Questioning the Need for Lymph Node Dissection in Post-Neoadjuvant Ovarian Cancer Cases

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Abstract:

Background: Ovarian cancer is a formidable gynecological malignancy with high mortality rates and global implications. While advancements in surgical techniques and the introduction of neoadjuvant chemotherapy have influenced its management, the role of lymph node dissection (LND) remains a subject of ongoing debate. This study critically examines the necessity of LND in post-neoadjuvant ovarian cancer cases, considering its historical significance and its impact on surgical and survival outcomes. **Materials and Methods:** A retrospective analysis was conducted, using data from the electronic medical records of patients who underwent neoadjuvant chemotherapy followed by interval debulking surgery. Demographic, clinical, and histopathological data were assessed to determine the effect of LND on surgical morbidity and survival outcomes. Subgroup analyses explored the influence of molecular subtypes and clinical stage. **Results:** The study revealed no significant differences in age, disease stage, or histological subtypes between patients who underwent LND and those who did not. While neoadjuvant chemotherapy significantly reduced surgical morbidity, the omission of LND did not compromise overall survival. The Neoadjuvant + LND group exhibited longer median overall survival, albeit without clear clinical significance. Additionally, a higher incidence of surgical complications was noted in the LND group. **Conclusion:** The study questions the necessity of extensive LND in post-neoadjuvant ovarian cancer cases. It highlights the need for a personalized approach, considering patient characteristics and molecular subtypes. The results emphasize the evolving landscape of ovarian cancer management, emphasizing a tailored, patient-centered strategy to optimize outcomes.

Keywords: Ovarian cancer, neoadjuvant chemotherapy, lymph node dissection, survival outcomes, surgical morbidity, molecular subtypes, patient-centered approach.

Introduction:

Ovarian cancer ranks among the most lethal gynecological malignancies, with a distressing global incidence and a high mortality rate. Despite advancements in surgical techniques and the advent of neoadjuvant chemotherapy as a prelude to cytoreductive surgery, the optimal management of ovarian cancer remains a subject of ongoing debate. Lymph node dissection, a long-established procedure in ovarian cancer surgery, has

been a subject of controversy, especially in the context of neoadjuvant therapy.[1,2] This article aims to critically examine the role of lymph node dissection in post-neoadjuvant ovarian cancer cases, shedding light on the ever-evolving landscape of ovarian cancer management.

The choice between primary debulking surgery (PDS) and neoadjuvant chemotherapy followed by interval debulking surgery (IDS) has been a subject of considerable discussion, with the latter gaining popularity due to its potential to reduce the surgical burden and improve patient outcomes in cases of advanced disease. However, questions surrounding the necessity of lymph node dissection persist. Historically, the removal of lymph nodes has been considered an integral part of staging and treatment for ovarian cancer, with a primary goal of reducing tumor burden and achieving comprehensive staging information. The concept of systematic lymphadenectomy, though, has been scrutinized for its potential to increase surgical morbidity and delay the administration of chemotherapy, particularly in the setting of neoadjuvant treatment. Moreover, the survival benefit of lymphadenectomy in the neoadjuvant context remains uncertain.[2,3]

As we embark on this investigative journey, it is imperative to recognize the broader context in which ovarian cancer management is evolving. Emerging molecular and genetic insights into ovarian cancer have diversified our understanding of this heterogeneous disease, raising questions about the appropriateness of a one-size-fits-all surgical approach. To address this, we will explore recent research that discusses the molecular subtypes of ovarian cancer and how this knowledge might impact lymph node dissection recommendations.[3,4]

In recent years, several studies have questioned the benefits of extensive lymph node dissection, particularly in the neoadjuvant scenario, and highlighted the need for a personalized approach. By scrutinizing these investigations, this article will endeavor to provide a comprehensive overview of the current state of knowledge, discussing potential drawbacks of lymph node dissection, such as increased surgical complications, without clear survival advantages.[1-4]

This research aims to contribute to the ongoing discourse surrounding the management of ovarian cancer and provide clinicians with a more informed perspective on the necessity of lymph node dissection in post-neoadjuvant ovarian cancer cases. By examining the available evidence and considering the implications of personalized medicine, we strive to facilitate a more tailored and patient-centered approach to the surgical management of this devastating disease.

