



## Original Article

# Comparative Study of Mastectomy Using Conventional Techniques, Multiport and Single-Port Robotic Surgical Systems

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**Purpose** Oncologic and surgical outcomes of robot-assisted nipple-sparing mastectomy (RNSM) compared to conventional nipple-sparing mastectomy (CNSM) is under investigation. This study compared the clinical outcomes of recurrence-free survival and postoperative complication after RNSM and CNSM.

**Materials and Methods** We retrospectively reviewed data of 401 patients who underwent da Vinci Si/Xi/SP-assisted RNSM or CNSM with immediate reconstruction between November 2016 and November 2020 at a single institute. Oncological outcomes were collected until March 2022. Primary endpoints were long-term outcomes, such as local recurrence, distant metastasis, disease-free survival, overall survival, and postoperative complications, while secondary endpoints were pathology results, and oncological outcomes.

**Results** Patients underwent RNSM (n=162) or CNSM (n=239). Of RNSM cases, nine (5.6%) were performed using the da Vinci Si System, 96 (59.3%) using the da Vinci Xi System, and 57 (35.2%) using the da Vinci SP System. No significant difference in recurrence-free survival was found between the RNSM and CNSM group, and both groups had a median follow-up of 37 months. The recurrence rate in RNSM patients after a median follow-up of 24.5 months was 3.8%, compared with 5.9% in CNSM patients after a median follow-up of 42 months. No difference in recurrence was seen among RNSM patients with respect to surgical systems (multiport vs. SP, p=0.136). In addition, grade III postoperative complication rate was lower in patients with RNSM than in those with CNSM. Transfusion was only applied in 6.2% of patients.

**Conclusion** Robot-assisted surgical systems can be safely used to perform nipple-sparing mastectomy in patients with early breast cancer.

**Key words** Breast neoplasms, Nipple-sparing mastectomy, Robotic mastectomy, Multiport robotic surgical system, Single-port robotic surgical system

## Introduction

In breast cancer surgery, nipple-sparing mastectomy (NSM) is preferred over conventional mastectomy because it enhances patients' quality of life and satisfaction with surgical outcomes [1]. NSM was introduced as a subcutaneous mastectomy technique in the 1960s and has been widely applied since [2,3]. Several retrospective studies have found that long-term outcomes of NSM are not significantly inferior to those of conventional total mastectomy [4-6]. According to U.S. National Comprehensive Cancer Network guidelines [4], NSM can be recommended to selected patients. However, a long scar overlying the skin persists after conventional NSM (CNSM), resulting in reduced patient satisfaction. Endoscopic mastectomy, a form of minimally invasive

breast surgery, was introduced in the 1990s; it uses smaller incisions located in the axilla or periareolar area, which can minimize or hide scars [7]. However, traditional endoscopic devices with a rigid shaft and short articulated tip require a long learning curve. Therefore, this method has only been used by a few surgeons in East Asia, where patient breasts are relatively small [7].

The da Vinci Surgical System provides surgeons with enhanced visualization, fully-wristed articulating instrumentation, intuitive user interface, and improved surgeon ergonomics, compared with traditional endoscopic surgery. Further, the system provides the usual benefits of endoscopy over open surgery, such as improved cosmesis, lower blood loss, and shorter length of hospital stay. Other surgical specialties, such as urologic, thyroid, colorectal,

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and gynecologic surgery, have utilized this system as well. Robot-assisted NSM (RNSM) was first introduced by Toesca et al. in 2017 [8], and has additionally been reported by other surgeons [9-11]. In RNSM, the incision is located at the midaxillary line, hidden by the arm and invisible from the front. At Severance Hospital, cadaveric practice for RNSM was initiated in 2013, with the first surgery performed in 2016 [12,13]. RNSM was applied to candidates for NSM due to early breast cancer, or for prophylactic mastectomy due to germline *BRCA1/2* mutations. Since then, over 300 RNSM surgeries have been performed [14]. Further, RNSM has been reported to be oncologically and surgically safer than conventional methods [15,16]. In two studies, fewer cases of nipple necrosis were observed in RNSM patients than in CNSM patients. This may have been due to the location of the incision site, which does not allow blood supply to the skin and nipple-areolar complex to deteriorate [17,18]. According to a randomized controlled study conducted in Italy, patient satisfaction was higher after RNSM [19]. However, limited data

is available on surgical or oncological outcomes > 30 days after surgery [10]. Therefore, the current study evaluated and compared oncological outcomes of recurrence-free survival (RFS) and postoperative complication rate after RNSM and CNSM using high-volume, single-center data.

