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Review Article

Measuring Quality in Thyroid Cancer Surgery

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Many of the surgical quality measures currently in use are not disease specific. For thyroid cancer, mortality and even recurrence are difficult to measure since mortality is rare and recurrence can take decades to occur. Therefore, there is a critical need for quality indicators in thyroid cancer surgery that are easily measured and disease specific. Here we will review recent research on two potential quality indicators in thyroid cancer surgery. The uptake percentage on postoperative radioactive iodine scans indicates the completeness of resection. Another measure, the lymph node ratio, is the proportion of metastatic nodes to the total number of nodes dissected. This serves as a more global measure of quality since it indicates not only the completeness of lymph node dissection but also the preoperative lymph node evaluation and decision-making. Together, these two quality measures offer a more accurate, disease-specific oncologic indicator of quality that can help guide quality assurance and improvement.

1. Introduction

Survival from differentiated thyroid cancer (DTC) remains excellent, with 5-year disease-specific survival exceeding 95%. However, the incidence of DTC continues to rise. Based on trends over the last 10 years, researchers at the American Cancer Society estimate that there will be nearly 63,000 new cases of thyroid cancer diagnosed in 2014 in the United States [1]. Thyroid cancer preferentially affects women and is now the 5th most common cancer among females [1]. Although mortality from thyroid cancer is relatively low, recurrence is more common. Large series report recurrence rates between 2 and 14% [2–5]. Therefore, recurrence becomes a more relevant outcome measure for patients with thyroid cancer.

Multiple factors influence recurrence including tumor histology, extent of disease at presentation, and the initial treatment. The mainstays of treatment include thyroidectomy and radioactive iodine (RAI) [6]. This review will focus on surgery. Specifically, we will discuss recent research that seeks to identify novel ways of measuring quality in thyroid cancer surgery.

2. Defining Quality

In order to discuss the optimal measures of surgical quality for thyroid cancer, we must first define healthcare quality. The Institute of Medicine defines quality as the degree to which health services improve desired health outcomes. In short, this means doing the right thing for the patient in a timely manner while minimizing complications [7]. Therefore, quality healthcare delivery involves achieving desirable outcomes in a safe and timely manner.

For thyroid cancer surgery, like all oncologic surgeries, mortality and recurrence remain valuable outcome measures. As mentioned above, recurrence is probably more reflective of surgical quality for most thyroid cancer patients since mortality rates remain quite low. This leaves recurrence, an outcome that is more common than mortality, but one that is harder to measure. Recurrence in thyroid cancer can occur years or even decades after the initial treatment, thereby adding to the difficulty in tracking this outcome.

Much of the quality literature related to thyroidectomy for benign and malignant disease revolves around complications. Complications specific to thyroid surgery include injury to the recurrent laryngeal nerves, causing hoarseness and dysphagia, and injury to the parathyroids causing hypocalcemia. Both complication types are considered permanent if they persist beyond six months postoperatively. Since thyroid cancer is unlikely to kill the patient, a permanent complication translates into lifelong, life-changing complications. In the case of permanent hypocalcemia, this means taking medications multiple times per day to stave off the symptoms and maintain normal serum calcium levels so that cardiac and nervous tissues function properly. Patients suffering permanent recurrent laryngeal nerve injury will have chronic problems with communication, swallowing, and aspiration often necessitating procedures like vocal cord injection and/or medialization. These complications, while specific to thyroidectomy, really do not reflect oncologic outcomes specific to thyroid cancer since they can occur regardless of the indication for thyroidectomy. They indicate nothing about the adequacy of resection and/or lymph node dissection for the amount of disease present at surgery.

Hence, the current literature lacks outcome measures specific to thyroid cancer surgery. The ideal quality indicator for thyroid cancer surgery would be readily available, specific to thyroid oncology, and easily measured. In the following sections, we discuss some novel approaches to measuring quality for thyroid cancer surgery. These new measures address some of the shortcomings seen with traditionally used outcome measures for thyroid cancer surgery.

3. Extent of Resection

Guidelines for treatment of differentiated thyroid cancer (DTC) recommend near-total or total thyroidectomy for patients with tumors greater than one centimeter in size or for patients with other high-risk features such as multifocality, metastases, history of radiation exposure, or family history of thyroid cancer [8]. These recommendations exist because complete resection of the entire gland resulted in improved survival and lower recurrence rates [2, 3, 9–11]. Although the appropriate extent of thyroidectomy continues to be debated for low risk tumors, removal of the entire gland facilitates adjuvant therapy with radioactive iodine ablation (RAI) and the ability to detect recurrence using thyroglobulin levels [12–15]. On the other hand, total thyroidectomy can result in potentially life-long complications including recurrent laryngeal nerve injury and hypoparathyroidism, since both recurrent laryngeal nerves and all four parathyroid glands are at risk during complete removal of the entire gland. Numerous patient, disease, and surgeon factors determine the magnitude of complication risk. For example, the risk of complication diminishes when a high-volume or experienced surgeon performs the thyroidectomy [16–21].

