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Surgery alone for papillary thyroid microcarcinoma is less costly and more effective than long term active surveillance

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A R T I C L E I N F O

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A B S T R A C T

Background: Papillary thyroid microcarcinoma is a subtype of thyroid cancer that may be managed with active surveillance rather than immediate surgery. Active surveillance decreases complication rates and may decrease health care costs. This study aims to analyze complication rates of thyroid surgery, papillary thyroid microcarcinoma recurrence, and survival rates. Additionally, the costs of surgery versus hypothetic active surveillance for papillary thyroid microcarcinoma are compared in an Australian cohort.
Methods: Papillary thyroid microcarcinoma patients were included from a prospectively collected surgical cohort of patients treated for papillary thyroid cancer between 1985 and 2017. The primary outcomes were the complications of thyroid surgery, recurrence-free survival, overall survival, and cost of surgical treatment and active surveillance.
Results: In a total of 349 patients with papillary microcarcinoma with a median age of 48 years (range, 18–90 years), the permanent operative complications rate was 3.7%. Postoperative radioactive iodine did not decrease recurrence-free survival ($P = .3$). The total cost of surgical treatment was $10,226 Australian dollars, whereas hypothetic active surveillance was at a yearly cost of $756 Australian dollars. Estimated cost of surgical papillary thyroid microcarcinoma treatment was equivalent to the cost of 16.2 years of active surveillance.
Conclusion: Surgery may have a long-term economic advantage for younger Australian patients with papillary thyroid microcarcinoma who are likely to require more than 16.2 years of follow-up in an active surveillance scheme.

Introduction

Papillary thyroid cancer (PTC) is the most commonly encountered histologic type of thyroid cancer. Its incidence in the United States has nearly tripled from 3.4 per 100,000 in 1973 to 12.5 per 100,000 in 2009.[1] More than 50% of PTCs have a size <1 cm and are classified as papillary microcarcinoma (PMC).[2] In recent decades, the increased PMC incidence did not seem to affect morbidity or mortality rates, suggesting overdiagnosis, overtreatment, and possibly avoidable treatment-related morbidity.[3] Additionally, it may contribute to an increased economic burden on both individuals and the health care system.[4]

The current American Thyroid Association (ATA) guidelines recommend hemithyroidectomy for low-risk, unifocal, intrathyroidal microcarcinomas with the absence of clinically detectable cervical node metastasis.[5] Total thyroidectomy may be opted for high-risk PMC (locoregional nodal metastases or gross extrathyroidal extension), multifocal PMC, or to enhance radioactive iodine (RAI).[5] The most common complication after a total

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thyroidectomy is iatrogenic hypoparathyroidism (7%–37%) followed by permanent recurrent laryngeal nerve palsy (0.9%–5.9%).[6–8]

A recent Japanese study offered the suggestion of managing these patients with PMC without high-risk features, such as distant or nodal metastasis, extrathyroidal extension, or aggressive cytology, with a program of active surveillance (AS). Operative intervention was performed if there was a >3 mm increase of tumor size or occurrence of lymph node metastasis.[9]

The rapidly increasing incidence and recognition of PMCs arouses a debate over the optimal management of patients with this low-risk thyroid cancer. The option for optimal PMC management with operation or AS may depend on local factors, such as complication rates or national health care systems. Therefore, studies are warranted to assess the local feasibility in relation to both benefits and costs of an AS program for PMC. The aim of this study is to retrospectively analyze several important health outcomes, including thyroid surgery complication rates, recurrence-free survival, and overall survival of patients with PMC in a high-volume Australian tertiary referral center. Additionally, we assessed the economic feasibility of an AS program for PMC by comparing the cost of surgery versus AS in the Australian health care system.

