Thyroid Cancer Treatment Audit

An audit of thyroid cancer treatment by a private group against best practice guidelines

Marcus Lombard - University of Notre Dame Australia – Audit Report

Introduction

Thyroid cancer represents the most common endocrine malignancy in Australia and the seventh most common malignancy in females in 2014 (Australian Institute of Health and Welfare, 2014; Sherman, 2003). The incidence of thyroid cancer is increasing at an alarming rate with the incidence increasing by 281% between 1982 and 2014, the greatest increase in incidence amongst cancers in Australia (Australian Institute of Health and Welfare, 2014).

Thyroid cancer typically has a good prognosis with a 97.3% one year survival and 95.8% five year survival in Australia (Australian Institute of Health and Welfare, 2014). The mortality rate decreased between 2002 and 2012 by ~20% (Australian Institute of Health and Welfare, 2014). This is contrasted by a high recurrence rate of 5-20% (Schlumberger 1998).

Cancer treatment is advancing rapidly and optimal treatments are constantly being updated. There are updated evidence-based guidelines from the American Thyroid Association (ATA) indicating points of best practice in the management of differentiated thyroid cancer. Private multi-disciplinary groups via the private practice of endocrine surgeons and nuclear physicians treating approximately 50 new cases each year are required to incorporate updates and changes in these guidelines. Audits represent a critical tool in analyzing the uptake of these guidelines and are critical in analyzing the practice of private cancer groups. The chosen location contains a private group of multi-disciplinary practitioners striving for world leading practice of thyroid cancer.

The audit topic was chosen due to a personal interest in oncology. Having previously performed research into oncological treatment and realizing how often new developments occur, I'm interested to see the uptake of new treatments into practice.

Aim: To ensure private practice treatment is using best practice in their treatment of thyroid cancer and to assess whether practice is inline with worldwide standards.

Objective: In Thyroid cancer patients treated at a Perth tertiary hospital; do they receive treatment in line with best practice according to ATA clinical standards?

Methods

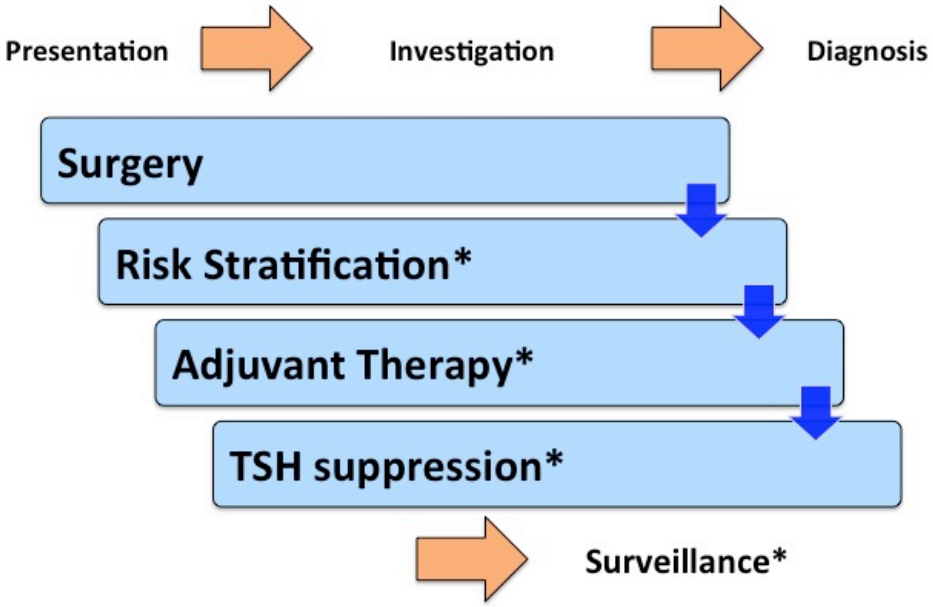
Standards

This audit addressed the treatment of thyroid cancer patients against the most recently released guidelines of the American Thyroid Association 2015 clinical guidelines released in 2016. They are freely accessible at the ATA website (http://www.thyroid.org/professionals/ata-professional-guidelines/). This audit addressed the 2015 guidelines an update of 2009 guidelines that do not significantly differ in the specifics audited.

This audit addressed different elements of the guidelines independently, not in an 'all or nothing' fashion and due to the broad and comprehensive nature of the guidelines targeted pertinent elements that were identified as critical by the supervisor and primary auditor.

