International Journal of Surgery 12 (2014) 837–842

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Total thyroidectomy versus hemithyroidectomy for patients with follicular neoplasm. A cost-utility analysis

C. Corso [a], X. Gomez [b], A. Sanabria [a, c, *], V. Vega [a], L.C. Dominguez [a], C. Osorio [a]

[a] Department of Surgery, Universidad de La Sabana, Chia, Colombia
[b] Education and Research Division, Fundacion Abood Shaio, Bogota, Colombia
[c] Oncology Unit, Hospital Pablo Tobon Uribe, Department of Surgery, Universidad de Antioquia, Medellin, Colombia

ARTICLE INFO

Article history:
Received 28 January 2014
Accepted 9 July 2014
Available online 11 July 2014

Keywords:
Thyroidectomy
Thyroid cancer
Goiter
Cost-benefit

ABSTRACT

Introduction: Thyroid nodules are a common condition. Overall, 20% of the nodules assessed with FNAB correspond to the follicular pattern. A partial thyroidectomy is the minimal procedure that should be performed to determine the nature of these nodules. Some authors have suggested performing a total thyroidectomy based on the elimination of reoperation and ultrasound follow-up. The aim of this study was to evaluate the most cost-useful surgical strategy in a patient with an undetermined nodule, assessing complications, reoperation, recurrence and costs.

Material and methods: A cost-utility study was designed to compare hemithyroidectomy and total thyroidectomy. The outcomes were complications (definitive RLN palsy, permanent hypoparathyroidism, reoperation for cancer, and recurrence of the disease), direct costs and utility. We used the payer perspective at 5 years. A deterministic and probabilistic sensitivity analysis was completed.

Results: In a deterministic analysis, the cost, utility and cost-utility ratio was COP $12.981.801, 44.5 and COP $291.310 for total thyroidectomy and COP $14.309.889, 42.0 and $340.044 for partial thyroidectomy, respectively. The incremental cost-utility ratio was −$535.302 favoring total thyroidectomy. Partial thyroidectomy was more cost-effective when the risks of RLN injury and definitive hypoparathyroidism were greater than 8% and 9% in total thyroidectomy, respectively. In total, 46.8% of the simulations for partial thyroidectomy were located in the quadrant of more costly and less effective.

Conclusion: Under a common range of complications, and considering the patient's preference and costs, total thyroidectomy should be selected as the most cost-effective treatment for patients with thyroid nodules and follicular patterns.

1. Introduction

Thyroid nodules are a very common condition. It is estimated that 3–7% of world population have palpable thyroid nodules, and this prevalence may reach 76% when ultrasonography is used as a screening tool [1]. When a thyroid nodule is detected, the most important step in the assessment is to determine whether this nodule is a carcinoma or an adenoma, which is determined via fine needle aspiration biopsy (FNAB). It is accepted that 5–7% of all nodules are malignant [2]. However, in 15–20% of nodules assessed with FNAB, it is not possible to determine the true condition of the malignancy or benignity; these are assessed by follicular patterns or undetermined nodules. Recently, these nodules were included into category 4 in the Bethesda system [3]. The nodules may be malignant in 20–30% of cases [4,5]. Currently, it is accepted that in these cases, a partial thyroidectomy is the minimum surgical procedure that should be performed to determine the nature of the nodule. This strategy has some advantages, such as the maintenance of thyroid function without hormone supplementation, the lower risk of recurrent laryngeal nerve (RLN) injury and the null risk of hypoparathyroidism. However, it also has some disadvantages, such as the need to reoperate on the patient if the pathology report confirms a malignancy, the obligation to perform an ultrasonographic follow-up of the remnant lobe and the later risk of reoperation if another suspicious nodule appears in this lobe, which could reach 50% at 10 years [6]. Consequently, some authors

* Corresponding author. Department of Surgery, School of Medicine, Universidad de La Sabana, Campus Puente del Comun, Km 21 Autopista norte, Chia, Colombia.
E-mail addresses: alvaro.sanabria@unisabana.edu.co, asanabriq@hotmail.com (A. Sanabria).

