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Association of Estrogen Receptor Expression with Early Postoperative Inflammation within the First 24 Hours after Lumpectomy

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ABSTRACT

Introduction: Early postoperative inflammation after lumpectomy may be influenced by tumor biology, particularly estrogen receptor expression, which modulates immune signaling and cytokine activity. However, its relationship with surgical inflammation remains unclear. This study aimed to evaluate the association between estrogen receptor expression and inflammatory responses during the first 24-hour postoperative period.

Material and methods: This descriptive cross-sectional study was conducted at Tabriz University of Medical Sciences in 2026 on 45 women undergoing lumpectomy, selected by convenience sampling. Estrogen receptor expression was assessed immunohistochemically in surgical specimens, while early postoperative inflammation was evaluated by 24-hour serum C-reactive protein measurement. Additional variables included age, body mass index, menopausal status, tumor characteristics, operative duration, white blood cell count, temperature, drainage volume, and pain score.

Results: Our study demonstrated that ER-negative patients exhibited a more pronounced inflammatory response post-lumpectomy. The ER-negative group showed significantly higher 24-hour CRP (16.83 vs. 12.46 mg/L; p=0.001) and WBC counts (10.08 vs. 8.71 × 10^3/μL; p=0.017) than ER-positive patients. Regression analysis confirmed an independent inverse association between ER expression and postoperative CRP levels (adjusted β=3.92; p=0.003), underscoring a distinct link between molecular phenotype and acute systemic inflammatory intensity.

Conclusion: ER-negative status in breast cancer patients significantly exacerbates the systemic inflammatory response during the first 24 hours after lumpectomy. This association suggests that ER expression serves as a critical molecular biomarker for early postoperative recovery. Consequently, patients with ER-negative tumors may require heightened clinical surveillance and targeted anti-inflammatory interventions to manage the observed surge in acute inflammatory markers following surgical resection.

Introduction

Breast-conserving surgery, particularly lumpectomy, remains a cornerstone in the management of early-stage breast lesions and malignancies because it offers effective local disease control while preserving breast tissue and improving postoperative body image and quality of life.

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As survival outcomes have improved, increasing attention has shifted toward perioperative factors that may influence recovery, short-term complications, and the biological milieu immediately after surgery. Among these factors, early postoperative inflammation has emerged as a clinically relevant process because it reflects the host response to tissue injury and may shape both symptom burden and subsequent healing trajectories in women undergoing breast surgery [1].

The inflammatory response that follows surgery is a tightly regulated yet highly dynamic process involving cytokine release, acute-phase reactants, leukocyte mobilization, and neuroendocrine activation. During the first 24 hours after an operation, local tissue disruption and systemic stress signaling stimulate the production of mediators such as interleukin-6, tumor necrosis factor-alpha, and C-reactive protein, which together provide measurable insight into the extent of surgical stress. Although this response is physiologically necessary for tissue repair, excessive or prolonged inflammation may contribute to poorer recovery, delayed wound healing, and a greater likelihood of adverse postoperative outcomes [2].

In the context of lumpectomy, postoperative inflammation is generally considered less severe than in major oncologic or abdominal procedures, yet it should not be regarded as biologically trivial. Even limited breast surgery involves tissue dissection, vascular injury, electrocautery exposure, and nociceptive activation, all of which can provoke measurable inflammatory changes within hours after the procedure. Moreover, because lumpectomy is frequently performed in women with heterogeneous tumor biology and hormonal receptor status, the immediate postoperative inflammatory response may vary according to underlying host and tumor-related characteristics that are not fully understood [3].

One biological factor of particular interest is estrogen receptor expression. Estrogen receptors, especially estrogen receptor alpha, are central regulators of mammary epithelial biology and play a defining role in the classification, prognosis, and treatment responsiveness of breast neoplasms. In routine oncology practice, estrogen receptor status is primarily used to guide endocrine therapy decisions and estimate long-term disease behavior. However, its potential relationship with perioperative physiological responses, including inflammation during the acute postoperative period, has received comparatively limited attention despite plausible mechanistic links [4].

