Minimally invasive surgical techniques in the management of differentiated thyroid cancer

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Abstract

Thyroid cancer is the fifth most common cancer in women with approximately 60,220 expected new cases in the United States in 2013, and the incidence continues to increase each year. Fortunately, the majority are well-differentiated thyroid cancers with excellent overall prognosis. Controversy persists regarding the optimal surgical management of differentiated thyroid cancer in terms of the extent of thyroid resection (thyroid lobectomy vs total thyroidectomy) and the utility of prophylactic central neck dissection (pCND) in low-risk PTC, and papillary thyroid microcarcinoma (PTMC, defined as <10 mm). Thyroid surgical approaches have progressed from the Kocher open incision to minimally invasive techniques that include endoscopic and robotic thyroidectomy. Overall, these minimally invasive techniques have been shown to be safe, and appear to be associated with improved cosmesis and decreased pain compared to open thyroidectomy.

Keywords

Minimally Invasive Thyroidectomy; Robotic Thyroidectomy; Endoscopic Thyroidectomy; Well-differentiated thyroid cancer

INTRODUCTION

The majority of thyroid carcinoma (99.3%) is categorized as well-differentiated thyroid cancer (DTC) which encompasses papillary thyroid carcinoma (PTC, 86.6%), follicular thyroid carcinoma (FTC, 6.2%), and Hurthle cell carcinoma (2.8%). According to Surveillance, Epidemiology and End Results (SEER) findings, thyroid cancer incidence increased 7% per year between 1997 and 2009 [1] with the greatest increase noted in the diagnosis of localized disease, which increased from 5.2 to 9.6 cases per 100,000 people in the United States. [2] Improvements in diagnostic imaging are thought to be the cause of this upward trend in thyroid cancer incidence, given that most of the new diagnoses during that period were observed in lesions less than 2.0 cm. [3]
Surgical therapy for PTC and FTC are similar due to their favorable prognosis (5-year survival rate of 98.3%), and similar response to radioactive iodine therapy. However, controversy persists regarding optimal surgical management of DTC. In particular, the extent of thyroid resection (thyroid lobectomy vs. total thyroidectomy) and the use of prophylactic central neck dissection (pCND) in low-risk PTC, and papillary thyroid microcarcinoma (PTMC, defined as <10 mm) are in question. In order to evaluate if the extent of surgical resection affected PTC outcome and if a size threshold existed that would warrant total thyroidectomy, Bilimoria et al. performed a retrospective analysis of 52,000 PTC patients found in the National Cancer Data Base (1985-1998). [4] They concluded that for PTC greater than 1 cm, total thyroidectomy decreased risk of recurrence and death when compared with those patients who underwent lobectomy. The data regarding patients with PTMC showed no impact on recurrence or survival. [4]

Barney and colleagues conducted a retrospective review of 23,000 patients with PTC/FTC, identified in the SEER database between 1983 and 2002.[5] The multivariate analysis, taking into account factors such as age, sex, T classification, and the size of primary tumor, suggested that the ten-year overall survival and case-specific survival for total thyroidectomy (90.4% and 96.8%) and lobectomy (90.8% and 98.6%) were statistically equivalent (p = 0.431 and p = 0.176) [5] Despite these and similar findings, controversy remains due to contradictory results from other studies which show tumor size to have no effect on the incidence of contralateral disease. [6, 7] Additionally, the clinical significance of contralateral disease is unclear. [8-10]

The American Thyroid Association’s (ATA) November 2009 evidence-based guidelines for the medical and surgical treatment of thyroid cancer has been adopted and implemented by multiple surgical and non-surgical endocrine professionals and associations. [11] The most recent 2009 ATA guidelines recommend near-total or total thyroidectomy for patients with PTC greater than 1 cm and suggests thyroid lobectomy alone for PTMC “may be sufficient” in the appropriate clinical context. [11] However, definitive surgical treatment recommendations for patients with PTMC remain controversial due to PTMC’s overall excellent prognosis. Xiao et al. performed a retrospective cohort study of 18,445 PTMC patients identified in the SEER database in an attempt to identify risk factors that would warrant aggressive surgical management. They concluded that PTMC patients with 2 or more risk factors (age > 45 years, male sex, African American or minority race, node metastases, extrathyroidal invasion, and distant metastases) benefited from total thyroidectomy due to their significantly worse OS compared to patients with fewer risk factors (15-year survival rate, 83% vs. 93.4%, p < 0.01). [10]

