Review Article

Bilateral axillo-breast approach robotic thyroidectomy: review of evidences

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Abstract: The bilateral axillo-breast approach (BABA) is one of the most popular contemporary remote-access thyroidectomy techniques. While the initial experiences with BABA endoscopic thyroidectomy (ET) were associated with some technical challenges and safety concerns, many limitations of the technique could now be substantially overcome by BABA robotic thyroidectomy (RT). In this review, the current literature evidences of BABA RT were analyzed. Data regarding the patient selection, the learning curve, and the comparison with open thyroidectomy (OT) and BABA ET were examined. Careful case selection for BABA RT should be undertaken according to factors related to the patient and the thyroid pathology. The learning curve of BABA RT was about 40 cases. Comparing to OT, BABA RT was comparable to OT for the complication profiles and most perioperative outcomes. But it was associated with longer operative time, higher cost and possibly inferior oncological control with lower number of central lymph node (LN) retrieved. When compared to BABA ET, BABA RT was comparable for most perioperative outcomes except longer operative time and higher cost. Yet, BABA RT was superior to BABA ET for better oncological control. BABA RT is a safe and effective procedure for most benign thyroid conditions and low-risk differentiated thyroid cancers (DTC).

Keywords: Bilateral axillo-breast approach (BABA); endocrine surgical procedures; robotics; thyroid neoplasms; thyroidectomy

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Introduction

The bilateral axillo-breast approach (BABA) for thyroidectomy was developed in 2007 by Choe and Youn *et al*. as a modification of the axillo-bilateral breast approach by Shimazu *et al*. (1,2). It is currently one of the most popular remote-access thyroidectomy techniques in the world, particularly in Korea (3,4). Among different techniques of remote access thyroidectomy, BABA has several unique advantages (5). Using a midline approach, BABA provides a symmetrical view to both thyroid lobes for optimal visualization and dissection of vital structures. Such midline access also allows a familiar operation process to surgeons as the dissection method closely resembles that of conventional open thyroidectomy (OT). In contrast to other techniques, BABA enables the largest operative angles between instruments that can distinctively prevent instrument crowding or fighting. Excellent cosmesis can also be easily achieved because four separate small wounds are adopted instead of a single long scar in the neck or other

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remote sites.

The initial experiences with BABA endoscopic thyroidectomy (ET) were associated with many technical challenges and safety concerns. Due to the limitations of narrow working space, two-dimensional operative view and restricted instrument manipulation, BABA endoscopic procedures could be applied to a small subset of patients only (5,6). With the advent of the Da Vinci robotic system (Intuitive Surgical, Inc., Sunnyvale, CA, USA), many technical disadvantages of BABA ET could be substantially overcome and the indications of BABA robotic thyroidectomy (RT) could be largely extended (7). With the eminent technology of multi-articulated endo-wrist function, hand tremor filtration and three-dimensional magnification, BABA RT can now be safely and effectively applied to the management of benign and malignant thyroid conditions (8-14).

While the outcomes of RT and OT have been extensively compared in the literature (15-24), none of the reports provides specific focus on BABA RT. In this review, we analyzed the current literature evidences about BABA RT, including its patient selection, the learning curve, and the comparison data with conventional OT and BABA ET.

Patient selection

Because BABA RT is not technically feasible on every patient, patients should be carefully selected according to the patient factors and the thyroid pathology (4,15). For patient related factors, there is no age limit for BABA RT but most surgeons apply the procedure on patients below 70 years of age (10,12). Although BABA RT can be safely conducted on both genders without restriction, male gender was an independent factor predicting difficult surgery (25). Prior surgery or irradiations at the neck or breast are absolute contraindications. Obesity is generally considered as a relative contraindication for BABA RT. Yet, a study by Lee *et al*. confirmed that obesity (BMI ≥25 kg/m^2) was not an adverse factor associated with increased complications or unfavorable outcomes (26).