Estrogen signaling is known to influence inflammatory pathways in a context-dependent manner. Experimental and clinical evidence suggests that estrogen and its receptors can modulate cytokine production, immune cell recruitment, endothelial reactivity, and oxidative stress responses. In some settings, estrogen receptor activity appears to attenuate inflammatory signaling, whereas in others it may amplify or redirect immune responses depending on tissue type, menopausal status, receptor subtype distribution, and the surrounding hormonal environment. This complexity raises the possibility that estrogen receptor expression in women undergoing lumpectomy may be associated with distinct postoperative inflammatory profiles rather than a uniform biological effect [5].

The relevance of this question becomes even greater when considering that many women undergoing lumpectomy are peri- or postmenopausal, a period characterized by marked endocrine transition and altered immune regulation. Reduced systemic estrogen exposure after menopause has been linked to changes in adipose tissue distribution, vascular function, inflammatory mediator production, and innate immune balance. In such a setting, the expression of estrogen receptors at the tumor or tissue level may reflect more than oncologic phenotype alone; it may also correspond to differences in local tissue biology and host inflammatory responsiveness during the perioperative period [6].

From a surgical perspective, early postoperative inflammation is not merely a laboratory phenomenon but a clinically meaningful indicator of tissue stress and recovery. Higher inflammatory activity in the first postoperative day has been associated in various surgical populations with greater pain burden, delayed mobilization, increased need for supportive care, and, in some cases, heightened risk of wound complications. Although lumpectomy is typically associated with brief hospitalization and rapid discharge, variability in early inflammatory response may still influence immediate comfort, recovery quality, and resource utilization, particularly in patients with additional biological or metabolic vulnerabilities [7].

C-reactive protein and related biomarkers are commonly used to assess early postoperative inflammation because they are widely available, reproducible, and responsive to tissue injury. Measurement within the first 24 hours after surgery provides a practical snapshot of the systemic acute-phase response and can serve as a surrogate marker of operative stress and immune activation. In breast surgery, however, the determinants of postoperative inflammatory marker elevation remain insufficiently characterized. Traditional predictors such as age, body mass index, operative duration, and extent of tissue manipulation likely contribute, but tumor receptor biology may represent an additional and underexplored source of variation [8].

The possible association between estrogen receptor expression and postoperative inflammation is biologically plausible for several reasons. Estrogen receptor signaling has been implicated in transcriptional control of inflammatory genes, cross-talk with nuclear factor kappa B pathways, and modulation of macrophage and lymphocyte behavior. Furthermore, estrogen-responsive tumors may exist within microenvironments that differ in stromal composition, vascularity, immune cell infiltration, and extracellular matrix remodeling. These microenvironmental differences may influence how surrounding tissues respond to surgical injury, thereby contributing to measurable variation in inflammatory markers during the first 24 postoperative hours [9].

Another important consideration is that receptor-defined breast cancer subtypes are increasingly recognized as biologically distinct entities with differing interactions between malignant cells and the immune system. Estrogen receptor-positive and estrogen receptor-negative tumors differ in proliferation patterns, cytokine milieu, immune infiltration, and genomic programs linked to host response. Although most studies have focused on prognosis and treatment sensitivity, these subtype-related differences may also extend into the perioperative period. If so, estrogen receptor expression could serve as a readily accessible clinicopathologic indicator of early postoperative inflammatory behavior after lumpectomy [10].

Despite these theoretical and translational implications, the existing literature offers limited direct evidence on the relationship between estrogen receptor expression and immediate postoperative inflammatory changes in women undergoing breast-conserving surgery. Most prior investigations have emphasized long-term oncologic outcomes, endocrine responsiveness, or broad immunohistochemical correlations rather than acute surgical recovery. As a result, clinicians currently have little evidence to determine whether estrogen receptor expression is associated with a lower, higher, or qualitatively different inflammatory response during the first postoperative day. This gap in knowledge limits the integration of tumor biology into perioperative risk assessment [11].

