Editorial

Surgical Management of Graves' Disease: A Contemporary Perspective

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Historically, thyroid surgery was feared as a "foolhardy undertaking"[1] with a mortality rate of 40%[2] until Theodore Kocher pioneered the technique of capsular dissection in the late 1880s, transforming total thyroidectomy into a safe and effective procedure. However, after noticing that total thyroidectomy resulted in "cachexia strumipriva"—a failure to thrive original attributed to chronic asphyxia before the discovery of thyroxine—he abandoned total thyroidectomy and instead utilized a bilateral subtotal approach, in order to avoid hypothyroidism. Kocher reported a series of 900 thyroid operations with a mortality rate of 1% and in 1909 was the first surgeon to be awarded, the Nobel Prize for medicine.[2]

In 1913, through his observation of "thousands of patients with goitre, numerous cases of cretins and myxedematous patients,"[1] Henry Plummer made the revolutionary discovery that cellular energy production is controlled by the amount of thyroid hormone acting within the cells of the body. This compound, later named thyroxin, was isolated in 1914 by Kendall[3] and was extracted from animal thyroid in an inefficient and expensive process. A decade later, Harrington and Barger[4] corrected Kendall's description of its chemical structure, allowing synthesis of human thyroid hormone, which was initially available for US$350 per gram.

Subtotal thyroidectomy for the management of Graves' disease was the mainstay of treatment for most of the 20th century until Perzik[5] advocated total thyroidectomy after demonstrating an equivalent complication profile in a series of 909 patients. Bilateral subtotal thyroidectomy aims to minimize the risk of permanent hypoparathyroidism and recurrent laryngeal nerve injury by avoiding dissection of the tubercle of Zuckerkandl and Berry's ligament, leaving a posterosuperior thyroid remnant. In addition, it may obviate the need for long-term thyroid hormone replacement. These potential advantages must be balanced against the risk of recurrent hyperthyroidism (5–10%)[6] and goiter, and the increased risk of complications inherent with re-operative thyroid surgery.[7] Furthermore, long-term remnant failure occurs in 40 to 60% of patients after subtotal thyroidectomy, eliminating the theoretical benefit of avoiding thyroid hormone replacement.[8,9]

Through refinement of the technique of capsular dissection, an embryologic approach to remove all thyroid tissue, and parathyroid identification and preservation, the complication profile of total thyroidectomy has improved dramatically since Kocher's era. Surgeon experience is also significantly associated with decreased complication rates[10] and improved outcomes have coincided with trends toward surgeon specialization, with an increasing proportion of thyroid surgery being performed in more specialized centers. In a meta-analysis of the efficacy of thyroidectomy for Graves' disease, Palit et al[11] found no significant difference in complication rates between total and subtotal thyroidectomy. Koyuncu et al[9] prospectively randomized 200 patients with benign thyroid disease to undergo bilateral subtotal thyroidectomy, Dunhill's procedure, or total thyroidectomy, and found no difference in the rate of recurrent laryngeal nerve injury or hypoparathyroidism. A Cochrane review performed by Liu et al[6] aiming to compare different surgical techniques for the treatment of Graves' disease reported total thyroidectomy to be more effective than subtotal thyroidectomy at preventing recurrent hyperthyroidism with no difference in the rate of recurrent laryngeal nerve injury. However, a slightly greater risk of permanent hypoparathyroidism was noted, affecting 8/172 and 3/221 in the total thyroidectomy and subtotal thyroidectomy groups respectively. This finding was qualified with the statement that accurate conclusions were difficult to draw, as the evidence was of low quality and the event rate was exceedingly low.

In this retrospective review of 117 consecutive thyroidectomies performed for Graves' disease by the endocrine surgery unit at a tertiary university hospital in Singapore, Liu et al[6] compare the postoperative outcomes of total (n = 38) and subtotal (n = 79) thyroidectomy over a 25-year period. The study period included the transition in practice from routine subtotal thyroidectomy prior to 2006 to routine total thyroidectomy after 2009. No patient in the total thyroidectomy group had persistent disease, whereas among patients who underwent subtotal thyroidectomy, 22 (28%) suffered persistent or recurrent hyperthyroidism and 50 (63%) required long-term thyroxine replacement. There were no permanent vocal cord palsies in either group. Seventeen of the 117 patients (15%) developed permanent hypocalcemia; however, the breakdown of this data was not included in the manuscript. The authors report

that total thyroidectomy did not independently predict the development of permanent hypocalcemia; however, it was associated with increased odds of developing hypocalcemia (either temporary or permanent). Perhaps some of the difficulty in interpreting this data may be related to the low sample size in the total thyroidectomy group. The authors acknowledge that the study is inadequately powered to confidently draw conclusions from these results.

The aim of surgery for Graves' disease is to permanently cure the hyperthyroidism, minimize complications, and maximize patients' quality of life. In current clinical practice, reliable synthetic human thyroid hormone is widely available, and in many health care settings, experienced thyroid surgeons are also accessible. This study adds to the growing body of literature supporting total thyroidectomy as the operation of choice in the surgical treatment of Graves' disease. It results in significantly better outcomes in terms of permanent cure of hyperthyroidism and avoids the significant risks associated with reoperative thyroid surgery. The rates of permanent hypoparathyroidism after total and subtotal thyroidectomy are not definitively compared in this study, but in most previous studies have been shown to be similar. The authors should be commended for reviewing and publishing their own experience.

REFERENCES

1. Grant CS. Presidential address: boiling water to iodine—a story of unparalleled collaboration. Surgery 2002 Dec;132(6):909-915.
2. Welbourn, R. The history of endocrine surgery. New York: Praeger Publishers; 1990.
3. Kendall EC. The isolation in crystalline form of the compound containing iodine, which occurs in the thyroid: its chemical nature and physiologic activity. J Am Med Assoc 1915 Jun;64(25):2042-2043.
4. Harington CR, Barger G. Chemistry of thyroxine: constitution and synthesis of thyroxine. Biochem J 1927;21(1):169-183.
5. Perzik S. The place of total thyroidectomy in the management of 909 patients with thyroid disease. Am J Surg 1976 Oct;132(4):480-483.
6. Liu ZW, Masterson L, Fish B, Jani P, Chatterjee K. Thyroid surgery for Graves' disease and Graves' ophthalmopathy. Cochrane Database Syst Rev 2015 Nov;11:CD010576.
7. Menegaux F, Turpin G, Dahman M, Leenhardt L, Chadarevian R, Aurengo A, du Pasquier L, Chigot JP. Secondary thyroidectomy in patients with prior thyroid surgery for benign disease: a study of 203 cases. Surgery 1999 Sep;126(3):479-483.
8. Delbridge L. Total thyroidectomy: the evolution of surgical technique. ANZ J Surg 2003 Sep;73(9):761-768.
9. Koyuncu A, Dökmetas HS, Turan M, Aydin C, Karadayi K, Budak E, Gökgöz S, Sen M. Comparison of different thyroidectomy techniques for benign thyroid disease. Endocr J 2003 Dec;50(6):723-727.
10. Sosa JA, Bowman HM, Tielsch JM, Powe NR, Gordon TA, Udelsman R. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. Ann Surg 1998 Sep;228(3):320-330.
11. Palit TK, Miller CC 3rd, Miltenburg DM. The efficacy of thyroidectomy for Graves' disease: a meta-analysis. J Surg Res 2000 May;90(2):161-165.

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