석 사 학 위 논 문

Survival of Mastectomy Skin Flap According to Incision Methods and Other Risk Factors

계 명 대 학 교 대 학 원

의 학 과

김 태 기

지도교수 손 대 구

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지도교수 손 대 구

이 논문을 석사학위 논문으로 제출함

2022년 2월

계명대학교 대학원
의학과

김 태 기

김태기의 석사학위 논문을 인준함

주 심 최 재 훈

부 심 손 대 구

부 심 조 태 희

계 명 대 학 교 대 학 원

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1. Introduction

The mastectomy technique in breast cancer patients has gradually developed from traditional radical mastectomy to skin-sparing mastectomy (SSM) and the most recent, nipple-sparing mastectomy (NSM). SSM was first described by Toth and Lappert in 1991 (1), the possibility of preserving the breast skin envelope was the greatest advantage compared to radical mastectomy. In addition to the improvement in aesthetic outcomes, the oncologic safety of SSM has been established by a number of studies conducted to date, in that there is no difference in local recurrence or survival rate compared to conventional mastectomy (2,3). Subsequently, the NSM technique was popularized by Lynn Hartmann (4) and is widely performed, even as prophylactic mastectomy. Its advantages are that it can preserve the nipple-areolar complex and results in fewer scars, leading to an increase in patient satisfaction with respect to the aesthetic outcomes and quality of life.

For both methods, although the oncologic safety has been proven (5,6), complications such as mastectomy skin flap necrosis, nipple necrosis, infection, and hematoma are often observed after immediate breast reconstruction following mastectomy. Among these, mastectomy flap skin necrosis (MFSN) is a major complication with a reported incidence of up to 15.8% following various methods of breast reconstruction (7). When MFSN occurs, it not only leads to scar formation and deformation of the breast, but also cancer treatment such as additional chemotherapy or radiation therapy is delayed, resulting in a longer treatment and follow-up period. Consequently, it is important to

reduce the incidence of necrosis not only in terms of the aesthetic results, but also in terms of the overall cost and treatment efficiency.

Patient factors such as age, body mass index (BMI), smoking history, breast size, and radiation history are known to affect the incidence of MFSN (8-11). Since there is no formal or standardized surgical approach yet, the operation is performed using various methods depending on the general surgeon's preference. The aim of this single institution study was to analyze the effect of the type of incision used for mastectomy on the occurrence of MFSN, and to provide additional evidence for the selection of an optimal incision method for mastectomy followed by immediate breast reconstruction.

2. Patients and Methods

A total of 179 breast cancer patients treated with unilateral total mastectomy and immediate breast reconstruction between January 2010 and December 2018 at the Keimyung University Dongsan Medical Center were reviewed. A retrospective review of the medical records and the classification of the incision types were performed by a single surgeon. The exclusion criteria were a lack of demographic data or medical records including clinical photographs, which made it difficult to judge the type of incision clearly, and a previous medical history of all types of breast surgery before undergoing unilateral total mastectomy. Data including demographics, type of breast cancer, type of reconstruction, weight, height, body mass index, history of tobacco use, neoadjuvant chemotherapy, postoperative radiation, and operative characteristics were collected through electronic medical records. Clinical photographs were used to classify the type of incision. This study was approved by the Institutional Review Board of the Keimyung University Dongsan Hospital.

2.1. Incision type classification and detection of MFSN

To evaluate the type of mastectomy incision, operative notes and immediate postoperative clinical photographs were meticulously reviewed. First, to compare the differences in the incidence of MFSN between SSM and NSM, the cases were divided into two groups according to the type of mastectomy. The incisions were classified as follows:

inframammary fold, superolateral radial, radial incisions other than superolateral, horizontal linear, and peri-areolar incisions in NSM; and elliptical, elliptical superolateral, round, and circumareolar incisions in SSM (Figure 1). Incisions that did not belong to these types were excluded.

