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Impact of Neoadjuvant Chemotherapy on Wound Healing in Modified Radical Mastectomy

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Abstract

Introduction: *Breast cancer is the second most common cancer among females in India. Neoadjuvant chemotherapy is the standard of care for patients with LABC but its effect on post operative wound healing is debatable.*

Aim: *In this study we aimed to analyze the wound problems in patients undergoing modified radical mastectomy following neoadjuvant chemotherapy in comparison with patients undergoing primary modified radical mastectomy in terms of wound infection, seroma, flap necrosis, wound dehiscence, and delay in initiation /restarting chemotherapy post surgery.*

Materials and Methods: *We prospectively analyzed 60 patients undergoing modified radical mastectomy following neoadjuvant chemotherapy in comparison with patients undergoing primary modified radical mastectomy for carcinoma breast with 30 in each arm from june 2014 to September 2016. All patients in the neoadjuvant chemotherapy arm received 4 cycles of Inj. Adriamycin 60mg/m^2, Inj.Cyclophosphamide 600mg/m^2. Variables analysed include wound infection, seroma, flap necrosis, wound dehiscence, and delay in initiation /restarting chemotherapy post surgery. Sub analyses of the other tumor and patient factors which impact wound healing was done.*

Results: *In our study none of the variables analysed were statistically significant. The sub analysis of number of nodes removed and seroma formation, patient factors like BMI and diabetes showed statistical significance.*

Conclusion: *With the limitation of a small sample size the study concluded that the rate of wound complications in modified radical mastectomy following neoadjuvant chemotherapy is not significantly different from that of primary modified radical mastectomy.*

Keywords: *Locally advanced, neoadjuvant, chemotherapy, chemoradiation. retrospective.*

Introduction

Breast cancer is the second most common cancer among females in India. It is a devastating illness both physically and mentally for tens of thousands of women around the world. The morbidity and mortality of breast cancer make it a leading cause of death in women. It accounts for 33% of all female cancers and is responsible for 20% of cancer related death in women.[2,3] Neoadjuvant chemotherapy is said to have a number of theoretical and practical advantages in treatment of locally advance breast cancer including [7,8,9,10]

- Early treatment of micro metastasis
- Limiting the rapid growth of metastatic foci after removal of primary tumor

- Decreased emergence of chemo resistant clones
- Extension of breast conservation surgery to more patients with larger tumors.

Neoadjuvant chemotherapy is the standard of care for patients with LABC but its effect on post operative wound healing is debatable. Our study analysed the wound problems in patients undergoing modified radical mastectomy following neoadjuvant chemotherapy in comparison with patients undergoing primary modified radical mastectomy in terms of

- wound infection,
- seroma,
- flap necrosis,
- wound dehiscence, and
- delay in initiation /restarting chemotherapy post surgery

Materials and Methods

We prospectively analyzed 60 patients undergoing modified radical patients undergoing primary modified radical mastectomy for carcinoma breast with 30 in each arm from june 2014 to September 2016.

Inclusion criteria

- Patients undergoing modified radical mastectomy with or without neoadjuvant chemotherapy
- All patients above the age of 18 years

Exclusion criteria

Patients with

- Chronic kidney disease
- Altered liver functions
- On steroid therapy
- On radiotherapy
- Collagen disorders
- Skin diseases involving the chest wall

All patients in the neoadjuvant chemotherapy arm received 4 cycles of

- Inj.Adriamycin 60mg/m^2
- Inj.Cyclophosphamide 600mg/m^2.with an interval of 21 days between each cycle, prior to surgery, according to NSABP 27 PROTOCOL

Variables analysed include

- wound infection,
- seroma,
- flap necrosis,
- wound dehiscence, and
- delay in initiation /restarting chemotherapy post surgery

Sub analyses of the other tumor and patient factors which impact wound healing was done.

