

Thyroidectomy Then and Now: A 50-Year Australian Perspective

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Abstract

Background Since the mid-1800s, thyroidectomy has transformed from a procedure associated with high to near-zero mortality. Nonetheless, surgeons must continue to strive to improve patient care. Using historical records and contemporary data, this study compares the practice and outcomes of thyroid surgery at a tertiary institution during two periods, 50 years apart.

Methods ‘The Alfred Hospital Clinical Reports’ recorded all cases of surgically managed thyroid disease from 1946 to 1959. These *historical* cases were compared to *contemporary* thyroidectomy cases at the Alfred Hospital from 2007 to 2016. Cases were compared for surgical indication and post-operative outcomes.

Results There were 746 patients in the *historical group* (mean age 53 years; 87% female) and 787 patients in the *contemporary group* (mean age 52 years; 80% female). The most common indication for thyroidectomy in both groups was non-toxic nodular goitre. A greater proportion of the *contemporary group* were diagnosed with thyroid malignancy (27% vs. 8%; $p < 0.001$). The *contemporary group* recorded significantly fewer cases of thyrotoxic crisis (2.1% vs. 0%; $p = 0.001$), permanent nerve palsy (4.6% vs. 0.4%; $p < 0.001$) and bilateral nerve palsy (1.2% vs. 0%; $p = 0.01$). There were no mortalities in the *contemporary group*, while the historical data recorded three deaths (0.44%).

Conclusions This study compared thyroid surgery in two cohorts separated by a 50-year period. While it is not surprising that outcomes of thyroidectomy have improved, this study uniquely demonstrates trends of thyroid surgery over time and areas in which further improvements may be made.

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Introduction

Thyroid surgery has travelled a long and contentious path through time. The earliest documented attempts at thyroidectomy are attributed to Albucasis, a tenth century Moorish surgeon [1]. While others strived to advance the

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procedure over the coming centuries, early thyroidectomies produced frightening results with high mortality and morbidity [2]. Eventually, the procedure was reserved for the most severe cases of goitre [3].

With the advent of antiseptic surgical technique, Theodor Billroth (1829–1894), the famed Austrian surgeon, reduced his mortality rate from 40 to 8% in 1877 [4]. Theodor Kocher (1841–1917) of Switzerland continued to advance the procedure [5]. By the end of his career, over 5000 thyroidectomies were attributed to Kocher with a mortality rate of < 0.5% [5, 6]. Thomas Dunhill (1876–1957), an Australian surgeon, contributed significantly to the field during the same period with his experience with thyroidectomy in thyrotoxicosis. He operated on acutely toxic patients and, despite this, had a mortality of < 1% [7].

Thyroidectomy has undergone major evolutions and transformed from a procedure associated with high mortality and morbidity to near-zero mortality in modern practice. Nonetheless, surgeons should endeavour to improve patient care and outcomes.

Using historical records and analysis of contemporaneous data, this study aimed to compare the practice and outcomes of thyroid surgery at an Australian tertiary institution during two periods, 50 years apart, with the objectives of better understanding the advances made and identifying areas for improvement.

Methods

Historical cases

The ‘Alfred Hospital Clinical Reports’ were a series of hardbound publications that recorded areas of work undertaken at The Alfred Hospital, a tertiary referral centre in Melbourne, Australia, from 1949 to 1967. Included in the 1960 volume was a report titled ‘Review of thyroidectomy at the Alfred Hospital: 1946–1959’ (Fig. 1) [8]. This report was compiled by general surgeon Dr Nicholas Hamilton and detailed all cases of thyroidectomy during this 14-year period. There was no specific unit for the management of thyroid disease at this time. The report summarized the surgical indications and outcomes with data obtained from the notes of 25 surgeons who performed the operations. Cases in this report comprised the *historical group* of this study.

