# Тематическое контролируемое исследование безопасности тотальной тиреоидэктомии для лечения амиодарон-индуцированного тиреотоксикоза

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**Цель.** Амиодарон является жизненно важным лекарством, но способным провоцировать развитие амиодарониндуцированного тиреотоксикоза (АмИТ) – угрожающего жизни побочного эффекта, который может вызвать серьезную сердечную дисфункцию и привести к развитию сердечной недостаточности. Небольшая часть пациентов не отвечает на терапию, а степень сердечной дисфункции у них продолжает расти. Больным из этой группы обычно выполняют тотальную тиреоидэктомию. Без хирургического удаления щитовидной железы смертность этих пациентов достигает 30–50%. Хотя хирургические вмешательства считаются более безопасными у эутиреоидных пациентов, продление медикаментозной терапии может привести к ухудшению сердечной функции и повышению хирургических рисков. Исследование направлено на изучение безопасности хирургического лечения АмИТ у пациентов, для которых медикаментозная терапия оказалась неэффективной.

**Методы.** Мы проводили сравнение пациентов, подвергшихся хирургическому лечению АмИТ, и пациентов, перенесших тотальную тиреоидэктомию по другим показаниям. Нами были проанализированы демографические данные пациентов, сведения об их ASA-статусах, весе щитовидной железы, осложнениях (возникших в результате хирургического лечения и наркоза) и частоте тиреотоксического криза.

**Результаты.** Это исследование позволило продемонстрировать, что тотальная тиреоидэктомия является относительно безопасной процедурой для лечения АмИТ, который не поддается медикаментозной терапии. Выявлена сходная частота развития осложнений у пациентов двух групп.

**Выводы.** Тотальная тиреоидэктомия является безопасной процедурой и может выполняться у пациентов с АмИТ. **Актуальность.** Наши данные дают хирургам возможность объяснить пациенту реальные риски при данной операции. Они также обеспечивают лечащему врачу уверенность в безопасности процедуры у больных с амиодарон-индуцированным тиреотоксикозом.

Ключевые слова: тиреоидэктомия, амиодарон, безопасность, случай-контроль.

## Case-control study of the safety of total thyroidectomy for amiodarone-induced thyroiditis

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**Aim.** Amiodarone, can be a life-saving medication however it can also cause amiodarone-induced thyroiditis (AIT). AIT is a complex and life-threatening side effect which can cause significant cardiac dysfunction and lead to cardiac failure. A small sub-group do not respond to medical therapy and their cardiovascular function continues to deteriorate. This select group is referred for a semi-elective total thyroidectomy. Without surgical removal of their thyroid gland these patients have a 30-50% mortality rate. Though surgery is known to be safer in euthyroid patients, prolongation of medical therapy can lead to worsening of heart function and higher surgical risk. This research aims to evaluate the safety of surgical management of AIT in those who have failed medical treatment.

**Method.** A comparison was made between a group of surgically-treated AIT patients to a group of patients undergoing total thyroidectomies for alternate reasons. The patient demographics, ASA states, weight of the thyroid gland, surgical complications, anaesthetic complications and incidence of thyrotoxic crisis were assessed.

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**Results.** This research has shown that a total thyroidectomy is a relatively safe procedure to treat AIT that is not responding to medical therapy. Similar complication rates between the two groups were evident. **Coinclusion.** Total thyroidectomy is an equivocally safe procedure to perform in patients with AIT. **Clinical Significance.** Surgeons can consult their patients with realistic risks for their surgery. treating physicians can feel confident that surgery is a safe option for their patients with amiodarone-induced thyroiditis. **Key words:** thyroidectomy, amiodarone, safety, case-control.

### Introduction

Amiodarone, can be a life-saving medication in the treatment of tachy-arrhythmias and has been shown to improve survival rates in patients with heart failure, however it has multiple side effects [1]. Amiodarone is 37% iodine and this iodine load can trigger increased thyroid hormone synthesis and release. Yet amiodarone also decreases peripheral de-iodination of thyroxine  $(T_4)$  to triiodothyronine  $(T_3)$  by inhibiting liver type I iodothyronine 5'-deiodination of  $T_4$  [2].