Thyroid cancer patient management is made up of both immediate treatment and long-term surveillance (Figure 1.). This audit assessed multiple elements of the treatment pathway for concordance with best practice. The standard of practice is 100% of patients will have risk stratification following surgery, post-surgical serum thyroglobulin testing; TSH suppression to guideline levels and follow up via serum Tg testing within 6-12 months.

Figure 1. Thyroid cancer patient pathway. * refers to elements audited.



1. An Initial Post-Surgery Risk Stratification System for DTC patients treated with thyroidectomy, based on its utility in predicting risk of disease recurrence and/or persistence.

Level III-3 evidence from a retrospective study validated the risk stratification system developed by the ATA in response to a perceived need for a stratification system that adequately predicted risk of recurrence (Baek et al., 2010; Haugen et al., 2016; Orlov et al., 2009; Tuttle et al., 2010). The ATA system correctly predicted structural disease or recurrence finding rates of 3% in low-risk patients, 21% in intermediate-risk patients and 68% in high-risk patients (Tuttle et al., 2010). Other risk stratification tools have also been validated and previously used, they include the Mayo clinics MACIS scoring and AJCC/TNM scoring. The equivalent ATA risk category is listed in table 2 (Haugen et al., 2016; Silberstein et al., 2012; Tuttle et al., 2010).

2. Radioactive iodine adjuvant therapy is recommended after total thyroidectomy for ATA high-risk DTC patients.

Level III-1 evidence has shown that RAI adjuvant therapy following total thyroidectomy for ATA high-risk patients is beneficial. A prospective multicenter

study reported a significant improvement in overall and disease-specific mortality, as well as disease-free survival in stage III and IV patients (Haugen et al., 2016; Jonklaas et al., 2006).

3. Thyroid cancer patients should have TSH suppression to below 2mU/L and high-risk thyroid patients below 0.1 mU/L

Level I evidence of a meta-analysis supported the efficacy of TSH suppression therapy in preventing adverse clinical events (Haugen et al., 2016; McGriff et al., 2002). This rationale is disputed by level II evidence from a RCT in Japan that found normal TSH levels gave equivalent outcomes to those suppressed, in thyroid cancer patients (Sugitani & Fujimoto, 2011). This RCTs relevance to American/Australian patients is disputed due to treatment arms differing from conventional guidelines (Sugitani & Fujimoto, 2011).

4. During initial follow-up, serum thyroglobulin (Tg) on thyroxine therapy should be measured every 6–12 months in patients with DTC. High-risk patients may be even more frequent.

Level I evidence has shown that Tg level gives good sensitivity and specificity for detecting persistent disease over time. The trend in serum Tg will typically identify patients with clinically significant residual disease (Haugen et al., 2016). Previous studies have shown that serum Tg alone in the presence of rhTSH stimulation alone had a diagnostic sensitivity of 85% and a negative predictive value of 98.2% (Pacini et al., 2003; Schlumberger et al., 2004). When combined with neck ultrasound the sensitivity increased to 96.3% and the negative predictive value increased to 99.5% (Pacini et al., 2003; Schlumberger et al., 2004), showing the value of serum Tg for detection of recurrent thyroid cancer (Pacini et al., 2003; Schlumberger et al., 2004).

Case Definition

Every adult patients, who had their first appointment with a nuclear physician between 10th of January 2013 and 5th of January 2015 (n=30), who were operated on by a stake-holding surgeon of the treatment group with a confirmed diagnosis of thyroid cancer 2016 ICD Code CM C73.

Patient Selection

Cases were selected from a private file system, where the supervisor was the primary nuclear medicine physician and the surgery was performed by a stake-holding surgeon. This surgeon performs the bulk of thyroid cancer surgery in WA performing approximately 150 surgeries per year across the state. The combination of the nuclear physician and surgeon treat approximately 50 patients per year, but only 10 required further follow up for radioablation.

All cases, had their first appointment with a nuclear physician between 10th of January 2013 and 5th of January 2015 (n=30). These cases were the first 30 after the 1st of January 2013 found by chronological appointment on the Geanie Pro electronic filing system. No coding system was used to determine eligible patients. Thirty patients were deemed to be an acceptable sample size, as it constituted all patients treated across multiple years.

This represented an overview of patients seen by this treatment team but emphasized higher risk cases requiring both surgery and RAI. This is not a replication of a previous audit and therefore the methodology was novel for this audit. There were no conflicts of interest identified by either the primary auditor or the supervisor, but the supervisor represents a key member of the group who are being audited which represents a potential conflict of interest, due to a potential bias towards positive results.