The importance of the extent of resection is underscored by its inclusion in some prognostic scoring systems. For example, in the MACIS prognostic scoring system, incomplete resection negatively impacts thyroid cancer-specific mortality [9]. A more recent and often cited study is that of Bilimoria et al. Using the National Cancer Database, these authors found that, for tumors ≥1 cm, total thyroidectomy resulted in lower recurrence rates and improved survival [2]. Extent of resection also affects recurrence. Hay et al. found that patients treated with lobectomy experienced significantly higher recurrence rates (14%) compared to patients treated with total thyroidectomy (2%) [22].

Studies analyzing the extent of thyroidectomy only compare lobectomy to total thyroidectomy. It is difficult to quantify the amount of tissue left behind, and the definitions of subtotal versus near-total versus total thyroidectomy are not exact [23, 24]. Often surgeons will leave some thyroid tissue near the upper parathyroid and the insertion of the recurrent laryngeal nerve to protect these structures, and this is termed "near-total thyroidectomy." In this scenario, the remnant is often ablated with radioactive iodine (RAI) [25]. Total thyroidectomy, on the other hand, eliminates the need to administer an ablative RAI dose to destroy the thyroid remnant, and any RAI that is given is more effective in destroying metastatic disease [23, 26]. Operations labeled as total thyroidectomy in administrative or cancer registries may really be a mixture of subtotal, near-total, and total thyroidectomies.

Most thyroid surgeons understand the wide variation in the extent of thyroid tissue left behind even for procedures labeled as "total thyroidectomy." This relates to each individual's practice habits, training, and comfort level with thyroid operations. Consensus guidelines recommend RAI for high-risk patients (tumors greater than 4 cm in size, gross extrathyroidal extension, or distant metastases). RAI is not recommended for the lowest risk patients (well-differentiated tumors <1 cm, confined to the thyroid gland, and without lymph node or distant metastases). Selective use is recommended for patients who do not fall into either the high or low risk categories [8].

When radioactive iodine is given a whole body scan is obtained three to seven days after administration of the radioisotope to evaluate the remnant uptake within the neck and to evaluate distant metastases [27–29]. The remnant uptake is the percentage of the total dose administered detected within the thyroid bed after adjusting for decay [30, 31]. This provides a quantitative assessment of how much thyroid tissue remains. Erbil and colleagues found that remnant thyroid volume assessed by ultrasound correlated with remnant uptake in benign diseases [32].

We evaluated the remnant uptake as an oncologic indicator since it reflects the volume of thyroid tissue left behind after surgery. The primary outcome was disease recurrence, and we also compared remnant uptake between high- and low-volume thyroid surgeons. In this retrospective review of 223 patients undergoing total thyroidectomy for DTC, we found that those who recurred had a tenfold higher remnant uptake compared to those who did not recur ($P = 0.001$). Similarly, we found that those with increasing postoperative thyroglobulin measurements ($P < 0.01$) or those requiring additional neck surgery ($P < 0.01$) also had higher remnant uptake compared to patients without these characteristics [33]. Thus, a higher remnant uptake was associated with recurrence, measured in a variety of different ways. In multivariate analysis, the remnant uptake independently predicted recurrence (OR 3.71, $P = 0.04$) when controlling for other factors associated with recurrence in thyroid cancer [33].

Since remnant uptake serves as a measure of the extent of resection, we also hypothesized that high-volume surgeons would perform a more complete resection compared to low-volume surgeons. Not only did high-volume surgeons have significantly lower uptakes ($P = 0.002$), but they also maintained a low level of permanent complications compared to low-volume surgeons, who in addition to having higher uptakes had a significantly higher rate of permanent complications. Achieving a lower uptake is not without consequences since there was a stepwise increase in permanent complications as the remnant uptake decreased [33]. To incorporate patient safety into this quality measure, the temporary and permanent complications should be considered alongside the remnant uptake.

