

## Efficiency of Platelet Rich Plasma in Prevention of Seroma Formation in Patients with Mastectomy

### Mastektomi Yapılan Hastalarda Seroma Oluşumunun Önlenmesinde Trombositten Zengin Plazmanın Etkinliği

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#### ABSTRACT

**Objective:** Seroma is the most frequent complication after breast surgery which may sometimes lead to delay in wound healing and adjuvant therapies. We aimed to investigate the effect of platelet rich plasma in patients performed mastectomy which is proved to be effective on wound healing.

**Methods:** Forty-one patients with breast cancer were included. All of them were performed mastectomy by the same surgical team and using electrocotery for flap dissection. After mastectomies and placing the drains, platelet rich plasma was sprayed on pectoralis muscle, under skin flaps, and incisions were closed by sutures routinely in 13 patients (study group). The control group (28 patients) and study group were followed-up by a blind surgeon to the groups and the drainage measures, drain removal dates and wound complications were recorded.

**Results:** There were no differences between the groups in terms of mean axillary and flap drainage amounts, mean axillary and flap drains' removal dates, and aspirated seroma amounts after drain removal. No other complications as infection or flap necrosis were recorded in both groups.

**Conclusion:** In breast cancer, some complications related to surgery like poor wound healing and prolonged seroma formation, may cause delay in setting of adjuvant therapy. Platelet rich plasma is known to be effective in wound healing and we wanted to adapt its good sides for patients undergoing mastectomies. Although the results are promising in the study group, there were no differences statistically between two groups.

**Key words:** Breast cancer, platelet rich plasma, seroma

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#### ÖZET

**Amaç:** Seroma, mastektomi ameliyatından sonra bazen yara iyileşmesinde ve adjuvant tedavilerde gecikmeye neden olabilecek en sık görülen komplikasyondur. Bu çalışmada, yara iyileşmesinde etkili olduğu kanıtlanan trombositten zengin plazmanın mastektomi yapılan hastalarda seroma oluşumu üzerine etkisini araştırmayı amaçladık.

**Yöntem:** Meme kanserli kırk bir hasta çalışmaya dahil edildi. Hepsine aynı cerrahi ekip tarafından mastektomi yapıldı ve flep diseksiyonu için elektrokoter kullanıldı. Mastektomi ve drenlerin yerleştirilmesinden sonra 13 hastada (Çalışma Grubu) trombositten zengini plazma pektoralis kası üzerine, deri fleplerinin altına püskürtüldü ve insizyonlar rutin olarak sütürlerle kapatıldı. Kontrol grubu (28 hasta) ve çalışma grubunu gruplara kör bir cerrah takip etti ve drenaj miktarları, dren çekilme süreleri ve yara komplikasyonları kaydedildi.

**Bulgular:** Gruplar arasında ortalama aksiller ve flep drenaj miktarları, ortalama aksiller ve flep drenlerin çıkarılma tarihleri ve dren çıkarıldıktan sonra aspire edilen seroma miktarları açısından fark yoktu. Her iki grupta da enfeksiyon veya flep nekrozu gibi bir komplikasyon kaydedilmedi.

**Sonuç:** Meme kanserinde, zayıf yara iyileşmesi ve uzun süreli seroma oluşumu gibi ameliyatla ilgili bazı komplikasyonlar, adjuvan tedavinin başlanmasında gecikmeye neden olabilir. Trombositten zengin plazmanın yara iyileşmesinde etkili olduğu bilinmektedir ve biz de mastektomi yapılan hastalar için bunun iyi taraflarını uyarlamak istedik. Sonuçlar çalışma grubunda ümit verici olmasına rağmen, iki grup arasında istatistiksel olarak fark yoktu.

**Anahtar Sözcükler:** Meme kanseri, trombositten zengin plazma, seroma

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## INTRODUCTION

Seroma is the most frequent complication (30%) after breast surgery which may sometimes lead to wound infection, pain, delayed wound healing, prolonged hospitalization, flap necrosis and delay in adjuvant therapy setting. Up to now, there have been no surgical procedure or application found to prevent seroma yet. Platelet rich plasma (PRP) is rich in growth factors like platelet derived growth factor, transforming growth factor  $\alpha$  and  $\beta$ , epidermal growth factor, vascular endothelial growth factor and also cytokines. It can be prepared simply and quickly from the one's own peripheral blood. It has positive effects on wound healing by increasing angiogenesis and activating coagulation cascade so in many fields like plastic and reconstructive surgery, orthopedic surgery, craniofacial surgery, and dermatology it is used in chronic ischemic wounds to ensure the viability of bone and skin grafts and flaps (1-5).

In our study, we aimed to investigate the possible effect of PRP if any, on prevention of seroma patients with mastectomy.