## Materials and Methods

### 1. Study population

We retrospectively reviewed the data of patients who underwent da Vinci Si/Xi/SP RNSM with immediate reconstruction performed by experienced breast surgeons between November 2016 and November 2020 at Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea. Patients lost to follow-up, those with insufficient medical records for analysis, those presenting with distant metastasis at diagnosis, and those who were ineligible to participate in this study according to investigators, were excluded. Finally,

**Table 1.** Baseline patient demographics and preoperative characteristics

Variable	RNSM (n=162)			CNSM (n=239)	p-values			
	Total	Si/Xi (n=105)	SP (n=57)		p-value <sup>a)</sup>	p-value <sup>b)</sup>	p-value <sup>c)</sup>	p-value <sup>d)</sup>
Age (yr)	44.76±7.81	45.04±7.95	44.25±7.59	46.75±8.34	0.017	0.077	0.039	0.534
BMI (kg/m <sup>2</sup> )	22.17±3.00	22.27±3.20	22.01±2.6	22.51±3.11	0.282	0.507	0.257	0.598
<b>Breast ptosis grade</b>								
Normal to mild	153 (94.4)	103 (98.1)	50 (87.7)	168 (70.3)	< 0.001 <sup>e)</sup>	< 0.001 <sup>e)</sup>	0.011 <sup>e)</sup>	0.01 <sup>e)</sup>
Moderate to severe	9 (5.6)	2 (1.9)	7 (12.3)	70 (29.3)				
Pseudoptosis		0	0	1 (0.4)				
<b>Germline mutation status</b>								
Negative	58 (35.8)	35 (33.3)	23 (40.4)	69 (28.9)	0.172	0.618	0.091	0.404 <sup>e)</sup>
Positive	7 (4.3)	6 (5.7)	1 (1.8)	19 (7.9)				
Test not done	97 (59.9)	64 (61.0)	33 (57.9)	151 (63.2)				
<b>Preoperative diagnosis</b>								
Benign <sup>d)</sup>	1 (0.6)	1 (1.0)	0	1 (0.4)	0.299 <sup>e)</sup>	0.499 <sup>e)</sup>	0.044 <sup>e)</sup>	0.05 <sup>e)</sup>
DCIS	55 (34.0)	30 (28.6)	25 (44.6)	63 (26.4)				
Invasive cancer	105 (64.8)	74 (70.5)	31 (55.4)	171 (71.5)				
Other <sup>e)</sup>	1 (0.6)	0	1 (1.8)	4 (1.7)				
<b>Bilateral NSM</b>	24 (100)	20 (100)	4 (100)	25 (100)	0.393	0.239	> 0.999 <sup>e)</sup>	0.590 <sup>e)</sup>
Bilateral cancer	12 (50.0)	11 (55.0)	1 (25.0)	9 (36.0)				
Unilateral cancer with contralateral RRM	12 (50.0)	9 (45.0)	3 (75.0)	16 (64.0)				
<b>Neoadjuvant therapy</b>								
Done	18 (11.1)	10 (9.5)	8 (14.0)	33 (13.8)	0.450	0.294	> 0.999	0.436
Not done	144 (88.9)	95 (90.5)	49 (86.0)	206 (86.2)				

Values are presented as mean±SD or number (%). BMI, body mass index; CNSM, conventional nipple-sparing mastectomy; DCIS, ductal carcinoma *in situ*; NSM, nipple-sparing mastectomy; RNSM, robot-assisted nipple-sparing mastectomy; RRM, risk-reducing mastectomy; SD, standard deviation. <sup>a)</sup>p-value in comparison of RNSM and CNSM, <sup>b)</sup>P1 for Si/Xi vs. CNSM, <sup>c)</sup>p-value for SP vs. CNSM, <sup>d)</sup>p-value for Si/Xi vs. SP, <sup>e)</sup>Fisher's exact test was performed, <sup>f)</sup>Preoperative benign (e.g., atypical ductal hyperplasia) but malignant at the final postoperative pathology, <sup>g)</sup>Papillary cancer, invasive uncertain.

