

RESEARCH ARTICLE

Editorial Process: Submission:06/09/2025 Acceptance:12/17/2025 Published:12/27/2025

Multimodal Prehabilitation in Indian Women with Advanced Ovarian Cancer: Enhancing Nutritional, Psychological, and Surgical Recovery

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Abstract

Background: Malnutrition is common among women with gynecologic cancers, particularly advanced ovarian cancer, and adversely impacts treatment tolerance, surgical recovery, and quality of life. The neoadjuvant chemotherapy (NACT) phase provides a unique opportunity to introduce prehabilitation interventions to improve perioperative outcomes. **Objective:** To evaluate the feasibility and impact of a culturally tailored, home-based multimodal prehabilitation program on perioperative outcomes in Indian women with advanced ovarian cancer undergoing NACT. **Methods:** Sixty women planned for NACT were enrolled and allocated to either a prehabilitation group (n = 30) or control group (n = 30). The intervention include yoga-based physiotherapy, individualized nutritional counseling, and psychological support. Outcomes assessed pre- and post-NACT included body mass index (BMI), hemoglobin, serum albumin, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), skeletal muscle index (SMI), Hospital Anxiety and Depression Scale (HADS) scores, in each group and between group comparisons of perioperative outcomes. **Results:** Both groups showed significant within-group improvements in nutritional and inflammatory markers. Between-group comparisons revealed a smaller decline in BMI (−1.29 vs. −4.51; $p < 0.001$) and a greater reduction in HADS scores (−4.5 vs. −1.5; $p = 0.013$) in the prehabilitation group. Hospital stay was significantly shorter in the prehabilitation group (median: 4 vs. 5.5 days; $p = 0.005$), while reductions in intraoperative blood loss and postoperative complications did not reach statistical significance. Greater physiotherapy session attendance correlated with reduced BMI loss ($\rho = -0.4187$, $p = 0.022$). Multivariable analysis showed that prehabilitation and physiotherapy adherence were associated with smaller BMI declines, and prehabilitation reduced the odds of prolonged hospitalization. **Conclusion:** Implementing a culturally adapted multimodal prehabilitation program is feasible and improves short-term nutritional, psychological, and perioperative outcomes in women undergoing NACT for advanced ovarian cancer.

Keywords: Ovarian Neoplasms- Preoperative Care- Prehabilitation- Nutritional Support- Psychological Adaptation

Asian Pac J Cancer Prev, 26 (12), 4575-4583

Introduction

Malnutrition is present at diagnosis in 56.2% of women with gynecologic cancers, with the highest rates observed in ovarian cancer 49.12% experiencing moderate and 19.3% severe malnutrition [1]. This high prevalence of nutritional deficiency, combined with the physical and psychological toll of the disease, significantly compromises treatment tolerance, surgical recovery, quality of life and overall outcomes in this patient population. Prehabilitation programs are emerging as a vital component of comprehensive cancer care, designed to enhance patients' functional and metabolic reserves

prior to undergoing major treatments. In the context of advanced ovarian cancer a condition marked by high symptom burden and extensive surgical requirements there exists a critical need to optimize patients' physical, nutritional, and psychological health before definitive surgery.

The neoadjuvant chemotherapy (NACT) phase, typically spanning 9–12 weeks before interval debulking surgery, presents a unique window of opportunity to introduce prehabilitation strategies. By leveraging this period, targeted interventions can mitigate the adverse effects of chemotherapy, preserve muscle mass, improve nutritional status, and bolster psychological resilience

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ultimately enhancing surgical readiness and recovery. While prehabilitation has demonstrated significant benefits in colorectal malignancies [2], its role in ovarian cancer remains underexplored. This gap is particularly striking in low- and middle-income countries like India, where cultural, socioeconomic, and logistical barriers often hinder access to structured preoperative care. Indian women with ovarian cancer frequently face challenges such as limited mobility, poor nutritional reserves, inadequate social support, and a high pre treatment-related fatigue, all of which can compromise treatment outcomes.

To address these gaps, we proposed the development and evaluation of a home-based, multimodal prehabilitation program tailored to the needs of Indian women undergoing NACT for advanced ovarian cancer. This program incorporated individualized exercise regimens, nutritional counseling, and psychological support delivered in a manner that is culturally sensitive, resource-appropriate, and logistically feasible. This pilot study aims to enhance perioperative fitness, nutritional performance, and short-term clinical outcomes, while offering a replicable model for use in similar low-resource settings.

