

# Evaluation of Post-operative wound complications in patients getting neoadjuvant chemotherapy

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## ABSTRACT:

**Aim:** To analyse the post-operative wound complications in patients getting neoadjuvant chemotherapy in respect to those patients who underwent surgery without any neoadjuvant chemotherapy.

**Material and method:** The present prospective observational study was conducted in GMCH AMRITSAR Punjab. It consisted of 50 female patients admitted with breast carcinoma divided into group of 25 each, one group that received neoadjuvant chemotherapy and the other group which underwent surgery first.

**Results:** The mean age of the patients was  $50.16 \pm 11.57$  years. no significant difference was observed in age, wound complications, healing time between the two groups. Flap necrosis was seen in 4% cases and 12% cases in group 1 (primary surgery) and 2 (NACT) respectively. Seroma was seen in 16% and 8% cases in group 1 and 2 respectively. 12% cases of group 1 and 20% cases of group 2 presented with wound infection. Patients with DM presented with more complication in both the groups. The difference between both the groups was significant which shows that diabetic patient without NACT have more risk of developing wound complications than with NACT. No significant difference was observed between the mean of healing time in both the groups.

**Conclusion:** In conclusion, our study revealed that a factor, like diabetes mellitus was associated with an increased risk of wound complications for patients undergoing mastectomy. However, neoadjuvant chemotherapy was not associated with an increased risk of wound complications.

## Introduction

Locally advanced breast cancers are an extremely heterogeneous group, ranging from neglected, relatively slow-growing, large primary tumours to small breast tumours presenting with extensive, nodal metastases. LABCs are usually defined by size >5 cm(T3), or primary cancer that involve skin/chest wall/inflammatory breast carcinoma (T4) independent of node status and/or cancer that are associated with fixed or matted axillary lymph nodes (N2a) or internal mammary lymph nodes(N2b/N3b).<sup>1</sup>

Surgical treatment for breast cancer includes breast conservation surgery and mastectomy with or without axillary dissection depending on disease stage. Often, the surgical treatment of breast cancer is accompanied by adjuvant or neoadjuvant therapy, including hormonal therapy, chemotherapy, and/or radiation therapy.<sup>2</sup>

In practice, the neoadjuvant approach is used routinely for patients with inoperable locally advanced breast cancer, including those with inflammatory breast cancer, those with large fixed or erosive lesions, not amenable to mastectomy and those with advanced nodal disease that is fixed, bulky or causing arm edema.<sup>3</sup>It can downgrade the tumours, making it resectable with margin clearance. By reducing tumour burden in both the breast and the axilla, women may achieve complete resections with less extensive operations.<sup>4</sup>

Various clinical trials have shown that preoperative cytotoxic chemotherapy may have undesirable effects on surgical outcomes. It can delay the wound healing and increase the susceptibility to infections, thus raising concerns about the possible increased incidence of complications post-operatively. Delayed healing could be attributed to various side effects of preoperative chemotherapeutics, neutropenia being the most common one.<sup>5</sup> Additionally, surgery associated complications may delay the initiation of adjuvant therapies, principally radiotherapy, which has been shown to reduce local recurrence rates, thus compromising the oncologic outcomes.<sup>6</sup>Thus, in present study, an attempt has been made to analyse the post-operative wound complications in patients getting neoadjuvant chemotherapy in respect to those patients who underwent surgery without any neoadjuvant chemotherapy.

## Material and Methods

The present prospective observational study was conducted in GMCH AMRITSAR Punjab. After approval from institutional ethical committee. It consisted of 50 female patients admitted with breast carcinoma, (with or without receiving neoadjuvant chemotherapy) in Department of General Surgery, GMCH AMRITSAR. Patients were divided into group of 25 each, one group that received neoadjuvant chemotherapy and the other group which underwent surgery first.

## Inclusion and Exclusion Criteria

Female patients diagnosed with breast carcinoma, with or without neoadjuvant chemotherapy, giving valid written informed consent for surgery. Female recurrent breast carcinoma patients and Metastatic breast carcinomas were excluded from the study.