The occurrence of skin necrosis in the mastectomy flap was confirmed after reviewing the medical records from the postoperative care period. It was considered that skin necrosis had occurred if one or more of the following was recorded: 'necrosis', 'revision', and 'debridement'. To distinguish MFSN from necrosis in flaps used for breast reconstruction, cases without the word 'mastectomy flap' in the records were excluded. Major mastectomy flap necrosis and minor lesions were distinguished based on the history of surgical debridement. Even if the size of the necrotic skin lesion was large, mastectomy flap necrosis that was managed noninvasively was classified into the minor necrosis group. Likewise, even if the size of the necrotic skin flap was quite small, if surgical debridement was performed, it was considered to belong to the major necrosis group.

2.2. Intraoperative risk factors

To analyze the intraoperative risk factors other than the type of incision, the intraoperative notes of the general surgeon who performed the unilateral mastectomy were reviewed. This was done to evaluate the impact of tissue damage or the thickness of the flap, which may vary depending on the surgeon's technique.

A history of indigo carmine blue dye injection for detecting the sentinel lymph nodes was also considered a possible risk factor for necrosis, and data were collected through operation notes in the

electronic medical records.

2.3. Statistical analysis

All statistical analyses were performed using the SAS version 9.2 (SAS, Cary, NC). To analyze the differences in the incidence of skin necrosis and risk factors between the NSM and SSM groups, Student's t-test and chi-square test were used. We also analyzed the associations of demographic data and intraoperative characteristics, including the incision type, with the occurrence of MFSN. A multivariate logistic regression model was used to analyze the risk factors while controlling for other risk factors that may affect the results. Statistical significance was set at $P < 0.05$.

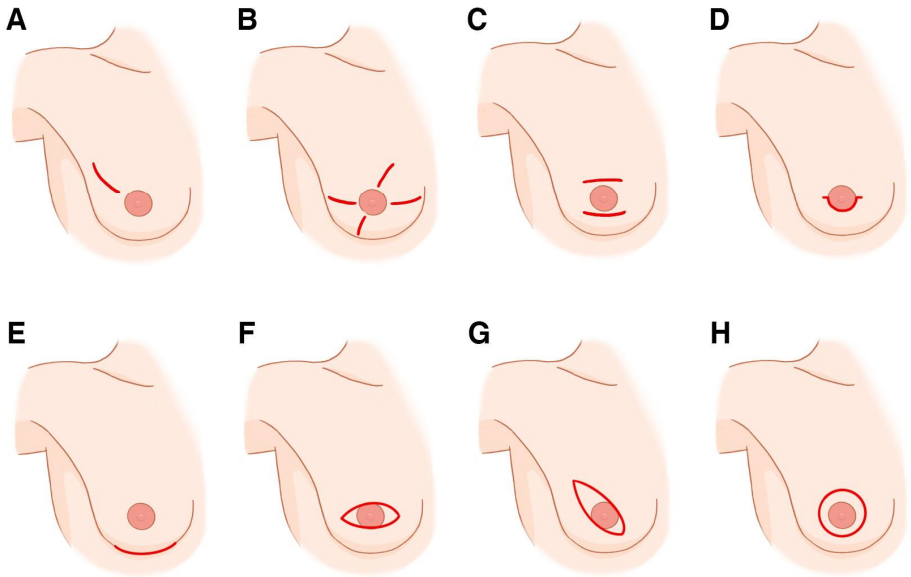

Figure 1. Classification of the type of incisions for mastectomy. A: superolateral radial; B: other radial incisions; C: horizontal linear; D: peri-areolar; E: inframammary fold; F: elliptical; G: elliptical superolateral; H: round and circumareolar. A to E incisions are for nipple sparing mastectomy and F to H incisions are for skin sparing mastectomy.

