy, and cosmetic reasons. However, there is an increase in asymptomatic SG patients detected incidentally

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due to the increase in neck and thorax imaging.[1]

The treatment and untreated natural course of the SG mass in these asymptomatic patients are still not well described.[3]

Most authors advocate that SG alone is a surgical indication, even if it is asymptomatic.[4,5]

On the other hand, there are some studies in the literature suggesting that there is no need for surgery for SG and that medical follow-up may be sufficient in asymptomatic patients.[6]

Patients with asymptomatic SG that can be followed;

- Patients who do not want surgery,
- Patients with normal flow volume curve and goiter at or above the level of the brachiocephalic vein
- High-risk patients who cannot tolerate general anesthesia for surgery.[7,8]

Arguments of studies advocating surgery in asymptomatic SG patients;

- In patients with SG, it is difficult to follow the mediastinal component with physical examination and follow-up with fine needle aspiration biopsy,[9]
- Although SG is strongly associated with tracheal compression or deviation, approximately 40% of patients with multinodular goiter with airway obstruction may be clinically asymptomatic,[10]
- Since the thyroid size will increase more when obstructive symptoms develop, surgical resection may become more difficult than in the asymptomatic period,
- Other suppressive therapies have low efficacy and are associated with significant morbidity, particularly in elderly patients,
- Patients are more prone to surgical complications that may be required at a later age than surgery to be performed at the time of first diagnosis,
- Theoretically, sudden bleeding into the substernal nodule can cause acute airway obstruction,
- Most SGs can be removed by the cervical route safely and with low complication rates.[8,11]

In addition to these studies in the literature, we believe that the treatment should be individualized in patients with SG and that surgery would be appropriate even if they are asymptomatic as long as there are no contraindications for surgery (Table 1).

Table 1. Indications for surgery in substernal goiter

Patients with obstructive symptoms
Symptoms related to the respiratory system
Symptoms related to the gastrointestinal system
Symptoms related to vascular obstruction
Symptoms related to pressure on neural structures
Patients with hyperthyroidism
Patients with suspected or proven malignancy
Patients with cosmetic requests
Asymptomatic patients
All patients without contraindication for surgery
Patients who can tolerate general anesthesia and surgery

Preoperative Evaluation and Investigation

Pre-operative evaluation of the patient should be multidisciplinary and detailed. Surgical team and other relevant clinics should be in communication for optimal surgery and minimizing complications.

Radiological Evaluation

Although ultrasonography is the primary imaging modality in the evaluation of multinodular goiter, cross-sectional imaging methods such as computed tomography (CT) and/or magnetic resonance imaging (MRI) are the basic imaging methods in determining the most appropriate surgical approach in SG. These imaging methods could also contribute significantly to the determination of the strategy for anesthesia and intubation.[3]

In most of studies, CT is defined as the gold standard method in the preoperative evaluation of patients with SG and is used more frequently.[2,12]

Pregnant women or patients with contraindication to CT and allergic to iodinated contrast material; MRI can be used instead of CT. Although MRI provides better information about soft tissue compared to the CT; respiratory motion artifacts, high cost and inability of claustrophobic patients to enter to non-open MR devices can be counted as disadvantages.

Important points can be identified and evaluated in cross-sectional imaging;

- Bilateral or unilateral substernal extension: If the SG is involved in one lobe and the other lobe is normal, it is appropriate to plan hemithyroidectomy, and if it is bilateral, total thyroidectomy should be planned.
    - It is important to distinguish between deviation and compression of the trachea due to thyroid compression. Deviation is more common in unilateral growth and has less clinical significance. Compression is more common in bilateral enlargements.[3]
- Determination of the cervical and mediastinal borders of the goiter: The extension, localization and borders of the SG should be clearly defined. The continuity of the cervical part and the mediastinal part should be evaluated. It should be defined whether SG is secondary (types I, II), primary (type III), mixed (both primary and secondary)

SG. In addition, the mediastinal portion of the secondary SG may be connected to the cervical thyroid with minimal fibrotic tissue. Especially in this situation, extrathyroidal approaches could be necessary since the mediastinal parts of the primary type and mixed types cannot be removed by the cervical incision.[2,13]

- However, sternotomy may be required in the presence of mediastinal ectopic nodules, especially in recurrent goiters.[14,15]