Materials and Methods

A prospective study was conducted at the All-India Institute of Medical Sciences (AIIMS), New Delhi from July 2022 to June 2024, following approval from the Institutional Ethics Committee (IECPG–500/30.06.2022). A total of 60 consecutive women newly diagnosed with advanced ovarian cancer and planned for neoadjuvant chemotherapy (NACT) were recruited. Patients aged ≥ 18 years with an ECOG performance status of 0–3 who were willing to comply with the study protocol were included. Those with pre-existing inflammatory disorders, myopathy, malabsorption syndromes, recent pulse steroid therapy, or major surgery within the past 30 days were excluded.

Baseline Assessment

At recruitment, anthropometric measurements height, weight, and body mass index (BMI) were recorded. Biochemical assessments included serum albumin, hemoglobin, and calculation of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).

Nutritional Status Evaluation

Nutritional status was assessed using the Patient-Generated Subjective Global Assessment (PG-SGA) tool. Scores were derived from weight loss, nutritional impact symptoms, reduced intake, functional capacity, and physical evidence of muscle or fat loss or fluid retention. Based on these scores, patients were categorized as well-nourished, moderately malnourished or severely malnourished. Skeletal Muscle Index (SMI) was assessed via CT scans at the L3 vertebra using Core-Slicer software [3] (Figure 1). An SMI $< 38.5 \text{ cm}^2/\text{m}^2$ was defined as indicative of sarcopenia [4].

Thirty patients were enrolled in the intervention group. A structured multimodal prehabilitation program was implemented, comprising the following components:

Medical Optimization

Management of comorbid conditions such as diabetes, hypertension, and hypothyroidism.

Yoga-Based Physical Therapy

A regimen consisting of at least 150 minutes of light to moderate aerobic activity per week, conducted over 2–3 sessions of ~60 minutes each. Sessions were available on all weekdays and could be attended either in person during hospital visits for follow-up or chemotherapy, or remotely from home under supervision of a physiotherapist via an online platform. These sessions included aerobic exercises, static and dynamic stretches (Yogasana), and breathing techniques (Pranayama). Patients also underwent inspiratory muscle training using an incentive spirometer for 10-minute sessions every 8 hours, as per American College of Sports Medicine guidelines.

Nutritional Intervention

Individual dietary consultations were aimed to achieve a minimum intake of 25 kcal/kg and 1–1.2 g protein/kg per day through food and oral nutritional supplements. Nutrition impact symptoms were addressed during one-on-one counseling, and patients were encouraged to follow a high-protein, high-energy diet. A 3-day food diary (including 1 weekend and 2 weekdays) was maintained and evaluated within a week. Ongoing monitoring was conducted via telephone follow-up, with supplementation of vitamin D, vitamin B complex, and iron as needed to maintain hemoglobin $\geq 11 \text{ g/dL}$.

Psychological Support

Patients were taught relaxation and deep breathing techniques, to be practiced at least three times a week and during periods of heightened stress. Psychological distress was evaluated using the Hospital Anxiety and Depression Scale (HADS). Patients with HADS scores > 7 were referred for psychiatric evaluation and treated with cognitive behavioral therapy or medication, if necessary.

The control group received standard preoperative instructions, which included a high-protein diet, daily walking for 30 minutes, and regular use of an incentive spirometer.

Outcome Assessment

The impact of the prehabilitation program was evaluated using pre- and post-intervention comparisons of anthropometric measurements (weight, BMI), skeletal muscle index, inflammatory markers (albumin, NLR, PLR) and HADS scores. Following completion of 9–12 weeks of NACT, all patients underwent interval cytoreductive surgery. All cytoreductive surgeries were conducted by experienced gynecologic oncologists. Surgical complexity was assessed using the Aletti score [5], and the peritoneal cancer index (PCI) was calculated based on the European Society of Gynaecological Oncology's Ovarian Cancer Operative Report [6]. Intraoperative blood loss and duration of hospital stay were recorded. Postoperative complications within 30 days were assessed and graded using the Clavien-Dindo classification [7].

Statistical Analysis

Data were analyzed using Stata 18. Results are presented as mean \pm standard deviation, median (interquartile range), or frequency (%), as appropriate. Categorical variables were compared using the chi-square or Fisher's exact test, and within-group changes were assessed using McNemar's test. Continuous variables were analyzed using t-tests for normally distributed data, and the Wilcoxon rank-sum test for non-normal distributions. Correlation between continuous variable was assessed by Spearman correlation coefficient. Paired tests were used for within-group comparisons. A p-value <0.05 was considered statistically significant.