Data Collection

The primary auditor retrospectively collected the data from a private electronic patient file system. This file system was examined for notation of the required information which was transcribed into an excel spreadsheet. This contained correspondence between practitioners, surgery reports, MDT reports, pathology results and appointment notations. The primary auditor subsequently bolstered any missing information with information from the surgeons private file system.

The results were compared to the standards through the use of percentages, allowing for graphical and tabular display and clear comparison of compliance to standards.

The audit includes three exposure variables and six outcome variables outlined in table 1 and table 2.

Exposure Variable	**Use**
Unique Identifier	Confidential form of patient identification allowing for identification if required.
Date of treatment	
Pathological Cancer Type	

Table 1. Exposure variables and their use.

Outcome Variable	**Definition**
1. Post Surgical Risk Identified	
A) Yes	Post surgical risk identified for patient with ATA, AJCC or MASIC
B) No	Post surgical risk NOT identified for patient.
2. ATA Post Surgical Risk	
A) High Risk	Gross extrathyroidal extension (Gross ETE), incomplete tumor resection, distant metastases, or lymph node >3cm. TNM equivalent = T4 (Gross ETE), OR Distant metastases (M1) MACIS equivalent = >6
B) Intermediate Risk	Aggressive histology, minor extrathyroidal extension, vascular invasion or >5 involved lymph nodes (0.2-3 cm) TNM = anything not defined by other categories.

C) Low Risk	Intrathyroidal DTC less than or equal to give lymph node micrometastases (<0.2 cm) TNM equivalent = T1a, N0/x, M0/x OR T1b/2, N0/x, M0/x MASIC equivalent = <6
3. Ablative 131-1 given	
A) Yes	RAI was given to patient.
B) No	RAI treatment was **NOT** given to patient or it is not recorded.
4. Post-Surgical Serum Thyroglobulin detection	
A) Yes	Blood test for serum thyroglobulin was performed within 4 weeks of surgery.
B) No	The blood test for serum thyroglobulin performed more than 4 weeks of after surgery.
5. TSH Suppression	
A) Adequate – Deemed as TSH below threshold on at least one of the first three TSH blood tests measured post RAI.	TSH was adequately suppressed following surgery. (High thyroid cancer patients <0.1 mU/L. Intermediate <0.5mU/L. Low risk patients with TSH levels < 2mU/L).
B) Inadequate – No TSH blood tests below threshold in the first three TSH blood tests measured post RAI.	TSH suppression was **NOT** below required levels. (High thyroid cancer patients <0.1 mU/L. Intermediate <0.5mU/L. Low risk patients with TSH levels < 2mU/L).
C) Unknown	The information was not recorded as to the indication or administration of the TSH

	suppression.
6. Follow up Serum Thyroglobulin	
A) Adequate	Serum Tg measured within 12 months post surgery.
B) Inadequate	Serum Tg was **NOT** measured within 12 months post surgery.

Table 2. Outcome variables and their definition.

Other issues

The data was stored on a locked excel spreadsheet maintaining confidentiality and accessed using confidential unique identifier numbers stored on a separate locked excel spreadsheet. The data was not accessible to anyone except the primary auditor and the supervisor. The primary auditor gave all of the data to the primary supervisor at the conclusion of the audit. No patient consent was obtained as NHMRC ethical guidelines state that maintenance of standards of practice in a blinded setting does not require patient consent, if aspects of research were included such as survival, both patient consent and ethical application would be required (National Health and Medical Research Council, 2014, 2015).

All patient identity remained blind to the auditor after initial generation of the unique identifier numbers.

Data collection tool and dictionary are attached as in appendix 3 and 4 respectively. Data pilot description attached as appendix 5.

Stakeholder consultation, results dissemination and feedback.

The stakeholders for the audit included: Head and neck surgeons, endocrinologists, nuclear medicine physicians, pathologists and managers of clinical governance. Stakeholders further include multi-disciplinary teams, which include speech therapists and clinical nurses.

The main stakeholders have been met with personally or email and feedback/input has been incorporated.

Data was collected and analyzed, with executive summaries of results sent to the key stakeholders. Feedback was sought regarding the results of the audit, the reasons for the results, how they believe the team should change and the barriers to change and input into the audit process. There was limited feedback received, other than from the primary supervisor. Feedback was incorporated into the final report and emailed to the stakeholders. Furthermore, results of the audit will be displayed on the private cancer groups website as evidence of their ongoing endeavor for clinical improvement.

