Section: General Surgery

Original Research Article

EFFECT OF PRE-OPERATIVE CHEMOTHERAPY ON HEALING OF SURGICAL WOUNDS: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: The impact of pre-operative chemotherapy on surgical wound healing remains controversial, with limited evidence from diverse cancer populations. Understanding wound healing complications in chemotherapy-treated patients is crucial for optimizing perioperative care and surgical outcomes. **Aim:** To examine the risk of post-surgical wound complications in patients receiving pre-operative chemotherapy and compare wound healing outcomes with patients undergoing primary surgery without prior chemotherapy.

Materials and Methods: A prospective observational study was conducted at a tertiary care center in Eastern India between July 2023 and November 2024. The study included 175 cancer patients requiring surgery, divided into two groups: those receiving pre-operative chemotherapy (n=87) and those undergoing primary surgery without pre-operative chemotherapy (n=88). Primary outcomes were wound infection and dehiscence rates. Secondary outcomes included post-operative erythema on days 3 and 7. Statistical analysis employed independent t-tests and chi-square tests, with significance set at $p<0.05$.

Results: Wound dehiscence was significantly higher in the pre-operative chemotherapy group (21.8% vs 6.8%, p=0.005), representing a three-fold increased risk. Early post-operative erythema was more frequent in the pre-operative chemotherapy group on day 3 (28.7% vs 14.8%, p=0.025), but this difference resolved by day 7 (20.7% vs 13.6%, p=0.216). Wound infection rates showed no significant difference (19.5% vs 12.5%, p=0.204). Baseline demographics and comorbidities were comparable between groups.

Conclusion: Pre-operative chemotherapy significantly increases the risk of wound dehiscence and early post-operative inflammation but does not affect wound infection rates. Enhanced wound closure techniques and vigilant post-operative monitoring should be implemented in this high-risk population.

Keywords: Neoadjuvant Chemotherapy; Surgical Wound Dehiscence; Surgical Wound Infection; Postoperative Complications; Wound Healing.

INTRODUCTION

Cancer remains a significant global health challenge, with increasing incidence and evolving treatment paradigms that combine multimodal therapeutic approaches. In India, cancer incidence stands at approximately 111 per 100,000 males and 116 per 100,000 females, with regional variations reflecting diverse epidemiological patterns.[1] Neoadjuvant chemotherapy (NACT) has emerged as a cornerstone in contemporary oncological practice, administered prior to definitive surgical resection to reduce tumor burden, eradicate micrometastatic disease, and improve surgical resectability. While this treatment strategy has demonstrated oncological benefits across various malignancies, concerns persist regarding its potential impact on post-operative wound healing.[12]

Wound healing represents a complex, tightly orchestrated biological process involving sequential phases of hemostasis, inflammation, proliferation, and tissue remodeling. Each phase requires precise coordination of cellular activities, growth factor signaling, cytokine networks, and extracellular matrix remodeling to achieve successful tissue repair.[3] Disruption of this intricate process can result in significant complications including delayed healing, surgical site infections, and wound dehiscence, each carrying substantial clinical implications including prolonged hospitalization, increased healthcare costs, and potential delays in adjuvant cancer treatment.[4,5]

Chemotherapeutic agents, while designed to target rapidly dividing cancer cells, exert non-selective effects on normal proliferating cells essential for wound repair, including keratinocytes, fibroblasts, and endothelial cells. These agents can impair critical cellular processes necessary for wound healing, including cellular metabolism, cell division, angiogenesis, and extracellular matrix production. Animal studies have consistently demonstrated adverse effects of chemotherapy on wound healing, with evidence of reduced wound tensile strength and delayed healing trajectories. However, clinical evidence regarding the impact of pre-operative chemotherapy on surgical wound complications remains inconsistent and controversial.[6,7]