Addressing this question may have practical value beyond descriptive biology. If estrogen receptor expression is found to correlate with early postoperative inflammation, this information could help refine perioperative monitoring, identify patients who may benefit from closer biochemical follow-up, and support more individualized recovery protocols after lumpectomy. Such insights might also stimulate further investigation into how tumor receptor status intersects with surgical stress, tissue repair, and short-term recovery outcomes. In the broader context of personalized medicine, linking molecular tumor characteristics with perioperative physiology represents a meaningful extension of precision oncology into the surgical setting [12].

The study of early inflammation after lumpectomy is also relevant because breast surgery is often performed in high-volume clinical environments where subtle improvements in perioperative stratification can yield meaningful benefits. Identifying biological markers that predict inflammatory intensity within the first 24 hours could contribute to more efficient postoperative planning, more rational use of laboratory testing, and earlier recognition of patients at risk for exaggerated inflammatory responses. Even in relatively low-morbidity procedures, these refinements may improve patient reassurance, streamline discharge decisions, and support enhanced recovery pathways tailored to individual biological profiles [13].

Given the multifactorial nature of postoperative inflammation, any investigation of its relationship with estrogen receptor expression must also consider relevant clinical and perioperative covariates. Age, menopausal status, body mass index, comorbid disease burden, operative duration, anesthetic technique, extent of resection, and baseline inflammatory status may all influence postoperative biomarker levels. Nevertheless, exploring the independent or associated contribution of estrogen receptor expression remains worthwhile because it may reveal a previously underappreciated link between tumor phenotype and acute host response to surgery [14].

Accordingly, the present study was designed to evaluate the association of estrogen receptor expression with early postoperative inflammation within the first 24 hours after lumpectomy. By examining inflammatory markers in women undergoing this common breast-conserving procedure, the study seeks to clarify whether estrogen receptor status is linked to differential acute inflammatory activation in the immediate postoperative period. A better understanding of this relationship may broaden current perspectives on perioperative breast cancer care by connecting receptor-defined tumor biology with short-term surgical recovery processes.

Material and methods

Study Design:

This descriptive, cross-sectional investigation was conducted at the tertiary care teaching hospitals affiliated with Tabriz University of Medical Sciences during the year 2026. The study aimed to assess the relationship between molecular tumor characteristics and early postoperative inflammatory

response in female patients undergoing breast-conserving surgery. By utilizing a cross-sectional framework, the clinical, biochemical, and histopathological data of the patients were evaluated concurrently, providing an epidemiological snapshot of the association between receptor status and the acute-phase inflammatory cascade within the immediate postoperative window.

Sampling

Study participants were selected utilizing a convenience sampling technique from the population of female patients scheduled for lumpectomy. The sample size was calculated based on the standard single-group descriptive cross-sectional estimation formula, specifically Cochran's sample size determination formula for a single proportion. Using an anticipated proportion of high estrogen receptor expression based on historical institutional data, an alpha level of 0.05, and a margin of error of 10% to ensure clinical feasibility within the study period, the minimum sample size required was determined to be 45 patients. Consequently, 45 eligible women who met the predefined selection criteria were prospectively enrolled in the study.

Inclusion and Exclusion Criteria

To ensure a homogeneous sample representative of early-stage breast lesion management, eligible participants were required to meet the following inclusion criteria: biological females aged 18 to 75 years, histologically confirmed diagnosis of breast lesions amenable to lumpectomy, candidates for elective breast-conserving surgery, and written informed consent to participate. Conversely, patients were excluded from the study if they met any of the following criteria: history of prior breast surgery or radiation therapy, presence of active systemic infection or chronic autoimmune disease, advanced metastatic disease, current or recent use of systemic anti-inflammatory agents, corticosteroids, or immunomodulatory therapy within 30 days prior to surgery, pre-existing chronic renal or hepatic failure, and secondary conversion from breast-conserving surgery to total mastectomy during the operation.

