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Effect of surgical volume on short-term outcomes of cytoreductive surgery for advanced-stage ovarian cancer: A population-based study from the Dutch Gynecological Oncology Audit

M.D. Algera [a,b,c,*], W.J. van Driel [d], B.F.M. Slangen [b,c], M.W.J.M. Wouters [a,e,f], R.F.P.M. Kruitwagen [b,c]
On behalf of the participants of the Dutch Gynecological Oncology Audit Collaborator Group:

A.J. Kruse [1], R. Yigit [2], M.J.A. Engelen [3], L.S. Nooij [4], J.W.M. Mens [5], M.A.A. de Jong [6], M.A.D. Haverkort [7], M. van der Aa [8], J. Diepstraten [9], M.A.P.C. van Ham [10], H.P.M. Smedts [11], N. Reesink [12], K.N. Gaarenstroom [4], P.M.L.H. Vencken [13], D. Boll [14], G. Fons [15], A. Baalbergen [16], E.B.L. van Dorst [17], E.M. Roes [5], H.T.C. Nagel [18], A. van Ginkel [19], J. de Waard [20], L.N. Hofman [21]

[1] *Isala Klinieken, Zwolle, the Netherlands*
[2] *University Medical Center Groningen, Groningen, the Netherlands*
[3] *Zuyderland Medical Center, Heerlen, the Netherlands*
[4] *Leiden University Medical Center, Leiden, the Netherlands*
[5] *Erasmus Medical Center Cancer Institute, Rotterdam, the Netherlands*
[6] *Radiotherapeutisch Instituut Friesland, Leeuwarden, the Netherlands*
[7] *Radiotherapy Group, Arnhem, the Netherlands*
[8] *Netherlands Comprehensive Cancer Organization, Utrecht, the Netherlands*
[9] *Stichting Olijf, Utrecht, the Netherlands*
[10] *Radboud University Medical Center, Nijmegen, the Netherlands*
[11] *Amphia Ziekenhuis, Breda, the Netherlands*
[12] *Medical Center Twente, Enschede, the Netherlands*
[13] *Bravis Ziekenhuis, Roosendaal, the Netherlands*
[14] *Catharina Ziekenhuis, Eindhoven, the Netherlands*
[15] *Amsterdam University Medical Center, Amsterdam, the Netherlands*
[16] *Reinier de Graaf Group, Delft, the Netherlands*
[17] *University Medical Center Utrecht, Utrecht, the Netherlands*
[18] *Haaglanden Medical Center, The Hague, the Netherlands*
[19] *Rijnstate Ziekenhuis, Arnhem, the Netherlands*
[20] *Fransiscus Gasthuis & Vlietland, Rotterdam, the Netherlands*
[21] *Albert Schweitzer Ziekenhuis, Dordrecht, the Netherlands*

[a] *Dutch Institute for Clinical Auditing (DICA), Scientific Bureau, Leiden, the Netherlands*
[b] *Maastricht University Medical Center (MUMC+), Department of Obstetrics and Gynecology, Maastricht, the Netherlands*
[c] *GROW- School for Oncology and Reproduction, Maastricht, the Netherlands*
[d] *Center for Gynecological Oncology Amsterdam, Netherlands Cancer Institute, Department of Gynecology, Amsterdam, the Netherlands*
[e] *Netherlands Cancer Institute, Department of Surgical Oncology, Amsterdam, the Netherlands*
[f] *Leiden University Medical Center, Department of Biomedical Data Sciences, Leiden, the Netherlands*

HIGHLIGHTS

- In the centralized Dutch healthcare, surgical volume did not affect short-term outcomes in patients undergoing interval CRS.
- Regarding primary CRS, high-volume was associated with higher complete CRS rates compared to low-volume hospitals.
- However, high-volume hospitals were also associated with increased length of stay and increased severe complications.
- Several case-mix factors were significantly associated with the outcomes, therefore adjusting for case-mix is essential.
- Enhancing the quality of care is multifactorial and should not solely be focused on increasing surgical volumes.

* Corresponding author at: Dutch Institute for Clinical Auditing, Rijnsburgerweg 10, 2333 AA Leiden, the Netherlands.
E-mail address: m.algera@nki.nl (M.D. Algera).

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ABSTRACT

Objective. Despite lacking clinical data, the Dutch government is considering increasing the minimum annual surgical volume per center from twenty to fifty cytoreductive surgeries (CRS) for advanced-stage ovarian cancer (OC). This study aims to evaluate whether this increase is warranted.

Methods. This population-based study included all CRS for FIGO-stage IIB-IVB OC registered in eighteen Dutch hospitals between 2019 and 2022. Short-term outcomes included result of CRS, length of stay, severe complications, 30-day mortality, time to adjuvant chemotherapy, and textbook outcome. Patients were stratified by annual volume: low-volume (nine hospitals, <25), medium-volume (four hospitals, 29–37), and high-volume (five hospitals, 54–84). Descriptive statistics and multilevel logistic regressions were used to assess the (case-mix adjusted) associations of surgical volume and outcomes.

Results. A total of 1646 interval CRS (iCRS) and 789 primary CRS (pCRS) were included. No associations were found between surgical volume and different outcomes in the iCRS cohort. In the pCRS cohort, high-volume was associated with increased complete CRS rates (aOR 1.9, 95%-CI 1.2–3.1, $p = 0.010$). Furthermore, high-volume was associated with increased severe complication rates (aOR 2.3, 1.1–4.6, 95%-CI 1.3–4.2, $p = 0.022$) and prolonged length of stay (aOR 2.3, 95%-CI 1.3–4.2, $p = 0.005$). 30-day mortality, time to adjuvant chemotherapy, and textbook outcome were not associated with surgical volume in the pCRS cohort. Subgroup analyses (FIGO-stage IIIC-IVB) showed similar results. Various case-mix factors significantly impacted outcomes, warranting case-mix adjustment.

Conclusions. Our analyses do not support further centralization of iCRS for advanced-stage OC. High-volume was associated with higher complete pCRS, suggesting either a more accurate selection in these hospitals or a more aggressive approach. The higher completeness rates were at the expense of higher severe complications and prolonged admissions.

