Surgical Endoscopy (2020) 34:622–627
https://doi.org/10.1007/s00464-019-06808-9

Comparison of robot-assisted modified radical neck dissection using a bilateral axillary breast approach with a conventional open procedure after propensity score matching

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Received: 7 November 2018 / Accepted: 29 April 2019 / Published online: 7 May 2019

Abstract

Background There is ongoing debate about whether or not robot-assisted thyroidectomy is appropriate for modified radical neck dissection (MRND). The purpose of this study was to compare the surgical outcomes of robot-assisted MRND with those of a conventional open procedure.

Methods One hundred and forty-five patients who underwent total thyroidectomy, bilateral central neck dissection, and MRND (robotic, $n=28$; open, $n=117$) at our institution from June 2011 to June 2015 were enrolled in the study. The surgical completeness and complication rates in the robotic and open groups were retrospectively compared after 1:3 propensity score matching for age, sex, body mass index, tumor size, and extrathyroidal extension.

Results The complication rates, including transient or permanent hypoparathyroidism and recurrent laryngeal nerve palsy, were comparable between the study groups ($p>0.05$). The operating time was significantly longer in the robotic group than in the open group ($p<0.001$). There was no significant difference in the number of retrieved lymph nodes, metastatic lymph nodes, or stimulated serum thyroglobulin level between the two groups ($p=0.733$, $p=0.663$, and $p=0.285$, respectively).

Conclusions The surgical outcomes, including complication and completeness rates, were comparable between robot-assisted MRND using a bilateral axillary breast approach and conventional open surgery. Robot-assisted MRND can be recommended as an alternative to a conventional open procedure for thyroidectomy.

Keywords Bilateral axillary breast approach · da Vinci robot · Modified radical neck dissection · Propensity score matching · Thyroidectomy

Since the initial reports in 2009 [1, 2], studies of robot-assisted thyroidectomy have reported good clinical outcomes, and the popularity of this approach in the treatment of thyroid tumors has rapidly increased [3]. The indications for robotic thyroidectomy were initially limited to low-risk, well-differentiated thyroid cancers. However, more recent studies have demonstrated the feasibility and safety of robot-assisted thyroidectomy in patients with more advanced thyroid cancer [3–6].

The indications for robot-assisted thyroid surgery have now expanded to include more complicated procedures, including lateral neck dissection and modified radical neck dissection (MRND). An increasing number of surgeons are taking the initiative to perform robot-assisted thyroidectomy with lateral neck dissection [6–11].

Patients with thyroid carcinoma and metastatic lateral cervical lymphadenopathy require MRND. A conventional open MRND procedure results in a long external neck scar, and most patients, particularly young women, are concerned about surgical scarring as well as oncologic completeness. Robot-assisted thyroidectomy, bilateral central neck dissection, and MRND using a bilateral axillary breast approach (BABA) can be performed successfully with good cosmetic

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results, and we have described this procedure in previous reports [7–9, 12].

However, concern remains regarding whether or not robot-assisted thyroidectomy is appropriate for MRND. The purpose of this study was to compare the safety of robotic MRND with that of a conventional open procedure. An exact 1:3 propensity score matching analysis according to age, sex, body mass index, tumor size, and extrathyroidal extension was performed to decrease the risk of confounding variables and minimize selection bias.

Materials and methods

Patients

One hundred and forty-five consecutive patients who underwent total thyroidectomy, bilateral central neck dissection, and MRND (robotic, $n=28$; open, $n=117$) at our institution from June 2011 to June 2015 were enrolled in the study. Lateral lymph node (LN) metastasis was confirmed preoperatively in all patients by fine needle aspiration with or without a washout thyroglobulin (Tg) test. All the operations were performed by the same surgeon. Patients with vessel invasion and/or vagus nerve invasion of a lateral cervical LN were excluded. All patients were offered a choice between an open or robotic procedure preoperatively after being given an explanation of the pros and cons of robotic-assisted surgery, i.e., a good cosmetic effect vs. high cost and the possibility of conversion to an open procedure and informed consents were acquired. The study protocol was approved by the relevant institutional review board and informed consents from patients were waived due to the retrospective design of this study.