- Anterior or posterior substernal extension (Fig. 1): In patients with posterior mediastinal extension, it is more difficult to perform dissection from the cervical incision and to reveal the anatomy.[11]
  - For this reason, the possibility of an extrathyroidal approach may be higher in posterior mediastinal type II SG.[15]
  - In addition, the risk of extracervical intervention is higher in posteriorly located (Type II) SGs, especially in type IIB with contralateral extension.[2,5]]
  - Rarely, the SG may sit on the brachiocephalic vessels and causing potential distortion of the RLN, also extend both anteriorly and posteriorly (Fig. 1). In this type of SG, the possibility of extracervical approach need is high since direct view of anatomical structures may not be achieved with cervical dissection.[11]
  - In posterior mediastinal goiters, the recurrent laryngeal nerve trajectory may be in an anterior position and the risk of injury is higher in these cases.[5,11]

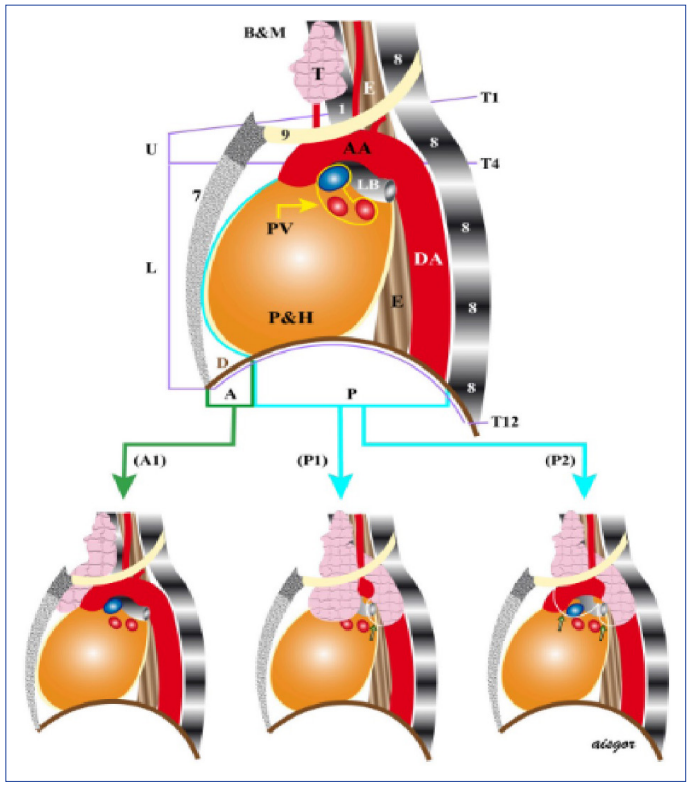

Figure 1. Substernal goiter. Lateral view of mediastinal regions and borders **(a)** Anterior mediastinum, P: posterior mediastinum, A1: Anterior Mediastinal Substernal Goiter, P1: Anterior and posterior mediastinal substernal goiter, and P2: Posterior mediastinal substernal goiter).

- Relationship of SG with surrounding organs: The mass effect of SG, its relationship with the aortic arch, vena cava and other main vascular structures, trachea, esophagus, main bronchi, lungs and pericardium; displacement of these structures and the direction of displacement should be evaluated. Evaluation of potential difficulties before surgery and solutions could be planned by evaluating the relationship of SG with these structures.
  - Respiratory distress may not develop until the diameter of the tracheal lumen has narrowed to 4 mm. For this reason, the presence of tortiosity or narrowing of the trachea, its localization, and the diameter of the trachea should be evaluated in cross-sectional imaging. This especially contributes to the planning of anesthesia, too.[3]
  - The level of the SG mass descends and its relationship with the organs in this region may contribute to predicting the possibility of extra cervical approach. In some studies, it has been reported that the possibility of need for an extracervical approach increases in SGs descending to the level of aortic arch and its inferior.[16]
  - Riffat et al. suggested that the extension of the mediastinal part of SG to the carina level should be used instead of the aortic arch to determine the possibility of the need for an extracervical approach in SG. According to this study, there are two reasons for this recommendation; first of all, it may be difficult to reach this area in dissection because the distance from the neck to the carina level and the sense of touch are not sufficient; second, due to intense adhesions in the esophagus and carina region, safe dissection cannot be performed in this region and an extracervical approach is recommended.[17,18]
  - Visual dissection is necessary not to open the pleura in SGs that come into contact with the pleura posterior to the trachea. Transcervically, sternotomy may be needed for safe dissection, as vision is limited in this region.[3]

