Oncologic Safety of Robot Thyroid Surgery for Papillary Thyroid Carcinoma: A Comparative Study of Robot vs Open Thyroid Surgery using Inverse Probability of Treatment Weighting

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BACKGROUND AND AIMS
To compare robot vs open thyroid surgery using inverse probability of treatment weighting (IPTW) with regard to oncologic safety in papillary thyroid carcinoma (PTC) patients.

METHODS
We enrolled 722 patients with PTC who underwent a total thyroidectomy with central compartment node dissection (CCND) at the Asan Medical Center in Korea from January 2009 to December 2010. These patients were classified into open thyroid surgery (n = 610) or robot thyroid surgery (n = 112) groups. We verified the impact of robot thyroid surgery on clinical recurrence and ablation/control-stimulated thyroglobulin (sTg) levels predictive of non-recurrence using weighted logistic regression models with IPTW.

RESULTS
Age, sex, thyroid weight, extent of CCND, and TNM stage were significantly different between the two groups (p < 0.05); however, there was no significant difference in the recurrence rate between the open and robot groups (1.5 vs 2.7%; p = 0.608). The proportion of patients with ablation sTg < 10.0 ng/mL and control sTg < 1.0 ng/mL was comparable between the two groups (p > 0.05). Logistic regression with IPTW using the propensity scores estimated by adjusting all of the parameters demonstrated that robot thyroid surgery did not influence the clinical recurrence (OR: 0.784; 95% CI: 0.150–3.403; p = 0.750), ablation sTg (OR: 0.950; 95% CI: 0.361–2.399; p = 0.914), and control sTg levels (OR: 0.498; 95% CI: 0.190–1.189; p = 0.130).

CONCLUSION
Robot thyroid surgery is comparable to open thyroid surgery with regard to oncologic safety in PTC patients.

Long-term Outcome in Patients following Endoscopic Thyroidectomy for Papillary Thyroid Carcinoma

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BACKGROUND AND AIMS
Over the last decade, several minimally invasive techniques for thyroid and parathyroid surgery have expanded to improve primarily the cosmetic results of neck surgical procedures. We have been developing a totally gasless endoscopic surgical technique for thyroid tumors that uses an anterior neck skin lifting method since 1998. We called this technique the video-assisted neck surgery (VANS) method. We reported the validity and safety of this method for malignant tumors. More than 700 cases were experienced since the initial case. Based on this experience, we would like to discuss the application and indication for the treatment of malignant thyroid tumors, including lymph node dissection.

METHODS
A retrospective review was done of 77 patients who underwent the VANS method for papillary thyroid carcinoma.

RESULTS
The mean age was 42.5 years and the male-to-female ratio was 1:76. Three cases underwent lobectomy with lateral neck dissection, 7 cases total thyroidectomy, and 64 cases lobectomy with central node dissection. Three cases were converted to open surgery.
due to tracheal invasion. Two cases had transient recurrent laryngeal nerve palsy. The mean time of lobectomy + MRND by this method was much longer than conventional lobectomy + MRND procedures. We discontinued the MRND procedure by VANS method based on relevant aspects of minimally invasive and surgical application. The mean following time was 1,764 days. One case of lateral lymph node metastasis was detected. None of the patients had permanent hypoparathyroidism. All of the patients were satisfied with good cosmetic outcomes.

CONCLUSION
The VANS method is an efficient, feasible, and safe procedure. This technique may be a suitable surgical option for low-risk patients with papillary thyroid carcinoma.

Endoscopic-assisted Thyroid Surgery via Small Incision of the Neck (Experience of 2,103 Cases)

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BACKGROUND AND AIMS
The endoscopic-assisted neck minimally invasive thyroid surgery is one of the advances in the development of thyroid surgery in recent years. The greatest significance of this kind of operation is to solve the patient’s disease by a truly minimally invasive and comparatively cosmetic way, which is in accordance with modern requirements for high-quality living standards and esthetic views. We will discuss skills of endoscopic-assisted minimally invasive thyroid surgery of the neck and summarize the relevant experience in this article.

METHODS
We analyzed clinical data of 2,103 cases (1,595 women and 508 men with a mean age of 42.5 years) of endoscopic-assisted minimally invasive thyroid surgery of the neck at the First Hospital of Jilin University in China from June 2006 to October 2015. The operation was performed under general anesthesia and tracheal intubation. During treatment, we recorded the operation time, blood loss, incision size, postoperative drainage, beauty score, the use of analgesics, postoperative time to discharge, hospitalization costs, presence or absence of tumor recurrence, wound infection, and other complications.