3. Results

3.1. Patients demographics and non-operative characteristics

A total 144 cases of immediate breast reconstruction after unilateral mastectomy were analyzed. Thirty five cases were excluded because the incision method could not be clearly distinguished due to poor medical records. The mean age was 47 ± 8.43 years (range, 25 to 84 years), and mean follow up period was 14.78 ± 14.27 days (range, 7 to 118). The mean height and weight were 157.89 ± 5.96 cm (range, 130.8 - 173 cm) and 58.55 ± 9.64 kg (range, 38.9 - 108.8 kg) and the mean BMI was 23.5 ± 3.55 (range, 17.8 - 39.1). There were 45 cases in SSM group and 99 patients in NSM group. Only three patients (2% of total cases) had a history of tobacco use. Seven patients (4.86%) had chemotherapy history before surgery and eighteen patients (12.5%) underwent radiation therapy after breast reconstruction. Fourteen of the patients had hypertension and four others had hyperlipidemia, four thyroid-related disease, three diabetes, two ovarian cancers and one three-vessel disease (Table 1).

3.2. Operative characteristics

Five types of breast reconstruction had performed. In 76 cases, pedicled latissimus dorsi musculocutaneous flap was performed followed by 40 cases of immediate breast augmentation with implant, 17 cases of pedicled transverse rectus abdominis musculocutaneous flap, 8 cases of partial pedicled latissimus dorsi flap and 3 of pedicled latissimus dorsi flap with implant augmentation. In the NSM surgery, the 'superolateral radial' incision method was most common with 44 cases. Next, the 'radial(others)' method was second most with 17 cases followed by 14 cases of the 'periareolar', 12 cases of the 'inframammary' and 9 cases of 'horizontal linear' method. Three different general surgeons performed mastectomy surgery, in each 104, 35 and 5 cases (Table 2).

3.3. Characteristics comparison between NSM group and SSM group

To compare the rate of mastectomy skin flap necrosis, student's t and chi-quare test between NSM and SSM group were performed and results are detailed in Table 3. In NSM group, MFSN occurred in 30 cases (30.3%), of which 9 cases were minor necrosis and 21 cases were major. In SSM group, MFSN occurred in 8 cases (17.8%), of which 1 case was minor and 7 cases were major necrosis. As a result, it turned out that the mastectomy type had no significant positive correlation with MFSN (P=0.195). Factors that were thought to have an effect on the difference in MFSN incidence, age, BMI, underlying diseases, smoking history of patients, general surgeon and dye injection showed no

significant difference between two groups.

3.4. Univariate analysis of risk factors associated with skin flap necrosis

In NSM group, the MFSN rate according to the incision method was largest in 'periareolar' with 42.9%, followed by IMF (41.7%), horizontal linear (33.3%), superolateral radial (27.3%) and radial(others) (17.7%). In SSM group, elliptical superolateral group was largest with 35.7%. But there was no significant correlation between incision method and the rate of MFSN (P=0.300). Other risk factors including age, smoking history, BMI, underlying disease, general surgeon and dye injection also turned out to have no significant correlation with the rate of MFSN (Table 4).

3.5. Multivariate logistic regression analysis

In multivariate logistic regression analysis, controlling variables those seem to have a slightly different distribution according to the type of mastectomy, NSM group showed higher rate of MFSN than SSM group (OR=2.67), but there was no significant correlation (P=0.055). Likewise, type of incision, underlying disease, BMI and dye injection also turned out that they have no significant correlation with MFSN (Table 5).

Table 1. Patient Demographics and Non-operative Characteristics

Characteristics	Value
No.	144
Mean age ± SD, year	47 ± 8.43
Mean follow-up ± SD, day	14.78 ± 14.27
Mean BMI ± SD	23.5 ± 3.55
Smoking history	3 (2%)
Neoadjuvant chemotherapy	7 (4.86%)
Postoperative radiation	18 (12.5%)
Underlying disease	
Hypertension	14
Hyperlipidemia	4
Hyper/hypothyroidism	4
Diabetes	3
Ovarian cancer	2
3-vessel disease	1

BMI: body mass index.