- Internal composition of SG: Features of SG such as internal composition of the mediastinal part, presence of calcification, irregular border, or extrathyroidal spread

can be evaluated. Because of its high iodine content, it is fundamentally hyperdense (8–100 Hounsfield units) compared to the surrounding muscles in non-contrast CT.[19] This high attenuation may contribute to the differentiation of other mediastinal masses such as lymphoma, thymoma, which is not characteristic in these lesions.[20]

- Since the thyroid is hypervascular, contrast enhancement increases in the thyroid when contrast is given.[19]
- Calcifications may be seen in both malignant and benign lesions on CT. The presence of peripheral capsular calcification could be associated with difficulty in dissection from surrounding organs and should be taken into account when deciding on the extracervical approach.[11]
- In a retrospective study, intrathyroidal calcification was detected in 35% of preoperative CT, and thyroid cancer was detected in 48% of those with calcifications. The incidence of calcified nodules was significantly higher in thyroid cancer and lymph node metastasis. Calcification type in nodules with thyroid cancer was 79% multiple punctate calcification, 58% single point calcification, 21% coarse calcification, and 22% peripheral calcification.[21]
- Although the majority of SGs are benign, malignancy can occur up to 25%.[11]
- In CT, features such as irregular border, heterogeneous internal structure, presence of microcalcification, extrathyroidal spread, invasion of surrounding organs, and lymph node involvement, which may be associated with malignancy in the mediastinal part, could be evaluated. However, absence of these features could not exclude malignancy.[19]
- Although, pre-operative fine-needle aspiration biopsy (FNAB) is the most appropriate method for cervical lesions which are suspicious for malignancy in SGs, FNAB is not routinely performed due to difficulties in accessing the intrathoracic lesions and complications related to major vascular structures.
- Shape and size of the substernal part (Fig. 2a, b): Simo described three different shapes as oval, tubular, cone, or iceberg for SG (Fig. 3a-f).[22]
- The cone or iceberg shape of the SG is an important factor that increases the risk of extracervical intervention.[16,22]
- In particular, the fact that the thoracic component is wider than the thoracic inlet is associated with the risk of extracervical approach.[12]
- Flati et al. reported that sternotomy is inevitable when the SG is iceberg-shaped and more than 70% of the thyroid volume is below the thoracic inlet.[23]
- Apart from the shape of the thyroid, thyroid gland weight could also increase the risk of extracervical approach. Sancho et al. stated thyroid gland weight as an independent risk factor for sternotomy; and over 260 g thyroid gland weight has been determined significant predictive factor, statistically.[24]
- According to the study by Lee et al., pre-operative semiautomated 3D CT can reliably measure the thyroid volume as well as determine the shape, position, and extent of the SG.[25]

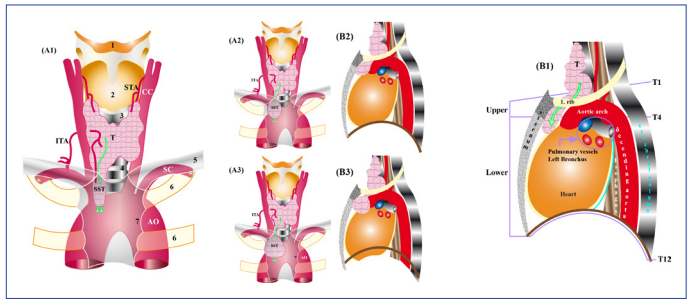

Figure 2. (a) Anteroposterior view of the three shapes of the intrathoracic part of the substernal goiter described by Simoi and Sanchez.[22] A1: Tubular shape, A2: Oval shape, A3: Cone or Iceberg shape, **(b)** Lateral view of the three shapes of the intrathoracic part of the anterior mediastinal located substernal goiter described by Simoi and Sanchez.[22] B1: Tubular shape, B2: Oval shape, B3: Cone or Iceberg shape.