1. Introduction

Centralization of care for patients undergoing cytoreductive surgery (CRS) for advanced-stage ovarian cancer has been a subject of ongoing discussion for the past two decades [1–9]. In the Netherlands, the centralization of surgical care for ovarian cancer was initiated in 2010, following two studies by Vernooij et al. in 2008 and 2009, demonstrating improved outcomes for patients treated in (semi-)specialized hospitals [8,9]. Consequently, the Dutch Gynecological Oncology Society established a minimum annual surgical volume of twenty CRS procedures per hospital in 2012 (CRS for International Federation of Gynecology and Obstetrics (FIGO) stage IIB-IVB) [10]. Partly due to this criterion, the number of hospitals performing CRS has decreased from over one hundred before centralization to eighteen in 2023.

The quality of care for patients with ovarian cancer in the Netherlands has been monitored since 2014 by the Dutch Gynecological Oncology Audit (DGOA). The DGOA is a mandatory population-based quality registry that covers all cases of ovarian cancer (as well as vulva, corpus uteri, and cervix cancer) in the Netherlands. The DGOA performs clinical auditing, which has been recognized as a critical tool to improve the quality of healthcare [11,12]. Benchmarked data are reported annually to facilitate comparisons of hospital performances and identify and address outliers. To compare and enhance quality of care for patients with advanced-stage ovarian cancer, the following short-term outcome indicators are monitored by the DGOA: result of CRS, length of hospital stay, severe complications, 30-day mortality, and textbook outcome [13]. Variations in the quality of care regarding complete result of CRS, complications, and textbook outcome have been described using DGOA data [13–15]. However, the impact of surgical volume on these short-term outcomes has yet to be assessed within the current centralized care system.

Following the centralization of care in 2012, improved outcomes have been observed, including an increased Dutch benchmark for the complete result of CRS (no macroscopic residual disease). Completeness rates rose from <50% in 2008, to up to 70% in 2017–2020, with even higher rates observed in 2022 (unpublished data) [13,15–17]. It should be noted that, besides the concentration of surgical care, other requirements were imposed by the Dutch Gynecological Oncology Society. Starting in 2012, hospitals treating patients with ovarian cancer were required to 1) be part of a regional network, 2) hold weekly multidisciplinary team meetings (involving gynecologic oncologists, medical oncologists, radiologists, radiation oncologists, pathologists, and case-managers), 3) ensure the presence of a gynecologic oncologist during all CRS procedures, 4) have a gastro-intestinal surgeon on call or available during CRS, 5) provide frozen-section availability during surgery, 6) have intensive care unit personnel competent in treating patients undergoing complex gynecologic surgery, and 7) participate in the DGOA quality registry [10]. Furthermore, until now it is unclear whether the use of neoadjuvant chemotherapy has increased in the Netherlands. As a result, it remains uncertain whether the improved quality of care for patients with advanced-stage ovarian cancer is solely attributed to the volume norms or to other factors.

Currently, care for patients with ovarian cancer in the Netherlands is regionally organized, in which gynecologic oncology centers collaborate with referring centers. CRS (and staging surgeries) are performed in gynecologic oncology centers, and chemotherapy and maintenance therapy are most often administered in referring hospitals according to a shared-care model. Recently, the Dutch government released an agreement on the future of health care (Integral Care Agreement), suggesting that a minimum of fifty surgeries per hospital per year should be mandated for complex surgical procedures such as CRS [18]. However, this recommendation lacks clinical data support. The Dutch Gynecological Oncology Society has not yet issued a statement regarding further centralizing care, as it remains uncertain whether short-term outcomes of Dutch patients would improve with treatment at relatively high-volume hospitals within the current centralized care system. Therefore, the primary objective of this study is to assess whether hospitals with low-, medium-, or high-volume correlate with improved short-term outcomes for patients with advanced-stage ovarian cancer undergoing CRS in the Netherlands."

2. Methods

2.1. Study design

This population-based study used data from the DGOA registry. The DGOA is a population-based and prospectively maintained quality registry, facilitated by the Dutch Institute for Clinical Auditing, that contains

reliable, detailed clinical data on all surgical procedures for ovarian cancer in the Netherlands [12]. Since January 2014, the DGOA has been a mandatory registry for all Dutch hospitals treating ovarian cancer patients and women with other gynecological malignancies. According to Dutch legislation, ethical approval or informed consent was not required for this study.

2.2. Patient selection

All interval and primary CRS (iCRS and pCRS) for advanced-stage ovarian cancer (FIGO-stage IIB-IVB) that were performed between October 1st, 2018, and September 30th, 2022, were included in this study. Separately, subgroup analyses were performed on patients with FIGO-stage IIIC-IVB because these patients underwent more extensive surgery compared to patients with FIGO-stage IIB-IIIB.

Only patients treated in the eighteen Dutch hospitals licensed to perform CRS as of January 1st, 2023, were considered for inclusion. In 2018, twenty-two hospitals performed CRS for advanced-stage ovarian cancer. However, between 2019 and 2022, four institutions stopped performing CRS because they could not meet the minimum annual volume requirement. Consequently, data from patients treated in these four hospitals were excluded from the current study because the study focused solely on the potential benefits and implications of further centralization for advanced-stage ovarian cancer. CRS after an initial incomplete pCRS or iCRS (i.e., macroscopic disease present after surgery) were included. That way, both procedures of patients were included. Further exclusion criteria were patients with borderline ovarian tumors, surgical treatment with palliative intent, missing type of CRS, and patients with missing date of surgery.

2.3. Outcomes

This study focused on short-term outcomes, since long-term outcomes such as overall survival could be impacted by factors which are not related to centralized surgical care. Short-term outcomes were the result of CRS, length of hospital stay, severe complications, time to adjuvant chemotherapy, 30-day mortality, and textbook outcome. The complete result of CRS was defined as the absence of macroscopically visible residual disease after surgery. A prolonged length of stay was defined as ≥10 days. The cut-off of 10 days was used because a prolonged length of stay ≥10 days is associated with a postponed start of adjuvant chemotherapy, resulting in a worse overall survival [19]. Severe complications were defined as complications with re-intervention, or any complication combined with a prolonged length of Intensive Care Unit (ICU) stay (Clavien-Dindo grade 3–4) [20]. Postponed start of adjuvant chemotherapy was defined as ≥42 days after surgery [19]. 30-day mortality was defined as death within 30 days after the surgical procedure and/or death during the admission related to the surgery (in-hospital mortality). Textbook outcome was defined as the presence of a complete result of CRS and the absence of 30-day mortality, severe complications, and prolonged length of stay. Time to adjuvant chemotherapy was excluded from textbook outcome because of substantial missing values.