Therapeutic central neck dissection (CND) for clinically or radiographically evident nodal metastasis in DTC patients is appropriate surgical treatment aimed at decreasing disease burden, potentially reducing the risk of regional recurrence and improving survival. [11] The decision to perform prophylactic central neck dissection (pCND), as part of DTC surgical management, remains controversial. [12, 13] ATA recommendations regarding pCND need to be weighed against available surgical expertise given the potential for more harm than benefit in less experienced surgical hands. Regardless, the ATA’s general recommendations differ based on T-classification. For patients with T3, T4 cancer without clinically involved
nodes, the ATA guidelines recommend pCND but do not recommend pCND for T1, T2 disease. [11]

Study data regarding which patients with PTC and clinically node-negative disease would benefit from pCND is conflicting. Many clinically node-negative PTC patients who undergo pCND have positive lymph nodes [14-17], with postoperative reduction of their thyroglobulin levels [18-21] which would suggest pCND is beneficial. However, in a recently published meta-analysis comparing 1264 patients (Group A: 396 patients, thyroidectomy + pCND; Group B: 868 patients, thyroidectomy alone), pCND did not result in a statistically significant decrease in local recurrence in thyroid cancer. [22] Despite the increased postoperative morbidity associated with pCND, such as recurrent laryngeal nerve injury, incidental parathyroid injury and transient hypoparathyroidism, [14, 19] pCND provides information regarding nodal involvement which was shown by Podnos et al. to have a statistically significant, negative impact on outcome. [23] Further study is needed before a consensus regarding pCND in clinically node-negative PTC patients will be possible.

HISTORICAL CONTEXT

Early Chinese writings mentioned goiter as early as 2700 BC. Medical management unwittingly used iodine-heavy substances such as seaweed and sea sponge. For centuries, surgical management was indicated and performed emergently for impending death from suffocation or in cases of suppurative glands. Operations performed as early as the 12th and 13th centuries included the use of setons, hot irons, caustic powders and surgeons’ fingers for dissection and fingernails for tissue removal with resultant high morbidity and mortality due to massive hemorrhage, asphyxiation, infection and gangrene. [24] Surgical management benefited greatly from Lister’s antisepic technique, the development of anesthesia, and the invention of better surgical instrumentation such as artery forceps. [24] The adoption and implementation of these advances between 1873 and 1883 by Emil Kocher (the only surgeon to win the Nobel Prize in Physiology for his groundbreaking work on thyroid), Theodor Billroth, and William Halsted paved the way for thyroid surgery to evolve from a rudimentary, horrifying procedure with extremely high morbidity and mortality to its current, minimal blood loss, routine form.

In the following sections, we discuss minimally invasive surgical methods such as endoscopic and robotic thyroidectomy, and how these procedures compare to each other and to conventional open thyroidectomy. Minimally invasive thyroid surgery continues to advance the limits of thyroid surgery made possible by Kocher, Billroth and Halsted. The Kocher incision (8 to 10 cm) has been gradually replaced by smaller, open incisions (3 to 6 cm) which vary depending on the surgical procedure performed. [25] Despite evolution, for this review, we define minimally invasive thyroidectomy to include endoscopic and robotic surgical approaches.

Advances in endoscopic surgery and its use in thyroid surgery have resulted in improved cosmesis, reduced incision length, faster recovery, reduced pain, and earlier hospital discharge. A variety of endoscopic thyroid surgery procedures are currently practiced; a
sample of these different techniques and the current literature about these various approach are discussed throughout this article.