In a related study, we evaluated the remnant uptake after completion thyroidectomy. When compared to total thyroidectomy, completion thyroidectomy had significantly higher remnant uptake ($P = 0.04$), but this greater remnant uptake was mitigated with the involvement of a high-volume surgeon during all or part of the surgical management [34]. Thus, an initial total thyroidectomy provides a more complete resection compared to a staged operation (i.e., lobectomy followed by completion thyroidectomy). Due to the limitations of FNA for distinguishing benign from malignant follicular lesions, completion thyroidectomy cannot always be avoided. In these cases, surgeon volume influences the completeness of resection.

The remnant uptake serves as a useful oncologic indicator after thyroidectomy for DTC since it correlated with the extent of resection and recurrence rates. Rather than waiting years or even decades for recurrence and mortality outcomes, the remnant uptake is more immediately available, measured at six to eight weeks postoperatively. Together with other clinical and pathologic data, the remnant uptake is another piece of information providers can use to determine a patient's risk for recurrence and schedule surveillance appropriately. Remnant uptake also indicates useful benchmarks for surgical quality. Since lower uptake was inversely proportional to surgeon volume, surgeons with less experience can use uptake as feedback regarding their performance while still on their learning curve. Alternatively, it may prompt lower volume surgeons to refer more difficult cancer cases or completion thyroidectomies to high-volume centers. Finally, the remnant uptake can be useful in evaluating newer surgical techniques such as transaxillary thyroidectomy for their oncologic quality. Again, this is a much more immediate measure rather than waiting years for recurrence. This will ensure that newer techniques are utilized appropriately without compromising oncologic quality.

An important limitation of using the remnant uptake is that not all patients require radioactive iodine, an adjuvant therapy reserved for higher risk tumors. As practice patterns shift toward more restrictive use of radioactive iodine, this quality measure will only apply to a subset of patients. However, the higher risk tumors probably require a more complete resection and are more likely to receive radioactive iodine. Perhaps this quality measure will remain useful in cases where evaluating the extent of resection matters most.

4. Lymph Node Ratio

The prognostic significance and appropriate treatment of metastatic lymph nodes for papillary thyroid cancer (PTC) continue to spark much debate. Lymph node metastases are relatively common, occurring in 20–50% of cases of PTC, but this rate depends on the level and intensity by which one searches for evidence of metastases in the nodes [35–37]. For example, up to 90% of patients will have micrometastatic disease [37, 38]. Lymph node metastases are associated with a 15–20% recurrence rate [39, 40]. Although their impact on recurrence is generally accepted, the significance of lymph node metastases on mortality remains debatable. Much of the older literature suggests that lymph node metastases do not influence survival, but more recent population-based data report a small but real negative impact on survival [4, 5, 41, 42]. Regardless of their impact on survival, disease in the lymph nodes does change management and can impact recurrence that has significant morbidity for patients since it often requires reoperation.

Numerous staging systems exist for DTC, but many of these do not even consider the status of cervical lymph nodes [43]. When lymph nodes are included, they are only considered in a binary sense (presence versus absence of metastases) based on anatomic location, but not on the extent of nodes involved [44–48]. In the commonly used AJCC staging system, patients with cervical lymph node metastases are labeled as either N1a (level VI) or N1b (levels I-V and VII), and a patient with two of 30 lymph nodes positive is grouped with a patient who has 30 of 30 lymph nodes positive [44].

Over the last 7 years, many have advocated routine, prophylactic central compartment (level VI) lymph node dissection for PTC [49–52], but the optimal approach to the central neck lymph nodes remains controversial, and practice patterns vary widely [53]. Amidst this debate and variations in care, we lack a means to understand and measure how the *extent* of lymph node metastases impacts oncologic outcomes. Just as there were no specific measures for the adequacy of resection, we also lack quality measures for the surgeon's evaluation of lymph node compartments and the performance of an oncologically sound lymph node dissection.

The lymph node ratio (LNR) is the number of metastatic lymph nodes divided by the total number of nodes harvested, and it has been used in several other cancers where lymph node dissection is performed [54, 55]. In some cancers like colorectal cancer, a minimum number of lymph nodes harvested have become a quality indicator. In studying both institutional and national datasets, a huge variability in nodal yield exists, especially in the central compartment. Instead of the absolute number of nodes, we studied how the lymph node ratio may be used to predict the likelihood of disease recurrence and mortality using both institutional and population-based datasets.

Again using the SEER database, we examined patients undergoing total thyroidectomy for PTC and lymph node dissection. Since SEER does not contain data on recurrence, disease-specific mortality (DSM) was the outcome of interest. By comparing Kaplan-Meier survival estimates, we found that a lymph node ratio ≥0.42 best divided those with lymph node metastasis based on disease-specific mortality ($P < 0.01$). Patients with a lymph node ratio ≥0.42 experienced a 77% higher DSM rate compared to those with metastatic lymph nodes as a whole. When combined with other known determinants of prognosis in a multivariate analysis, we found that lymph node ratio was strongly associated with DSM (HR 4.33, $P < 0.01$) [56].