This interference in thyroid function can lead to amiodarone-induced thyrotoxicosis (AIT), a complex and life-threatening side effect with an incidence of 3–5% in Australia [3]. It is difficult to manage due lack of response to medication, worsening of tachy-arrhythmias in patients with poor cardiac function and the possibility of needing to continue amiodarone to control an arrhythmia [3]. The duration between amiodarone use and the presentation of AIT is variable and can range from two to 47 months [4].

The onset is rapid and fulminant. TFTs usually show a low thyroid-stimulating hormone (TSH), a high  $T_4$  and normal or slightly high  $T_3$ . Other forms of iodine-induced thyrotoxicosis are generally managed conservatively due to their self-limiting nature. The long half-life of amiodarone (~107days) means that patients are still exposed to the rapeutic levels for a long time after cessation. Conservative management may not be suitable due to the associated cardiac dysfunction as AIT can worsen pre-existing arrhythmias, cardiac failure, angina pectoris and cardiomyopathy [1]. Current practice is to withdraw amiodarone when feasible, however due to the inhibiting effect on the peripheral de-iodination, there can be a paradoxical worsening of the patient's condition on cessation of therapy.

There is a male predisposition with a male: female ratio of ~ 3: 1 and a tendency to occur in iodine-deficient areas. AIT manifests as three types; type I occurs in abnormal thyroid glands via a Jod-Basedow phenomenon, where the iodine loading unmasks underlying thyroid autonomy. Type II is a destructive thyroiditis leading to the release of preformed hormones from an intrinsically normal thyroid gland and type three is a mixed type. The histopathology for all types' shows marked destruction of follicles, with inflammation and fibrosis [5].

The medical management is challenging, poorly understood and lacks a proven, consistent therapeutic armamentarium, though the literature reports 20% of cases remit spontaneously [1]. Radioiodine therapy is not feasible due to the suppressed iodine uptake, delayed effect, and potential for further hormone release [6].

Treatment may take up to four months to become effective and no regimens have demonstrated reliable success. These patients have pre-existing cardiac dysfunction and do not tolerate hyperthyroidism well; they require timely resolution of their AIT [7]. Chemical treatment also has significant side effects.

Overall, the difficulties with medical management are:

- 1. amiodarone may be the only effective agent and cannot be ceased:
- 2. cessation of amiodarone can cause paradoxical rise in T<sub>3</sub>, worsening thyrotoxicosis;
- 3. it may take months for the patient to achieve a euthyroid state with medication;
- 4. the medication may never induce a response:
  - 5. the medication has known side effects.

Plasmapheresis and haemodialysis, can provide acute but transient relief but are extremely expensive and impractical in the long term.

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The small selection of patients who do not respond to medical treatments have uncontrolled thyrotoxicosis, the potential to develop a thyrotoxic crisis, and generally end-stage cardiac failure. This select group is referred for a semi-elective total thyroidectomy [8]. There is minimal research on this subset of patients and no guidelines as to when surgery is indicated.

With increasing levels of  $T_4/T_3$  there is increased systemic vascular resistance, heart rate, ejection fraction, cardiac output and blood volume but a decrease in isovolumetric relaxation time [9]. Though surgery is known to be safer in euthyroid patients, there is evidence that a general anaesthetic can be safely undertaken in patients with thyrotoxicosis and severe cardiac disease [9].

Without a thyroidectomy these patients will continue to deteriorate, and have a mortality rate of 30–50% [6]. This rate is reduced to 0–13% when a thyroidectomy is performed [10]. Surgery should be considered before complete failure of medical therapy occurs, to avoid intra-operative anaesthetic complications associated with the cardiovascular status of the advanced condition [11].

Current agreed upon indications for surgery are:

- 1. when amiodarone is essential despite thyrotoxicosis;
- 2. type I or mixed AIT, since the thyroid disorder may maintain the thyrotoxicosis to which amiodarone contributes:
  - 3. patients awaiting heart transplant;
  - 4. failure of anti-thyroid treatment.