http://dx.doi.org/10.1016/j.ijsu.2014.07.005
1743-9191/

have suggested the performance of a total thyroidectomy based on the elimination of the possibility of reoperation and ultrasound follow-up; however, this option runs the risk of an increased rate of RLN injury and definitive hypoparathyroidism and of the need for hormone supplementation for the rest of the patient's life. There is no agreement as to which of these alternatives should be chosen. In the scenario of a patient with goiter, which is common in some iodine-deficient areas, such as Latin America, Europe and Asia, the conditions of the patient modify the baseline in favor of one or the other procedure. In this specific case, the advantage of preserving the thyroid function is lost, and therefore, leaving a remnant lobe will still carry the risk of reoperation, only securing the advantage of less RLN injury. To date, there is no information directly comparing the two surgical procedures and assessing their clinical and cost outcomes concomitantly.

The aim of this study was to evaluate the most cost-effective surgical strategy in a patient with an undetermined nodule in the FNAB, considering the complications, reoperation, recurrence and hormonal support in the long term.

2. Material and methods

This is a cost-utility study. The protocol was approved by the ethics committee and supported by Universidad de La Sabana. The cases on which the study is based involve adult patients with a thyroid nodule and a reported follicular pattern in the FNAB in a general hospital in a developing country as Colombia. Based on this scenario, we excluded patients with comorbidities, previous neck or thyroid surgery, previous radioiodine therapy and pregnancy.

2.1. Alternatives

A decision tree with a Markov chain was assembled with the Treeage Pro (Treeage software, Inc; Williamstown, MA, USA) to compare two strategies, hemithyroidectomy and total thyroidectomy, as the initial surgical procedure (Fig. 1). The Markov nodes were introduced for the risk of recurrence on the contralateral lobe after partial thyroidectomy. The outcomes included were complications (definitive RLN palsy, permanent hypoparathyroidism, reoperation for cancer, and recurrence of the disease in the contralateral lobe), direct costs and utility. The time period selected was 5 years.

2.2. Complications and follow up

We completed a systematic review of the literature in the PubMed database with the terms “hypothyroidism”, “thyroid nodule”, “therapeutics”, “treatment” and “thyroidectomy,” searching for data on the incidence of complications for each alternative. We assumed that total thyroidectomy could produce definitive RLN and permanent hypoparathyroidism, but the possibility of reoperation and the necessity of follow-up were null. On the contrary, hemithyroidectomy could have RLN palsy, but not permanent hypoparathyroidism; a risk of early reoperation was present if a