Results

The baseline characteristics of the intervention and control groups were largely comparable, with no significant differences in age, BMI, comorbidities, smoking or alcohol use, disease stage, or biochemical markers including albumin, NLR, and PLR. However, haemoglobin was significantly lower in the control group (11.28 ± 1.41 vs. 10.43 ± 1.72 ; $p = 0.040$). CA125 levels, reflecting disease burden, and skeletal muscle index were similar between groups. The prevalence and severity of malnutrition, assessed by PG-SGA scores, were also comparable (Table 1).

Patients in the intervention group participated in a multimodal prehabilitation program over 9–12 weeks while receiving neoadjuvant chemotherapy. Participants were encouraged to attend three physiotherapy sessions per week, targeting 27 to 36 sessions across the program duration. The median number of sessions attended was 14, with a range of 3 to 66 sessions. Attendance varied: 40% attended fewer than 10 sessions, 33.3% attended between 20 and 30, 16.7% attended 30 to 40, and 10% exceeded 40 sessions. Patients underwent baseline assessments of caloric and protein intake, received individualized diet plans, and were reassessed after a median of 28 days

(IQR: 21–38 days). At baseline, the median caloric deficit was 27.75% (range: 3.71%–63.75%), which improved to 15.81% (range: 0.71%–57.50%) at follow-up. Similarly, the median protein deficit decreased from 32.86% (range: 5.45%–63.08%) to 25.00% (range: 6.67%–56.67%) post-intervention. A comparison of markers before and after NACT in both the experimental and control groups is presented in Table 2.

Following neoadjuvant chemotherapy and the prehabilitation program, both groups experienced a reduction in BMI following neoadjuvant chemotherapy, the decline was significantly smaller in the prehabilitation group (-1.29 ± 2.70 vs. -4.51 ± 2.38 ; $p < 0.001$). Haemoglobin levels decreased in the prehabilitation group but increased in the control group (-0.69 ± 1.97 vs. $+0.47 \pm 1.73$; $p = 0.018$). Both groups showed improvements in serum albumin levels, though the intergroup difference was not significant ($p = 0.740$). Inflammatory markers, including the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio, declined significantly within each group, but without a significant difference between groups. The skeletal muscle index decreased slightly in both arms, with no statistically significant change observed. Nutritional status, as assessed by PG-SGA scores and categories, improved significantly in both groups following neoadjuvant chemotherapy, with 70% of patients in each group achieving PG-SGA Category A (no malnutrition) post-NACT. Psychological outcomes also improved more in the prehabilitation group, with a greater reduction in HADS scores (-4.5 vs. -1.5 ; $p = 0.013$) and a higher proportion of patients achieving normal scores (56.7% vs. 36.7%; $p = 0.006$). These findings highlight the potential of prehabilitation to attenuate nutritional and psychological decline during neoadjuvant chemotherapy for advanced ovarian cancer.

In the prehabilitation group, Spearman's rank correlation demonstrated a moderate, statistically significant inverse relationship between the number of physiotherapy sessions and BMI change ($\rho = -0.4187$, p

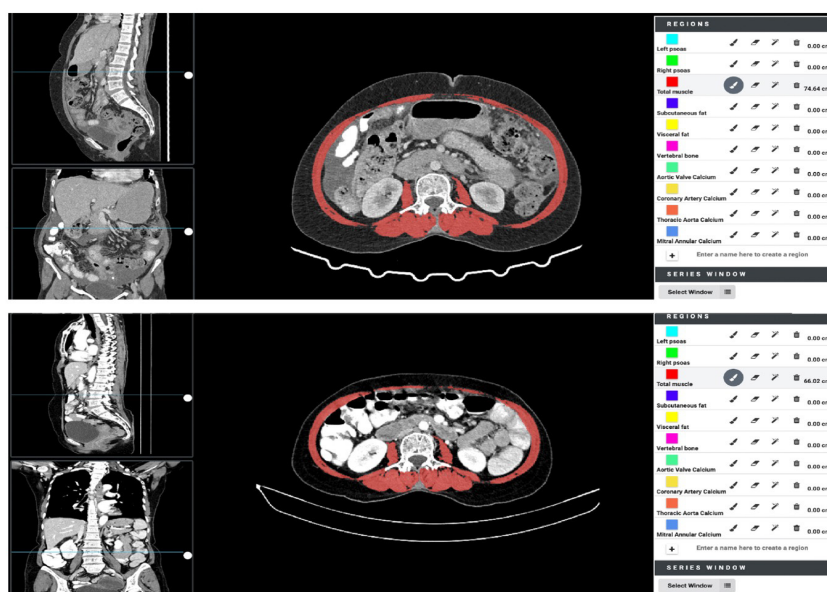


Figure 1. Evaluation of Skeletal Muscle Area Using the CoreSlicer Web Tool in a Participant at Baseline and after Prehabilitation

