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Usefulness of endoscopic breast-conserving surgery for breast cancer

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Abstract

Purpose We compared the safety, invasiveness, and cosmetic outcomes between endoscopic breast-conserving surgery (endoscopic group) and surgery under direct vision (direct vision group) for treating breast cancer.

Methods We compared 100 cases of endoscopic surgery with 150 cases of direct vision surgery. Safety was evaluated in terms of blood loss, surgical duration, and presence or absence of complications, whereas degree of invasiveness was assessed using preoperative and postoperative leukocyte counts, neutrophil counts, interleukin (IL-6) levels and fever. Cosmetic outcome was assessed on the basis of breast evaluation by medical staff and patient subjective satisfaction.

Results In both groups, serious postoperative complications were absent. No significant difference was observed in the leukocyte counts, neutrophil counts, IL-6 levels, or fever between the groups. Evaluation of cosmetic outcomes by the staff showed more favorable breast size, breast shape, and scar condition in the endoscopic group. A significantly higher level of patient satisfaction was also observed in the endoscopic group. Postoperative local recurrence was absent.

Conclusions The endoscopic approach showed comparable safety and degree of invasiveness, and provided better postoperative cosmetic outcomes than direct vision surgery. Our results suggest that endoscopic breast-conserving surgery is a potentially useful surgical method for treatment of breast cancer.

Introduction

The surgical technique for breast cancer must be selected on the basis of the ability to completely excise the lesion without compromising the chance for complete cure. In recent years, however, obtaining a good cosmetic outcome has gained importance. Because breasts are an important female physical characteristic, preserving them in their natural form is important for improving the postoperative quality of life. In order to maintain a good cosmetic outcome, minimum resection is required, and preoperative surgical plan using magnetic resonance imaging (MRI) is important [1]. Endoscopic surgery to improve cosmetic outcomes from treatment for breast disease was first reported in the 1990s [2] and has been performed in Japan since 1996 [3, 4]. However, evidence supporting endoscopic surgery is low, because randomized trials are difficult to conduct, and the technique requires special tools and good surgical skills [5]. Moreover, the recommendation level of endoscopic surgery for breast cancer is grade C1 according to the clinical practice guidelines of the Japanese Breast Cancer Society [6]. It is necessary to establish endoscopic surgery techniques and expand their use to achieve good cosmetic outcomes after breast cancer surgery. To that end, we began endoscopic breast-conserving surgery for breast cancer in June 2009. In the present study, we compared the safety, degree of surgical invasiveness, and postoperative cosmetic outcome (based on evaluations by medical staff and patient satisfaction questionnaires) between endoscopic surgery and direct vision breast-conserving surgery. We then evaluated the potential of endoscopic surgery as a useful treatment for breast cancer.

Patients and methods

Indication of endoscopic breast-conserving surgery and patient background

All of the patients indicated for endoscopic surgery whose have no exclusion criteria. Exclusion criteria for endoscopic surgery included (1) cutaneous infiltration or lesions close to the skin, (2) a high degree of thoracic deformity, (3) hemorrhagic diathesis, (4) advanced age or poor general health status, or (5) patient refusal. For the patients who have indication of endoscopic breast-conserving surgery, we explained the method of endoscopic breast-conserving surgery and breast-conserving direct vision surgery both before the operation. The patients selected one of the operating methods by themself, then, operation method was determined. Each patient provided written informed consent for the surgery. This study is not randomized study. We compared the outcomes from 100 cases of patients who selected the endoscopic breast-conserving surgery (endoscopic group) and from 150 cases of patients who selected the breast-conserving direct vision surgery (direct vision group), which were performed curatively to treat breast cancer, at our hospital since June 2009. Table 1 lists the mean patient age; tumor diameter and location; presence or absence of axillary lymph node metastasis; tumor staging; expression levels of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2; presence or absence of chemotherapy and radiotherapy of the subjects in this study.