Table 2. Operative Characteristics

Characteristics	Number
Reconstruction type	
Latissimus dorsi flap	76
Immediate implant insertion	40
TRAM flap	17
Partial latissimus dorsi flap	8
Latissimus dorsi flap with implant	3
Incision type	
NSM	
Superolateral radial	44
Radial (others)	17
Periareolar	14
Inframammary	12
Horizontal linear	9
SSM	
Elliptical	18
Elliptical superolateral	14
Circumareolar	6
Round	6
General surgeon	
surgeon A	104
surgeon B	35
surgeon C	5

TRAM: transverse rectus abdominis musculocutaneous flap; NSM: nipple sparing mastecomy; SSM: skin sparing mastectomy.

Table 3. Characteristics Comparison between Nipple Sparing Mastectomy and Skin Sparing Mastectomy Group

		Mastectomy type		
		NSM (N, %)	SSM (N, %)	*P*
MFSN	No	69 (69.7)	37 (82.2)	0.114
	Yes	30 (30.3)	8 (17.8)	
Degree of necrosis	Major	21 (21.2)	7 (15.6)	0.195
	Minor	9 (9.1)	1 (2.2)	
Age		46.9 ± 8.5	47.3 ± 8.4	0.7714
BMI		23.2 ± 3.3	24.2 ± 4.0	0.1000
Smoking	No	98 (99.0)	43 (95.6)	0.181
	Yes	1 (1.0)	2 (4.4)	
Underlying disease	No	72 (72.7)	39 (86.7)	0.065
	Yes	27 (27.3)	6 (13.3)	
Breast surgeon	A	70 (70.7)	34 (75.6)	0.774
	B	4 (4.0)	1 (2.2)	
	C	25 (25.3)	10 (22.2)	
Dye injection	No	22 (22.2)	16 (35.6)	0.092
	Yes	77 (77.8)	29 (64.4)	

MFSN: mastecotmy flap skin necrosis; NSM: nipple sparing mastectomy; SSM: skin sparing mastectomy; BMI: body mass index.

Table 4. Univariate Analysis of Risk Factors Associated with Skin Flap Necrosis

		MFSN		
		N (N, %)	Y (N, %)	*P*
Mastectomy type	NSM	69 (69.7)	30 (30.3)	0.114
	SSM	37 (82.2)	8 (17.8)	
Incision type				0.300
	NSM			
	Periareolar	8 (57.1)	6 (42.9)	
	IMF	7 (58.3)	5 (41.7)	
	Horizontal linear	6 (66.7)	3 (33.3)	
	Superolateral radial	32 (72.7)	12 (27.3)	
	Radial (others)	14 (82.4)	3 (17.7)	
	SSM			
	Elliptical superolateral	9 (64.3)	5 (35.7)	
	Elliptical	16 (88.9)	2 (11.1)	
	Round	6 (100.0)	0 (0.0)	
	Circumareolar	5 (83.3)	1 (16.7)	
General surgeon	A	75 (72.1)	29 (27.9)	0.799
	B	4 (80.0)	1 (20.0)	
	C	27 (77.1)	8 (22.9)	
Age		46.6 ± 8.3	48.2 ± 8.7	0.328
Smoking	No	104 (73.8)	37 (26.2)	0.783
	Yes	2 (66.7)	1 (33.3)	
BMI		23.2 ± 3.3	24.4 ± 4.1	0.065
Underlying disease	No	84 (75.7)	27 (24.3)	0.303
	Yes	22 (66.7)	11 (33.3)	
Dye injection	No	25(65.8)	13(34.2)	0.202
	Yes	81(76.4)	25(23.6)	

MFSN: mastecotmy flap skin necrosis; NSM: nipple sparing mastectomy; SSM: skin sparing mastectomy; IMF: inframammary fold; BMI: body mass index.

