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INTRODUCTION

Thyroid nodules are a common clinical condition with approximate prevalence of 6% in females and 1.5% in males.1 The primary concern in the assessment of thyroid nodule is to exclude malignancy. According to the 2017 Bethesda System for Reporting Thyroid Cytopathology, a thyroid nodule with fine-needle aspiration (FNA) biopsy reading suspicious for malignancy, which is classified as Bethesda V, implies risk of malignancy ranging from 50% to 75%.2 Risk factors that predict malignancy include clinical features (size >4 cm, family history, and history of irradiation),3 sonographic features,4 and molecular markers testing if performed. In a patient with low-risk papillary thyroid cancer (PTC), <4 cm without extrathyroidal extension and without lymph node metastasis (cN0), the initial surgical procedure could be either near-total/total thyroidectomy or thyroid lobectomy (American Thyroid Association [ATA] REC 35).5 The same recommendation applies if the FNA biopsy of the nodule shows suspicious for PTC (ATA REC 17).5

The strategy of initial thyroid lobectomy has some advantages, such as retaining some of the thyroid tissue, the nil probability of hypoparathyroidism, and the lower risk of injuring the recurrent laryngeal nerve (RLN). However, following thyroid lobectomy, the patient may need reoperation to undergo completion thyroidectomy in case the surgical histopathology revealed evidence of presence of moderate- or high-risk thyroid cancer. The need for frequent sonographic follow-up on the remnant lobe in anticipation of any suspicious nodule is another concern. Consequently, some patients and surgeons opt to proceed with total thyroidectomy, despite the higher risk of RLN injury and hypoparathyroidism, to eliminate the possible inconvenience of reoperation or compliance with ultrasound follow-up.

The study aim was to assess the cost-effectiveness of managing a single thyroid nodule suspicious for PTC on FNA by comparing lobectomy and total thyroidectomy approaches.

MATERIALS AND METHODS

The study is based on discrete-time Markov chain (MC) comparing the cost-effectiveness of two strategies, lobectomy versus total thyroidectomy for a predefined base-case (Fig. 1). The base-case is a 40-year-old female who presented with a 2.0-cm single
thyroid nodule after a preoperative FNA biopsy that was suspicious for PTC (Bethesda V). The patient is otherwise healthy, no clinical or sonographic evidence of cervical lymphadenopathy, and no previous history of radiation exposures, thyroid cancer, or any other type of cancers. It was proposed that if the base-case underwent lobectomy and histopathology revealed benign disease or low-risk PTC defined as tumor size <4 cm, no extrathyroidal extension, and was clinical N0, the base-case would be conservatively followed without completion thyroidectomy. Otherwise, if histopathology demonstrated high-risk PTC, the base-case would undergo completion thyroidectomy. We assumed that all the completion thyroidectomies were to be performed within the same year, and the

Fig. 1. Decision tree using the Markov model. FNA = fine-needle aspiration; PTC = papillary thyroid carcinoma; RLN = recurrent laryngeal nerve.
TABLE I.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign surgical pathology</td>
<td>40.0</td>
<td>2</td>
</tr>
<tr>
<td>PTC stage I or II on surgical pathology</td>
<td>48.0</td>
<td>6</td>
</tr>
<tr>
<td>PTC stage III or IV on surgical pathology</td>
<td>12.0</td>
<td>6</td>
</tr>
<tr>
<td>PTC, any stage, on surgical pathology</td>
<td>60.0</td>
<td>2</td>
</tr>
<tr>
<td>Unilateral RLN injury</td>
<td>1.0</td>
<td>7–9</td>
</tr>
<tr>
<td>Bilateral RLN injury</td>
<td>0.5</td>
<td>7–9</td>
</tr>
<tr>
<td>Hypothyroidism after thyroid lobectomy</td>
<td>22.0</td>
<td>9</td>
</tr>
<tr>
<td>Hypoparathyroidism after total thyroidectomy</td>
<td>1.0</td>
<td>9</td>
</tr>
</tbody>
</table>

Probabilities (%) from published literature (Table I).7

TABLE II.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Net Cost</th>
<th>Δ Cost</th>
<th>QALYs</th>
<th>Δ QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobectomy</td>
<td>$12,392.90</td>
<td>N/A</td>
<td>19.93</td>
<td>N/A</td>
</tr>
<tr>
<td>Total thyroidectomy</td>
<td>$15,074.26</td>
<td>$2,681.36</td>
<td>19.69</td>
<td>−0.24</td>
</tr>
</tbody>
</table>