Table 1. Baseline Characteristics of Prehabilitation and Control Groups in Patients with Epithelial Ovarian Cancer Undergoing Neoadjuvant Chemotherapy

	Prehabilitation Group (n=30)	Control Group (n=30)	p-value
Age (years) (Mean + SD)	52.63 + 10.69	51.1 + 8.54	0.542*
BMI (Mean + SD)	24.63 + 6.05	25.59 + 4.43	0.486*
Comorbidities:			
Diabetes mellitus	4 (13.33%)	8 (26.67%)	0.333†
Number of comorbidities:			
0	17 (56.67%)	17 (56.67%)	0.707†
1	4 (13.33%)	6 (20.00%)	
>2	9 (30.00%)	7 (23.33%)	
Regular Smoker	2 (6.67%)	1 (3.33%)	1.000‡
Alcohol Consumption	0 (0.00%)	0 (0.00%)	
Disease Stage			
IIIC	19 (63.33%)	23 (76.67%)	0.612†
IVA	4 (13.33%)	3 (10.00%)	
IVB	7 (23.33%)	4 (13.33%)	
Histology			
High grade serous	28 (93.33%)	29 (96.67%)	0.167†
Low grade serous	1 (3.33%)	1 (3.33%)	
High grade endometrioid	1 (3.33%)	0 (0.00%)	
ECOG	1 (1-2)	1 (0-1)	0.036‡
CA125 (U/mL) [Median (IQR)]	1136 (559, 2624)	651.5 (328, 1526)	0.098‡
Haemoglobin (g/dL) (Mean + SD)	11.28 + 1.41	10.43 + 1.72	0.040*
Albumin (g/dL) (Mean + SD)	3.69 + 0.54	3.71 + 0.55	0.860*
Neutrophil-to-Lymphocyte Ratio [Median (IQR)]	3.62 (2.51, 6.45)	4.49 (2.70, 7.56)	0.605‡
Platelet-to-Lymphocyte Ratio [Median (IQR)]	222.49 (145.68, 386.03)	248.28 (137.93, 433.56)	0.989‡
Skeletal Muscle Index (Mean + SD)	38.64 + 7.21	38.41 + 5.28	0.885*
PG-SGA Scores	15 (10, 20)	12.5 (9, 19)	0.454‡
PG-SGA Category:			
A (No Malnutrition)	2 (6.67%)	0 (0.00%)	0.389†
B (Moderate Malnutrition)	14 (46.67%)	18 (60.00%)	
C (Severe Malnutrition)	14 (46.67%)	12 (40.00%)	

*Independent Samples t-test †Fisher's Exact Test ‡Mann-Whitney U Test

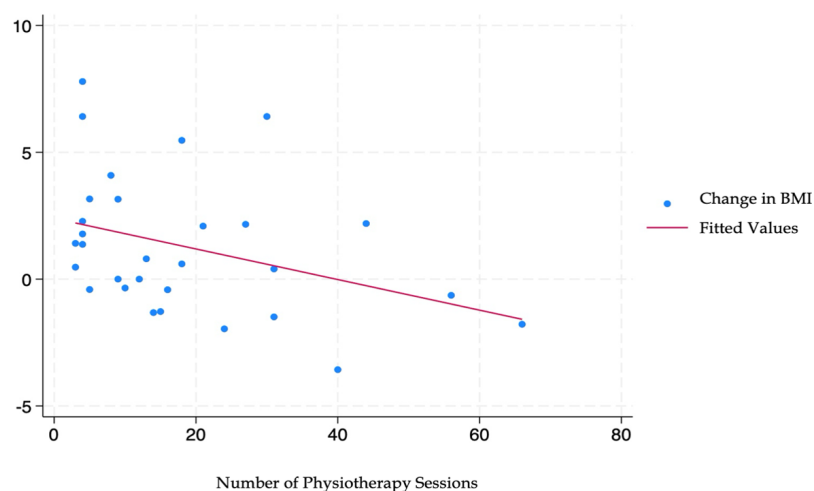


Figure 2. Scatter Plot Showing the Relationship between the Number of Physiotherapy Sessions Attended and Change in BMI in the Prehabilitation Group

Table 2. Comparison of Nutritional and Inflammatory Markers, and Skeletal Muscle Index in Prehabilitation vs. Control Groups at Baseline and Post-NACT

