PERSPECTIVE

Primary and interval cytoreductive surgery for advanced ovarian cancer

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ABSTRACT

The difficulty in doing Cytoreductive Surgery (CRS) is balancing the advantages and disadvantages. This study's objective was to document postoperative morbidity and mortality in the short term in relation to surgical outcome in patients having primary Debulking Surgery (PDS) or Interval Debulking Surgery (IDS) in the Netherlands. Retrospective analysis was performed using data from the Dutch Gynecological Oncology Audit (DGOA). Postoperative problems were common as a result. The prognosis of CRS was correlated with the median time to adjuvant chemotherapy and the degree of sequelae. Case mix was adjusted while an analysis of Clavien-Dindo complications by region was conducted. Patients undergoing interval debulking as well as primary debulking surgery were included in the statistical analysis, which was done in Studio. In primary debulking surgery as compared to interval debulking, complications with re-invention were much higher.

Key Words: *Surgical care; Virtual reality; Neuro surgery; Cytroreductive surgery*

INTRODUCTION

A combination of Cytoreductive Surgery (CRS) and (neo) adjuvant chemotherapy is used to treat the majority of patients with advanced-stage ovarian cancer (FIGO stages IIb-IV) (NACT). There is no debate over the fact that CRS offers patients the highest chance of survival when all visible illness is removed [1, 2]. There is still some disagreement as to whether interval debulking surgery (IDS) and neoadjuvant chemotherapy come first before Primary Debulking Surgery (PDS). The current standard of care, however, is to perform PDS when pre-operative CT scan results indicate that a complete CRS is possible. This is based on the fact that individuals with complete PDS exhibit a higher rate of survival, and it is unclear if NACT and IDS are harmful to this particular subgroup of patients. More extensive surgery, which may have a higher risk of complications, may be required to achieve complete CRS. Co-morbidity and/or performance status are influencing variables. Therefore, the difficulty in doing CRS is to strike a compromise between the advantages (obtaining complete cytoreduction) and disadvantages (perioperative problems), particularly given that delaying adjuvant chemotherapy has a detrimental impact on survival. A recent systematic evaluation also revealed that the day readmission rates for IDS and PDS varied, with lower percentages for IDS. Although this systematic review also observed that some of the studies had small population sizes and that not all studies had recorded the results of the cytoreductive surgery, it may suggest that patients who have IDS have less postoperative problems. The centralization of surgical care for ovarian cancer patients was adopted in The Netherlands with the goal of enhancing patient outcomes. Only gynecological oncologists were allowed to do cytoreductive surgery in centers that annually perform cytoreductive surgery due to criteria that were specified. On a national level, centralization led to eight regions that each had one gynecooncological center and a number of local hospitals working together as part of a gyneco-oncological network. The Dutch Gynecological Oncology Audit was started in order to acquire insight into the caliber of care provided to patients with gynecological malignancies. Information on the surgical result and complications of every patient is gathered through this national

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registration. All hospitals that treat patients with gynecological malignancies are required to participate in the DGOA, and these facilities receive benchmarked evaluation on their performance. This study's objective was to report and compare short-term postoperative morbidity and mortality in patients receiving PDS or IDS in the eight regions of the Netherlands in relation to the surgical result. Retrospective analysis is done using a population-based prospective database called the DGOA. Ovarian, cervical, endometrial, and vulvar cancers are the four gynecological malignancies that the database tracks surgery results for. Gynecologists or skilled data managers under their supervision collect data prospectively. Included were all ovarian cancer patients with advanced stages (FIGO IIB-IV) undergoing PDS or IDS in the Netherlands and recorded in DGOA. For this analysis, patients having dubious histology were not included. Patients with a single PDS, a single IDS, and patients with numerous attempted cytoreductive procedures were the three groups of patients in this study who underwent CRS for ovarian cancer (MCS). CRS was described as a procedure with the goal of eliminating all visible disease, including removing the uterus, ovaries, and tubes, performing an infrasonic and supracolic omentectomy, resecting all macroscopically significant tumors in the abdomen, and removing pathological abdominal retroperitoneal lymph nodes. Complete CRS (macroscopically no remaining tumor), ideal CRS, and imperfect CRS were the three categories used to categorize the CRS outcome. Following at least three cycles of neoadjuvant chemotherapy, IDS is defined as a CRS. The frequency of postoperative problems recorded in the DGOA was one result of the study. The Clavien-Dindo scale was employed to categorize the complications' level of seriousness. Additionally, day-in/day-out hospital mortality, the type of readmissions, re-interventions, and ICU stay duration, as well as difficult course, were employed.