Methods

Patient and surgery outcomes

After approval by the human research ethics committee of the Northern Sydney Area, we performed a retrospective analysis of PTC patients included in the Endocrine Database of the University of Sydney Endocrine Surgery Unit. Patients with at least 3 months of follow-up treated with primary operation and diagnosed with PMC defined as PTC <1 cm were included. Histopathology reports of all PMC patients were reviewed to confirm the diagnosis. Patient charts were reviewed to verify patient characteristics, treatment details, complications, recurrences, recurrence-free survival (RFS), and overall survival (OS). Complications were defined as temporary or permanent. Temporary hypocalcemia and hypothyroidism were defined as the need for calcium or calcitriol or L-thyroxine supplementation within 12 months postoperatively. Pre- and postoperative fiber-optic vocal cord assessments were performed on all patients. Recurrent laryngeal nerve injuries were defined as postoperative vocal cord paralysis (uni- or bilateral). All complications lasting more than 12 months were considered as permanent. Structural recurrence was defined as locoregional or distant and was confirmed by computed tomography (CT), magnetic resonance imaging, positron emission tomography, or radioactive iodine (RAI) scanning.

Costs

The cost of surgery and a hypothetic AS are derived from anonymized data provided by the clinical costing team from the Royal North Shore Hospital and the University of Sydney. Medical costs of all parts of the operative treatment included all medical costs of preoperative examinations, anesthesia, pathologic examination, and inpatient stay. Treatment cost are expressed in Australian dollars (AUD $).

Currently, AS is not actively offered to low-risk PMC patients as a treatment option at the Endocrine Surgery Unit of the University of Sydney, Royal North Shore Hospital. The aim of this study was to compare costs of operative treatment according to the 2015 ATA guidelines versus hypothetic active surveillance. The hypothetic AS protocol and standard protocols for surgical treatment are shown in Table I. Hemi- or total thyroidectomy is performed for low- and high-risk PMC patients, respectively. Patients having an uncomplicated hemithyroidectomy receive a 5-year clinical follow-up with ultrasonographic examination and were considered cured thereafter. Patients managed with total thyroidectomy undergo routine central lymph node dissection (CLND). After implementation of the 2015 ATA guidelines, prophylactic central lymph node dissection was omitted. Lateral lymph node dissection was opted preoperatively based on clinical or ultrasonographic grounds, and intraoperatively when grossly involved lymph node disease was found. Patients undergoing total thyroidectomy have follow-up visits at 1 month, 6 months, and once yearly thereafter. After their release in 2015, the ATA guidelines are widely implemented among Australian endocrine surgeons[10]; however, we hypothesized that the number of PMC patients treated in our unit after implementation of the new guidelines would be small compared to patients treated with the previous guidelines. For a representative estimation of the ratio of total versus hemithyroidectomy for PMC treated according to current guidelines, all PMCs included in the retrospective cohort were reclassified according to the 2015 ATA guidelines as low (unifocal, intrathyroidal carcinomas without lymph node metastases) or high risk (extrathyroidal extension, lymph node metastases, and multifocality) based on histopathologic results.[5] Based on the reclassification, the ratio of total versus hemithyroidectomy for PMC after implementation of the 2015 ATA guidelines was estimated. Data of complications and recurrence rates from the previously described PMC cohort were used as input for the cost-effectiveness analysis, thereby providing a representative overview of costs of immediate operative treatment according to the current ATA guidelines for our unit.

Patients undergoing hypothetic AS are included in a program of biannual follow-up with an ultrasonographic examination and biochemical testing by an endocrinologist. Operative intervention would occur if there is disease progression or if the patient has a preference for operative treatment. The operative intervention rate was estimated at 8% according to previous literature and is performed 2 years after the initiation of AS.[11] The total costs of the AS and immediate operative management were calculated for the amount of years weighed by the frequencies of the events (recurrence, reoperation, and complications) based on local clinical data (Fig S1). Cost calculations for AS were based on the AS program proposed by Oda et al.[11] Additionally, a sensitivity analysis was performed to analyze the robustness of the cost analysis. Biannual follow-up for AS has been changed to annual follow-up after 2 years of biannual follow-up. This interval was based on the recommendation for yearly follow-up for PMC by the ATA Guidelines. In the second sensitivity analysis, the risk of disease progression per age decade was used to compare the cost of hypothetic AS versus immediate operative treatment. The estimated risk for disease progression per age decade in PMC patients during AS was based on recent Japanese data.[9] This approach allows for an accurate comparison between costs of operative treatment according to the 2015 ATA guidelines and a hypothetic AS program for patients treated at our unit.