Patients attending the surgical OPD were first examined clinically and relevant investigations like USG of both breasts with axilla, Mammogram and FNAC, besides routine investigations were done. Then according to NCCN (National Comprehensive Cancer Network) guidelines,

breast cancer patients operated without neoadjuvant chemotherapy and patients with locally advanced breast cancer received neoadjuvant chemotherapy first, followed by surgery. Neoadjuvant chemotherapy regimens were given according to the standard protocol followed in our hospital. In the postoperative period, the patients were treated in the ward according to standard protocol like antibiotics, i.v fluids, analgesics and the various parameters, particularly the wound related complications were examined and tabulated. All wounds were examined post-operatively after 72 hours. If there was any evidence of wound infection, and then antibiotic with a gram positive aerobic coverage was given intravenously. Wound swab for culture / sensitivity were sent thereafter, and antibiotics were changed according to the sensitivity reports. After discharge, patients were asked to visit OPD for regular follow up till 30 days or till complete healing of wound, whichever was longer.

## RESULTS AND OBSERVATIONS

Out of 50 patients, 36% belonged to the age group 51 to 60 years, making it the largest age group. 16 patients were in the 41 to 50 years age group. The mean age of the patients was  $50.16 \pm 11.57$  years. The mean age of patients, between both the groups (group 1 =  $53.12 \pm 9.5$  years and group 2 =  $51.6 \pm 10.6$  years) showed no significant difference. (graph 1)

Total 36% of patients developed some form of wound complication. 40 % of patients, who received NACT and 32 % of patients, who underwent primary surgery presented with wound complications. The difference between the two groups was statistically non-significant. (graph 2)

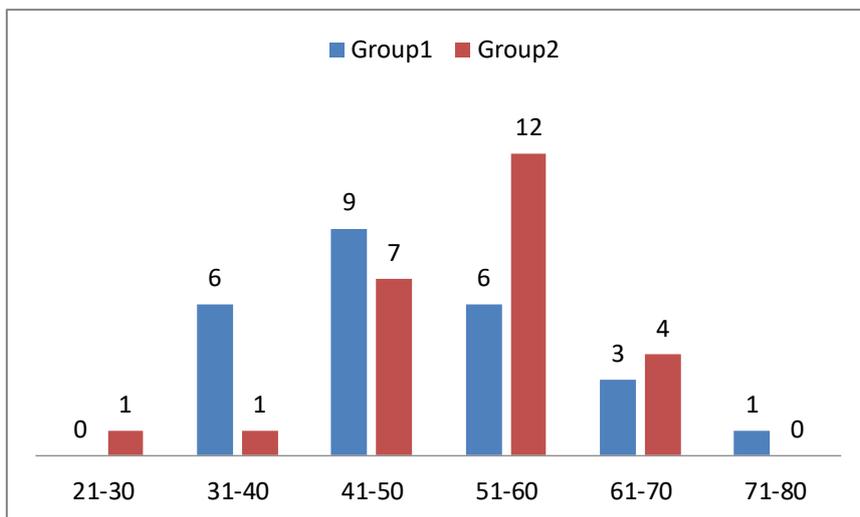
Table 1 shows that in each group 6 patients were hypertensive followed by 5 patients each who had diabetes. Obesity, Hyperthyroidism, CAD, HIV/HCV and MR were present in 1 patient from both groups. There was no significant difference observed in comorbidity.

Table 2 shows the different wound complications in different groups. Flap necrosis was seen in 4% cases and 12% cases in group 1(primary surgery) and 2(NACT) respectively. Seroma was seen in 16% and 8% cases in group 1 and 2 respectively. 12% cases of group 1 and 20% cases of group 2 presented with wound infection. No significant difference was observed among wound complications between both the groups.