Contemporary cases

Cases of total thyroidectomy were recruited from the Monash University Endocrine Surgery Unit (MUESU) database during a 10-year period (2007–2016). During this

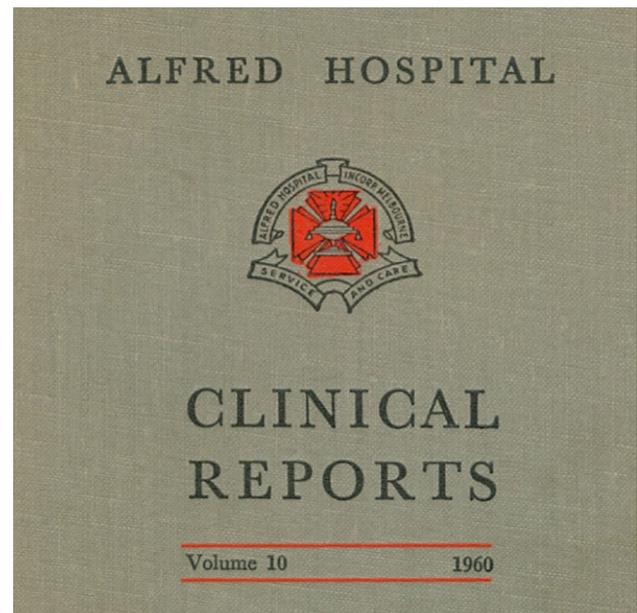


Fig. 1 Hardcover of the 1960 ‘Alfred Hospital Clinical Reports’ which contains the report by Nicholas Hamilton on thyroid surgery

period at the Alfred Hospital, thyroid surgery was performed by five surgeons in a dedicated Endocrine Surgery Unit. Data comparable to Hamilton’s report were extracted and the two groups compared.

Case file review

Cases in the *historical* and *contemporary* groups were compared for surgical indication and post-operative outcomes including rates of nerve palsy, hypocalcemia, haemorrhage, thyrotoxic crisis, wound infections and mortality.

Surgical indications in the *contemporary group* were categorized identically to Hamilton’s report to allow comparison—including Graves’ disease, toxic multinodular goitre (MNG), non-toxic nodular goitre, carcinoma and other. The historical paper did not describe pathologies included in the ‘other’ category. If a *contemporary* patient required thyroidectomy for an indication that could not be categorized into one of the categories, they were included in the ‘other’ category.

Hamilton reported post-operative complications in 680 patients, but excluded complications related to carcinoma and ‘other’ cases. Data detailing post-operative complications were available for all *contemporary* cases. To enable a true comparison, complications relating to carcinoma and ‘other’ cases were excluded from analysis.

In the *historical group*, 78% of patients underwent a post-operative laryngoscopy. The timing of the examination is not known. In calculating post-operative palsy rates, all relevant patients were included irrespective of whether

Table 1 Summary of demographics, data source, operator factors and surgical indications

Variable	Historical group	Contemporary group	<i>p</i> value
No. of patients	746	787	
Gender, <i>n</i> (%)			0.001
Female	646 (87)	632 (80)	
Male	100 (13)	155 (20)	
Mean age, years	53	52	
Data source	1960 Alfred Hospital Clinical Reports	MUESU Database	
Data period	1946–1959 (14-year period)	2007–2016 (10-year period)	
Surgical technique	Subtotal thyroidectomy ^a	Total thyroidectomy	
Number of surgeons	25	5	
Surgical indication, <i>n</i> (%)			
Graves' disease	146 (20)	133 (17)	0.18
Toxic multi-nodular goitre	111 (15)	121 (15)	0.79
Non-toxic nodular goitre	421 (56)	276 (35)	<0.001
Carcinoma	56 (8)	214 (27)	<0.001
Other	12 (2)	43 (5) ^b	<0.001

^aSurgical technique was not specified in the Hamilton Report, but approximately 80% involved bilateral surgery and were likely to be subtotal thyroidectomy as this was the common surgical technique for management of thyroid disease at the time [27]

^bThe 'other' thyroidectomy indications of the *contemporary group* included Hashimoto's thyroiditis, lymphocytic thyroiditis, amiodarone thyrotoxicosis, benign cysts, colloid/hyperplastic nodules, follicular adenomas, Hurthle cell adenomas and hyalinizing trabecular tumours

they had laryngoscopy. It was felt that if patients who did not have a laryngoscopy were excluded, we would likely be excluding many of those without a suspicion for palsy, and risk overestimating the palsy rate. All patients in the *contemporary group* had a laryngoscopy on post-operative day 1.