Statistical analysis

All statistical analyses were performed using IBM SPSS version 25.0.0.0 (IBM Corp, Armonk, NY). Categorical variables were compared using the χ^2 test. The Cox proportional hazard model was estimated to identify patient and tumor characteristics for disease recurrence. Both RFS and OS were estimated using

Table I
Follow-up schemes of hypothetic AS and immediate operative treatment

Time	Hypothetic AS	Total thyroidectomy	Hemithyroidectomy*
At presentation	C, BT, US, FNA	C, BT, US, FNA	C, BT, US, FNA
1 mo	-	C, BT, MEDS	C, BT, MEDS†
6 mo	C, BT, US	C, BT	C, BT
1 y annually	n/a	C, BT, MEDS	C, BT, MEDS†, US
1 y biannually	C, BT, US	n/a	n/a

Standard protocol of hypothetic AS and immediate operative treatment for groups of patients with PMC at University of Sydney and Royal North Shore Hospital, Australia.
BT, blood test; *C,* consult with an endocrinologist/endocrine surgeon; *FNA,* fine-needle aspiration; *MEDS,* use of L-thyroxine with or without calcium/vitamin D supplementation; *US,* ultrasonography.
* Patients who underwent hemithyroidectomy will receive a 5-year follow-up.
† Medication is prescribed for patients requiring L-thyroxine with or without calcium/vitamin D supplementation.

Kaplan-Meijer curves and tests for statistical significance were conducted using the log-rank test.

Results

Patient characteristics

Between 1985 and 2017, 2,079 patients underwent operative treatment for the management of PTC. All PTC >1 cm (n = 1,421) and patients with incidental PMC treated by operation for thyrotoxicosis or goiter (n = 244) were excluded. Only patients treated by operation for a thyroid malignancy were included, resulting in 414 patients. Of these, 349 patients had sufficient follow-up and were included for analysis (Fig S2). Patient demographics are summarized in Table II. The median age of the included patients was 48 years (range, 18–90 years), and 282 patients (81%) were female. Total thyroidectomy was performed in 301 patients (87%); from these patients, 233 (77%) had lymph node dissection, 135 (58%) had a CLND, and 98 (42%) underwent additional lateral lymph node dissection. The remaining 48 patients (13%) were treated with hemithyroidectomy (Table II).

Table II
Patient and treatment characteristics

Characteristic	Categories	Number (%)
Age (years)	Median	48
	Range	18–90
Sex	Female	282 (81%)
	Male	67 (19%)
Operative treatment	Total thyroidectomy	301 (87%)
	Hemithyroidectomy	48 (13%)
LND (total thyroidectomy)	CLND	135 (58%)
	LLND	98 (42%)
LND (hemithyroidectomy)	CLND	16 (76%)
	LLND	5 (24%)
Operative complications	Permanent	13 (3.7%)
	Temporary	45 (12.9%)
Radioactive iodine	Yes	237 (68%)
	No	113 (33%)

Patient and treatment characteristics are described in the first column. Numbers are given in percentages.
LLND, lateral lymph node dissection; *LND,* lymph node dissection.

Operative complications

Temporary complications occurred in 12.9% of the patients (Table III). Temporary hypocalcemia was the most frequent temporary complication (n = 27) and occurred more often in patients undergoing total thyroidectomy (P = .03). Permanent complications occurred in 13 (3.7%), the most common of which was permanent hypoparathyroidism that occurred in 8 patients (2.3%). Moreover, 1 patient had injury to the recurrent laryngeal nerve. Four (8.3%) of the 48 patients who underwent a hemithyroidectomy had permanent hypothyroidism and required thyroid hormone supplementation. Reoperation was required for 4 patients, 3 of whom (0.9%) developed a hematoma, and 1 a chyle leak.

