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Surgical safety and oncological completeness of robotic thyroidectomy for thyroid carcinoma larger than 2 cm

Young Jun Chai[1,2] · Hyunsuk Suh[3] · Jung-Woo Woo[4,5] · Hyeong Won Yu[2,4] · Ra-Yeong Song[2,4] · Hyungju Kwon[2,4] · Kyu Eun Lee[2,4]

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Abstract

Background The safety of robotic thyroidectomy (RT) for small-sized thyroid carcinomas has been well established. The surgical outcomes of bilateral axillo-breast approach RT for thyroid carcinomas larger than 2 cm were evaluated and compared with those of open thyroidectomy (OT).

Methods The medical records of patients who underwent total thyroidectomy or hemithyroidectomy followed by completion thyroidectomy for differentiated thyroid carcinomas measuring 2–4 cm were retrospectively reviewed.

Results The study included 86 patients who underwent RT ($n = 21$) or OT ($n = 65$) with mean ages of 30.8 and 51.6 years, respectively. The mean tumor size was 2.8 cm in both groups. There were no significant differences between the RT and OT groups in vocal cord palsy rate (transient, 19.0 vs. 9.2 %; permanent, 0 vs. 1.5 %), postoperative hypoparathyroidism rate (transient, 19.0 vs. 33.8 %; permanent, 4.8 vs. 1.5 %), and the number of retrieved central lymph nodes in papillary thyroid carcinoma patients (6.4 ± 3.5 vs. 6.1 ± 3.9, respectively). The proportion of the patients with serum stimulated thyroglobulin level of <1.0 ng/ml at the initial radioactive iodine treatment was 64.7 % (11/17) for RT group and 66.0 % (35/53) for OT group ($p = 0.920$). There were three patients (1 RT and 2 OT) who had a biochemical incomplete response, and there was no case of anatomical recurrence or mortality during the median follow-up period of 40.2 months.

Conclusion RT is a safe and oncologically sound treatment option for differentiated thyroid carcinomas measuring 2–4 cm in a selected group of patients. The role of RT should be evaluated in correlation with technological advances and increased experience.

Keywords Robotic · Thyroidectomy · Bilateral axillo-breast approach · BABA · Completeness · Large thyroid carcinoma

Young Jun Chai and Hyunsuk Suh have contributed equally to this study as co-first authors.

✉ Kyu Eun Lee
kyueunlee@snu.ac.kr

1 Department of Surgery, Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 156-70, Korea

2 Cancer Research Institute, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea

3 Department of Surgery, Mount Sinai Beth Israel Hospital, Icahn School of Medicine at Mount Sinai, New York, NY, USA

4 Department of Surgery, Seoul National University Hospital and College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea

5 Department of Surgery, Gyeongsang National University Changwon Hospital and Gyeongsang National University School of Medicine, Changwon 514-72, Korea

Thyroid surgery has become a common procedure in recent years because of the increasing incidence of thyroid carcinoma [1]. Conventional open thyroidectomy (OT) can be performed safely by experienced surgeons using a 4- to 6-cm transverse incision on the neck. However, the incision frequently results in a cosmetically undesirable scar on the neck despite the minimal incision length. Remote access thyroid surgeries were developed to avoid conspicuous neck scars, and the first endoscopic thyroid surgery was performed in 1996 [2]. Since then, various endoscopic approaches were developed, and the robotic system was adopted in 2007 [3].

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Among several methods of robotic thyroidectomy (RT), the bilateral axillo-breast approach (BABA) is one of the most widely used methods. BABA RT requires two 8 mm axillary incisions and two peri-areolar incisions measuring 8 mm on the left and 12 mm on the right [4, 5]. BABA RT is optimized for total thyroidectomy in that the camera offers a midline view, facilitating visualization of the bilateral recurrent laryngeal nerves and parathyroid glands [6]. However, similar to other RT methods, the application of BABA RT has been limited thus far although its safety and surgical completeness have been reported in the literatures [7, 8]. BABA RT is mainly used for the treatment of thyroid carcinomas measuring <2 cm or cancers with no evidence of local invasion or extensive lymph node metastasis [6, 7].