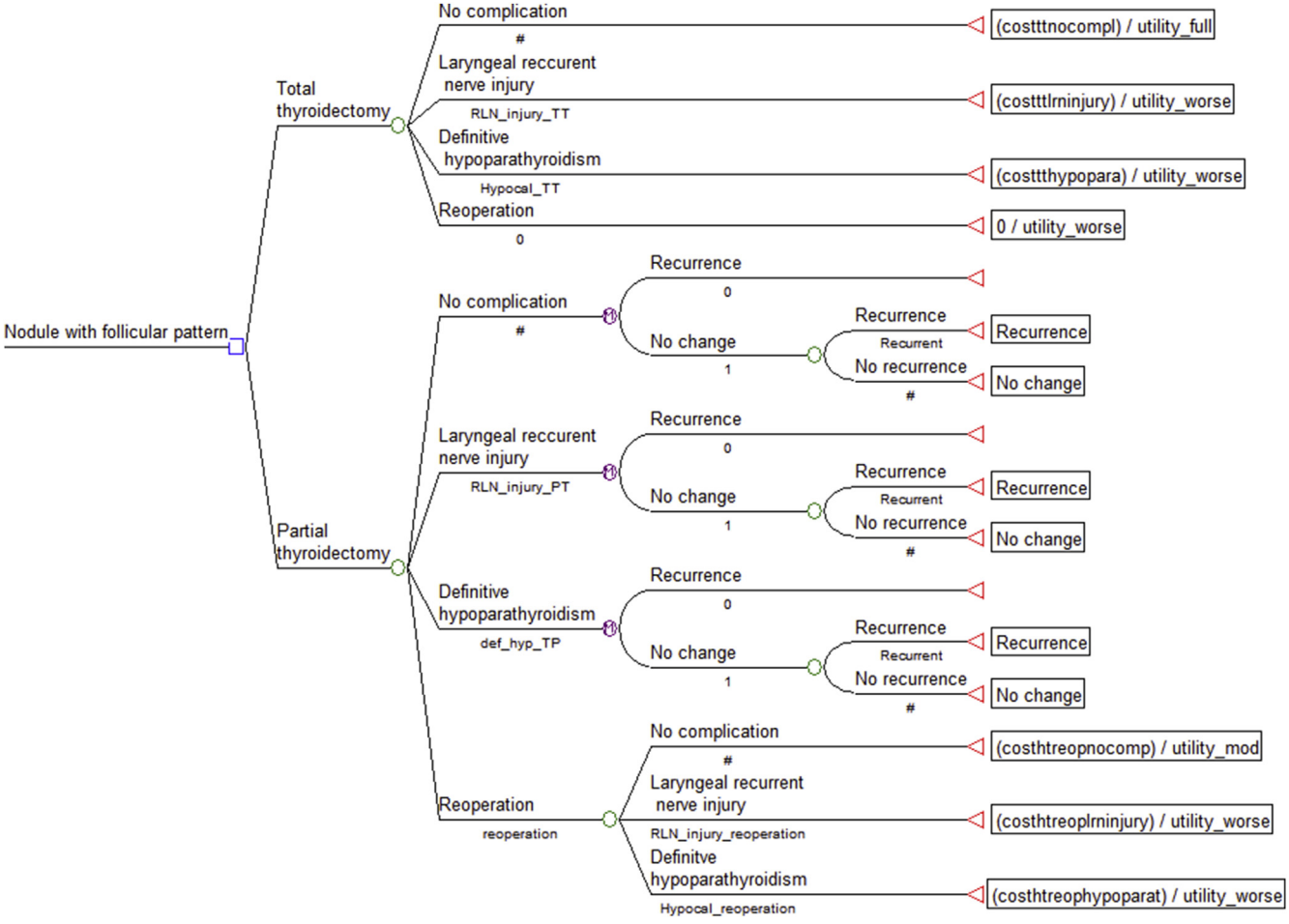

Fig. 1. Decision tree.

definitive pathological result of carcinoma was found, while the risk of late reoperation was present if a recurrence of the nodules in the remnant lobe was noted upon obligatory follow up. We also assumed that the rate of complications was higher in cases of reoperation. The follow up consisted of ultrasound and thyroid function tests every 6 months. The treatment complications were considered to include the following: for RLN injury, we considered vocal therapy up to 6 months; and for hypoparathyroidism, we considered the daily provision of 3600 mg of calcium and 0.5 mcg of vitamin D, with a trimestral measurement of serum calcium levels.

2.3. Costs

We used the payer perspective and considered only direct costs. We selected a cohort of 50 patients treated with each alternative by one of the authors and recorded the source used from clinical and administrative charts using a micro-costing method. Specific costs included honoraria and resources for the primary surgical procedure, operative time, inpatient length-of-stay, and resources of reoperation, follow-up tests (biochemical and imaging), treatment of complications and hormone supplementation. The total cost was calculated using the number of resources used and multiplying this value according to a national prizes manual (SOAT 2012), in comparison with the costs obtained from public contracts, as previously reported in other study [7]. For the cost calculation of the surgical procedure, we used a Monte Carlo probabilistic simulation with 500 iterations, with the primary data adjusted by operative time, to include the variability among hospitals and surgeons. For the follow up, we used a micro-costing method from the clinical charts, and an adjustment for the months of follow-up was made in order to calculate total costs. We used the mean, lowest and highest values obtained from this calculation for the sensitivity analysis. As the time period assessed was longer than a year, an annual 3% discount for costs and utility was applied. 1 dollar = 2800 COP (Colombian pesos).

2.4. Utility

For utility, we selected a preference measurement in a 1–10 visual analog scale using the following values: 1 for surgical procedures with any definitive complication, 10 for those without complication and 5 for cases which required a reoperation but had no complications. These preferences scales represent the weight a decision maker put in the outcome and have been widely used in other studies that assess utilities [8,9]. The numbers were obtained surveying surgeons involved in the management of thyroid diseases.