Survival

Median follow-up was 13.4 months (range 0–267.9 months); 55 patients (15.7%) had a follow-up greater than 5 years. The majority of patients (n = 237, 68%) were treated with RAI after operative treatment with a mean dosage of 4.0 (range, 0.9–7.0) GBq. All patients who received adjuvant RAI were treated previously with total thyroidectomy. The 5-year RFS, OS, and disease-specific survival were 94.5%, 97%, and 100%, respectively (Fig 1). Adjuvant RAI was administered more often in patients with tumor characteristics such as tumor size >5 mm, extrathyroidal extension, venous invasion, and multifocality (Table SI). Recurrence was diagnosed in 11 patients (3.2%). The majority of patients with recurrent disease presented with new distant metastases (n = 6, 1.7%); the remainder had locoregional lymph node recurrence (n = 5, 1.4%). All 11 patients with recurrence underwent prior lymph node dissection, 9 of whom had lymph node positivity postoperatively. Postoperative RAI was utilized for all 9 patients with positive lymph nodes 1 month postoperatively. Median time to recurrence was 14.3 months. Adjuvant RAI did not increase RFS (Fig 2, P = .104). Univariate analysis identified nodal positivity and extrathyroidal extension as being associated with PMC recurrence (P < .009 each; Table SII). Multivariate analysis did not indicate an association between recurrence and either age, sex, tumor size, lymph node involvement, extrathyroidal extension, venous invasion, multifocality, or adjuvant RAI.

Costs

The cost components of AS and immediate operative treatment are shown in Table IV. The average costs of 1 thyroid operative treatment using 3 years of data and excluding the admission for RAI treatment was calculated at AUD $9,041 (range, AUD $2,874–$26,881). Excluding the costs of complications and related operative intervention, the initial cost of AS was calculated to be AUD $950 and a yearly cost of AUD $756. Immediate operative treatment was estimated to be more costly at AUD $10,226, with a yearly cost of AUD $235. Assessment of the histopathology reports of the included PMC patients identified 141 low-risk patients (41%) who could be managed with a hemithyroidectomy. The remaining 208 (59%) high-risk patients would require thyroidectomy

Table III
Operative complications according to treatment

Operative complication	Number (%)	Total thyroidectomy (n = 301)	Hemithyroidectomy (n = 48)	P value
Hypocalcemia				
- Temporary	27 (7.8%)	27 (9.0%)	0	.03
- Permanent	8 (2.3%)	7 (2.3%)	1 (2%)	.95
RLN palsy				
- Temporary	9 (2.6%)	9 (3.0%)	0	.23
- Permanent	1 (0.3%)	1 (0.3%)	0	.70
Hypothyroidism*				
- Temporary	4 (8.3%)	-	4 (8.3%)	-
- Permanent	4 (8.3%)	-	4 (8.3%)	-
Other				
- Hematoma	3 (0.9%)	3 (1.0%)	0	.48
- Chyle leak	1 (0.3%)	1	0	.70

Operative complications are described in the first column and divided into the amount of complications in total thyroidectomies and hemithyroidectomies. Numbers are given in percentages.
RLN, recurrent laryngeal nerve.
* Patients presenting with permanent hypothyroidism after hemithyroidectomy.

