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Single-Port Transaxillary Robotic Bilateral Total Thyroidectomy (START) for Graves' Disease: First Initial 10 Cases Using da Vinci SP Robotic System

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

ABSTRACT

Purpose: Graves' disease (GD) is an autoimmune disorder and the most common cause of persistent hyperthyroidism. Recently, robotic transaxillary thyroidectomy has served as a minimally invasive surgical alternative to conventional open thyroidectomy, even for patients with GD. In 2019, we first performed single-port transaxillary bilateral total thyroidectomy using the da Vinci SP robotic system (START). This study aimed to evaluate the technical feasibility of START for GD.
Methods: This retrospective review included 10 patients with GD who underwent START at our institution between September 2020 and January 2022 by a single surgeon.
Results: All 10 patients were female, and the body-mass index was 22.3±3.6 kg/m^2 (range, 18.6–28.9). Seven patients (70%) had thyroid carcinoma, two (20%) had persistent hyperthyroidism despite medical control, and one patient (10%) had Graves' ophthalmopathy. The mean operation time was 173.4±26.8 min (range, 128–226), and the mean estimated blood loss was 102.0±185.1 mL (range, 10–600). There were no cases of conversion to open surgery. There were no intraoperative complications and six cases of postoperative complications, including transient hypocalcemia in three cases, bleeding with reoperation in two cases, and transient hoarseness in one case.
Conclusions: Patients with GD with large goiter and hypervascularity require delicate ligation, even of minor vessels, in a narrow space. START is feasible and safe for GD performed by high-volume expert surgeons.

Keywords: Single-port transaxillary robotic thyroidectomy; Graves' disease; Da Vinci SP robotic system

INTRODUCTION

Graves' disease (GD) was first described in the 19th century associated with overactive thyroid function, palpitations, goiter, and exophthalmos (1). Although there is not much information on GD incidence, it has been reported to be approximately 20 to 50 cases per 100,000 individuals per year (1-3). GD can affect any age; however, the incidence is most common between 30 and 50 years of age (2). GD occurs more frequently in women than men, and GD-associated ophthalmopathy (GO) is prevalent in women (4). Activating thyrotropin receptor

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Conceptualization: In A Lee, Jin Kyong Kim, Kee-Hyun Nam; Data curation: In A Lee, Jin Kyong Kim, Cho Rok Lee; Investigation: Cho Rok Lee, Sang-Wook Kang, Jong Ju Jeong; Methodology: Jong Ju Jeong, Kee-Hyun Nam, Woong Youn Chung; Project administration: Jong Ju Jeong, Kee-Hyun Nam, Woong Youn Chung; Resources: In A Lee, Jin Kyong Kim, Cho Rok Lee; Software: In A Lee, Jin Kyong Kim, Cho Rok Lee; Supervision: Jong Ju Jeong, Kee-Hyun Nam, Woong Youn Chung; Validation: Cho Rok Lee, Sang-Wook Kang; Visualization: In A Lee, Jin Kyong Kim, Cho Rok Lee; Writing - original draft: In A Lee, Cho Rok Lee, Kee-Hyun Nam; Writing - review & editing: In A Lee, Cho Rok Lee, Kee-Hyun Nam.

antibodies by interacting with genetic and environmental factors increases thyroid hormone levels. Increasing thyroid hormone levels cause various adverse effects, ranging from minor discomfort to death (5). The treatment of choice for GD includes radioactive iodine (RAI) therapy, antithyroid drugs, or thyroidectomy. Physicians should discuss treatment options with patients considering the best clinical judgment and patients' preferences (1,6).

GD's surgical treatments include subtotal thyroidectomy and total thyroidectomy; however, total thyroidectomy has recently been preferred (6-8). Because of the large cervical wound caused by total thyroidectomy, the demand for extra-cervical approaches for GD's surgical treatment is increasing. In the early 20th century, video-assisted endoscopic thyroidectomy was attempted for patients with GD; however, the discomfort associated with rigid instruments remains a problem (9-11). According to recent developments in robotic systems, a three-dimensional (3-D) working field with a magnified view and tremor-filtering multi-articulated instruments can permit meticulous manipulation of the thyroid gland with minimally invasive surgery (12-15). At the initial introduction of robotic thyroidectomy, GD was contraindicated because of the large thyroid gland and hypervascularity causing intraoperative bleeding with a high risk of open conversion (16,17). However, good results have recently been reported for robotic transaxillary thyroidectomy (RTT) in patients with GD using the da Vinci Si or Xi robotic system (Intuitive Surgical, Sunnyvale, CA, USA) (18-20).

