



Operative Management of Thyroid Disease in Older Adults

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ABSTRACT:

Background: As the population ages, both domestically and globally, clinicians will increasingly find themselves navigating treatment decisions for thyroid disease in older adults. When considering surgical treatment, individualizing risk assessment is particularly important, as older patients can present with very different health profiles. While fit, independent individuals may benefit from thyroidectomy with minimal risk, those with multiple comorbidities and poor functional status are at higher risk of perioperative complications, which can have adverse health effects and detract from long-term quality of life. In order to optimize surgical outcomes for older adults, strategies for accurate risk assessment and mitigation are being explored. Surgical decision-making also should consider the characteristics of the thyroid disease being treated, given many benign thyroid disorders and some well-differentiated thyroid cancers can be appropriately managed nonoperatively without compromising longevity. Shared decision-making becomes increasingly important to respect the health priorities and optimize outcomes for older adults with thyroid disease. This review summarizes the current knowledge of thyroid surgery in older adults to help inform decision-making among patients and their physicians.

Abbreviations: ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ATC, anaplastic thyroid cancer; DTC, differentiated thyroid cancer; GD, Graves' disease; MNG, multinodular goiter; MTC, medullary thyroid cancer; RFA, radiofrequency ablation; RLN, recurrent laryngeal nerve; SEER, Surveillance, Epidemiology, and End Results.

INTRODUCTION

The population of older adults (>65 years old) in the India is growing rapidly, with projections indicating that this group will close to double by the year 2060 and the population older than 85 years-old will almost triple in number [1]. As a result, endocrinologists and endocrine surgeons will encounter an increasing number of older adults with thyroid disease in a clinical setting. Treatment decisions in older adults may be unique from those of younger patients. Older adults are more likely to present with cardiovascular, neurologic, and metabolic comorbidities, which may increase the inherent risks of thyroid surgery and general anesthesia. In addition, older

adults may have limited life expectancy, which makes lag-time to benefit from invasive interventions, such as thyroidectomy, a key consideration when weighing the risks and benefits of operative and nonoperative treatment strategies. Lastly, the health priorities of older adults may prioritize preservation of function, cognition, and quality of life over rapid and definitive treatments that have the potential for side effects or complications that will affect their independence [2]. With this aging population, it is essential that clinicians familiarize themselves with unique considerations for the management of thyroid disorders in older adults to optimize their care and outcomes.



In older adults who are fit and functional, with few chronic conditions and a long (>10-year) life expectancy, it is reasonable for clinicians to proceed with surgical decision-making based on established disease-specific guidelines and a patient's specific goals and preferences. However, in patients with intermediate life expectancy (2-10 years), multiple comorbidities, and/or functional impairment, it is important to consider an individual patient's health priorities and the potential for adverse effects to their quality of life with thyroid surgery, such as the risks of systemic complications related to general anesthesia or recurrent laryngeal nerve (RLN) injury and hypoparathyroidism^[3]. Shared decision-making, in which patients are provided explicit information about treatment options and their associated benefits and harms and participate in final treatment choice with their clinician, allows patients to take a more active role in their care, reduces decisional conflict, and improves congruence between treatment choice and personal values^[4]. Incorporation of these principles into the clinical care of older adults with thyroid disorders should be the goal of the clinicians who care for them.

Although the prevalence of thyroid nodules increases with age, the risk that a nodule will prove malignant at initial evaluation decreases as patients grow older^[5, 6]. However, the proportion of thyroid malignancies that are higher-risk histologic subtypes, poorly differentiated, or anaplastic thyroid cancers (ATCs) increases with patient age^[6]. Given these age-based differences, the optimal approach to treating benign and malignant thyroid disease in older adults has not been established. The aim of this article is to review the current understanding of how older age can affect surgical outcomes of thyroidectomy, as well as expected disease-related outcomes, such as survival from low-risk thyroid cancer, and highlight important considerations in surgical decision-making for older adults. The overall goal of summarizing this information is to provide context for treatment decisions among older adults with thyroid disease to improve individualized and shared decision-making by patients and the clinicians who care for them.