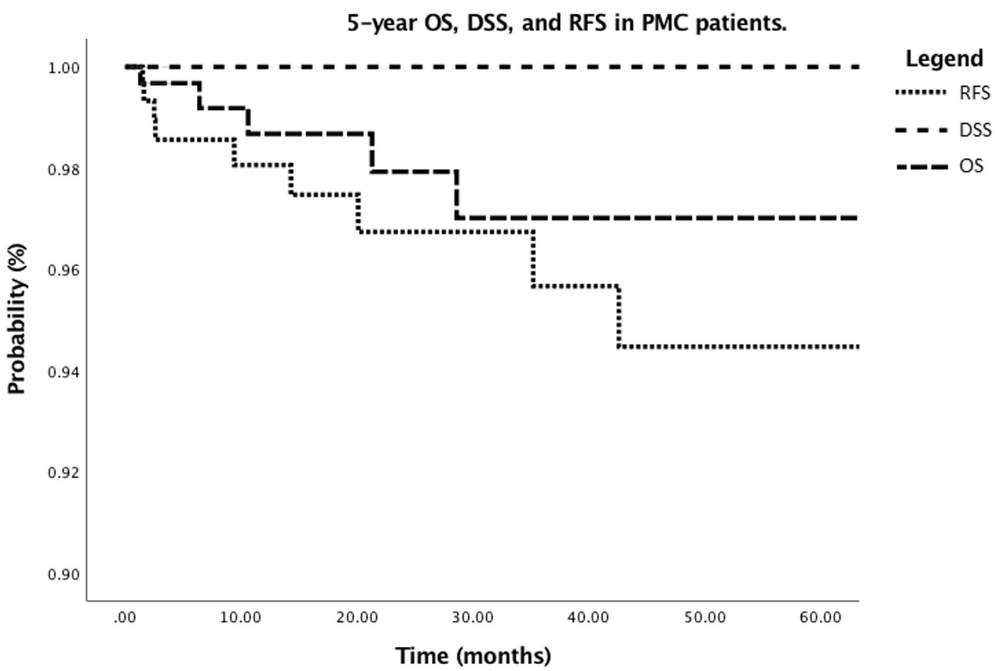

Fig 1. Kaplan Meier curve showing 5-year OS, DSS, and RFS in PMC patients. *DSS*, disease specific survival; *OS*, overall survival; *RFS*, recurrence free survival.

according to the current guidelines. From these patients, multifocality (n = 166) was the most prevalent, high-risk predisposition, followed by nodal metastases (n = 125) and extrathyroidal extension (n = 74). Based on an estimated hemi- and total thyroidectomy rate of 41% and 59% respectively and including complications, recurrences, and additional operative intervention, AS was estimated to be more expensive than operative treatment after 16.2 years (Fig 3). Additionally, a sensitivity analysis was performed to assess the cost efficiency of a decreased follow-up interval for AS from biannual to annual (Table V). This alteration markedly decreased the cost of AS when compared with operative treatment, with AS surpassing the cost of operative treatment of PMC after 45.1 years. Finally, a sensitivity analysis was performed to analyze the effect of the risk of disease progression during AS per age decade. The cost of AS in patients in the age group of 20 to 30 years exceeded the cost of immediate operative treatment after 8.0 years. In contrast, the cost of AS in patients between 70 to 80 years will exceed the cost of immediate operative treatment after 16.5 years (Table V).

Discussion

In this single-center study, we investigated the health outcomes and cost of immediate operative treatment versus AS for patients with PMC in the Australian setting. Permanent complications would be expected to occur in 3.7% of the patients and RAI would not appear to prevent recurrence. Immediate operative treatment appears to be less expensive when AS is expected to last more than 16.2 years.

Hypoparathyroidism is the most prevalent complication among our operatively treated patients. The rate of temporary hypoparathyroidism is greater in patients undergoing total thyroidectomy. These results are in concordance with the literature.[12] The overall complication rate of 14.9% reported in this study is similar to complication rates reported from other high-volume thyroid surgery centers.[13] The indolent biologic behavior of PMC was confirmed with a recurrence rate of 3.2%. Prior studies reported similar rates, ranging from 0% to 3%.[14,15] Our results confirm that adjuvant RAI does not decrease recurrence rates in PMC as reported