RESULTS
We analyzed clinical data of 2,103 cases (1,595 women and 508 men with a mean age of 42.5 years) of endoscopic-assisted minimally invasive thyroid surgery of the neck at the First Hospital of Jilin University in China from June 2006 to October 2015. The operation was performed under general anesthesia and tracheal intubation. During treatment, we recorded the operation time, blood loss, incision size, postoperative drainage, beauty score, the use of analgesics, postoperative time to discharge, hospitalization costs, presence or absence of tumor recurrence, wound infection, and other complications.

CONCLUSION
Endoscopic-assisted minimally invasive thyroid surgery of the neck is a practical, less-invasive surgery, which has advantages of safety, reliability, less bleeding, less pain, shorter hospital stay, fewer complications, and comparatively better cosmetic results. In the future, this kind of surgery would become widely used to treat thyroid diseases including some thyroid cancers.

Minimally Invasive Open Thyroidectomy: Surgical Completeness of Consecutive 108 Consecutive Patients

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BACKGROUND AND AIMS
The cosmetic consideration motivated the development of various minimally invasive thyroidectomies even in the thyroid cancer patients. We had performed a minimally invasive open thyroidectomy (MT; using mini-incision). This study describes the technique of its method and analyzes the surgical outcomes.

METHODS
Between January 2005 and February 2014, 4,257 patients with thyroid cancer (papillary and follicular thyroid cancer) underwent ipsilateral thyroidectomy. Of these patients, 108 patients have been performed. Minimally invasive open thyroidectomy (MT), and 2,805 underwent the conventional open thyroidectomy (OG).

The clinicopathologic characteristics and follow-up data between the two groups were retrospectively compared.
RESULTS
There were no significant difference in tumor size, multifocality, extrathyroidal invasion, central node metastasis, pathologic subtypes (PTC, FTC), and TNM stage between MG and other groups. The operation time and postoperative hospital day were significantly shorter in the MG group than in other groups. The retrieved LN number in MT was significantly smaller than in the open group and robotic group. And there were more recurrences in other operation methods compared to MT.

CONCLUSION
The early surgical outcomes of MT were comparable to other methods with excellent cosmesis. Although MT has shown benefits, a long-term follow-up data with more patients are is needed to assess of the surgical completeness of MT. The MT procedure can be safely performed for the selected patients with low-risk thyroid cancer such as less-than-total thyroidectomy.

Reliability of Intraoperative Angiography with Indocyanin Green after Thyroid Resection for the evaluation of Postoperative Parathyroid Function

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BACKGROUND AND AIMS
There are currently no peroperative methods to reliably predict the function of each parathyroid gland (PG) visualized during thyroid surgery. We have previously demonstrated that intraoperative angiography with the fluorescent dye indocyanin green (ICG) was feasible. We present here the results when patients underwent total thyroidectomy and in whom the four PGs were characterized with ICG angiography.

METHODS
Parathyroid angiography with intravenous administration of 3.5 ml of ICG was performed in consecutive patients undergoing total thyroidectomy. A near-infrared imaging endoscopic system (PinPoint, NOVADAQ) was used to characterize the vascularization of the identified PG after thyroid resection. Patients in whom four PGs were identified represent the study cohort. Data collection was done prospectively.

RESULTS
Between September 2014 and September 2015, four PGs were visualized in 39 of 196 patients undergoing total thyroidectomy. At least one well-perfused PG was demonstrated by ICG angiography in 30 patients (76.9%). None of these patients developed postoperative hypoparathyroidism. In the other nine patients, ICG angiography did not show a good vascularization in any of the four PGs, despite the fact that at least one PG was visually considered well-preserved in 4 of these 9 patients. Six of the 9 patients (including 2/4 with visually well-preserved PGs) were hypoparathyroid at POD1 and four of them at POD10. One patient was still hypoparathyroid after 6 months; the others recovered a good parathyroid function. In six patients, the PGs were autotransplanted. The positive predictive value of ICG angiography (absence of hypoparathyroidism with well-vascularized PG) was 100% and the negative predictive value (hypoparathyroidism when no PG was well-vascularized) was 67%.