Surgical procedures

The same surgeon performed all the conventional open and robotic thyroidectomies. All the patients underwent total thyroidectomy, routine bilateral central neck dissection, and MRND for lateral cervical LN metastasis. The BABA method with a verticalizing maneuver [9, 12] was used in all cases. The operative procedures used for open and robotic total thyroidectomy with MRND have been described in detail previously [8, 9, 12]; robotic MRND procedure requires a larger skin flap that extends up to the inferior border of the submandibular gland, superiorly to the angle of the mandible, and posteriorly to the anterior edge of the trapezius muscle. After the medial and lateral borders of the sternocleidomastoid (SCM) muscle are fully exposed, the SCM muscle is pulled with anchoring #0 polydioxanone sutures (PDS; Ethicon, San Angelo, TX, USA). Lifting of the SCM muscle ensures a sufficient workspace for LN dissection, which proceeds from level IV to level II. A slight clockwise or counterclockwise rotation of the camera port is helpful. The dissected LNs were removed using lap bags, and the sutures anchored by the PDS were released and removed through the areolar trocar. Vicryl sutures were used for midline closure, followed by placement of a Jackson-Pratt drain.

Assessment of surgical outcomes

The surgical complications (e.g., recurrent laryngeal nerve injury, hypocalcemia, postoperative bleeding, chyle leak, and wound infection) and completeness of surgery (mean numbers of retrieved and metastatic LNs, stimulated serum thyroglobulin (sTg) level on first radioactive iodine (RAI) treatment, and proportion of patients with sTg level < 1.0 ng/mL) were retrospectively compared between the two study groups after propensity score matching for age, sex, body mass index, tumor size, and extrathyroidal extension. Postoperative hypoparathyroidism was defined as any hypocalcemic symptom with decreased serum calcium level (less than 8.0 mg/dL) or ionized calcium (less than 1.00 mmol/L) level. Permanent hypoparathyroidism was defined as that requiring calcium medication more than 12 months after surgery. All patients underwent postoperatively vocal cord examination through laryngoscopy and vocal cord palsy lasting more than 6 months was defined as permanent. Spinal accessory nerve injury was evaluated through intraoperative neuromonitoring. Conservative management including bed rest and low fat diet were initiated immediately when a chyle leak is diagnosed following surgery. Fluid balance, electrolytes, and protein status were also monitored closely. If a chyle leak does not respond satisfactorily to conservative management alone, surgical control was applied.

All patients were encouraged to undergo RAI therapy in accordance with the published guidelines for RAI therapy of differentiated thyroid cancer [13, 14]. The RAI dose was based on pathologic aggressiveness. sTg was measured on the day of RAI treatment after 28 days of levothyroxine withdrawal or recombinant human TSH (Thyrogen, Genzyme, Cambridge, MA, USA) injection for TSH stimulation. Successful ablation was assumed when sTg was less than 1.0 ng/mL. Tumor recurrence was monitored regularly (every 6 months) by ultrasonography and by annually measuring Tg concentrations.

Statistical analysis

An exact 1:3 propensity score matching analysis according to age, sex, body mass index, tumor size, and extrathyroidal extension was performed to decrease the risk of confounding variables and minimize selection bias. The Student's *t* test and Chi-squared test were used to assess differences

between the open and robotic groups. All statistical analyses were performed using SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). A p value < 0.05 was considered statistically significant.

Results

Characteristics of the study groups before matching

The baseline characteristics of the 145 patients in the robotic ($n = 28$) and open ($n = 117$) groups are shown in Table 1. Patients in the robotic group were significantly younger (36.14 ± 8.04 vs. 43.51 ± 11.48 years; $p < 0.001$), had a significantly smaller tumor size (0.95 vs. 1.30 cm; $p = 0.020$), and had a significantly lower extrathyroidal extension rate (46.4% vs. 70.1%; $p = 0.032$). There were more women with a lower body mass index in the robotic group than in the open group; however, this difference was not statistically significant ($p = 0.247$ and $p = 0.150$, respectively).

The postoperative outcomes in the two study groups are shown in Table 2. Transient and permanent hypoparathyroidism occurred in 12.0% and 1.7% of patients in the open group and in 7.1% and 0% of patients in the robotic group ($p = 0.738$ and $p > 0.99$, respectively). Transient and permanent vocal cord palsy occurred in 9.4% and 1.7% of patients in the open group and in 10.7% and 3.6% of patients in the robotic group ($p = 0.734$ and $p = 0.477$, respectively). There was no significant between-group difference in the incidence of postoperative bleeding, wound infection, or chyle leak ($p > 0.05$). The mean operating time was significantly longer in the robotic group than in the open group (382.3 ± 41.5 min vs. 210.9 ± 44.3 min; $p < 0.001$) but the duration of hospital stay was not significantly different between the groups ($p = 0.593$).