2.5. Data analysis

Categorical variables were presented as percentages and ranges, and continuous variables, as means and standard deviations. A deterministic one-way, two-way and tornado sensitivity analysis was performed for complications, reoperation, recurrence, costs and utility of the intermediate outcome of reoperation without complication. The incremental cost-utility ratio was calculated at the end of the 5 years to make comparisons. We also made a simple Monte Carlo probabilistic analysis using distributions for the variables previously reported (Table 3). The incremental cost-utility distribution was represented in the fourth quadrant graphic.

3. Results

The values obtained from the systematic review for complications, reoperation and recurrence of the disease are shown in Table 1 [10–15]. The risk of RLN definitive palsy was 1% for total thyroidectomy and 0.5% for partial thyroidectomy; of permanent hypoparathyroidism in total thyroidectomy, 2%; of RLN definitive palsy in any reoperation, 5%; of permanent hypoparathyroidism in any reoperation, 9%; of reoperation for malignancy in partial thyroidectomy, 20%; and of recurrence at 5 years, 10%. The net present value for utility at five years was 45.8 for surgery without complications, 22.9 for reoperation without any complications and 4.58 for surgery with any complications. For all of these cases, we used the same range for sensitivity analysis (4.58–45.8). The net present values for the costs calculated for each final outcome are shown in Table 2. The higher cost was incurred for a patient with a partial thyroidectomy who required a reoperation for any cause and who had definitive hypoparathyroidism as a complication. The lowest cost was incurred for a patient with a partial thyroidectomy without any complications.

Table 1
Incidence of complications by surgical procedure.

Complications	Total thyroidectomy (%, range for sensitivity analysis)	Partial thyroidectomy (%, range for sensitivity analysis)
RLN definitive palsy in primary surgical procedure	1 (0–50)	0.5 (0–50)
Permanent hypoparathyroidism in primary surgical procedure	2 (1–50)	0
RLN definitive palsy in reoperation	0	5.0 (0–50)
Permanent hypoparathyroidism in reoperation	0	9.0 (0–50)
Reoperation for postoperative malignancy finding	0	20 (0–50)
Reoperation for recurrence of nodule on the contralateral lobe	0	10 (1–99)

After rolling back in a deterministic analysis, the cost, utility and cost-utility ratios were COP $12.981.801, 44.5 and COP $291.310 for total thyroidectomy and COP $14.309.889, 42.0 and $340.044 for partial thyroidectomy, respectively. The incremental cost-utility ratio was −535.302, favoring total thyroidectomy.

3.1. Deterministic sensitivity analysis

For RLN definitive palsy and permanent hypoparathyroidism, the single way sensitivity analysis showed that partial thyroidectomy was more cost-effective than total thyroidectomy when the risks were superior to 8% and 9%, respectively. In cases of reoperation for malignancy, partial thyroidectomy was superior when the risk was lower than 11% and for reoperation for recurrence when the risk was lower than 7%, respectively. The tornado diagram showed that the most relevant variables were the risk of permanent hypoparathyroidism and the risk of recurrence at 5 years, both of them dominated in most clinical scenarios by total thyroidectomy, as shown.

3.2. Probabilistic sensitivity analysis

The probabilistic cost-utility calculations are shown in Table 4. As shown, the cost was higher and the utility was lower for partial thyroidectomy, with the result of complete dominance by total thyroidectomy. Fig. 2 shows the four quadrant plane for cost-utility. Overall, 46.8% of the simulations for partial thyroidectomy were located in quadrant II (more costly and less effective).

4. Discussion

Thyroid nodules are very common in the general population. The Framingham study determined that at least 4–8% of adults

Table 2
Direct costs value. (Colombian pesos).