Antithyroid medications

In the *contemporary group*, pre-operative treatment for thyrotoxic patients was with carbimazole, with propylthiouracil as an alternative. Lugol's iodine was added for 7 to 10 days prior to thyroidectomy for patients with Graves' disease. In Hamilton's report, the use of these three agents was described in the subgroup of patients in whom thyrotoxic crisis occurred, but only for up to 3 weeks prior to thyroidectomy. The patient's functional status at the time of surgery was not known, and whether this approach was used in all clinically thyrotoxic patients was unclear.

Statistical analysis

Patient characteristics, surgical indications and post-operative outcomes were summarized using counts and proportions. Comparisons between the historical and contemporary cohorts were made using Chi-square test for equal proportions or Fisher's exact test where numbers

were small. A two-sided *p* value of < 0.05 was considered to be statistically significant. When insufficient details were available in the *historical group*, no *p* value is provided. Analysis was performed with Stata software version 14 (StataCorp, Texas, USA).

Results

There were 746 patients in the *historical group* and 787 patients in the *contemporary group* (Table 1). A female preponderance was noted in both the *historical* (87%) and *contemporary groups* (80%), with a mean age of 53 years and 52 years, respectively. There was insufficient information to calculate the standard deviation (SD) of age in the *historical group*, and hence SD and *p* value were not reported.

Surgical indication

The most common indication in both groups was non-toxic nodular goitre (Table 1), though a significantly higher proportion of *historical* patients underwent thyroidectomy for this indication (52% vs. 35%; *p* < 0.001).

In the *contemporary group*, a significantly higher proportion of patients were diagnosed with thyroid malignancy compared to the *historical group* (27% vs. 8%;

$p < 0.001$). This was true even if cases of microcarcinomas in the *contemporary group* were not considered to be malignant cases, thus reducing malignant rate of the *contemporary group* to 18% ($p < 0.001$). The size of cancers was not reported for the *historical group*.

There was a trend towards increasing rates of malignancy over time in both groups. In the *historical group*, 16 (4.4%) cases of thyroid malignancy were diagnosed in the first seven years, and 40 (10.5%) cases in the latter seven years. This trend was also seen in the *contemporary group* where 91 (24.4%) cases of malignancy were diagnosed in the first five years, and 123 (29.7%) cases in the subsequent 5 years.

Operative complications

Vocal cord palsy

In the *historical group*, recurrent laryngeal nerve (RLN) injury occurred in 36 (5.3%) patients (Table 2). Of these, 31 (4.6%) were permanent, and eight (1.2%) were bilateral. This equates to 44 (3.6%) nerve injuries out of 1210 nerves at risk (NAR). It was noted that a greater incidence of nerve injuries occurred in the toxic cases (6.6% of NAR). The incidence of vocal cord palsy varied among 25 surgeons from zero to 20% of NAR. However, the number of thyroidectomies per surgeon was not available.

By comparison, fewer palsies were noted in *contemporary* patients (21, 4.0%). There were significantly fewer cases of permanent palsy (2, 0.4%, $p < 0.001$) and no bilateral palsy. Only 2.0% of 1 060 NAR sustained a palsy,

significantly lower than the *historical group* ($p = 0.02$). It is worth noting that intraoperative neuromonitoring of the RLN has been routine practice at this institution since 2009. There was no significant difference in the rate of nerve palsy before or after the introduction of intraoperative neuromonitoring (1.1% vs 4.6%; $p = 0.15$).

Hypocalcemia

In the *historical group*, 20 (2.9%) patients developed tetany following thyroidectomy. Routine calcium monitoring was not performed in this group. In the *contemporary group*, hypocalcemia was detected by routine serum calcium measurements post-thyroid surgery in 38 (7.2%) patients. Permanent hypocalcemia rates were similar in both groups (0.4% and 0.6%, respectively).