The recently developed da Vinci SP robotic system (Intuitive Surgical) allows single-port access through a single 2.5 cm cannula. It has a single arm that delivers three multi-jointed instruments and a completely wristed 3-D high-definition (HD) camera for visibility and control in a narrow working space. Our institution first introduced this robotic system in 2018 and reported the operation method and good results for thyroidectomy using a 3.5 cm transaxillary single incision (21). This is the first report on the preliminary surgical outcomes of single-port transaxillary robotic bilateral total thyroidectomy (START) for GD; the initial 10 cases used the da Vinci SP robotic system.

MATERIALS AND METHODS

1. Patients

We evaluated the initial 10 Asian patients who underwent bilateral total thyroidectomy (BTT) with or without central compartment neck dissection (CCND) using the da Vinci SP robotic system for GD performed by a surgeon at the Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, between September 2020 and January 2022. Patient selection from an outpatient clinic included female preference and body mass index (BMI) <30 kg/m^2, and patient preference for START. The indications for surgical treatment included GD combined with thyroid cancer (n=7), persistent hyperthyroidism despite medical control (n=2), and severe GO (n=1). All patients took Lugol's solution 10 days before surgery to decrease thyroid blood flow, vascularity, and intraoperative blood loss and took methimazole (MMI) to maintain the euthyroid status according to the guidelines of the American Thyroid Association (6). We retrospectively collected the clinical and pathological data and stored them in a dedicated database for analysis. This study was conducted in accordance with the tenets of the Declaration of Helsinki (as revised in 2013) and approved by the institutional review board of Yonsei University (IRB No: 4-2021-1769). The need for informed consent was waived because of the study's retrospective design.

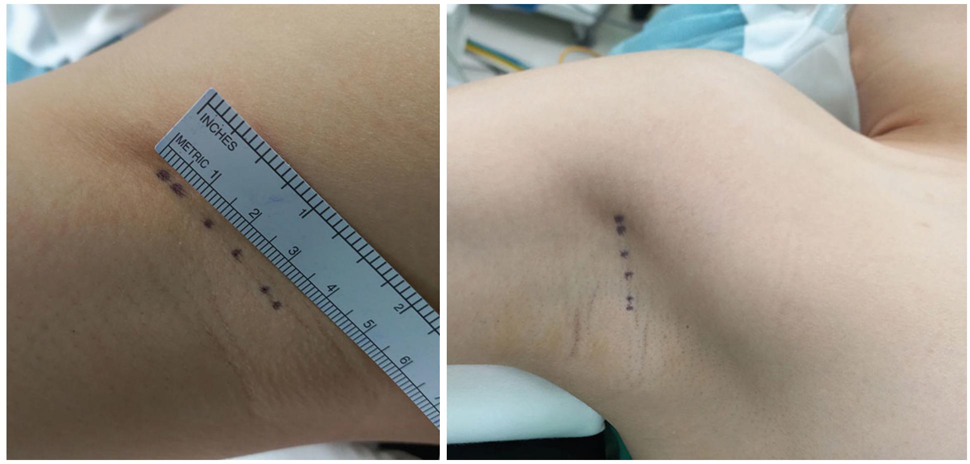

Fig. 1. Pictures of preoperative skin markings at the incision site.