2.4. Statistical analysis

Patients were categorized into quartiles, based on annual surgical volume (FIGO-stage IIB-IVB). Due to group sizes, patients treated in the 1st and 2nd volume quartiles (consisting of the nine hospitals with the lowest volumes) were grouped together as the low-volume group. Patients treated in the 3rd and 4th volume quartiles were categorized separately as the medium-volume (four hospitals) and high-volume groups (five hospitals).

Data were analyzed using RStudio version 1.4.1106 (RStudio, Boston, United States of America, 2021). Separate analyses were carried out for patients that underwent iCRS, and those who underwent pCRS. Subgroup analyses were performed for patients with FIGO-stage IIIC-IVB. Descriptive statistics were used to compare the case-mix factors and outcomes in the different surgical volume groups. Furthermore, the associations of surgical volume and case-mix factors with the different outcomes were analyzed using multilevel, multivariable logistic regression models. Multilevel logistic regression models with a random intercept were performed to adjust for clustering effects of patients within hospitals (using the hospital variable as multilevel variable). Due to a limited number of events, 30-day mortality was solely analyzed using descriptive statistics (Fisher exact test).

In the multilevel, multivariable logistic regression analyses, the short-term outcomes were adjusted for the following case-mix factors: patient and tumor characteristics such as age (continuous), Body Mass Index (continuous), Charlson Comorbidity Index (0 and 1+) [21], FIGO-stage (iCRS: IIB-IIIB, IIIC, IVA, and IVB; pCRS: IIB, IIIA, IIIB, IIIC, and IV), tumor histology (serous and other (clear cell, endometrioid, mucinous, mixed, non-epithelial, other)), and whether previous abdominal surgery had been performed prior to the CRS. The addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to iCRS was also included as a 'case-mix factor' in the iCRS analyses regarding length of stay and severe complications, because of the possible impact of HIPEC on these outcomes [22]. However, the addition of HIPEC to iCRS was excluded as case-mix factor in the analyses regarding complete result of CRS and textbook outcome because patients only received HIPEC when the result of CRS was complete (no macroscopic residual disease) or optimal (residual disease <1 cm), and HIPEC was not administered when the result of CRS was incomplete (residual disease ≥1 cm).

3. Results

3.1. Patients and characteristics

The selection flowcharts are displayed in Fig. 1A for iCRS and Fig. 1B for pCRS. A total of 2435 CRS were performed for FIGO-stage IIB-IVB ovarian cancer in the eighteen Dutch hospitals between October 1st, 2018, and September 30th, 2022. The majority were iCRS, 67.6% iCRS ($n = 1646$) vs. 32.4% pCRS ($n = 789$). These 2435 surgeries were performed on 2407 patients: twenty-eight patients had a second CRS after an initial incomplete CRS.

Annual surgical volumes of the eighteen Dutch hospitals are shown in Fig. 2 (FIGO-stage IIB-IVB) and Supplementary Fig. 1 (FIGO-stage IIIC-IVB). Five out of the eighteen hospitals did not reach the threshold of twenty CRS per year during 2019–2022.

For patients with FIGO-stage IIB-IIIB ovarian cancer ($n = 527$), low-volume hospitals performed 15.1% iCRS and 84.9% pCRS, medium-volume hospitals performed 11.0% iCRS and 89.0% pCRS, and high-volume hospitals performed 18.3% iCRS and 81.7% pCRS. For patients with FIGO-stage IIIC-IVB ovarian cancer ($n = 1908$), low-volume hospitals performed 76.6% iCRS and 23.4% pCRS, medium-volume hospitals performed 85.3% iCRS and 14.7% pCRS, and high-volume hospitals performed 82.9% iCRS and 17.1% pCRS.

Second surgery after incomplete pCRS occurred in 2.8% ($n = 22$ out of 789 pCRS). Breakdown per surgical volume as follows: low-volume 2.6% ($n = 7$ out of $n = 265$ pCRS) in low-volume hospitals, medium-volume 3.3% ($n = 5$ out of $n = 152$ pCRS), and high-volume 2.7% ($n = 10$ out of $n = 372$ pCRS) (no statistical test performed). Second surgery after incomplete iCRS, occurred 0.4% ($n = 7$ out of 1646).

Patient and tumor characteristics (case-mix factors) and treatment characteristics are displayed in Table 1 (FIGO-stage IIB-IVB) and Supplementary Table 1 (FIGO-stage IIIC-IVB). Regarding FIGO-stage IIB-IVB, most patients in both iCRS and pCRS cohorts were treated in high-volume hospitals. In the iCRS cohort, the case-mix was comparable in the different surgical volume groups regarding histology and whether previous abdominal surgeries had been performed; however, age, BMI, co-morbidity, FIGO-stage, and the addition of HIPEC differed significantly across the surgical volume groups (Table 1A). In the pCRS cohort,

