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OPTIMIZING PATIENT CARE PROTOCOLS: IMPORTANCE OF NUTRITIONAL MANAGEMENT AS PART OF COMPREHENSIVE BREAST CANCER TREATMENT

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Key words: nutritional support, nutritional status, quality of life, breast cancer, neoadjuvant chemotherapy**Ключові слова:** нутритивна підтримка, якість життя, рак молочної залози, неоад'ювантна хіміотерапія

Abstract. Optimizing patient care protocols: importance of nutritional management as part of comprehensive breast cancer treatment. Moroz O., Yin Q., Li X. Aim – to assess the influence of neoadjuvant chemotherapy (NAC) on nutritional status in breast cancer patients by analyzing changes in the prognostic nutritional index (PNI), serum albumin, and neutrophil-to-lymphocyte ratio (NLR) at standardized clinical time points. A retrospective study of 121 patients treated in 2008 and 2018 was conducted. Nutritional indicators were evaluated at baseline, before surgery, and seven days postoperatively. Baseline characteristics, including age, body mass index (BMI), albumin, NLR, and PNII, did not differ significantly between groups. NAC significantly reduced preoperative PNII levels (48.70±6.73 vs. 51.61±3.99; $p=0.0072$), while no significant differences were found at baseline or postoperative PNII ($p>0.05$). A weak negative correlation was observed between age and PNII ($r= -0.1817$; $p=0.0461$). BMI, chemotherapy regimen, and treatment-related complications did not correlate with PNII values ($p>0.05$). Generalized Linear Model analysis showed no independent effect of treatment year, BMI, or NAC protocol on PNII–PNI, whereas albumin and NLR were significantly associated with PNII across all time points, consistent with the PNII formula. Analysis of the 2018 cohort confirmed a significant decrease in PNII among NAC patients ($p=0.0076$) with no postoperative differences ($p=0.9916$). The results indicate that NAC causes a transient decline in nutritional reserves confined to the pre-surgical period, emphasizing the need for targeted nutritional assessment and support during NAC in breast cancer care.

Реферат. Оптимізація протоколів догляду за пацієнтами: важливість нутритивного менеджменту як складової комплексного лікування раку молочної залози. Мороз О., Інь Ц., Лі С. Мета дослідження – оцінити вплив неоад'ювантної хіміотерапії на харчовий статус пацієнтів з раком молочної залози шляхом аналізу змін прогнозистичного індексу харчування (PNI), сироваткового альбуміну та співвідношення нейтрофілів до лімфоцитів у стандартизовані клінічні моменти часу. Було проведено ретроспективне дослідження 121 пацієнтки, які отримували лікування у 2008 та 2018 роках. Показники харчування оцінювали на початковому етапі, перед операцією та через сім днів після операції. Вихідні характеристики, включаючи вік, індекс маси тіла (ІМТ), альбумін, співвідношення нейтрофілів до лімфоцитів і PNI, які оцінювали, суттєво не відрізнялися між групами. Неоад'ювантна хіміотерапія значно знишила передопераційні значення PNI (48,70±6,73 проти 51,61±3,99; $p=0,0072$), тоді як суттєвих відмінностей не було виявлено на початковому рівні або післяопераційному ($p>0,05$). Спостерігалася слабка негативна кореляція між віком і передопераційним PNI ($r= -0,1817$; $p=0,0461$). ІМТ, схема хіміотерапії та ускладнення, пов'язані з лікуванням, не корелювали зі значеннями PNI ($p>0,05$). Аналіз узагальненої лінійної моделі не показав незалежного впливу року лікування, ІМТ або протоколу хіміотерапії на PNI, тоді як альбумін і співвідношення нейтрофілів до лімфоцитів були тісно пов'язані з його значеннями в усі моменти часу, що узгоджується з формулою індексу. Аналіз когорти 2018 року підтвердив значне зниження PNII у пацієнтів, які отримували неоад'ювантну хіміотерапію ($p=0,0076$), без післяопераційних відмінностей ($p=0,9916$). Результати показують, що неоад'ювантна хіміотерапія спричиняє тимчасове зниження поживних резервів, обмежених доопераційним періодом, що наголошує на необхідності цілеспрямованого оцінювання харчування та підтримки під час неоад'ювантної хіміотерапії в лікуванні раку молочної залози.