The existing literature presents conflicting findings regarding the relationship between pre-operative chemotherapy and wound healing outcomes. Some studies suggest that adjuvant chemotherapy administered after surgery increases wound complication rates, while others report no significant increase in complications with neoadjuvant regimens. Additionally, concerns exist that immunosuppression induced by pre-operative chemotherapy may predispose patients to infectious complications in the post-operative period. This uncertainty is particularly relevant for specific surgical procedures including mastectomy with immediate reconstruction, abdominoperineal resection, and thoracic oncological surgeries, where wound complications can significantly impact both immediate surgical outcomes and long-term cancer management.[8,9,10]

Compounding these challenges, wound complications impose a substantial healthcare burden, with over six million patients in the United States experiencing delayed wound healing annually, translating to approximately 25 billion USD in healthcare expenditures. In the context of cancer surgery, wound complications can lead to increased morbidity, extended hospital stays, and critically, delays in initiating adjuvant therapy, potentially compromising oncological outcomes.[11]

Despite the widespread adoption of neoadjuvant chemotherapy across multiple cancer types and the recognized importance of optimal wound healing for surgical success, there remains a paucity of conclusive evidence regarding the specific effects of pre-operative chemotherapy on wound healing trajectories. This knowledge gap has significant clinical implications, as understanding these effects could inform treatment planning, enable implementation of preventive strategies, and optimize perioperative management for cancer patients receiving multimodal therapy.[8,11] Therefore, this study was designed to systematically evaluate the impact of pre-operative chemotherapy on surgical wound healing by comparing post-operative wound complications between cancer patients receiving neoadjuvant chemotherapy and those undergoing primary surgical resection without prior chemotherapy. By examining wound infection rates, dehiscence incidence, and temporal patterns of inflammatory response, this investigation aims to provide evidence-based insights that can guide clinical decision-making and contribute to improved surgical outcomes in the oncological patient population.

MATERIALS AND METHODS

Study Design and Setting

This prospective, observational study was conducted at the Department of General Surgery, IIMSAR Dr. B. C. Roy Hospital, Haldia, West Bengal, India, between July 2023 and November 2024. The study protocol received approval from the Institutional Ethical Committee of ICARE Institute of Medical Sciences and Research, Haldia. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

Study Population

The study population comprised patients with histopathologically confirmed malignancies requiring surgical intervention, attending both outpatient and inpatient departments of General Surgery. Participants were enrolled consecutively during the study period and allocated into two groups based on their treatment pathway: those receiving pre-operative chemotherapy prior to surgery (pre-operative chemotherapy group) and those undergoing primary surgical resection without pre-operative chemotherapy (non-pre-operative chemotherapy group). Patients aged ≥18 years with confirmed malignancy, scheduled for surgical resection with or without pre-operative chemotherapy, and provided written informed consent were included in the study. Patients with uncontrolled diabetes mellitus, history of radiotherapy to the surgical site, peripheral vascular disease, chronic liver disease, chronic kidney disease, or declined consent were excluded from the study.

Sample Size Calculation

Sample size was determined using the formula for estimating a single proportion:

n=Z2×p×(1−p)D2$n=D2Z2\times p\times(1-p)$

Where:

- Level of significance (α) = 5% (0.05)
- Confidence level = 95% (1-α = 0.95)
- Z = 1.96 (from Z table at 5% type 1 error)
- Prevalence (p) of wound complications in patients receiving pre-operative chemotherapy = 0.87
- Absolute precision (D) = 5% (0.05)

This calculation yielded a required sample size of approximately 175 participants, comprising 87 patients in the pre-operative chemotherapy group and 88 patients in the non-pre-operative chemotherapy group.

Data Collection

Following informed consent, patient data were collected using pre-designed proformas including demographics (age, gender, weight, height, BMI), comorbidities (COPD, dyslipidemia, hypertension), oncological characteristics (cancer type, stage), chemotherapy details (regimen, number of cycles), and surgical information.

Outcome Measures

Primary outcomes were wound complications assessed post-operatively:

- Wound infection: Defined per CDC criteria, including purulent drainage, positive culture, or clinical signs requiring antibiotics
- Wound dehiscence: Partial or complete wound separation requiring intervention

Secondary outcomes included post-operative erythema assessed on days 3 and 7 to evaluate inflammatory response. Wound assessments were performed by trained surgical staff using standardized protocols, with photographic documentation when feasible.