CONCLUSION
Indocyanin green angiography evaluation of the PG function is reliable and better than visual evaluation alone. The procedure could help the surgeon decide which PG should be autotransplanted and could be a reliable tool to adapt the postoperative management of patients according to the results.

Antioxidant Status Analyses in Patients with Thyroid Disorders

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BACKGROUND AND AIMS
Thyroid hormones regulate oxidative metabolism, an important role in free-radical production. They are linked with the synthesis and degradation of antioxidant enzymes, proteins, and vitamins. As the synthesis of thyroid hormones involves hydrogen peroxide, thyroid disorders (TD) may alter levels of cellular oxidative stress. The body contains a network of antioxidant systems that counters the detrimental effects of reactive oxygen species (ROS). Inflammation and tumor cell proliferation could alter the antioxidant status and therefore the redox balance, favoring oxidative stress. This could induce oxidative cellular damage,
including membrane lipids. The antioxidant status of TD patients may elucidate the effects of ROS on thyroid gland dysfunction. This study aimed to measure antioxidant activities and biomarkers of oxidative stress in serum of patients with benign and malignant thyroid disorders.

METHODS

Forty-one TD patients from the University of Malaya Medical Centre were recruited. They were categorized into four groups: multinodular goiter (MNG; n = 18), follicular thyroid adenoma (FTA; n = 7), papillary thyroid cancer (PTC; n = 10), and follicular thyroid cancer (FTC; n = 6). Patient’s serum were analyzed for antioxidant activities, antioxidant enzymes, and biomarkers of oxidative stress and the results compared with the control group (n = 14) (Table 1).

RESULTS

Compared to the control group, TD patients had significantly higher superoxide dismutase (SOD) and catalase (CAT) activities, with no significant changes in glutathione peroxidase (GPx) activity. Although the FTA group had the highest GPx activity, this was not significant. Antioxidant activity levels were significantly decreased and the MDA equivalents (as indicators of lipid peroxidation) were increased in all four TD groups. The ROS levels in MNG and PTC groups were significantly higher than in the control group. Reactive oxygen species levels in the PTC group were significantly higher than in the MNG group (Table 2).

CONCLUSION

Thyroid gland dysfunction can influence serum antioxidant activities levels. Oxidative stress levels may provide an indication into the effectiveness of endogenous antioxidant defense mechanisms in scavenging ROS, providing an insight into the development of thyroid disorders.

Table 1: Details of patients and healthy subjects with their thyroid function test (TFT) results

<table>
<thead>
<tr>
<th>Groups</th>
<th>n = x</th>
<th>Mean age</th>
<th>TSH (mU/L)</th>
<th>fT4 (pmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MNG</td>
<td>18</td>
<td>52.77 ± 12.44</td>
<td>1.349444</td>
<td>16.22778</td>
</tr>
<tr>
<td>PTC</td>
<td>10</td>
<td>46 ± 14.55</td>
<td>1.925</td>
<td>16.36</td>
</tr>
<tr>
<td>FTA</td>
<td>7</td>
<td>40.14 ± 15.17</td>
<td>1.685714</td>
<td>16.58571</td>
</tr>
<tr>
<td>FTC</td>
<td>6</td>
<td>55.00 ± 22.45</td>
<td>1.23</td>
<td>19.8</td>
</tr>
<tr>
<td>CONTROL</td>
<td>14</td>
<td>39.93 ± 11.74</td>
<td>1.416667</td>
<td>16.83333</td>
</tr>
</tbody>
</table>

Note: TSH: Thyroid-stimulating hormone (normal range: 0.55–4.78 mU/L); fT4: Free thyroxine (normal range: 11.5–22.7 pmol/L).

Table 2: Antioxidant assays for all four groups of thyroid disorders in comparison to control group