**Table 2.** Intraoperative details and postoperative complications

Variable	RNSM (n=162)		CNSM (n=239)	p-values				
	Total	Si/Xi (n=105)		SP (n=57)	p-value <sup>a)</sup>	p-value <sup>b)</sup>	p-value <sup>c)</sup>	p-value <sup>d)</sup>
<b>Total operation time</b>	370.63±157.11	360.94±145.95	388.47±175.80	319.34±203.48	0.005	0.033	0.019	0.316
GS operation time <sup>e)</sup>	155.06±64.80	151.23±45.65	162.11±90.13	104.67±39.46	<0.001	<0.001	<0.001	0.310
PS operation time <sup>f)</sup>	182.29±148.10	169.91±133.82	205.09±170.25	213.41±190.16	0.067	0.016	0.762	0.180
<b>Reconstruction type<sup>g)</sup></b>								
Implant-based	136 (83.9)	94 (89.5)	42 (73.6)	165 (69.1)	0.001	<0.001	<0.001	0.013
Flap harvest	26 (16.1)	11 (10.5)	15 (26.4)	74 (30.9)				
Deep inferior epigastric perforator flap	23 (14.2)	9 (8.6)	14 (24.6)	72 (30.1)				
Latissimus dorsi flap	3 (1.9)	2 (1.9)	1 (1.8)	2 (0.8)				
<b>Grade III complications within 30 days after surgery</b>	8 (4.9)	7 (6.7)	1 (1.8)	70 (29.3)	<0.001	<0.001	<0.001	0.268
Partial nipple necrosis	1 (0.6)	1 (0.95)		4 (5.7)				
Total nipple necrosis	0	0		29 (41.4)				
Skin ischemia	0	0		5 (7.1)				
Skin necrosis	4 (2.4)	4 (3.8)		32 (45.7)				
Thermal injury	1 (0.6)	1 (0.95)		0				
Bleeding/Hematoma	2 (1.2)	1 (0.95)	1 (1.8)	0				
<b>Transfusion (any grade within POD 30 days)<sup>h)</sup></b>	10 (6.2)	3 (2.9)	7 (12.3)	16 (6.7)	>0.99	0.202	0.170	0.034
<b>Cause of transfusion</b>								
Intraoperative blood loss	3 (1.9)	1 (0.95)	2 (3.5)	4 (1.7)				
Acute blood loss (within 24-hour post-surgery)	1 (0.6)	0	1 (1.8)	2 (0.8)				
Delayed hemoglobin down (after 24-hour post-surgery)	6 (3.7)	2 (1.9)	4 (7.0)	10 (4.2)				
		DIEP (1), Implant (1)	DIEP (2), Implant (2)	DIEP (7), T / E (3)				

Values are presented as mean±SD or number (%). CNSM, conventional nipple-sparing mastectomy; DIEP, deep inferior epigastric perforator flap harvest; POD, postoperative day; RNSM, robot-assisted nipple-sparing mastectomy; T/E, tissue expander. <sup>a)</sup>p-value in comparison of RNSM and CNSM, <sup>b)</sup>p-value for Si/Xi vs. CNSM, <sup>c)</sup>p-value for SP vs. CNSM, <sup>d)</sup>p-value for Si/Xi vs. SP, <sup>e)</sup>GS operation time: general surgery (nipple-sparing mastectomy), <sup>f)</sup>PS operation time: plastic surgery (reconstruction), <sup>g)</sup>In the RNSM group, transfusion was performed in seven cases using the SP system and three cases using multiport systems (Si/Xi). Five out of seven cases with the SP system (71.4%) and two out of three (66.7%) cases with multiport systems were reconstructed using DIEP flaps.