Table 5. Multivariate Logistic Regression Analysis

		Crude			Adjusted		
		OR	95% CI	*P*	OR	95% CI	*P*
Mastectomy type	NSM	2.01	0.84-4.83	0.118	2.67	0.98-7.30	0.055
	SSM	1			1		
Incision type	Others	1			1		
	Supero-lateral radial	1.07	0.48-2.37	0.873	1.27	0.52-3.12	0.596
Underlying disease	No	1			1		
	Yes	1.56	0.67-3.62	0.305	1.39	0.58-3.33	0.466
BMI		1.10	0.99-1.22	0.072	1.11	1.00-1.24	0.062
Dye injection	No	1.69	0.75-3.77	0.205	1.68	0.71-3.97	0.234
	Yes	1			1		

NSM: nipple sparing mastectomy; SSM: skin sparing mastecomy; BMI : body mass index.

4. Discussion

Blood supply to the breast parenchyma is derived from multiple arterial sources. The internal mammary artery predominantly supplies the superomedial portion, the lateral thoracic artery supplies the superolateral portion, and the intercostal artery supplies the central, inferior, and lateral portions of the breast as the anterior/lateral intercostal perforators. The skin of the breast is supplied by the subdermal plexus, which communicates with the perforators from the deep arteries mentioned above (12,13). After mastectomy is performed, the axial pattern of perfusion is disrupted, and the skin of the breast can only rely on the random blood supply from the subdermal plexus. The basis of this study was the idea that the different types of mastectomy incisions could affect the subdermal plexus differently, and therefore, have different effects on the rate of MFSN occurrence.

In this study, there was no significant difference in MFSN occurrence between the NSM and SSM groups. Although not statistically significant, the NSM group showed a higher rate of MFSN occurrence than the SSM group, with an odds ratio of 2.67. The risk of flap necrosis in NSM has been reported in several studies (14-16). Matsen et al. (15) compared the rate of skin flap necrosis between 95 cases of NSM and 509 cases of SSM. Their results showed that the rate and severity of skin flap necrosis were higher in the NSM group. The reason for this is thought to be the considerably smaller incision used in NSM, which can cause more damage to the skin envelope compared to the incision used in SSM.

The type of incision was not found to be an independent factor affecting MFSN in this study. In our institution, NSM is performed

more often than SSM, and the superolateral radial incision is most commonly used. In our clinical experience, flap necrosis was detected often, and therefore, we hypothesized that the rate of MFSN would be higher with this type of incision; however, no difference was found in both univariate and multivariate analyses. The rate of MFSN in NSM was the highest with the periareolar incision and lowest with the radial incision and the superolateral incision, although this was not statistically significant. Lee et al. (16) systematically analyzed 44 articles about NSM and revealed that there was a significant relationship between the incision type and MFSN; they found that the highest rate of MFSN was associated with the transareolar incision followed by periareolar with radial incision, radial incision only, lateral, inframammary fold, vertical, and periareolar incisions. These results contradicted our study findings. However, it is necessary to consider that the study by Lee et al. was not a single institution study. Recently, Frey et al. (17) analyzed 1207 NSM cases and partially proved the association between the incision type and MFSN. According to their findings, lateral radial incisions had a greater rate of necrosis than vertical radial incisions, and wise-pattern incisions had a greater rate of necrosis than lateral and vertical radial incisions. Furthermore, periareolar incisions had a higher rate of MFSN occurrence compared to lateral, vertical radial, wise-pattern, and IMF incisions. However, they focused on the overall incidence of complications rather than on MFSN alone, and no separate multivariate analysis of the incision type with regard to other complications was performed. Therefore, it is possible that their results differ from those of the present study.

In studies conducted so far, MFSN has been found to be caused by a combination of various factors. It is possible that the length of the incision, rather than its location, affects the rate of MFSN occurrence.

However, due to a lack of data, the length of the incision was excluded from this analysis. Although there was no relation between the length of the incision and MFSN in a previously reported study (15), it can be assumed that a long incision could damage the subdermal plexus and disturb the perfusion of the breast skin envelope. On the other hand, a longer incision can make it easier to handle the mastectomy skin flap properly and preserve it during mastectomy, making it difficult to determine how these two conflicting factors affect the incidence of MFSN.