	Prehabilitation Group				Control Group				Intergroup p-value
	(n=30)				(n=30)				
	Baseline	Post-NACT	Δ (Change) [†]	Within group p-value	Baseline	Post-NACT	Δ (Change) [†]	Within group p-value	
BMI (Mean + SD)	24.63 + 6.05	23.34+5.08	1.41	0.014*	25.59 + 4.43	21.09 + 3.72	-2.13	0.000*	0.000§
Haemoglobin (Mean + SD)	11.28 + 1.41	10.59+1.25	1.28	0.065*	10.43 + 1.72	10.91 + 1.019	0.47 + 1.73	0.141*	0.018§
Albumin (g/dL) (Mean + SD)	3.69 + 0.54	4.1 + 0.57	0.41 + 0.74	0.005*	3.71 + 0.55	4.19 + 0.78	0.48 + 0.78	0.002*	0.740§
Neutrophil-to-Lymphocyte Ratio [Median (IQR)]	3.62 (2.51, 6.45)	1.73 (1.55, 3.1)	-1.75 (-4.69, -0.79)	0.002‡	4.49 (2.70, 7.56)	1.65 (1.11, 2.41)	-2.57 (-5.08, -0.97)	0.000‡	0.344‡
Platelet-to-Lymphocyte Ratio [Median (IQR)]	222.49 (145.68, 386.03)	106.73 (88.94, 132.05)	-116.38 (-213.17, -40.05)	0.000‡	248.28 (137.93, 433.56)	144.93 (83.13, 194.37)	-144.94 (-238.83, 6.97)	0.002‡	0.183§
Skeletal Muscle Index (Mean + SD)	38.64 + 7.21	37.31+7.05	2.88	0.093*	38.41 + 5.28	38.04 + 5.17	1.43	0.268*	0.254§
PG-SGA Scores [Median (IQR)]	15 (10, 20)	1 (1, 5)	-11 (-17, -6)	0.000‡	12.5 (9, 19)	3 (1, 5)	-9.5 (-15, -4)	0.000‡	0.343‡
PG-SGA Category:									
A (No Malnutrition)	2 (6.67%)	21 (70.00%)		0.000 ^{III}	0 (0.00%)	21 (70.00%)		0.000 ^{III}	
B (Moderate Malnutrition)	16 (53.3%)	8 (26.67%)			18 (60.00%)	8 (26.67%)			
C (Severe Malnutrition)	12 (40.0%)	1 (3.33%)			12 (40.00%)	1 (3.33%)			
HADS Score [Median (IQR)]	10 (7, 14)	6.5 (3, 10)	-4.5 (-9, -2)	0.000‡	10 (6, 14)	10 (6, 13)	-1.5 (-5, 2)	0.103‡	0.013‡
Normal Score (0-7)	8 (26.7%)	17 (56.7%)		0.000 ^{III}	8 (26.7%)	11 (36.7%)		0.098 ^{III}	
Mild distress (8-11)	9 (30.0%)	7 (23.3%)			9 (30.0%)	7 (23.3%)			
Moderate distress (11-15)	6 (20.0%)	4 (13.3%)			6 (20.0%)	6 (20.0%)			
Severe distress (>16)	7 (23.3%)	2 (6.7%)			7 (23.3%)	6 (20.0%)			

† Δ (Change) = Post-NACT value – Baseline value. Negative values indicate a reduction * Paired t-test ‡ Wilcoxon rank-sum test § Independent t-test; III, McNemar Test

Table 3. Surgical Characteristics and Perioperative Outcomes of Patients Undergoing Interval Cytoreduction for Advanced Ovarian Cancer: Comparison between Multimodal Prehabilitation and Control Groups

	Prehabilitation Group (n=30)	Control Group (n=30)	p-value
Peritoneal Carcinomatosis Index [Median (Range)]	9 (4–18)	9 (3–20)	0.732*
Procedures Performed			
Hysterectomy – salpingo-oophorectomy	30 (100.00%)	30 (100.00%)	
Total Omentectomy	30 (100.00%)	30 (100.00%)	
Excision of Pelvic Lymph Nodes	12 (40.00%)	11 (36.67%)	
Excision of Para-aortic Lymph Nodes	10 (33.33%)	9 (30.00%)	
Pelvic Peritoneum Stripping	15 (50.00%)	13 (43.33%)	
Abdominal Peritoneum Stripping	9 (30.00%)	10 (33.33%)	
Diaphragm Stripping	6 (20.00%)	7 (23.33%)	
Rectosigmoidectomy	4 (13.33%)	5 (16.67%)	
Splenectomy	2 (6.67%)	1 (3.33%)	
Surgical Complexity Score [Median (Range)]	5 (3–8)	5 (2–9)	0.899*
Complexity Score Groups:			
Low (<3)	5 (16.67%)	6 (20.00%)	
Intermediate (4-7)	19 (63.33%)	18 (60.00%)	
High (>8)	6 (20.00%)	6 (20.00%)	
Residual Disease:			0.313†
CC0	21 (70.00%)	19 (63.33%)	
CC1	5 (16.67%)	5 (16.67%)	
CC2	3 (10.00%)	1 (3.33%)	
CC3	1 (3.33%)	5 (16.67%)	
Intraoperative Blood Loss (ml) [Median (IQR)]	500 (400-750)	700 (300-800)	0.744*
Hospital Stay (days) [Median (IQR)]	4 (4-5)	5.5 (5-7)	0.005*
Postoperative Complication <30 days (Clavien-Dindo Classification)	11 (36.67%)	15 (50.00%)	0.674†
Grade 1	0 (0.00%)	1 (3.33%)	
Grade 2	7 (23.33%)	9 (30.00%)	
Grade 3	4 (13.33%)	5 (16.67%)	
Type of Complication			
Surgical Site Infections	3 (10.00%)	5 (16.6%)	0.706†
Blood Transfusions	6 (20.00%)	7 (23.33)	1.000†
Paralytic Ileus	1 (3.33%)	1 (3.33%)	1.000†
Urinary Retention	1 (3.33%)	0 (0.00%)	1.000†
Febrile Illness	0 (0.00%)	1 (3.33%)	1.000†