The current difficulty lies in defining the criteria of medical treatment failure in a standardised manner, to avoid emergency thyroidectomy [12].

Further research is needed to develop guidelines for which patients should trial chemical management and for what duration. This research may demonstrate that surgery is safer than natural history and sometimes medical treatment, for this potentially lethal disease [13]. The aim of this case-control study is to determine if a total thyroidectomy is a comparably safe procedure for patients with AIT. It is expected that total thyroidectomies for patients with AIT will show comparable clinical outcomes

to total thyroidectomies performed to alternative indications.

### **Clinical Significance**

The clinical significance of this research is that it demonstrates the safety in performing total thyroidectomies in patients with amiodarone-induced thyroiditis. The risks have been shown to be comparable to performing a thyroidectomy in patients for alternative indications. This allows the surgeon to consult the patient with realistic risks for their surgery. It also provides treating physicians with confidence that surgery is a safe option for their patients with amiodarone-induced thyroiditis.

### **Methods**

A retrospective case series was performed. From January 1998 To November 2015, pathology records were screened for thyroid tissue and the records of patients who had a total thyroidectomy at The Prince Charles Hospital (TPCH), Australia were selected and reviewed. Ethics approval was obtained from the Human Research and Ethics Committee (HREC) at TPCH.

### **Pre-operatively**

The patients' demographics, amiodarone use, indications, doses and duration prior to the diagnosis were noted.

### **Anaesthesia and Surgery**

Pre-operatively the American Society of Anaesthesiology (ASA) status was also noted. All surgeries were performed under general anaesthesia. Thyroidectomy was as total as possible in each case.

#### Post-operatively

Post-operatively, the histopathology, weight of the gland and incidence of surgical, anaesthetic and other complications were recorded. Surgical complications included; infection, bleeding, hypocalcaemia, recurrent laryngeal nerve palsy, thyrotoxic crisis, return to theatre, deep vein thromboses and death within 30 days. Anaesthetic complications included; aspiration pneumonia, drug reactions, heart attacks, stroke and death within 30 days. These complications were chosen due to their frequency in

total thyroidectomies performed under general anaesthetic.

These results were compared with the results from all patients undergoing total thyroid-ectomies during the same period at TPCH.

### **Results**

### **AIT** group

Eleven patients underwent total thyroidectomies under general anaesthetic for amiodarone-induced thyroiditis (AIT) from January 1998 to November 2015. The salient features of the data are summarised in the following tables. Table one illustrates the range of patient demographics and their amiodarone use.

There were 32 patients who underwent total thyroidectomies for non-AIT diagnoses from January 1998 to Novemer 2015. Figure 1 documents the distribution of diagnoses between the 32 patients.

Table 2 provides a comparison of the demographics, ASA statuses, weight of the thyroid glands and complications encountered due to surgical treatment between the AIT and non-AIT groups. The values are representated as percentages to allow for ease in comparing between the different sized groups. Figure 2 provides a pictorial description of the complication rates between the two groups.

### **Discussion**

### Background on the Prince Charles Hospital

This research was performed at The Prince Charles Hospital (TPCH). TPCH is 630 bed, major, tertiary referral hospital, located 10 kilometres from Brisbane city (the capital of the state of Queensland). It is the premier cardiac service for the state of Queensland, as well as northern New South Wales. It is the centre for specialised state-wide services including heart and lung transplantation; adult cystic fibrosis; adult congenital heart disease; advanced heart failure; percutaneous valve therapies and complex cardiac care.

This background provides the foundation to a better understanding of this group of patients. The patients identified at TPCH with AIT came from a cohort of cardiac cripples; each one with significant cardiac comorbidities. This is considerably different from other hospitals which do not treat such patients and thus the results must be interpreted with this knowledge in mind.