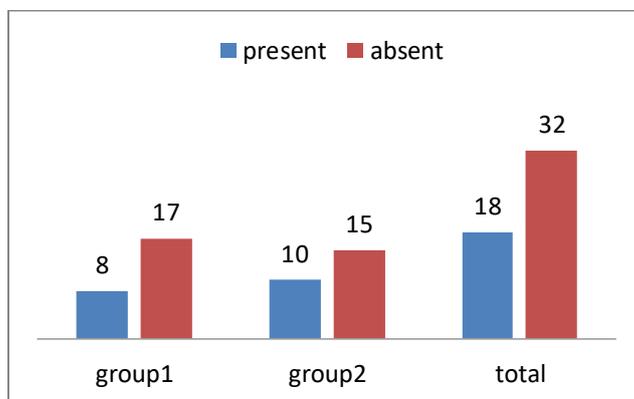
On comparing wound complications with diabetes mellitus it was observed that patients with DM presented with more complication in both the groups. The difference between both the groups was significant which shows that diabetic patient without NACT have more risk of developing wound complications than with NACT. (Table 3)

In patients with NACT 16 patients underwent 3 cycles whereas 9 patients underwent 6 cycles. Out of 16 patients with 3 cycles, 7 patients presented with wound complications as compared to 3 patients with 6 cycles. The difference between the two was non significant (Table 4). The mean healing time for patients in group 1 was 15.84 days and that for group 2 was 18 days. No significant difference was observed between the mean of healing time in both the groups however, in group 2(NACT) the healing time was more than in group 1(primary surgery). (Table 5)

Graph 3 shows the comparison of gap between last NACT cycle and surgery in weeks. Total 14 patients had a gap of 3 weeks between last NACT cycle and surgery, out of which 7 presented with wound complications and 11 had a gap of 4 weeks between last NACT cycle and surgery out of which 3 patients presented with wound complications. Graph 4 shows the comparison of NACT regimen and wound complications. No statistically significant association was seen between the two regimens.



**Graph 1: Age group**



**Graph 2: Incidence of wound complications in breast cancer patients with and without NACT**

Comorbidity	Group 1		Group 2		Total		P-Value Chi- Square
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Diabetes	5	20%	5	20%	10	20%	1(non-significant)
Hypertension	6	24.0%	6	24.0%	12	24%	1(non-significant)
HIV/HCV	1	4%	0	0%	1	2%	.3(non-significant)
Obesity	1	4%	0	0%	1	2%	.3(non-significant)

							significant)
Hyperthyroidism	0	0%	1	4%	1	2%	.3(non significant)
CAD	0	0%	1	4%	1	2%	.3(non significant)
MR	1	4%	0	0%	1	2%	.3(non significant)

**Table 1: Co-morbidities in breast cancer patients**

Complication	Group 1		Group 2		Total		P-Value Chi-Square
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Flap Necrosis	1	4%	3	12%	4	8%	.5
Seroma	4	16%	2	8%	6	12%	
Wound Infection	3	12%	5	20%	8	16%	
None	17	68%	15	60%	32	64%	
Total	25	100%	25	100%	100%	100%	

**Table 2: Different wound complications in both groups of patients**

Groups	Diabetes mellitus	Wound complications				Total	Percentage
		Absent	%Age	Present	Percentage		
1	Absent	17	85.0%	3	15.0%	20	100.0%
	Present	0	0%	5	100.0%	5	100.0%
	Total	17	68.0%	8	32.0%	25	100.0%
2	Absent	14	70.0%	6	30.0%	20	100.0%
	Present	1	20.0%	4	80%	5	100.0%
	Total	15	60.0%	10	40.0%	25	100.0%

p- value= .0001\*\*

**Table 3: Correlation of diabetes mellitus with wound complications**

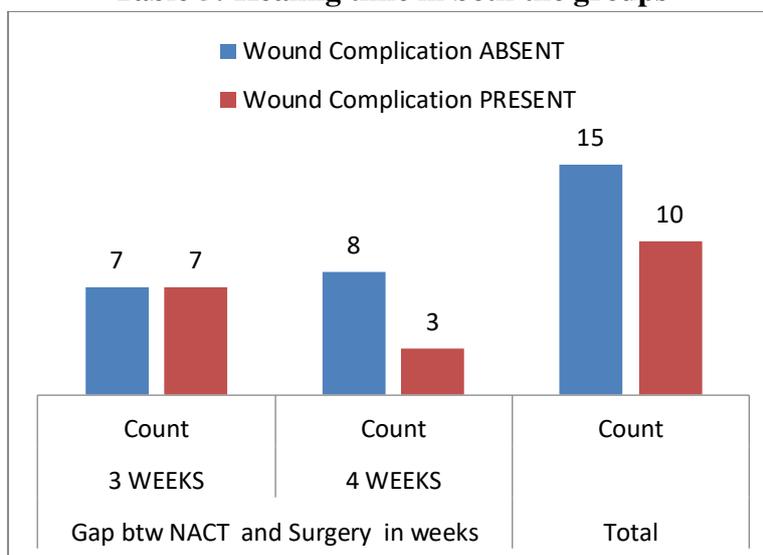
Groups	No. OF CYCLES	Wound complications				Total	Percentage
		Absent	%Age	Present	%Age		
2	3	9	56.3%	7	43.7%	16	100.0%
	6	6	66.7%	3	33.3%	9	100.0%
	Total	15	60.0%	10	40.0%	25	100.0%