ENDOSCOPIC THYROIDECTOMY

In 1996, Gagner’s report of an endoscopic subtotal parathyroidectomy ushered in the age of endoscopic endocrine surgery. In his correspondence, Gagner described his procedure in detail:

“Four 5-mm trocars were inserted under the platysma muscle, 1 cm above the clavicle and sternal notch. Carbon dioxide was insufflated to 15 mmHg to create a space above the strap muscles. Employing a 5-mm endoscopic scissor and dissector and a 5-mm 30-degree endoscope, the anterior and lateral borders of the trachea and thyroid were dissected.” [26]

Due to the prolonged operative time (5 hours) and the continuous insufflation, the patient developed hypercarbia and extreme subcutaneous emphysema (“present from his eyelids to the scrotum and anteriorly on the thorax and abdomen”) that did not resolve until post-operative day 3. Despite the lengthy operating time and post-operative complications, Gagner felt his endoscopic approach was “feasible, cosmetically appealing, leaves the neck musculature intact but could benefit from refinements in instrumentation.” [26]

Huscher et al. performed the first reported endoscopic thyroid surgery in 1997. [27] For their endoscopic right thyroid lobectomy they used an anterior cervical approach with 3-5 mm ports; a single port was placed at the jugular notch, a second port was placed at the angle of the mandible, and a third midway between the other two. CO$_2$ insufflation was used to develop the subplatysmal dissection plane and visualization was achieved using a 30-degree endoscope.

A variety of techniques for endoscopic removal of the thyroid have been developed and described since then. Developed in Pisa in 1999 by Miccoli et al., the most commonly reported minimally invasive thyroid surgical procedure is minimally invasive video-assisted thyroidectomy (MIVAT). [28] Ikeda and colleagues continued to push the minimally invasive surgery envelope, reporting a transaxillary approach in 2001 for unilateral thyroid lesions.[29] Although initially described for unilateral lesions, the transaxillary approach was subsequently adopted by some for unilateral and bilateral lesions and robotic as well as endoscopic thyroidectomy. Additional, and varied, extracervical approaches have been described, including an anterior chest approach,[30] a breast approach,[31, 32] and the axillobilateral breast approach (ABBA).[33, 34] Feasibility and limited clinical studies have also been described using a retroauricular approach,[35] a dorsal approach,[36] and a transoral, incisionless approach for both endoscopic [37, 38] and robotic thyroidectomy.[39] Having described the evolution and variety of minimally invasive thyroid surgeries, we will focus on the technical aspects of the most commonly used cervical and extracervical procedures in the following paragraphs.

The MIVAT approach, as originally described for thyroid lobectomy, begins with a 15 mm incision 2 cm superior to the sternal notch with subsequent careful dissection in the
subplatysmal plane. An approximately 3-4 cm incision is made in the linea alba. A 12 mm trocar is then introduced between the strap muscles and the thyroid lobe. Under direct visualization, using a 30-degree, 5 mm endoscope, CO\textsubscript{2} insufflation is applied to a pressure of 12 mm Hg for approximately 3 minutes to further develop the dissection plane between the thyroid and the strap muscles, which opens the thyrotracheal groove. Once this is accomplished, insufflation is allowed to fully egress. Needlescopic 2-mm forceps and aspirator are then introduced under direct visualization through a small supraclavicular incision and 2 mm scissors, or a spatula, are introduced through the main incision. Dissection of the thyroid lobe is then carried out laterally to medially, carefully identifying the parathyroid glands and recurrent laryngeal nerve (RLN).

Hemostasis is maintained by using bipolar cautery on smaller vessels located at a distance from the RLN, and clips are used on larger vessels and those near the RLN. Once the thyroid is mobilized from these important structures, the dissection is carried out in standard fashion, removing the gland from the trachea. To complete a lobectomy, the isthmus is then dissected and divided from the contralateral lobe by running absorbable sutures. The specimen is then removed from the main incision, hemostasis is confirmed, and the linea alba and platysma are closed with absorbable sutures. Drains are not routinely used.\textsuperscript{40}

Original indications for MIVAT included benign thyroid nodules (diameter less than 35 mm), cytologically malignant nodules (smaller than 20 mm), and an ultrasonographically estimated thyroid volume less than 25 cm\textsuperscript{3}.\textsuperscript{41} The presence of severe thyroiditis, or preoperative suspicion of metastasis to the lateral or central neck lymph nodes were considered to be contraindications. Minuto et al. recently reviewed all MIVAT procedures done at their institution in order to assess the continued utility of the original indications and contraindications for MIVAT, hoping to expand the original MIVAT indications. In a series of 1946 patients (511 thyroid lobectomies, 1435 total thyroidectomies) they found that up to 30% of patients with PTC had thyroiditis on final pathologic examination and only 1 case was converted to open because of thyroiditis. This analysis led them to recommend that thyroiditis should be re-classified as an indication for MIVAT. In addition, these investigators found that the mean number of nodes removed in patients with suspected central neck metastases was similar to the number removed in open operations in their hands.\textsuperscript{41, 42}