In breast cancer surgery, blue dye and radioisotopes are commonly used to detect sentinel lymph nodes for biopsy. Blue dye injection is associated with complications such as skin necrosis, tattooing, and anaphylaxis (18) of the few blue dyes in use, there have been some reports that methylene blue injection can cause skin necrosis (19-21). Methylene blue has a vasoconstrictive effect, which is thought to be the cause of skin necrosis (22), but its mechanism and independent effect on MFSN have not been clearly identified. In the present study, all three general surgeons injected indigo carmine blue dye into the subareolar area in all patients who needed a sentinel lymph node biopsy; but its effect on MFSN has not been studied so far. The results of the analyses revealed that indigo carmine was not a factor that significantly influenced MFSN. Consequently, it cannot be considered an intraoperative factor that affects skin necrosis after mastectomy.

Surgical techniques that may affect skin necrosis differ depending on the surgical techniques used by the surgeon performing mastectomy and include the thickness of the mastectomy skin flap, dissection method, and preferred incision type. A thick mastectomy skin flap is important in that it can reduce skin flap necrosis by preserving the tissue blood supply; and previous studies have shown that it plays an important role

in skin flap viability and the final aesthetic results (23,24). Regarding the dissection method, there is still controversy between sharp dissection and electrocautery dissection. Sharp dissection was shown to be associated with MFSN in a few studies (25,26) because the blood supply was sacrificed in thin flaps made by sharp dissection. On the other hand, there is an opinion that sharp dissection is more traumatic to the skin and increases skin necrosis compared to electrocautery (27). In the operations included in this study, the flap thickness could not be measured because no standard measurement tool was available. There was no noticeable difference clinically, and they all used 'electrocautery' for dissection. However, there were differences in the preferred incision type, and each of the three surgeons preferred the supralateral radial, lateral radial, and inframammary fold incisions, respectively. Despite this, in the statistical analysis, there were no significant differences in the rates of MFSN occurrence between the three different general surgeons. It can be inferred that flap thickness and tissue damage, which depend on the surgeon's proficiency, may be more important intraoperative risk factors for MFSN than the incision type.

In addition to the intraoperative factors, patient factors such as age, BMI, smoking, and preoperative radiation have already been shown to be risk factors for MFSN in previous studies (8-11); however, our findings were inconsistent with those of previous studies with regard to age, BMI, and smoking history. However, although there was no statistical significance, MFSN was more frequent in patients with a high BMI. Such patients tend to have larger breasts than the patients in the lower BMI group, and may require more skin reduction or a larger incision. A larger mastectomy skin flap may be more susceptible to impaired perfusion and ischemic sequelae. Non-nipple-sparing mastectomy may be better suited to these patients than NSM (17).

Smoking is a well-known significant risk factor for MFSN and impairs cutaneous vascularity in a time-and dose-dependent manner (8,11,15,16). The reason for the inconsistent results of our study is that the proportion of smokers was small. This seems to be due to the low smoking rate among women in Korea as well as the reluctance to reveal the smoking history due to social constraints.

This study has some limitations. Since it was a retrospective study, there may have been classification errors as we relied only on postoperative clinical photographs and operation notes for classifying the incision type. However, to reduce this error, a single surgeon closely analyzed the clinical data of the subjects more than once. This study focused on the type of incision according to its location and direction. However, as revealed by the results of other studies as well as those of the present study, an approach that focuses on intraoperative factors other than the incision type is required. A new approach, which involves the development of standardized tools for measuring the mastectomy flap thickness or recording the length of the incision during surgery, could be more helpful in lowering the incidence of MFSN after mastectomy and breast reconstruction.

5. Summary

In summary, this retrospective study showed that there was no significant association between the different types of mastectomy incisions and MFSN. Efforts are needed to reduce the incidence of MFSN because it increases the duration of treatment after surgery and can affect the aesthetic results. Therefore, it is important to control the known risk factors, such as a high BMI and smoking before surgery. Further research on other intraoperative risk factors, such as flap thickness and length of incision, in addition to the incision type, may help in improving the postoperative care of patients undergoing immediate breast reconstruction after total mastectomy.