Major potential barriers to the implementation of these audits results, will be the small sample size. Furthermore, the ATA guidelines for best practice are published regularly and this project will audit cases from three years ago due to the low levels of cases each year. In some cases the results of the audit may have already been implemented to the practice. Another major barrier to change is the inability of the guidelines to reflect individual cases where they may not fit snugly into criteria. The multidisciplinary meeting involves large discussion of the patients and their options using the latest research, to advise their decision. The identification of lower than expected guideline compliance would be the first step in implementing change, via identification of an initial problem that can easily be shown to the primary stakeholders. Their state of mind is one open and compliant with change. They were interested to see the results of the audit making barriers to change minimal. No resources were required to implement change that had not already been developed or put into place. Data managers and data systems were beginning to be developed during the auditing process.

Results

This audit successfully analyzed 30 patients treated at a private treatment group associated with a tertiary hospital in Perth. The patients were seen at between 10th of January 2013 and 5th of January 2015. The demographics of those audited were not collected as they have no relevance in determining the thyroid cancer treatment given and as such sex and age weren't collected. The thyroid cancers across the 30 cases analyzed were predominately Papillary thyroid cancers with some follicular including one rare case that represented a subtype of follicular cancer (Figure 1.).

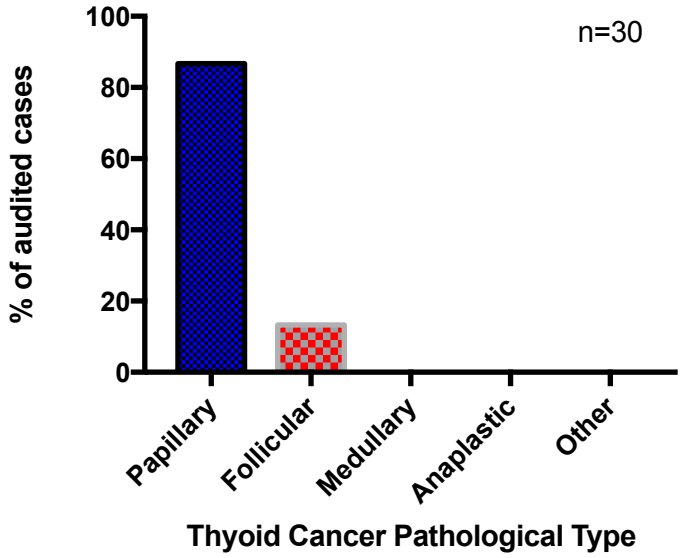


Figure 1. Pathological cancer type per percentage of cases audited

Overall compliance with the audited aspects of the ATA guidelines was on average 97.5% (Table 3). Further breakdown of each area follows.

Table 3. Summary of ATA guideline compliance with each audited element.

Audited Area	ATA Guideline Compliance
Risk stratification	96.7%
Post-surgical serum thyroglobulin	100%
TSH Suppression	93.3%
Follow up serum thyroglobulin	100%

Risk stratification systems were applied to the majority of patients with only 1 patient file not showing signs of risk stratification (Figure 2.), and of those stratified the most common converted ATA classification was high (50%) followed by low (33%) with the intermediate category and those without a defined classification taking the minority (Figure 3.).

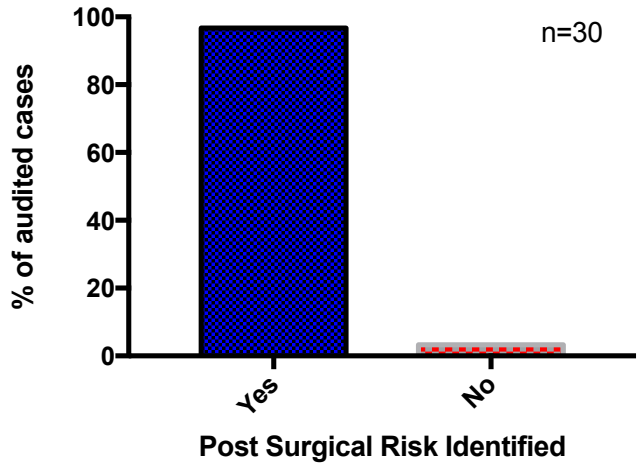


Figure 2. Identification of post surgical risk in cases of thyroid cancer audited