Haemorrhage

When the *historical* and *contemporary* groups were compared, no difference in the number of patients with post-operative haemorrhage was noted (1.8 vs 2.3%; $p = 0.54$). In the *historical group*, haemorrhage requiring operative wound exploration occurred in 12 cases (1.8%). A bleeding vessel was identified in one case, and the remaining 11 cases were packed, with three requiring a tracheostomy. In the *contemporary group*, 12 cases (2.3%) had post-operative bleeding requiring return to theatre for exploration. Three of these were delayed haematomas, occurring more than 48 h after operation. Of note, five patients were on anticoagulants pre-operatively; all had Graves' disease,

Table 2 Operative complications

Complication	Historical group (<i>N</i> = 680)	Contemporary group (<i>N</i> = 530 ^a)	<i>P</i> value
Vocal cord palsy, <i>n</i> (%)	36 (5.3)	21 (4.0)	0.28
Permanent palsy, <i>n</i> (%)	31 (4.6)	2 (0.4)	<0.001
Bilateral palsy, <i>n</i> (%)	8 (1.2)	0 (0.0)	0.01
Nerve injuries per NAR, <i>n</i> (%)	44 (3.6)	21 (2.0)	0.02
	(<i>N</i> = 1210)	(<i>N</i> = 1060)	
Hypocalcemia, <i>n</i> (%) ^b	20 (2.9)	38 (7.2)	0.001
Haemorrhage, <i>n</i> (%)	12 (1.8)	12 (2.3)	0.54
Thyrotoxic crisis, <i>n</i> (%)	14 (2.1)	0 (0.0)	0.001
Wound infection, <i>n</i> (%)	15 (2.2)	0 (0.0)	0.001
Mortality, <i>n</i> (%)	3 (0.4)	0 (0.0)	0.26

NAR Nerves at risk

^aThe number of *contemporary* cases is smaller compared to Table 1. Cases of carcinoma and 'other' pathology were excluded from analysis to allow an accurate comparison to the *historical group*

^bHamilton's report only included cases of tetany (severe hypocalcemia). All *contemporary* cases underwent routine post-operative calcium monitoring. Comparing tetany to contemporary hypocalcemia detected by routine post-operative blood tests is not a fair comparison

retrosternal goitres or both; and one patient had a previously undiagnosed bleeding diathesis. None in the *contemporary group* required tracheostomy and all were closed primarily with insertion of drains after exploration.

Thyrotoxic crisis

Thyrotoxic crisis only occurred in the *historical group* (2.1%)—nine of these patients had Graves' disease, and five had a toxic MNG. Two of these cases were fatal.

In the *contemporary group*, all patients were clinically euthyroid at the time of surgery; however, 37 patients had mildly deranged thyroid function tests. Of these, 14 patients had subclinical hypothyroidism (suppressed TSH with normal T3/T4), and 23 had elevated T3 and/or T4 levels.

Wound infection

No patient in the *contemporary group* suffered wound infections, while 15 patients in the *historical group* (2.2%) had a wound infection. It was reported that all these were secondary to a haematoma, and three required operative treatment. In the *contemporary group*, only one wound infection was recorded for the period. However, this patient had thyroidectomy for carcinoma and was therefore excluded from this comparison.

Mortality

There were three deaths in the *historical group*. Two cases were due to inadequate pre-operative preparation of thyrotoxicosis, while the cause of death for the third case was pulmonary embolism in the setting of post-operative pneumonia. No deaths were recorded in the *contemporary group*.

Discussion

Our study identified a changing pattern in indications for thyroidectomy. Furthermore, analysis identified significantly fewer cases of operative complications including permanent and bilateral nerve palsy, thyrotoxic crisis, wound infection and mortality.

Non-toxic MNG remained the most common indication in both time periods while the incidence of thyroidectomy for malignancy in the *contemporary group* more than tripled compared to the *historical group* (27% vs. 8%; $p < 0.001$). Data released by the Australian Institute of Health and Welfare support this trend. Between 1982 and 2017, the incidence of thyroid cancer in Australia rose from 2.7 to 12 per 100 000 persons [9]. A recent study

reported the incidence of thyroid cancer in the USA increasing by 3% annually over a 40-year period to 2013 [10].