Procedure

Eligible patients underwent standard preoperative clinical evaluation and baseline testing. Estrogen receptor expression was determined quantitatively using immunohistochemical analysis of formalin-fixed, paraffin-embedded tumor tissue specimens obtained from the primary lumpectomy specimen. The tissue sections were processed and incubated with primary antibodies against the estrogen receptor, and the expression levels were evaluated by a senior pathologist blinded to the clinical outcomes, recording the percentage of positively stained malignant cells and the intensity of staining. Preoperative demographic details, body mass index, menopausal status, tumor size, histopathological subtype, baseline C-reactive protein levels, and intraoperative variables such as operative duration, surgical margin status, and anesthetic agents were recorded. Postoperative inflammation was systematically assessed through the measurement of systemic inflammatory markers, specifically serum high-sensitivity C-reactive protein, at the 24-hour postoperative mark. Venous blood samples were collected under sterile conditions exactly 24 hours following the completion of the surgical procedure, centrifuged, and analyzed using standard laboratory immunoturbidimetric assays. In addition to C-reactive protein levels, early postoperative pain scores, surgical site drainage volumes, temperature, and white blood cell counts were recorded during the initial 24 hours. The collected data allowed for a comprehensive assessment of the acute postoperative inflammatory response and its potential correlation with the baseline estrogen receptor status of the excised tissue.

Data Analysis

Statistical analysis was performed using SPSS software. The normality of continuous variables was assessed using the Shapiro-Wilk test and visual inspection of histograms. Continuous data with a normal distribution were expressed as mean ± standard deviation and analyzed using the independent-samples t-test or analysis of variance, whereas non-normally distributed data were presented as median and interquartile range and analyzed using the Mann-Whitney U test or Kruskal-Walli's test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's exact test. Correlation between estrogen receptor expression levels and C-reactive protein values was evaluated using Pearson's or Spearman's correlation coefficient. Multivariable linear regression analysis was conducted to control for potential confounding variables, and statistical significance was set at $p<0.05$.

Ethical Considerations

The study protocol was reviewed and formally approved by the regional research ethics committee of Tabriz University of Medical Sciences under the ethics code IR.TBZMED.FMD.REC.1405.161. The study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki. All eligible participants were provided with comprehensive information regarding the study objectives, risks, benefits, and data confidentiality,

and written informed consent was obtained from each patient prior to enrollment and data collection.

Results

The study included 45 women undergoing lumpectomy, of whom 29 (64.44%) had ER-positive tumors and 16 (35.56%) had ER-negative tumors. No statistically significant differences were observed between the groups in age, body mass index, menopausal status, comorbidities, tumor size, histopathological subtype, or tumor grade (all $p>0.05$). Preoperative CRP and WBC values and operative duration were also comparable, indicating generally balanced baseline and perioperative characteristics between the ER groups (Table 1).

Table 1. Baseline Demographic, Clinical, and Tumor Characteristics According to Estrogen Receptor Status

Variable	ER-Positive (n = 29)	ER-Negative (n = 16)	p-value
Age (years), mean ± SD	53.72 ± 8.46	51.19 ± 9.13	0.356
Body mass index (kg/m²), mean ± SD	27.83 ± 4.17	26.91 ± 4.08	0.482
Postmenopausal status, n (%)	19 (65.52)	9 (56.25)	0.542
Hypertension, n (%)	8 (27.59)	3 (18.75)	0.514
Diabetes mellitus, n (%)	5 (17.24)	2 (12.50)	0.674
Tumor size (cm), mean ± SD	2.36 ± 0.81	2.58 ± 0.77	0.383
Histopathological subtype, n (%)	-	-	0.681
Invasive ductal carcinoma	23 (79.31)	11 (68.75)	
Invasive lobular carcinoma	4 (13.79)	3 (18.75)	
Other histological subtypes	2 (6.90)	2 (12.50)	
Histological grade, n (%)	-	-	0.238
Grade I	8 (27.59)	2 (12.50)	
Grade II	16 (55.17)	8 (50.00)	
Grade III	5 (17.24)	6 (37.50)	
Preoperative CRP (mg/L),84 ± 1.37	7.12 ± 1.49	0.527	
Operative0.603	-	-	
Preoperative WBC count (×10³/µL), mean ± SD	6.84 ± 1.37	7.12 ± 1.49	0.527
Operative duration (minutes), mean ± SD	74.62 ± 15.83	78.31 ± 14.27	0.443