Breast cancer, which is the most frequently diagnosed malignancy among women globally, continues to be a significant public health burden [1], despite the fact that diagnostic and therapeutic strategies have advanced [2]. According to the International Agency for Research on Cancer's global epidemiological projections, there is a constant increase in both incidence and mortality across all age groups, with particularly sharp increases observed in developing regions where late-stage presentations remain frequent [3].

Neoadjuvant chemotherapy (NAC), chemotherapy administered before surgery, has become an integral component of modern breast cancer management. Beyond facilitating tumor downstaging and increasing eligibility for breast-conserving surgery [4], NAC provides early insight into tumor biology and treatment responsiveness, offering prognostic information that is not available in the adjuvant setting [5]. Over the past decade, significant progress in imaging technologies, systemic therapies, and surgical techniques has contributed to improved clinical outcomes for breast cancer patients [2, 6]. Despite these advances, the nutritional care of patients undergoing oncologic treatment has lagged behind [7]. This stagnation is particularly concerning given the widespread use of NAC, which, despite its therapeutic benefits, is accompanied by numerous adverse effects, such as bone marrow suppression, reduced immunity, and malnutrition [8], and diminishes treatment tolerance, expands hospitalization, increases postoperative complications, and has a negative impact on overall quality of life [9].

The existing literature suggests that several nutritional assessment tools, such as the Prognostic Nutritional index (PNI) – a composite measure incorporating serum albumin concentration and peripheral lymphocyte count – provide a comprehensive snapshot of nutritional and immune health, with the potential to predict treatment outcomes and survival in breast cancer patients. Increasing evidence suggests that PNI correlates with treatment response, postoperative recovery, and long-term survival in breast cancer patients [10, 11]. Nevertheless, limited data exist regarding how PNI and related biochemical indicators fluctuate throughout the full treatment continuum, particularly during NAC and the preoperative period.

To address this gap, the present study aims to retrospectively evaluate the effect of NAC on key nutritional parameters in breast cancer patients. By analyzing PNI, albumin levels, body mass index (BMI), and related hematologic indices measured before NAC, immediately prior to surgery, and during early postoperative recovery, this study seeks to quantify the extent of nutritional deterioration associated with NAC – primarily due to its adverse side effects – and

identify clinical factors influencing these changes. These findings are intended to highlight the critical need for integrating structured, timely nutritional support into patient care protocols to optimize tolerance to treatment and improve overall outcomes.

MATERIALS AND METHODS OF RESEARCH

This retrospective study that analyzed clinical data from breast cancer patients treated at a tertiary hospital between 2008 and 2018. Treatment strategies for patients were managed according to institutional and national breast cancer treatment guidelines [12]. Depending on the clinical stage of the disease, tumor subtype, and the patient's baseline condition, patients either received standardized NAC (Anthracycline, Taxane, or Platinum-based regimens selected based on tumor subtype) followed by definitive surgery (NAC group), or proceeded directly to surgery (non-NAC group). Both groups followed identical surgical and postoperative care protocols, enabling comparison of nutritional indicators across two standard treatment pathways. All patients included in the study were hospitalized and treated under the supervision of the authors (board-certified physicians with 20+ years of experience), and the research was conducted retrospectively using existing clinical data. No experimental therapies or interventions were applied; treatment plans followed institutional protocols and were regularly reviewed by the department team. Cross-disciplinary consultations (e.g., oncology, pathology, hematology, etc.) were obtained as needed.

Specifically a total of 140 medical records were randomly selected from a larger pool of individuals diagnosed with breast cancer during this period. Inclusion criteria were: 1) histologically confirmed breast cancer; 2) receipt of NAC followed by surgery for the NAC group, or surgery alone for the non-NAC group; 3) complete laboratory data for the Prognostic Nutritional Index (PNI), serum Albumin (ALB), neutrophil-to-lymphocyte ratio (NLR), and body mass index at specified time points. Exclusion criteria included incomplete clinical data or missing PNI measurements. Therefore, after applying these criteria, 121 patients were included in the final analysis.

Nutritional and inflammatory indicators were assessed at three checkpoints predefined by institutional and clinical guidelines [12, 13]. Baseline measurements (PNI1, ALB1, NLR1) were taken the day before the first NAC cycle in the NAC group, representing the patient's initial nutritional and immunologic status. Preoperative measurements (PNI2, ALB2, NLR2) were obtained the day before surgery for both groups as part of mandatory preoperative evaluation to exclude contraindications to anesthesia and surgical procedures. Postoperative measurements (PNI3, ALB3, NLR3) were collected seven

days after surgery, when patients were clinically stable and evaluated for discharge readiness. The use of predefined institutional measurement time points minimized variability related to chemotherapy-induced fluctuations in cell counts, particularly in neutrophils, thereby improving comparability across patients.