The mean number of retrieved LNs was 41.00 (29.00–50.00) in the open group and 36.50 (31.00–50.50) in the robotic group, and the respective mean numbers of metastatic LNs were 8.00 (5.00–14.00) and 8.00 (6.50–10.00); there was no statistically significant difference in the

Table 1 Clinicopathological characteristics

Variable	Open group ($n = 117$)	Robot-assisted group ($n = 28$)	p value
Mean age (years)	43.51 ± 11.48	36.14 ± 8.04	< 0.001
Sex [M:F (*F%*)]	41:76 (65.0%)	6:22 (78.6%)	0.247
Body mass index	24.26 ± 4.08	23.04 ± 3.56	0.150
Tumor size (cm)†	1.30 (0.75–2.00)	0.95 (0.50–1.40)	0.020
Extrathyroidal extension	82 (70.1%)	13 (46.4%)	0.032
LN metastasis	100%	100%	N/A

LN lymph node, *N/A* not available

†Results presented as median with interquartile range and p values obtained by Mann–Whitney U test

Table 2 Comparison of surgical outcomes between robot-assisted and open thyroidectomy groups before matching

Variable	Open group ($n = 117$)	Robot-assisted group ($n = 28$)	p value
Transient hypoparathyroidism	14 (12.0%)	2 (7.1%)	0.738‡
Permanent hypoparathyroidism	2 (1.7%)	0 (0%)	> 0.99‡
Transient VC palsy	11 (9.4%)	3 (10.7%)	0.734‡
Permanent VC palsy	2 (1.7%)	1 (3.6%)	0.477‡
Postoperative bleeding	0	0	N/A
Wound infection	0	0	N/A
Chyle leak	2 (1.7%)	1 (3.6%)	0.477‡
Operating time, mean (min)	210.9 ± 44.3	382.3 ± 41.5	< 0.001
Hospital stay (days)	4.00 (4.00–6.00)	4.50 (3.00–6.00)	0.593
Mean retrieved LNs (n)	41.00 (29.00–50.00)	36.50 (31.00–50.50)	0.869
Metastatic LNs (n)	8.00 (5.00–14.00)	8.00 (6.50–10.00)	0.526
Stimulated Tg level, ng/mL, mean	4.92	1.67	0.366
Proportion of stimulated Tg < 1.0 ng/mL	80/116 (69.0%)	20/27 (74.1%)	0.371

LN lymph node, *Tg* thyroglobulin, *VC* vocal cord

†Results presented as median with interquartile range and p values obtained by Mann–Whitney U test

‡p values obtained by Fisher's exact test

numbers of retrieved or metastatic LNs between the two groups ($p=0.869$ and $p=0.526$, respectively). All patients in both study groups received RAI therapy. The mean sTg level on first RAI therapy was 4.92 ng/mL in the open group and 1.67 ng/mL in the robotic group ($p=0.366$). There was no statistically significant difference in the proportion of patients with sTg levels < 1 ng/mL between the open group and the robotic group (69.0% vs. 74.1%; $p=0.371$).

Outcomes in the matched cohorts (Table 3)

After 1:3 propensity score matching analysis for age, sex, body mass index, tumor size, and extrathyroidal extension, the matched study cohorts did not differ in any clinicopathologic parameter, indicating that the surgical outcome parameters are likely to have been unaffected.

Transient and permanent hypoparathyroidism occurred in 10.7% and 1.2% of patients in the open group and in 7.1% and 0% of patients in the robotic group ($p=0.728$ and $p>0.99$, respectively). Transient and permanent vocal cord palsy occurred in 7.1% and 2.4% of patients in the open group and in 10.7% and 3.6% of patients in the robotic group ($p=0.688$ and $p>0.99$, respectively). There was no statistically significant difference in the incidence of postoperative bleeding, chyle leak, or wound infection ($p>0.05$) between the groups. The mean operating time was significantly longer in the robotic group than in the open group (382.3 ± 41.5 min vs. 195.9 ± 34.1 min, $p<0.001$) but the duration of hospital stay was not significantly different between the groups ($p=0.815$).

The mean number of retrieved LNs was 40.00 (29.00–50.00) in the open group and 36.50 (31.00–50.50) in the robotic group, and the respective mean numbers of metastatic LNs were 8.00 (5.00–14.00) and 8.00 (6.50–10.00). There were no statistically significant differences in the numbers of retrieved and metastatic LNs between the two groups ($p=0.733$ and $p=0.663$, respectively). The mean sTg level on first RAI treatment was 3.44 ng/mL in the open group and 1.67 ng/mL in the robotic group ($p=0.285$). There was no significant between-group difference in the proportion of patients with a sTg level < 1 ng/mL (67.5% in the open group, 74.1% in the robotic group; $p=0.354$).