Although this study emphasized the impact of lymph node ratio on mortality, the use of SEER to really evaluate lymph node dissection was somewhat problematic. First, it is difficult to discern the surgeon's intentions in a large, national dataset, since it cannot reliably distinguish formal lymph node dissection from incidentally removed lymph nodes or "berry-picking." The other issue is that the mortality differences were quite small, and recurrence is a more relevant outcome for PTC. Therefore, we performed a similar study from our large institutional dataset where we knew exactly which patients underwent lymph node dissection. The downside to using an institutional dataset was a much smaller number, with only 69 patients undergoing total thyroidectomy and concomitant neck dissection. Instead of disease-specific mortality, the outcome of interest was cytology- or pathology-proven disease recurrence. We found that patients with a total lymph node ratio ≥0.7 ($P < 0.01$) or a central compartment lymph node ratio ≥0.86 ($P = 0.04$) experienced significantly worse disease-free survival than patients with lymph node ratios below these thresholds. Considering other known predictors of recurrence, lymph node ratio was significantly associated with recurrence (OR 19.5, $P < 0.01$) on multivariate analysis [57].

An elevated lymph node ratio is associated with *both* recurrence and disease-specific mortality in DTC. The lymph node ratio therefore becomes a valuable tool for clinicians to risk/stratify patients for additional therapy like radioactive iodine or in deciding the appropriate follow-up and surveillance schedule. As a measure of surgical quality, the lymph node ratio indicates the "margin" of negative nodes the surgeon obtained. Multiple factors determine this margin including the extent of disease present. In addition, the thoroughness of pathologic examination also impacts LNR. A thorough search and accounting of all lymph nodes provides a true measure of the extent of dissection. Therefore, the LNR can also be seen as a system-level measure of quality.

Assuming that the pathologic examination is thorough, the lymph node ratio encompasses the surgeon's pre- and intraoperative assessment of the lymph node compartments along with the technical ability to perform an adequate compartment-oriented lymph node dissection. Hence, it is a quality measure that accounts for decision-making, imaging interpretation, and operative planning, in addition to technical skills. Of course, there will be some patients where the LNR represents the aggressive biology of disease despite optimal surgical care. For patients with poorly differentiated and aggressive forms of DTC, the LNR may simply reflect the biology of the disease, but, for low risk tumors, LNR can account for several phases of surgical care including the preoperative evaluation.

5. Conclusions

The ideal quality indicator for thyroid cancer surgery would be easily measured, immediately available after surgery, and specific to thyroid cancer. Recent research on the remnant uptake and lymph node ratio demonstrates that these measures directly relate to thyroid cancer recurrence, a relevant outcome measure for DTC. The remnant uptake is available within a few months after surgery and indicates the completeness of thyroid resection. The lymph node ratio can be calculated as soon as the final pathology is reported and indicates the adequacy of lymph node dissection.

These thyroid cancer-specific quality indicators can assist quality improvement efforts at both the individual and institution level. Surgeons with less experience can evaluate and track their own lymph node ratio or remnant uptake to improve their own practice. Alternatively, these measures can evaluate surgeons who perform thyroid surgery for cancer as part of a quality assurance program so that hospitals or cancer centers can assure that they are providing the best oncologic care for thyroid cancer. In the evolving pay for performance environment, surgeons need to identify disease- or organ-specific quality measures appropriate for their specialty. Providers who care for patients with thyroid cancer may face pressure to utilize generic outcome measures such as mortality or infectious complications. Such measures seldom apply to thyroid cancer patients. Even thyroidectomy specific complications such as hypocalcemia or hoarseness indicate very little about the oncologic aspects of the surgery or fail to risk/adjust the complications for the level of disease present. Both the LNR and remnant uptake must be considered along with these disease-specific complications in order to encompass the true definition of quality. Otherwise, these are simply outcome measures. Additionally, one must consider patient-centered outcomes such as quality of life when developing quality measures. This certainly plays an important role in DTC where mortality is quite low so survivorship and patient-reported quality of life remain lasting issues.

While the remnant uptake or the lymph node ratio each has drawbacks and requires further validation, the studies outlined here suggest that they are useful thyroid cancer surgery quality measures that provide specific information about recurrence, the completeness of resection, and the adequacy of lymph node dissection.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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