The use of BABA RT for thyroid carcinomas larger than 2 cm is not contraindicated, and the procedure has been performed in patients with a strong aversion to neck scars. Furthermore, RT has been performed for thyroid carcinomas larger than 2 cm that were indeterminate preoperatively and revealed as such after surgery. There are currently no reports on the surgical outcomes of RT for the treatment of thyroid carcinomas measuring > 2 cm. In the present study, the surgical outcomes of BABA RT in patients with differentiated thyroid carcinomas, including papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), larger than 2 cm were evaluated and compared with those of conventional OT.

Patients and methods

Patients

The medical records of patients who underwent total thyroidectomy or hemithyroidectomy followed by completion thyroidectomy for the treatment of PTC or FTC between April 2009 and January 2014 at Seoul National University Hospital were retrospectively reviewed. Patients with PTC or FTC measuring 2.1–4.0 cm were enrolled. Patients who had lateral neck lymph node metastasis were excluded. Clinicopathologic data and postoperative complications were recorded to evaluate surgical safety. Recurrence and the outcomes of radioactive iodine (RAI) treatment were analyzed for oncological completeness evaluation. The Institutional Review Board of the Seoul National University Hospital approved the study protocol.

Operative procedure

For OT, thyroidectomy was performed following conventional procedures, using a 4- to 6-cm transverse midline incision. BABA RT was performed as described previously [9]. Ipsilateral prophylactic central neck dissection was performed routinely when carcinoma was suspected preoperatively. Intraoperative frozen biopsy was routinely performed, and total thyroidectomy was performed when the results were suggestive of malignancy.

Postoperative follow-up

Patients visited the outpatient clinic 2 weeks after discharge for immediate postsurgical care, and follow-up examinations were performed at 3 and 6 months thereafter. Patients were treated with levothyroxine for thyroid stimulating hormone (TSH) suppression. A thyroid function test and thyroglobulin (Tg) and anti-Tg antibody level were checked every 6 months. Ultrasound was performed yearly. A routine indirect laryngoscopic examination was performed preoperatively and at the first outpatient clinic visit. Laryngoscopic examinations were repeated in patients with vocal cord palsy until the vocal cord movement normalized. Vocal cord palsy lasting more than 6 months was defined as permanent. Serum calcium and parathyroid hormone (PTH) levels were checked routinely for 1 year. Transient hypoparathyroidism was diagnosed when the serum total calcium level was below 8 mg/dl with hypocalcemic symptoms. Permanent hypoparathyroidism was diagnosed when the serum calcium and PTH level were below the normal range with ongoing calcium therapy for more than 6 months after surgery. Anatomical recurrence was defined as the anatomical reappearance of disease with following cytological confirmation or as the suspicious distant metastasis on imaging studies. A biochemical incomplete response was defined as a serum Tg level that was continually higher than 1.0 ng/ml or an increase in the anti-Tg antibody level in the absence of localizable disease, as suggested in the 2015 American Thyroid Association management guidelines [10].

RAI treatment protocol

RAI treatment was performed as described previously [11]. The first RAI treatment was performed at 3 months after surgery, the second RAI treatment at 6 months after the first RAI treatment. Stimulate Tg was measured on the day of each RAI treatment after 28 days levothyroxine withdrawal or recombinant human TSH (Thyrogen, Genzyme, Cambridge, MA, USA) injection for TSH stimulation. Successful ablation was assumed when serum Tg was <1.0 ng/ml.

Statistical analysis

Results were analyzed with SPSS version 20 (SPSS, Inc. Chicago, IL, USA). Continuous variables were expressed as the mean with standard deviation, and the groups were compared using Mann–Whitney test. Categorical variables were expressed as the number and percentage and compared using Fisher's exact or Chi-square test according to sample size. p values of <0.05 were considered statistically significant.