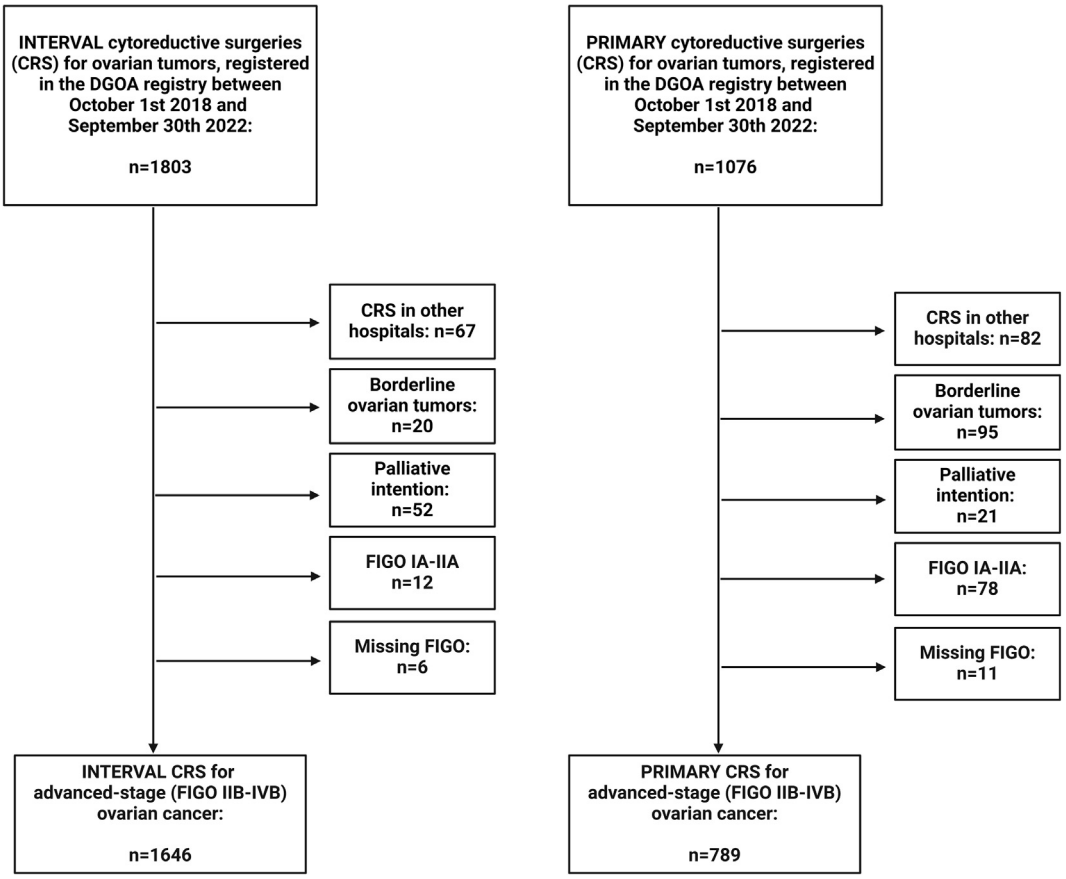

Fig. 1. A & B: Patient selection flowcharts.

all case-mix factors were comparable across the surgical volume groups (Table 1B).

Regarding the subgroup analysis (FIGO-stage IIIC-IVB), the case-mix was comparable in the different surgical volume groups regarding age, BMI, histology, and whether previous abdominal surgeries had been performed in the iCRS cohort. However, co-morbidity, FIGO-stage, and the addition of HIPEC differed significantly across the surgical volume groups (Supplementary Table 1A). In the pCRS cohort, the case-mix was comparable across the surgical volume groups regarding age, BMI, histology, co-morbidity, and FIGO-stage; however, whether previous abdominal surgeries had been performed differed across surgical volume groups (Supplementary Table 1B).

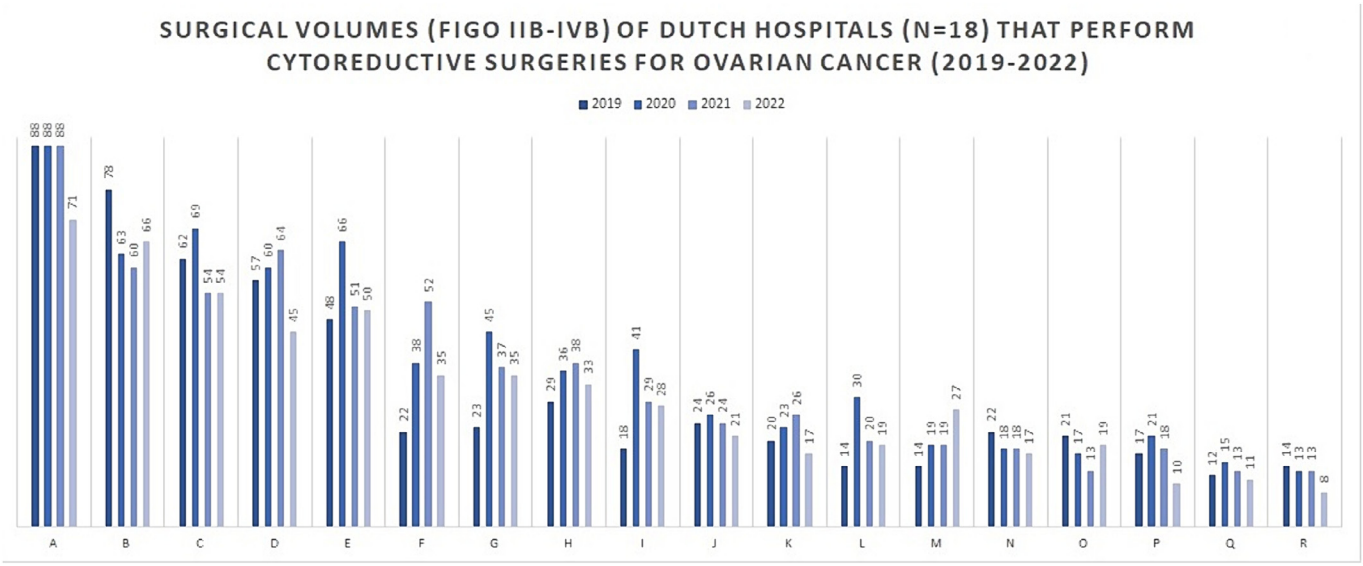

Fig. 2. Surgical volumes (FIGO IIB-IVB) of Dutch ovarian cancer hospitals ($n = 18$) (2019–2022). X-axis: hospitals. Y-axis: number of annual surgeries.

Table 1
Patient, tumor, and treatment characteristics of patients undergoing INTERVAL (A) and PRIMARY (B) cytoreductive surgery for FIGO IIB-IVB advanced-stage ovarian cancer in the Netherlands (2019–2022). Patients were categorized in low-volume (1st and 2nd quartiles), medium-volume (3rd quartile), and high-volume (4th quartile) hospitals.