* Wilcoxon rank-sum test † Fisher's Exact Test

= 0.022), indicating that greater session attendance was associated with less reduction in BMI. This relationship is illustrated in the scatter plot (Figure 2), with a fitted regression line showing the trend. In multivariable linear regression, higher baseline BMI was associated with greater BMI loss during chemotherapy. In contrast, prehabilitation and greater physiotherapy adherence were independently associated with significantly smaller declines in BMI, with each additional physiotherapy session linked to a 0.07-unit lesser BMI loss. (Supplementary Table 1)

All 30 patients underwent interval cytoreductive surgery. The prehabilitation and control groups were comparable in surgical characteristics, including intraoperative disease burden (PCI), types of surgical

procedures performed, and surgical complexity scores. (Table 3).

The prehabilitation group had a significantly shorter hospital stay (median 4.0 vs. 5.5 days, $p = 0.005$). The intraoperative blood loss (median 500 mL vs. 700 mL, $p = 0.744$) and the incidence of postoperative complications (36.7% vs. 50.0%, $p = 0.674$) were also lower in the prehabilitation group, although these differences did not reach statistical significance.

Multivariable logistic regression was performed to assess predictors of prolonged hospital stay (>4 days), including clinical factors (preoperative BMI, comorbidities, skeletal muscle index, malnutrition), biochemical markers (preoperative serum albumin, neutrophil-to-lymphocyte

Table 4. Summary of Study Findings on Prehabilitation in Advanced Epithelial Ovarian Cancer

Study Details	Prehabilitation Program	Key Outcomes
Miralpeix et al., 2022 (Spain) [11] • Retrospective, single-center study • 29 patients (14 prehabilitation, 15 control)	• Individualized dietary plan with homemade protein supplements • VO2max-based exercise: walking, resistance training, inspiratory muscle training; supervised or home-based • Psychological support (relaxation, mindfulness)	• Higher in prehabilitation group: serum protein (4.9 ± 0.6 vs. 4.3 ± 0.7 , $p = 0.005$), albumin (2.8 ± 0.4 vs. 2.4 ± 0.6 , $p = 0.021$) • Lower intraoperative transfusion rate (2 vs. 8, $p = 0.027$) • Non-significant reduction in complications (14.3% vs. 40%, $p = 0.518$) • No significant difference in hospital stays (7.4 ± 5.0 vs. 7.8 ± 6.8 days, $p = 0.700$)
Diaz-Feijoo et al., 2022 (Spain) [12] • Prospective, single-center study • 34 patients (15 prehabilitation, 19 control) • Duration: 2–4 weeks	• Personalized nutritional plan with whey protein and immunomodulatory formula • Functional capacity-guided exercise (6-MWT, VO2max), inspiratory muscle training, hospital/home-based plan • Psychological support	• Higher in prehabilitation group: prealbumin (0.235 vs. 0.180 g/L, $p = 0.007$), shorter time to chemotherapy (25 vs. 35 days, $p = 0.03$) • Non-significant reduction in complications (40% vs. 63%, $p = 0.3$); no grade III events in prehabilitation group • Shorter hospital stays (5 vs. 7 days, $p = 0.04$)
Sebio-Garcia et al., 2025 (Spain) [13] • Ambispective, single-center cohort • 62 patients underwent prehabilitation • Duration: 4–7 weeks	• Dietary counseling, whey protein, immunomodulatory formula • Supervised endurance and resistance training • Psychological support (coping strategies, stress reduction)	• Improved 6-minute walk test post-intervention • In a subset ($n = 23$), significant muscle mass gain by BIA ($+0.33$ kg; 95% CI: 0.1–0.6; $p = 0.015$)
Current Study • Prospective, single-center study • 60 patients (30 prehabilitation, 30 control) • Duration: 9–12 weeks	• Personalized nutritional plan with home-based protein supplementation • Home-based yoga (3 sessions/week), adapted to patient capacity • Psychological support	• Higher in prehabilitation group: reduced calorie and protein deficits, improved mental health, and smaller BMI decline during NACT (-1.29 vs. -4.51 , $p < 0.001$) • Non-significant reduction in complications (36.7% vs. 42.9%, $p = 0.674$) and blood loss (500 vs. 700 ml, $p = 0.744$) • Significantly shorter hospital stays (4 vs. 5.5 days, $p = 0.000$)