Additional recorded variables included age, BMI, treatment year (2008 or 2018), chemotherapy regimen (for patients receiving NAC), total duration of surgical hospitalization, and chemotherapy-related complications. The primary objective of the analysis was to examine changes in PNI across the three time points and determine whether NAC exerted a measurable effect on nutritional status compared with surgery alone. Secondary analyses evaluated the contribution of albumin, NLR, BMI, age, and treatment year to observed nutritional changes. A correlation analysis was also performed between patient age and PNI at each time point.

Statistical analyses were conducted using SAS® OnDemand for Academics (Release 3.81, Enterprise Edition). The distribution of continuous variables was assessed, independent samples t-tests or Mann-Whitney U tests were applied for comparisons between groups. Categorical variables were analyzed using Chi-square or Fisher's exact tests [14, 15]. Descriptive statistics included means, standard deviations, and ranges. A General Linear Model (GLM) was used to evaluate the combined effects of NAC status, albumin, NLR, BMI, and treatment year on PNI. Statistical significance was set at $p<0.05$.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (Protocol No. TJ-IRB20221234). Given the retrospective nature of the study and the use of anonymized clinical data, the requirement for written informed consent was waived.

RESULTS AND DISCUSSION

Baseline clinical and nutritional characteristics of the study population are presented in Table 1. The distribution of patients across treatment years and treatment pathways is shown, with 18 patients receiving NAC in 2008 and 53 in 2018, while 50 patients in 2018 underwent surgery without NAC. Age and BMI values were similar across groups, with no significant pre-treatment differences in demographic characteristics. Furthermore, baseline nutritional status was also comparable: PNI1 values exceeded 50 in both treatment years, and baseline albumin and neutrophil-to-lymphocyte ratio (NLR) levels showed no significant differences. The length of stay during surgical hospitalization was shorter in 2018 compared with 2008, while baseline nutritional markers remained unchanged. These findings address the primary research questions and underline important considerations for patient care, including nutritional monitoring and treatment planning [10, 11, 16]. The overall similarity of baseline indicators strengthens the validity of subsequent comparisons of how neoadjuvant chemotherapy influenced nutritional status at later time points.

Table 1

Clinical and nutritional characteristics of patients stratified by NAC status and year of treatment (2008 vs. 2018)

Indicator	2008		2018	
	NAC	Non-NAC	NAC	Non-NAC
Amount of patients (amount)	18	-	53	50
Age (years)	48.94±8.03	-	44.45±9.94	49.60±9.03
BMI (kg/m ²)	-	-	22.16±2.64	23.02±3.57
Total length of stay for surgery admission (days)	19±5	-	12±5	13±7
Prognostic Nutritional Index	PNI1	51.42±4.94	-	51.33±4.12
	PNI2	49.27±5.82	-	48.51±7.06
	PNI3	46.07±4.33	-	46.77±5.28
Albumin levels (g/L)	ALB1	43.95±3.49	-	43.11±3.61
	ALB2	44.43±5.19	-	41.05±3.63
	ALB3	40.58±3.97	-	40.74±4.37
Neutrophil-to-lymphocyte ratio	NLR1	2.26±0.84	-	2.30±1.40
	NLR2	3.27±2.80	-	2.73±2.64
	NLR3	2.66±1.20	-	3.64±4.04
				2.34±1.49

Changes in nutritional indicators associated with NAC are summarized in Table 2. NAC significantly reduced pre-surgery PNI (PNI2) levels (mean difference -2.91; $p=0.0072$), indicating a notable depletion in nutritional reserves before surgery. In

contrast, no significant differences were seen for PNI1 (pre-NAC; $p>0.05$) or PNI3 (post-surgery; $p=0.8507$), suggesting that NAC's impact on nutritional status is transient and primarily concentrated during the pre-surgical phase.