Evaluation of the Need for an Extracervical Approach

Although pre-operative CT cannot detect all cases requiring extracervical intervention, it is still one of the best imaging methods to identify the factors that may increase the risk of extracervical approach and determine appropriate surgical intervention. These risk factors are discussed in detail under the heading of radiological evaluation above.[12,26]

According to prospective data in literature, although the majority of SGs can be removed by the cervical approach, an extracervical approach may be required in approximately 2% of patients to safely remove SGs by experienced endocrine surgeons.[4]

Whether the SG can be delivered through the thoracic inlet, the SG can be removed with minimal morbidity, and the ability to control unexpected bleeding in the mediastinum are the main factors to be considered in the selection of the surgical approach.[27]

Simo and Sanchez classified patients with SG into 3 main categories based on the experience of the surgical team and multiplanary CT data, according to clinical, surgical, and anatomical features. High-risk patients for the extra-

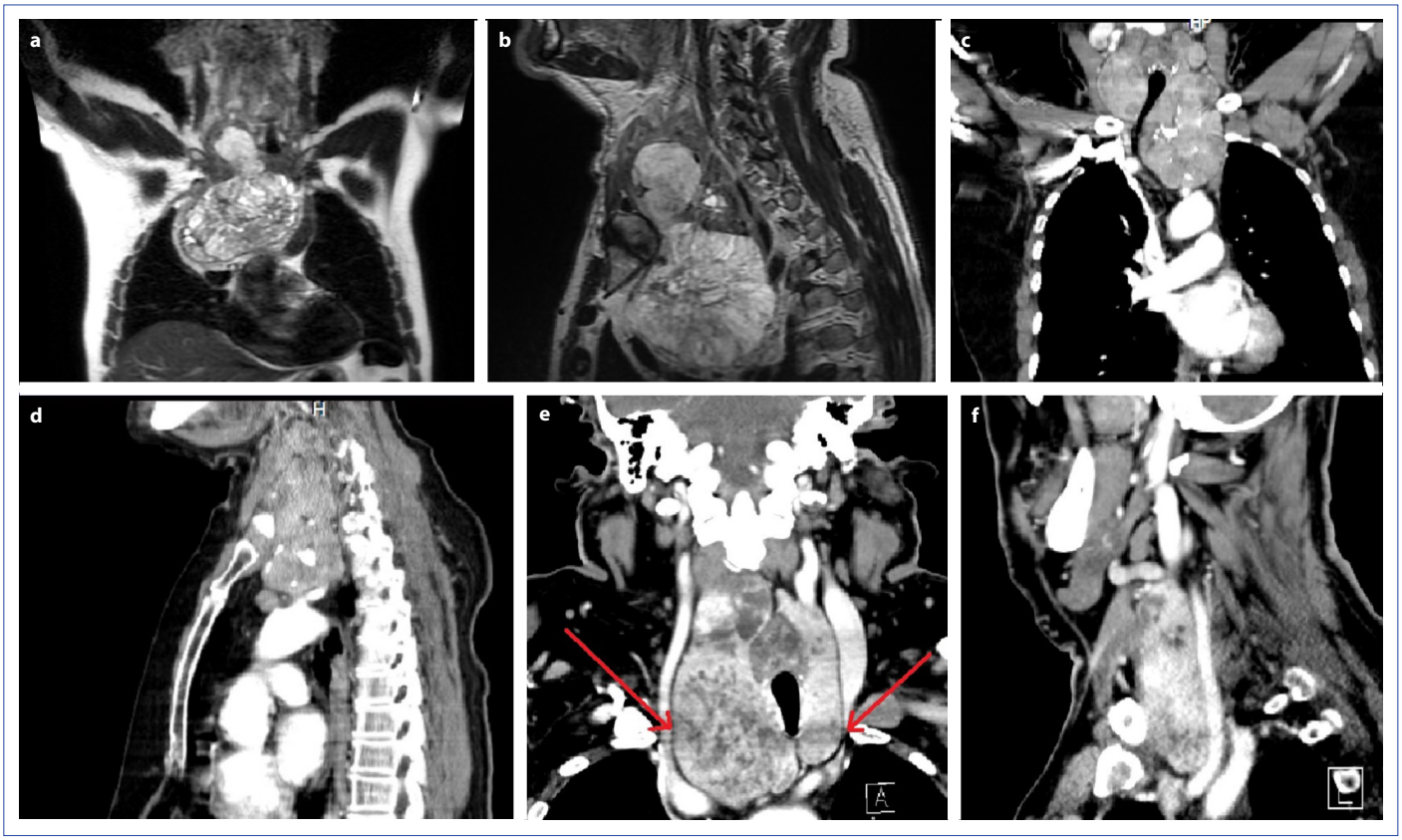

Figure 3. (a) Cone or iceberg shape of substernal goiter coronal magnetic resonance image, **(b)** Cone or iceberg shape of substernal goiter sagittal magnetic resonance image, **(c)** Oval shape of substernal goiter coronal computer tomography image, **(d)** Oval shape of substernal goiter sagittal computer tomography image, **(e)** Tubular and oval shape of substernal goiter coronal computer tomography image (The intrathoracic part marked with a red arrow on the left side of the substernal goiter is formed tubular, and the substernal part marked with a red arrow on the right is formed oval), **(f)** Tubular shape of substernal goiter sagittal computer tomography image.