In terms of disease factors, BABA RT is applicable exclusively on benign conditions and low-risk differentiated thyroid cancers (DTC). For benign thyroid pathology, the upper size limit is usually set at 6–8 cm (9). Although BABA RT may be technically more demanding on patients with Graves' disease or thyroiditis, these are no longer a contraindication (14,27-29). For low-risk DTC, most surgeons limit the size to ≤4 cm. Posteriorly located tumors are not suitable as there is an unpredictable risk of recurrent laryngeal nerve (RLN) involvement. Extrathyroidal invasions to larynx, trachea, esophagus, or RLN are also absolute contraindications. Minimal anterior strap muscle invasion and lateral cervical nodal metastasis are still feasible because en bloc resection of strap muscles and modified radical neck dissection (MRND) can both be safely accomplished by the BABA robotic technique (30).

Learning curve

Similar to other minimally invasive procedures, the operative time of BABA procedures is expected to decrease with increasing experiences of surgeons and the operating team (31). As demonstrated in a study analyzing the learning curve of BABA RT in 100 cases by a single surgeon, the mean operative time decreased significantly from 232.6 minutes in the first 40 cases to 188.9 minutes in the next 60 cases (P=0.001) (13). In another study by Kim *et al*. on 300 cases by a single surgeon, the operative time also reduced remarkably after 35–40 cases of BABA RT (31). The learning curve of BABA RT was therefore about 40 cases.

Comparison with conventional OT

In the literature, there are 11 studies comparing the outcomes between BABA RT and OT (*Table 1*) (27-37). All except one study are originated from South Korea which represents the major and leading body of worldwide experiences and evidences (27-36). One study was conducted in China and it is the only randomized controlled trial (RCT) available (37). All the other studies are non-randomized retrospective comparisons which are subjected to selection biases. To eliminate these biases, the authors in four studies had conducted a matched comparison using propensity score matching (27,28,32,33). While most studies focused on patients with papillary thyroid carcinoma (PTC), one study by Kwon *et al*. compared the differences between BABA RT and OT on patients with Graves' disease (32). All these evidences about the comparisons between BABA RT and OT on the perioperative results, complication profiles, oncological outcomes, and cost differences are to be reviewed.

Perioperative outcomes

Operative time

Because of the need for skin flap dissection and robotic

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Table 1 Comparison of outcomes between BABA RT and OT (Data are BABA RT versus OT)