ratio [NLR], platelet-to-lymphocyte ratio [PLR]), disease burden (FIGO stage, CA125, peritoneal cancer index [PCI]), surgical complexity score, prehabilitation status, and occurrence of postoperative complications. Among these, only prehabilitation was significantly associated with reduced odds of prolonged hospitalization (OR = 9.47, 95% CI: 1.87–48.01, $p = 0.007$). No other clinical, biochemical, or surgical factors were independently associated with length of stay. (Supplementary Table 2).

Discussion

Prehabilitation is increasingly recognized as a vital component of multidisciplinary cancer care, with growing evidence supporting its role across various tumor types. A meta-analysis of randomized controlled trials on prehabilitation reported that lung cancer accounted for the largest share (38%), followed by colorectal (27%) and prostate cancer (18%). Other cancers, such as esophageal (5%), and bladder, pancreatic, breast, stomach, and liver cancers (2% each), were less commonly represented [8]. In lung cancer, pulmonary prehabilitation has demonstrated benefits in improving lung function, reducing postoperative complications, and shortening hospital stays [9]. In colorectal cancer, prehabilitation has been associated with improved preoperative functional status and shorter postoperative hospitalization, although its effect on postoperative complications remains

inconclusive [2, 9].

Among gynecologic malignancies, few studies have assessed perioperative outcomes following prehabilitation, primarily in endometrial and ovarian cancers. In endometrial cancer, combining prehabilitation with ERAS protocols significantly reduced hospital stay by one day ($p < 0.001$) and led to earlier initiation of normal oral intake by 3.6 hours ($p = 0.005$) [10].

Patients with advanced ovarian cancer are particularly vulnerable to perioperative complications due to extensive surgical requirements, high symptom burden, and chemotherapy-induced immunosuppression. A few pilot studies (Table 4) have evaluated prehabilitation in this group. Despite variations in the duration (2 to 12 weeks) and components of the interventions, all trials integrated multimodal strategies involving nutrition, exercise, and psychological support.

Improvement in nutritional biomarkers was a consistent finding across studies. Functional gains and improvements in body composition were reported by Sebio-Garcia et al. [13], with significant increases in 6-minute walk test performance and muscle mass. Our study similarly showed smaller BMI decline and improved mental health during NACT in the prehabilitation group. Significant reductions in hospital stay were observed across the studies, reflecting faster surgical recovery with prehabilitation. Although postoperative complications were numerically lower in the prehabilitation groups,

the differences were not statistically significant a pattern also noted in meta-analyses of prehabilitation trials in colorectal cancer.

In our study, inflammatory indices (NLR and PLR) declined, and serum albumin improved comparably in both prehabilitation and control groups following NACT, reflecting the inflammatory basis of cancer and its partial resolution with chemotherapy. The similar rise in albumin levels in both arms reinforces its role as a negative acute-phase reactant rather than a sensitive nutritional marker. Although Miralpeix et al. reported higher albumin levels in the prehabilitation group, mean albumin values before surgery still fell within the hypoalbuminemic range, indicating persistent nutritional compromise despite intervention. Diaz-Feijoo et al. [12] additionally assessed prealbumin, a more sensitive indicator of nutritional improvement, which was significantly higher in the prehabilitation arm.

We did not observe a significant change in skeletal muscle index post-intervention. In contrast, Sebío-García et al. reported muscle mass gains in a subset of 23 patients assessed by bioimpedance analysis before and after prehabilitation, despite a shorter intervention period. Skeletal muscle serves as the body's primary protein reservoir, and its loss is a defining feature of disease-related malnutrition. Further insights are expected from the ongoing OPTIMOVA trial (NCT05415527), which is investigating sarcopenia prevention through personalized nutrition and physical activity in patients with inoperable ovarian cancer.

