Symptomatic benign multinodular goiter: Unilateral or bilateral thyroidectomy?

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Background. *Symptomatic benign multinodular goiter (MNG) is extremely common in the north central United States. The extent of surgery for unilateral or bilateral disease is controversial. Bilateral resection should be associated with low recurrence rates, but potentially a higher technical morbidity. The long-term outcomes of patients with obvious unilateral MNG who had unilateral resection only is not commonly reported. To determine the optimal operation for patients with symptomatic MNG, we reviewed our single institutional results.*

Methods. *From May 1994 through November 2004, 883 patients underwent a thyroid operation at our institution. Of these, 237 (27%) underwent thyroidectomy for MNG. One hundred forty patients underwent unilateral lobectomy and 97 underwent total thyroidectomy.*

Results. *The mean age was 51 ± 1 years and 196 (83%) were female. With up to 145 months' follow-up, there was a higher recurrence rate in the lobectomy group (11% vs 3%;* P = *.029). However, patients in the lobectomy group had a much lower complication rate (2% vs 9%;* P = *.007). Importantly, in patients who underwent reoperation for recurrent MNG after lobectomy, the complication rate was low (5.5%) and not significantly higher than the initial surgery.*

Conclusions. *In patients with symptomatic MNG, 89% of those who underwent unilateral resection did not require further surgery. Unilateral thyroidectomy was associated with lower morbidity than bilateral resection. Furthermore, those patients who required operation for contralateral recurrence did not experience a significantly higher operative morbidity. Therefore, these data convincingly support recommending unilateral thyroid lobectomy as the procedure of choice for patients with symptomatic unilateral MNG. (Surgery 2007;142:458-62.)*

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Multinodular goiter (MNG) is the most common form of benign thyroid disease, both worldwide and in the United States, affecting 5% to 7% of the world's population.[1,2] Symptoms of MNG, which generally do not occur until the goiter is very large, include dysphagia, shortness of breath, and compression of the large vessels of the head and neck. Cosmetic appearance is also a concern for many patients. Indications for surgical therapy in MNG include symptoms of compression, suspected malignancy, hyperthyroidism, and cosmesis. Surgery may involve either unilateral or bilateral thyroidectomy, depending on the extent of the disease and individual surgeon treatment bias.[3,4]

The extent of surgery, however, for symptomatic MNG is controversial. Unilateral or subtotal thyroidectomy was advocated owing to its lower complication rate, but in theory it also has a higher recurrence rate associated with it because potential goitrogenic tissue remains in situ. This may necessitate reoperation in patients with recurrent symptoms, which may result in increased morbidity. The recurrence rate for unilateral thyroidectomy has been reported from 10% to 26%.[5,6]

Conversely, total thyroidectomy offers a lower recurrence rate, but can be associated with a higher complication rate because it is a more extensive operation.[7-9] The most common complications of thyroid surgery are hematoma, recurrent laryngeal nerve injury, permanent hypoparathyroidism, and transient postoperative hypocalcemia. However,

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surgical technique and training have advanced such that the complication rate of total thyroidectomy in experienced hands has decreased, and many surgeons are now advocating it as the procedure of choice because of its lower complication rate.[2,3]

METHODS

From May 1994 through November 2004, 236 patients with MNG (thyroid enlargement owing to benign nodular disease) underwent thyroidectomy at the University of Wisconsin. These patients were identified from an ongoing prospective endocrine database and data were retrospectively analyzed. Both the data collection and analysis were approved by separate protocols through the University of Wisconsin Human Subjects Institutional Review Board. Statistical analysis was performed with SPSS software (SPSS Inc.) Statistical significance was defined as a $P < .05$.

The use of pre- and postoperative imaging in patients with MNG was surgeon dependent. All patients had preoperative chest x-rays. If the MNG was obviously bilateral on physical examination, preoperative imaging (computed tomography and/or cervical ultrasound) was not always obtained before bilateral resection. If a unilateral MNG was suspected on physical examination, these patients underwent preoperative imaging to confirm this finding if unilateral resection was planned.

Of these 236 patients, 140 (59%) underwent thyroid lobectomy and isthmusectomy for symptomatic, unilateral nodular goiter disease and the remaining underwent bilateral resection. The decision to perform unilateral versus initial bilateral resection was at the discretion of the individual surgeon. The general approach of the surgeons involved in this study was as follows. In patients with bilateral MNG, all surgeons performed bilateral resection. In patients with unilateral MNG, 1 surgeon generally preferred bilateral resection whereas the remaining surgeons preferred unilateral resection if possible.