Results

Patient demographics and clinical characteristics

A total of 86 patients were enrolled in the study, including 21 for RT and 65 for OT. Patient demographics and clinicopathological characteristics are listed in Table 1. Patients who underwent RT were younger than those who underwent OT (30.8 ± 12.0 vs. 51.6 ± 12.4, $p < 0.001$), and RT patients had a lower body mass index (BMI) than OT patients (21.0 ± 2.8 vs. 24.8 ± 3.2, $p = 0.012$). There were no significant differences between the RT and OT groups in the pathologic diagnosis, mean tumor size, tumor stage, or nodal stage.

Surgical outcomes

Table 2 shows the surgical outcomes of RT and OT patients. Operation times were longer in the RT group than in the OT group (165.1 ± 43.9 vs. 93.5 ± 30.8 min, $p < 0.001$). There was no conversion to open surgery from RT. No significant differences between the RT and OT groups were observed in the number of retrieved central lymph nodes in PTC patients (6.4 ± 3.5 vs. 6.1 ± 3.9, $p = 0.816$), transient vocal cord palsy rates (19.0 %; 4/21 vs. 9.2 %; 6/65, $p = 0.250$), permanent vocal cord palsy rates (0 %; 0/21 vs. 1.5 %; 1/65, $p = 1.000$), transient hypoparathyroidism rates (19.0 %; 4/21 vs. 33.8 %; 22/65, $p = 0.199$) or permanent hypoparathyroidism rates (4.8 %; 1/21 vs. 1.5 %; 1/65, $p = 0.431$). There were no complications, including tracheal injury, or postoperative bleeding, in either group. Hospital stay was similar in the two groups (RT 3.2 ± 0.6 vs. OT 3.4 ± 0.9 days, $p = 0.241$). There were 3 patients (1 RT and 2 OT patients) who had a biochemical incomplete response. All of these patients had an elevated suppressed-Tg level higher than 1.0 ng/ml without evidence of anatomical recurrence. There was no anatomical recurrence or mortality during the median follow-up period of 40.2 months.

Outcomes of RAI treatment

RAI treatment was performed in 17 RT and 53 OT patients. Table 3 shows the outcomes of RAI treatment. The mean number of RAI treatments was 1.9 ± 0.7 (range, 1–4) for RT and 1.7 ± 0.6 (range, 1–3) for OT patients ($p = 0.446$). The mean total dose of RAI was 61.2 mCi (range, 30–100) for RT, and 74.3 mCi (range, 30–350) for OT patients ($p = 0.114$). There were no significant differences in the TSH stimulation methods between the two groups. The median serum stimulated Tg level at the first RAI treatment was 0.26 ng/ml (range 0.1–15.7) for RT and

Table 1 Clinicopathological characteristics of the patients

	RT ($n = 21$)	OT ($n = 65$)	p value
Age (mean ± SD), years	30.8 ± 12.0	51.6 ± 12.4	<0.001*
Gender			
Male	2 (9.5 %)	13 (20.0 %)	0.341†
Female	19 (90.5 %)	52 (80.0 %)	
Body mass index (mean ± SD), kg/m^2	21.0 ± 2.8	24.8 ± 3.2	0.012*
Pathologic diagnosis			
Papillary thyroid carcinoma	17 (81.0 %)	54 (83.1 %)	1.000†
Follicular thyroid carcinoma	4 (19.0 %)	11 (16.9 %)	
Tumor size (mean ± SD), cm	2.8 ± 0.6	2.8 ± 0.6	0.991*
Tumor stage			
T2	9 (42.9 %)	17 (26.2 %)	0.147‡
T3	12 (57.1 %)	48 (73.8 %)	
Nodal stage			
N0	11 (52.4 %)	22 (33.8 %)	0.315†
N1a	8 (38.1 %)	34 (52.3 %)	
NX	2 (9.5 %)	9 (13.8 %)	