	Total	NPV at 5 years	Lower value	Higher value
Total thyroidectomy without complications	$ 2.823.511	$ (12.930.856)	$ (9.308.176)	$ (30.822.842)
Partial thyroidectomy without complications	$ 1.671.847	$ (7.656.568)	$ (5.408.596)	$ (11.180.809)
Total thyroidectomy with RLN palsy	$ 2.839.363	$ (13.003.453)	$ (7.823.307)	$ (26.567.286)
Total thyroidectomy with hypoparathyroidism	$ 3.371.791	$ (15.441.818)	$ (12.415.855)	$ (26.567.286)
Partial thyroidectomy with RLN palsy	$ 2.157.331	$ (9.879.943)	$ (4.739.061)	$ (16.168.385)
Partial thyroidectomy with hypoparathyroidism	$ 2.689.759	$ (12.318.307)	$ (9.331.610)	$ (16.168.385)
Partial thyroidectomy with reoperation and without complications	$ 3.813.325	$ (17.463.913)	$ (11.632.526)	$ (31.604.750)
Partial thyroidectomy with reoperation and with RLN palsy	$ 3.829.177	$ (17.536.511)	$ (10.147.657)	$ (27.349.195)
Partial thyroidectomy with reoperation and with hypoparathyroidism	$ 4.361.605	$ (19.974.875)	$ (14.740.206)	$ (27.349.195)
Partial thyroidectomy with late reoperation and without complications	$ 3.343.693	$ (15.313.136)	$ (10.817.192)	$ (22.361.619)

have a clinically palpable nodules [2], and this number can reach almost 76% if ultrasonography is used [1]. These numbers can ever be higher if the population lives in iodine-deficient areas, such as Latin America, Asia and Europe [12]. The most relevant challenge for surgeons facing a patient with a thyroid nodule is to define whether it is malignant or benign. This classification is routinely performed with a FNAB, which has a high sensitivity and specificity [16]. However, in at least 15–20% of cases [17], the cytological results do not offer enough information to determine the type of nodule, resulting in what is currently called an undetermined, follicular pattern or a follicular neoplasm, under the recent Bethesda classification [18]. In these cases, the final diagnosis can only be made through a histopathological study of the surgical specimen. The most accepted approach in these cases is the performance of a partial thyroidectomy of the suspicious side, with or without frozen biopsy, to define the true pathological result and extent of the surgery (total or partial thyroidectomy). If the definitive result confirms a malignant nodule, a total thyroidectomy is indicated, but if the results discard this conclusion, the surgical procedure can finish with a partial resection. The avoidance of a total thyroidectomy in a benign condition offers the advantage of preserving at least 50% of the gland volume. This option allows the consequent preservation of its function without hormone supplementation and a decrease in the risk of definitive hypoparathyroidism and bilateral RLN palsy rates to zero, but it also carries the risk of an early reoperation due to a malignancy rate of approximately 30%. Long term follow-up of the remnant lobe is necessary, and the latent risk of a late reoperation due to nodule recurrence in the remaining lobe could reach 50% at 180 months [13]. Many authors have recommended choosing a total thyroidectomy, based on the advantages of reducing the rates of reoperation for malignancy or recurrence and reducing the need for follow-up to zero, but this choice incurs the price of a higher risk of bilateral RLN palsy and permanent hypoparathyroidism. However, factors outside of the potential complications should also be considered when making a decision. These strategies have different costs. In total thyroidectomy, the costs associated with complication management could be high, but in partial thyroidectomy, the cost of a reintervention and follow-up could also be important. Additionally, both strategies have different impacts on the quality of life. While a complication can be devastating, reoperation and permanent uncertainty about the condition of the remaining lobe can also cause significant anxiety. Up to now, we have been unable to identify a randomized controlled trial comparing these alternatives and considering all outcomes, and so our decision is based on our own personal criteria and experience.

Table 3
Values used in distributions for the probabilistic analysis.