Adherence to prehabilitation protocols remains a critical challenge, necessitating context-specific strategies to enhance participation. Diaz-Feijoo et al. reported that 86.7% of participants attended over 75% of sessions, despite the requirement for hospital-based supervision [12]. However, in low- and middle-income countries (LMICs), where many women come from socioeconomically disadvantaged backgrounds, additional hospital visits impose a significant financial burden and contribute to physical and emotional fatigue for both patients and caregivers. A systematic review identified several factors influencing adherence, including individual-level motivators (such as perceived benefit and personal commitment) and the delivery model of the intervention. Home-based prehabilitation, supported by remote professional supervision, offers a practical and accessible alternative. The use of mobile technology often referred to as 'digital' or 'e-prehabilitation' can further improve engagement by enabling communication, feedback, and automated reminders [14].

In our study, adherence was enhanced by aligning the prehabilitation program with the existing neoadjuvant chemotherapy schedule, thereby eliminating the need for additional hospital visits. In fact, we observed an inverse relationship between the number of physiotherapy sessions attended and the magnitude of BMI decline, suggesting a dose-response effect and underscoring the importance of sustained participation. Nutritional counseling was tailored to regional dietary habits, and cost-effective, home-based protein and micronutrient supplements replaced commercial formulations to

improve both cultural acceptability and affordability. Yoga formed the cornerstone of our physiotherapy protocol. As a culturally ingrained practice in India, yoga provided a holistic approach to physical and psychological conditioning. It incorporates dynamic movements (e.g., Vinyasa), static strength-based postures (e.g., Hatha yoga), breathing exercises (pranayama), and mindfulness techniques elements shown to reduce cancer-related fatigue, psychological distress [15], cognitive dysfunction [16], and sleep disturbances [17]. Notably, two patients in our cohort continued regular yoga practice even after remission, underscoring its long-term acceptability and potential for sustained benefit.

While our findings are encouraging, certain limitations must be acknowledged. The relatively small sample size may limit the power to detect statistically significant differences in outcomes such as intraoperative blood loss and postoperative complications. The non-randomized, single-center design introduces potential for selection bias and reduces generalizability. Lack of blinding may have affected subjective assessments, such as HADS scores. Finally, the study focused on short-term perioperative outcomes; long-term effects on recovery, recurrence, or survival were not evaluated.

Several ongoing randomized trials (the PADOVA trial (NTR6300), PHOCUS (NCT04789694), TEAL (NCT05761561), and PROADAPT (NCT04284969)) are anticipated to clarify the role of prehabilitation and contribute to standardizing its structure within gynecologic oncology.

In conclusion, our study supports the feasibility and effectiveness of a culturally adapted, multimodal prehabilitation program for Indian women with advanced ovarian cancer undergoing neoadjuvant chemotherapy. By integrating personalized dietary counseling, home-based supplementation, psychological support, and yoga-based physiotherapy into routine care without additional hospital visits, we demonstrated improvements in nutritional intake, mental well-being, and length of hospital stay. These findings add to the growing body of evidence supporting individualized, low-cost, and scalable prehabilitation strategies in resource-limited settings. Future multicentric, randomized trials with standardized protocols and objective functional metrics are warranted to validate these outcomes and further define the role of prehabilitation in gynecologic oncology.

Author Contribution Statement

Saroj Rajan – Conceptualization, Methodology, Formal Analysis, Investigation, Data Curation, Writing – Original Draft. Neena Malhotra – Supervision. Ekta Dhamija – Validation, Resources. Parmeet Kaur – Investigation, Resources. Raj Kumar Yadav – Investigation, Resources. Nilanchali Singh – Resources. Sachin Khurana – Resources. Koushik Sinha Deb – Investigation, Resources. Ashish Datt Upadhyay – Formal Analysis. Neerja Bhatla – Supervision. Seema Singhal – Conceptualization, Methodology, Validation, Formal Analysis, Writing – Review & Editing, Supervision

Acknowledgements

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Scientific Body/Thesis Statement

This study was conducted as part of the MCh Gynaecologic Oncology thesis submitted to the All India Institute of Medical Sciences, New Delhi.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Presentations

This study has been submitted as an abstract to the IGCS 2025 Annual Global Meeting.

Trial Registration

This trial was prospectively registered with the Clinical Trials Registry – India (CTRI), Reference Number: REF/2023/02/063825.

Ethical Approval

This study was approved by the Institute Ethics Committee of All India Institute of Medical Sciences, New Delhi (Ref. No. IEC-888/03.09.2021, RP-40/2021).

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