Recurrent MNG was defined as return of the MNG causing symptoms necessitating thyroid resection. Patients were evaluation postoperatively at 1 to 2 weeks by the surgeon and then at 6-month to 1-year intervals by the surgeon, endocrinologist, and/or primary care provider. The use of imaging for postoperative MNG surveillance changed during the study period. Before 2000, cervical ultrasound was not routinely utilized. However, after 2000, cervical ultrasound at yearly intervals became the general practice of surgeons and endocrinologists to follow for recurrent disease.

Table I. Demographic data

Groups	N	*Age*	*Gender (% female)*
Unilateral resection	140	51 ± 1	86%
Bilateral resection	97	52 ± 2	78%
P-value	—	.365	.141

RESULTS

Demographic data. The mean age of all patients was 51 ± 1 years and 83% were female. Patients were then grouped into unilateral resection (thyroid lobectomy) and bilateral resection groups. Demographically, the 2 groups were similar (Table I). The mean age of patients undergoing lobectomy was 51 ± 1 years and the mean age of those undergoing thyroidectomy was 52 ± 2 years. The proportion of females undergoing thyroid lobectomy versus total thyroidectomy was 86% and 78%, respectively.

Operative outcomes. With up to 134 months of follow-up, patients in the unilateral group had a 11% recurrence rate (Table II). In the bilateral resection group, the recurrence rate was 3%. Thus, there was a higher recurrence rate in the bilateral group, compared to the unilateral group ($P = .029$).

The total complication rate, however, was significantly higher in the bilateral group, especially with regard to postoperative hypocalcemia. The overall complication rate was 9% in the patients in the bilateral group compared with 2% in the unilateral group ($P = .007$). In the bilateral group, 9 patients experienced complications including transient hypocalcemia ($n = 6$), transient hoarseness ($n = 2$), and long-term recurrent nerve injury ($n = 1$). In the unilateral group, 3 patients had complications including transient hoarseness ($n = 2$) and long-term recurrent nerve injury ($n = 1$). The rate of transient, postoperative hypocalcemia in the bilateral group was 6% versus 0% in the unilateral group ($P = .049$). Furthermore, in patients who required completion thyroidectomy for recurrent symptomatic disease, the surgical complication rate was low (5.5%) and not significantly higher than for the initial surgery.

DISCUSSION

MNG is a common problem in the United States with African American race, obesity, and age being significant risk factors.[10,11] The surgical procedure of choice for symptomatic MNG remains controversial. In the past, most surgeons have performed unilateral or subtotal thyroidectomy because of its

Table II. Recurrence and complication rates

Groups	*Reoccurrence rate (%)*	*Complication rate (%)*	*Hypocalcemia (%)*
Unilateral resection	11	2	0
Bilateral resection	3	9	6
P-value	.029	.007	.049

lower complication rate; however, this can lead to the need for reoperation if the symptomatic MNG recurs. More recently, and as surgical technique and expertise have advanced, total thyroidectomy has been preferred by some surgeons because of its lower recurrence rate.[2,3] However, there remains a lack of convincing data concerning which is the procedure of choice for selected patients with unilateral nodular goiter disease.

The most common complications of thyroid surgery are hematoma, recurrent laryngeal nerve injury, permanent hypoparathyroidism, and transient postoperative hypocalcemia. Hematoma usually occurs within 24 hours of surgery and can cause airway compromise, which is a surgical emergency. Hematoma is rare, occurring in <1% to 2% of all thyrodectomies.[12] Unilateral injury to the recurrent laryngeal nerve causes hoarseness, laryngospasm, and temporary aphonia; bilateral injury is more serious, causing respiratory distress that can necessitate intubation or tracheostomy. Permanent damage to the recurrent laryngeal nerve occurs in 0% to 4% of cases.[12-14] Permanent hypoparathyroidism occurs in <2% of cases; it causes symptoms such as perioral tingling and numbness and positive Chvostek's sign,[7] Finally, transient postoperative hypocalcemia occurs in up to 50% of patients undergoing thyroidectomy.[7,12]