Table 2

Comparison and statistical results of indicators between groups under NAC for breast cancer

Time Point	NAC Status	Sample Size (N)	Mean \pm Standard Deviation (PNI)	Test Value (p-value)	Significance	Related Variables
PNI1 (Pre-NAC)	NAC Group	71	51.35 \pm 4.31	> 0.05	None	ALB1, NLR1 (significant predictors)
	Non-NAC Group	50	-			
PNI2 (Pre-surgery)	NAC Group	71	48.70 \pm 6.73	0.0072	Significant	NAC, ALB2, NLR2
	Non-NAC Group	50	51.61 \pm 3.99			
PNI3 (Post-surgery)	NAC Group	71	46.60 \pm 5.03	0.8507	None	ALB3, NLR3 (significant predictors)
	Non-NAC Group	50	46.76 \pm 4.14			

Correlation analysis showed a negative association between age and PNI2 ($r= -0.1817$; $p=0.0461$) (Table 3), indicating that older patients exhibited slightly poorer nutritional status at the pre-surgery.

No significant correlations were observed between BMI, NAC protocol, treatment-related complications, or length of hospital stay and any of the PNI indicators (all $p>0.05$).

Table 3

Pearson Correlation Coefficients Between PNI Values and Clinical Variables

	PNI1	PNI2	PNI3
Age	-0.1719 ($p=0.1528$)	-0.1817 ($p=0.0461$)	-0.0863 ($p=0.3469$)
BMI1	0.04557 ($p=0.7459$)	N/A	N/A
BMI2	N/A	-0.0589 ($p=0.5547$)	N/A
BMI3	N/A	N/A	0.1099 ($p=0.2692$)
NAC protocol	-0.0246 ($p=0.8412$)	0.0085 ($p=0.9292$)	-0.0347 ($p=0.7161$)
Treatment related complications	-0.0063 ($p=0.9585$)	0.1118 ($p=0.2222$)	-0.0419 ($p=0.6486$)
Length of stay for surgery admission	0.2129 ($p=0.0746$)	0.0848 ($p=0.3550$)	0.1274 ($p=0.1636$)

Note: Correlation coefficients (r) with $p<0.05$ were considered statistically significant.

Generalized Linear Model analysis showed that BMI, treatment year, and chemotherapy regimens had no statistically significant impact on PNI1, PNI2, or PNI3 ($p>0.05$). In contrast, albumin and NLR

demonstrated significant associations with PNI across all three time points, which is expected given that PNI is directly calculated from serum albumin and lymphocyte count [17] (Table 4).

Table 4

The impact of NAC status and other indicators on PNI indicators during 2008 and 2018

Indicator	PNI1 (Pre-NAC)	PNI2 (Pre-surgery)	PNI3 (Post-surgery)
Treatment year	F=0, Not Statistically Significant	F=0, Not Statistically Significant	F=0, Not Statistically Significant
NAC status	F=0, Not Statistically Significant	F=0, Not Statistically Significant	F=0, Not Statistically Significant
ALB	F=181.28, p<0.0001	F=149.31, p<0.0001	F=387.86, p<0.0001
NLR	F=23.14, p<0.0001	F=8.58, p=0.0045	F=26.19, p<0.0001
BMI	F=0.62, p=0.4380	F=0.44, p=0.5092	F=1.00, p=0.3199

The comparative analysis of patients treated in 2018 is presented in Table 5. The negative effect of NAC on PNI2 was statistically significant between the two treatment groups – those receiving standard chemotherapy alone and those receiving without

neoadjuvant chemotherapy (p=0.0076), while no significant difference was observed in PNI3 (p=0.9916). These findings indicate that the influence of NAC was confined to the pre-surgery phase.

Table 5

Effect of NAC on PNI index among patients in 2018

Time Point	NAC Group (n=53)	Non-NAC Group (n=50)	Mean Difference	t-test (p-value)	Cohen's d	Significance
PNI2 (Pre-surgery)	48.51±7.06	51.61±3.99	-3.10	0.0076	-0.54	Moderate
PNI3 (Post-surgery)	46.77±5.28	46.76±4.14	0.01	0.9916	0.01	None

Neoadjuvant chemotherapy (NAC) remains a key component in the management of locally advanced and biologically aggressive breast cancer [4]. Its therapeutic benefits extend beyond direct cytotoxic effects on rapidly proliferating tumor cells. NAC also influences the tumor microenvironment and modulates systemic immune responses, thereby enhancing tumor immunogenicity and increasing susceptibility to immune-mediated clearance [18-22]. Through these combined mechanisms, NAC contributes to higher rates of pathological complete response (pCR), which is strongly associated with improved long-term outcomes and survival [4, 23]. The type, sequence, and timing of chemotherapy regimens can affect these therapeutic responses, with some strategies demonstrating enhanced efficacy in tumor downstaging and control of micrometastatic disease [20].