Table 1A: INTERVAL	Low-volume <25 /year (n = 379)	Medium-volume 29–37 /year (n = 377)	High-volume 54–84 / year (n = 890)	Total (n = 1646)	p-value
Age (years)					
Median [Q1,Q3]	71 [64,76]	67 [58,73]	68 [61,74]	69 [61,74]	**<0.001**
BMI					
Median [Q1,Q3]	26 [23,29]	25 [23,28]	25 [22,28]	25 [22,28]	**0.015**
Missing*	33 (9%)	3 (1%)	52 (6%)	88 (5%)	
CCI					
0	236 (62%)	225 (60%)	597 (67%)	1058 (64%)	**0.028**
1+	143 (38%)	152 (40%)	293 (33%)	588 (36%)	
FIGO (2014)					
Stage IIB-IIIB	28 (7%)	11 (3%)	44 (5%)	83 (5%)	**<0.001**
Stage IIIC	166 (44%)	248 (66%)	506 (57%)	920 (56%)	
Stage IVA	120 (32%)	65 (17%)	120 (13%)	305 (18%)	
Stage IVB	65 (17%)	53 (14%)	220 (25%)	338 (21%)	
Histology					
Serous	341 (90%)	347 (92%)	814 (92%)	1502 (91%)	0.535
Other†	38 (10%)	30 (8%)	74 (8%)	142 (9%)	
Missing*			2 (0.2%)	2 (0.1%)	
Abdominal surgery					
No	205 (54%)	212 (56%)	469 (53%)	886 (54%)	0.559
Yes	142 (38%)	165 (44%)	373 (42%)	680 (41%)	
Missing*	32 (8%)		48 (5%)	80 (5%)	
Type of CRS					
Interval	352 (93%)	200 (53%)	583 (66%)	1135 (69%)	**<0.001**
Interval + HIPEC	27 (7%)	177 (47%)	307 (34%)	511 (31%)	
Table 1B: PRIMARY	**Low-volume <25 /year (n = 265)**	**Medium-volume 29–37 /year (n = 152)**	**High-volume 54–84 /year (n = 372)**	**Total (n = 789)**	**p-value**
Age (years)					
Median [Q1,Q3]	64 [56,73]	63 [54,71]	64 [55,71]	64 [55,72]	0.375
BMI					
Median [Q1, Q3]	25 [23,30]	25 [23,28]	25 [23,29]	25 [23,29]	0.563
Missing*	31 (12%)	0 (0%)	28 (8%)	59 (7%)	
CCI					
0	190 (72%)	102 (67%)	258 (69%)	550 (70%)	0.605
1+	75 (28%)	50 (33%)	114 (31%)	239 (30%)	
FIGO (2014)					
Stage IIB	93 (35%)	50 (33%)	99 (27%)	242 (31%)	0.512
Stage IIIA	26 (10%)	15 (10%)	36 (10%)	77 (10%)	
Stage IIIB	39 (15%)	24 (16%)	62 (17%)	125 (16%)	
Stage IIIC	93 (35%)	51 (34%)	150 (40%)	294 (37%)	
Stage IV	14 (5%)	12 (8%)	25 (7)	51 (7%)	
Histology					
Serous	176 (66%)	92 (60%)	258 (69%)	526 (67%)	0.137
Other†	89 (34%)	60 (40%)	113 (30%)	262 (33%)	
Missing*			1 (0.3%)	1 (0.1%)	
Abdominal surgery					
No	133 (50%)	75 (49%)	200 (54%)	408 (52%)	0.180
Yes	101 (38%)	77 (51%)	144 (39%)	322 (41%)	
Missing*	31 (12%)		28 (8%)	59 (7%)	

Abbreviations: BMI = Body Mass Index; FIGO = International Federation of Gynecology and Obstetrics; CCI = Charlson Comorbidity Index.
Definitions: †Other histology = clear cell, endometrioid, mucinous, mixed, non-epithelial, and 'other' histology.
* = Not tested. Abdominal surgery = previous abdominal surgery before the cytoreductive surgery.
Based on group sizes, categorical data were compared using Chi-squared or Fisher's exact tests. Non-parametric comparisons of non-normally distributed continuous variables were performed using the Kruskal-Wallis test. A two-sided p-value of <0.05 was considered statistically significant.

3.2. Unadjusted associations of surgical volume and short-term outcomes

The unadjusted, univariate analyses regarding the associations between short-term outcomes and surgical volume for patients with FIGO-stage IIB-IVB are shown in Table 2A and B. In the iCRS analyses, no significant associations were observed between most outcomes and the surgical volume groups. However, in the medium-volume hospitals, patients had a postponed start of adjuvant chemotherapy significantly less frequently compared to patients treated in low- and high-volume hospitals. In the pCRS analyses, a prolonged length of stay occurred significantly more frequently in patients treated in medium- and high-volume hospitals compared to low-volume hospitals. The other outcomes were comparable across the surgical volume groups. The analyses displayed in Table 2 were not adjusted for case-mix factors or clustering effects within hospitals.

Similar unadjusted analyses focusing on patients with FIGO-stage IIIC-IVB are displayed in Supplementary Table 2. Like the previous analyses, in the iCRS analyses, no significant associations were observed between most outcomes and the surgical volume groups (FIGO-stage IIIC-IVB). In the medium-volume hospitals, patients had a postponed start of adjuvant chemotherapy significantly less frequently compared to patients in low- and high-volume hospitals.

3.3. Case-mix adjusted associations of surgical volume and short-term outcomes

The multivariable multilevel logistic regression analyses of the iCRS cohort are shown in Table 3. No associations between surgical volume and result of CRS, length of stay, severe complications, interval to adjuvant chemotherapy, and textbook outcome were observed. Older age

Table 2
Outcomes for patients undergoing INTERVAL (A) and PRIMARY (B) cytoreductive surgery for FIGO IIB-IVB advanced-stage ovarian cancer in the Netherlands (2019–2022). Patients were categorized in low-volume (1st and 2nd quartiles), medium-volume (3rd quartile), and high-volume (4th quartile) hospitals.