**Table 3.** Postoperative pathological details

Variable	RNSM (n=162)			CNSM (n=239)	p-values			
	Total	Si/Xi (n=105)	SP (n=57)		p-value <sup>a)</sup>	p-value <sup>b)</sup>	p-value <sup>c)</sup>	p-value <sup>d)</sup>
<b>T category</b>								
T0/Tis	44 (27.1)	25 (23.8)	19 (33.3)	60 (25.1)	0.423	0.463	0.383	0.395
T1	98 (60.5)	67 (63.8)	31 (54.4)	138 (57.7)				
T2	20 (12.3)	13 (12.4)	7 (12.3)	41 (17.2)				
<b>N category</b>								
N0	136 (84.0)	92 (87.6)	44 (77.2)	195 (81.6)	0.913 <sup>e)</sup>	0.537 <sup>e)</sup>	0.426 <sup>e)</sup>	0.109 <sup>e)</sup>
N1	21 (13.0)	10 (9.5)	11 (19.3)	36 (15.1)				
N2	4 (2.5)	3 (2.9)	1 (1.8)	7 (2.9)				
N3	1 (0.6)	0	1 (1.8)	1 (0.4)				
<b>No. of positive nodes</b>	2.26±2.03	2.15±1.57	2.38±2.46	2.54±2.52	0.637	0.600	0.840	0.779
<b>TNM stage</b>								
0	43 (26.5)	24 (22.9)	19 (33.3)	59 (24.7)	0.727 <sup>e)</sup>	0.455 <sup>e)</sup>	0.472 <sup>e)</sup>	0.255 <sup>e)</sup>
IA	80 (49.4)	58 (55.2)	22 (38.6)	115 (48.1)				
IB	1 (0.6)	1 (1.0)	0	0				
IIA	27 (16.7)	16 (15.2)	11 (19.3)	40 (16.7)				
IIB	6 (3.7)	3 (2.9)	3 (5.3)	17 (7.1)				
IIIA	4 (2.5)	3 (2.9)	1 (1.8)	7 (2.9)				
IIIC	1 (0.6)	0	1 (1.8)	1 (0.4)				
<b>Estrogen receptor</b>								
Negative	30 (18.5)	14 (13.3)	16 (28.1)	59 (24.5)	0.178	0.021	0.613	0.033
Positive	132 (81.5)	91 (86.7)	41 (71.9)	180 (75.3)				
<b>Progesterone receptor</b>								
Negative	45 (27.8)	25 (23.8)	20 (35.1)	82 (34.3)	0.190	0.058	> 0.999	0.144
Positive	117 (72.2)	80 (76.2)	37 (64.9)	157 (65.7)				
<b>Human epidermal growth factor receptor 2</b>								
Negative	112 (73.7)	73 (73.0)	39 (75.0)	174 (76.7)	0.543	0.488	0.857	0.848
Overexpression	40 (26.3)	27 (27.0)	13 (25.0)	53 (23.3)				
<b>Ki-67</b>								
Low (< 14%)	78 (48.1)	44 (41.9)	34 (59.6)	109 (45.6)	0.918	0.409	0.105	0.034
High (≥ 14%)	84 (51.9)	61 (58.1)	23 (40.4)	122 (51.0)				
<b>Histologic grade</b>								
I-II	126 (77.8)	84 (80.0)	42 (73.7)	173 (80.1)	0.611	> 0.999	0.362	0.429
III	36 (22.2)	21 (20.0)	15 (26.3)	43 (19.9)				
<b>Positive surgical margin (superficial)</b>	1 (0.6)	1 (1.0)	0	1 (0.4)	> 0.999 <sup>e)</sup>	0.518 <sup>e)</sup>	> 0.999 <sup>e)</sup>	> 0.999 <sup>e)</sup>
<b>NAC involvement</b>	0	0	0	1 (0.4)	> 0.999 <sup>e)</sup>	> 0.999 <sup>e)</sup>	> 0.999 <sup>e)</sup>	N/A

Values are presented as number (%) or mean±SD. CNSM, conventional nipple-sparing mastectomy; NAC, nipple-areolar complex; N/A, not available; RNSM, robot-assisted nipple-sparing mastectomy; SD, standard deviation. <sup>a)</sup>p-value comparison of RNSM and CNSM, <sup>b)</sup>p-value for Si/Xi vs. CNSM, <sup>c)</sup>p-value for SP vs. CNSM, <sup>d)</sup>p-value for Si/Xi vs. SP, <sup>e)</sup>Fisher's exact test was performed.

the analysis included 401 patients, whose oncological outcomes were monitored up to March 2022. The survival data was obtained from the medical record of Severance Hospital.