MATERIALS AND METHODS

To assess the current literature relevant to the operative management of thyroid disease in older adults, we reviewed articles accessed via Pubmed and Google Scholar using the following search terms: "thyroid" and

"older adult," "elderly," or "geriatric," with at least 1 of the following: "surgery," "cancer," "goiter," "hyperthyroidism," or "Graves." Abstracts published in English between January 1, 1992, to December 31, 2022, were reviewed, and scientific merit was assessed by the authors based on the population included, study design, statistical analysis, and relevance to the review topic. All study designs (including prospective trials, observational studies, meta-analyses, and case series), practice guidelines, consensus statements, and other review articles were considered for inclusion. The references from all articles reviewed in full text were also evaluated and included as appropriate. Additional sources related to shared decision-making and surgical optimization in older adults were also reviewed and incorporated into our findings.

Challenges of Thyroid Surgery in Older Adults

While thyroidectomy now is accepted as a low risk, outpatient procedure, it is still associated with complications that can impact quality of life and increase medical costs. Older adults have been found to experience higher rates of general and procedure-specific postoperative complications after thyroidectomy, which may be related to the higher prevalence of comorbidities, poorer functional status, and malnutrition^[7]. In a 2005-2014 American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) study of 40 025 thyroidectomy patients, the most common complication documented was readmission, and patients ≥ 70 years old experienced 1.5 times more general complications within 30 days of surgery than patients younger than 70^[8]. In another ACS NSQIP study, the presence of a concomitant comorbidity in a patient ≥ 65 years of age increased the risk of postoperative complications, suggesting that comorbidities act as effect modifiers that compound the effect of older age on adverse outcomes^[9].

The higher risk of complications, especially readmission, can detract from quality of life postoperatively and create financial burden for older patients. A study of patients over 65 years of age undergoing surgery for thyroid cancer in the Surveillance, Epidemiology, and End Results (SEER)- Medicare database from 1997 to 2002 found an unplanned readmission rate of 8%, which was more common in those with comorbidities and advanced stage disease^[10]. On average, each readmission lasted 3.5



days and cost \$5921, with readmissions for pulmonary complications costing the most (\$9684), suggesting readmission among older adults undergoing thyroid surgery for cancer is prevalent and costly.

While older age has been associated with higher general complication rates for thyroid operations, data are mixed on the impact of older age on thyroidectomy-specific complications, namely RLN injury, neck hematoma, and hypoparathyroidism. Current data from European and US surgical quality databases are equivocal on whether older age is associated with a higher risk of RLN injury. In a cohort study of 5252 patients undergoing thyroidectomy from the 2009-2013 Scandinavian Quality Register for Thyroid, Parathyroid, and Adrenal Surgery, patient age was not independently associated with permanent RLN palsy [11]. In contrast, in a study of 11 370 patients from the 2016-2017 ACS NSQIP thyroidectomy-specific database, patients ≥ 65 years of age had a higher rate of RLN injury than those < 65 years (8.0% vs 5.4%, $P < .001$), and age ≥ 65 years was independently associated with RLN injury [12]. An increased rate of RLN injury among older adults was also shown in a 1991-2009 SEER–Medicare study, which found the overall incidence of RLN injury to be 9.5% among Medicare beneficiaries after thyroidectomy for thyroid cancer, with the adjusted odds of vocal cord paralysis increasing with each additional year of age (odds ratio 1.03, 95% CI 1.01-1.04) [13]. While it is unclear whether older age is associated with RLN injury, it is important to note that this thyroidectomy-specific complication can significantly reduce quality of life. Not only does RLN injury cause alterations in voice, swallowing, and breathing, it also leads to feelings of social isolation, which could be exacerbated in older adults.

Limited data are available on the association between older age and neck hematoma or hypocalcemia. There may be a higher risk of neck hematoma in older adults. In a study of 147 344 thyroid and parathyroid operations in the 2000-2009 Nationwide Inpatient Sample database, age > 65 years was identified as an independent risk factor for postoperative neck hematoma, with these older adults having 1.8 times the odds of experiencing this adverse outcome [14]. Patients who experienced neck hematoma also had longer, costlier hospital stays and a higher mortality rate than their younger counterparts. It has been hypothesized that the association between older

age and neck hematoma is related to more frequent use of anticoagulation and antiplatelet therapy. Older age has not been identified as an independent risk factor for developing post-thyroidectomy hypocalcemia due to hypoparathyroidism. In a 2021 meta-analysis of 23 studies, age was not identified as a risk factor for post-thyroidectomy hypocalcemia [15].