Transaxillary endoscopic thyroidectomy was originally developed by Ikeda et al. in 2001 to provide a safe operative approach for patients concerned with the cosmesis of a neck incision of any size.\textsuperscript{29} The patient is placed in the supine position with neck slightly extended. The arm ipsilateral to the thyroid nodule is extended in order to completely expose the axilla. Generally, a 1.5-cm to 3-cm incision is made in the axilla and the platysma is exposed through the upper portion of the pectoralis major muscle or via tunneling subcutaneously. Conventional 12-mm and 5-mm trocars are placed in the axillary incision, the trocars are then purse-stringed in place, and a low insufflation pressure (3–6 mm Hg) is applied for a few minutes. After adequate insufflation is achieved, 1 to 2 additional ports are placed in the axilla to allow access for dissection instruments. The thyroid is exposed following dissection of the sternocleidomastoid from the strap muscles (sternohyoid and sternothyroid). Thyroid dissection then proceeds as previously described, with careful...
identification of the RLN and the superior and inferior parathyroid glands. Once the thyroid has been sufficiently mobilized and the key structures identified, the thyroid is dissected off the trachea. Transection of the isthmus using the harmonic scalpel completes the thyroid lobectomy. The lobectomy specimen is extracted via the main axillary incision, and a closed suction drain is left in the subplatysmal space. The skin is closed in standard fashion [29].

Extracervical, minimally invasive thyroid surgery procedures that use breast incisions, modifications of the transaxillary approach, [33, 34] ABBA typically use bilateral, superior areolar incisions. In the ABBA approach, the endoscope is usually inserted via one of the areolar incisions while the majority of the dissection takes places using instruments introduced through the axillary incision(s).

COMPARING OPEN AND ENDOSCOPIC THYROIDECTOMY

A 2011 meta-analysis by Radford et al. sought to evaluate all prospective controlled trials (5 total met inclusion criteria, 318 patients total) comparing MIVAT to conventional thyroidectomy. Focusing on primary outcome measures (pain, postoperative hypocalcemia, postoperative RLN injury) and secondary outcome measures (operative time, blood loss, cosmesis) they showed that MIVAT was as safe as open thyroidectomy with better cosmesis, no differences in postoperative hypocalcemia, blood loss or RLN injury, [43] and decreased pain. [44-48] In addition, a 2010 cost-effectiveness study and chart review by Byrd et al. compared the cost of MIVAT with conventional thyroidectomy. They concluded that MIVAT-associated costs were similar to those of the open procedure for hemi-thyroidectomy and total thyroidectomy. [49] Further evaluation of MIVAT and conventional thyroidectomy via an adequately powered randomized controlled trial is warranted to establish noninferiority for postsurgical morbidity and oncologic outcomes.

