A systematic review and meta-analysis of total thyroidectomy versus bilateral subtotal thyroidectomy for Graves' disease

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Background. *Our aim was to perform a meta-analysis of high-quality published trials, randomized and observational, comparing total thyroidectomy (TT) and bilateral subtotal thyroidectomy (ST) for Graves' disease.*
Methods. *All studies published from 1970 to August 2012 were identified. All randomized controlled trials (RCTs) were included. Selection of high-quality, nonrandomized comparative studies (NRCTs) was based on a validated tool (Methodological Index for Nonrandomized Studies). Recurrent hyperthyroidism during follow-up, progression of ophthalmopathy, postoperative temporary and permanent hypoparathyroidism, and permanent recurrent laryngeal nerve (RLN) palsy were compared using odds ratios (ORs).*
Results. *Twenty-three studies were included (4 RCTs and 19 NRCTs) compromising 3,242 patients (1,665 TT, 1,577 ST). TT was associated with a decrease in recurrent hyperthyroidism (*$P < .00001$*; OR, 0.10; 95% confidence interval [CI], 0.06–0.18), but with an increase in both temporary (*$P < .00001$*; OR, 2.70; 95% CI, 2.04–3.56) and permanent hypoparathyroidism (*$P = .005$*; OR, 2.91; 95% CI, 1.59–5.32). Progression of ophthalmopathy (*$P = .76$*; OR, 0.90; 95% CI, 0.48–1.71) and permanent RLN palsy (*$P = .82$*; OR, 0.91; 95% CI, 0.41–2.02) were similar.*
Conclusion. *TT offers a better chance of cure of hyperthyroidism than bilateral ST and can be accomplished safely with only a small increase in temporary and permanent hypoparathyroidism. (Surgery 2014;155:529-40.)*

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Graves' disease (GD), the most common cause of hyperthyroidism, is an autoimmune disorder characterized by circulating thyroid-stimulating immunoglobulins that bind the thyrotropin receptor.[1] This inhibition leads to sustained hyperfunctioning of the thyroid gland with a resultant oversecretion of thyroid hormone. Options for treatment include antithyroid medication or definitive treatment via radioactive iodine ablation or thyroidectomy, and the method of choice differs dramatically depending on regional preference.[2]

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Radioactive iodine ablation with ^{131}I is usually preferred in the United States, whereas in Europe and Asia, antithyroid drugs or thyroidectomy tend to be favoured.[3] Generally, antithyroid medication is the preferred initial therapy, with thyroidectomy or radioactive iodine ablation considered as a second choice when drug therapy fails or in cases of recurrence.[2] Traditionally, the operative procedure for GD has been bilateral, subtotal thyroidectomy (ST), but during the last decade, many endocrine surgeons have advocated total thyroidectomy (TT) as the gold standard.[4-11] The extent of resection in patients with GD is an important and widely debated question. TT for GD decreases recurrence rates; however, this benefit should be balanced against an assumed greater risk of complications after more radical thyroid resection.[2,4,5,8-11]

The aim of our study was to perform an updated evaluation of all available, high-quality, published trials, randomised and observational, that

Table. Modified Methodological Index for Nonrandomized Studies scale used for quality assessment of NRCT

Item	*Points*		
	0	*1*	*2*
Statement of the study aim	Not reported	Unclearly stated	Clearly stated
Consecutive patients	Not reported	Patients are not consecutive	Patients are consecutive
Prospective data	Not reported	Collection Data is obtain from retrospective review of medical history	Data is obtained from prospectively maintained database
Reported endpoints	Not reported	Only secondary or incomplete primary outcomes reported	Complete primary outcomes reported
Unbiased assessment of the study endpoints	Not reported	Non blind evaluation of endpoints	Blind evaluation of endpoints
Appropriate controls	Not reported	Incomplete report of the standard intervention	Complete report of the standard intervention
Contemporary groups	Not reported	Study group compared with historical control group	Study group compared with contemporary control group
Groups equivalent*	No matching analysis performed	Matching incomplete	Matching complete
Sample size	<50 thyroidectomies	50–100 thyroidectomies	>100 thyroidectomies
Adequacy of statistical methods	Not reported	Inadequate	Adequate
Adequate follow-up period†	Not reported	Inadequate	Adequate
Follow-up loss <5%	Not reported	>5%	<5%

*Factors considered: Demographics (age, gender), mean thyroid resected (g), mean operative time (min), Mean BLOOD loss (mL), mean hospital stay (d).
†At least 12 months.

compared TT with bilateral ST for GD. The potential advantages of each technique were quantified using the meta-analytical method.

METHODS

Eligibility criteria. *Types of studies.* We evaluated all randomised (RCT) and nonrandomized (NRCT) controlled trials with no restrictions on languages or regions published from 1970 through December 1, 2012, comparing TT to ST for GD. Noncomparative studies, animal studies, and grey literature (written material that is difficult to find via conventional channels because it is unpublished or inaccessible) were excluded. Studies were excluded from the analysis when the primary outcome of interest for the 2 techniques was not reported. If 2 studies from the same institution were identified, the most recent or the most informative was selected, unless they were reports from different time periods or the data of overlapping patients could be removed selectively.

Types of interventions. Only TT and bilateral ST for GD were considered. Other interventions, such as unilateral thyroid lobectomy or total lobectomy on 1 side with a subtotal lobectomy on the other side,[12] were excluded unless the data were presented separately. Data concerning the weight of the remnant thyroid tissue after ST were collected.

Types of outcome measures. The primary outcome measure was recurrent hyperthyroidism during follow-up and progression of ophthalmopathy. The secondary outcome measure was postoperative temporary and permanent hypoparathyroidism and permanent, recurrent laryngeal nerve (RLN) palsy (Appendix 1).

Because only 1 study defined temporary RLN palsy and only 1 other study defined postoperative bleeding, these variables could be equally evaluated in a meta-analysis in the same way other outcomes defined in multiple studies are compared. As such, their statistical relevance and comparison is not well-justified to report out in same way as the other more well-characterized variables/outcomes.

Search. Two authors (MR and AB) conducted the electronic bibliographic research independently according to the validated methods of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement[13] using the following databases: Medline, Embase, Web of Science, and The Cochrane Library. The database search (date range,