In summary, the risk of general complications, especially readmission, after thyroidectomy appears to be more dependent on the patient's age, comorbidities, and functional status, than thyroidectomy-specific complications. Comprehensive risk assessment in geriatric patients considering thyroidectomy is important in order to achieve best postoperative outcomes.

Frailty is defined by the presence of three or more of the following:

- Unintentional weight loss greater than 10 pounds in 1 year
- Self-reported exhaustion
- Weakness
- Slow walking speed
- Low physical activity

Figure 1: Frailty phenotype as described by Fried et al. [22]

Assessment of Risk of Thyroid Surgery in Older Adults

Accurate assessment of patient-specific risks of thyroid surgery also are essential to informed consent discussions with older adults who have benign and malignant thyroid conditions. Although thyroid operations are most commonly performed in the ambulatory setting and require minimal time in the hospital, the risk of thyroid surgery increases with patient age and, more notably, frailty, a measure of physiologic reserve that is distinct from comorbidity or disability and is associated with vulnerability to adverse health outcomes in response to stressors [16]. The risks of invasive interventions and surgery overall, in addition to thyroid surgery specifically, are best predicted based on patient frailty rather than age and comorbidity alone. In a population of more than 400 000 Veterans undergoing noncardiac surgery, frailty was associated with increased 30-, 90-, and 180-day mortality across all levels of operative stress, with 30-day mortality among frail patients undergoing the lowest-stress operations being 1.55% (95% CI 1.20-1.97%) [17]. This suggests that patient frailty should be assessed and considered in patient evaluation for even “low-risk” operations, such as



thyroidectomy. In a study of over 30 000 adults who underwent thyroid surgery for thyroid cancer in the 2005-2014 US Nationwide Inpatient Sample, those who were frail had a higher risk of prolonged length of stay, in-hospital mortality, surgical complications, and 6 times the odds of medical complications [18]. Frailty has also been associated with an increased risk of neck hematoma and RLN injury among older adults undergoing surgery for multinodular goiter (MNG) [19].

The prevalence of frailty in community-dwelling adults older than 65 is estimated to be around 10%, with 41% of patients in the community estimated to be prefrail, showing some, but not all, characteristics of frailty [20]. Frailty can be easily assessed in the clinical setting using the Risk Analysis Index, a validated frailty assessment tool that is rooted in the deficit accumulation model of frailty that takes less than 1 minute to calculate during a patient interview, or through the assessment for a frailty phenotype (see Fig. 1) [21, 22]. Identifying frail patients in the preoperative setting allows surgeons the opportunity to divert perioperative resources for preoperative optimization in an effort to improve surgical outcomes or to counsel high-risk patients about nonoperative treatment strategies with less associated risk. Additional measures that may contribute to risk stratification for older adults planned for thyroid surgery include the American Society of Anesthesiologists score and multimorbidity [23, 24].

Mitigating the Risk of Thyroid Surgery in Older Adults

General strategies to reduce the risks associated with thyroid surgery in older adults include modifying the surgical approach or anesthetic, seeking out experienced thyroid surgeons, and avoiding unnecessary surgery in higher-risk patients when there is treatment equipoise with alternative nonoperative strategies. Thyroid lobectomy is associated with a decreased risk of complications compared with total thyroidectomy and should be considered as an alternative treatment option in appropriate older adults. In a cohort of 60 000 adults with thyroid disease, total thyroidectomy was associated with twice the odds of postoperative complications, with increased rates of hypocalcemia, neck hematoma, respiratory complications, and tracheostomy [25]. In addition to eliminating the risk of permanent hypoparathyroidism and bilateral RLN injury, only 30%

of patients treated with thyroid lobectomy for benign thyroid conditions will require postoperative thyroid hormone replacement [26]. This will reduce the contribution of thyroid hormone supplementation to polypharmacy, which is associated with adverse clinical consequences in older adults [27], and avoid potential complications from exogenous hypothyroidism or hyperthyroidism, such as cardiovascular events and fractures [28, 29]. Pathology that can be considered for thyroid lobectomy over total thyroidectomy in older adults include MNG with predominantly unilateral involvement, indeterminate thyroid nodules, and malignancies with unilateral involvement. In a study using the 2000-2009 SEER database, advancing age was associated with an increasing likelihood to undergo less than total thyroidectomy for treatment of papillary thyroid cancer, with patients 85 years and older least likely to undergo total thyroidectomy [30]. This suggests that surgeons may be prioritizing local control of disease over strategies that focus on long-term recurrence risk-reduction and ease of surveillance in patients with limited life expectancy.

