MORBIDITY AFTER TOTAL THYROIDECTOMY FOR BENIGN THYROID DISEASE: COMPARISON OF GRAVES’ DISEASE AND NON-GRAVES’ DISEASE

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The purpose of this study was to review the safety of total thyroidectomies for benign thyroid disease, with special emphasis on the comparison between Graves’ disease and non-Graves’ disease. In this study, 107 patients who underwent total thyroidectomies for clinically benign thyroid disease performed by the same surgeon between January 1987 and December 2004 were enrolled; 48 had Graves’ disease and 59 had non-Graves’ disease. The rates of temporary vs. permanent hypoparathyroidism, hematoma requiring surgical intervention, and temporary vs. permanent recurrent laryngeal nerve palsy (RLNP) after total thyroidectomy for benign thyroid disease were 34.6% vs. 3.7%, 6.5%, and 6.5% vs. 1.85%, respectively. The rates of permanent hypoparathyroidism and temporary RLNP in the Graves’ disease group were significantly different when compared with the non-Graves’ disease group (8.3% vs. 0% and 11.5% vs. 2.5%, respectively). However, comparing the rates of temporary hypoparathyroidism and permanent RLNP, and postoperative hematoma, there was no statistically significant difference. Compared with total lobectomy, the rates of postoperative hematoma increased significantly for total thyroidectomy (6.5% vs. 0.48%). Total thyroidectomy for non-Graves’ benign thyroid disease may be performed with minimal morbidity as has been advocated by many authors. For patients with Graves’ disease in this study, however, the complication rates of permanent hypoparathyroidism and temporary RLNP were significantly increased. Therefore, we suggest that total thyroidectomy for Graves’ disease should be performed by an experienced surgeon.

Key Words: Graves’ disease, hypocalcemia, recurrent laryngeal nerve palsy, thyroid, thyroidectomy

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Total thyroidectomy is increasingly accepted for the management of patients with benign disease when both lobes of the thyroid gland are involved (such as multinodular goiter, thyroiditis, Graves’ disease). This approach can avoid disease recurrence and eliminate any subsequent risk of malignant change. Several authors [1–6] have reported that total thyroidectomy can be performed safely for treatment of bilateral benign thyroid disease, and that a low complication rate can be achieved with a meticulous surgical technique. However, few studies compare the complication rates after total thyroidectomy between Graves’ disease and other benign thyroid variants (non-Graves’ disease). The purpose of the present study is to review the results of our total thyroidectomies for benign
thyroid disease and compare the complication rates between Graves’ and non-Graves’ disease groups.

**Patients and Methods**

Between January 1987 and December 2004, a total of 601 thyroidectomies were performed by the same surgeon at our institution. Among them, 417 had total lobectomies and 184 had total thyroidectomies. This study was confined to 107 total thyroidectomies for clinically benign thyroid disease (48 for Graves’ disease and 59 for non-Graves’ disease). Patients with Graves’ disease received antithyroid medication to achieve a euthyroid state before operation. All patients underwent total thyroidectomy under general anesthesia. Routine identification of the recurrent laryngeal nerve (RLN) was performed during all operative procedures. Autotransplantation of the parathyroid gland was performed routinely when vascular injury was identified or when the glands were incidentally removed.

Free calcium levels were measured daily preoperatively and for at least 4 days postoperatively. All patients underwent pre- and postoperative laryngoscopic examinations of the vocal cords. When recurrent laryngeal nerve palsy (RLNP) or hypocalcemia was identified, follow-up was weekly at the beginning, and every 3–4 weeks thereafter until complete recovery was achieved. RLNP was considered to be permanent if it persisted after 6 months. Hypocalcemia was defined as free calcium level less than 4.0 mg/dL on at least two consecutive measurements. Temporary hypoparathyroidism was defined as hypocalcemia associated with or without symptoms of perioral paresthesia, tingling of distal extremities or muscle spasm, and free calcium level that returned to normal within 6 months. Permanent hypoparathyroidism was defined as hypocalcemia that persisted for over 6 months and that required active vitamin D and calcium supplementation. The term “hematoma” in this paper is defined as hematoma requiring surgical intervention. In this study, the calculation of the RLNP rate was based on the number of nerves at risk. Intergroup difference was assessed using the $\chi^2$ and Fisher exact tests. A $p$ value of 0.05 or less was regarded as statistically significant.