Statistics Analysis

The association between neoadjuvant chemotherapy arm and primary MRM arm for the variables under study were determined using chi square tests

Results

Age Distribution

In this study mean age of patients in the neoadjuvant arm is 52.03 years

In this study mean age of patients in the primary MRM arm is 52.13 years [table 1]

Wound site infection

In this study wound infection was seen in 10% of the patients who underwent neo adjuvant chemotherapy and in 6.7%of the patients who underwent primary MRM [table 2]

Seroma

IN this study the seroma formation rates in the neoadjuvant chemotherapy arm were 16.7%and that of the primary MRM were 30.0% [table 3]

Flap necrosis

In this study the flap necrosis rates in the neoadjuvant chemotherapy arm were 13.3% and that of the primary MRM were 6.7% [table 4]

Wound dehiscence

In this study the wound dehiscence rates in the neoadjuvant chemotherapy arm were 13.3% and that of the primary MRM were 3.3% [table 5]

Delay in initiation /restarting chemotherapy

In this study it was observed that 33% of patients in the neoadjuvant chemotherapy arm had delay in initiation /restarting chemotherapy

In the primary MRM 23.3% of patients had delay in initiation /restarting chemotherapy [table 6]

Number of nodes removed vs. seroma

the number of nodes removed and seroma formation showed statistical significance with a p value of 0.000 [table 7]

Node positivity vs. seroma formation in axilla

The incidence of seroma axilla is greater in the positive group. However the p value 0.709 was not statistically significant [table 8]

Volume of specimen vs. wound infection

There was no statistical significance in the incidence of wound infections and the breast volume. [table 9]

Volume of specimen vs. seroma

Analysis showed a statistical significance between the incidence of seroma and breast volume (p value-0.002) [table 10]

Volume of breast vs. flap necrosis

There was no statistical significance between volume of breast and flap necrosis [table 11]

Volume of breast vs. wound dehiscence

None of the patients who had breast volume >500mg had wound dehiscence. The p value was 0.494 which is not statistically significant [table 12]

T staging vs. wound complications

There was no statistical significance found [table 13]

Wound complication rates-BMI

There was a significant association between BMI of the patient and the incidence of wound complication p value 0.000 [table 14]

Wound complication rates in diabetes

There was a significant association in the incidence of wound complication in diabetic patient p value 0.000 [table 15]

Wound complication rates in hypertension

There was no statistical significance found [table 16]

Table 1 Group statistics

Group	N	MEAN	Std deviation	Std Error Mean
Age neoadjuvant chemotherapy	30	52.03	8.381	1.530
primary MRM	30	52.13	12.939	2.362

Table 2

			Group		Total
			Neoadjuvant chemotherapy	Primary MRM	
Wound site infection	Present	Count % within group	3 10.0%	2 6.7%	5 8.3%
	absent	Count % within group	27 90.0%	28 93.3%	55 91.7%
Total		Count % within group	30 100.0%	30 100.0%	60 100.0%

Table 3

			Group		Total
			Neoadjuvant chemotherapy	Primary MRM	
seroma	Present	Count % within group	5 16.7%	9 30.0%	14 23.3%
	absent	Count % within group	25 83.3%	21 70.0%	46 76.7%
Total		Count % within group	30 100.0%	30 100.0%	60 100.0%

Table 4

			Group		Total
			Neoadjuvant chemotherapy	Primary MRM	
Flap necrosis	Present	Count % within group	4 13.3%	2 6.7%	6 10.0%
	absent	Count % within group	26 86.7%	28 93.3%	54 90.0%
		Count % within group	30 100.0%	30 100.0%	60 100.0%

Table 5

			Group		Total
			Neoadjuvant chemotherapy	Primary MRM	
Wound dehiscence	Present	Count % within group	4 13.3%	1 3.3%	5 8.3%
	absent	Count % within group	26 86.7%	29 96.7%	55 91.7%
Total		Count % within group	30 100.0%	30 100.0%	60 100.0%

Table 6

			Group		Total
			Neoadjuvant chemotherapy	Primary MRM	
Time taken to restart /initiate chemotherapy	<=30days	Count % within group	20 66.7%	23 76.7%	43 71.7%
	>30days	Count % within group	10 33.3%	7 23.3%	17 28.3%
Total		Count % within group	30 100.0%	30 100.0%	60 100.0%

Table 7

			seroma		Total
			present	absent	
Total number of nodes removed	<=15	Count % within total number of nodes removed	4 9.1%	40 90.9%	44 100.0%
	>15	Count % within total number of nodes removed	10 62.5%	6 37.5%	16 100.0%
Total		Count % within total number of nodes removed	14 23.3%	46 76.7%	60 100.0%

Table 8

			seroma axilla		Total
			present	absent	
Nodal status	positive	Count % within Nodal status	9 25.0%	27 75.0%	36 100.0%
	negative	Count % within Nodal status	5 20.8%	19 79.2%	24 100.0%
Total		Count % within Nodal status removed	14 23.3%	46 76.7%	60 100.0%