Despite these therapeutic advantages, NAC often imposes considerable physiological stress, particularly on nutritional and immunologic reserves. Several nutritional markers, including the PNI, albumin, and BMI, can be adversely affected during chemotherapy, contributing to declines in patient well-being and functional status [10, 11, 16]. Therefore, moni-

toring these indicators is essential to ensure optimal patient management.

In the present study, NAC was associated with a significant decrease in preoperative PNI (PNI2), indicating a measurable reduction in nutritional reserves by the time of surgery. This pattern is consistent with known effects of cytotoxic drugs, which may reduce appetite, alter gastrointestinal function, and increase metabolic demands. Although the PNI values remained above the conventional “normal” threshold (>45), even a decline within this range can represent a meaningful reduction in physiological reserves [24]. Small decreases in PNI may lower tolerance to surgical stress, impair immune function, and increase vulnerability to complications. An additional point of interest is that postoperative PNI values were lower than preoperative values in both groups. This postoperative decline reflects the expected acute metabolic response to surgical trauma rather than treatment-induced deterioration. These findings are consistent with previous researches, where early postoperative reductions in nutritional indices reflect acute inflammatory and catabolic responses [25, 26]. Importantly, the magnitude of

decline was similar in NAC and non-NAC patients, indicating that NAC did not negatively affect post-operative recovery of nutritional status.

Moreover, older patients showed slightly lower PNI2 values, suggesting increased vulnerability in this subgroup. However, no significant differences were observed between NAC and non-NAC patients at baseline (PNI1) or at the early postoperative stage (PNI3). The absence of postoperative differences suggests partial recovery of nutritional status within the first week after surgery and indicates that the impact of NAC is largely confined to the pre-surgical interval.

The GLM analysis demonstrated that treatment year (2008 vs. 2018), BMI, and chemotherapy protocol did not exert independent effects on PNI. This absence of year-to-year variation implies that broader institutional practices, including nutritional monitoring and perioperative support, remained relatively consistent over time. In contrast, albumin and NLR were significantly associated with PNI across all time points, which aligns with their direct involvement in the PNI formula(17) and highlights their combined importance as indicators of nutritional and inflammatory status.

Taken together, these findings emphasize the importance of timely nutritional assessment and support in breast cancer patients receiving NAC. As PNI and albumin decline during chemotherapy, targeted interventions during the NAC period may help maintain physiological stability, improve tolerance to treatment, and prepare patients for surgery. While long-term nutritional impairment, defined as persisting beyond the immediate postoperative period, may not be universal among breast cancer patients, short-term, focused support, particularly in the pre-operative phase, may prevent deterioration and facilitate recovery. Future research should continue exploring structured, individualized nutritional strategies, including supplementation and routine monitoring of biochemical markers, to optimize treatment readiness and overall clinical outcomes.

CONCLUSION

1. This study demonstrates that neoadjuvant chemotherapy has a measurable impact on the nutritional status of breast cancer patients, primarily reflected by a significant reduction in preoperative prognostic nutritional index values. Although baseline and postoperative nutritional indicators did not differ between neoadjuvant chemotherapy and non-NAC groups, the decline observed at the pre-surgical phase highlights a critical period of increased physiological vulnerability. Age showed a modest association with lower preoperative prognostic nutritional index, while body mass index, treatment complications, and year of treatment did not independently influence nutritional outcomes. Albumin and neutrophil-to-lymphocyte ratio remained the strongest determinants of prognostic nutritional index across all time points.

2. These findings emphasize the need for timely nutritional assessment and targeted support during the neoadjuvant chemotherapy period to help preserve metabolic reserves and optimize readiness for surgery. Integrating structured nutritional strategies into routine breast cancer care may improve treatment tolerance and contribute to enhanced clinical outcomes

Contributors:

Moroz O. – conceptualization, investigation, methodology, software, visualization, writing – original draft;

Yin Q. – data curation, formal analysis, project administration, resources, supervision, writing – review & editing;

Li X. – formal analysis, funding acquisition, supervision, validation, writing – review & editing.

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