### **Demographics**

A review of the AIT cases demonstrated several features that have previously been documented in the literature. Firstly, as shown in table 2, AIT is seen more frequently in male patients. This study showed a male: female ratio of 9:2 and this is consistent with the literature which quotes a distribution of 3:1 [3]. This is suspected to be due to the higher frequency of males suffering from cardiovascular disease and being treated with amiodarone. The reverse can be seen with non-AIT cases, showing a female predominance, as is well known for other thyroid pathologies.

Secondly that there is a variable duration of amiodarone use before onset of symptoms. This has been previously documented by Mariotti et al (1999), who found the duration of time before onset ranged between 2-47 months and as shown in table 1, all the values from this study fall within that range [4]. Thirdly, the time between diagnosis and surgery is also highly variable. This is likely related to the lack of guidelines available to direct management of these patients. However, all patients were operated on within the half-life of amiodarone (~107days), thus despite all patients being able to cease amiodarone, there may have been a residual amount in each patient's system. This means that no comment can be made about self-resolution of AIT after complete elimination of amiodarone in these patients.

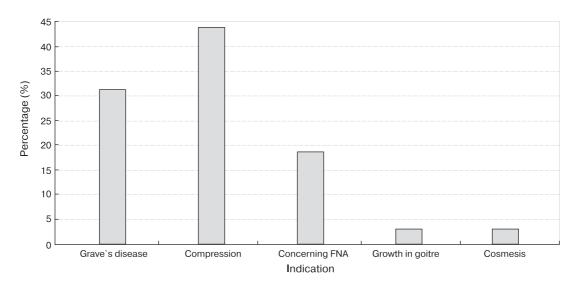
### Non-AIT causes

Thirty-two patients were found to have undergone total thyroidectomies under general anaesthetic between the dates of January 1998 to November 2015. Most of these surgeries were for symptoms of compression. The second most common indication was unresponsive Grave's disease or Grave's disease where the patient no longer wanted medical therapy and had requested surgery. All the non-AIT patients were confirmed to be biochemically euthyroid prior to their total thyroidectomies. Due to the

Table 1. Demographics and amiodarone use

Patient	Age	Sex	Indication for amiodarone therapy	Duration of amiodarone therapy before surgery (months)	Duration of thyrotoxicosis before surgery (weeks)
1	70	М	VT	40.5	8
2	82	М	AFib	38	9
3	51	М	SVT/AFlutter	5	11
4	52	М	VF	9	1.5
5	68	М	AFib	20	13
6	51	F	VT	>29	2
7	59	М	AFib	15	7
8	52	М	VT	43	6
9	48	М	AFib	21	2.5
10	63	М	AFib	33	7.5
11	34	F	Aflutter	14	14

Notes: VT — ventricular tachycardia; Afib — Atrial fibrillation; SVT — supraventricular tachycardia; Aflutter — Atrial flutter; VF — Ventricular fibrillation.



**Fig. 1.** Indications for non-AIT total thyroidectomies.

Table 2. Comparison between AIT and non-AIT group

Comparisons	AIT	Non-AIT
Age range	34-82	25-78
Average age	57	52.1
Male	82%	16%
Female	18%	84%
ASA status (2 no	ot documented)	
ASA 2	0%	47%
ASA 3	64%	47%
ASA 4	36%	0%
Average weight of thyroid gland	34.1	66.4
Compli	cations	
Haematoma	9%	6%
Return to OT	0%	3%
Hypocalcaemia (total)	27%	41%
Mild (PO replacement)	18%	34%
Moderate (IV RX or admit)	9%	6%
Nerve palsy	0%	3%
Infection	0%	3%
Readmission	0%	6%
Deceased within 30 days	9%	0%
Aspiration pneumonia	0%	3%
Thyroid storm	0%	0%

*Notes:* ASA — American society of anaesthesiologists; PO — per oral; IV — intravenous; RX — treatment.