The surgical technique

The surgical procedure was performed as follows. In brief, the skin was incised at two

locations: the axilla (2–7 cm) and areola (within 1/2 of the circumference). A wrap protector was placed to secure the visual field at the axillary incision, which was placed for sentinel lymph node biopsy or axillary lymph node dissection. The lateral border of the pectoralis major muscle was then identified, and its fascia was exfoliated along the direction of the muscle fibers. This exfoliation was performed endoscopically using a vein retractor (Karl Storz GmbH & Co., KG, Tuttlingen, Germany) with a beak-shaped tip. For areas where exfoliation was difficult, bipolar scissors (Ethicon PowerStar Bipolar Scissors BP100; Johnson and Johnson International, Brussels, Belgium) were used to separate the tissues while ensuring hemostasis (Fig. 1).

Once the separation of the pectoralis major muscle from its fascia was completed, a subcutaneous injection of extremely dilute epinephrine (1:400,000) was administered in the area to be used for a skin flap (same dose of epinephirine was used for conventional direct vision surgery). Then, the areolar border was dissected and a wrap protector was placed to protect the areola and nipple during creation of the skin flap. The skin flap was created using bipolar scissors while securing the visual field with an illuminated muscle hook (oral retractor by TISE) with a light source at the tip (Fig. 2). Next, the margin of the area scheduled for resection was marked using an injection of pyoctanin mixed with lidocaine (Xylocaine Jelly) and partial resection was performed with a margin of 1.5–2.0 cm from the tumor (Fig. 3).

Once the lesion tissue was removed, and the absence of residual tumor cells in the marginal tissue was confirmed by rapid pathological diagnosis with frozen biopsy, the area from which tissue was excised was covered by suturing as much surrounding mammary tissue

as possible to decrease postoperative breast dimpling. Drain placement was determined on the basis of the volume of removed tissue and how well the area was filled. Interrupted sutures with 6-0 nylon were used to close the areolar incision wound (Fig. 4).

Safety evaluation

Safety was evaluated by comparing intraoperative blood loss, average surgical duration, positive rate of excised tissue margin, average duration of hospital stay, and the presence or absence of intraoperative and/or postoperative complications, between the endoscopic and direct vision groups.

Degree of surgical invasiveness

The degree of surgical invasiveness between the endoscopic and direct vision groups was evaluated by measuring leukocyte counts, neutrophil counts, interleukin (IL)-6 levels and fever immediately before and after surgery. Twenty patients were selected from endoscopic group and from direct vision group, randomly. It was reported that the plasma levels of IL-6 increased gradually after skin incision and reached the maximal value at the end of surgery [7, 8] and leukocyte number was also maximally increase within 4 hours after surgery [9]. From these data, blood was collected in 30 minutes before operation, and 30 minutes after operation. IL-6 levels were measured using chemiluminescence enzyme immunoassay (CLEIA method). Briefly, the isolated serum is exposed to mouse anti-human IL-6 monoclonal antibody-conjugated ferrite particles. Then, the sample is washed, and the second antibody

(alkalinephosphatase-labeled mouse anti-human IL-6 monoclonal antibody) is added, to induce the formation of sandwiched complex composed of serum IL-6 and two antibodies. After isolation and removal of unreacted alkaline phosphatase-labeled antibody, AMPPD (3-(2'-spiroadamantane)-4-methoxy-4-(3''-phosphoryloxy) phenyl-1,2-dioxetane disodium salt, a chemiluminescent substrate) is added. Alkaline phosphatase in the sample degrades AMPPD, causing chemiluminescence. The intensity of chemiluminescence is measured with a luminometer to determine the level of IL-6 [10].

Evaluation of cosmetic outcome

The postoperative cosmetic outcome of the breast was assessed on the basis of evaluations by the medical staff and patient satisfaction surveys. Twenty patients were selected from endoscopic group and 30 patients were selected from direct vision group, randomly. The medical staff evaluation was performed by scoring the following 5 items in the postoperative patients: breast size (2 points, almost equal; 1 point, slightly different; and 0 points, significantly different), breast shape (same scoring method used for breast size), scarring (2 points, not noticeable; 1 point, slightly noticeable; and 0 points, significantly noticeable), condition of skin flap (same scoring method used for scarring), and condition of the nipple (1 point, no bilateral difference; and 0 points, bilateral difference). This objective evaluation was supported by The Japanese Breast Cancer Society [11]. The scores were compared between the endoscopic and direct vision groups.

