Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios as Predictive Markers for Capsular Contracture after Nipple-Sparing Mastectomy with Immediate Implant-Based Reconstruction

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Abstract

Background

Capsular contracture remains a significant complication of nipple-sparing mastectomy(NSM) with immediate direct-to-implant(DTI) reconstruction. Although local inflammation is known to contribute to its development, the role of systemic inflammatory markers remains unclear. This study aimed to evaluate whether preoperative systemic inflammatory markers, such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), are associated with the increased risk of developing capsular contracture.

Methods

The medical records of 376 patients who underwent NSM with DTI reconstruction were retrospectively reviewed. The patients were divided into the non-contracture group (grades 1 and 2) and the contracture group (grades 3 and 4) based on Baker's classification. Clinicopathological variables, including the preoperative NLR and PLR, were analyzed.

Results

Among the 376 patients, 43 (11.4%) developed grade 3 or 4 capsular contractures. The contracture group showed significantly higher proportions of patients who underwent radiotherapy or chemotherapy and those with elevated preoperative NLR and PLR levels. Multivariate analysis identified radiation therapy and elevated NLR and PLR as independent risk factors of capsular contracture. Subgroup analysis revealed that NLR and PLR were not predictive of contracture among patients who did not undergo radiotherapy, but remained significant predictors among those who did.

Conclusion

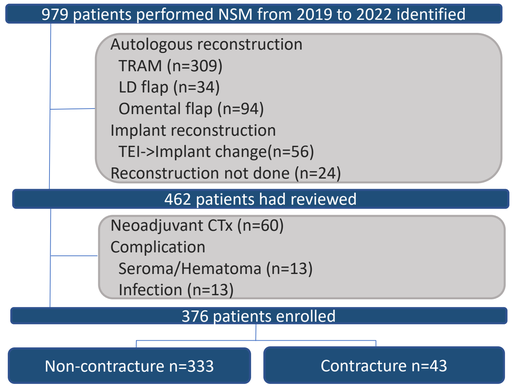
Elevated preoperative NLR and PLR are associated with an increased risk of capsular contracture, particularly in patients receiving radiotherapy. These findings suggest that systemic inflammation, which is potentially exacerbated by radiation-induced fibrosis, may play a synergistic role in the development of capsular contracture. These markers may aid in preoperative risk stratification and support more personalized surgical planning.

Introduction

- **Capsular contracture:**
  Significant complication following NSM with DTI reconstruction
- **Inflammation:**
  Plays a pivotal role in the pathogenesis of capsular contracture
- **Systemic inflammatory markers:**
  Emerging biomarkers that are associated with various disease
- This study evaluates whether **preoperative NLR and PLR can predict capsular contracture in patients undergoing NSM with DTI reconstruction**.

Methods and Materials

- **Study Design:** Retrospective single-center study
- **Patients:** 376 patients who underwent NSM with DTI reconstruction
- **Groups:** Non-contracture group (Baker grade 1–2) and contracture group (Baker grade 3–4)
- **Receiver Operating Characteristic (ROC) analysis:**
  To determine the optimal cut-off values for NLR and PLR as predictors of capsular contracture
- **Analysis:** Preoperative NLR and PLR levels were analyzed, along with clinical and treatment factors. Multivariate logistic regression was used to identify independent risk factors for capsular contracture.



Results

- **Patient Characteristics:**
  43 (11.4%) patients developed grade 3 or 4 capsular contracture.
  Patients in the contracture group had significantly higher rates of radiation therapy (79.1%) and chemotherapy (46.5%).
- **Systemic Inflammatory Markers:**
  Higher NLR and PLR levels were significantly associated with the development of capsular contracture.
- **Multivariate Analysis:**
  Radiation therapy, elevated NLR, and PLR were identified as independent risk factors for capsular contracture.