ICER = $2,681.36/−0.24 = −$11,172.33

DISCUSSION

The choice of surgery for thyroid nodule depends on several factors. The FNA biopsy is crucial in determining the initial surgical procedure.2 A solitary thyroid nodule reported by FNA biopsy to be suspicious for malignancy can be stratified based on clinical and sonographic risk factors into low-, moderate-, or high-risk for malignancy. Accordingly, the extent of surgical resection (thyroid lobectomy versus total/near-total thyroidectomy) is decided.13 Both strategies have costs and benefits that should be taken into consideration when making a decision. The possible complications associated with total thyroidectomy could be costly, as well the possible need for reoperation, and regular follow-up after thyroid lobectomy might be devastating. Therefore, it is necessary to study the cost-effectiveness of both strategies that will provide efficient management.

Our base-case was hypothesized to be an adult female patient, aged 40 years, with solitary thyroid nodule (2 cm) reported by FNA biopsy as suspicious for PTC, with no previous history of thyroid surgery or neck irradiation, and with a time horizon of a 20-year follow-up. The frozen section is most helpful in cases of classic PTC histopathology; therefore, we assumed that the frozen section was not done during thyroid lobectomy. We also did not implement the molecular markers testing in our model, as its use on thyroid nodules suspicious for malignancy is not standardized yet.5

Under the base-case modeling assumptions, the QALYs gained after performing total thyroidectomy were 19.69, and 19.93 after thyroid lobectomy. This
demonstrated that a slight difference in utility existed between the two strategies. Net costs were $15,074.26 for total thyroidectomy and $12,392.90 for thyroid lobectomy. ICER calculation resulted in a negative value, revealing lobectomy to be superior to total thyroidectomy.

In a similar study conducted by Leiker et al.,9 they concluded that the cost-effective initial approach for a solitary thyroid nodule read as suspicious for PTC on FNA (Bethesda V) is the total thyroidectomy. However, there are significant issues with their model. They did not specify a size for the thyroid nodule of the base-case, and they included the frozen section in the analysis as a variable performed during thyroid lobectomy. Their model was most sensitive to changes in accuracy of frozen section, which is not routinely performed by most thyroid surgeons. They also did not account for the probable long-term use of thyroid hormone replacement therapy and calcium supplementation and incurred costs for only 12 months.9

Our Markov model was most sensitive to changes in rate of PTC stage III or IV on surgical pathology after thyroid lobectomy. However, total thyroidectomy would become the preferred strategy only when the probability of PTC stage III or IV on surgical pathology went beyond 82.4%, an extremely high rate not supported by the previous studies.6 The model also showed sensitivity to hypothyroidism probability, hypoparathyroidism probability, and unilateral RLN injury probability after thyroid lobectomy. For total thyroidectomy to be more cost-effective, each of the aforementioned probabilities should be 50% or higher, which was not appreciated by any prior study examining the complications after thyroid surgery.7–9

Generally, cost-effectiveness analysis studies are hypothetical in nature and reductive of real practice. The study is limited to truthfully replicating a real-life situation, which ultimately limits its generalizability. Cost-effectiveness analyses also have inherent limitation with reproducibility, mainly because of changes in values (probability and cost) over time and model design. It is worth mentioning that cost-effectiveness analysis outcomes are not meant to be applied at the individual level or guide clinical judgement. Rather, the outcomes described might be realized if the proposed intervention is applied at the population level.

Our analysis has some limitations to be considered. First, the current literature data discussing the clinical probabilities and patient utilities after thyroid surgery show variable ranges of percentages. We obtained our inputs from the best available sources. Second, we limited...
our base-case to the small thyroid nodules not exceeding 2 cm. To address the first and second limitations, we recommend further studies that have more detailed data regarding different sizes using different resources. Third, we did not include molecular testing, which may further stratify risk of malignancy preoperatively.

CONCLUSION

Thyroid lobectomy is a cost-effective strategy in patients with a solitary thyroid nodule cytologically diagnosed as suspicious for PTC on FNA biopsy. Total thyroidectomy is not just cost prohibitive, but is also associated with lower effectiveness compared with thyroid lobectomy.

BIBLIOGRAPHY