2. Operative procedures

Under general anesthesia, the patient was placed in a supine position with a backrest to extend the neck. Intraoperative nerve monitoring is routinely applied because the thyroid gland in GD usually has large masses and hypervascularity (22). The arm on the lesion side was draped without fixation to adjust it during flap dissection and the robotic console time. A 3.5 to 4.0 cm incision was made along the natural skin crease (**Fig. 1**). Usually, a 3.5 cm incision is sufficient for START; however, in the case of a large thyroid gland due to GD, a skin incision of up to 4.0 cm is inserted. Skin flap dissection was performed using a two-step procedure. The detailed procedure has been described in previous studies (21,23). After flap dissection along the anterior surface of the pectoralis major muscle to the sternal notch, a narrow version of Chung's retractor was inserted between the dividing heads of the sternocleidomastoid muscle (SCM). After docking the robot, the strap muscles were elevated from the thyroid gland until the contralateral thyroid gland was exposed through the avascular space between the two SCM heads. The surgical assistant then reinserted Chung's retractor under the strap muscles in the surgical field. When both steps were completed, robotic thyroidectomy was performed as conventional transaxillary robotic surgery (15,21,24). The camera was inserted into the bottom lumen, and the Maryland bipolar forceps were inserted into both lateral lumens. Cardiere forceps for traction are usually introduced into the top lumen. Maryland dissectors were connected to a bipolar energy source, Erbe (Erbe USA Inc., Marietta, GA, USA), in the SWIFT COAG mode. Because the thyroid gland in GD is sometimes larger than the size of the skin incision, the robot was pulled back to extract the specimen (**Fig. 2**). After surgery, all patients underwent drainage to prevent the accumulation of hematoma or seroma, and the drain was removed on the morning of discharge (**Fig. 3**).

3. Statistical analyses

All statistical analyses were performed using Statistical Package for the Social Sciences software for Windows version 26.0 (IBM Corp., Armonk, NY, USA). Continuous quantitative data were expressed as mean ± standard deviation. Categorical qualitative data were expressed as percentages. Statistical significance was set at $P<0.05$.

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Fig. 2. Images of the specimen immediately after the operation.

Fig. 3. Picture of the postoperative incision wound.

RESULTS

1. Baseline clinical characteristics and preoperative laboratory results

All 10 patients were female. The mean age was 32.1±6.9 years (range, 21–43), and BMI was 22.3±3.6 kg/m^2 (range, 18.6–28.9). All patients received medication for GD by a clinical endocrinologist. Before operation, patients took 12.0±7.6 mg/day (range, 2.5–25.0) of MMI for 3.6±2.9 years (range, 0.2–8.0). Preoperative laboratory results of free T4 (normal range, 0.80–1.23 ng/dL), T3 (normal range, 0.61–1.16 ng/mL), thyroid-stimulating hormone (TSH) (normal range, 0.41–4.30 mIU/L), TSH receptor antibody (Ab) (0–1.75 IU/L), and thyroid peroxidase Ab (normal range, 0–13.7 IU/mL) were 1.27±0.45 ng/dL (range, 0.78–2.26), 1.69±1.16 ng/mL (range, 0.68–4.06), 0.48±0.93 mIU/L (range, 0.01–2.27), 12.03±8.85 IU/L (range, 0.80–29.20), and 90.83±76.56 IU/mL (range, 9.00–241.00), respectively. Papillary thyroid carcinoma (PTC) coexisted with fine-needle aspiration during follow-up in seven patients. Three of seven patients had PTC in both thyroid lobes, and four patients were diagnosed with PTC in only one lobe. Two patients underwent surgery because of thyroid function control failure despite high-dose (10–20 mg daily) MMI treatment for more than

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Table 1. Clinical characteristics, preoperative laboratory results, indications, and scope of operation in patients with Graves' disease

Variables	Values
Sex, male:female	0:10
Age (yr)	32.1±6.9 (21–43)
BMI (kg/m^2)	22.3±3.6 (18.6–28.9)
Preoperative methimazole intake	
Dose (mg/day)	12.0±7.6 (2.5–25.0)
Duration (yr)	3.6±2.9 (0.2–8.0)
Preoperative laboratory results	
Free T4 (ng/dL)	1.27±0.45 (0.78–2.26)
T3 (ng/mL)	1.69±1.16 (0.68–4.06)
TSH (mIU/L)	0.48±0.93 (0.01–2.27)
TSH receptor Ab (IU/L)	12.03±8.85 (0.80–29.20)
Thyroid peroxidase Ab (IU/mL)	90.83±76.56 (9.00–241.00)
Indication for the decision on surgery	
Diagnosed PTC	7 (70)
Recurrent disease with a large goiter	2 (20)
GD with severe GO	1 (10)
Scope of operation	
BTT	3 (30)
BTT with CCND	7 (70)

Data are expressed as number of patients (%) or mean ± SD (range).
BMI = body mass index; TSH = thyroid-stimulating hormone; Ab = antibody; PTC = papillary thyroid cancer; GD = Graves' disease; GO = Graves' ophthalmopathy; BTT = bilateral total thyroidectomy; CCND = central compartment neck dissection.