## PATIENTS and METHODS

The approval of the study was obtained from the local Ethical Committee (XXXX University, Ethic Committee: 23/2014). Informed Consent: Written informed consent was obtained from patients who participated in this study. The study is planned as a prospective study in a single center. The patients who were planned to undergo mastectomies because of breast cancer were enrolled in the study. The demographic data, body mass index (BMI), and breast size of each patient were recorded. All operations were performed by the same surgical team and by using electrocotery for flap dissection. The patients with axillary dissection were also recorded. The patients who underwent breast conserving surgery, which have diabetes mellitus; chronic renal failure, collagen tissue diseases, immune deficiency diseases, chronic steroid and/or anticoagulant drug administration were excluded. Also having neoadjuvant chemotherapy because of breast or another malignancy, having high BMI and unwilling to participate in the study were exclusion criteria. Forty-one patients with breast cancer were included in the study.

## Preparation of PRP (5-7)

1. Obtain 30 cc venous bloods from the patient just before the surgery, use tubes with 3.8% citrate phosphate dextrose adenine.
2. Centrifugation for 10 minutes at 1000 rpm/min. The whole blood separates into three layers: an upper layer contains mostly platelets and WBC, intermediate thin layer is known as the buffy coat and is rich in WBCs, and a bottom layer consists mostly of RBCs.
3. Transfer the upper layer and superficial buffy coat to an empty sterile tube.
4. Centrifugation for 10 minutes at 1300 rpm/min. afterwards the upper portion of the volume that is composed mostly of PPP (platelet-poor plasma) is removed. Remaining part at the bottom is PRP.
5. There is no consensus on platelet activation before their application and with which agonist. Some authors activate platelets with thrombin or calcium, whereas others apply platelets without being previously activated, arguing that better results are obtained. We use 10% calcium gluconate for activation. Just 2-3 minutes before application.

After mastectomies and placing the drains, PRP was sprayed on pectoralis major muscle, under skin flaps, and the incisions were closed by sutures routinely in 13 patients (*Study Group*). The Control Group was 28 patients. Both groups were followed-up by a blind surgeon to the groups. The drainage measures, drain removal dates and wound complications were recorded.

## Statistical analysis

The Statistical Package for the Social Sciences version 18.0 (SPSS Inc.; Chicago, IL, USA) was used to analyze the statistical data. Along with descriptive statistical methods (Median, Mean, Standard deviation), t-test or Mann

Whitney U test was used to compare the quantitative data for evaluation of the study data. Results were evaluated within 95% confidence interval with a statistical significance value of  $p < 0.05$ .

## RESULTS

Forty-one patients undergoing mastectomies for breast cancer were enrolled in this study. The age of the study group were ranging from 31 to 75 years with a median age of 47 year, and the age of the control group were ranging between 27 and 73 years with a median age of 48 year. Both groups' characteristics features were given in Table 1.

Table 1: The patients' characteristics

	Study Group (n: 13)	Control Group (n: 28)
Median age (years)	47	48
(minimum-maximum)	(31-75)	(27-73)
BMI (kg/m <sup>2</sup> )	28.8	30.05
(minimum-maximum)	(18.7-38)	(21.4-42)
Breast volume, median	95A (75A-110F)	95A (75C-115F)
MRM	4	22
Simple mastectomy	9	6

BMI: Body mass index, MRM: Modified radical mastectomy

The axillary drain removal day of the study and control groups were ranging from 1 to 18 days (median 7 days) and from 3 to 18 days (median 6 days), respectively (Table 2). The flap drain removal day of the study and control groups were ranging from 3 to 22 days (median, 10 days), and from 3 to 35 days (median 7 days), respectively. Although there seems to be difference, the differences between the groups in terms of median axillary and flap drain removal dates were statistically not significant.

Table 2: The groups' median drain removal days and complications

	Study Group	Control Group	p
Axillary drain median removal, day (min-max)	7 (1-18)	6 (3-18)	NS
Flap drain median removal, day (min-max)	10 (3-22)	7 (3-35)	NS
Hematoma	-	-	NS
Median duration of seroma (min-max)	9 (0-228)	9.5 (0-41)	NS
Flap necrosis	-	-	NS
Wound infection	-	-	NS

NS: not significant

The mean volume of the axillary drainage on the first postoperative day of the study and control groups were  $92.91 \pm 72.62$  cc and  $101.25 \pm 41.73$  cc, respectively (Table 3). On the second day, they were  $78.33 \pm 52.62$  cc and  $85.53 \pm 38.47$  cc, respectively. The mean volume of the flap drainage on the first day of the study and control groups were  $145.38 \pm 108.39$  cc and  $80.35 \pm 39.17$  cc, respectively. On the second day, they were  $102.69 \pm 67.78$  cc and  $81.42 \pm 59.11$  cc, respectively. There were no differences between the groups in terms of mean axillary and flap drainage amounts, statistically.