Author/year	Sample size	Age (years)	Tumor size (cm)	Operative time (min)	Hospital stay (days)	Transient RLN injury (%)	Permanent RLN injury (%)	Transient hypoPTH (%)	Permanent hypoPTH (%)	Bleeding (%)	No of central LN retrieved	sTg (ng/mL)	Ablative sTg <1 ng/mL (%)	Cost (USD)
Lee *et al*. 2011 (27)	108:108	43.8:43.7 (P=0.93)	0.82:0.83 (P=0.82)	NR	NR	NR	NR	NR	NR	NR	NR	1.4:1.4 (P=0.56)	64.2:69.0 (P=0.59)	NR
Kim *et al*. 2014 (28)	123:123	38.9:39.8 (P=0.19)	0.78:0.74 (P=0.55)	NR	NR	4.9:5.7 (P=1.00)	0:0.3 (P=1.00)	23.4:21.1 (P=0.65)	0:0 (P=NS)	0:0 (P=NS)	8.7:10.7 (P=0.006)	1.3:1.1 (P=0.65)	75.7:76.4 (P=0.93)	NR
Chai *et al*. 2016 (29)	27:27	36.0:38.9 (P=0.19)	0.80:0.90 (P=0.43)	142:79 (P<0.001)	3.3:3.1 (P=0.04)	11.1:11.1 (P=1.00)	0:0 (P=NS)	37.0:22.2 (P=0.37)	0:0 (P=NS)	NR	5.3:7.4 (P=0.13)	NR	NR	NR
Seup Kim *et al*. 2015 (30)	13:65	38.9:43.5 (P=0.21)	1.10:1.47 (P=0.24)	382:210 (P<0.001)	5.4:6.9 (P=0.30)	0:4.6 (P=NS)	0:3.1 (P=NS)	0:15.4 (P=NS)	0:1.5 (P=NS)	0:0 (P=NS)	12.8:12.7 (P=0.97)†	2.5:2.8 (P=NS)	69.2:54.0 (P=NS)	13,608:4,704 (P<0.001)
Kim *et al.* 2015 (31)	300:300	39.5:48.5 (P=0.001)	0.60:0.94 (P=0.47)	175:115 (P<0.001)	3.9:3.5 (P=0.09)	2.6:1.3 (P=0.08)	0:0.7 (P=NS)	23.0:36.3 (P=0.01)	1.3:1.3 (P=NS)	0.3:0.3 (P=NS)	6.7:8.9 (P<0.001)	0.8:1.7 (P=0.001)	86.6:67.6 (P=0.004)	NR
Kwon *et al.* 2016 (32)	44:44	35.1:36.4 (P=0.56)	NR	178:89 (P<0.001)	3.4:3.3 (P=0.56)	11.4:11.4 (P=1.00)	0:2.3 (P=0.31)	18.2:20.5 (P=0.78)	2.3:2.3 (P=1.00)	0:0 (P=NS)	NR	NR	NR	NR
Cho *et al.* 2016 (33)	109:109	41.7:40.8 (P=0.25)	0.70:0.70 (P=0.33)	290:107 (P<0.001)	3.5:3.4 (P=0.29)	6.4:5.5 (P=NR)	0.9:0.9 (P=NR)	33.0:26.6 (P=NR)	1.8:1.8 (P=NR)	0.9:0.9 (P=NR)	3.5:5.2 (P=0.002)	0.2:0.2 (P=0.95)	NR	7,632:2,995 (P<0.001)
Kim *et al.* 2011 (34)	69:138	41.3:51.8 (P<0.001)	0.60:0.70 (P=0.03)	196:81 (P<0.001)	3.1:2.8 (P=0.09)	1.4:0.7 (P=0.62)	0:0 (P=1.00)	33.3:27.5 (P=NS)	1.4:2.9 (P=NS)	0:0 (P=1.00)	4.7:4.8 (P=0.80)	0.8:0.8 (P=0.97)	NR	NR
Kwak *et al*. 2015 (35)	206:634	40.0:51.4 (P<0.001)	0.79:1.01 (P=0.14)	239:115 (P<0.001)	3.4:3.3 (P=0.71)	0.5:0.9 (P=0.36)	NR	14.6:15.0 (P=0.29)	0.5:0.3 (P=0.08)	0:0.9 (P=0.16)	5.8:8.4 (P=0.001)	NR	NR	9,198:1,489 (P<0.001)
Chai *et al*. 2017 (36)	21:65	30.8:51.6 (P<0.001)	2.80:2.80 (P=0.99)	165:93 (P<0.001)	3.2:3.4 (P=0.24)	19.0:9.2 (P=0.25)	0:1.5 (P=1.00)	19.0:33.8 (P=0.19)	4.8:1.5 (P=0.43)	0:0 (P=NS)	6.4:6.1 (P=0.81)	0.2:0.3 (P=0.67)	64.7:66.0 (P=0.92)	NR
He *et al*. 2016 (37)	50:50	40.9:41.5 (P=NS)	0.50:0.49 (P=NS)	118:90 (P<0.05)	5.1:5.3 (P=NS)	2.0:0 (P=NS)	0:0 (P=NS)	20.0:34.0 (P=NR)	0:0 (P=NS)	0:0 (P=NS)	6.7:6.8 (P=NS)	NR	NR	NR

BABA, bilateral axillo-breast approach; RT, robotic thyroidectomy; OT, open thyroidectomy; RLN, recurrent laryngeal nerve; hypoPTH, hypoparathyroidism; LN, lymph node; sTg, stimulated thyroglobulin; NR, not reported; NS, not significant. †Data are lateral compartment lymph nodes.

docking, the operative time of BABA RT was consistently longer than that of OT in nine comparative studies (29-31,33-37). The mean operative time of BABA RT was almost 1.3 to 2.4 times longer than that of OT. In a study evaluating robotic BABA and open total thyroidectomy with MRND, Seup Kim *et al.* also found a significantly longer operative time in BABA procedure than in open approach (30). Although cumulating experiences could shorten the operative time of BABA RT, the remarkable differences on operative time between BABA RT and OT could hardly be eliminated.