Index	Variable name	Description	Type	Parameter 1	Parameter 2	Parameter 3
1	RLN_injury_TT	RLN injury total thyroidectomy	Triangular	0	0.01	0.05
2	RLN_injury_PT	RLN injury partial thyroidectomy	Triangular	0	0.005	0.01
3	RLN_injury_reoperation	RLN injury reoperation	Triangular	0	0.005	0.01
4	Hypocal_TT	Hypocalcemia after total thyroidectomy	Triangular	0	0.02	0.05
5	Hypocal_reoperation	Hypocalcemia after reoperation	Triangular	0	0.05	0.1
6	reoperation	Reoperation rate	Beta	20	80	
7	utility_reoperation	Utility for reoperation	Normal	5	3	
8	Recurrent	Recurrence rate	Beta	10	90	
9	costttnocompl	Costs in total thyroidectomy without complication	Log-normal	16.38	0.245	
10	costhtnocomp	Costs in partial thyroidectomy without complications	Log-normal	15.85	0.245	
11	costttlrninjury	Costs in total thyroidectomy with RLN injury	Log-normal	16.38	0.245	
12	costtthypopara	Costs in total thyroidectomy with hypoparathyroidism	Log-normal	16.55	0.245	
13	costhtrecurnocomp	Costs in partial thyroidectomy after recurrence and without complications	Log-normal	16.54	0.245	
14	costhtlrninjury	Costs in partial thyroidectomy with RLN injury	Log-normal	16.11	0.245	
15	cosththypop	Costs in partial thyroidectomy and hypoparathyroidism	Log-normal	16.33	0.245	
16	costhtreopnocomp	Cost in partial thyroidectomy and reoperation without complications	Log-normal	16.68	0.245	
17	costhtreoplrninjury	Costs in partial thyroidectomy and reoperation with RLN injury	Log-normal	16.68	0.245	
18	costhtreophypoparat	Costs in partial thyroidectomy after reoperation and hypoparathyroidism	Log-normal	16.81	0.245	

Table 4
Probabilistic incremental cost-utility values.

Strategy	Cost	Incremental cost	Utility	Incremental utility	C/E ratio	Incremental C/E ratio (ICER)
Total thyroidectomy	$13.447.811		44.01		$305.536	
Partial thyroidectomy	$14.713.565	$1.265.754	42.39	−1.61	$347.068	−$786.182

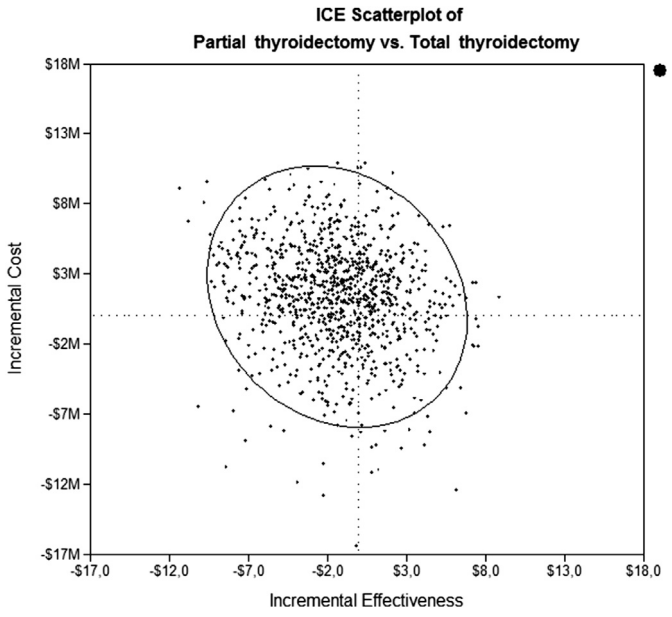

Fig. 2. Probabilistic quadrant plane for cost-utility.

Decision theory has shown that the human mind is not able to manage more than three variables simultaneously when making a decision [19]. Therefore, in this particular problem, the number of variables to take into account when choosing the best surgical alternative is sufficiently high to make the decision very difficult. An approach to these cases is the use of decision analysis. This methodology allows the introduction of a higher number of variables, facilitating a sensitivity analysis for the different clinical scenarios. As among the important variables are cost and preference, this method also allows their inclusion into the model.

This study showed that, with the accepted frequency of complications reported at high volume centers, approximately 2%, the cost-utility of the total thyroidectomy is the best option. Even in scenarios where the frequency could be even higher, total thyroidectomy maintains its dominance. Only in improbable cases of rates of permanent hypoparathyroidism of RLN palsy higher than 9% would partial thyroidectomy be a good option. In conditions, such as Graves' disease and goiter, some authors [20–22] have shown in randomized controlled trials that more extensive procedures (total or near total thyroidectomy) have the same rate of complications but a lower rate of late recurrence. However, these trials did not introduce the cost factor into their design.