**Table 4: correlation of wound complications with number of cycles**

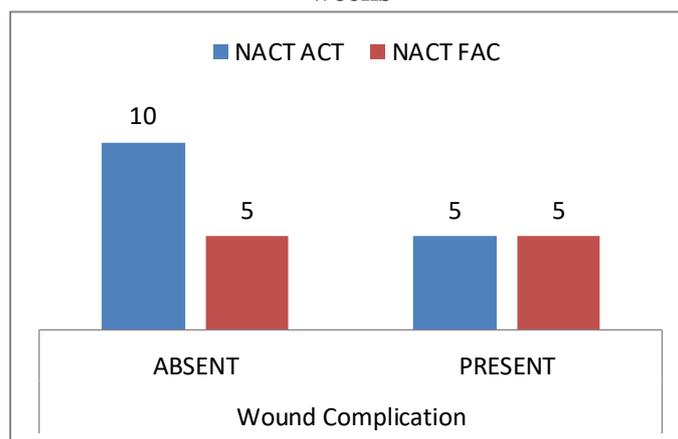
	Mean healing time(Days)	Standard Deviation	t-test	P-value
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Group 1	15.84	5.186	-1.338	.187
Group 2	18.00	6.185		

**Table 5: Healing time in both the groups**



**Graph 3: Association of wound complications with gap between NACT and surgery in weeks**



**Graph 5 : NACT regimen And Wound Complications**

**Discussion**

The present study was conducted at GOVERNMENT MEDICAL COLLEGE AND HOSPITAL, AMRITSAR. It included 50 female patients of breast carcinoma, who were fulfilling the selection criteria. In our study, the mean age of the study population was 51.6±10.6 years. The results of our study were in accordance with Kumar et al who conducted the study to determine wound complications in cancer breast surgery following neoadjuvant chemotherapy. In their study, 63.3% of patients belonged to age group 41-60 years which is comparable to 68% in current study.<sup>7</sup>In our study, the mean age was 51.6 years, which was comparable to the study conducted by Chandrakar and Shinde<sup>8</sup> where the mean age was 50.9 years and maximum patients were in age group 51-60 years similar to the present study. In a study of 150 patients by Dahri FJ et al, maximum patients were 40-60 years of age with a mean age of 52 years.<sup>9</sup> In another the study conducted by Bowen et al, the mean age of the patient was 58.6 years.<sup>10</sup>

In the present study, 36% of total patients from both the groups presented with some form of wound complications. 40% of patients receiving NACT developed some form of wound complications, in comparison to 32% of patients, who underwent primary surgery. The difference between the two groups were statistically non significant. The similar results were obtained by Marszalek D et al,<sup>11</sup> and Decker MR<sup>12</sup> et al who observed no statistically significant difference between both groups in post-operative recovery or the rates of wound complications in patients who underwent NACT and patients with primary surgery.<sup>12</sup>

In the present study, total 16% patients have wound infection, 12% have seroma formation and 8% patients presented with flap necrosis. No significant difference was observed among wound complications between both the groups.

In a study by Chadrakar et al, 24.39% of patients presented with a wound infection post mastectomy which was comparable to the present study.<sup>8</sup> The increased number of wound infections in present study was higher in spite of all sterile precautions, it may be due to patient factors like malnutrition, improper hygiene of the patient.