Table 2A: INTERVAL CRS	Low-volume <25 /year (n = 379)	Medium-volume 29–37 /year (n = 377)	High-volume 54–84 / year (n = 890)	Total (n = 1646)	p-value
Complete CRS					
Yes	259 (68%)	266 (71%)	641 (72%)	1166 (71%)	0.457
No	118 (31%)	108 (29%)	247 (28%)	473 (29%)	
Missing*	2 (1%)	3 (1%)	2 (0.2%)	7 (0.4%)	
Length of stay					
<10 days	303 (80%)	286 (76%)	676 (76%)	1265 (77%)	0.273
≥10 days	49 (13%)	63 (17%)	141 (16%)	253 (15%)	
Missing*	27 (7%)	28 (7%)	73 (8%)	128 (8%)	
Severe complications					
No	347 (92%)	356 (94%)	811 (91%)	1514 (92%)	0.132
Yes	32 (8%)	21 (6%)	79 (9%)	132 (8%)	
Time to adjuvant chemotherapy					
<42 days	208 (55%)	245 (65%)	636 (72%)	1089 (66%)	**0.004**
≥42 days	62 (16%)	35 (9%)	163 (18%)	260 (16%)	
Missing †	109 (29%)	97 (26%)	91 (10%)	297 (18%)	
30-day mortality					
Alive	377 (99.5%)	375 (99.5%)	884 (99.3%)	1636 (99.4%)	1.000
Dead	2 (0.5%)	2 (0.5%)	6 (0.7%)	10 (0.6%)	
Textbook outcome					
Yes	192 (51%)	191 (51%)	463 (52%)	846 (51%)	0.770
No	166 (44%)	167 (44%)	374 (42%)	707 (43%)	
Missing*	21 (5%)	19 (5%)	53 (6%)	93 (6%)	
Table 2B: PRIMARY CRS	**Low-volume <25 /year (n = 265)**	**Medium-volume 29–37 /year (n = 152)**	**High-volume 54–84 /year (n = 372)**	**Total (n = 789)**	**p-value**
Complete CRS					
Yes	213 (80%)	131 (86%)	324 (87%)	668 (85%)	0.108
No	48 (18%)	21 (14%)	46 (12%)	115 (15%)	
Missing*	4 (2%)		2 (1%)	6 (1%)	
Length of stay					
<10 days	233 (88%)	122 (80%)	288 (77%)	643 (82%)	**0.029**
≥10 days	21 (8%)	18 (12%)	53 (14%)	92 (12%)	
Missing*	11 (4%)	12 (8%)	31 (8%)	54 (7%)	
Severe complications					
No	250 (94%)	138 (91%)	332 (89%)	720 (91%)	0.079
Yes	15 (6%)	14 (9%)	40 (11%)	69 (9%)	
Time to adjuvant chemotherapy					
<42 days	158 (60%)	96 (63%)	226 (61%)	480 (61%)	0.464
≥42 days	49 (19%)	38 (21%)	89 (24%)	176 (22%)	
Missing †	58 (22%)	18 (12%)	57 (15%)	133 (17%)	
30-day mortality					
Alive	261 (98.5%)	152 (100%)	371 (99.7%)	784 (99.4%)	0.135
Dead	4 (1.5%)	0 (0%)	1 (0.3%)	5 (0.6%)	
Textbook outcome					
Yes	180 (68%)	99 (65%)	238 (64%)	517 (66%)	0.811
No	72 (27%)	43 (28%)	107 (29%)	222 (28%)	
Missing*	13 (5%)	10 (7%)	27 (7%)	50 (6%)	

Abbreviations: CRS = cytoreductive surgery. Definition: Textbook outcome: the presence of a complete result of CRS, and the absence of 30-day mortality, severe complications, and prolonged length of stay. * = Not tested. † = tested as category.
Based on group sizes, categorical data were compared using Chi-squared or Fisher's exact tests. A two-sided p-value of <0.05 was considered statistically significant. Missing data below 5% were excluded for analysis.

was associated with fewer complete CRS, fewer textbook outcomes, increased length of stay, and increased interval to adjuvant chemotherapy. The addition of HIPEC to iCRS was associated with increased length of stay and increased severe complications rates.

The subgroup analysis regarding patients with FIGO-stage IIIC-IVB undergoing iCRS is displayed in Supplementary Table 3. No associations between surgical volume and result of CRS, length of stay, severe complications, interval to adjuvant chemotherapy, and textbook outcome were observed. Older age was associated with fewer complete CRS, fewer textbook outcomes, increased length of stay, and increased interval to adjuvant chemotherapy. FIGO stage IVA was associated with fewer complete CRS. The addition of HIPEC to iCRS was associated with increased length of stay and increased severe complications.

The multivariable multilevel logistic regression analyses of the pCRS cohort are shown in Table 4. An association was found between surgical volume and result of CRS: high-volume hospitals were associated with increased complete CRS rates (adjusted Odds Ratio (aOR) 1.9, 95% Confidence Interval (CI) 1.2–3.1, $p = 0.010$). Furthermore, high-volume was associated with increased length of stay ≥10 days (aOR 2.3, 95% CI 1.3–4.2, $p = 0.005$), and severe complications (aOR 2.3, 95% CI 1.1–4.6, $p = 0.022$). No significant volume-related associations were observed for time to adjuvant chemotherapy and textbook outcome. Like the iCRS cohort, older age was associated with fewer complete CRS, fewer textbook outcome, increased length of stay, and increased interval to adjuvant chemotherapy.

The subgroup analysis regarding patients with FIGO-stage IIIC-IVB undergoing pCRS is displayed in Supplementary Table 4. An association

Table 3
Multilevel, multivariable logistic regression analyses regarding patients with FIGO IIB-IVB advanced-stage ovarian cancer undergoing INTERVAL cytoreductive surgery. Multilevel variable: hospital id.

INTERVAL CRS		Complete result of CRS			Length of stay ≥10 days			Time to adjuvant chemotherapy ≥42 days		
	No of patients	aOR	95% CI	*p*	aOR	95% CI	*p*	aOR	95% CI	*p*
Annual volume										
Low (<25)	379 (23%)	1			1			1		
Medium (29–37)	377 (23%)	0.9	0.6–1.5	0.793	0.9	0.5–1.9	0.851	0.5	0.2–1.3	0.149
High (54–84)	890 (54%)	1.0	0.7–1.6	0.926	1.1	0.6–2.1	0.758	0.9	0.4–1.8	0.699
Age (continuous)	1646 (100%)	**0.98**	**0.97–0.99**	**0.001**	**1.02**	**1.00–1.04**	**0.020**	**1.03**	**1.01–1.05**	**0.001**
BMI (continuous)	1558 (95%)	0.99	0.99–1.00	0.124	1.00	0.99–1.01	0.526	1.00	0.98–1.01	0.494
Missing	88 (5%)									
CCI										
0	1058 (64%)	1			1			1		
1+	588 (36%)	1.2	0.9–1.5	0.159	1.1	0.8–1.5	0.396	1.1	0.8–1.5	0.595
FIGO (2014)										
Stage IIB-IIIB	83 (5%)	1			1			1		
Stage IIIC	920 (56%)	**0.5**	**0.2–0.9**	**0.029**	1.0	0.5–1.9	0.952	0.9	0.5–1.7	0.823
Stage IVA	305 (19%)	**0.3**	**0.1–0.5**	**<0.001**	1.0	0.5–2.0	0.991	0.7	0.4–1.5	0.383
Stage IVB	338 (21%)	**0.4**	**0.2–0.7**	**0.007**	0.7	0.4–1.6	0.430	0.7	0.4–1.5	0.351
Histology										
Serous	1502 (91%)	1			1			1		
Other	142 (9%)	1.3	0.8–2.0	0.276	1.6	1.0–2.5	0.070	1.4	0.9–2.4	0.169
Missing	2 (0.1%)									
Abdominal surgery										
No	886 (54%)	1			1			1		
Yes	680 (41%)	1.0	0.8–1.2	0.773	1.2	0.9–1.6	0.301	**0.6**	**0.5–0.9**	**0.006**
Missing	80 (5%)									
Type of CRS										
Interval	1135 (69%)				1			1		
Interval + HIPEC	511 (31%)	NT	NT	NT	**2.3**	**1.6–3.4**	**<0.001**	1.2	0.8–1.8	0.313