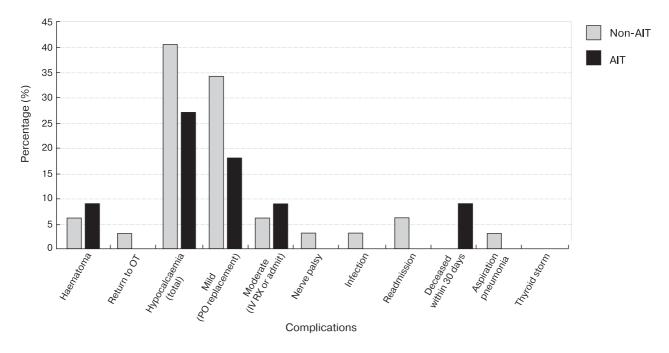


Fig. 2. Graphical representation of the complication rates between the two groups.

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non-urgent nature of medically controlled Grave's disease, a comparison between the duration of medical treatment prior to operation for these patients and the AIT cases cannot be made. The remainder of the patients in the non-AIT group were not on anti-thyroid medication. However, comparisons can be made between the two groups with respect to surgical complications as the same surgery was performed for each patient.

### Comparison between AIT and non-AIT

By comparing the surgical outcomes between the two groups, the relative safety of performing a total thyroidectomy for AIT patients in comparison to other pathology requiring the same procedure can be made.

### **Complications**

The complication rates shown in table 2 and fig. 2 demonstrate similar results between the AIT and non-AIT groups. Due to the small sample size, there is lack of power in this study to confidently determine if there are any statistical differences between the two groups. However, what can be seen are the similar trends between the two groups.

Also, by comparing this study to an Australian study, similar complication rates were found. The most commonly encountered complication for both studies was temporary hypocalcaemia. Serpell and Phan (2007) [14] reported rates of permanent unilateral recurrent laryngeal nerve palsy of 0.3% (AIT = 0% and non-AIT = 0%) and permanent hypocalcaemia as 1.8% (AIT = 0% and non-AIT = 0%). They also reported rates of significant temporary hypocalcaemia of 13.4% (AIT = 9% and non-AIT = 6%), non-significant temporary hypocalcaemia of 23.8% (AIT = 18%) and non-AIT = 34%) and an overall hypocalcaemia rate of 38.9% (AIT = 27% and non-AIT = 41%). The rates of postoperative haemorrhage and wound infection were quoted at 0.9% (AIT = 9% and non-AIT = 6%) and 1.5% (AIT = 0%)and non-AIT = 3%) respectively.

A comparison of the rates of hypocalcaemia between the two groups show that there was a higher rate of total and mild hypocalcaemia in the non-AIT group (n = 3 (27.3%) AIT, n = 13 (40.6%) non-AIT). However, there was a higher

proportion of moderate hypocalcaemia among the AIT group (n = 1, 9% for AIT and n = 2, 6.3% for non-AIT). Multiple factors may have contributed to this difference between the two groups.

### Weights of thyroid

A hypothesis to explain the difference in number of hypocalcaemic episodes experienced between the two groups is that the indication for almost half of the surgeries for the non-AIT group was compression symptoms. This would indicate that the thyroid is guite large and the operation may have been more difficult. A larger thyroid would require greater dissection and retraction to obtain optimal vision for safe excision, which may place the parathyroid glands at greater risk of being damaged or inadvertently removed. To support this hypothesis the average weights of the thyroid glands were compared between the two groups. The findings showed the average weight of the thyroid for the AIT group (34.1 grams (range of 14.15-62 g)) was almost half that of the weight of the non-AIT group (66.4g (range of 10.7–182.6 g). This finding supports the hypothesis and may also explain the higher rate of nerve palsy in the non-AIT group.

The AIT group appeared to suffer more moderate hypocalcaemia, though didn't require readmission, unlike the non-AIT group. This may be explained by the AIT patient's having less physiological reserve or a lower pre-operation calcium level due to their significant comorbidities. The AIT patients are also more likely to be monitored for longer postoperatively due to their comorbidities. Hence, they may have developed hypocalcaemia at a similar time to the non-AIT patients, but due to a prolonged admission, this may have been detected as an inpatient compared to an outpatient (as in the non-AIT group).