Seroma formation is a side effect of breast and axilla surgery rather than complication but can delay patient recovery and can cause unpleasant symptoms. Rate of seroma formation can be reduced/prevented by insertion of suction drain deep to mastectomy flaps in axilla. In a study conducted by Kumar et al,<sup>7</sup> the percentage of seroma seen was 20%. In a study by Ranisavljević et al,<sup>13</sup> 4.43% patients had seroma formation. In another study by Chandrakar et al,<sup>8</sup> 26.82% patients presented with seroma formation. Dahri FJ et al in their study observed 33.33% of seroma formation post mastectomy.<sup>9</sup>

8% patients in the present study presented with flap necrosis. In a study by Kumar et al,<sup>7</sup> no patients had flap necrosis while in a study by Ranisavljević et al,<sup>13</sup> and Decker et al<sup>12</sup>, it was 14% and 15% respectively. In a study by Chandrakar N et al,<sup>13</sup> 3% of patients presented with flap necrosis. In a study by Shaikh BF et al 7% of patients presented with flap necrosis.<sup>14</sup>

In present study, 42% of the patients had some form of co-morbidities. 47.6% among these patients had diabetes mellitus as a co-morbidity. Out of these patients, 80% of the patients developed wound complications. In a study by Decker et al, diabetes was present in 5.5% and 8.8% patients with and without NACT respectively. In a study by Kumar et al,<sup>7</sup> the patients with co-morbidities within NACT were 8.3% for hypertension and 10% for diabetes mellitus.

On comparing the wound complications with the co-morbidities, it was observed that patients with DM presented with more complications in both the groups. This could be, as the microangiopathy seen in diabetes mellitus and associated alterations in immune status of the patients lead to an unfavourable environment for wound healing. On comparing two groups the in respect to diabetes mellitus it was seen that diabetic patient with primary surgery had more risk of developing wound complications than with NACT before surgery (p value < 0.001).

In our study, we also analysed the relationship between the duration of last cycle of NACT and surgery to the wound complications. Majority of the wound complications occurred when the duration between last cycle and surgery was 3 weeks than 4 weeks. However, there was no statistically significant difference seen. This might be due to the fact that less patients fell in the 4 week category.

Similarly, the relationship between number of cycles of NACT a patient took and wound complications associated with them could not be analysed correctly, due to majority of patients falling in three cycle regimen than six cycle category.

In the present study, it was observed that 33.3% patients on ACT presented with wound complications where as in FAC 50% patients presented with wound complications. However, more wound complications were observed within FAC group, the difference was not statistically significant.

Most chemotherapeutic drugs are designed to inhibit cellular metabolism, rapid cell division, and angiogenesis and thus inhibit many of the pathways that are critical to appropriate wound repair. These medications inhibit DNA, RNA, or protein synthesis, resulting in decreased fibroplasia and neovascularization of wounds. Chemotherapeutic drugs delay cell migration into the wound, decrease early wound matrix formation, lower collagen production, impair proliferation of fibroblasts and inhibit contraction of wounds. In addition, these agents weaken the immune functions of the patients, and thereby impede the inflammatory phase of healing and increase the risk of wound infection. Chemotherapy induces neutropenia, anaemia, and thrombocytopenia, thus leaving wounds vulnerable to infection, causing less oxygen delivery to the wound, and also making patients vulnerable to excessive bleeding at the wound site.

In our study, we analysed the average wound healing time of NACT patients and primary surgery patients. The difference in the average healing time in days was not statistically different (18.00 days for NACT patients versus 15.84 days for primary surgery patients), however, the patients who had NACT took more time for healing than patients with primary surgery.

### **Conclusion**

In conclusion, our study revealed that a factor, like diabetes mellitus was associated with an increased risk of wound complications for patients undergoing mastectomy. However, neoadjuvant chemotherapy was not associated with an increased risk of wound complications.

Although it did not reach statistical significance, a trend towards increased risk of wound complications after mastectomy for patients who received neoadjuvant chemotherapy was observed. Although the association between neoadjuvant chemotherapy and post-operative wound complications was much less strong than that observed for other clinical factors (like diabetes mellitus), it represents one among many factors that must be considered by surgeons while planning treatment for patients with breast cancer.

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