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Survival of Mastectomy Skin Flap According to Incision Methods and Other Affecting Risk Factors

Taeki Kim

Department of Plastic and Reconstructive surgery
Graduate School

Keimyung University

(Supervised by Professor Daegu Son)

(Abstract)

Various incision methods of mastectomy have been used for mastectomy surgery for breast cancer patients. And mastectomy skin flap necrosis is one of important postoperative complication after immediate breast reconstruction after mastectomy. We analyzed the effect of the incision type on mastectomy skin flap necrosis to provide additional evidence for the selection of incision method.

A retrospective review of medical records of 179 breast cancer patients who treated with unilateral total mastectomy and immediate breast reconstruction were performed. To compare incidence differences of mastectomy flap necrosis between skin sparing mastectomy and nipple sparing mastectomy, cases were divided into two groups. And types of incisions were subdivided according to their location and direction. Data of body mass index, smoking history, underlying disease and intraoperative dye injection were collected through medical records as other factors that could affect necrosis. And we analyzed which factors affected the mastectomy

flap skin necrosis using statistical analyses. In multivariate analysis, nipple sparing mastectomy group showed higher flap necrosis than skin sparing mastectomy, but there was no significant difference. And between subdivided incision methods, there was no significant difference with necrosis too. Other risk factors including dye injection also turned out to be not dependent factor of mastectomy skin flap necrosis.

So, rather than incision type, further studies are needed on the effect of other intraoperative risk factors such as flap thickness and length of incision on mastectomy skin flap necrosis. And this may help to make postoperative care easier and bring good aesthetic results after immediate breast reconstruction following mastectomy.

유방전절제술과 즉시유방재건술 후 피판의 괴사에 있어 절개법에 따른 차이와 이에 영향을 미치는 위험인자

김 태 기
계명대학교 대학원
의학과 성형외과학 전공

(지도교수 손 대 구)

(초록)

유방암 환자의 유방전절제술에는 다양한 절개법이 사용되어왔다. 유방즉시재건술 후에 피판의 괴사는 중요한 합병증 중 하나이다. 따라서 우리는 유방전절제술에 시행되는 절개방법이 재건술 후 피판의 괴사에 미치는 영향을 후향적 분석하였다.

179명의 유방전절제술 후 즉시재건술을 받은 유방암 환자의 의무기록 및 임상 사진이 사용되었다. 유두보존절제술과 피부보존절제술의 괴사 차이 비교를 위해 두 그룹으로 분류하였으며 절개법에 따른 괴사 발생률을 비교하기 위해 절개법을 세분화하여 분류하였다. 이 외에 괴사에 영향을 미칠 수 있는 위험인자로 체질량 지수, 흡연력, 지병, 염색약 주입에 관한 데이터가 수집되었다. 단변량분석 및 다중회귀분석을 이용하여 절개법을 포함한 위험인자가 피판의 괴사에 미치는 영향에 대해 분석하였다.

유두보존절제술에서 피부보존절제술보다 피판의 괴사율이 높은 결과를 보였으나 통계적으로 유의한 결과를 보이지는 않았다. 세분화된 절개법 사이에도 피판 괴사율에 있어 유의미한 차이를 찾을 수는 없었다. 이 외의 위험인자들 또한 피판의 괴사에 독립적인 영향을 주지는 못하는 것으로 드러났다.

따라서 유방절제술 시 절개창의 위치와 방향은 피판의 괴사에 유의미한 요소는 아니며, 절개창의 길이, 피판의 두께 등에 관한 추가적인 연구와 관심이 필요할 것이다.

□ 저자 약력

1987년 포항 출생

계명대학교 의과대학 의학과 졸업

계명대학교 동산병원 인턴 수료

계명대학교 동산병원 성형외과 전공의(현)

계명대학교 대학원 의학과 석사과정 수료