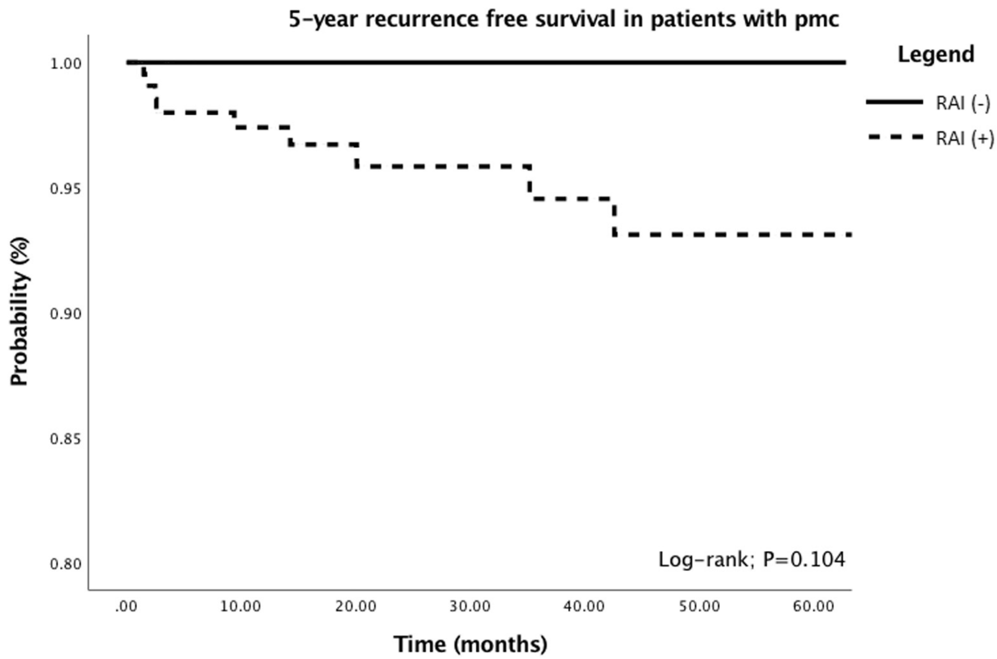

Fig 2. Meier curve showing 5-year recurrence free survival with (+) and without (-) radioactive iodine.

Table IV
Cost of clinical practices, AS, and immediate operative treatment

	Cost (AUD)	Cost (USD)
Clinical practice leading to diagnosis	950	675
Visit to endocrinologist	165	117
Blood tests	70	50
US	143	102
FNA	572	406
Thyroid surgery for malignancy	9,041	6,428
Follow-up		
Visit to endocrinologist	165	117
Blood tests	70	50
US	143	102
L-thyroxine*	26	19
Calcium and vitamin D supplementation*	19	14

The total costs are given by each modality outlined in the first column. The second and third column describes the cost of clinical practices given in Australian Dollars and US dollars, respectively.
FNA, fine-needle aspiration; *US*, ultrasound.
* Cost are as per 12 mo; these drugs do not include overhead costs or pharmacy costs.

in earlier studies.[16,17] These studies reported that the efficacy of postoperative RAI does not result in prevention of recurrent PTC, which is also in concordance with our data. Conversely, Xue et al showed that RAI does decrease recurrence rates in PMC patients with lateral and mediastinal lymph node metastases, suggesting that RAI can be beneficial for high-risk PMC patients.[18]

To date, there has been limited research and no studies comparing the costs and effectiveness of AS versus immediate operative treatment in the context of the Australian health care systems. We estimated that the initial cost of immediate operative treatment is greater than performing AS. A recent study in Japan suggested that initial operative treatment of PMC is 4.1 times more expensive than AS over a time span of 10 years.[11] Interestingly, Oda et al did not compare the costs and effectiveness of AS after 10 years. Our results confirm that immediate operative treatment of PMC in Australia is more expensive than AS during the initial 10 years after diagnosis. With the need for biannual follow-up and the possibility of operative intervention, we estimated that the costs of AS will exceed the cost of immediate operative treatment after 16.2 years. These numbers are concordant with a study from Wong et al,[19] suggesting that AS for PMC is more expensive compared with initial operative treatment when practiced more than 16.2 years after diagnosis. A recent study outlined that the growth kinetics of PMCs under AS appear to be predictable.[20] This information may help in guiding clinical decision making between operative intervention or observation, raising the question whether patients need a long follow-up during AS. The recent pioneering publications on AS of PMC are shifting the paradigms of worldwide treatment.[9,20] Nevertheless, determination of the optimal and most cost-effective treatment of PMC remain both patient and country-specific.