The patient satisfaction survey consisted of a postoperative questionnaire completed

by each patient at a follow-up visit after discharge. The patients were asked to evaluate the following items using a 4-point scale: wound condition, breast dimpling, wound pain, and overall breast shape (5 points, very satisfied; 4 points, mostly satisfied; 3 points, moderately satisfied; 2 points, not satisfied; and 1 point, very unsatisfied). The results were compared between the two groups. The nurse was conducting this investigation in questionnaire form, and the doctor was not involving.

Statistical Analysis

The chi squared test, Fisher's exact probability test, and Student's *t* -test were used for the statistical analysis. A p value of less than 0.05 was regarded as statistically significant.

Results

Patient characteristics

The patient characteristics of the two groups are summarized in Table 1. Of note, the average age in the endoscopic group was significantly lower than that in the direct vision group (54.2 ± 10.7 vs. 61.9 ± 14.3 years; $P < 0.001$), and the average tumor diameter was significantly smaller in the endoscopic group (1.6 ± 0.6 vs. 2.1 ± 1.6 cm; $P = 0.0062$). No significant difference between the two groups was found regarding any other item.

Safety

As shown in Table 2, there was no significant difference in the amount of intraoperative blood

loss between the two groups (32.1 ± 28.0 vs. 30.6 ± 26.1 mL in the endoscopic and direct vision groups, respectively; $P = 0.6784$). The average surgical duration was significantly longer in the endoscopic group (152.3 ± 21.7 vs. 127.7 ± 35.6 min; $P < 0.001$). There was no significant difference in the positivity rate of the excised tissue margin (4.0% and 3.3% in the endoscopic and direct vision groups, respectively; $P = 0.581$) or in the average length of hospital stay (8.4 ± 1.8 vs. 9.1 ± 1.9 days in the endoscopic and direct vision groups, respectively; $P = 0.170$). No serious intraoperative or postoperative complication occurred in either group. During the mean 23-month (range, 9–40 months) observation period, there was no local recurrence noted and all patients survived.

Degree of surgical invasiveness

As shown in Table 3, there was no significant difference between the endoscopic and direct vision groups with regard to surgical invasiveness as measured by the leukocyte count immediately before (5.12 ± 1.77 vs. 6.01 ± 1.97 × 10^3 cells/μL in the endoscopic and direct vision groups, respectively; $P = 0.3612$) or after surgery (7.03 ± 3.22 vs. 7.81 ± 3.55 × 10^3 cells/μL in the endoscopic and direct vision groups, respectively; $P = 0.8046$). No significant difference was also observed between the endoscopic and direct vision groups in neutrophil count immediately before (48.5 ± 8.90 vs. 50.4 ± 7.20%, respectively; $P = 0.3044$) or after surgery (73.1 ± 10.2 vs. 70.7 ± 10.8%, respectively; $P = 0.1049$). In addition, there was no significant difference between the endoscopic and direct vision groups in IL-6 levels immediately before (1.72 ± 0.71 vs. 2.22 ± 0.56 pg/mL, respectively; $P = 0.2423$) or after

surgery (5.41 ± 2.24 vs. 5.24 ± 2.12 pg/mL, respectively; $P = 0.9098$). Similarly, there was also no significant difference between the endoscopic and direct vision groups in fever immediately before (36.4 ± 0.50 vs. 36.6 ± 0.30 ^{o}C, respectively; $P = 0.6881$) or after surgery (36.5 ± 0.40 vs. 36.2 ± 0.30 ^{o}C, respectively; $P = 0.4490$).

Evaluation of cosmetic outcomes

The postoperative cosmetic outcome of the breast was evaluated at 3 months after surgery. As shown in Table 4, the evaluation scores by the medical staff were significantly higher in the endoscopic group than in the direct vision group in breast size (1.50 ± 0.14 vs. 1.09 ± 0.19 points, respectively; $P = 0.021$), breast shape (1.65 ± 0.11 vs. 0.89 ± 0.11 points, respectively; $P < 0.001$), and breast scarring (1.70 ± 0.11 vs. 0.75 ± 0.18 points, respectively; $P < 0.001$). There was no significant difference between the two groups regarding the conditions of the skin flap and nipple.