**2. Data collection and endpoints**

All clinical data and surgical complications were retrospectively collected from medical records. All eligible partici-

pants were included in the analysis regardless of completeness of data. Primary endpoints were long-term outcomes, such as local recurrence, distant metastasis, disease-free survival, overall survival, and postoperative complications, while secondary endpoints were subject demographics, clinical characteristics, inter/postoperative information, pathology results, and oncological outcomes.

**Table 4.** Adjuvant therapy and recurrence

Variable	RNSM (n=162)			CNSM (n=239)	p-values			
	Total	Si/Xi (n=105)	SP (n=57)		p-value <sup>a)</sup>	p-value <sup>b)</sup>	p-value <sup>c)</sup>	p-value <sup>d)</sup>
<b>Adjuvant therapy</b>								
Chemotherapy	39 (24.1)	27 (25.7)	12 (21.1)	74 (31.0)	0.143	0.369	0.148	0.568
Targeted therapy	22 (13.6)	17 (16.2)	5 (8.8)	23 (9.6)	0.259	0.100	> 0.999	0.234
Radiotherapy	36 (22.2)	21 (20.0)	15 (26.3)	45 (18.8)	0.448	0.882	0.270	0.429
Endocrine therapy	127 (78.4)	87 (82.9)	40 (70.2)	177 (74.1)	0.343	0.096	0.617	0.073
<b>Disease status</b>								
Recurrence <sup>e)</sup>	6 (3.8)	3 (2.9)	3 (5.3)	14 (5.9)	0.624 <sup>f)</sup>	0.783 <sup>f)</sup>	0.209 <sup>f)</sup>	0.196 <sup>f)</sup>
Local recurrence	3 (1.9)	1 (1.0)	2 (3.5)	5 (2.1)				
Regional recurrence	1 (0.6)	0	1 (1.8)	1 (0.4)				
Distant recurrence	2 (1.2)	2 (1.9)	0	8 (3.3)				
No recurrence	156 (96.3)	102 (97.1)	54 (94.7)	225 (94.1)				

Values are presented as number (%). CNSM, conventional nipple-sparing mastectomy; RNSM, robot-assisted nipple-sparing mastectomy. <sup>a)</sup>p-value in comparison of RNSM and CNSM, <sup>b)</sup>p-value for Si/Xi versus CNSM, <sup>c)</sup>p-value for SP versus CNSM, <sup>d)</sup>p-value for Si / Xi versus SP, <sup>e)</sup>Recurrence: locoregional and distant, <sup>f)</sup>Fisher's exact test was performed.

### 3. Statistical analysis

Analyses were based on preoperative, intraoperative, and postoperative characteristics. Continuous variables (e.g., age and operation time) are described as medians and interquartile ranges. Discrete variables (e.g., sex and conversion rate) are described as a proportion of the total.

## Results

### 1. Preoperative information

Patients underwent RNSM (n=162) or CNSM (n=239). Of RNSM cases, nine (5.6%) were performed using the da Vinci Si Surgical System, 96 (59.3%) using the da Vinci Xi Surgical System, and 57 (35.2%) using the da Vinci SP Surgical System (S1 Table). The mean age of the patients was 44.7 and 46.7 years in the RNSM and CNSM groups respectively (p=0.017). Bilateral NSM was performed on 25 and 24 patients in the CNSM and RNSM groups respectively. Among them, contralateral risk-reducing mastectomy was performed in 16 CNSM patients (64%) and 12 RNSM patients (50%), with no significant difference between groups (p=0.322). The mean body mass index (BMI) of the RNSM and CNSM arms were 22.17±3.00 and 22.51±3.11, respectively. Most women had normal-to-mild breast ptosis. More women reported moderate-to-severe ptosis in the CNSM group compared with the RNSM group (29.3% vs. 5.6%). Germline mutations were found in 4.3%, 7.9% of the RNSM and CNSM groups respectively. One-quarter to one-third of patients in each group had ductal carcinoma *in situ*, and most patients had invasive cancer at diagnosis. Preoperative factors, including BMI, germline mutations, preoperative diagnosis, bilaterali-

ty, and neoadjuvant chemotherapy, did not vary significantly between the groups (Table 1).