Statistical Analysis

Statistical analysis was performed using SPSS version 23.0. Categorical variables were presented as frequencies and percentages; continuous variables as means ± standard deviations. Independent t-tests compared continuous variables between groups, while chi-square tests assessed associations between categorical variables. Statistical significance was set at $p<0.05$.

Ethical Considerations

All participants provided written informed consent after detailed explanation of study objectives, procedures, risks, and benefits. Patient confidentiality was maintained throughout, with data anonymized using unique study identification numbers. Study materials were securely stored under principal investigator supervision at ICARE Institute of Medical Sciences and Research, Haldia.

RESULTS

A total of 175 cancer patients undergoing surgery were enrolled in this prospective observational study, with 87 patients (49.7%) receiving pre-operative chemotherapy and 88 patients (50.3%) undergoing primary surgery without pre-operative chemotherapy. Statistical analysis was performed using SPSS version 23.0, with categorical variables presented as frequencies and percentages, and continuous variables as means ± standard deviations. Independent t-tests were used for continuous variables and chi-square tests for categorical variables, with statistical significance set at $p<0.05$.

Table 1: Baseline demographic characteristics of study participants

Variable	Pre-operative Chemotherapy (n=87)	Non-pre-operative Chemotherapy (n=88)	Test Statistic	p-value
Age (years), mean ± SD	53.05 ± 14.91	49.34 ± 15.19	t = 1.628	0.105
Gender, n (%)			χ^2 = 0.053	0.818
Female	46 (52.9)	45 (51.1)		
Male	41 (47.1)	43 (48.9)		
Weight (kg), mean ± SD	68.06 ± 12.09	71.08 ± 12.59	t = 1.619	0.107
Height (cm), mean ± SD	168.17 ± 11.01	168.19 ± 10.40	t = 0.013	0.990
BMI (kg/m²), mean ± SD	24.50 ± 6.05	25.43 ± 5.66	t = 1.046	0.297

SD: Standard deviation; BMI: Body mass index

The baseline demographic characteristics were comparable between both groups. The mean age was 53.05 ± 14.91 years in the pre-operative chemotherapy group compared to 49.34 ± 15.19 years in the non-pre-operative chemotherapy group, with no statistically significant difference (p=0.105). Gender distribution was nearly equal in both groups, with females comprising 52.9% and 51.1% of the pre-operative and non-pre-operative groups, respectively (p=0.818). Similarly, no significant differences were observed in weight, height, or BMI between the two groups.

Table 2: Distribution of comorbidities and cancer types

Variable	Pre-operative Chemotherapy (n=87), n (%)	Non-pre-operative Chemotherapy (n=88), n (%)	χ²	p-value
Comorbidities			0.866	0.929
COPD	15 (17.2)	15 (17.0)		
Dyslipidemia	16 (18.4)	19 (21.6)		
Hypertension	21 (24.1)	19 (21.6)		
None	16 (18.4)	19 (21.6)		
Other	19 (21.8)	16 (18.2)		
Cancer Type			8.158	0.086
Breast Cancer	18 (20.7)	7 (8.0)		
Cholangiocarcinoma	21 (24.1)	17 (19.3)		
Colon Cancer	16 (18.4)	26 (29.5)		
Lung Cancer	18 (20.7)	21 (23.9)		
Stomach Cancer	14 (16.1)	17 (19.3)		

COPD: Chronic obstructive pulmonary disease

The distribution of comorbidities showed no significant difference between groups (p=0.929), with hypertension being the most common comorbidity in the pre-operative chemotherapy group (24.1%). The distribution of cancer types was also similar between groups (p=0.086), with cholangiocarcinoma (24.1%) and breast cancer (20.7%) being most prevalent in the pre-operative chemotherapy group, while colon cancer (29.5%) and lung cancer (23.9%) were most common in the non-pre-operative group.