Postoperative pain

Postoperative pain between BABA RT and OT was analyzed in three studies (29,33,37). In a RCT, He *et al.* reported a significantly lower pain score in BABA RT than in OT during the first 24 hours after surgery (37). In a cohort study using propensity score matching, Cho *et al.* observed no differences in pain scores during the first two postoperative days (33). In another comparative study specifically analyzing postoperative pain, Chai *et al.* also found no differences between the two procedures for both throat pain and neck pain (29). Overall evidences suggested that BABA RT was at least equivalent to OT for postoperative pain.

Drain output

While one study found a significantly higher volume of drain output in BABA RT than in OT (34), He *et al.* and Kim *et al.* reported comparable results between the two procedures (30,37). The duration of keeping drainage tube was also similar as shown in the RCT by He *et al.* (37).

Hospital stay

In the largest series of 1,026 cases of BABA RT, Lee *et al.* reported a mean hospital stay of 3.3 days (10). None of the available studies showed a significant difference between BABA RT and OT on the length of hospital stay (29-35). Their reported mean hospital stay after BABA RT was also about 3 to 5 days.

Cosmetic satisfaction

The essence of remote access thyroidectomy entails better patients' satisfaction on cosmetic outcomes. Using different measurement scales, BABA RT was found to be significantly better than OT on cosmetic satisfaction in four comparative studies (29,35,37,38). In a prospective study focusing on postoperative scarring and psychological distress, Koo *et al.* observed a significantly better result in BABA RT than in OT (38). These evidences concluded that BABA RT was objectively superior to OT on cosmetic excellence.

Sensory change

Anterior chest paresthesia is notoriously common after BABA procedures due to the need of skin flap dissection. Two prospective observational studies by Kim *et al.* suggested that 41.2% of patients experienced sensory impairment after BABA procedures but such sensory disturbance could be normalized completely by 3 months (39,40). As for the comparison with OT, no study provided data on sensory change.

Complication profiles

The rates of RLN injury, hypoparathyroidism and other specific complications often represent the hallmark of operative safety in BABA RT. In the largest series of 1,026 cases of BABA RT, Lee *et al.* reported the complication rates of total thyroidectomy with central compartment nodal dissection (CCD), including transient RLN injury (14.2%), permanent RLN injury (0.2%), transient hypoparathyroidism (39.1%), and permanent hypoparathyroidism (1.5%).

RLN injury

Although there was no universal consensus in defining transient and permanent RLN injuries, no significant difference was observed between BABA RT and OT for the rates of transient and permanent RLN injuries in ten reported studies (28-37). The current evidences therefore suggested that the risk of RLN injury was not increased by BABA RT.

Hypoparathyroidism

The difference between BABA RT and OT for the rate of inadvertent parathyroid gland removal was compared in four studies (28,33,35,37). Except for the study by Kwak *et al.* (35), no difference was observed between the two procedures in one RCT and two propensity score matched

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comparisons (28,33,37). In terms of transient and permanent hypoparathyroidism, their definitions were also variable in the literature. Except for one study by Kim *et al*. (31), the rates of transient hypoparathyroidism were similar between BABA RT and OT (28-30,32-37). As reported in all ten studies, the rates of permanent hypoparathyroidism were comparable between BABA RT and OT (28-37). Hence, BABA RT did not seem to pose additional risks on hypoparathyroidism and hypocalcemia.

Bleeding and hematoma

The reported rates of postoperative bleeding and hematoma in BABA RT were well below 1%. In the largest case series of BABA RT by Lee *et al*., the risk was only 0.19% (10). In nine studies comparing BABA RT and OT, the rates of postoperative bleeding and hematoma after BABA RT were 0–0.9% (28,30-37). No significant difference was found between the two procedures in all nine studies.

Other specific complications

Seroma formation was compared between BABA RT and OT in four studies and no significant difference was observed (33-35,37). The rate of seroma formation after BABA RT was 0–1.4% only. Chyle leakage after BABA robotic and open total thyroidectomy with central compartment nodal dissection (CCD) was compared in four studies and no difference was found (31,33,34,37). In a study comparing BABA robotic and open total thyroidectomy with MRND, Kim *et al*. also found comparable rates of chyle leakage (30). Seven studies also analyzed the wound infection rates and reported no difference between BABA RT and OT (28,30,31,33-35,37). Based on the current evidences, the complication risks of BABA RT were comparable to conventional OT. Criticisms against the safety of BABA RT were therefore not justified.