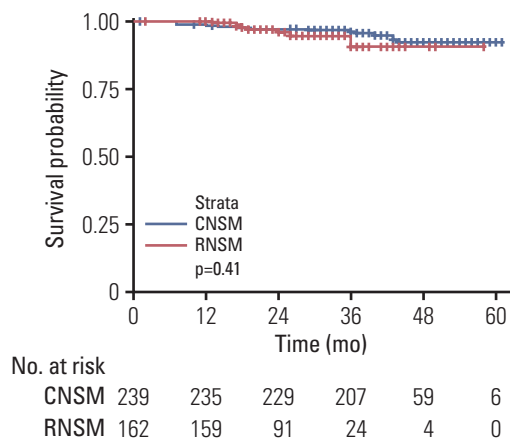
### 2. Intraoperative information

Table 2 describes operative outcomes such as operation time and reconstruction type. The total operation time and operation time for mastectomy varied significantly between the two groups, being approximately 50 minutes longer in RNSM than in CNSM. Meanwhile, reconstruction time did not vary significantly between groups, and there was no significant difference in the total and NSM operative time between the multiport and SP systems. Implant-based reconstruction was performed more frequently in both groups, although deep inferior epigastric perforator flap harvest (DIEP) was performed more frequently in CNSM. Additionally, the rate of grade III postoperative complications within 30 days after surgery (G3-Cx-PO30D) was assessed, and was found to be higher in the CNSM group compared with the RNSM group (29.3% vs. 4.9%) (Table 2). Of these, partial skin necrosis was the most common complication in the RNSM group; to treat it, revision was performed in three cases and implant was removed in one case. In cases of thermal injury, vancomycin was administered, and debridement was performed. For hematoma, evacuation and drain insertion were initially performed. Later, vancomycin was injected, and the implant was removed due to combined infection. Transfusions of packed red blood cell were conducted in 16 (6.7%) cases in the CNSM group and 10 (6.2%) in the RNSM group (p=0.835). Nineteen patients (19/26, 73.1%) requiring transfusion underwent reconstruction using the DIEP method (p < 0.001). Only 26.9% of transfusions were related to NSM with tissue expander (T/E) implant reconstruction. Transfu-

**Table 5.** Details of recurrence cases

Case No.	Group	Initial recurrence type	Recurrence site	Recurrence interval (mo)	Diagnostic tool
1	CNSM	Distant	Supraclavicular lymph nodes, both axillary lymph nodes, mediastinal lymph nodes, bone, liver, chest wall, lung	37	Chest CT, abdomen pelvic CT, neck ultrasonography, fine needle aspiration
2	CNSM	Distant	Brain, spinal cord with leptomeningeal seeding	14	Brain MRI
3	CNSM	Local	IBTR	13	Excisional biopsy
4	CNSM	Distant	Visceral metastasis (2019.04) brain metastasis	7	PET-CT
5	CNSM	Local	IBTR	44	Breast ultrasonography, core needle biopsy
6	CNSM	Distant	Lung	44	Chest CT
7	CNSM	Distant	Brain, lymph nodes, lung, pleura, liver	14	Brain MRI, PET-CT
8	CNSM	Distant	Liver	20	Abdomen pelvic CT
9	CNSM	Local	IBTR	31	Breast ultrasonography
10	CNSM	Distant	Lung	45	Chest CT, biopsy
11	CNSM	Local	Chest wall, lung	18	Excisional biopsy
12	CNSM	Distant	Axillary lymph nodes, subcarinal lymph node, liver	41	Chest CT, abdomen pelvic CT
13	CNSM	Local	Nipple areolar complex	38	Physical exam, biopsy
14	CNSM	Regional	Axillary lymph nodes, mediastinal lymph nodes, lung, brain	12	PET-CT
15	RNSM (Xi)	Local	IBTR	26	Breast MRI, breast ultrasonography
16	RNSM (Xi)	Distant	Lung, brain, liver	20	Chest CT
17	RNSM (SP)	Local	Nipple areolar complex	25	Physical exam, biopsy
18	RNSM (SP)	Distant	Distant multiple lymph nodes, supraclavicular lymph nodes, mediastinal, retroperitoneal, neck node, lung	19	Chest CT
19	RNSM (SP)	Regional	Axillary lymph nodes	22	Breast ultrasonography, fine needle aspiration
20	RNSM (Xi)	Local	Chest wall, axillary lymph nodes	13	Breast MRI, breast ultrasonography, excisional biopsy

CNSM, conventional nipple-sparing mastectomy; CT, computed tomography; IBTR, in breast tumor recurrence (residual breast tissue, pectoralis m, chest wall, overlying skin, and chest wall); MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; RNSM, robot-assisted nipple-sparing mastectomy.



