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Unilateral thyroidectomy for the treatment of benign multinodular goiter

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Abstract

BACKGROUND—Benign multinodular goiter (MNG) is one of the most commonly treated thyroid disorders. While bilateral resection is the accepted surgical treatment for bilateral MNG, the appropriate surgical resection for unilateral MNG continues to be debated. Bilateral resection generally has lower recurrence rates but higher complication rates than unilateral resection. Therefore, the purpose of this study was to define the recurrence and complication rates of unilateral and bilateral resections in order to determine the appropriate intervention for patients with unilateral, benign MNG.

METHODS—We reviewed a prospectively maintained database of all patients who underwent a thyroidectomy for treatment of benign MNG at a single institution between May 1994 and December 2011. All patients with bilateral MNG were treated with bilateral resection. Surgical treatment for unilateral MNG was determined by surgeon preference, with all but one surgeon opting for unilateral resection to treat unilateral MNG. Data were reported as means $\pm$ standard error of the mean. Chi-squared analysis was used to determine statistical significance at a level of $p < 0.05$.

RESULTS—A total of 683 patients underwent thyroidectomy for MNG. Of these patients, 420 (61%) underwent unilateral resection and 263 patients (39%) underwent total thyroidectomy. The mean age was 52 ± 17 years, and 542 patients (79%) were female. The mean follow-up time was 46.1 ± 1.9 months. The rate of recurrent disease was similar between unilateral (2%, $n=10$) and bilateral (1%, $n=3$) resections ($p=0.248$). Unilateral resection patients had a lower total complication rate than patients with bilateral resections (8% vs. 26%, $p < 0.001$); however, there was no difference in the rate of permanent complications (0.2% vs. 1%, $p=0.133$). Thyroid hormone replacement was rare in unilateral resection patients, but necessary in all patients with bilateral resection (19% vs. 100%, $p < 0.001$).

CONCLUSIONS—Patients that had unilateral resections endured less overall morbidities than those who had bilateral resections, and their risk of recurrent disease was similar. They were also significantly less likely to require lifelong hormone replacement therapy post-operatively. Although bilateral resection remains the recommended treatment for bilateral MNG, this data strongly supports the use of unilateral thyroidectomy for the treatment of unilateral, benign MNG.

Keywords

thyroidectomy; lobectomy; multinodular; goiter; MNG; resection; thyroid; complications; recurrence; levothyroxine

Introduction

Multinodular goiter (MNG) is one of the most common endocrine disorders, and it often presents only after the goiter has become large and symptomatic [1, 2]. Symptoms of MNG include dysphagia and shortness of breath due to compression of the esophagus and trachea, as well as obstruction of venous flow in the head and neck [3]. Once these compressive symptoms occur, surgical resection is recommended. Additional indications for surgical intervention include suspected malignancy, hyperthyroidism, a large substernal component, and cosmetic concerns [4,5].

Bilateral thyroidectomy has become the accepted surgical therapy for bilateral MNG due to the lower complication rates attained by more experienced surgeons, as well as the lower reported recurrence rates when compared with unilateral or subtotal resection [1,2,6–8]. However, the favored surgical treatment for unilateral goiter continues to be of debate [1,2,9]. Unilateral thyroidectomy may be preferred in order to retain some function of the thyroid, allowing patients to avoid lifelong hormone replacement therapy. We have previously reported that 14.3% of patients undergoing lobectomy require thyroid hormone replacement in the form of levothyroxine, compared with 100% of patients that undergo total thyroidectomy [9]. Opponents of unilateral resection are concerned with the higher recurrence rates associated with this operation due to the presence of remaining thyroid tissue. Previous studies report a wide range of recurrence rates, from 1.5–34% [3,10–13]. Given this risk, some surgeons prefer to perform a bilateral thyroidectomy in order to decrease the possibility of developing a recurrent goiter and, thus, avoid further surgical intervention. Although the rate of recurrence is lower for bilateral resection, a more extensive surgery generally leads to higher rates of post-operative complications [1,3,8,14–16]. The most common complications with thyroid resection are hematoma, voice hoarseness due to damage to the recurrent laryngeal nerve with subsequent vocal fold paralysis, permanent hypoparathyroidism, and transient hypocalcemia due to parathyroidal ischemia or inadvertent damage to the parathyroids [17]. Higher complication rates with bilateral resection lead some surgeons to recommend unilateral thyroidectomy whenever possible, such as in the case of a well-defined, unilateral goiter.