cervical approach need has classified as; SGs below the aortic arch, with intrathoracic extension and recurrent goiter below the aortic arch, recurrent goiter not associated with the cervical thyroid, primary SG, SG with greater mediastinal extension, SG with multiple mediastinal compartment, goiter with separate components, iceberg or cone-shaped SG, patients with SG extending to the posterior pleura. Patients with intermediate risk for the extracervical approach need have classified as those with SG reaching the aortic arch, oval or tubular SG reaching the aortic arch, SG with minimal posterior mediastinal or retrotracheal extension, and patients with low risk were those with retroclavicular extension SG.[22]

In addition, it should be kept in mind that extrathyroidal approach may also be necessary; in the presence of potential fibrosis or scar tissue in the thorax due to the previous neck or chest intervention or radiation therapy, when the intrathoracic component is wider than the thoracic inlet, when there is no clear plan around the goiter, when extrathyroidal extension or invasion is suspected, and when the intrathoracic thyroid cancer.[1,27]]

Since many SGs with high risk features can be removed by cervical method, except in cases such as primary SG which can only be removed by mediastinal intervention, these operations should be started with cervical intervention. The classifications proposed by this and other authors for the determining surgical approach to SG are not absolute rules. An extracervical approach should be used if the SG cannot be safely removed by cervical incision.[27] Before these operations, patients should be informed that extracervical intervention may be required.

Preoperative Laboratory Evaluation

Like all goiter patients, thyroid function should be evaluated in SG, and hypothyroidism and hyperthyroidism should be excluded.[2]

Before elective surgery, hyperthyroid and hypothyroid patients should be treated and rendered euthyroid.

In patients with subclinical hyperthyroidism, iodinated contrast material given to the patient in contrast-enhanced CT may cause iatrogenic overt hyperthyroidism. Therefore, exposure to iatrogenic iodine in these patients, especially

in elderly patients, should be avoided.[5]

If autoimmune thyroid disease is suspected, TSH receptor antibody and thyroid peroxidase should be checked. In particular, chronic thyroiditis may be an additional factor complicating thyroid surgery when removing the SG from the neck. Calcitonin measurement should be performed when medullary cancer is suspected.[1]

Vocal Cord Examination

Pre-operative vocal cord examination should be performed in patients with SG. SG patients with preoperative vocal cord paralysis (VCP) should be carefully evaluated for malignancy. Although pre-operative VCP is generally thought to be associated with locally invasive thyroid malignancy, 2–3% of patients with benign nodular goiter or SG who have not had prior neck surgery may be seen VCP. Up to 50% of patients may be asymptomatic, as VCP develops gradually due to the compression effect of the large mass on the recurrent laryngeal nerve and is compensated by the laryngeal muscles.[28]

Although there are no clinical findings, the diagnosis of VCP could be made accurately with the examination of CT sections by the experienced radiologist according to the key findings at the level of the true vocal cord and aryepglottic fold.[29]

Knowledge of vocal cord function before surgery may affect the extent of surgery. Documentation of pre-operative vocal cord function could be used as evidence in post-operative iatrogenic VCP accusations. The American Society for Head and Neck Surgery recommends pre-operative vocal cord examination in all patients at high risk for nerve injury.[30]

Since SG surgery is a high-risk thyroidectomy, it should be performed under the guidance of intraoperative nerve monitoring (IONM). Pre-operative vocal cord examination is among the standards of IONM for optimal application of IONM.[31]

Surgery for SG

Position of the Patient

For the best exposure during the SG surgery, a transverse pillow should be placed under the shoulder in the supine position and the neck is positioned in maximal passive extension. To reduce venous compression in the neck, the patient should be placed in a semi-sitting position and both arms should be closed on both sides of the patient. This position has been defined as the beach chair position. Extending the arms 90 degrees laterally may increase venous pressure by narrowing the thoracic inlet compared to lateral closure. Depending on the possibility of extrathyroidal approach to the patient and the type of extracervical intervention; the neck and thorax should be wiped and sterilized with antiseptic solution.[32,33]

Intubation

Preoperatively, the otorhinolaryngologist (ENT specialist) should be asked to evaluate the current condition of upper air-way such as larynx appearance and deviation, together with vocal cord examination.