Oncological outcomes

Lymph node (LN) retrieval

Adequate LN retrieval during CCD is crucial for optimal oncological control in PTC. In nine studies comparing the number of LN retrieved during CCD in BABA RT and OT, five studies reported a comparable number between the two procedures (29,30,34,36,37) but four studies found a significantly lower number in BABA RT than in OT (28,31,33,35). In two propensity score matched comparisons, the number of central LN retrieved was consistently lower in BABA RT than in OT (28,33). As the study populations in these two studies were matched for demographic details and disease stages, their results were expected to be more convincing. However, no difference was found in the only available RCT comparing a relatively small sample of 100 patients (50 BABA RT versus 50 OT) (37). Based on the current evidences available, BABA RT might be inferior to OT for the number of central LN retrieved.

Surgical completeness of resection

The thyrotropin-(TSH-) stimulated thyroglobulin (Tg) levels and the radioiodine (RAI) uptake levels on post-therapy whole-body scan (RxWBS) during RAI ablation are common surrogate markers for the completeness of surgical resection. In seven studies reporting the absolute levels of stimulated Tg (sTg) measured, no difference was observed between BABA RT and OT in six studies (27,28,30,31,33,34,36). Five of these seven studies also compared the proportions of patients having undetectable sTg (<1 ng/mL) and four studies reported a similar result between BABA RT and OT (27,28,30,31,36). As for the RAI uptake levels on RxWBS, only one study had reported the comparison between BABA RT and OT (27). Lee *et al*. found no difference between the two procedures for the levels of RAI uptake, the RAI ablation dose and the number of RAI sessions required (27). Hence, the current evidences suggested that BABA RT was comparable to OT for the completeness of surgical resection.

Disease recurrence and survival

Due to the lack of long-term follow-up studies, the literature evidence on locoregional recurrence and disease survival after BABA RT was extremely limited. In a study comparing BABA RT and OT for PTC measuring 2–4 cm, Chai *et al*. reported no recurrence in both treatment arms in a median follow-up of 40.2 months (36). Yet, Kim *et al*. found two regional recurrences at lateral neck LN in 300 cases of BABA RT (30). None of the available studies had compared the survival data between BABA RT and OT.

Cost

One of the greatest criticisms on remote access thyroidectomy is cost. With the extra expenses on prolonged operative

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time, specific robotic equipment, consumable charges, and equipment maintenance, the cost of RT is invariably higher than that of OT. As consistently shown in three studies, the cost of BABA RT was significantly higher than that of OT (30,33,35). BABA RT was 2.5 to 6.2 times more expensive than OT.

Comparison with BABA ET

BABA RT was compared with BABA ET in two retrospective studies (34,41). No significant difference was observed between the two techniques on the length of hospital stay and all postoperative complications, including the rates of RLN injury, hypoparathyroidism and bleeding. However, RT could be inferior to ET for a significantly longer operative time by 1.4 to 1.5 times. In terms of oncological control, RT might be superior to ET. In a cohort comparative study by Kim *et al*., RT was shown to have significantly lower sTg levels than ET (0.8 *vs*. 2.4 ng/mL, P=0.026) (34). In another propensity score matched comparison of 289 RT versus 289 ET, Kim *et al*. found a significantly higher number of central LN retrieved in RT than in ET (5.3 *vs*. 4.4, P=0.003) (41). The same authors also analyzed the costs of both procedures. RT was 2.8 and 2.6 times more expensive than ET for total thyroidectomy and unilateral lobectomy respectively (41).

Conclusions

Robotic BABA thyroidectomy is a safe and effective procedure with a reasonable learning curve. Based on the current literature evidences, it is comparable to conventional open surgery for safety and most perioperative outcomes. Despite a definite superiority on cosmesis, BABA RT is associated with longer operative time, higher cost and possibly inferior oncological control with lower number of central LN retrieved. Nevertheless, long-term follow-up studies are warranted to evaluate the outcomes on recurrence and survival. Prospective randomized trials are also imperative to provide unbiased comparisons between BABA RT and conventional open procedures.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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