INTERVAL CRS		Severe complications			Textbook outcome			Missing values of the short-term outcomes were excluded from analysis.
	No of patients	aOR	95% CI	*p*	aOR	95% CI	*p*	
Annual volume								
Low (<25)	379 (23%)	1			1			
Medium (29–37)	377 (23%)	0.5	0.2–1.2	0.131	0.8	0.5–1.4	0.497	
High (54–84)	890 (54%)	0.9	0.4–1.9	0.684	0.9	0.5–1.4	0.590	
Age (continuous)	1646 (100%)	1.00	0.99–1.02	0.685	**0.98**	**0.97–0.98**	**<0.001**	
BMI (continuous)	1558 (95%)	1.00	1.00–1.01	0.454	1.00	0.99–1.00	0.230	
Missing	88 (5%)							
CCI								
0	1058 (64%)	1			1			
1+	588 (36%)	1.2	0.8–1.7	0.409	1.1	0.8–1.3	0.692	
FIGO (2014)								
Stage IIB-IIIB	83 (5%)	1			1			
Stage IIIC	920 (56%)	1.3	0.6–3.1	0.489	0.7	0.4–1.1	0.110	
Stage IVA	305 (19%)	1.1	0.4–2.8	0.883	**0.5**	**0.3–0.9**	**0.025**	
Stage IVB	338 (21%)	1.2	0.4–3.1	0.755	0.8	0.4–1.4	0.371	
Histology								
Serous	1502 (91%)	1			1			
Other	142 (9%)	1.3	0.7–2.5	0.354	1.0	0.7–1.4	0.909	
Missing	2 (0.1%)							
Abdominal surgery								
No	886 (54%)	1			1			
Yes	680 (41%)	0.9	0.6–1.3	0.634	0.9	0.7–1.1	0.268	
Missing	80 (5%)							
Type of CRS								
Interval	1135 (69%)	1						
Interval + HIPEC	511 (31%)	**1.9**	**1.2–3.1**	**0.009**	NT	NT	NT	

Abbreviations: BMI = Body Mass Index; FIGO = International Federation of Gynecology and Obstetrics; CCI = Charlson Comorbidity Index. Abdominal surgery = previous abdominal surgery before the cytoreductive surgery.

was found between surgical volume and result of CRS: medium and high-volume were associated with increased complete CRS rates (medium-volume adjusted aOR 2.2, 95% CI 1.0–4.8, $p = 0.038$; high-volume aOR 1.9, 95% CI 1.0–3.3, $p = 0.038$). Furthermore, high-volume was associated with increased length of stay ≥10 days (aOR 3.1, 95% CI 1.3–7.3, $p = 0.009$), and severe complications (aOR 4.5, 95% CI 1.5–13.5, $p = 0.007$). No significant associations were observed between surgical volume and textbook outcome, and no significant associations were observed between case-mix factors and all outcomes in the pCRS analyses.

4. Discussion

The present population-based cohort study aimed to assess the correlation between surgical volume and various short-term outcomes for patients undergoing CRS for advanced-stage ovarian cancer. The findings of this study indicate that, after adjusting for case-mix factors, no significant associations were observed between surgical volume and short-term outcomes for patients undergoing iCRS. However, in patients undergoing pCRS, an association between surgical volume and higher rates of complete CRS was found, specifically in high-volume

Table 4
Multilevel, multivariable logistic regression analyses regarding patients with FIGO IIB-IVB advanced-stage ovarian cancer undergoing PRIMARY cytoreductive surgery. Multilevel variable: hospital id.

PRIMARY CRS		Complete result of CRS			Length of stay ≥10 days			Time to adjuvant chemotherapy ≥42 days		
	No of patients	aOR	95% CI	*p*	aOR	95% CI	*p*	aOR	95% CI	*p*
Annual volume										
Low (<25)	265 (34%)	1			1			1		
Medium (29–37)	152 (19%)	1.6	0.9–3.0	0.120	1.9	0.9–3.9	0.082	1.5	0.8–2.9	0.249
High (54–84)	372 (47%)	**1.9**	**1.2–3.1**	**0.010**	**2.3**	**1.3–4.2**	**0.005**	1.5	0.8–2.7	0.189
Age (continuous)	789 (100%)	**0.98**	**0.96–0.99**	**0.012**	**1.03**	**1.00–1.05**	**0.015**	**1.02**	**1.01–1.04**	**0.007**
BMI (continuous)	730 (93%)	1.02	0.98–1.07	0.325	1.02	0.97–1.07	0.480	1.02	0.99–1.06	0.209
Missing	59 (7%)									
CCI										
0	550 (70%)	1			1			1		
1+	239 (30%)	0.8	0.5–1.3	0.389	1.3	0.8–2.1	0.295	1.0	0.7–1.5	0.970
FIGO (2014)										
Stage IIB	242 (31%)	1			1			1		
Stage IIIA	77 (10%)	0.5	0.2–1.7	0.289	**4.0**	**1.6–10.2**	**0.004**	0.9	0.4–1.8	0.713
Stage IIIB	125 (16%)	**0.3**	**0.1–0.8**	**0.020**	**2.6**	**1.1–6.4**	**0.036**	**0.5**	**0.3–0.9**	**0.025**
Stage IIIC	294 (37%)	**0.1**	**0.1–0.2**	**<0.001**	**4.0**	**1.9–8.3**	**<0.001**	0.8	0.5–1.3	0.327
Stage IV	51 (7%)	**0.1**	**0.0–0.3**	**<0.001**	**4.7**	**1.7–12.7**	**0.002**	1.2	0.5–2.5	0.705
Histology										
Serous	526 (67%)	1			1			1		
Other	262 (33%)	1.1	0.6–1.8	0.783	1.1	0.7–1.9	0.663	1.2	0.8–1.9	0.311
Missing	1 (0.1%)									
Abdominal surgery										
No	408 (52%)	1			1			1		
Yes	322 (41%)	0.6	0.4–1.0	0.053	0.8	0.5–1.3	0.360	0.8	0.6–1.2	0.322
Missing	59 (7%)									