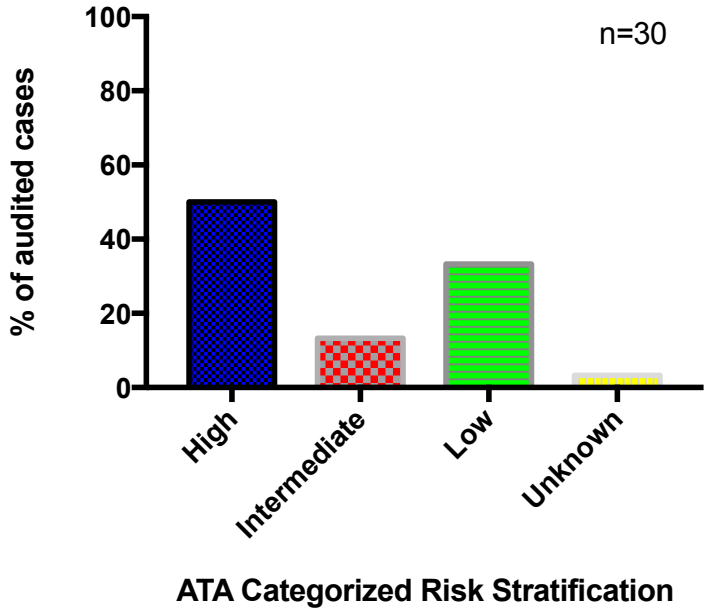


Figure 3. ATA Post Surgical Risk in % of thyroid cancer cases audited

Following surgery all patients had serum thyroglobulin levels tested in line with ATA guidelines (100%). There was one case of testing the serum thyroglobulin prematurely before 4 weeks post surgery, but this value was not used and appropriate testing was performed weeks later so was this case was categorized as appropriately greater than 4 weeks. Serum thyroglobulin has previously been shown not to reach its nadir prior to 3-4 weeks post surgery so using the premature value could potentially have been artificially elevated. Critically this premature result was not used in the MDT risk stratification and treatment-planning phase, therefore not impacting the overall outcomes of the patient. The serum thyroglobulin tested after 4 weeks of surgery was tested either before, or at the time of radioactive iodine treatment, in line with the ATA guidelines (Figure 4.). There were no instances where it was not performed.

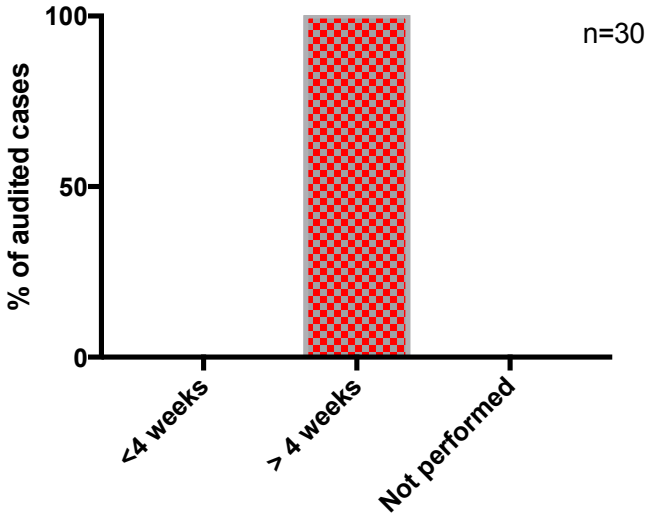


Figure 4. Post-surgical serum thyroglobulin per percentage of cases audited

The patients, as expected, were all treated with radioactive iodine (Figure 5.), and replacement thyroxine that suppressed their TSH as indicated in 2016 ATA guidelines (Figure 6.). The thyroxine suppression analysis showed that 93% of patients were suppressed to guideline levels in the 12 months following surgery. For high-risk patients this was a TSH below 0.1, and for low and medium risk this was below 2 mU/L. One cases did not have results listed to determine whether the FSH was adequately suppressed other than initially after surgery, and one case was defined as high risk but was only suppressed below 2 mU/L, the threshold for medium and low risk cases.

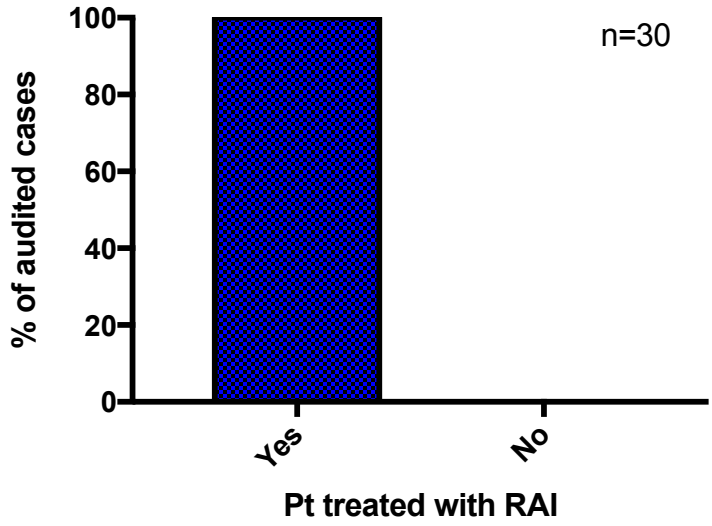


Figure 5. Number of patients treated with radioactive iodine per percentage of cases audited