<table>
<thead>
<tr>
<th>Antioxidant assays</th>
<th>Control</th>
<th>MNG</th>
<th>PTC</th>
<th>FTA</th>
<th>FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD (Activity U/ml)</td>
<td>3.12 ± 0.01</td>
<td>14.74 ± 0.20*</td>
<td>15.07 ± 0.08*</td>
<td>11.34 ± 0.22*</td>
<td>15.67 ± 0.51*</td>
</tr>
<tr>
<td>GPx (Activity nmol/min/ml)</td>
<td>122.86 ± 0.01</td>
<td>92.07 ± 0.01</td>
<td>128.45 ± 0.01</td>
<td>156.07 ± 0.01</td>
<td>114.61 ± 0.01</td>
</tr>
<tr>
<td>CAT (Activity nmol/min/ml)</td>
<td>67.89 ± 0.27</td>
<td>162.82 ± 0.85*</td>
<td>210.67 ± 0.64*</td>
<td>158.01 ± 0.45</td>
<td>246.21 ± 1.13*</td>
</tr>
<tr>
<td>ABTS</td>
<td>1.63 ± 0.02</td>
<td>0.98 ± 0.07*</td>
<td>0.59 ± 0.01**</td>
<td>1.30 ± 0.01*</td>
<td>1.35 ± 0.01*</td>
</tr>
<tr>
<td>TEAC value (mmol Trolox/μl sample)</td>
<td>0.016 ± 0.00</td>
<td>0.019 ± 0.00*</td>
<td>0.019 ± 0.00*</td>
<td>0.021 ± 0.00*</td>
<td>0.022 ± 0.00*</td>
</tr>
<tr>
<td>MDA (MDA equivalent (ng/mg of protein))</td>
<td>90.62 ± 0.42</td>
<td>107.93 ± 0.48*</td>
<td>131.27 ± 0.48**</td>
<td>102.29 ± 0.53</td>
<td>87.78 ± 0.94</td>
</tr>
</tbody>
</table>

*Indicates significant difference (p < 0.05) between the diseased groups of benign and malignant thyroid disorders (MNG vs PTC, FTA vs FTC).

#Indicates significant difference (p < 0.05) between control and the diseased groups.

MNG: Multinodular goiter; PTC: Papillary thyroid cancer; FTA: follicular thyroid adenoma, FTC: Follicular thyroid cancer.
Effect of Postoperative Period and the Radioiodine Uptake of the Metastatic Lesions

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BACKGROUND AND AIMS
It is well known that when radioiodine therapy is performed, younger patients have a higher uptake than elder ones. But even in some elder patients, radioiodine accumulation to the inetastatic lesions could be seen. T. Higashi et al reported (J Nucl Med 2011 May;52(5):683-689) that the uptake of radioiodine is higher when the therapy is given within 6 months after the last operation.

METHODS
A retrospective survey was performed using 112 differentiated thyroid cancer (DTC) patients who had had radioiodine therapy for metastasis. Of the 112 cases, 99 were papillary cancer and 13 were follicular cancer. There were 24 male and 88 female patients with the average age of 58.6 years. We evaluated the effect of period from the first surgery of DTC to the radioiodine therapy for inetastasis and also evaluated if the age of the patient would have any effect on the uptake rate.

RESULTS
In the 112 cases, the average of the postoperative period was 88.2 months (1–556) and the uptake rate of radioiodine was only 33.9%. When divided by 24 months of postoperative period, the group that had radioiodine therapy before 24 months had an uptake rate of 51.1% and the group that had therapy after 24 months had an uptake rate of only 19.0%. When divided by age, the group younger than 45 years had an uptake rate of 51.9% and the group older than 45 years had a rate of only 28.8%. But even in the elder group, when radioiodine therapy was given before 24 months, the uptake rate was 51.4%.

CONCLUSION
This study suggested that the uptake rate of radioiodine therapy for metastatic DTC is due to not only age but also the postoperative period.

Cosmetic High-neck (Hyoid-level) Incision Ante-grade Ligature-less Thyroidectomy Technique

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BACKGROUND AND AIMS
Most of our patients present late with large goiters that are not suitable for endoscopic thyroidectomy. The classical Kocher’s low-neck incision is visible as our people do not cover their neck due to hot weather. It is also prone to Keloid formation. Hence, an alternative high-neck incision at the level of the hyoid was tried on December 26, 2007, as this is a flexural area and is in the shadow of the face and chin and is not seen.

METHODS
For total or hemithyroidectomy, a 4 to 8 cm (depending on the size of the goiter) incision is made in the upper most skin crease in the anterior aspect of the neck. Flaps are raised and strap muscles cut or retracted. Pyramidalis and right upper pole are dissected first with ultrasonic shears followed by lateral mobilization of the right lobe, then lower pole dissection, and then isthmus and the left lobe in similar ante-grade (upper pole to lower pole) sequence. The parathyroids and the laryngeal nerves (EBSLN and RLN) are identified and preserved.