**Table 3:** Axillary and flap drainage amounts (cc)

Days	Axillary drainage cc (mean ± SD)			Flap drainage cc (mean ± SD)		
	Study group	Control group	P	Study group	Control group	P
1	92.91 ± 72.62	101.25 ± 41.73	NS	145.38 ± 108.39	80.35 ± 39.17	NS
2	78.33 ± 52.62	85.53 ± 38.47	NS	102.69 ± 67.78	81.42 ± 59.11	NS
3	60.00 ± 34.96	59.64 ± 46.12	NS	86.81 ± 46.59	59.64 ± 41.94	NS
4	52.00 ± 28.88	59.61 ± 46.1		94.58 ± 70.56	52.80 ± 34.67	
5	56.66 ± 37.9	83.00 ± 62.67		83.00 ± 52.23	54.58 ± 24.44	

The duration of the seroma of the study and control groups were ranging from 0 to 228 days (median, 9 days) and from 0 to 51 (median 9.5 days), respectively. There were no differences between the groups in terms of aspirated seroma amounts after drain removal. No other complications as infection or flap necrosis were recorded in both groups.

## DISCUSSION

Breast carcinoma is the most common malign disease in women and its main part of the treatment is surgery. Some complications such as poor wound healing, infection and intractable seroma may be seen after surgery. Seroma, collected lymphovascular fluid into the dead space is annoying and important complication after breast surgery especially mastectomy and axillary dissection (8). These complications especially seroma may cause delay in setting of adjuvant therapy, both chemo and/or radiotherapy, unfortunately. Also, seroma increases the risk of the lymphedema (9). Different techniques including external compression, immobilization of the arm, ligation of the lymphatics, flap fixation, fibrin glue application, steroid (local or systemic), and intraoperative boost radiation have been used to prevent seroma formation up to now (10-12). In our study, we aimed to investigate the effect of PRP on seroma formation, in patients with mastectomy.

The effects of local or systemic steroid applications were investigated. Local methylprednisolone application to prevent seroma formation was investigated in a randomized clinical trial by Qvamme and colleagues (1). Local methylprednisolone was effective in patients performed mastectomy plus sentinel lymph node biopsy, however, it was not effective in patients underwent mastectomy plus axillary lymph node dissection. The effects of preoperatively systemic steroid to prevent the seroma were investigated by Khan (10). In this randomized study, study group administered methylprednisolone (120 mg) preoperatively and control group (conventional group, did not administer methylprednisolone) were compared. The volume of the drainage in the study group was lower than control group significantly. Also, total drainage days and seroma incidence were reduced statistically in study group. But, wound infection developed in three patients in study group just as expected.

The effect of the fibrin sealant to prevent developing seroma was evaluated in a systemic review by Carless and Henry (2). No effect of fibrin sealant was determined to prevent developing seroma unfortunately.

Flap fixation is another technique that was used to prevent seroma formation. The patients with modified radical mastectomies were divided into two groups. The groups were defined as study group (flaps were fixed to the underlying muscles with absorbable sutures) and control group (performed conventional surgery). Low incidence of the seroma formation, short duration of drain stay and low drainage volume were found in study group (3). Also, van Bastelaar and colleagues (11) reviewed the flap fixation techniques in reducing seroma formation with a meta-analysis. Thirty-seven articles were reviewed and they found mechanical flap fixation technique reduced seroma formation and seroma aspiration after breast surgery. In another study by van Bastelaar and colleagues (12), the patients undergoing mastectomy were divided into three groups as FF-1 (using flap fixation with Vicryl sutures), FF-2 (using flap fixation with ARTISS tissue glue and DO (drain only)). They determined that the flap fixation techniques both using ARTISS tissue glue and sutures reduce seroma formation.

In an experimental study by Agalar and colleagues (8), the effect of Porcine

Dermal Collagen to prevent seroma formation was investigated. They found that it reduces the seroma formation.

The platelets contain a large number of proteins in their granules. These proteins are platelet-derived growth factor, transforming growth factor, platelet factor 4, interleukin-1, platelet-derived angiogenesis factor, vascular endothelial growth factor, epidermal growth factor, platelet-derived endothelial growth factor, epithelial cell growth factor, insulin-like growth factor, osteocalcin, osteonectin, fibrinogen, vitronectin, fibronectin, and thrombospondin-1. The role of these proteins on wound healing has been reported recently. Also, platelet rich plasma is known to be effective in wound healing especially in chronic, ischemic wounds and non-healing skin, bone flaps and grafts. Using of the PRP is common in especially periodontal and oral surgery and aesthetic plastic surgery (5-7, 13, 14). So we wanted to adapt its therapeutic effect for patients undergoing mastectomies in order to force the wound healing, and prevent seroma formation to not to cause any delay in treatment because of wound complications. Although the results are promising in study group, there were no differences statistically between two groups by means of decrease in drain removal time and seroma formation.

In conclusion, seroma formation after breast surgery is one of the most frequent complications and it is an annoying event not only for patients, but also for the medical team because of delay in adjuvant treatments. Until now many kinds of methods were tried but nothing has found to solve this problem completely.

## Conflict of interest

No conflict of interest was declared by the authors.

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