Local and regional anesthesia with monitored anesthesia care are associated with a reduced risk of systemic complications when compared with general anesthesia and can be considered for very selected older adults requiring thyroid surgery by surgeons with experience with this technique [16, 31]. However, it should be noted that this anesthetic technique does not allow for the use of RLN monitoring, which has been associated with a reduction in nerve injury in some but not all studies [32, 33], and older adults with back pain or pulmonary disease may not be able to lay flat for the duration of the operation. Lastly, some thyroid pathologies will not be appropriate to manage with this approach.

Higher surgeon operative volume has been associated with improved outcomes for many operations, including thyroidectomy. In a study using the 2003-2004 Nationwide Inpatient Sample, high-volume thyroid surgeons had fewer complications, but performed fewer thyroidectomies in older adults [34]. While high-volume surgeons performed 29% of thyroidectomies in patients younger than 65 years, they performed only 23% of thyroidectomies in patients 65-79 years and 15% in patients 80 years and older, suggesting barriers to access skilled surgeons. Lower utilization of high-volume thyroid surgical care among older adults was also



demonstrated in a study of over 800 patients referred to a high-volume thyroid center in Germany. Machens *et al.* showed that the distance traveled to this high-volume center was much greater in younger patients than older patients, indicating that older adults were less inclined to travel for high-volume thyroid surgery despite their increased risk of aggressive cancers [35]. In a survey of members of the Endocrine Society, American College of Physicians, and American Academy of Family Practice, patient preference, transportation barriers, and confidence in a local surgeon were the most commonly cited factors discouraging referral to a high-volume surgeon [36]. Given older adults may be less resilient to perioperative complications, seeking out a high-volume surgeon is an important strategy to mitigate the risks of thyroid surgery. This may require targeted efforts to address barriers to receiving specialty thyroid care. A recent study showed that complication rates increase up to a yearly surgeon volume of 25 thyroidectomies, above which there was no difference in the adjusted risk of adverse outcomes [37], which provides older adults considering thyroid surgery a benchmark for assessment of potential surgeons.

Thyroid Cancer

When discussing surgical risk for older adults, the indication for thyroidectomy is important, as the expected natural history and disease-specific mortality should be taken into account and compared to the competing risk of mortality from other causes. Thyroid disease-specific mortality can be drastically different based on the cancer subtype and often will inform treatment decisions in thyroid cancer.

In differentiated thyroid cancer (DTC), especially papillary thyroid carcinoma, the low disease-specific mortality should be weighed against the potential complications from thyroidectomy, which can be more common in older patients, as discussed earlier in this review. Shared decision making is especially important in older adults who present with DTC in the setting of multiple comorbidities or functional impairment, as they are at higher perioperative risk and may find that nonsurgical management is preferable to preserve their quality of life without compromising longevity. In a 2000-2015 SEER database study of over 20 000 patients >65 years with thyroid cancer (papillary, follicular, Hurthle cell, medullary, anaplastic, and other), 19.4%

died of other causes while 12.3% died of thyroid cancer with a median follow-up of 50 months [38]. For patients with DTC, the likelihood of dying from other causes exceeded the likelihood of dying from thyroid cancer, especially among those with comorbidities, highlighting the indolent nature of this cancer and important context for surgical decision-making in this population. Similarly, a 1992-2013 SEER-Medicare study of 3280 patients >65 years who received surgery for low-risk papillary thyroid carcinoma found these older adults had excellent disease-specific survival (98.5%), but overall survival was significantly lower (38.2%) and life expectancy was less than 15 years for any patient >80 years old, regardless of the presence of comorbidities [39]. Based on these findings, surgeons should consider each patient's operative risk and tumor characteristics carefully to determine the approach that best aligns with a patient's preferences and life expectancy. Local control of disease should be a priority but may be accomplished with a more conservative operative approach (ie, lobectomy) and less associated morbidity in patients at high risk of complications.