**Fig. 1.** Kaplan-Meier curves of recurrence-free survival in robot-assisted (RNSM) and conventional nipple-sparing mastectomy (CNSM) case.

sion was done for three reasons: intraoperative blood loss, acute blood loss, (i.e., bleeding within 24 hours post-surgery) and delayed blood loss (i.e., bleeding after 24 hours post-surgery). Seven (1.7%), three (1.0%), and 16 (4.0%) patients experienced intraoperative, acute and delayed blood loss, respectively. Regarding reconstruction type, all seven cases of intraoperative bleeding were related to the DIEP flap. One case of acute bleeding (1/3, 33.3%) was related to T/E, while the others (2/3, 66.7%) were related to DIEP flap. Regarding preoperative condition, 10 (10/26, 38.5%) cases requiring transfusion underwent neoadjuvant chemotherapy before surgery.

### 3. Postoperative outcomes and follow-up

In the postoperative pathological review (Table 3), T1 disease was found to be the most common T category in both groups. Approximately 80% of patients in both groups had node-negative disease. The mean number of metastatic lymph nodes did not differ significantly between the groups ( $2.26 \pm 2.03$  RNSM vs.  $2.54 \pm 2.52$  CNSM). Most patients in both groups had hormone receptor-positive disease. Human epidermal growth factor receptor 2 (HER2) overexpression was observed in approximately one-quarter of patients in both groups (26.3% for RNSM vs. 23.3% for CNSM). High Ki-67 levels were observed in approximately half the tumors (51.9% for RNSM vs. 51.0% for CNSM). The majority of tumors were grade I-II tumors (77.8% for RNSM and 80.1% for CNSM). Hormone receptor levels, HER2 status, Ki-67 levels, and histological grade did not vary significantly between the two groups. Superficial margin involvement was observed in one case in each group, and only one case with nipple-areolar complex involvement was observed in the CNSM group.

Adjuvant chemotherapy was performed in 24.1% of

RNSM patients and 31.0% of CNSM patients. HER2 targeted therapy was administered to 13.6% of RNSM patients and 9.6% of CNSM patients. Approximately 20% of patients received adjuvant radiation therapy, while approximately 75% received adjuvant endocrine therapy. The status of adjuvant therapy was not significantly different between the two groups (all  $p > 0.05$ ). Recurrence was observed in six RNSM patients and 14 CNSM patients, being approximately 5% (20/401 patients) of the whole cohort (Table 4). Among recurrent RNSM patients, three used the Xi system and the other three used the SP system. Details of recurrence are described in Table 5.

Kaplan-Meier curves (Fig. 1) illustrate RFS in the two groups. Local recurrence, including ipsilateral breast tumor recurrence, regional recurrence in the ipsilateral axilla, and distant recurrence, was evaluated. Local recurrence rate of RNSM patients was 1.9% (3 cases), and that of CNSM patients was 2.1% (5 cases). With a median follow-up of 37 months (24.5 months for RNSM patients vs. 42 months for CNSM patients), no significant differences were observed in RFS between the two groups ( $p=0.41$ ). The 3-year RFS rate in the RNSM group were 95.7%, and that in the CNSM group was 94.1%. In the CNSM group, five patients died due to systemic recurrence, while no patient died in the RNSM group. Overall survival was not analyzed due to the low rate of events in each group.