**Results**

The rates of temporary vs. permanent hypoparathyroidism, hematoma requiring surgical intervention, and temporary vs. permanent RLNP after total thyroidectomy for benign thyroid disease were 34.6% vs. 3.7%, 6.5%, and 6.5% vs. 1.85%, respectively. Table 1 shows the morbidity of total thyroidectomy for the Graves’ and non-Graves’ disease groups. Rates of temporary/permanent hypoparathyroidism were 37.5%/8.3% for Graves’ disease and 32.2%/0% for non-Graves’ disease. Rates of temporary/permanent RLNP were 11.5%/2.0% for Graves’ disease and 2.5%/1.7% for non-Graves’ disease. The rates of postoperative hematoma were 10.4% for Graves’ disease and 3.4% for non-Graves’ disease. One of the Graves’ disease patients suffered from thyroid storm with postoperative hematoma. Compared to the non-Graves’ disease group, the rates of permanent hypoparathyroidism and temporary RLNP were significantly higher for the Graves’ disease group (8.3% vs. 0% and 11.5% vs. 2.5%, respectively; $p<0.05$). There were no significant differences in temporary hypoparathyroidism, permanent RLNP, and

| Table 1. Morbidity of total thyroidectomy for benign thyroid disease |
|-------------------------|-------------------------|-------------------------|-------------------------|
|                         | Non-GD ($n=59$) | GD ($n=48$) | GD ($n=62$) | GD ($n=119$) |
| Temporary hypocalcemia | 19 (32.2) | 18 (37.5) | 22 (35.4) | 25 (21) |
| Permanent hypocalcemia | 0 | 4 (8.3) | 1 (1.06) | 1 (0.8) |
| Temporary cord palsy   | 3 (2.5)* | 11 (11.5)* | 9 (14.4) | 2 (1.7) |
| Permanent cord palsy   | 2 (1.7)* | 2 (2.0)* | 1 (1.6) | 1 (0.8) |
| Hematoma               | 2 (3.4) | 5 (10.4) | 0 | 7 (5.9) |
| Thyroid storm          | 0 | 1 (2.0) | |

*Palsy rates according to number of nerves at risk. GD = Graves’ disease.
postoperative hematoma ($p > 0.05$). The rate of postoperative hematoma was 6.5% for patients who had undergone total thyroidectomy, with a significant increase when compared to the analogous rate for total lobectomy (6.5% vs. 0.48%; $p < 0.05$). All patients who developed hypothyroidism after total thyroidectomy underwent thyroxine replacement. There was no mortality in this series.

**DISCUSSION**

Subtotal thyroidectomy has been considered the treatment of choice for benign thyroid disorders, such as multinodular goiter, thyroiditis, and Graves’ disease. Lower complication rates after subtotal thyroidectomy were advocated as compared to total thyroidectomy. With long follow-up of these cases, however, recurrence is often observed after subtotal thyroidectomy, with rates of 12–45% for nodular goiter [6–11] and 15–27.9% for Graves’ disease [12–15]. Several authors [16–19] have proposed that reoperation for recurrent disease carries a very significant risk of damage to the RLN and parathyroid glands. Therefore, total thyroidectomy has been widely adopted for the management of patients with benign disease when both lobes of the thyroid gland are involved. Total lobectomy with routine RLN identification is our basic procedure for solitary thyroid nodules [19]. When both lobes of the thyroid gland are involved, total thyroidectomy is our preferred option.

The reported complication rates after thyroid surgery are often underestimated because of the lack of routine perioperative examination of free calcium levels and vocal cords to document hypoparathyroidism and RLNP. In addition, many reports are retrospective and include operations performed by a number of surgeons using different surgical techniques over a long period. Thus, in this study, all the operations were performed by the same surgeon and perioperative free calcium levels and vocal cords were routinely examined, with the calculation of the RLNP rate based on the number of nerves at risk. The calculation of RLNP rate based on the number of nerves at risk seems to be a more logical method that allows meaningful comparison between different studies [16,19,20].