Characteristic	Non-contracture (group 1) n=333	Contracture (group 2) n=43	p-value
Age at diagnosis	45.8±7.0	45.6±8.1	0.829
BMI at operation			0.541
<25	290 (87.1%)	36 (83.7%)	
≥25	43 (12.9%)	7 (16.3%)	
Radiation therapy			**<0.001**
No	250 (75.1%)	9 (20.9%)	
Yes	83 (24.9%)	34 (79.1%)	
Anti-hormonal therapy			0.380
No	65 (19.5%)	6 (14.0%)	
Yes	268 (80.5%)	37 (86.0%)	
Chemotherapy			0.005
No	246 (73.9%)	23 (53.5%)	
Yes	87 (26.1%)	20 (46.5%)	
Systemic inflammatory marker			
NLR			**0.004**
Low	137 (41.1%)	8 (18.6%)	
High	196 (58.9%)	35 (81.4%)	
PLR			**0.005**
Low	234 (70.3%)	21 (48.8%)	
High	99 (29.7%)	22 (51.2%)	

Variable	Univariate		Multivariate	
	OR(95% CI)	p-value	OR(95% CI)	p-value
BMI		0.542		
≤25	Ref.		-	
>25	1.311(0.549 - 3.132)		-	
Adjuvant RTx		<0.001		**<0.001**
No	Ref.		Ref.	
Yes	11.379(5.239 - 24.712)		11.203(5.028 - 24.960)	
Adjuvant HTx		0.383		
No	Ref.		-	
Yes	1.496(0.606 - 3.694)		-	
Adjuvant CTx		0.006		0.060
No	Ref.		Ref.	
Yes	2.4599(1.287 - 4.697)		2.010(0.972 - 4.155)	
NLR+PLR				
Both low	Ref.		Ref.	
One high	2.109(0.831 - 5.350)	0.116	2.152(0.799 - 5.794)	0.129
Both high	4.341(1.767 - 10.666)	0.001	5.287(1.983 - 14.091)	**0.001**

	Radiotherapy not done		Radiotherapy done			
Variable	Univariate		Univariate		Multivariate	
	OR(95% CI)	p-value	OR(95% CI)	p-value	OR(95% CI)	p-value
BMI		0.908		0.665		
≤25	Ref.		Ref.			
>25	0.883 (0.107 - 7.303)		1.268 (0.434 - 3.708)			
Adjuvant HTx		0.410		0.316		
No	Ref.		Ref.			
Yes	2.417 (0.296 - 19.725)		0.534 (0.157 - 1.818)			
Adjuvant CTx		0.138		0.332		
No	Ref.		Ref.			
Yes	2.771 (0.720 - 10.669)		1.491 (0.665 - 3.342)			
NLR+PLR						
Both low	Ref.		Ref.		Ref.	
One high	0.978 (0.135 - 7.095)	0.983	2.600 (0.830 - 8.145)	0.101	3.203(0.953 - 10.765)	0.060
Both high	3.447 (0.649 - 18.314)	0.146	5.389(1.701 - 17.081)	0.004	7.334(2.086 - 25.782)	**0.002**

- **Subgroup analysis:**
  Elevated NLR and PLR were significant predictors of capsular contracture in the **radiotherapy group**
  No such association was found in the **non-radiotherapy group**
- **Synergistic Role of NLR and PLR in RT and Capsular Contracture:**
  Elevated NLR and PLR suggest a pro-fibrotic systemic environment, **particularly in patients receiving radiation therapy**
- **Clinical implications:**
  NLR and PLR may assist in **preoperative risk stratification and patient counseling**

Conclusions

- **Elevated preoperative NLR and PLR** were significantly associated with an **increased risk of capsular contracture** after NSM with DTI reconstruction, especially in patients receiving radiation therapy.
- These markers **reflect systemic inflammation and may serve as predictive biomarkers for fibrotic responses**.
- **Further multicenter prospective studies are needed to validate** these findings and explore inflammation-guided preventive strategies.

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