Table 3: Chemotherapy regimen and treatment characteristics in pre-operative chemotherapy group (n=87)

Variable	n	%
Chemotherapy Regimen		
Regimen A	31	35.6
Regimen B	23	26.4
Regimen C	18	20.7
Regimen D	15	17.2
Number of Chemotherapy Cycles		
1 cycle	8	9.2
2 cycles	21	24.1
3 cycles	14	16.1
4 cycles	14	16.1
5 cycles	16	18.4
6 cycles	14	16.1

Among patients receiving pre-operative chemotherapy, Regimen A was the most commonly administered (35.6%), followed by Regimen B (26.4%). The majority of patients received 2 cycles of chemotherapy (24.1%), followed by 5 cycles (18.4%), with the number of cycles ranging from 1 to 6.

Table 4: Comparison of wound complications between groups

Outcome	Pre-operative Chemotherapy (n=87), n (%)	Non-pre-operative Chemotherapy (n=88), n (%)	χ²	p-value
Wound Infection			1.613	0.204
Present	17 (19.5)	11 (12.5)		
Absent	70 (80.5)	77 (87.5)		
Wound Dehiscence			8.061	**0.005**
Present	19 (21.8)	6 (6.8)		
Absent	68 (78.2)	82 (93.2)		

The incidence of wound infection was 19.5% in the pre-operative chemotherapy group compared to 12.5% in the non-pre-operative group, but this difference did not reach statistical significance (p=0.204). However, wound dehiscence occurred significantly more frequently in patients who received pre-operative chemotherapy (21.8% vs. 6.8%, p=0.005), representing a more than three-fold increase in risk.

Table 5: Post-operative erythema assessment

Time Point	Pre-operative Chemotherapy (n=87), n (%)	Non-pre-operative Chemotherapy (n=88), n (%)	χ²	p-value
Post-operative Day 3			5.017	**0.025**
Erythema present	25 (28.7)	13 (14.8)		
Erythema absent	62 (71.3)	75 (85.2)		
Post-operative Day 7			1.532	0.216
Erythema present	18 (20.7)	12 (13.6)		
Erythema absent	69 (79.3)	76 (86.4)		

Early post-operative erythema on day 3 was significantly more common in the pre-operative chemotherapy group (28.7% vs. 14.8%, p=0.025), indicating heightened inflammatory response in the immediate post-operative period. However, by post-operative day 7, the difference in erythema rates between groups was no longer statistically significant (20.7% vs. 13.6%, p=0.216), suggesting resolution of the early inflammatory response.

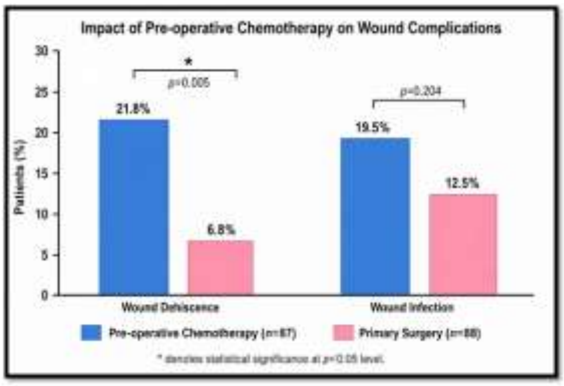

Figure 1: Comparison of primary wound complications between study groups

Figure 1 illustrates the differential impact of pre-operative chemotherapy on wound complications, with wound dehiscence showing a statistically significant three-fold increase while wound infection rates remained comparable between groups.