Discussion

This study compared the surgical outcomes of patients who underwent robotic or conventional open thyroidectomy plus MRND, with all procedures performed by the same surgeon. Patients in the robotic group were significantly younger, reflecting a potentially greater concern for cosmetic outcomes [7, 15, 16]. For a more balanced comparison, an exact 1:3 matching analysis was applied for age, sex, body mass index, tumor size, and extrathyroidal extension. Propensity score matching has been confirmed to minimize selection bias and increase the efficiency of estimates in non-randomized retrospective studies, allowing comparison between different groups [17]. The significant between-group differences initially observed in age, tumor size, and extrathyroidal extension were no longer present in the matched cohorts.

The perioperative complication rates were similar between the study groups. Transient hypoparathyroidism was the most common complication in both groups, and only two patients in the open group experienced permanent hypocalcemia. Transient and permanent vocal cord palsy occurred in 7.1% and 2.4% of patients in the open group and in 10.7% and 3.6% of patients in the robotic group ($p=0.688$ and $p>0.99$, respectively). The incidences of postoperative

Table 3 Comparison of surgical outcomes between robotic and open groups after propensity score matching

Variable	Open group ($n=84$)	Robot-assisted group ($n=28$)	p value
Transient hypoparathyroidism	9 (10.7%)	2 (7.1%)	0.728‡
Permanent hypoparathyroidism	1 (1.2%)	0	> 0.99‡
Transient VC palsy	6 (7.1%)	3 (10.7%)	0.688‡
Permanent VC palsy	2 (2.4%)	1 (3.6%)	> 0.99‡
Postoperative bleeding	0	0	N/A
Wound infection	0	0	N/A
Chyle leak	2 (2.4%)	1 (3.6%)	> 0.99‡
Operating time, mean (min)	195.9 ± 34.1	382.3 ± 41.5	< 0.001
Hospital stay (days)	4.10 (4.00–6.00)	4.50 (3.00–6.00)	0.815
Retrieved LNs, *n*, mean	40.00 (29.00–50.00)	36.50 (31.00–50.50)	0.733
Metastatic LNs, *n*, mean	8.00 (5.00–14.00)	8.00 (6.50–10.00)	0.663
Stimulated Tg level, ng/mL, mean	3.44	1.67	0.285
Proportion of stimulated Tg < 1.0 ng/mL	56/83 (67.5%)	20/27 (74.1%)	0.354

LN lymph node, *Tg* thyroglobulin, *VC* vocal cord

‡*p* values obtained by Fisher's exact test

bleeding, chyle leak, and wound infection were also similar between the two groups. There were no instances of injury to the trachea or esophagus in either study group.

The thyroid-stimulating hormone (TSH)-stimulated Tg level has been shown to be a reliable marker of remnant thyroid tissue after total thyroidectomy with MRND when evaluating the completeness of surgery. [5, 14, 18]. In our study, there was no significant between-group difference in the sTg level and the proportion of patients with sTg levels < 1 ng/mL. Moreover, there was no significant difference in the number of retrieved LNs between the study groups, indicating that the robotic and open techniques were equivalent in terms of their performance for total thyroidectomy with MRND.

Our study has some limitations that should be taken into account when interpreting the findings. First, it had a single-institution and non-randomized design, so the possibility that there were other sources of non-uniformity between the robotic cohort and the open cohort cannot be excluded. Some other factors such as body habitus and comorbidities may have been neglected also. Second, the sample size was relatively small and all data were derived from procedures performed by the same surgeon. Also, only short-term outcomes were acquired and this could be a limitation of our study. Longer-term multicenter studies using validated instruments will be essential to confirm our findings.

To date, the surgical outcomes of robot-assisted MRND using BABA in patients with papillary thyroid cancer and lateral LN metastasis have been unclear. Our study reports successful experience using a da Vinci robotic approach [7–9, 12], which permits the surgeon to perform operations by maneuvering the robot arms while seated at a control panel without needing to hold and manipulate an endoscope or other surgical instruments.

In summary, robot-assisted MRND using BABA has surgical completeness and complication rates that are similar to those of a conventional open procedure. Given the cosmetic advantage of robotic thyroidectomy with MRND over conventional open surgery, robotic MRND can be recommended as an alternative surgical option.

Compliance with ethical standards

Disclosures Drs. Se Hyun Paek, Hye Ah Lee, Hyungju Kwon, Kyung Ho Kang, and Sung Jun Park have no conflicts of interest or financial ties to disclose.

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