RESULTS
Four hundred thyroidectomies (nearly all of them total) have been performed by this technique and the cosmetic and functional results have been excellent with residual thyroid needing re-exploration in only one patient. Immediate and late follow-up images of the neck show excellent cosmetic results. PTH and thyroglobulin levels are routinely checked before and after surgery to monitor the safety and adequacy of the procedure. Vocal cords are routinely checked before the surgery. During follow-up, the patient and family members are asked about any voice change noticed.

CONCLUSION
Numerous referrals of new patients by operated patients show the popularity of this technique among patients. The scar is so well hidden that it is virtually a scarless surgery. It is safe and complete (no residual thyroid tissue) and provides an intact specimen to the pathologist.
Proper Timing of Postoperative Vocal Cords Assessment by Transcutaneous Laryngeal Ultrasonography

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BACKGROUND AND AIMs

Transcutaneous laryngeal ultrasound (TLUSG) is an innovative tool to assess vocal cords (VC) after thyroidectomy or parathyroidectomy. However, it is unclear when postoperative TLUSG should be done to provide better visualization and accuracy.

METHODS

We prospectively evaluated 227 patients undergoing thyroidectomy or parathyroidectomy. Transcutaneous laryngeal ultrasound was performed on postoperative day (D0), one day after operation (D1), and on follow-up 7 to 10 days after operation (Dfu). On follow-up, direct laryngoscopy (DL) was performed after TLUSG as validation. Findings of TLUSG at different timings were correlated with DL findings. The VC visualization rate and accuracy at different timings were compared.

RESULTS

D0 TLUSG had a lower VC visualization rate than D1 or Dfu (84.1 vs 92.5 vs 92.5%, p = 0.005). A total of 30, 28, and 26 patients were found to have Vocal code palsy (VCP) by TLUSG on D0, D1, and Dfu respectively. While 19 patients were diagnosed with VC palsy by laryngoscopy, sensitivity was comparable between D0, D1, and Dfu. On Dfu, TLUSG has a comparable accuracy to D1 (93.3 vs 86.4%, p = 0.0199). Comparing to D0 TLUSG performed after 1 hour of skin closure (D0-b), D0 TLUSG performed within 1 hour of skin closure (D0-a) had a lower rate of VCs visualization (77.1 vs 88.2%, p = 0.028) and a trend of inferior sensitivity (25.0 vs 87.5%, p = 0.067) and specificity (81.7 vs 90.8%, p = 0.094). While there was no difference in the rate of VCs visualization, sensitivity and specificity between Dfu TLUSG performed within 1 weeks (Dfu-I) and after 1 weeks (Dfu-II) Was significantly different.

CONCLUSION

To assess postoperative VCs function, TLUSG within 1 hour of operation should be avoided. Performing TLUSG at about 1 week postoperatively was preferred as it offered a higher visualization rate and specificity.

Intraoperative Nerve Monitoring during Thyroidectomy: An Attitude Survey in Turkey

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BACKGROUND AND AIMs

Intraoperative neuromonitoring (IONM) is a helpful method during thyroid surgery. It has been mentioned in current guidelines, with the aim to protect potential damage to the nerves. We aimed to determine personal approaches of surgeons of Turkey dealing with thyroid surgery regarding IONM, with a survey prepared by the National IONM Study Group.

METHODS

The survey consisted of 20 questions, concerning the participation rate for IONM, the reason of usage, and case preference. Besides, the preference for the type of monitoring (intermittent or continuous), intraoperative decision after loss of signal and attitude toward routine postoperative laryngeal exam were questioned.

RESULTS

A total of 214 surgeons replied. The majority were from the western regions. More than a half remarked performed over 50 thyroidectomies a year. The rate of those who preferred to use IONM due to medicolegal concern was 52%. Another 65% used the IONM in believing the system helps to protect nerve injury. The rate of using continuous monitoring was 16%. The rate of IONM users remarking that they use IONM in all cases was 21%. Surgeon rate using IONM in the difficult case was 58%. Interestingly, 33% of the participants remarked that they do not check the ipsilateral vagus (V2) signal after lobectomy. More
than half of the surgeons would not use the system for identifying the external branch of the superior laryngeal nerve. Besides, 16% preferred routine laryngeal examination, while 68% were supporters of selective laryngeal examination. After loss of signal in the malignant case, only 28% of surgeons believed in staged thyroidectomy.

CONCLUSION

Although guidelines are in use, there seems to be individual differences in the practice of IONM between Turkish surgeons.