Recognizing the indolent natural history of DTC, active surveillance of papillary thyroid microcarcinoma is also an accepted management approach by current guidelines and becoming more accepted by patients [40, 41]. Just as with discussing thyroidectomy, shared decision-making is important in discussing active surveillance for DTC with older patients, and consequently, understanding patients' priorities in their decision-making also becomes important. In an institutional study that examined patient decision-making about papillary thyroid microcarcinoma in focus groups, patients who opted for active surveillance expressed more concerns regarding the impact of surgery on their overall function and quality of life [42], which is consistent with data regarding other treatment decisions in older patients with serious illness [43].

In contrast to DTC, medullary thyroid cancer (MTC) and ATC are more aggressive cancers that can harbor significant mortality risk for older adults [38]. Patients >65 years of age with MTC are more likely to die from their thyroid cancer within the first 6.25 years of diagnosis, consistent with progression of many to distant disease, although after 6.25 years they are more likely to die from other causes [38]. Older age has been shown to be an independent risk factor for disease-specific mortality in



MTC [44, 45]. As a result, following guideline recommendations for the operative management of MTC may be more critical to achieving appropriate short- and long-term outcomes for older patients. Older adults with ATC are as a group more likely to die from their thyroid cancer than other causes; in a systematic review of patients ≥ 65 years treated for ATC between 2009 and 2019, median overall survival was 3 months [38,46]. Given this extremely poor prognosis, establishing goals of care and pain management may take precedence over surgical intervention in older adults diagnosed with ATC.

Management of thyroid cancer, regardless of subtype, should balance the expected mortality associated with thyroid cancer, the patient's personal values, and the potential risks of surgery (see Fig. 2). Using this balanced approach, surgeons will need to engage in a shared decision-making process with their patients, which may be enhanced with decision aids and other tools. For instance, a clinical tool called Thyroid Cancer Treatment Choice was developed at the Memorial Sloan Kettering Cancer Center to aid decision-making between physicians and patients about surgery vs active surveillance for papillary thyroid microcarcinomas [47]. The clinical tool was then implemented at 1 of 2 hospitals in Seoul, South Korea, in a prospective study, which enrolled 278 patients of varying ages and evaluated differences in rates of active surveillance between the clinics. Patients who used the clinical tool were more likely to choose active surveillance, despite having more patients with larger papillary thyroid microcarcinomas, suggesting this tool may increase acceptance of active surveillance. This type of decision support could be tailored for older adults, who may have age-specific quality of life concerns or comorbidities that would be important to include in the discussion (see Fig. 3).

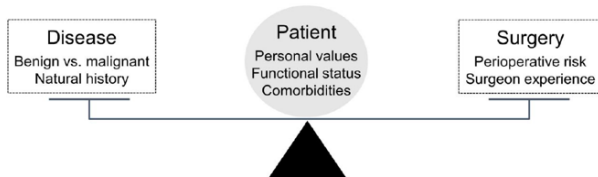


Figure 2: Perioperative factors to consider when making treatment decisions in older adults with thyroid disorders.

Talking Points for Shared Decision-Making in Older Adults Considering Thyroidectomy

- Elicit patient values and goals of care
- Describe treatment options and tradeoffs of operative and non-operative management
- Discuss expected postoperative outcomes based on patient-specific preoperative risk assessment
- Consider actions to mitigate the risks of thyroid surgery

Figure 3: Talking points for shared decision -making in older adults considering thyroidectomy