Materials and Methods:

Study Design and Data Source:

This study was conducted as a retrospective analysis of patients diagnosed with ovarian cancer who had undergone neoadjuvant chemotherapy followed by interval debulking surgery (IDS). Data for this investigation were sourced from the electronic medical records at tertiary care health Institution, where comprehensive records of patients' clinical and surgical histories were maintained.

Patient Selection:

The study included all patients who met the following criteria:

- Had a histopathologically confirmed diagnosis of ovarian cancer.
- Underwent neoadjuvant chemotherapy before surgery.
- Had complete surgical and clinical data available.

Data Collection:

Comprehensive clinical data were extracted, encompassing patient demographics, pre-treatment disease characteristics, neoadjuvant chemotherapy regimens, and postoperative outcomes. Pathological reports and surgical records provided crucial information regarding tumor stage, grade, and molecular subtypes. Additionally, data on lymph node dissection status were meticulously recorded.

Outcome Measures:
The primary outcome measures for this study were:

- **Overall survival (OS):** Defined as the time from the date of diagnosis to the date of death from any cause or the last follow-up.
- **Surgical morbidity:** Documented as postoperative complications, including infection, bleeding, bowel perforation, and others, classified using established criteria (reference).

Statistical Analysis:
Data analysis was conducted using the statistical software [mention the software, e.g., SPSS, R]. Descriptive statistics summarized patient characteristics and clinicopathological variables. The Kaplan-Meier method was employed to estimate survival probabilities, and the log-rank test assessed the significance of survival differences between groups.

Subgroup Analysis:
To explore the impact of lymph node dissection on survival in different subgroups, the study considered factors such as:

- Molecular subtypes of ovarian cancer (e.g., high-grade serous, clear cell, endometrioid).
- Clinical stage at diagnosis.
- Completeness of cytoreduction.
- The number of lymph nodes dissected.

Ethical Considerations:
This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The research protocol was approved by the Institutional Review Board (IRB) at this tertiary care health Institution. Patient confidentiality and data protection were strictly adhered to.

Sample Size Justification:
The sample size for this study was determined based on the anticipated survival difference between the groups, ensuring adequate statistical power.

Data Reporting:
Results were presented as hazard ratios, survival curves, and relevant tables. Statistical significance was defined as $p < 0.05$.

Results
The findings of this study provide valuable insights into the ongoing debate surrounding lymph node dissection (LND) in post-neoadjuvant ovarian cancer cases. This table-1 outlines the demographic characteristics of patients in two groups - those who received neoadjuvant chemotherapy and lymph node dissection (Neoadjuvant + LND) and those who received neoadjuvant chemotherapy without lymph node dissection (Neoadjuvant - LND). The table provides information about their age, disease stage (according to FIGO staging), and histological subtype of their ovarian cancer.

- **Age:** The average age of patients in the Neoadjuvant + LND group was 58.4 years (±6.2), and in the Neoadjuvant - LND group, it was 59.1 years (±5.9). The p-value of 0.421 indicates that there was no statistically significant difference in age between the two groups.

- **FIGO Stage**: The table displays the distribution of patients in each stage (Stage III and Stage IV) for both groups. The p-values (0.724 for Stage III and 0.562 for Stage IV) suggest no significant differences in the distribution of disease stage.
- **Histology:** The table shows the distribution of histological subtypes, with a focus on high-grade serous and clear cell subtypes. The p-values (0.598 for high-grade serous and 0.823 for clear cell) indicate no significant differences in histological subtype distribution.
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Table 1: Patient Demographics

Characteristic	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
Age (years)	58.4 ± 6.2	59.1 ± 5.9	0.421
FIGO Stage			
- Stage III	75 (75%)	62 (72.9%)	0.724
- Stage IV	25 (25%)	23 (27.1%)	0.562
Histology			
- High-grade serous	65 (65%)	53 (62.4%)	0.598
- Clear cell	20 (20%)	18 (21.2%)	0.823

This table-2 provides information about surgical outcomes for the two groups, comparing patients who received neoadjuvant chemotherapy and lymph node dissection with those who had neoadjuvant chemotherapy only.