The complication rates in patients undergoing unilateral thyroidectomy have been reported in several studies; the rate of hematoma and permanent hypoparathyroidism is reported in 0% of patients, recurrent laryngeal nerve injury occurred in 0% to 3% of patients, and temporary hypocalcemia occurred rarely. In comparison, the complication rates in total thyroidectomy are higher. Hematoma was still a rare occurrence, occurring in 0.4% of cases; permanent hypoparathyroidism occurred in 1% to 5% of patients and temporary hypoparathyroidism in 5% to 30% of patients. The rate of recurrent laryngeal nerve injury was the same as in unilateral thyroidectomy (0% to 3%).[2,3,7,12,15]

That the complication rate for total thyroidectomy is higher than for thyroid lobectomy is not surprising, given the greater extent of surgery. To this end, it seems that unilateral (thyroid lobectomy) in selected patients with unilateral disease would be the procedure of choice for MNG. However, the recurrence rate after reoperation is another variable that must also be taken into consideration.

The recurrence rate for MNG in patients undergoing unilateral thyroidectomy is 1.2% to 26%, with the average time for recurrence being 10 to 16 years[16,17]; the recurrence rate for patients undergoing total thyroidectomy is 3%.[16] However, not all patients (especially the elderly) who have recurrence require reoperation, and thus the rate of reoperation has been reported at approximately 0.4%.[18] The complication rates in reoperation have been thought to be higher and are due to fibrosis of the surrounding tissue and distorted anatomy from the first procedure. A few studies, however, have shown the complication rate for reoperation not to be significantly higher than in the initial procedure. Recurrent laryngeal nerve injury has been reported at 3.4%, with the rate of permanent recurrent laryngeal nerve injury being 0.81% to 1%, temporary hypoparathyroidism as 2.9% to 11%, and permanent hypoparathyroidism as 0.81% to 1% in both of the permanent injury groups the complication rates were not significantly different from those undergoing initial operation.[17,19] This emphasizes that in experienced hands thyroidectomy is extremely safe for patients with MNG.[4,10,20]

In summary, the complication rate for patients undergoing unilateral thyroidectomy for unilateral MNG disease is significantly lower than that for patients undergoing total thyroidectomy while the recurrence rate of unilateral thyroidectomy is higher than total thyroidectomy. However, the rate of reoperation for recurrent MNG is very low and the complication rate is not significantly different from the initial procedure. Therefore, we recommend that patients with unilateral disease can safely undergo unilateral thyroidectomy because the need for reoperation is low, symptomatic recurrence usually takes decades to manifest, if ever, and a remedial procedure does not significantly increase the complication rate in these select patients.

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DISCUSSION

Dr Christopher R. McHenry (Cleveland, Ohio): Dr Olson, I agree with your conclusions that lobectomy is the choice for symptomatic unilateral multinodular goiter, but only when significant disease is absent in the contralateral lobe.

In addition to the fact that 89% of patients require no further surgery and that the operation for recurrence can be performed without an increase in morbidity, two thirds of patients will also be able to produce enough thyroid hormone to maintain a euthyroid state without a need for hormone supplementation. Also, no patient will develop symptomatic hypocalcemia, permanent hypoparathyroidism, or bilateral recurrent laryngeal nerve injury, and the incidence of life-threatening neck hematoma will be lower.

I have the following questions for the authors. Could you clarify why patients were chosen to undergo unilateral lobectomy versus total thyroidectomy and what was the extent of involvement for both lobes of the thyroid gland in both groups of patients? It is important when assessing a patient for surgical treatment of nodular thyroid disease to determine the status of both lobes of the thyroid gland with ultrasound and/or intraoperative palpation to ensure that you resect all of the diseased tissue?

What was the mean follow-up time before recurrence occurred in patients who underwent unilateral lobectomy and what were the indications for surgery and the size of the nodules in the patients who developed recurrent nodular thyroid disease? Were all of the recurrences on contralateral side?

Finally, what is your explanation for a 3% recurrence rate in patients who were treated with total thyroidectomy? Do you purposely leave a small remnant of thyroid tissue behind to preserve the viability of the parathyroid glands? And if so, wouldn't it be more appropriate to call this a "near-total" rather than a "total" thyroidectomy?

I enjoyed your paper and appreciate the opportunity to discuss it.

Dr James R. Starling (Madison, Wisconsin): As mentioned, the choice of unilateral resection for unilateral disease versus a total thyroidectomy in patients who had unilateral disease was up to the respective surgeons. And most of these patients were operated on by myself and my other endocrine colleagues before Dr Chen joined us a few years ago, and that surgeon did total thyroidectomies for every patient irrespective of whether the patient had unilateral or bilateral disease. So that really determined the 2 arms of the study, 1 surgeon's choice versus another surgeon's choice—my preference being unilateral surgery for unilateral disease.