## Discussion

This study demonstrated no significant difference in RFS between the CNSM and RNSM groups, with a median follow-up period of 37 months. The medical community has not yet reached a definitive consensus on the oncologic outcomes of RNSM compared with CNSM [20]. However, our study showed a recurrence rate of 3.8% in RNSM patients after a median follow-up of 24.5 months, compared with 5.9% in CNSM patients after 42 months. No difference in recurrence was observed within the RNSM group with respect to robotic surgical system (multiport vs. SP,  $p=0.136$ ). A previous international pooled analysis supported this finding [16]. Therefore, our data suggest that RNSM is a feasible option for selected patients with early-stage breast cancer.

In addition, the rate of grade III postoperative complications was lower in patients with RNSM than in those with CNSM, and results of the SORI study supported this finding [16]. The low complication rate in the RNSM group in the study by Lee et al. [18] was mainly due to low nipple necrosis rate. As the incision site in the axillary area is located far from the nipple-areolar complex, this procedure does not disturb blood supply to the nipple. Furthermore, RNSM requires less

mechanical traction than CNSM, which explains the lower rate of skin necrosis. Lower complication rates have been reported in previous studies as well; this may be an advantage of RNSM [15,18].

Transfusion was applied in approximately 6% of patients. Most cases underwent reconstruction using the DIEP flap method. In general, an autologous DIEP flap requires more transfusion than an implant-based reconstruction, because it requires vessel harvesting and anastomosis.

Our study had some limitations. First, this was a single-center retrospective study; hence, its results cannot be generalized. Despite an overall mean follow-up of 37 months, which is longer than follow-ups in previous studies, mean follow-up in RNSM patients was 24 months, which is a relatively short period. Nevertheless, in selected patients with early-stage breast cancer, RNSM showed lower postoperative complication rates and more favorable oncologic outcomes compared with CNSM in a single institution. Furthermore, we evaluated SP cases separately for comparison with multiport robotic-assisted surgery cases by experienced surgeons at a high-volume center, finding comparable results in terms of operation time. Among robotic surgical devices, SP has advantages over multiport, being suitable for narrow spaces as well as ergonomic. Compared to the multiport system, the SP system may offer enhanced visualization with the “cobra” camera position proving especially helpful for visualizing the medial aspect of the breast. Additionally, the SP platform supports various camera modes and clutch functions, enabling greater instrument maneuverability, improved surgical efficiency, and a more compact patient cart [21]. These features may lead to decreased technical difficulty and reduced surgeon fatigue and instrument collisions, suggesting that the benefits of the SP system could become even more pronounced with increasing surgical experience. Only the initial RNSM cases in this study used the SP system, showing no difference in operative times compared with the multiport system. Additionally, lower rates of grade III postoperative complication were observed in SP cases than in multiport system.

Several prospective studies are currently underway to overcome those limitations. The MARRES (NCT 04585074) study is a prospective cohort study evaluating postoperative complication rates in patients undergoing RNSM and CNSM as primary endpoints, and long-term oncologic outcomes as secondary endpoints [22]. The ROM trial (NCT 05490433) is a multicenter randomized clinical trial elucidating long-term oncologic outcomes between RNSM and CNSM, with five-year disease-free survival as a primary endpoint. These studies aim to provide high-level evidence for the use of robot-assisted surgical systems in NSM.

In conclusion, robot-assisted surgical systems represent

a feasible option for NSM, in selected patients with early-stage breast cancer. However, given the study’s retrospective design, short-term follow-up, and lack of randomization by tumor characteristics, these findings should be interpreted with caution, particularly with respect to oncologic outcomes.

#### Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (<https://www.e-crt.org>).




#### Ethical Statement

The survival data was obtained from the medical record of Severance Hospital. This study was approved by the Institutional Review Board of our institution (approval No. 4-2021-1609) and the requirement for informed consent was waived owing to the retrospective study design.

#### Author Contributions

Conceived and designed the analysis: Park HS.  
Collected the data: Lee SJ, Kwon Y, Kim NH, Park HS.  
Contributed data or analysis tools: Kwon Y, Kim NH.  
Performed the analysis: Kwon Y, Kim NH.  
Wrote the paper: Lee J, Go J, Lee SJ, Kim JY, Park HS.  
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#### Conflicts of Interest

Hyung Seok Park received honoraria from AstraZeneca, Takeda, Medtronic, and Intuitive Surgical. No other relationships or activities that could appear to have influenced the submitted work are reported. All remaining authors have declared no conflicts of interest.

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