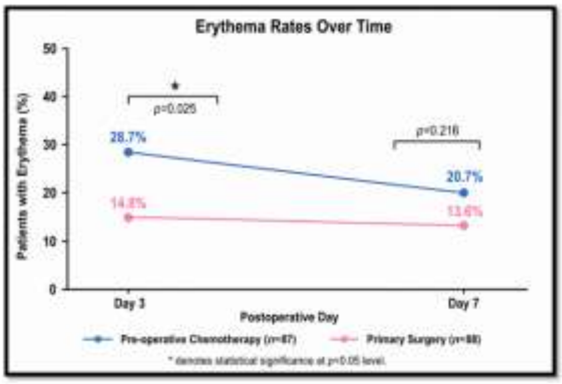

Figure 2: Temporal progression of post-operative erythema

Figure 2 demonstrates the temporal pattern of post-operative inflammation, showing that while early erythema was significantly elevated in the pre-operative chemotherapy group, this difference diminished by post-operative day 7, suggesting resolution of the acute inflammatory response.

DISCUSSION

This prospective observational study investigated the impact of pre-operative chemotherapy on surgical wound healing in cancer patients. Our study enrolled 175 patients over 15 months at a tertiary care center in Eastern India, with 87 patients receiving pre-operative chemotherapy and 88 undergoing primary surgery without prior chemotherapy. The primary aim was to examine the risk of post-surgical wound complications and compare wound healing outcomes between groups. The findings revealed significant differences in wound dehiscence and early post-operative erythema, providing important insights into perioperative management of cancer patients.

Our study demonstrated that pre-operative chemotherapy significantly increased wound dehiscence risk, with incidence of 21.8% compared to 6.8% in the non-pre-operative chemotherapy group (p=0.005). This represents a more than three-fold increase, suggesting that pre-operative chemotherapy substantially compromises wound integrity. This finding contrasts with several previous studies reporting no significant association between neoadjuvant chemotherapy and wound complications. Decker et al., in a large multicenter study of 44,533 patients from the American College of Surgeons National Surgical Quality Improvement Program database, found that wound complications were comparable between neoadjuvant and non-neoadjuvant groups (3.4% vs 3.1%, p=0.4), with no significant association on multivariable analysis (OR 1.01, CI 0.78-1.32).[8] Similarly, Kumar et al. reported wound dehiscence rates of only 3.3% in their Indian study of 60 breast cancer patients, concluding that neoadjuvant chemotherapy did not obviously increase complications.[10] Kaushik et al. also found no statistically significant difference in wound dehiscence between neoadjuvant and primary surgery groups (13.3% vs 3.3%).[12] These discrepancies may be attributed to differences in patient populations, cancer heterogeneity in our cohort which included breast, cholangiocarcinoma, colon, lung, and stomach cancers, and potentially different chemotherapy regimens and surgical approaches.

Regarding wound infection, our study found no statistically significant difference between groups (19.5% vs 12.5%, p=0.204), although there was a trend toward higher infection rates in the pre-operative chemotherapy group. This finding aligns with several previous studies. Kumar et al. reported superficial surgical site infection rates of 6.67% and deep surgical site infection rates of 3.33% in neoadjuvant chemotherapy patients, with no obvious increase compared to controls.[10] Ghosh et al. found that 62.5% of patients who received neoadjuvant chemotherapy developed wound infections compared to 37.5% without neoadjuvant therapy.[13] Kaushik et al. reported wound infection rates of 10% in the neoadjuvant arm versus 6.7% in primary surgery.[12] Saad et al. reported higher infection rates in the adjuvant chemotherapy group (45%) compared to neoadjuvant (25%) and no chemotherapy groups (24%), with p=0.05.[14] The variability in infection rates across studies may reflect differences in antibiotic prophylaxis protocols, surgical sterility measures, operative techniques, and patient comorbidity profiles.

Early post-operative inflammation, assessed as erythema on day 3, was significantly more common in our pre-operative chemotherapy group (28.7% vs 14.8%, p=0.025). However, by post-operative day 7, this difference was no longer statistically significant (20.7% vs 13.6%, p=0.216), suggesting that while pre-operative chemotherapy may trigger a more robust early inflammatory response, this effect resolves within the first week. This temporal pattern of inflammation has not been extensively reported in previous studies, representing a novel contribution of our research. The resolution of erythema by day 7 suggests that the inflammatory cascade initiated by chemotherapy-induced cellular injury is transient, though it may still contribute to the increased dehiscence risk observed in our cohort.[15,16]

Our patient demographics showed comparable baseline characteristics between groups, with mean ages of 53.05 years in the pre-operative chemotherapy group and 49.34 years in controls (p=0.105). This is consistent with Kumar et al. who reported mean age of 41-50 years in 40% of patients, and Kaushik et al. whose study population had mean ages of 52.03 and 52.13 years in neoadjuvant and primary surgery arms respectively.[10,12] The similarity in comorbidity distribution between our groups (p=0.929) strengthens the internal validity of our findings, as confounding by baseline patient characteristics was minimized.