5 years and increasing multiple goiters. Despite good control of thyroid function with medication, one patient developed severe GO and underwent surgery. Seven patients underwent BTT with CCND for PTC with GD, and three underwent BTT for GD (**Table 1**).

2. Surgical outcomes

Table 2 summarizes the intraoperative and pathological findings of the patients with GD. The immediate postoperative specimen weight was 83.0±34.8 mg (range, 55–122 mg), and the weight of the specimen measured during the pathologic examination was 40.4±23.4 mg (range, 13.6–92.0). The thyroid gland's maximum horizontal and vertical lengths measured in pathologic examination were 3.7±0.9 cm (range, 2.0–5.0) and 6.0±1.6 cm (range, 3.0–8.7), respectively. Three patients were diagnosed with diffuse follicular hyperplasia, consistent with GD and seven patients had PTC with GD on the final pathologic findings.

The mean operation time was 173.4±26.8 minutes (range, 128–226), including 24.8±13.7 minutes (range, 13–53), 3.5±1.2 minutes (range, 2–6), and 112.4±17.6 minutes (range, 83–136) of working space making, docking, and console time, respectively. The mean estimated

Table 2. Intraoperative and pathological specimen findings

Pathology	Values
Immediately postoperative specimen weight (mg)	83.0±34.8 (55–122)
Pathologic specimen	
Total weight (mg)	40.4±23.4 (13.6–92.0)
Maximum width (cm)	3.7±0.9 (2.0–5.0)
Maximum length (cm)	6.0±1.6 (3.0–8.7)
Pathologic diagnosis	
Diffuse follicular hyperplasia, consistent with GD	3 (30)
PTC with GD	7 (70)

Data are expressed as number of patients (%) or mean ± SD (range).
GD = Graves' disease; PTC = papillary thyroid cancer.

Table 3. Operation time and intraoperative and postoperative surgical outcomes of patients

Operation	Values
Operation time (min)	173.4±26.8 (128–226)
Working space	24.8±13.7 (13–53)
Docking	3.5±1.2 (2–6)
Console	112.4±17.6 (83–136)
Estimated blood loss (mL)	102.0±185.1 (10–600)
Intraoperative complications	0 (0)
Postoperative complications	6 (60)
Transient hypocalcemia	3 (30)
Bleeding with reoperation	2 (20)
Transient hoarseness	1 (10)
Length of hospital stays (days)	3.5±1.3 (3–7)

Data are expressed as number of patients (%) or mean ± SD (range).

blood loss (EBL) was 102.0±185.1 mL (range, 10–600 mL), and there were no intraoperative complications and no open conversion in all patients. Postoperative complications included transient hypocalcemia (three cases, 30%), bleeding with reoperation (two cases, 20%), and transient hoarseness (one case, 10%). In two cases of postoperative bleeding, the hematoma was evacuated through the operative axillary wound without a neck incision. In addition, the length of hospitalization was 3.5±1.3 days (range, 3–7) (**Table 3**).

DISCUSSION

GD affects multiple organ systems and presents with subclinical hyperthyroidism, a rare but potentially life-threatening complication. Thyrotoxicosis can appear as stable remission after medical treatment, relapse, or an unremitting course. The indications of surgical management for GD include symptomatic compression or large goiter, moderate to severe active GO, relatively low uptake of RAI, suspected thyroid malignancy, and woman planning a pregnancy (6). Minimally invasive surgery for thyroidectomy was developed because of cosmetic considerations and related quality of life outcomes. Many reports on the advantages of RTT have been published over the past two decades (12-15,25-27). Until 2019, all robotic surgeries were based on a multi-armed robotic surgical system. The da Vinci SP robotic system was approved and introduced in late 2018 by the Food and Drug Administration. The first surgery was performed in September 2020 by applying this robotic system to the BTT for patients with GD. Consequently, 10 patients underwent surgery performed by one surgeon until January 2022. This novel system uses a 2.5 cm cannula to introduce three multi-jointed instruments and a wristed 3-D HD camera, which can move up to the wrist and elbow in the operation field. The three instruments and camera facilitate an excellent internal range of motion, angulated around the target organ to visualize blind spots.