Given the comparable baseline characteristics presented in Table 1, ER-negative patients demonstrated a more pronounced inflammatory response during the first 24 postoperative hours. Their mean CRP level (16.83 ± 4.27 vs. 12.46 ± 3.18 mg/L; $p=0.001$), WBC count (10.08 ± 1.86 vs. 8.71 ± 1.54 ×10³/µL; $p=0.017$), and body temperature (37.41 ± 0.38 vs. 37.18 ± 0.31°C; $p=0.047$) were significantly higher than those of ER-positive patients. CRP levels above 15 mg/L and leukocytosis were also more frequent in the ER-negative group. However, drain output, postoperative pain, and fever incidence did not differ significantly between the groups (Table 2).

Table 2. Early Postoperative Inflammatory and Clinical Outcomes According to Estrogen Receptor Status

Variable	ER-Positive (n = 29)	ER-Negative (n = 16)	p-value
CRP at 24 hours (mg/L), mean ± SD	12.46 ± 3.18	16.83 ± 4.27	0.001
WBC count at 24 hours (×10³/µL), mean ± SD	8.71 ± 1.54	10.08 ± 1.86	0.017
Body temperature at 24 hours (°C), mean ± SD	37.18 ± 0.31	37.41 ± 0.38	0.047
Surgical drain output at 24 hours (mL), mean ± SD	82.63 ± 24.71	96.44 ± 28.16	0.111
Postoperative pain score at 24 hours, mean ± SD	3.79 ± 1.24	4.31 ± 1.30	0.187
CRP >15 mg/L at 24 hours, n (%)	6 (20.69)	9 (56.25)	0.015
Leukocytosis at 24 hours, n (%)	4 (13.79)	7 (43.75)	0.026
Postoperative fever, n (%)	2 (6.90)	4 (25.00)	0.091

Correlation analysis showed a significant inverse association between estrogen receptor expression percentage and 24-hour postoperative CRP level ($r=-0.41$; $p=0.006$), indicating that lower ER expression was associated with greater early inflammatory activity. ER expression was also

inversely correlated with 24-hour WBC count (r=−0.32; p=0.034), whereas its association with body temperature was not statistically significant. In adjusted regression analysis, ER-negative status remained independently associated with higher 24-hour CRP levels (adjusted β=3.92; 95% CI:1.41-6.43; p=0.003) and increased odds of CRP elevation above 15 mg/L (adjusted OR=4.21; p=0.034), supporting an independent relationship between ER negativity and intensified early postoperative inflammation (Table 3).

Table 3. Correlation and Regression Analysis of Estrogen Receptor Expression with 24-Hour Postoperative Inflammation

Variable / Model	Statistical Measure	Estimate	95% CI	p-value
ER expression percentage and 24-hour CRP	Spearman's correlation coefficient	-0.41	—	0.006
ER expression percentage and 24-hour WBC count	Spearman's correlation coefficient	-0.32	—	0.034
ER expression percentage and 24-hour body temperature	Spearman's correlation coefficient	-0.21	—	0.169
ER-negative status and 24-hour CRP	Unadjusted β coefficient	4.37	1.98 to 6.76	0.001
ER-negative status and 24-hour CRP	Adjusted β coefficient	3.92	1.41 to 6.43	0.003
ER-negative status and leukocytosis at 24 hours	Adjusted odds ratio	3.86	1.04 to 14.39	0.044
ER-negative status and CRP >15 mg/L at 24 hours	Adjusted odds ratio	4.21	1.12 to 15.84	0.034

Discussion

This study aimed to investigate the correlation between estrogen receptor (ER) expression in breast tissue and the intensity of the systemic inflammatory response, as measured by C-reactive protein (CRP) levels and white blood cell (WBC) counts, during the critical first 24 hours following lumpectomy [15]. By shifting the clinical focus from analgesic requirements to objective inflammatory markers, our findings elucidate how molecular characteristics of the tumor microenvironment may influence postoperative physiological recovery [16].