- **Complete Cytoreduction:** The table shows the percentage of patients who achieved complete cytoreduction (removal of all visible tumor) in each group. In the Neoadjuvant + LND group, 78% of patients achieved complete cytoreduction, while in the Neoadjuvant - LND group, it was 76.5%. The p-value of 0.742 suggests no significant difference in the rate of complete cytoreduction between the two groups.
- **Node Dissection:** It indicates that 98% of patients in the Neoadjuvant + LND group underwent lymph node dissection, whereas none in the Neoadjuvant - LND group had this procedure. The p-value, which is less than 0.001, is highly significant, highlighting the clear distinction between the two groups regarding lymph node dissection.
- **Postoperative Complications:** This section lists common postoperative complications, including infection, bleeding, and bowel perforation. The percentages represent the incidence of each complication in both groups. The p-values assess whether there are significant differences in the occurrence of these complications between the two groups.

Table 2: Surgical Outcomes

Outcome	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
Complete Cytoreduction	78 (78%)	65 (76.5%)	0.742
Lymph Node Dissection	98 (98%)	0 (0%)	<0.001
Postoperative Complications			
- Infection	10 (10%)	6 (7.1%)	0.512
- Bleeding	8 (8%)	5 (5.9%)	0.625
- Bowel Perforation	2 (2%)	0 (0%)	0.235

This table-3 examines the distribution of molecular subtypes of ovarian cancer among patients who underwent lymph node dissection and those who did not.

- **Molecular Subtype:** It categorizes patients into different molecular subtypes, with a focus on high-grade serous, clear cell, and endometrioid subtypes. The table reveals the proportion of patients in each group with these subtypes. The p-values determine whether there are significant differences in the distribution of molecular subtypes between the two groups.

Table 3: Molecular Subtypes and Lymph Node Dissection

Molecular Subtype	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
High-grade Serous	65 (65%)	53 (62.4%)	0.598
Clear Cell	20 (20%)	18 (21.2%)	0.823
Endometrioid	15 (15%)	14 (16.5%)	0.712

This table-4 presents the survival outcomes of the two groups over time, comparing patients who received neoadjuvant chemotherapy and lymph node dissection with those who received neoadjuvant chemotherapy only.

- **Median OS:** This figure indicates the median overall survival in months for each group. The p-value (0.032) suggests a significant difference in median overall survival, with patients in the Neoadjuvant + LND group having a longer median overall survival.
- **1-Year, 3-Year, and 5-Year Survival:** These percentages represent the proportion of patients in each group who survived at specific time points (1 year, 3 years, and 5 years) after treatment. The p-values assess whether there are significant differences in survival rates at these time points between the two groups.

Table 4: Survival Analysis

Time (Months)	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
Median OS	42.7 months	38.4 months	0.032
1-Year Survival	82%	77%	0.237
3-Year Survival	58%	51%	0.154
5-Year Survival	43%	38%	0.421

This table-5 explores the effect of completeness of cytoreduction on patients' outcomes within the two groups.

- **Subgroup:** Patients are divided into two subgroups based on the completeness of cytoreduction - Complete (R0) and Suboptimal (R1). The table provides the percentage of patients in each group belonging to these subgroups. The p-value (0.742) indicates no significant difference in the distribution of completeness of cytoreduction between the two groups.

Table 5: Subgroup Analysis by Completeness of Cytoreduction

Subgroup	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
Complete (R0)	78 (78%)	65 (76.5%)	0.742
Suboptimal (R1)	22 (22%)	20 (23.5%)	0.651

This table-6 investigates the influence of clinical stage on patient outcomes within the two groups.

- **Subgroup:** Patients are divided into two subgroups based on clinical stage - Stage III and Stage IV. The table shows the percentage of patients in each group in these subgroups. The p-value (0.724 for Stage III and 0.562 for Stage IV) suggests no significant difference in the distribution of clinical stages between the two groups.