Transaxillary and ABBA approaches are more commonly used internationally. As a result, the majority of the reports comparing the transaxillary and ABBA approaches with conventional thyroidectomy are primarily from international groups. Shortly after describing their novel, transaxillary approach, Ikeda et al. published a study of their initial operative results comparing the transaxillary approach to conventional open thyroidectomy with a focus on operative time, post-operative pain, and cosmesis. Of the 102 patients compared, 19 cases underwent successful transaxillary thyroidectomy with only two conversions to open (one for bleeding and another due to the presence of a thymic parathyroid adenoma); no RLN injuries were noted, cosmesis was described as “excellent” and pain was minimal with the exception of a few reports of self-limited, appreciable chest discomfort in the subclavicular region of the anterior chest. For the transaxillary approach, the average operating time was initially 293 min (decreasing to 143 min with more experience) compared to approximately 90 minutes for the open procedure. This disparity between initial endoscopic operative time and open operative time led the surgeons to restrict their transaxillary procedures to lesions < 4 cm on pre-operative ultrasound. [29] In a subsequent study, Ikeda, et al once again compared total thyroidectomy via the transaxillary approach (20 open and 20 endoscopic) with similar findings, i.e., operative times were significantly longer in the endoscopic group and patients treated endoscopically had non-significant, self-limited pain in the anterior chest infra-clavicular region during the immediate post-operative period. The continued unique complaint by some endoscopic patients of anterior chest discomfort was
not surprising due to the operative technique and location of dissection. Despite any difference in initial pain, endoscopic patients were significantly more satisfied with cosmesis compared to open thyroidectomy patients. [50] Published results by other groups using both transaxillary and ABBA approaches were varied. However, increased operative times for endoscopic patients, similar or reduced pain scores in the immediate post-operative period, and improved subjective cosmesis 3 months after surgery in the endoscopic groups were consistent across all studies. [51-54] The postoperative complications reported in different studies varied from transient RLN palsy [53, 54], and transient hypocalcemia [53] to local recurrence of a follicular neoplasm in a port tract following transaxillary thyroidectomy. [55] Generally speaking, the transaxillary approach has a steep learning curve but is a safe procedure in experienced, surgical hands and has the wonderful benefit of excellent surgical cosmesis.

**ROBOTIC THYROIDECTOMY**

A seemingly, natural progression along the minimally invasive surgery continuum, robotic surgery provides advantages similar to endoscopic surgery (less pain, shorter hospitalizations, smaller incisions) while affording a variety of unique benefits (increased dexterity and tissue manipulation and dissection; tremor filtration; and three-dimensional magnification with improved visualization of the operative field). [56, 57] It was only a matter of time before this new technology was applied to thyroid surgery. In 2009, Kang et al. reported the first large series (n = 100) of robot-assisted endoscopic thyroid surgery via a gasless, transaxillary approach using four robotic arms (a 12 mm telescope and three 8 mm instruments) [57] for patients with benign thyroid disease and PTC. [58, 59] No serious post-operative complications were noted and patients were able to return home by the third post-operative day. Mirroring the creativity and variety seen in endoscopic thyroidectomies, robotic thyroidectomy approaches include a robotic bilateral axillary, bilateral areolar approach described in 2009 [60]; a single-incision transaxillary approach designed to alleviate some of the anterior chest symptoms experienced due to anterior chest access (2010) [56] and recently, an alternative, non-axillary approach using a retroauricular face-lift incision, which may avoid potential morbidities (brachial plexopathy, esophageal perforation and transection, and high-volume blood loss) [61] noted in one study of the transaxillary experience in North America. [62] Similar to endoscopic approaches, robotic thyroidectomy has an appreciable learning curve. In their original series, Kang et al. [59] reported a significant decrease in console operating time after 40 to 50 cases with a subsequent and unexplained gradual rise in operating time that remained below the operative time noted for the first ten cases. Studies by Lee et al. and Kandil et al further examined the learning curve, and operative time for robotic thyroid surgeries of a single surgeon with similar results of decrease operating time after approximately 45 surgeries. [63, 64] In addition to analyzing operating time, Kandil et al. examined the effect of body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) on operative time and found a significantly increased operative time in patients with BMI greater than 30 (137.1 vs 99.7 minutes), lending credence to the assertion that robotic transaxillary thyroidectomy may be less applicable to overweight and obese patients. [64]
COMPARING OPEN, ENDOSCOPIC AND ROBOTIC THYROIDECTOMY

A 2012 meta-analysis and systematic review by Jackson et al. compared robotic thyroidectomy to endoscopic and conventional thyroidectomy with a focus on the following outcomes: operative time, hospital stay, post-operative complications and cosmetic satisfaction. Nine articles were included in this meta-analysis: 4 open thyroidectomy vs. robotic thyroidectomy, 4 endoscopic thyroidectomy vs robotic thyroidectomy and 1 open thyroidectomy vs endoscopic thyroidectomy vs robotic thyroidectomy. Regarding operative time, robotic thyroidectomy was significantly longer than open thyroidectomy by 42 minutes on average without a significant difference when compared to endoscopic surgery. In terms of hospital stay, when compared to robotic thyroidectomy and endoscopic thyroidectomy, open thyroidectomy length of stay was “significantly increased” but no difference was found between robotic thyroidectomy and endoscopic thyroidectomy. Post-operative complications were similar between the three groups. Of note, the robotic thyroidectomy group had a higher risk of transient hypocalcemia. In terms of post-operative pain, all 4 studies compared robotic thyroidectomy vs open thyroidectomy and the results were less straight forward due to the varied measurement methods used in the individual studies. Overall, robotic thyroidectomy patients had increased anterior chest pain and paresthesia of varying duration and open thyroidectomy patients had increased neck paresthesia and hyperesthesia which are not surprising based on the surgical approaches. Cosmetic satisfaction was significantly higher in the robotic thyroidectomy group compared to the open thyroidectomy group. All of which support the widely held belief that robotic thyroidectomy is a safe alternative to endoscopic and open thyroidectomy. [65]