RT robotic thyroidectomy, *OT* open thyroidectomy, *FNA* fine needle aspiration

* Mann–Whitney test, † Fisher's exact test, ‡ Chi-square test

Table 2 Surgical outcomes of patients in the RT and OT groups

	RT ($n = 21$)	OT ($n = 65$)	p value
Operation time (mean ± SD), min	165.1 ± 43.9	93.5 ± 30.8	<0.001*
Number of retrieved central lymph nodes in PTC patients (mean ± SD)	6.4 ± 3.5	6.1 ± 3.9	0.816*
Vocal cord palsy			
Transient	4 (19.0 %)	6 (9.2 %)	0.250†
Permanent	0 (0 %)	1 (1.5 %)	1.000†
Hypoparathyroidism			
Transient	4 (19.0 %)	22 (33.8 %)	0.199‡
Permanent	1 (4.8 %)	1 (1.5 %)	0.431†
Hospital stay (mean ± SD), days	3.2 ± 0.6	3.4 ± 0.9	0.960*

RT robotic thyroidectomy, *OT* open thyroidectomy

* Mann–Whitney test, † Fisher's exact test, ‡ Chi-square test

Table 3 Outcomes of radioactive iodine treatment

	RT ($n = 17$)	OT ($n = 53$)	p value
Mean number of RAI treatment (range)	1.9 ± 0.7 (1–4)	1.7 ± 0.6 (1–3)	0.757*
Mean of total RAI dose, mCi (range)	61.2 ± 17.6 (30–100)	74.3 ± 51.1 (30–350)	0.290*
TSH stimulation method for the first ablation			
T4-off	15 (88.2 %)	42 (79.2 %)	0.498†
Recombinant human TSH	2 (11.8 %)	11 (20.8 %)	
Median serum stimulated Tg level at the first RAI treatment, ng/ml (range)	0.26 (0.1–15.7)	0.31 (0.1–53.4)	1.000*
Serum stimulated Tg < 1.0 ng/ml at the first RAI treatment	11/17 (64.7 %)	35/53 (66.0 %)	0.920‡

RT robotic thyroidectomy, OT open thyroidectomy, *RAI* radioactive iodine, *TSH* thyroid stimulating hormone, *Tg* thyroglobulin

* Mann–Whitney test, † Fisher's exact test, ‡ Chi-square test

0.31 ng/ml (range 0.1–53.4) for OT patients, respectively ($p = 0.672$). There was no significant difference in the proportion of patients with serum stimulated Tg of <1.0 ng/ml at the first RAI treatment (RT 64.7 %; 11/17 vs. OT 66.0 %; 35/53, $p = 0.920$).

Discussion

The surgical safety and oncologic completeness of robotic thyroid surgery for the treatment of early stage differentiated thyroid carcinomas have been well documented [12–17]. The role of the RT procedure in thyroid carcinoma is largely attributed to the advantages of the robotic system, such as endo-wrist articulation and a three-dimensional magnified stable operative view in a constrained neck space. However, despite such advantages, RT is primarily recommended for small-sized thyroid carcinomas because of several technical limitations associated with the surgical resection of large thyroid carcinomas [7, 18, 19]. In addition to the innate limitations of endoscopic and robotic surgeries, such as lack of haptic feedback, limited instruments, narrow working space, and difficulties in bleeding control, there are limitations originating from the nature of thyroid surgery. In RT, one robotic arm typically retracts the thyroid gland to the contralateral side to identify the recurrent laryngeal nerve or parathyroid glands. This maneuver is hampered when the tumor is large because of the sheer size and density of the tumor. Furthermore, PTCs larger than 2 cm are associated with lymph node metastasis [20] and require meticulous lymph node dissection. The reported inferiority of RT to OT for retrieving lymph nodes is one of the reasons for selecting OT for the treatment of large thyroid carcinomas [21–23].