The distribution of cancer types in our study was diverse, with cholangiocarcinoma (24.1%) and breast cancer (20.7%) being most prevalent in the pre-operative chemotherapy group, while colon cancer (29.5%) was most common in the non-pre-operative group. This heterogeneity differs from most previous studies which focused exclusively on breast cancer surgery. Kumar et al., Kaushik et al., Ghosh et al., and Saad et al. all studied only breast cancer patients, limiting the generalizability of their findings.[10,12,13,14] Our inclusion of multiple cancer types provides broader insights but also introduces variability in surgical complexity and chemotherapy regimens that may have influenced wound healing outcomes.

Comparison with regional studies is particularly relevant. Reji et al. reported overall surgical site infection rates of 11% in South Indian tertiary hospital settings (13% emergency, 9% elective), with Staphylococcus aureus being the most common organism (36.37%).[17] Tekam et al. found overall SSI incidence of 42.51% in Central Indian gastrointestinal surgeries, with Klebsiella being the predominant pathogen.[18] These higher infection rates in Indian settings compared to Western studies may reflect resource constraints, antibiotic stewardship challenges, and patient factors such as nutritional status and delayed presentation.

Global studies have also examined treatment timing effects. Chen et al. recently reported that neoadjuvant immunochemotherapy was associated with significantly reduced major wound complications (9.2%) compared to neoadjuvant chemotherapy alone (17.8%) and upfront surgery (21.5%) in oral cancer patients (p<0.001), suggesting immunomodulatory benefits.19 Miyazaki et al. found that preoperative radiotherapy and molecular-targeted therapy were significant risk factors for wound dehiscence in spinal metastasis surgery, with patients receiving both modalities having a 62.5% dehiscence rate.[20]

Our study has several limitations. The sample size of 175 patients, while statistically adequate, is relatively small for subgroup analyses by cancer type or chemotherapy regimen. The single-center design limits generalizability to other healthcare settings. We did not analyze specific chemotherapy agents or regimens, which may have differential effects on wound healing. The observational design precludes causal inference, and residual confounding cannot be excluded despite comparable baseline characteristics. We did not assess nutritional status or albumin levels, which are known predictors of wound healing outcomes.

Despite these limitations, our study has important advantages and clinical implications. The prospective design ensured systematic data collection and minimized recall bias. The inclusion of multiple cancer types enhances external validity compared to single-cancer studies. The assessment of temporal inflammation patterns provides novel insights into wound healing dynamics in chemotherapy-treated patients. Clinically, the significantly elevated risk of wound dehiscence (21.8% vs 6.8%) in patients receiving pre-operative chemotherapy should prompt heightened vigilance during surgical planning and post-operative monitoring. Surgeons should consider implementing enhanced wound closure techniques, such as tension-reducing sutures or prophylactic negative pressure wound therapy, in this high-risk population. Patient counseling should include realistic expectations regarding wound healing complications to facilitate shared decision-making. The transient nature of early inflammatory response suggests that delaying surgery beyond the acute inflammatory phase may not be necessary, though optimal timing warrants further investigation.[21,22]

CONCLUSION

In conclusion, this study demonstrates that pre-operative chemotherapy significantly increases the risk of wound dehiscence and early post-operative inflammation in cancer patients, though wound infection rates remain comparable between groups. These findings underscore the importance of individualized perioperative risk assessment and implementation of evidence-based strategies to optimize wound healing in this vulnerable population.

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