The objective of this study was to describe the recurrence and complication rates of unilateral and bilateral thyroidectomies in order to determine the appropriate surgical intervention for patients with unilateral, benign MNG. A secondary objective included determining the rate of post-operative thyroid hormone replacement in both patient populations.

Methods

Data Collection and Analysis

A prospective database of all thyroidectomies was used to retrospectively analyze 683 patients who underwent unilateral or bilateral resection for benign MNG. Information collected included patient demographics, surgical procedure, pathology, follow-up surveillance, post-operative thyroid hormone replacement, recurrence, and re-operation. Surgeries were performed at the University of Wisconsin from May 1994 through December 2011. All patients diagnosed with benign MNG on final pathology were included. Benign MNG was defined as any thyroid enlargement due to benign nodular disease. Patients with hyperthyroidism (toxic MNG) were excluded, as were those with carcinoma or microcarcinoma on final pathology. The University of Wisconsin Institutional Review Board approved both data collection and analysis. Continuous variables are presented as means $\pm$ standard error of the mean (SEM). Analysis of data was performed using SPSS

Version 17 statistical software (SPSS, Inc., Chicago, IL). Chi squared test and student's t-test were used for univariate analysis. Statistical significance was defined as $p < 0.05$.

Treatments

The decision to treat with unilateral versus bilateral resection was made at the discretion of each individual surgeon. A bilateral resection was defined as a total or near-total thyroidectomy, and a unilateral resection was defined as a lobectomy with isthmusectomy. The tubercle of Zuckerkandl was always resected. One surgeon used a nerve stimulator for all operations, while other surgeons preferred not to. Bilateral resection was always performed when thyroid enlargement was apparent in both lobes on physical inspection and/or imaging. Unilateral disease was defined as either the absence of nodules in the contralateral lobe on cervical ultrasound, or the presence of clinically insignificant contralateral nodules (generally, $< 1\text{ cm}$ in diameter). In cases of unilateral disease, one surgeon preferred bilateral resection, whereas the other surgeons performed unilateral resection. All patients with bilateral resections were discharged with levothyroxine prescriptions for post-operative hypothyroidism, per our institutional protocol.

Follow-up

In general, patients were seen by the operating surgeon 1 to 2 weeks after resection. At 6 months post-operatively, patients were seen by their surgeon, endocrinologist, or primary care physician. Annual visits were then recommended with an endocrinologist or primary care physician to evaluate for recurrent disease. Thyroid stimulating hormone (TSH) levels were closely monitored to determine if thyroid hormone replacement was necessary, and if so, determine the appropriate dosage.

Hypocalcemia was defined within this study as symptomatic hypocalcemia manifested as numbness or tingling in the extremities or lips. This was distinguished from hypoparathyroidism, which was defined as undetectable parathyroid hormone or the requirement of calcitriol treatment. Transient complications were defined as those resolving within 6 months of surgery, while permanent complications were present after 6 months. In addition, the designation of permanent voice hoarseness required documented vocal fold dysfunction and/or a subsequent procedure to attempt correction.

Notably, during the study period, the standard of care for post-operative thyroidectomy surveillance changed. Prior to 2000, post-operative cervical ultrasound was not always used to evaluate for recurrence; however, after 2000, it became standard for physicians to use cervical ultrasound at annual follow-ups. As expected, the increased use of post-operative ultrasound increased the detection of recurrent nodules; however, for the purposes of this study, we defined recurrence as the return of MNG on imaging that necessitated reoperation.

Results

Patient Demographics

A total of 683 patients underwent thyroidectomy for MNG and had benign disease on final pathology. Of these patients, 61% ($n=420$) underwent unilateral resection and 39% ($n=263$) underwent bilateral resection. Patient demographics are similar between the two groups (Table 1).

Recurrent MNG and Post-Operative Complications

The mean follow-up time was 46.1 ± 1.9 months. The recurrence and complication rates for each operation are listed in Table 2. As shown, there was no significant difference in recurrence rates between the two operations. Transient complications were more likely after

bilateral resections ($p<0.001$), but permanent complications occurred at a similar frequency after both operations ($p=0.131$). Transient hypocalcemia, voice hoarseness, hypothyroidism, and hematoma were all more common in patients undergoing bilateral resection (Table 3).