The conclusion is also similar when the reported rates of reoperation for an unexpected malignancy found after hemithyroidectomy were included in the model. Classically, a risk of malignancy of 20% has been accepted. The recent introduction of the Bethesda classification [3], with its more specific categories of AUS and suspicious follicular neoplasms, has produced little change in this risk, decreasing the former to approximately 15% and increasing the latter to 30%. Even under these scenarios, total thyroidectomy stills maintain its dominance. Today, it seems impossible to reach rates of malignancy lower than 4%, although some genetic tests could change this situation in the future [23].

Additionally, when the risk of recurrence of goiter and the need of later reoperation were considered, total thyroidectomy was also the ideal alternative. We used a rate of recurrence of 10%, but this number can be higher in select populations, in which goiter is endemic [24,25]. Only in cases of less than 7% risk of recurrence would partial thyroidectomy be a good alternative. Additionally, the anxiety produced by a reoperation can differ between patients and populations, resulting in our fixing this value as intermediate between the two limits. A sensitivity analysis was performed with these variables, showing that even in cases where the patient was indifferent to undergoing a reoperation or not, total thyroidectomy was still always dominant.

A probabilistic analysis that also introduced the random variations that occur in real life confirmed the results of the deterministic analysis and showed that in almost 50% of cases, the strategy of partial thyroidectomy results in a more costly and less effective intervention. Only in 13% of cases were its results better than total thyroidectomy. This helps us to generalize the present results to other settings with similar conditions to those presented in this study.

However, some weaknesses of this study should be realized. The first is that the data were taken from only one surgeon and within the specific cost structure of a reference center. We tried to solve this difficulty by performing a probabilistic sensitivity analysis, but we understand that this approach can leave some particular situations out of the analysis. The same risk was run regarding the utility, which was specifically fixed by the authors. Second, this analysis did not include other variables, such as the surgeons' experience and case mix of patients. It is clear that more experienced surgeons will accept these conclusions easier than those at the beginning of their training curve; depending on the hospital, the number of difficult patients will be higher or lower. The base case corresponded to a mean patient, and all conclusions should be analyzed in consideration of this condition.

In conclusion, under the commonly accepted range of complications and considering the patient's preference and health system costs, total thyroidectomy should be selected as the most cost-effective treatment for patients with thyroid nodules with follicular patterns.

Ethical approval

Approved by ethics in research committee of Universidad de La Sabana.

Sources of funding

Universidad de La Sabana.

Author contribution

X Gomez, C. Corso participated in the design, collected information, participated in the analysis and writing of the article, reviewed the final version.

A Sanabria, V Vega, Luis C Dominguez and C Osorio participated in the design, participated in the analysis and writing of the article, reviewed the final version.

Conflicts of interest

None.

References

[1] H. Gharib, E. Papini, Thyroid nodules: clinical importance, assessment, and treatment, Endocrinol. Metab. Clin. N. Am. 36 (2007) 707–735 vi.
[2] M.D. Coltrera, Evaluation and imaging of a thyroid nodule, Surg. Oncol. Clin. N. Am. 17 (2008) 37 viii.
[3] E.S. Cibas, S.Z. Ali, The Bethesda system for reporting thyroid cytopathology, Am. J. Clin. Pathol. 132 (2009) 658–665.
[4] G.V. Teixeira, H. Chikota, T. Teixeira, et al., Incidence of malignancy in thyroid nodules determined to be follicular lesions of undetermined significance on fine-needle aspiration, World J. Surg. 36 (2012) 69–74.