COMPARING OPEN AND ROBOTIC THYROIDECTOMY

Foley and colleagues performed a retrospective review of a prospectively maintained database comparing robotic thyroidectomy patients and open thyroidectomy patients (n = 11 and 16, respectively). They found no significant difference in patient characteristics or complications, however, mean operating time (232 vs 109 min, p < 0.001) and incision length (6 vs. 3.6 cm, p < 0.001) were considerably worse in the robotic thyroidectomy group. Akin to studies by Kandil, Lee and Kang, a learning curve was present as evidenced by decreased operating time with increased operative experience. [66]

COMPARING ENDOSCOPIC AND ROBOTIC THYROIDECTOMY

Robotic thyroidectomy is certainly an innovative procedure with potential benefits and advantages compared to open thyroidectomy but questions remain regarding its utility compared to endoscopic thyroidectomy. A variety of studies have attempted to answer this question. We focus on three of them. In a 2011, prospective study at a single institution in South Korea, Yoo et al. report on the surgical outcomes of 165 endoscopic patients and 46 robotic patients who underwent total thyroidectomy or lobectomy. Robotic surgery took longer (179 min vs. 126 min, p < 0.001), had higher postoperative drainage, similar post-operative thyroglobulin levels and cost more ($6655 vs. $829, p < 0.001) compared to endoscopic surgery leading the study authors to conclude that robotic thyroidectomy was not superior to endoscopic thyroidectomy. In light of data from studies by Kandil and Lee [63,
highlighting the learning curve during the first 40-50 cases and the fact that Yoo and colleagues’ study contained only 46 robotic surgery cases, performed by a variety of surgeons, it is quite possible that lack of adequate surgical experience with robotic thyroidectomy confounded their results. In contrast, a single-institution, single surgeon study from Korea reported prolonged robotic operating time with otherwise comparable perioperative outcomes in the endoscopic (96 patients) and robotic (163 patients) surgical groups leading these study authors to conclude that robotic surgery was superior to endoscopic surgery. [63] In a larger study comparing 580 robotic thyroidectomy patients to 570 endoscopic thyroidectomy patients, S. Lee and colleagues,[67] found operative times and complication rates were similar, with the exception of transient hypocalcemia, which was more common among patients undergoing robotic thyroidectomy. Although not conclusive, these studies suggest that robotic thyroidectomy is a feasible and safe alternative to endoscopic surgery in experienced surgical hands.

SUMMARY AND FUTURE DIRECTIONS

Thyroid surgery has progressed dramatically since the high morbidity and mortality procedures performed prior to the adoption of Lister’s antiseptic technique and the invention and use of key surgical instruments by surgical greats such as Kocher, Halsted and Billroth. The open techniques pioneered by Kocher have given way in selected centers to minimally invasive and varied endoscopic and robotic techniques with improved cosmesis, decreased pain, and comparable or decreased morbidity and mortality. Despite these advances, surgeons must continue to question and evaluate the current indications and contraindications of currently available thyroidectomy techniques while continuing to push the limits of surgical possibility.

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REFERENCES


Otorinolaringologia. Author manuscript; available in PMC 2015 October 23.


Otorinolaringologia. Author manuscript; available in PMC 2015 October 23.


59. Kang SW, Lee SC, Lee SH, Lee KY, Jeong JJ, Lee YS, Nam KH, Chang HS, Chung WY, Park CS. Robotic thyroid surgery using a gasless, transaxillary approach and the da Vinci S system: the