Four patients (0.6%) had permanent complications as a result of their thyroidectomies. These permanent complications occurred after both types of resections (Table 3). Among those undergoing bilateral resection, 2 patients were left with permanent hypoparathyroidism, and another had permanent hoarseness due to left vocal cord paralysis that required a laryngoplasty. The one permanent complication resulting from unilateral resection was permanent voice hoarseness due to vocal fold paralysis. This patient had a follow-up laryngoplasty.

Of the 13 patients requiring reoperation for recurrence, only 2 had complications associated with the secondary operation. Both of these patients had transient voice hoarseness. There were no permanent complications as a result of reoperation.

Post-operative Thyroid Hormone Replacement

The rate of post-operative thyroid hormone replacement therapy is reported in Table 2. Levothyroxine was used for all patients requiring replacement. As shown, post-operative hypothyroidism requiring thyroid hormone replacement was much less prevalent for patients undergoing unilateral resection ($p<0.001$).

Discussion

Thyroidectomy is indicated for patients with MNG that causes compressive symptoms, hyperthyroidism, or cosmetic concerns. Surgical resection is also indicated if there is suspicion of malignancy. Patients with bilateral MNG typically undergo a bilateral resection, followed by lifelong thyroid hormone replacement therapy. Alternatively, patients with unilateral MNG can be treated with either unilateral or bilateral resection, depending on surgeon preference. Unilateral resection is often chosen to limit post-operative complications and avoid lifelong hormone replacement therapy, while bilateral resection may be preferred to limit the risk of recurrence. In this study, we found that there was no significant difference in the rate of MNG recurrence between the two operations. Transient post-operative complications occurred more frequently following bilateral resection, however, there was no difference in the rate of permanent complications between the two operations. In addition, far fewer patients required thyroid hormone replacement after unilateral resection.

Possible complications from thyroidectomy include hypoparathyroidism, hypocalcemia, voice hoarseness due to recurrent laryngeal nerve damage, and hematoma. The complication rate after bilateral resection has been reported to be between 5–33%, congruent with our rate of 26.2% in this study [3,6,8]. The lower rate of post-operative complications after unilateral thyroidectomy, 8% in our series and previously reported between 2–3%, is an advantage of this operation over bilateral resection [3,15]. The difference can be attributed to higher incidences of transient complications following bilateral resection, as the rates of permanent complications from each operation were not statistically different. Our rates were similar to previously reported ranges for transient complications, which were more prevalent after bilateral resection. For a unilateral resection, transient hypocalcemia is reported in 0–18% of patients, voice hoarseness in 1–6%, and hematoma in 0–1%. In addition, transient hypoparathyroidism is uncommon [2,15,18,19]. These transient complications are all more common after bilateral resection, as hypocalcemia is seen in 9–35% of patients, voice hoarseness in 1–10%, hematoma in 0–3%, and hypoparathyroidism in 5–30% [2,3,6,8,20]. Only one parathyroid gland is necessary to maintain normal levels of parathyroid hormone

and calcium, therefore, the low rate of hypocalcemia and hypoparathyroidism in unilateral thyroidectomy patients is expected [21,22]. Lower rates of voice hoarseness and hematoma in these patients are most likely due to the lesser extent of the surgery.

Although the rate of total complications is higher for patients undergoing bilateral resection, we demonstrated that the rate of permanent complications in these patients is similar to those undergoing unilateral resection. Our rates for permanent complications were similar to previously reported ranges. For patients undergoing unilateral resections, permanent damage to the recurrent laryngeal nerve is reported in 0–3% of patients, with permanent hypoparathyroidism in 0–1% of patients, and permanent symptomatic hypocalcemia rarely reported [2,3,6,8]. These ranges are similar to those for bilateral resection, where the recurrent laryngeal nerve is permanently damaged in 0–3% of patients, permanent hypoparathyroidism occurs in 0–5%, and permanent symptomatic hypocalcemia is uncommon [2,15,18,19]. It is hypothesized that the low rate of permanent complications after total thyroidectomy seen in these studies is due to a higher skill level of more experienced surgeons.