The debate over the use of total thyroidectomy for the treatment of benign thyroid disease typically revolves around the higher complication rates, particularly hypoparathyroidism. In recent literature [1–4,20–22], the incidence of temporary vs. permanent hypoparathyroidism after total thyroidectomy for benign thyroid disease was 12.9–35.4% vs. 0–3.4% (Table 2). In our series, the incidence of temporary and permanent hypoparathyroidism was 34.6% and 3.7%, respectively. We found that all cases of permanent hypoparathyroidism were in the Graves’ disease group. The rates of permanent hypoparathyroidism in the Graves’ disease group were significantly higher than that in the non-Graves’ disease group (8.3% vs. 0%, respectively; $p < 0.05$). However, the analogous comparison for temporary hypoparathyroidism did not yield a statistically significant difference (37.5% vs. 32.2%; $p > 0.05$). Trupka and Sienel [23] have advocated autotransplantation of at least one parathyroid gland during total thyroidectomy in benign thyroid disease to minimize the risk of

<table>
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<tr>
<th>Authors</th>
<th>$n^{bt}$</th>
<th>$n^{GD}$</th>
<th>Hypoparathyroidism, $n$ (%)</th>
<th>RLNP, $n$ (%)</th>
<th>Hematoma, $n$ (%)</th>
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<td>28 (26.4)</td>
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<td>37</td>
<td>41 (32.3)</td>
<td>2 (1.6)</td>
<td>6 (4.7)</td>
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<td>119</td>
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<td>782</td>
<td>53</td>
<td>101 (12.9)</td>
<td>10 (1.27)</td>
<td>17 (2.17)</td>
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<td>Bron &amp; O’Brien 2004 [4]</td>
<td>834</td>
<td>47</td>
<td>120 (14.4)</td>
<td>20 (2.4)</td>
<td>19 (2.3)</td>
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<td>Chiang et al 2006 (this study)</td>
<td>107</td>
<td>48</td>
<td>37 (34.6)</td>
<td>4 (3.7)</td>
<td>14 (6.5)*</td>
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*Palsy rates according to number of nerves at risk. $n^{bt}$ = total number of patients with benign thyroid disease; $n^{GD}$ = number of Graves’ disease patients; $n$ = number of patients.
permanent hypoparathyroidism. In our study, four Graves’ disease patients with permanent hypoparathyroidism underwent at least one parathyroid autotransplantation (two had one, one had two, and the remaining one had three glands implanted). Although not statistically validated, this result suggests that parathyroid autotransplantation cannot guarantee avoidance of permanent hypoparathyroidism. In this study, the reason for why permanent hypoparathyroidism was more prevalent after total thyroidectomy for Graves’ disease is unclear. Among the four Graves’ disease patients with permanent hypoparathyroidism, we found that two patients (one patient had three glands, and the other had two glands implanted) suffered postoperative hematoma, and the other two patients who had one gland implanted underwent parathyroid autotransplantation at the end of the operation. This may indicate that postoperative hematoma and delayed autotransplantation might be the culprits of graft failure. We had already modified our surgical technique of parathyroid autotransplantation by: (1) transplanting the devascularized gland immediately; (2) preparing the muscle pocket carefully to prevent hematoma; (3) mincing the gland into pieces as small as possible; (4) transplanting the glands into bilateral sternocleidomastoid muscles if more than one gland needed autotransplantation.

The reported incidence of temporary RLNP after total thyroidectomy for benign thyroid disease varies from 1.7% to 14.4%, and the incidence of permanent RLNP ranges from 0.38% to 1.9% (Table 2). In our study, the incidences of temporary and permanent RLNP were 6.5% and 1.85% of the nerves at risk, respectively. The rate of temporary RLNP in the Graves’ disease group was significantly higher than that in the non-Graves’ disease group (11.5% vs. 2.5%; \( p \leq 0.05 \)); however, as to the rate of permanent RLNP (2.0% vs. 1.7%; \( p > 0.05 \)), there was no significant difference. Several authors [21,24–26] have also reported higher temporary RLNP rates (8–14.4%) after surgery for Graves’ disease. Furthermore, we found that stretching of the nerve occurred more frequently during dissection of the RLN from a large thyroid mass with increased vascularity, and it seems to be reasonable to suggest that this stretching phenomenon is the reason for the higher rate of temporary RLNP in these patients.