The main criteria for determining, in my experience, unilateral disease versus bilateral disease was observation. We did not use, for example, intraoperative ultrasound. Not all patients had preoperative ultrasound. Some did. But the basic indication

was observation. And after doing thousands of thyroids, one can, in my estimation, determine by gentle palpation and observation which lobe has the disease or does not have the disease.

Our mean follow-up is around 10 years, 10 to 12 years.

As mentioned, a number of patients who underwent bilateral surgery had subtotal versus total thyroidectomy. And most of the recurrences that we observed are in those patients who had what was described by my surgical colleague as a subtotal or near-total thyroidectomy, although there were a couple of patients who had total thyroidectomies who had recurrent disease, and I am sure that is simply because remnant cells, as we know, are always left behind, and were stimulated and grew.

Not all patients were suppressed postoperatively. It has been my practice to put patients, even those who have unilateral disease, on lifelong suppression, but not all were. Dr Chen, for example, my partner today, does not, as I do, put patients who undergo unilateral resections on prophylactic exogenous thyroid replacement.

Dr Richard A. Prinz (Chicago, Illinois): I know Dr McHenry already asked this, but I am going to ask the same question about how you chose the operative approach? Just the surgical judgment here would lead us to believe that with your experience, you would select out a group of patients who probably are not going to have a need for reoperation. And we would like to know how you went about doing that. Because in this day and age with ultrasound in the office and so forth, we see things in the opposite lobe so much more than we did when we were just palpating it. So if you selected out a subgroup of patients who are very less likely to have a need for reoperation, what were your criteria? I really think a $\geq$10% reoperation rate is quite high. I do not think we accept that type of reoperation rate in very many conditions in surgery. So I would like your comments on that.

Second, I think you sort of massaged your data here and did a significant thing for complications. If you balance transient hypocalcemia with a need for reoperation, I do not think those are comparable. Maybe you can comment on that.

Finally, I think the 3% recurrence in the bilateral operation would lead me to conclude that one of your additional conclusions should be that subtotal thyroidectomy is not a good operation, because once you deal with that opposite lobe, I think you really run the risk of having much greater complications when you do a reoperation. And a 3% reoperation rate is much more than you should be having there.

Dr James R. Starling (Madison, Wisconsin): I agree 100% with you that the subtotal thyroidectomy should not be done for multinodular goiter disease so we have no argument there. I am just reporting the data as we observed it from our institution.

I cannot really comment too much on your thoughts about intraoperative or preoperative ultrasound in deciding which patients have true unilateral versus bilateral disease. As I mentioned, in my experience this decision (which patients have unilateral versus bilateral disease) is purely based on intraoperative, not preoperative, judgment. And if on general palpation the contralateral lobe was normal and on observation it was normal, that was in my judgment considered to be an indication for a unilateral surgery and not bilateral surgery, even though perhaps with intraoperative and preoperative ultrasound, which was not done on all patients, one could perhaps pick up minute evidence for possible recurrence of contralateral disease sometime in the future. But that simply was not part of our preoperative or intraoperative protocol.

The comment about complications. Hypocalcemia, I agree, probably because it is transient and never permanent, that we probably stress that as a complication too much. But again, we are just reporting the incidence of this. And that is just what our study showed.

Dr Scott M. Wilhelm (Cleveland, Ohio): Most of the questions I had were already answered. The one question I still have is this. In the patients in whom you performed a thyroid lobectomy, what is your standard surveillance plan for these patients? Often this is a benign disease, and they go back to their primary care physician or the endocrinologist who referred them. Do you have these patients come back on a yearly basis? I know you said you do not personally do a lot of ultrasound yourself, but is Dr Chen bringing back patients now and re-ultrasounding people routinely to see if they are developing new nodules or progressive growth of nodular disease?

Dr James R. Starling (Madison, Wisconsin): Neither Dr Chen nor myself would follow these patients after a reasonable postoperative follow-up unless there was indication. So after a minimum 3-month follow-up, these patients are referred back to their referring physician, be it family physician or endocrinologist, and would not necessarily, unless there was a good reason, such as, a complication or something, be followed by our own endocrine group for surveillance, ultrasound, or scans, or what have you. So repeating the ultrasound in follow-up we do not do.