Levothyroxine was necessary post-operatively in 19% of our patients who underwent unilateral resection, which is consistent with previous studies showing a rate of 14–30% [9]. Conversely, all patients undergoing bilateral resection require thyroid hormone replacement post-operatively to prevent hypothyroidism. We discharge all total thyroidectomy patients on levothyroxine, assuming the operation leaves no remaining functional thyroid, thereby necessitating thyroid hormone supplementation. Levothyroxine requires regular check-ups and occasional medication adjustments, and overdosing may cause patients to experience side effects such as atrial fibrillation, osteoporosis, and osteopenia [9]. Given the possible negative effect on patients' quality of life, as well as the increased cost of treating post-operative hypothyroidism, avoiding the need for thyroid hormone replacement may be ideal.

The recurrence rate for patients with unilateral thyroidectomy has been reported to be between 1.5–34% in previous studies, although the definition of recurrence was not consistent [3,10–13]. For example, Rios and colleagues defined recurrence as recurrent nodules on imaging, but not necessarily requiring reoperation [10]. Our recurrence rate of 2.4% is within the lower margin of the previously reported range. In addition, our recurrence rate for bilateral thyroidectomies (1.1%) is consistent with previous studies ranging from 0.5–3% [3,6,15]. Interestingly, there was no significant difference in the rates of recurrence between the two operations. Although our follow-up period limits the interpretation of this result to an extent, we find it to be reliable, for when patients that had their initial operation from 2008–2011 were excluded (raising our mean follow-up time to 69.4 ± 2.9 months), there was still no statistical difference in recurrence rates (3% for bilateral resection and 2% for unilateral resection, $p=0.47$).

It is important to note that with the increased use of ultrasound post-operatively over the past 12 years, the rate of recurrent nodules detected in patients that underwent any thyroid resection is higher than previously reported. However, we chose to focus on recurrences that required reoperation, because a redo operation has more implications for the patients' safety and quality of life when compared to the recurrence of an asymptomatic nodule. Therefore, the increased use of post-operative ultrasound that occurred during our study period had little impact on our recurrence rates.

The main limitation of this study is the retrospective nature. In addition, as mentioned previously, long-term follow-up was unavailable in some patients, particularly those who had an operative procedure near the end of the study period. The lack of a true control group is also a limiting factor for this study. All but one surgeon in the study used unilateral

resection to treat unilateral goiter. Therefore, few patients with unilateral MNG were treated with bilateral resection, leading us to substitute patients with bilateral MNG as the control.

In conclusion, patients that had unilateral resections endured less post-operative complications than those who had bilateral resections, even though their risk of permanent complications was similar. The risk of recurrent goiter was also similar after either operation. In addition, the large majority of patients with unilateral resection avoided lifelong thyroid replacement therapy, while this therapy was necessary in all patients after bilateral resection. Therefore, although bilateral resection should remain the standard surgical intervention for bilateral MNG, we recommend that patients with unilateral, benign MNG be treated with unilateral resection.

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Table 1

Patient Demographics

Group	Unilateral resection	Bilateral resection	<i>P</i>
N	420	263	-
Age (mean±SEM)	50.7±0.8	52.9±1.0	0.10
Gender, Female (n, %)	327 (78)	216 (82)	0.18

Table 2

Rates of recurrence, post-operative complications, and thyroid hormone replacement

Group	Unilateral Resection (n=420)	Bilateral Resection (n=263)	P
Recurrence (%)	10 (2)	3 (1)	0.25
Complications (%)	32 (8)	68 (26)	<0.001
<i>Transient (%)</i>	31 (7)	64 (24)	<0.001
<i>Permanent (%)</i>	1 (0)	3 (1)	0.13
Hormone Replacement (%)	79 (19)	263 (100)	<0.001

Table 3

Post-operative complications

Group	Unilateral Resection (n=420)	Bilateral Resection (n=263)	P
Hypocalcemia			
<i>Transient (%)</i>	7 (2)	35 (13)	<0.001
<i>Permanent (%)</i>	0 (0)	0 (0)	-
Voice Hoarseness			
<i>Transient (%)</i>	19 (5)	25 (10)	0.01
<i>Permanent (%)</i>	1 (0)	1 (0)	0.74
Hypoparathyroidism			
<i>Transient (%)</i>	0 (0)	7 (3)	<0.001
<i>Permanent (%)</i>	0 (0)	2 (1)	0.07
Hematoma (%)	0 (0)	4 (2)	0.01