However, there was higher rates of haematoma formation in the AIT group. Despite the likely increased dissection in the non-AIT group, the higher haematoma formation rate could be explained by the hyperthyroid state in which the patients entered surgery. It has been documented in the literature that hyperthyroidism increases the risk of haematoma formation [15]. Though the non-AIT patients would have

likely undergone more dissection and more likely to have bled, these patients were euthyroid at the time of surgery. The single patient who required a return to theatre for re-operation was due to haematoma formation causing airway distress. This patient was on medical therapy for suspected Grave's disease but their histopathology results demonstrated no significant pathology.

A feature that has previously been used as a surrogate marker of surgical difficulty is, length of operation. However, this was not assessed in the current study due to the variety of surgeons and techniques used to complete the procedures. Over the period of 1998 to 2015, a variety of methods have been employed to complete a thyroidectomy, some; such as the use of LigaSure, have decreased the duration of the operation significantly [16]. Hence, using surgery duration as a marker for surgical complexity would be innately flawed.

A significant complication experienced by a member of the AIT group was death within 30 days of operation. As previously mentioned, patient 9 passed away four days after the operation due to the removal of a femoral line which resulted in haemorrhage. He was taken to theatre to treat the haemorrhage and he suffered a cardiac arrest on the table from which he could not be resuscitated.

There were single episodes of aspiration pneumonia and infection which both occurred in patients from the non-AIT group. Both pathologies are unfortunate complications of having surgery under a general anaesthetic. Without further research, it is unclear whether they would be more likely to occur in one group in preference to the other. Notably, the most feared complication of operating on hyperthyroid patients; the onset of a thyrotoxic crisis, did not occur in any of the AIT cases.

Overall, more complications did occur in the non-AIT group. These results may be linked to the size of the glands operated on.

### **ASA**

Reasons previously given to abstain from operating on AIT patients are that they are high risk and it is dangerous. When comparing the demographics and comorbidities of the patients between the two groups it is evident the AIT pa-

tients are of significantly higher risks for a general anaesthetic than the non-AIT patients. This is evident in the difference in the ASA scores between the two groups. The AIT patients were distributed with ~60% scoring an ASA 3 and 30% an ASA 4. In comparison, of the ASA scores documented for the non-AIT group, 50% of the non-AIT group were classified as ASA 2 and 50% were classifies as ASA 3; there were no patients classified as ASA 4 patients in the non-AIT group. However, the complications documented do not reflect this significant difference in ASA scores between the two groups. This would suggest, that despite their large list of risk factors, the surgery is of similar risk for both AIT and non-AIT patients and the apprehension in offering these patients a general anaesthetic may not be well-founded.

Yet what must be considered is that an ASA score is an incomplete and subjective assessment of the patient by a particular anaesthetist. The anaesthetist for each procedure would have been a different physician and may have graded a patient differently from their colleague. The ASA score also doesn't include all factors important to the patient's likely outcome from the surgery. Despite this, it is a tool that is regularly used to provide a summary of the patient's condition for everyday practice and in this study, supports what is already known about these two groups of patients.

As with the differences in anaesthetists, there was also different surgeons involved with the total thyroidectomy cases. This inter-surgeon variability in complication rates must be taken into consideration. A prospective study in which all operations were performed by the same surgeon and anaesthetist using the same techniques would remove this variable from the study.

### Reduce mortality

Part of the aim of this study was to assess if there was any indication as to when a thyroid-ectomy should be performed in AIT patients to reduce mortality. It was hypothesised that there is likely to become a time when the ongoing stress to the heart from thyrotoxicosis outweighs the perceived risks of surgery and it becomes beneficial to perform an operation. Tomisti et al (2012) has previously shown that

performing a thyroidectomy in AIT patients has improved their cardiac function; to such a degree as removing the need for cardiac transplant [6]. This contradicts the results from this study which show that the two patients who had documented LVEF values postoperatively (patients 2 and 10), had very similar preoperatively LVEF values.