The term "complicated course" refers to a composite metric that includes all patients who experienced a complication that required a further surgical or radiologic procedure, prolonged hospitalization, or day death. Days spent in the hospital were used to characterize a prolonged hospital stay. Finally, the median time from CRS to the first adjuvant chemotherapy was evaluated in relation to the outcome of CRS and complications. Postoperative results and patient and tumor characteristics were described for three groups (PDS, IDS, and MCS) using frequencies and percentages. Using the chi-square test, PDS and IDS were compared. It was thought to be statistically significant. Both PDS and IDS had median times to adjuvant chemotherapy that were measured in days. The likelihood of experiencing Clavien-Dindo problems for PDS and IDS independently was examined using univariable and multivariable logistic regression analysis. Clavien-Dindo was selected as the outcome because it can be compared internationally and is frequently used in the international literature to assess surgical complications. In this analysis, patients with a single PDS or IDS were included; individuals with MCS were removed due to a lack of cases. With appropriate confidence intervals, the results were presented as odds ratios. Age, BMI, Carlson Comorbidity Index, FIGO stage, to-logicalical type, differentiation grade, and debulking outcome were the variables selected for univariate analysis based on the literature and the opinions of experts. The results of univariate studies were utilized to select variables for multivariate analysis that were statistically significant. The addition of factors for multivariable analysis took degrees of freedom into consideration. The R statistical software version (R Foundation for Statistical Computing, Vienna, Austria) was used to analyses the data. The percentage of patients with serious complications, as rated by Clavien-Dindo, was given in observed vs. predicted funnel plots for PDS and IDS for each of the eight areas in the Netherlands after being adjusted for variations in case mix. By determining the "anticipated" number of Clavien-Dindo complications for each location based on the odds ratios discovered for the covariates in the multivariable analysis, the case mix adjustment was carried out. After that, funnel plots were used to calculate and display the observed/expected (O/E) ratio. The number of days till the start of adjuvant therapy. After PDS and IDS, pitied registered for adjuvant chemotherapy. Adjuvant chemotherapy was started by patients undergoing CRS (both PDS and IDS) without postoperative problems after days (median time), for PDS at days, and for IDS at days. In contrast to patients who had difficulties with re-intervention, patients with complications without re-intervention delayed starting adjuvant chemotherapy by days on average. The longest gap to adjuvant chemotherapy for all surgical outcomes of PDS and IDS was days, and it varied between and days for patients who had complications requiring re-intervention a similar tendency is seen for other debulking outcomes. The most common reason for the delay in starting adjuvant chemotherapy is re-intervention complications. Case mix adjusted funnel graphs for PDS and IDS for each of the eight centralized areas in the Netherlands.

Issues with using Clavier-Din for PDS. A Clavien-Dindo problem was experienced by 166 patients out of 1027. This allowed us to change the case mix categories. Because of this, we streamlined the categories to account for additional variables. We adjusted for variations in age, BMI, Charlton Comorbidity Index, FIGO stage, histological type, and CRS procedure outcome between the areas following univariable and multivariable analyses (supplement S1). The risk of complications graded Clavien-Dindo in one area was almost twice as high as the national norm after case mix correction. The performance of the other regions was within confidence ranges. The case mix corrects he ted Clavien-Dindo funnel plot for IDS with absent patients. Age, BMI, Charlton Comorbidity Index, FIGO stage, differentiation grade, and CRS procedure differences between the regions were adjusted for in IDS (supplement S2). Two regions fared outside the confidence intervals after accounting for the case mix. When compared to the mean of all regions, the risk for a ClavienDindo grade 3 complication was almost twice as high in one region. Compared to the national average, the risk of Clavien-Dindo complications was much lower in the other region. In relation to CRS outcomes for patients with advanced ovarian cancer, this is the first prospective population-based study conducted in the Netherlands. Although there was no significant difference between the Clavien-Dindo complication rates in the PDS and IDS, the PDS had a considerably greater rate of patients who experienced problems upon re-intervention. In relation to CRS outcomes for patients with advanced ovarian cancer, this is the first prospective population-based study conducted in the Netherlands. Although there was no significant difference between the Clavien-Dindo complication rates in the PDS and IDS, the PDS had a considerably greater rate of patients who experienced problems upon re-intervention. This demonstrates the significance of striking a