All wounds were closed with suction drainage routinely. One drain tube was used for total lobectomy and two for total thyroidectomy. In our study, all postoperative hematomas occurred within 24 hours of the operation, and it was unusual in patients after unilateral total lobectomy. Rates of postoperative hematoma were 0.48% (2/417) after total lobectomy and 6.5% (7/107) after total thyroidectomy. Postoperative hematoma appeared to be more common in the Graves’ disease group; however, no significant difference between the two groups was demonstrated (10.4% vs. 3.4%; \( p > 0.05 \)). We found that postoperative hematoma still occurred after thyroidectomy, even though meticulous hemostasis had been performed for every patient. For patients with Graves’ disease awaiting operation, oral potassium iodine (Lugol) may be considered before thyroidectomy to minimize postoperative hematoma. Thyroid storm has become a rare problem with the advent of antithyroid drugs. We operated only on patients whose thyrotoxic state had been brought under control. However, thyroid storm still occurs infrequently with surgical manipulation of the thyroid gland. Thyroid storm occurred in one of our Graves’ disease patients when the operation had just been completed. Hematoma, high fever, and tachycardia occurred suddenly before the patient was sent to the recovery room. Fortunately, this patient recovered uneventfully after emergent management.

Three strategies are now available for the treatment of Graves’ disease: antithyroid drugs, surgery, and radioactive iodine. None of them has been shown to be ideal or superior to the other two. Physicians in different countries use varying approaches to provide optimal treatment for Graves’ disease. Antithyroid drugs are our first line of therapy for this disease. Our indications for surgery in Graves’ disease were: (1) large goiter; (2) worsening ophthalmopathy; (3) suspected concomitant thyroid malignancy; (4) severe side effects of antithyroid drug treatment. Total thyroidectomy is our preferred option for Graves’ disease because it has the advantages of immediate cure of any hyperthyroidism, avoidance of recurrence, and diminution of cancer risk. The reported prevalence for coexistent thyroid cancer ranges from 2.1% to 5% of Graves’ disease patients [21,22, 27]. In this study, out of the 48 Graves’ disease cases, six (12.5%) were associated with occult thyroid cancer.

In conclusion, this study showed that total thyroidectomy may be performed with minimal morbidity.
in non-Graves’ disease cases with benign thyroid disease, as claimed by many surgeons. But the risks of permanent hypoparathyroidism and temporary RLNP increased significantly in Graves’ disease patients after total thyroidectomy. The risk of postoperative hematoma was also higher in patients with Graves’ disease, but this difference did not reach statistical significance. Therefore, the operation in Graves’ disease patients requires a more skilled technique because of the high vascularity of the thyroid gland. Our main point is that patients must participate fully in the choice of treatment for Graves’ disease and be fully informed with respect to the advantages and disadvantages of each form of therapy [21]. It is recommended that total thyroidectomy for Graves’ disease be performed by an experienced surgeon.

**REFERENCES**

良性甲狀腺疾病接受全甲狀腺切除後的
併發症：特別比較 Graves’氏病和
非 Graves’氏病的差異

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目前已有很多報告顯示全甲狀腺切除可以用來安全地處理一些良性的甲狀腺疾病。本
研究的目的為回顧本科以全甲狀腺切除處理良性的甲狀腺疾病時可能發生的併發症，
特別比較 Graves’氏病和非 Graves’氏病的差異。本研究共收集於 1987 年 1 月至
2004 年 12 月間因雙側良性的甲狀腺疾病而接受全甲狀腺切除的病人共 107 位，
所有的病人皆由同一術者手術，其中包括 48 位為 Graves’氏病、59 位為非
Graves’氏病。術後發生暫時性 / 永久性側甲狀腺功能低下和暫時性 / 永久性喉返
神經麻痺的機率分別為 34.6%/3.7% 和 6.5%/1.85%。比較永久性側甲狀腺功能低下
和暫時性喉返神經麻痺的發生率發現 Graves’氏病的人比非 Graves’氏病的人
有顯著較高的發生率。但於暫時性側甲狀腺功能低下、永久性喉返神經麻痺及術後血
腫的發生率，兩組之間則沒有顯著的差異。全甲狀腺切除可以用來安全地處理一些非
Graves’氏病的良性甲狀腺疾病。但對於 Graves’氏病的病人仍有較高的永久性側
甲狀腺功能低下和暫時性喉返神經麻痺的發生率。因此對於以全甲狀腺切除來治療
Graves’氏病仍需相當的小心。

關鍵詞：Graves’氏病、低血鈣、喉返神經麻痺、甲狀腺、甲狀腺切除術

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