[5] A. Sanabria, A.L. Carvalho, V. Piana dA, et al., Is galectin-3 a good method for the detection of malignancy in patients with thyroid nodules and a cytologic diagnosis of "follicular neoplasm"? A critical appraisal of the evidence, Head Neck 29 (2007) 1046–1054.
[6] A. Rios, J.M. Rodriguez, M.D. Balsalobre, et al., Results of surgery for toxic multinodular goiter, Surg. Today 35 (2005) 901–906.
[7] A. Sanabria, X. Gomez, L. Dominguez, et al., Tiroidectomía total basada en la evidencia, análisis de impacto presupuestario, Rev. Colomb. Cir. 27 (2012) 30–39.
[8] D. Parkin, N. Devlin, Is there a case for using visual analogue scale valuations in cost-utility analysis? Health Econ. 15 (2006) 653–664.
[9] G.W. Torrance, D. Feeny, W. Furlong, Visual analog scales: do they have a role in the measurement of preferences for health states? Med. Decis. Mak. 21 (2001) 329–334.
[10] T. Colak, T. Akca, A. Kanik, et al., Total versus subtotal thyroidectomy for the management of benign multinodular goiter in an endemic region, ANZ J. Surg. 74 (2004) 974–978.
[11] Y. Giles, H. Boztepe, T. Terzioglu, et al., The advantage of total thyroidectomy to avoid reoperation for incidental thyroid cancer in multinodular goiter, Arch. Surg. 139 (2004) 179–182.
[12] J. Moalem, I. Suh, Q.Y. Duh, Treatment and prevention of recurrence of multinodular goiter: an evidence-based review of the literature, World J. Surg. 32 (2008) 1301–1312.
[13] S. Ozbas, S. Kocak, S. Aydintug, et al., Comparison of the complications of subtotal, near total and total thyroidectomy in the surgical management of multinodular goitre, Endocr. J. 52 (2005) 199–205.
[14] M. Barczynski, A. Konturek, A. Hubalewska-Dydejczyk, et al., Five-year follow-up of a randomized clinical trial of total thyroidectomy versus Dunhill operation versus bilateral subtotal thyroidectomy for multinodular nontoxic goiter, World J. Surg. 34 (2010) 1203–1213.
[15] G. Agarwal, V. Aggarwal, Is total thyroidectomy the surgical procedure of choice for benign multinodular goiter? An evidence-based review, World J. Surg. 32 (2008) 1313–1324.
[16] G.A. de Carvalho, G. Paz-Filho, T.C. Cavalcanti, et al., Adequacy and diagnostic accuracy of aspiration vs. capillary fine needle thyroid biopsies, Endocr. Pathol. 20 (2009) 204–208.
[17] Z.W. Baloch, V.A. LiVolsi, Follicular-patterned lesions of the thyroid: the bane of the pathologist, Am. J. Clin. Pathol. 117 (2002) 143–150.
[18] B.K. Richmond, B.A. O'Brien, W. Mangano, et al., The impact of implementation of the Bethesda system for reporting thyroid cytopathology on the surgical treatment of thyroid nodules, Am. Surg. 78 (2012) 706–710.
[19] J.D. Birkmeyer, N.O. Birkmeyer, Decision analysis in surgery, Surgery 120 (1996) 7–15.
[20] M. Barczynski, A. Konturek, A. Hubalewska-Dydejczyk, et al., Randomized clinical trial of bilateral subtotal thyroidectomy versus total thyroidectomy for Graves' disease with a 5-year follow-up, Br. J. Surg. 99 (2012) 515–522.
[21] N. Rayes, T. Steinmuller, S. Schroder, et al., Bilateral subtotal thyroidectomy versus hemithyroidectomy plus subtotal resection (Dunhill procedure) for benign goiter: long-term results of a prospective, randomized study, World J. Surg. 37 (2013) 84–90.
[22] J.J. Sancho, R. Prieto, J.P. Duenas, et al., A randomized trial of hemithyroidectomy versus Dunhill for the surgical management of asymmetrical multinodular goiter, Ann. Surg. 256 (2012) 846–851.
[23] M. Xing, A.S. Alzahrani, K.A. Carson, et al., Association between BRAF V600E mutation and mortality in patients with papillary thyroid cancer, J. Am. Med. Assoc. 309 (2013) 1493–1501.
[24] Y. Erbil, A. Bozbora, B.T. Yanik, et al., Predictive factors for recurrent non-toxic goitre in an endemic region, J. Laryngol. Otol. 121 (2007) 231–236.
[25] R. Bellantone, C.P. Lombardi, M. Boscherini, et al., Predictive factors for recurrence after thyroid lobectomy for unilateral non-toxic goiter in an endemic area: results of a multivariate analysis, Surgery 136 (2004) 1247–1251.