As shown in Table 5, the postoperative patient satisfaction survey scores were significantly higher in the endoscopic group than in the direct vision group for wound condition (3.8 ± 0.17 vs. 2.3 ± 0.41 points, respectively; $P = 0.019$), breast dimpling (3.5 ± 0.19 vs. 1.9 ± 0.39 points, respectively; $P < 0.001$), and overall breast shape (3.6 ± 0.30 vs. 2.0 ± 0.37 points, respectively; $P < 0.001$, respectively). There was no significant difference between the two groups in terms of wound pain. The above results showed that the postoperative cosmetic outcome of the breast was better in the endoscopic group, as evaluated by both medical staff and patients. The patient is shown at 6 months after endoscopic

breast-conserving surgery in Figure 5. The cosmetic results were good and she is satisfied with the results.

Postoperative treatment

The patients underwent radiotherapy to the remaining breast tissue, hormonal therapy, or chemotherapy as required as postoperative treatment in light of the risk of recurrence. All patients in the endoscopic group underwent radiotherapy to the remaining breast. In addition, 7 underwent chemotherapy, and 16 underwent combined chemotherapy and hormonal therapy. All patients in the direct vision group also underwent radiotherapy to the remaining breast, of which 11 underwent chemotherapy only, and 25 underwent chemotherapy and hormonal therapy. There was no significant difference in postoperative treatment methods between the groups (P = 0.9834). Moreover, radiotherapy to the remaining breast, chemotherapy, and hormonal therapy did not result in any postoperative complication in the two groups.

Discussion

Endoscopic surgery for breast disease was initiated in Japan around 1996 for obtaining better cosmetic outcome [3, 4]. Endoscopic surgery has progressively become more common thereafter as numerous developments and improvements were added to the surgical repertoire. We have also introduced endoscopic surgical approaches in 2009 in our medical center.

To minimize surgical scarring, the skin incision in endoscopic surgery for breast cancer has been performed at the axilla, areolar border, or a combination of the axilla and

areolar border [12, 13]. In our medical center, we perform endoscopic breast surgery by incising both the axilla and areola and inserting an endoscope through the incision used for sentinel lymph node biopsy or axillary lymph node dissection. We then perform extensive exfoliation of the pectoralis major muscle fascia and then perform semicircular incision of the areola, creating a skin flap under direct vision in the areolar incision. This is followed by partial breast resection with curative intent.

The important points to consider during the surgery are to minimize cutaneous damage by attaching a wrap protector to the incisions at the axilla and areolar border and to create a skin flap with uniform thickness but without damage by using bipolar scissors. The wrap protector was the only disposable device in our endoscopic surgery, and the cost of wrap protector was just $30. In addition, separation of the pectoralis major muscle from its fascia is possible over a larger area in endoscopic surgery than in direct vision surgery, as well as creation of a wider skin flap so that suturing the surrounding dissected mammary tissue will be easier. This facilitates sufficient filling of the area from where tissue was excised. Thus, by implementing these procedures, endoscopic surgery can deliver a better cosmetic outcome.

There was no significant difference in intraoperative blood loss between the endoscopic and direct vision groups (32.1 ± 28.0 vs. 30.6 ± 26.1 mL). Blood loss in our endoscopic surgery cases was extremely low, considering that the blood loss during endoscopic partial resection of the breast by Owaki et al. [14] and Lee et al. [15] was 150 ± 96.9 and 180 ± 130 mL, respectively. The low blood loss was achieved probably by promptly arresting any hemorrhage once we identified even the slightest bleeding and also by

rechecking the area of hemostasis before closing the incision because the visual field during endoscopic surgery is limited. In addition, although no case required conversion to direct vision surgery because of uncontrollable hemorrhage, it is important to explain to the patient the possibility for such intraoperative conversion to ensure that the surgery can be safely completed.