The results of this study should be addressed with respect to the limitations of our study based on retrospective data analysis and study biases. Patients were treated in a high-volume tertiary referral center by highly specialized endocrine surgeons. Therefore, complication rates may be less when compared with lesser volume centers. Furthermore, data used to calculate the costs in this study are likely to differ from that for other countries. To control the variation of costs, we validated the cost inputs with those in the published literature. Although most of the patients received adjuvant RAI, we did not include this RAI treatment in the cost analysis. Current practices do not recommend adjuvant RAI in low-risk patients. The cost of operative treatment was calculated from an estimated ratio of hemi- versus total thyroidectomy based on the prevalence of histology-proven low- and high-risk PMC in this cohort. This approach might underestimate the rate of hemithyroidectomies in current daily practice and in the future owing to adherence to the new guideline.[10] Based on the low risk of recurrence aftertreatment for PMC, we calculated follow-up costs after hemithyroidectomy based on discharge, when no recurrence is detected during a 5-year follow-up. Prospective studies are warranted to validate the optimal duration of follow-up needed.

Currently, no consensus about guidelines for AS versus immediate operative treatment are available internationally. This lack of consensus may affect the results of this cost and effectiveness

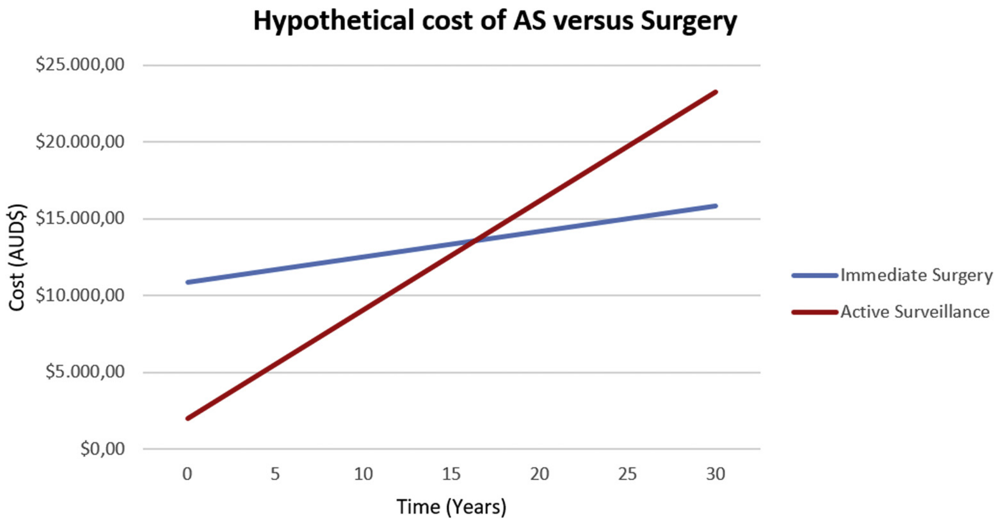

Fig 3. Hypothetical cost of active surveillance and immediate surgery, including complications, recurrences, and additional surgical intervention for active surveillance. *Blue line* represents the cost of active surveillance. *Red line* represents the cost of immediate surgery. Cost of active surveillance surpasses the cost of immediate surgery at 16.2 years. Costs are given in Australian Dollars.

Table V
Sensitivity analysis of AS versus immediate operative treatment

Category	Fixed cost of AS	Fixed costs of operative treatment	Cost of AS per year	Cost of operative treatment per year	Cost of AS > cost of operative treatment (years from diagnosis)
2015 ATA guidelines	AUD$2,014	AUD$10,837	AUD$709	AUD$165	16.2
Hypothetic AS interval of 1 y	AUD$2,014	AUD$10,837	AUD$361	AUD$165	45.1 y
RoD in 20s (60.3%)	AUD$8,969	AUD$10,837	AUD$400	AUD$165	8.0 y
RoD in 30s (37.1%)	AUD$5,883	AUD$10,837	AUD$537	AUD$165	13.3 y
RoD in 40s (27.3%)	AUD$4,580	AUD$10,837	AUD$595	AUD$165	14.6 y
RoD in 50s (14.9%)	AUD$2,932	AUD$10,837	AUD$668	AUD$165	15.7 y
RoD in 60s (9.9%)	AUD$2,267	AUD$10,837	AUD$698	AUD$165	16.1 y
RoD in 70s (3.5%)	AUD$1,416	AUD$10,837	AUD$735	AUD$165	16.5 y