Because this was the first experience using the new technique, the patient's selection preferred only women who usually had easy tissue manipulation. The BMI varied from 18.6 to 28.9 kg/m^2. Excessively patients with obesity have thick and heavy flaps; thus, using the narrow version of Chung's retractor in START does not secure sufficient surgical space. Therefore, BMI was limited to less than 30 kg/m^2. PTC was diagnosed in seven patients (70%), and CCND was required during the operation. Operation time was 173.4±26.8 minutes (range, 128–226), which was faster than the operation time 182.5±58.1 min by the RTT for GD using da Vinci Xi or Si robotic system announced by our institution in 2021 (20). START can be performed with only a narrow working space through the two-step flap dissection method using a small 3.5 cm incision. Therefore, the working space-time was shorter (24.8±13.7 minutes [range, 13–53]) than that of the conventional robotic system, while the console time was long (112.4±17.6 minutes [range, 83–136]) because of increasing the robot dependence on a narrow space (28). The mean EBL was 102.0±185.1 mL (range, 10–600 mL). Maximum EBL appeared in the first case of recurrent disease with a large goiter, and it seems that the learning time for applying a new technique was necessary. There were two cases (20%) of postoperative bleeding with reoperation the day after surgery. These patients were diagnosed with PTC using CCND. One patient had prelaryngeal artery bleeding, and the other had no specific focus on bleeding; therefore, the reoperation was terminated after hematoma evacuation. The reoperation and hematoma evacuation were performed using the operative axillary wound without new incision in the neck, and a robot and endoscopic devices were used to perform the bleeder ligation. After reoperation, this patient received a transfusion because of decreased hemoglobin levels and was discharged on the seventh day of the first operation. The thyroid with GD has hypervascular tissues. Accordingly, pretreatment with Lugol's solution must be performed. In addition, the minor vessels should be delicately ligated to prevent postoperative bleeding. Three (30%) patients had transient postoperative hypocalcemia. According to Al Qubaisi et al. (29), patients with GD are at twice the risk of hypocalcemia than patients without GD. This is due to sex (especially women), the degree of parathyroid gland manipulation at the time of surgery, size of the goiter, and vitamin D deficiency. In patients with GD, the surgical view of the field is poor due to bleeding during surgery, and the surgical space is narrow due to the thyroid goiter; therefore, parathyroid preservation should be performed carefully. In this respect, robotic surgery is advantageous for magnified views and meticulous manipulations. One patient (10%) had postoperative transient hoarseness because her thyroid cancer had invaded the recurrent laryngeal nerve and shaved it off. The average length of hospital stay after RTT at our institution was 2–3 days. Most patients with GD who underwent START were discharged 3 days after surgery; however, only two patients who underwent reoperation with postoperative bleeding were discharged 4 and 7 days after surgery.

The longest thyroid with GD performed at our institution was 5.0×8.5 cm in length and width, and this specimen was removed with an incision of less than 4.0 cm while preserving its original shape. Because of the skin's elasticity, even if the shortest distance of the specimen is about 1.5 to 2 times the size of the incision, it can come out as a small incision. As patients with GD are mostly young women, they are sensitive to wounds. Therefore, an incision size of 3.5 to 4.0 cm is sufficient for START, which showed high patient satisfaction in our clinic.

Hypervascularity with a large thyroid gland in patients with GD is challenging for surgeons. In addition, the need for a large incision and the prevalence in women make them consider the cosmetic aspects. In line with all these circumstances, START for GD enhanced the cosmetic effect on patients and facilitated an easier and more convenient operation for surgeons.

A limitation of this study is that it was an initial retrospective review of 10 cases. In the future, further prospective or multicenter studies are warranted to evaluate operative outcomes and verify their technical feasibility.

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CONCLUSION

To our knowledge, this is the first report of the preliminary surgical results of START for GD. START is an effective surgical technique that specializes in a narrow space by the hands of high-volume surgeons. Therefore, the novel technique using the da Vinci SP robotic system is feasible and safe for BTT with GD.

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