An echocardiogram provides a snapshot of a patient's health and it is difficult to convey all the dynamic factors of a patient's clinical course via these measurements objectively. Echocardiograms don't account for the patient's functional status, the health of their other end-organs, their present clinical state or propensity for fatal arrhythmias. It is unlikely that a single measurement of level of cardiovascular function; such as an ejection fraction, could be used as an indicator for surgery. Performing a total thyroidectomy didn't appear to affect the patient's cardiac function in this study but it did significantly improve the patient's symptoms and this would be an indication to perform the surgery, sooner rather than later.

Five (patients 1, 29, 10 and 11) of the eleven (45%) AIT patients died within two years of the operation, compared with no deaths for patients who had a total thyroidectomy for alternate indications. Though this is quite a sobering number it is not entirely unexpected. O'Sullivan, Lewis and Diamond, (2006) demonstrated a mortality rate of 10%; and subgroup analysis showed a 50% mortality rate for patients with severe cardiac dysfunction (LVEF <30%) [17]. Not all of patients who died in this study were patients with LVEF of <30%. Patients 1 and 11, both had LVEF < 30%, however, the other three patients had LVEF values close to normal. This contradicts the findings of O'Sullivan, Lewis and Diamond (2006) but as previously mentioned, a LVEF value doesn't capture the entire clinical scenario of a patient [17].

None of the patients died from causes directly related to the total thyroidectomy. Patient 1 died from end-stage cardiac disease 22months after the operation. Patient 2 died from severe cardiogenic shock 6weeks after the operation. Patient 9 died from a cardiac arrest after he was taken to theatre to treat a haemorrhage in his groin from the removal of a femoral line. Patient 10 developed multiple organ dys-

function syndrome and died 10 weeks after the operation and patient 11 suffered primary cardiac graft failure after her heart transplant, 2 years after the operation. These deaths were not related to the operation but were related to heart dysfunction and AIT. This further emphasises the significance of these patients' initial cardiac comorbidities and questions the duration of thyrotoxicosis that is permitted.

Though not documented through echocardiographs, the time spent thyrotoxic may have weakened the already damaged hearts of the AIT patients. This may have led to a quicker demise in these patients' conditions over time and possibly contributed to their deaths. Tomisti et al (2012) has shown improvement in cardiac function after thyroidectomies are performed in AIT patients but all operations in that study were completed within 30 days of diagnosis and it is unclear when the preoperative echocardiograms were performed [6]. It is also unclear from that study whether all patients returned to baseline or whether irreversible damage was done to the patient's cardiac function due to AIT.

In comparison to Tomisti's (2012) study, some of the patients in this study were treated medically for significant periods of time; such as 11 weeks for patient 3 [6]. If the decline in cardiac function caused by AIT is reversible, then such a duration may be acceptable, provided the patient is haemodynamically stable. However, if some of the damage is irreversible then such a trial of medical treatment should not be attempted.

A study is needed which documents how much damage occurred over varying durations of time spent thyrotoxic and whether it is reversible. Such a study would hopefully identify a safe duration of a trial of medical therapy before recommending patients to surgery.

### **Limitations of study**

As previously mentioned, there were a few limiting features of this study. Firstly, the small sample size inhibits the performance of useful statistical analysis due to the lack of power in the study. This is a factor of studying rare diseases. A method to overcome this would be recruitment of more facilities to be involved in any prospective trials or to collate and analyse data from more facilities.

Another limitation is the inter-surgeon and anaesthetist variability, which ideally would be controlled. However due to the rarity of the disease this is an unrealistic aim and the intersurgeon and anaesthetist variability must be calculated into the analysis.

This study is a retrospective analysis of chart notes and this lends itself towards bias. There is bias in the interpretation of the chart notes and in what information was documented for each patient. Not all information was included for each patient and this resulted in an incomplete assessment of all the patients.

### **Conclusions**

Total thyroidectomy in patients with AIT demonstrated comparable clinical outcomes to total thyroidectomies for other indications. There was no evidence of mortality risk reduction by performing a total thyroidectomy or any correlation to the duration of medical therapy.

This study has also shown that patients with significant comorbidities and who are high surgical risks are still appropriate for surgery and in some cases, this may be the best method of treatment for them.

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