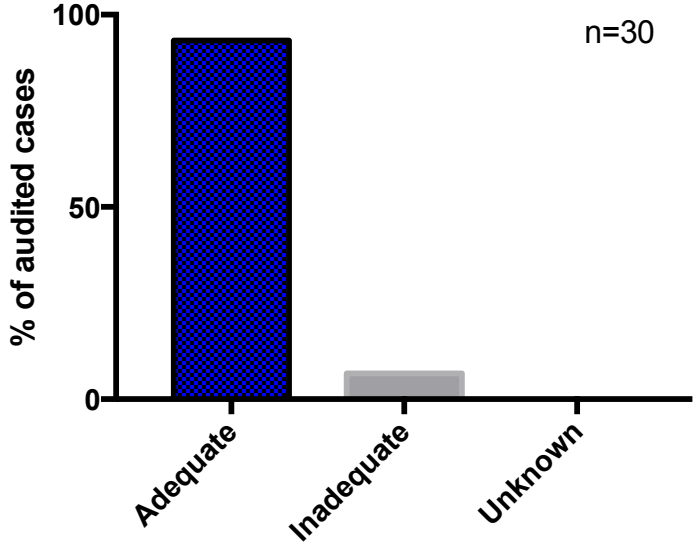


Figure 6. TSH Suppression per percentage of thyroid cancer cases audited

Finally, of the cases audited, the follow up ATA guideline for serum thyroxine was correctly followed up in all cases (Figure 7.), with no cases of sub-optimal follow up between the time frame of this audit.

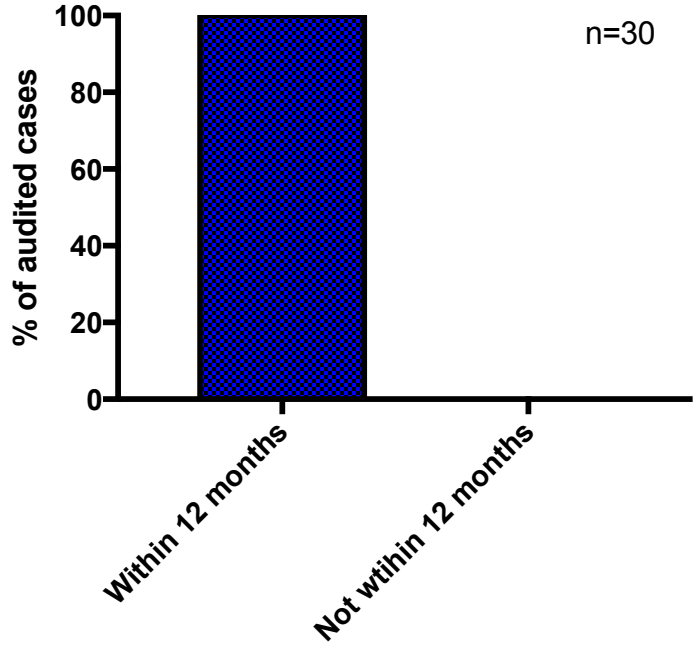


Figure 7. Follow up serum thyroglobulin within 12 months per percentage of cases audited

Discussion

The results of this audit represent exemplary standard for organizational practice in the treatment of thyroid cancer. The audit findings show that the group treats primarily differentiated thyroid cancers of varying risk stratifications and follows an extremely high compliance with the 2016 ATA thyroid cancer guidelines (Table 3).