The radiological and endoscopic findings of patients with large cervical goiter and/or SG should be discussed with the anesthesiologist and surgeon, and if necessary, with the ENT specialist and radiologist who performs the endoscopic examination of the larynx for airway and intubation plan. Intubation of these patients should be performed by an experienced anesthesiologist. The majority of these patients can be intubated transorally without significant difficulty. Apart from the effects of SG, classical patient-related factors such as Body mass index and Mallampati score associated with difficult intubation should also be considered.[34]

In SG patients, the larynx may be deviated, although there is usually no compression. There may be deviation or rarely compression in the trachea. Laryngeal deviation usually does not cause difficulty in intubation.[1,3,5]

Even if there is severe narrowing and compression in the trachea, the patient can be intubated without difficulty with a tube that 1–2 size smaller than the standard tube, and the distal of the tracheal compression can be easily passed with an endotracheal tube that contains guide stylet.[35]

If the patient is to be intubated with an endotracheal tube with electrodes for nerve monitoring, it should be kept in mind that the outer diameter of these tubes is thicker than normal intubation tubes. It should also be known that for optimal monitoring, the thickest tube for intubation should be selected. Considering both conditions in intubation, a suitable tube that can pass tracheal compression should be selected. In these patients who will undergo IONM, low-dose muscle relaxants should be administered at induction and then muscle relaxants should not be administered. Since inhaler anesthetics and narcotic analgesics do not affect EMG findings in IONM, depth of anesthesia should be maintained with inhalers and IV anesthetic drugs to prevent spontaneous vocal cord activity.[31]

However, large goiters growing toward the upper pole may cause notching of the supraglottic hypopharynx by compression, which may lead to difficult intubation.[1,3,5]

Intubation should perform under optimal general anesthe-

sia atraumatically, and in fact, awake fiberoptic intubation is not usually necessary, with the potential risk of multilevel trauma to the larynx.[3]

A rigid bronchoscope, fiberoptic intubation equipment, video laryngoscopes, and laryngeal mask equipment should be available to manage any difficulty in intubation or airway management. Fiberoptic intubation may be needed through a laryngeal mask.[1]

Awake fiberoptic intubation is rarely a necessary option, especially if there is doubt about airway maintenance with sedating mask anesthesia.[35]

This may occur especially in goiters that have grown superiorly and cause compression in the hypopharynx, and in obesity.[1,5]

In severe tracheal compression causing stridor, fiberoptic intubation does not facilitate passage of the endotracheal tube into the trachea. In this situation, the patient's being awake during fiberoptic intubation may help.[1]

In this technique, the patient is usually awake in an upright sitting position to protect his/her own airway. A wake fiberoptic intubation can be performed nasally or orally by adequately anesthetizing the upper airway with topical lidocaine. In this situation a team that can perform rigid bronchoscopy or a surgical team for performing tracheostomy should be presented.[1]

However, it should be kept in mind that emergency tracheostomy may be difficult due to the position of the SG. A double-lumen endotracheal tube suitable for selective pulmonary ventilation may be required in patients with the possibility of extensive mediastinal dissection.[11]

Long-term and significant laryngeal edema may develop if multiple traumatic intubations is attempted, especially in large bilaterally encircling cervical goiters or SGs.[35]

Prolonged edema is probably due to the reduction of chronic venous and lymphatic drainage due to the compression of the larynx by large goiter, which represents the distal part of the airway in the hypopharynx.[5]

This edema may last for a long time postoperatively, and the patient may even require a tracheostomy until the edema resolves.[35]

Results

Surgery is the main treatment in SG. In these patients, surgical methods benefits for patient is high due to it eliminates the compression symptoms and excludes the possibility of malignancy. Although SG surgery is considered as high-risk thyroidectomy, most of the SGs can be resected by the cervical approach by experienced surgeons with low risk and excellent results and an extracervical approach may be required in a small proportion of patients. Detailed preoperative evaluations of the SG may predict the high risk of the extracervical approach and surgery can be performed with minimal morbidity in these patients with the necessary consultations such as thoracic surgery and a careful, appropriate, and planned surgical technique.

Detailed evaluation of the cervical approach, extra-cervical approach methods, and complications of SG will be discussed in our next studies.

Disclosures

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