The effect of adjusting the surgical management according to the 2015 ATA guidelines is outlined in the first row of the table. The effect of changing the annual follow-up interval for AS to 1 y is outlined in the second row of the table. The subsequent rows show the cost of AS and immediate operative treatment when patients are stratified by age decade. Cost of conversion to operative intervention and complications are included.
RoD, risk of disease progression.

analysis and, therefore, the generalizability of findings.[11,19–21] Moreover, there is lack of evidence regarding the frequency of follow-up during AS. Sensitivity analysis on the effect of a yearly follow-up suggested that AS is more cost-efficient over a greater period; however, a biannual follow-up of surveillance could be well defended. Because AS is a new strategy for our patients, disease progression should be monitored closely, especially in younger patients, because they tend to have a greater risk of disease progression than elderly patients. The lifetime risk of disease progression is estimated to be over 60% in patients between 20 and 30 years old.[9] In our sensitivity analysis, we recognized that these younger patients would be less cost-efficient in an AS program. Currently, the difference in quality of life of patients undergoing AS versus initial operative treatment for PMC in an Australian setting is unclear. To address this, a prospectively conducted study including assessments of the quality of life of patients with AS would ensure a right step toward patient-tailored treatment plans for patients with PMC.

In conclusion, for PMC managed in the Australian setting, immediate operative treatment should still be considered and may have a long-term economic advantage for patients who are likely to require more than 16.2 years of follow-up in an AS scheme. Therefore, for some patients, immediate operative treatment appears to remain a cost-effective and safe treatment option for Australian PMC patients.

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Conflict of interest/Disclosure

The authors have no conflicts of interest to declare in relation to this work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2019.05.078.

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Discussion

Dr Mahsa Javid (Charleston, SC): I have 2 questions. Firstly, why is it that a lot of your patients were high risk? What in particular made them high risk? This seems unusual.

Jia Feng Lin: I think this may be from referral bias. Patients were treated at a very specialized endocrine surgery unit, so it's more likely that high-risk patients would be referred there.

Dr Mahsa Javid: But what specifically made them high risk? Did they have lymph node involvement? Was it extrathyroidal extension?

Jia Feng Lin: Yes. We reclassified them into high risk or low risk, and patients with high risk were considered as such because of extrathyroidal extension, lymph node metastasis, or multifocality on histopathology.

Dr Mahsa Javid: My second question is, assuming your hypothetical scenario of surveilling patients has to be based on actually diagnosing the PTC, who is diagnosing these and how? Presumably, you are not getting people off the street into specialized centers and ultrasounding everybody. Who is seeing this? Are you biopsying lesions under a centimeter that might look suspicious?

Jia Feng Lin: Thank you for your question. I don't think I can answer that.

Dr Ashok R. Shaha (New York, NY): Going back to the question Dr Javid asked, when you are observing these patients, you select out the patients which are truly low risk. So, putting the high-risk patient in the observation protocol is probably not appropriate. If there is indication by age or any other criteria that the patient is high risk, they need to go to surgery. So, the comparison is a bit incorrect. That is number one.

Number two, you have shown that the cost of observation is high. The patients who undergo surgery have the same observation protocol. They undergo ultrasound, they undergo whatever the treatment is necessary, and they undergo thyroglobulin blood testing. So, I am not convinced that you are increasing the cost by observation. The ultrasound and the CAT scan, also the blood tests, are done even in patients with total thyroidectomy or lobectomy.

The last point is that you have a high number of total thyroidectomies, 88%. But if you consider microcarcinoma, 88% total thyroidectomy is a very high number.

Jia Feng Lin: Thank you for those comments.

Dr Viktor Makarin (St. Petersburg, Russia): Thank you for your excellent presentation. You showed that there were 2 patients with hypoparathyroidism in the hemithyroidectomy group. Can you explain how that would happen after hemithyroidectomy?

Jia Feng Lin: There was 1 patient with permanent hypocalcemia. I cannot explain that.

Dr Viktor Makarin: There was no previous operation? Or was it the first operation on this patient?

Jia Feng Lin: No. We did not include the completion thyroidectomies.