Our analysis revealed that ER-negative patients experienced a significantly heightened inflammatory profile compared to their ER-positive counterparts. Specifically, those lacking estrogen receptor expression exhibited higher postoperative CRP levels (16.83 vs. 12.46 mg/L; p=0.001) and elevated WBC counts (10.08 vs. 8.71 × 10^3/μL; p=0.017) within the first day after surgery [17]. Furthermore, regression models confirmed that ER-negative status was independently associated with a pronounced inflammatory surge, evidenced by an increased risk of CRP levels exceeding 15 mg/L (OR=4.21; p=0.034), even after adjusting for confounding variables such as tumor size and operative duration [18].

The observed inverse relationship between ER expression and early postoperative inflammation can be attributed to the pleiotropic anti-inflammatory properties of estrogen signaling. Estrogen, acting through its receptors, is known to modulate the immune response by suppressing the production of proinflammatory cytokines such as Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-α), which are primary drivers of the hepatic synthesis of CRP [19]. In the absence of ER expression, the inhibitory control exerted by estrogen on these inflammatory pathways is diminished, potentially leading to an unchecked, exaggerated systemic inflammatory response following surgical trauma [20]. This dysregulation suggests that ER-negative breast tumors not only possess distinct clinical behaviors but may also confer a heightened physiological stress burden on the patient during the immediate postoperative period [21].

Moreover, the higher WBC counts observed in the ER-negative cohort likely reflect a more robust innate immune activation, consistent with recent literature suggesting that estrogen signaling dampens the maturation and mobilization of neutrophils and monocytes [22]. When this dampening effect is absent, surgical manipulation though localized during a lumpectomy triggers a more systemic, dysregulated immune cascade [23]. This phenomenon might also be related to the underlying biological aggressiveness of ER-negative subtypes, which often exhibit a more active stromal environment capable of secreting higher levels of damage-associated molecular patterns (DAMPs) upon tissue disruption, thereby

exacerbating the postoperative inflammatory milieu [24].

In addition, our finding that body temperature was slightly higher in the ER-negative group aligns with the thermoregulatory influence of systemic inflammatory cytokines that are more readily released in an estrogen-depleted molecular environment [25]. While variables such as drain output and patient-reported pain scores showed no statistically significant divergence between groups, the objective biomarker data strongly indicate that the systemic "stress" imposed by surgery is significantly more pronounced in the absence of ER expression [26]. These results imply that clinicians might consider ER status as a predictive factor for postoperative recovery dynamics, potentially identifying a subset of patients who could benefit from more targeted anti-inflammatory management strategies or closer monitoring in the immediate 24-hour postoperative window [27]. Future prospective research should further explore the specific intracellular signaling pathways through which ER expression modulates this acute inflammatory response to confirm whether prophylactic anti-inflammatory interventions could mitigate this disparity in clinical practice [28]. Furthermore, the consistency of our findings with existing molecular data suggests that the anti-inflammatory protection afforded by estrogen receptors is a fundamental aspect of breast cancer biology that extends beyond purely oncological outcomes, warranting consideration in holistic perioperative care planning [29]. Ultimately, understanding these molecular-physiological links underscores the necessity of personalized perioperative approaches, wherein the molecular phenotype of the tumor informs the expected inflammatory trajectory and subsequent supportive care requirements [30].

Conclusion

These findings broaden our understanding of the interplay between tumor biology and the systemic host response, demonstrating that the absence of estrogen receptor expression is a determinant of an intensified acute inflammatory trajectory. This suggests that the protective anti-inflammatory regulatory mechanisms mediated by estrogen signaling are compromised in ER-negative breast cancer, thereby predisposing these patients to heightened physiological stress following surgical intervention. Integrating ER status into clinical risk stratification could refine perioperative management, guiding more personalized strategies that mitigate the impact of surgery-induced inflammation, while paving the way for future studies to elucidate the exact intracellular pathways involved in this immune modulation.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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