Table 9

					volume of specimens(grams)		Total
			<=500	501-1000	1001-1500	>1500	
Wound site infection	Present	Count % within volume of specimens(grams)	0 .0%	2 6.7%	2 13.3%	1 20.0%	5 8.3%
	Absent	Count % within volume of specimens(grams)	10 100.0%	28 93.3%	13 86.7%	4 80.0%	55 91.7%
Total		Count % within volume of specimens(grams)	10 100.0%	30 100.0%	15 100.0%	5 100.0%	60 100.0%

Table 10

			seroma		Total
			present	absent	
Volume of specimen (grams)	<=500	Count % within volume of specimens(grams)	1 10.0%	9 90.0%	10 100.0%
	501-1000	Count % volume of specimens(grams)	3 10.0%	27 90.0%	30 100%
	1001-1500	Count % within volume of specimens(grams)	6 40.0%	9 60.0%	15 100.0%
	>1500	Count % volume of specimens(grams)	4 80.0%	1 20.0%	5 100.0%
Total		Count % within volume of specimens(grams)	14 23.3%	46 76.7%	60 100.0%

Table 11

					volume of specimens(gms)		Total
			<=500	501-1000	1001-1500	>1500	
Flap necrosis	Present	Count % within volume of specimens(grams)	1 10.0%	2 6.7%	2 13.3%	1 20.0%	6 10.0%
	Absent	Count % within volume of specimens(grams)	9 90.0%	28 93.3%	13 86.7%	4 80.0%	54 90.0%
Total		Count % within volume of specimens(grams)	10 100.0%	30 100.0%	15 100.0%	5 100.0%	60 100.0%

Table 12

					volume of specimens(gms)		Total
			<=500	501-1000	1001-1500	>1500	
Wound dehiscence	Present	Count % within volume of specimens(grams)	0 .0%	2 6.7%	2 13.3%	1 20.0%	5 8.3%
	Absent	Count % within volume of specimens(grams)	10 100.0%	28 93.3%	13 86.7%	4 80.0%	55 91.7%
Total		Count % within volume of specimens(grams)	10 100.0%	30 100.0%	15 100.0%	5 100.0%	60 100.0%

Table 13

			Wound complications		Total
			present	absent	
T staging	pT0	Count % within T staging	0 .0%	1 100.0%	1 100.0%
	pT1	Count %within T staging	4 66.7%	2 33.3%	6 100%
	pT2	Count %within T staging	6 20.7%	23 79.3%	29 100.0%
	pT3	Count %within T staging	3 20.0%	12 80.0%	15 100.0%
	pT4	Count %within T staging	2 22.2%	7 77.8%	9 100.0%
Total		Count %within T staging	15 25.0%	45 75.0%	60 100.0%

Table 14

			Wound complications		Total
			present	absent	
BMI	<19	Count % within BMI	2 10.0%	18 90.0%	20 100.0%
	19-25	Count % within BMI	3 12.0%	22 88.0%	25 100%
	>25	Count % within BMI	10 66.7%	5 33.3%	15 100.0%
Total		Count % within BMI	15 25.0%	45 75.0%	60 100.0%

Table 15

			Wound complications		Total
			present	absent	
DIABETES	present	Count % within diabetes	10 40.0%	15 60.0%	25 100.0%
	absent	Count % within diabetes	5 14.3%	130 85.7%	35 100.0%
Total		Count % within diabetes	15 25.0%	45 75.0%	60 100.0%

Table 16

			Wound complications		Total
			present	absent	
Hypertension	present	Count % within Hypertension	10 40.0%	15 60.0%	25 100.0%
	absent	Count % within Hypertension	5 14.3%	130 85.7%	35 100.0%
Total		Count % within Hypertension	15 25.0%	45 75.0%	60 100.0%

Conclusion

Following observations were made

There was no statistical significance

- in the incidence of wound infection
- incidence of seroma
- flap necrosis,
- wound dehiscence, and
- delay in initiation /restarting chemotherapy post surgery

The tumor factors associated with incidence of wound complications

- Volume of breast tissue had a significant association with occurrence of seroma (p value 0.002)

- Tumor size had no statistical significance
- Number of nodes removed was directly proportional to incidence of seroma which was statistically significant.(p value-0.000)
- There was no statistical significance between node positivity and incidence of axillary seroma

The patient factors like BMI and diabetes showed statistical significance on the incidence of wound complication

With the limitation of a small sample size the study concluded that the rate of wound complications in modified radical mastectomy following neoadjuvant chemotherapy is not significantly different from that of primary modified radical mastectomy

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