While the incidence of thyroid cancer is rising, it is difficult to ascertain whether this is a genuine increase in its prevalence, or an increase in the detection of subclinical cancers due to modern diagnostic technology. This is not supported by a New York Institute of Cancer study that reported while incidental detection may contribute, it does not explain significant rises observed in the incidence of larger cancers [11]. Our data also demonstrated a significant difference in malignancy rates between groups, even when microcarcinomas were excluded.

Morbidity and mortality improved in the *contemporary group* across the majority of measures used by Hamilton's report. This is not surprising as the principles of safe thyroid surgery have been well established. Moreover, in the *historical group*, surgery was performed by 25 surgeons presumably with varying degrees of training and experience in thyroid surgery. By comparison, five high-volume endocrine surgeons contributed cases to the *contemporary group*. This surgeon volume–outcome association is supported by a 2017 study that found the risk of post-operative complications increased by 87% if the surgeon only performed one thyroidectomy per year [12], and another study that found high-volume surgeons had a significantly lower incidence of nerve palsy and hypocalcemia [13].

The RLN is vulnerable to injury during thyroid surgery, and permanent nerve injury has been documented in up to 5% of cases [14, 15]. With high rates of post-operative laryngoscopy in both groups, RLN palsy rate was higher in the *historical group*, especially in permanent and bilateral palsies. These findings concur with studies that suggest avoiding permanent and bilateral palsies being the key benefits of intraoperative neuromonitoring, which was used in the majority of cases in the *contemporary group* [16, 17]. Other contributing factors may include operator volume and better understanding of RLN anatomy [18–20]. A recent study found a positive correlation between patient-reported voice change post-hemithyroidectomy and degree of RLN swelling, suggesting the importance of minimizing surgical trauma in preserving RLN function [21].

Although the overall rates of post-operative hypocalcemia cannot be accurately compared due to the Hamilton report only reporting tetany in the *historical group*, rates of permanent hypocalcemia were similar in the two groups. A multicentre analysis of over 14 000 patients reported temporary hypoparathyroidism in 8.3% and persistent hypoparathyroidism in 1.7% [14]. This suggests that our institution's respective rates of 5.6% and 0.4% are comparable to other high-volume institutions.

The reported incidence of post-thyroidectomy haemorrhage varies widely from 0.4 to 4.3% [22–24]. The rates of haemorrhage requiring return to theatre were similar between groups. Rates of post-operative haemorrhage during Hamilton's time were low, as principles of haemostasis were well established [25]. The use of Liga-Sure™ was introduced during the *contemporary* study period. Its introduction may have been accompanied by an operator learning curve, resulting in similar haemorrhage rates between groups. The overall rate for post-operative haemorrhage in the MUESU database has been previously reported as 1% [26]. This figure includes all 13 institutions where the five contributing surgeons work, whereas this study only includes patients from one of those institutions and only patients who had a total thyroidectomy. Therefore, this differential may reflect a selection bias where more complex cases are selectively booked at this tertiary institution.

The key challenge faced in this study was drawing conclusions from Hamilton's report to make comparisons to our contemporary data. Hamilton's grouping of indications and exclusion of 'carcinoma' and 'other' patients from post-operative complication analysis necessitated that we group and analyse the *contemporary group* in a similar fashion. Despite this difficulty, it is clear that the indications for thyroidectomy have evolved over time, and morbidity and mortality rates have improved.

Our institution is similar to many other high-volume endocrine surgery centres, and we believe that our results may be generalized to other health services. This will enable us to identify evolving patterns in thyroidectomy indications and facilitate surgeons to continue striving to optimize patient care by further reducing morbidity and mortality.

Conclusions

While it is not surprising that outcomes have improved as thyroid surgery has progressed, this study demonstrates that while morbidity and mortality rates were low, we can still strive to further improve patient outcomes. The improvement in rates of nerve palsy, thyrotoxic crisis, wound infection and mortality reflect multifactorial advancements in surgical technique, medical management of thyrotoxicosis and peri-operative care. Reflective practice is the foundation of professional development. It facilitates self-growth and the development of new skills, and this study allowed us to reflect on our collective progress over the past 50 years. We are indebted to the surgeons of the past whose efforts in advancing the field of thyroid surgery, both technically and academically, have enabled us to provide safe thyroid surgery to our patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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