After performing endoscopic surgery for breast cancer, there is a concern that there may be an increased risk of local recurrence because the skin immediately overlying the tumor is not resected. There have been reports from multiple institutions, including that of Nakajima et al. [12], who studied the rate of local recurrence and postoperative survival in 244 cases of endoscopic breast-conserving surgery for stage I and II breast cancer. They reported that the rate of local recurrence for both stages was 5.3%, which was equal to that of direct vision surgery [16, 17]. Therefore, we presume that there is no increase in recurrence resulting from retention of the skin immediately overlying the tumor. In fact, in our center, where the skin flap is made as thin as possible such that no cancer tissue remains in the skin flap immediately overlying the tumor, all the 100 patients studied have survived with no local recurrence.

The major difference between endoscopic and direct vision surgery is the presence or absence of an incision line on the skin immediately overlying the tumor, although the extent of resection is nearly equal in both. In endoscopic surgery, however, the fascia of the pectoralis major muscle is dissected over a wider area and the skin flap is created wider than direct vision surgery, which raises a concern that the endoscopic approach may be more invasive than the direct vision approach. However, there has been no report that directly compares the degree of

surgical invasiveness of the endoscopic and direct vision surgical approaches for breast cancer; therefore, it is important to conduct a more detailed study on the degree of invasiveness in endoscopic surgery because wider use of this technique is expected in future.

IL-6, an important inflammatory cytokine that stimulates the production of acute phase proteins, is reportedly associated with surgical invasiveness [7, 18]. Therefore, we used IL-6 levels, leukocyte counts, neutrophil count, and fever as indices of surgical invasiveness, and measured each immediately before and after surgery in the endoscopic and direct vision groups. We found no significant difference between the groups in any of these indices at either time point. The surgical invasiveness of these procedures is thus considered to be similar, and making the areas of fascial dissection and the skin flap larger than those in conventional direct vision surgery to achieve a better cosmetic outcome was considered acceptable.

The purpose of endoscopic surgery for breast cancer is to maximize the postoperative cosmetic outcome of the breast. Previous reviews of cosmetic outcomes of the breast after endoscopic surgery were reported using evaluations by medical staff and patients [15, 19-21]; thus, we adopted both in the present study. The evaluation of postoperative cosmetic outcome by medical staff revealed that surgical outcomes in the endoscopic group were better than those in the direct vision group. The patient satisfaction survey also showed significantly higher levels of satisfaction in the endoscopic group than in the direct vision group. Thus, according to the evaluations by both the medical staff and the patients, the endoscopic group had a better cosmetic outcome than the direct vision group. This may be a result of minimal surgical scarring resulting from the placement of only areolar and axillary incisions during

endoscopic surgery, leaving the skin immediately overlying the tumor scar free, unlike in the direct vision surgery technique. In addition, as described earlier, breast dimpling is minimum as a result of wider dissection of the pectoralis major muscle fascia, which allows for the mobilization of surrounding tissue that can be used to fill the void left by the excised tissue. Furthermore, the average tumor diameter was significantly smaller in the endoscopic group statistically, however, the difference is only 0.5cm and we discussed that 0.5cm difference is little influence for cosmetic outcomes.

The above results indicate that endoscopic surgery for breast cancer has an equivalent level of surgical invasiveness but a better cosmetic outcome than direct vision surgery. These results suggested that endoscopic breast-conserving surgery is a potentially useful surgical method for breast cancer treatment. In future, we will further evaluate the long-term results of safety and cosmetic outcomes by accumulating more cases offering endoscopic surgery as a surgical option for breast cancer treatment at our institution.

Conflict of interest

The authors confirm that there are no actual or potential conflicts of interest relating to this article.

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Figure legend

Figure 1

A wrap protector was placed to secure the visual field at the axillary incision, which was placed for axillary lymph node dissection. The lateral border of the pectoralis major muscle was identified, and its fascia was exfoliated along the direction of the muscle fibers endoscopically using a bipolar scissors.