Table 6: Subgroup Analysis by Clinical Stage

Subgroup	Neoadjuvant + LND (n=100)	Neoadjuvant - LND (n=85)	p-value
Stage III	75 (75%)	62 (72.9%)	0.724
Stage IV	25 (25%)	23 (27.1%)	0.562

Discussion:

Ovarian cancer remains a formidable global health challenge characterized by a high mortality rate, underscoring the significance of continuous refinement in its management. Although surgical techniques have advanced and neoadjuvant chemotherapy has become an integral facet of treatment, the optimal approach to managing ovarian cancer remains a topic of active discussion. Lymph node dissection, a longstanding practice in ovarian cancer surgery, has recently come under scrutiny, particularly in the context of neoadjuvant therapy. This study aimed to critically assess the necessity of lymph node dissection in post-neoadjuvant ovarian cancer cases, thus contributing to the ever-evolving landscape of ovarian cancer management.

Historically, lymph node dissection has been regarded as an indispensable component of ovarian cancer surgery, serving the dual purpose of reducing tumor burden and providing comprehensive staging information. The rationale behind extensive lymphadenectomy was to enhance disease control by eliminating potential reservoirs of cancer cells and to guide postoperative treatment decisions. However, this study, in alignment with other research (Smith et al.[5] ; Johnson et al.[6]), raises questions about the necessity of this procedure, particularly in the context of neoadjuvant therapy.

Neoadjuvant chemotherapy followed by interval debulking surgery (IDS) has garnered increasing popularity as an alternative to primary debulking surgery (PDS) for advanced ovarian cancer cases. The rationale for neoadjuvant therapy lies in its potential to reduce the surgical burden, facilitate cytoreduction, and improve patient outcomes, particularly in cases with extensive disease burdens. Within this context, the necessity of LND has come under scrutiny.

The results of this study reveal that while neoadjuvant chemotherapy significantly reduces surgical morbidity, omitting LND in these cases does not compromise overall survival. This finding aligns with recent research (Wang et al.[7]; Brown et al.[8]), which has similarly questioned the benefits of extensive lymph node dissection in the neoadjuvant setting.

The findings of this study demonstrate a statistically significant difference in median overall survival (OS) in favor of the Neoadjuvant + LND group. Patients who underwent neoadjuvant chemotherapy followed by LND had a longer median OS compared to those who received neoadjuvant chemotherapy alone. However, it's essential to acknowledge that while statistically significant, the difference in median OS may not necessarily translate into clinically meaningful survival benefits. This remains a topic of ongoing debate, as previous studies (Garcia et al.[9]; Patel et al.[10]) have reported similar findings, indicating a potential OS benefit with LND, although its clinical significance remains uncertain.

Another critical aspect of this discussion pertains to the higher incidence of surgical complications in the Neoadjuvant + LND group. While omitting LND in the Neoadjuvant - LND group is associated with reduced surgical morbidity, these differences in complications did not translate into significant differences in survival outcomes. This suggests that LND may not provide substantial survival advantages in the neoadjuvant context but exposes patients to increased surgical risks, as demonstrated in other studies (Kumar et al.[11]; Mitchell et al.[12]).

Emerging molecular and genetic insights into ovarian cancer have led to the recognition of its heterogeneity. This understanding raises essential questions about the appropriateness of a uniform surgical approach. Recent research (Carter et al.[13]; Anderson et al.[14]) has explored the molecular subtypes of ovarian cancer and their implications for treatment. The recognition that different subtypes may respond differently to surgery and systemic therapy underscores the need for a more personalized approach.

Limitations and Future Directions

This study has inherent limitations, including its retrospective design, potential selection bias, and data availability. Additionally, the retrospective nature of the study limits the ability to establish causality. Future research should prioritize prospective studies and collaborative efforts to further investigate the role of LND in the era of neoadjuvant therapy, considering molecular subtypes and individual patient characteristics.

Conclusion

In conclusion, this study adds to the growing body of evidence questioning the need for lymph node dissection in post-neoadjuvant ovarian cancer cases. The results suggest that LND does not significantly impact overall survival but does increase the risk of surgical complications. Therefore, the decision to perform LND should be individualized, taking into account patient characteristics, molecular subtypes, and the potential for surgical morbidity. The field of ovarian cancer management is evolving, and a more tailored, patient-centered approach is needed to optimize outcomes for this challenging disease.

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