There are some key limitations of this audit and data interpretation, which include where the data was collected and the novel nature. This audit was conducted on the patient file system of a nuclear physician and as such patients likely to require radioactive iodine ablation are referred to this clinic, therefore the radioactive iodine ablation may have been artificially elevated, creating a selection bias for higher risk stratification. The novel nature of the audit and therefore its methodology was only scrutinized with a small sample pilot and had not been rigorously scrutinized through previous audits. The audit only used key elements of the ATA guidelines with high quality evidence, which reflect key practices that are of high importance to thyroid cancer treatment. The audits retrospective nature and incomplete retrieval of information for some patients who received treatment occurred at multiple locations. One final key limitation of this audit was the multitude of laboratories used for blood testing. Each laboratory had a different reference ranges and sensitivity and specificity of their tests, as values may vary with testing in serum thyroglobulin and thyroid stimulating hormone levels with each laboratory or company. It was noted during the audit that one particular laboratory changed the method of their Thyroid Stimulating hormone test from the 17th of February 2014, producing values predicted to be approximately 15% less. This was not taken into account in the results and therefore cases before this date may have had elevated levels compared to those tested after this date.

A key strength of this audit was auditing against 2015 guidelines not the 2009 guidelines, which were the latest published and were likely updated during the timeframe of the audit. The private group therefore was performing at expectations of guidelines that were still being produced and represent a forward thinking and world-leading approach. The areas audited did not differ significantly between 2009 and 2015 guidelines with the exception of TSH suppression (Cooper et al., 2009; Haugen

et al., 2016). The 2009 method of TSH testing and guideline suppression levels are complex with more advanced and complex stimulated tests, but with similar levels of TSH required in the long term follow up (Cooper et al., 2009).

Presentation of the audit with the aid of slides to the primary stakeholder, received a response similar to that of the author of this audit. The results are of an extremely high standard and give validation to the novel methods used by this thyroid cancer group, showing them to possess extremely high standards.

The demographics of this audit showed 86.7% papillary and 13.3% follicular pathological cancer types. This reflects Australian statistics that show papillary cancer is approximately 80% whilst follicular thyroid cancer is approximately 10% (Australian Institute of Health and Welfare, 2014). There were no cases identified of medullary, anaplastic or lymphoma in the cohort audited. This represents less than 10% of all thyroid cancers in Australia (Australian Institute of Health and Welfare, 2014).

The ATA guidelines represent a gold standard for worldwide treatment of thyroid cancer, and due to their 2016 release no information regarding audits of this information is available. They are used for guidelines worldwide so other thyroid cancer audits published worldwide can be used as a comparison base. Unfortunately, they are not generally published and as such it is impossible to compare results with other hospitals.

The most relevant published thyroid audit was published in 2001. It was an extensive audit of 205 patients with differentiated thyroid cancer in the United Kingdom (Kumar et al., 2001). It found TSH suppression to be adequate in only 77.8% of cases (Kumar et al., 2001), and the follow up serum thyroglobulin to be monitored in only 85% of cases (Table 4.) (Kumar et al., 2001). There were key methodical differences compared to this audit, they used old guidelines, which required a TSH below 0.1 for all cases (they did not apply a risk stratification) (Kumar et al., 2001), but similar standards for serum thyroglobulin follow up. In comparison to the published material, this audit is extremely successful, showing high levels of compliance with guidelines and follow through with patients (Kumar et al., 2001).

Table 4. Comparison of audit results with Kumar et al. (Data taken from (Kumar et al., 2001))

	This audit	Kumar et al.
TSH	93.3%	77.8%
Follow up Serum Thyroglobulin	100%	85%

The difference between the two audit results may be due to the use of computer-based support systems at the point of care. This specialist multi-disciplinary team uses an automated computer-based stratification system to give specific treatment outputs for individuals in line with current management guidelines. A recent paper showed the need for computer-based systems such as the thyroid cancer care collaborative, to allow for fast uptake of guidelines into practice (Likhterov et al., 2016). This group of clinicians appears to currently be following best-practice in their clinical practice and secondly already use a computer-based system at the point of care to maintain this high standard to guidelines, showing their novel advanced standards.

The auditor expressed no conflict of interest, and potential positive results bias did not eventuate due to the objective and independent nature of the primary auditor from the primary supervisor. Decisions about methodology of the audit were made independently of the supervisor, before the audit was performed and analyzed independently of the supervisor. Positive selection bias therefore had no action or implication upon the results.

Discussion with stakeholders identified a number of follow up areas and ideas to uphold the high standard. The need for further audits to aid compliance to standards and maintenance of high standards was identified. Indication for RAI was outside of the scope of this audit due to it's complexity but was an area that the supervisor was concerned they did not conform fully to guidelines and therefore represented an ideal future audit target. The maintenance of the novel computer based MDT system and the creation of a database to track treatment but also give outcome values.

Table 5. Ideas for implementation to maintain audit standards.