The surgical safety of thyroidectomy is commonly evaluated based on two parameters, vocal cord palsy and hypoparathyroidism rates. In the present study, we firstly demonstrated that RT can be performed safely in thyroid carcinomas larger than 2 cm. The complication rates of RT were comparable to those of OT in terms of vocal cord palsy and hypoparathyroidism rates, which was in agreement with previous studies comparing RT with OT [7, 23]. However, a recent meta-analysis by Lang et al. reported that the transient vocal cord palsy rate of RT is higher than that of OT, whereas no differences in the permanent vocal cord palsy rates or transient and permanent hypoparathyroidism rates were detected between RT and OT patients [24]. In the present study, the transient vocal cord palsy rates were higher in RT than in OT patients (19.0 vs. 9.2 %), but the difference did not reach statistical significance. The potentially higher risk of transient vocal cord palsy in the RT group might be explained by the observation that 80 % of vocal cord palsy cases are caused by traction injury [25], and RT requires a longer operation time than OT. Careful attention is needed when performing RT to avoid retracting the thyroid gland for a prolonged time to minimize the risk of transient vocal cord palsy.

Along with safety issues, oncologic completeness is an important factor in the evaluation of the surgical outcomes of thyroid cancer operations. The most reliable parameters of surgical completeness are the number of retrieved lymph nodes and serum stimulated Tg levels. In previous studies, analysis of the number of retrieved lymph nodes indicated the inferiority of RT [22, 23]; however, in the present study, the number of retrieved central lymph nodes in PTC patients was similar between the RT and OT groups (RT 6.4 ± 3.5 vs. OT 6.1 ± 3.9, $p = 0.816$). Meanwhile, the level of serum stimulated Tg measured on the day of RAI treatment reflects the amount of residual thyroid tissue, and a level of <1.0 ng/ml is suggestive of successful ablation. In the present study, the proportion of patients with serum stimulated Tg of <1.0 ng/ml was similar between the two groups, which is in agreement with previous studies [7, 8, 14]. Taken together, these data indicate that RT has similar outcomes to OT regarding the number of retrieved lymph nodes and serum stimulated Tg levels. This is attributed to the fact that the BABA method allows a relatively symmetrical operative view of both lobes of the thyroid gland, which facilitates complete thyroid tissue removal [6, 8]. These results support the use of BABA RT as a remote access surgery method for thyroid carcinomas requiring total thyroidectomy.

A comparison of the surgical outcomes of RT and OT was difficult because the patient demographics of the two groups were different. The age and BMI of RT patients were lower than those of OT patients because RT is more popular among young patients. Given that the cost gap between the two procedures is significant, and RT is performed solely on the basis of patient preference, a randomized controlled study of patients undergoing RT and those undergoing OT is not possible. The impact of age and BMI differences on surgical outcomes cannot be determined; however, a previous study reported similar surgical outcomes of transaxillary approach RT and OT regardless of body habitus, indicating that BMI may not have a significant impact on the surgical outcomes of thyroidectomy [26].

This study has limitations. Firstly, the follow-up period was too short to evaluate fully the survival outcomes of PTC patients on the basis of anatomy or histologic appearance, which usually requires long-term surveillance. This was because robotic surgery was only adapted since 2008. Instead, we used the stimulated Tg level as a surrogate marker to evaluate oncologic completeness, which showed that 2- to 4-cm thyroid tumors can be removed by RT as effectively as by OT. Secondly, the results of this study should be interpreted carefully because all RT and OT procedures were performed by highly experienced surgeons. Based on the transaxillary approach RT study, 40–50 cases are needed to overcome the learning curve, and inexperience was associated with major complications such as permanent vocal cord palsy, permanent hypoparathyroidism, bleeding requiring reoperation, tracheal injury, or major vessel injury [27, 28]. In this regard, for less experienced surgeons, appropriate patient selection is essential to ensure good surgical outcomes.

Conclusion

The results of the present study indicate that RT can be performed safely with sound oncologic completeness for the treatment of differentiated thyroid carcinomas measuring 2–4 cm without lateral neck lymph node metastasis. As this procedure becomes more common, further studies should evaluate the expanding indications for RT.

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Compliance with ethical standards

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