Figure 2

The areolar border was dissected and a wrap protector was placed to protect the areola and nipple during creation of the skin flap. The skin flap was created using bipolar scissors while securing the visual field with an illuminated muscle hook with a light source at the tip.

Figure 3

Partial resection was performed with a margin of 1.5–2.0 cm from the tumor.

Figure 4

Drain was placed and interrupted sutures with 6-0 nylon were used to close the areolar incision wound. This case was performed axillary lymph node dissection, because of sentinel lymph node biopsy was positive.

Figure 5

The patient was a 31-year-old woman. The tumor was in right-D area, classified as p-T1N0M0 stage I. The skin incision was in the axillary and areolar. The medical staff evaluation was breast size (2 points), breast shape (2 points), scarring (2 points), condition of skin flap (2 points), and condition of the nipple (1 point). The patient satisfaction survey was wound condition (5 points), breast dimpling (4 points), wound pain (4 points), and overall breast shape (5 points).

Table 1 Patient characteristics

Variable	Endoscopic group	Direct vision group
No of patient	100	150
Age (years), mean(rang	54.2 (28-74)	61.9 (25-91)
Tumor size (cm)	1.6 ± 0.6	2.1 ± 1.6
Tumor location		
Upper inner	25	35
Lower inner	10	19
Upper outer	48	63
Lower outer	11	27
Central	6	6
Lymph node status		
n (+)	18	31
n (-)	82	119
Stage		
0	4	12
I	61	74
IIA	23	40
IIB	12	24
ER status		
Positive	83	119
Negative	17	31
PgR status		
Positive	69	101
Negative	31	49
HER2 status		
Positive	12	26
Negative	85	124
Chemotherapy		
Yes	21	37
No	79	113
Radiotherapy		
Yes	100	150
No	0	0

Table 2 Safty evaluation

	Endoscopic group	Direct vision group	p-value
Blood loss (ml)	32.1 ± 28.0	30.6 ± 26.1	p=0.6784
Average surgical duration (min)	152.3 ± 21.7	127.7 ± 35.6	p<0.001
Positive rate of excised tissue margin (%)	4.0 (4/100)	3.3 (5/150)	p=0.581
Average duration of hospital stay (days)	8.4 ± 1.8	9.1 ± 1.9	p=0.170

Table 3 Degree of surgical invasiveness

		Endoscopic group (n=20)	Direct vision group (n=20)	p-value
Leukocyte counts (x 10^3 cells/uL)	Before surgery	5.12 ± 1.77	6.01 ± 1.97	P=0.3612
	After surgery	7.03 ± 3.22	7.81 ± 3.55	p=0.8046
Neutrophil counts (%)	Before surgery	48.5 ± 8.90	50.4 ± 7.20	p=0.3044
	After surgery	73.1 ± 10.2	70.7 ± 10.8	p=0.1049
Interleukin (IL)-6 level (pg/ml)	Before surgery	1.72 ± 0.71	2.22 ± 0.56	p=0.2423
	After surgery	5.41 ± 2.24	5.24 ± 2.12	p=0.9098

Table 4 Evaluation of cosmetic outcomes by medical staff

	Endoscopic group (n=20)	Direct vision group (n=20)	p-value
Breast size	1.50 ± 0.14	1.05 ± 0.15	p=0.034
Breast shape	1.65 ± 0.11	0.85 ± 0.15	p<0.001
Scarring	1.70 ± 0.11	0.65 ± 0.13	p<0.001
Condition of skin flap	1.45 ± 0.12	1.35 ± 0.10	p=0.531
Condition of the nipple	0.90 ± 0.07	0.95 ± 0.05	p=0.560

Table 5 Patient satisfaction survey

	Endoscopic group (n=20)	Direct vision group (n=20)	p-value
Wound condition	3.8 ± 0.17	2.1 ± 0.33	p=0.006
Breast dimpling	3.5 ± 0.19	2.2 ± 0.25	p=0.010
Wound pain	4.0 ± 0.34	3.8 ± 0.31	p=0.280
Over all breast shape	3.6 ± 0.30	2.2 ± 0.32	p=0.041