Benign Thyroid Disease

In light of the increased risks of thyroidectomy in older patients, shared decision-making is important not only in malignant disease, but also in managing benign thyroid disorders, including hyperthyroidism due to Graves' disease (GD), toxic adenoma, and toxic MNG, in addition to nontoxic MNG. The goal of management for hyperthyroidism is to render patients euthyroid rapidly, considering the tradeoffs of each therapeutic option for the individual patient (including potential adverse treatment effects and the need for subsequent or ongoing treatment). Antithyroid drugs and radioactive iodine therapy may be good options for many older adults newly diagnosed with hyperthyroidism due to GD, toxic adenoma, and toxic MNG, especially those who are frail or who have significant comorbidities [48]. However, total thyroidectomy should be considered among older adults with GD or toxic MNG who have associated symptomatic goiters, Graves' orbitopathy, or concurrent primary hyperparathyroidism, as long as they have acceptable risk profiles for general anesthesia. A recent study of 4650 Medicare beneficiaries >65 years of age who underwent total thyroidectomy for GD from 2007 to 2017 showed that the rate of permanent hypoparathyroidism requiring calcitriol therapy was low (2.2%, 95% CI 1.8-2.7%), as were the rates of neck hematoma requiring operative decompression (0.9%, 95% CI 0.7-1.2%) and permanent RLN injury (1.6%, 95% CI 1.2-1.9%) [49]. These data suggest that older adults with GD who may benefit from operative management, which offers rapid resolution of hyperthyroidism with low recurrence rates, should be counseled on these geriatric-specific risks and the potential benefits of total thyroidectomy so that informed treatment decisions can be made.

MNGs present a particular challenge in older patients, as they can impact quality of life due to associated dyspnea or dysphagia but have no effective medical treatment.



Studies demonstrate that older patients tend to have bigger, more symptomatic goiters that require thyroidectomy [50, 51], but the benefit of surgery must be balanced against the potential risks. When older patients undergoing surgery for MNG have been specifically studied, they have a higher risk of cardiopulmonary complications, while thyroidectomy-specific complications are similar to those of younger patients [51–53]. Frailty, rather than the numerical age, has been associated with increased risk of neck hematoma in patients ≥ 65 years of age undergoing surgery for MNG, highlighting the importance of preoperative frailty assessment in older patients with this benign condition [19]. Goiters with substernal extension are often identified in older patients, either due to evaluation following the onset of associated symptoms or incidentally on imaging for other indications. When considering operative intervention vs observation, it is important to recognize that the vast majority of substernal goiters can be removed via a cervical incision, avoiding the risks associated with partial sternotomy, and thyroidectomy is often associated with symptomatic benefit and the avoidance of lifelong surveillance [50]. Given the tendency for ongoing substernal growth and challenges of surveillance, the risks and benefits of operative management should be considered at initial diagnosis of large substernal goiters in all older adults with appropriate surgical risk profiles and reasonable life expectancy (>5 years) to avoid higher risk operations at more advanced ages when symptoms and/or airway compromise develop.

As an alternative to surgery, thyroid radiofrequency ablation (RFA) has emerged in recent years as an alternative to operative management for cytologically confirmed benign thyroid nodules that cause compressive symptoms or cosmetic concerns [54–56]. RFA has been shown to be effective in reducing compressive symptoms related to benign thyroid nodules [57]. In addition, RFA is a second-line option for the management of toxic adenomas in patients who have contraindications to radioactive iodine or surgery, although the resolution of hyperthyroidism is less predictable and ranges from 24% to 72% [55, 56]. RFA allows many patients to preserve innate thyroid function and avoid general anesthesia, which are advantages over thyroid lobectomy or total thyroidectomy and may be especially beneficial for older adults. Data on the use of

thyroid RFA in older adults are limited but promising [58] and will likely expand as RFA becomes more common in clinical practice.

CONCLUSION

Surgical decision-making for older adults with benign and malignant thyroid disorders, especially those with comorbidities, functional impairment, or limited life expectancy, has unique considerations with which clinicians should be familiar. As the general population ages, endocrinologists and surgeons will need to consider perioperative risks within the context of a patient's age, frailty, and personal values. Older adults undergoing thyroidectomy may be more likely to experience postoperative complications on average, which can adversely affect their quality of life and lead to financial burden. Thorough preoperative risk assessment, informed consent discussions, and decision support may help individualize treatment decisions and improve acceptance of nonoperative management strategies in high-risk older adults. Referral to high-volume thyroid surgeons is an important strategy to mitigate risk from thyroidectomy in older adults. The expected natural history of thyroid malignancies is important to weigh the risks and benefits of operative and nonoperative management strategies. Shared decision-making is critical to optimize the management of thyroid disorders in individual older adults.

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