balance between the objective of achieving the best surgical outcome and the risk of complications associated with aggressive surgery, which improves survival but also increases the risk of re-intervention and consequently delays the start of adjuvant chemotherapy.

Another interesting finding was that more PDS patients had a "complex course" than IDS patients did. This is mostly because PDS patients spend more time in the hospital—a day longer than IDS patients—than IDS patients do. The discrepancy between the results of complications measured using the Clavien-Dindo classification (which is comparable for IDS and PDS) and "complicated course" as a composite measure demonstrates how hospitalization can affect the measuring and reporting of complications and can add another dimension to the investigation of postoperative complications and their effects In contrast to our findings, a single center study using Clavien-Dindo also found that PDS had much greater rates of grading and problems than IDS in advanced ovarian cancer.

Despite using the same problems grading system as our study, this study's population size is too small to be used as comparative literature (PDS patient's vs IDS patients).

In one area, the chance of developing a complication-rated ClavienDindo in both PDS and IDS was approximately two times higher. Especially after case mix correction, we did not anticipate such a significant difference because regions already geographically balance populations. With these findings, the clinical audit might conduct a more thorough analysis of the area and pinpoint potential reasons to reduce regional variation going forward.

It should be noted that confounding by indication can cause similarities and variations between PDS and IDS results. When comprehensive PDS is feasible based on preoperative data, the Dutch recommendation recommends PDS over IDS. In our study, compared to individuals treated with PDS, patients who underwent IDS were older, had a higher ASA classification, and had a more advanced FIGO stage. This might have had an impact on the surgical aggressiveness as well as the treatment strategy, leading to confounding by indication.

This confounding by indication is further demonstrated by the significantly greater rate of completion in PDS compared to IDS, despite the fact that other studies have found the contrary to be true that is, that complete IDS is more frequently attained than PDS. The superior selection of patients appropriate for PDS/IDS may be due to a higher FIGO stage with more widespread illness and lower differentiation grades of patients undergoing IDS and starting with NACT, which is one explanation.

Comparing PDS and IDS to other research, the high percentages of complete cytoreduction are very intriguing. Studied survival in a population-based cohort in Sweden before and after centralization. In addition to a greater relative survival after centralization, they mentioned a complete cytoreduction in PDS before centralization. The Netherlands and our entire PDS are concentrated for the treatment of ovarian cancer. These outcomes are difficult to compare because the beginning treatment arms are not comparable (decision to choose for either PDS or IDS). After centralization, the specific population in Sweden included patients with PDS and patients with IDS, whereas our sample had a more equitable distribution of population sizes. To better understand how the results of CRS relate to the volume of procedures in other nations, it would be interesting to compare theresults of CRS at high- and low-volume centers in the Netherlands with high- and low-volume centers in other nations. The strength of the current study is that, to our knowledge, no population-based comparison of postoperative complications between IDS and PDS in relation to adjuvant treatment has yet been described in the literature. This research offers insightful information on how the country performs in terms of surgical results, as well as how regional variations in postoperative outcomes can be identified. Gynecologists or skilled data managers doing registration in the DGOA could be a potential restriction of the current investigation. These two organizations' interpretations of the patient files or their rigor in registering complications may differ. However, gynecologists review the data that data managers enter.