Suggested Action	Person Responsible	Timeframe
Re-audit of the latest patient database	Primary Supervisor	Consider in 12 months
Creation of database for ease of future auditing	Primary Supervisor and data manager	Ongoing
Maintain MDT system	All team members	Ongoing
Audit of indications for RAI	Primary Supervisor	Consider in 12 months time.

Conclusion

This audit successfully determined the compliance with ATA guidelines of key areas of a private hospital thyroid cancer group, found them to be performing of a high standard and identified strategies for the maintenance of this standard.

Appendix 1. Data Collection Tool (retrospective audit)

1. Unique Identifier	Number from 1 to 50
2. Date of treatment	__/__/____ (dd/mm/yyyy)
3. Pathological cancer type	Confirmed DTC Papillary = 1 Confirmed DTC Follicular = 2 Confirmed Medullary = 3 Confirmed Anaplastic = 4 Other = 5 Missing data = 6

4. Post Surgical Risk Identified	Yes = 1 No = 2
5. ATA Post Surgical Risk	High Risk = 1 Intermediate Risk = 2 Low Risk = 3 Unknown = 4
6. RAI given	Yes = 1 No/Unknown = 2
7. Post-Surgical Serum Thyroglobulin recorded	Yes before 4 weeks = 1 Yes after 4 weeks = 2

	No/Unknown = 3
8. TSH Suppression	Adequate = 1 Inadequate = 2 Unknown = 4
9. Follow up Serum Thyroglobulin	Yes within 12 months = 1 No/Unknown = 2

Appendix 2. Data Dictionary

1. Unique Identifier
    a. Random number given to each patient that corresponds with their UMRN (though this information is kept on a separate database that is kept by the audit supervisor)
2. Date of treatment
    a. dd/mm/yyyy or 99/99/9999 if data missing
3. Pathological cancer type
    a. 1 - Confirmed differentiated Papillary
    b. 2 - Confirmed differentiated Follicular
    c. 3 - Confirmed differentiated Medullary
    d. 4 - Confirmed differentiated Anaplastic
    e. 5 - Other
    f. 6 - Missing data
4. Post Surgical Risk identified
    a. 1 – Yes the patient was risk stratified using a post surgical risk stratification chart.
    b. 2 – No the patient was not risk stratified using a post surgical risk stratification chart.
5. ATA Post Surgical Risk Identified
    a. 1 – The patients ATA post surgical risk when identified was in the high category or equivalent in another risk stratification tool
    b. 2 - The patients ATA post surgical risk when identified was in the intermediate risk category or equivalent in another risk stratification tool
    c. 3 – The patients ATA post surgical risk when identified was in the low risk group or equivalent in another risk stratification tool
    d. 4 – The information is unknown or incomplete.
6. RAI given
    a. 1 – The patient was treated with RAI
    b. 2 – The patient was not treated with RAI or it is unknown if the patient was treated with RAI

7. Post surgical serum thyroglobulin
    a. 1- There is notary evidence the patient's serum Tg level was tested for serum Tg within 4 weeks of surgery.
    b. 2 – There is notary evidence the patient's serum Tg level was tested for serum Tg after 4 weeks of surgery or at the time of RAI.
    c. 3 – There is no evidence of serum Tg level testing a the time of surgery or after it.
8. TSH suppression
    a. 1 – TSH was suppressed to an adequate level at one of the first three TSH pathological tests following surgery. (High <0.1mU/L, Intermediate <0.5mU/L, Low <2mU/L).
    b. 2 – TSH was **NOT** suppressed to an adequate level at one of the first three TSH pathological tests following surgery. (High <0.1mU/L, Intermediate <0.5mU/L, Low <2mU/L).
    c. 5 –The information was not recorded as to the indication or administration of the TSH suppression.
9. Serum thyroglobulin
    a. 1 – Yes, Serum Tg was tested within 12 months of first nuclear physician appointment (excluding post-surgical).
    b. 2 – There is **NO** notary evidence Serum Tg was tested within 12 months of first nuclear physician appointment (excluding post-surgical).

Appendix 3. Data Collection Tool Pilot

The data collection tool was piloted on 10 patient files on an electronic file database, under the supervision of clinical staff and the primary supervisor. The 10 files were of patients originally seen in 2011 and therefore excluded from the target audit cases. Alterations made included the removal of pre-surgery stage as a demographic due to low levels of recording, date of surgery was altered to first appointment with the nuclear medicine physician due to increased prevalence of information and risk stratification was altered to encompass multiple risk stratification systems that were used at the time of surgery.

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