PRIMARY CRS		Severe complications			Textbook outcome			Missing values of the short-term outcomes were excluded from analysis.
	No of patients	aOR	95% CI	*p*	aOR	95% CI	*p*	
Annual volume								
Low (<25)	265 (34%)	1			1			
Medium (29–37)	152 (19%)	2.1	0.9–4.8	0.083	0.9	0.5–1.5	0.702	
High (54–84)	372 (47%)	**2.3**	**1.1–4.6**	**0.022**	1.0	0.6–1.4	0.827	
Age (continuous)	789 (100%)	0.99	0.98–1.02	0.795	**0.98**	**0.96–0.99**	**0.001**	
BMI (continuous)	730 (93%)	1.03	0.98–1.09	0.247	1.02	0.98–1.05	0.378	
Missing	59 (7%)							
CCI								
0	550 (70%)	1			1			
1+	239 (30%)	1.0	0.5–1.7	0.872	0.92	0.6–1.3	0.666	
FIGO (2014)								
Stage IIB	242 (31%)	1			1			
Stage IIIA	77 (10%)	2.7	0.9–7.7	0.065	**0.4**	**0.2–0.9**	**0.020**	
Stage IIIB	125 (16%)	1.4	0.5–3.9	0.544	**0.5**	**0.2–0.9**	**0.028**	
Stage IIIC	294 (37%)	**3.2**	**1.4–6.9**	**0.004**	**0.2**	**0.3–0.9**	**<0.001**	
Stage IV	51 (7%)	2.0	0.6–6.8	0.295	**0.2**	**0.1–0.4**	**<0.001**	
Histology								
Serous	526 (67%)	1			1			
Other	262 (33%)	1.0	0.5–1.8	0.927	1.1	0.8–1.7	0.575	
Missing	1 (0.1%)							
Abdominal surgery								
No	408 (52%)	1			1			
Yes	322 (41%)	1.1	0.6–1.8	0.816	1.0	0.7–1.4	0.784	
Missing	59 (7%)							

Abbreviations: BMI = Body Mass Index; FIGO = International Federation of Gynecology and Obstetrics; CCI = Charlson Comorbidity Index. Abdominal surgery = previous abdominal surgery before the cytoreductive surgery.

hospitals. Furthermore, the current study observed associations between surgical volume and prolonged length of stay as well as increased severe complication rates in patients treated in high-volume hospitals. Focusing on patients with FIGO-stage IIIC-IVB undergoing pCRS only, medium- and high-volume were associated with increased rates of complete CRS, these increased completeness rates were at the expense of increased severe complications and prolonged admissions in high-volume hospitals. Therefore, increasing the annual surgical volume to fifty does not necessarily improve short-term outcomes. Moreover, the effect on long-term outcomes is yet unknown, and therefore, the implementation of increasing the surgical volume per hospital is subject to debate. Surgical capacity should be considered because lack of capacity could lead to longer waiting times and deterioration of the quality of care.

The fact that high-volume (combined with medium-volume in the subgroup analysis) was associated with increased complete pCRS rates could indicate that patients were appropriately selected for either neoadjuvant chemotherapy or upfront surgery in these hospitals. Medium- and high-volume hospitals had similar proportions of patients with FIGO IIIC-IVB ovarian cancer selected for primary surgery, while low-volume hospitals performed primary surgery more often. However, it should be noted that patients treated in high-volume hospitals were also associated with prolonged length of hospital stay and increased severe complications rates. This could be the result of more aggressive,

radical surgery in high-volume hospitals. One could argue that the 'best practice' for FIGO-stage IIIC-IVB was in medium-volume hospitals because patients treated in those hospitals were associated with higher complete CRS rates, without a concurrent increase in prolonged length of stay or severe complications rates. Clinical auditing and roundtable discussions with the aim to learn from best practices could reveal factors contributing to these hospitals' favorable outcomes.

It is important to realize that variation in outcomes exists among different hospitals within volume groups. For instance, low-volume was associated with significantly lower rates of complete pCRS for FIGO-stage IIIC-IVB. However, the range of complete CRS in low-volume hospitals was 43%–86%. In medium-volume hospitals, the range was 69%–90%, and in high-volume hospitals, the range was 67%–93% (FIGO-stage IIIC-IVB). Consequently, some low-volume hospitals could exhibit higher rates of complete CRS than various medium- and high-volume hospitals. This underscores the need not only to focus on increasing surgical volumes but rather on clinical auditing and learning from best practices.

Five out of the eighteen hospitals included in the current study did not reach the threshold of twenty CRS per hospital per year. On September 1st, 2023, one out of these hospitals stopped performing CRS because they could not meet this requirement. It remains unclear why the other four hospitals continued to perform CRS. This will be addressed during the next national roundtable discussion of the DGOA in June 2024 as part of the Plan-Do-Check-Act cycle.

The Dutch government released a report suggesting that the minimum should be increased from twenty to fifty surgeries due to multiple reasons [18]. The most important motivator was to enhance the quality of care while assuring affordable healthcare in the future. The authors of the government report hypothesized that further centralization would lead to cost reduction. However, results of this study might contradict this hypothesis, as patients treated in high-volume hospitals had higher prolonged length of stay rates and experienced more severe complications. This might suggest that further centralization may lead to higher healthcare costs.

Previous Dutch studies by Vernooij et al. on hospital volume and outcomes for patients with ovarian cancer showed significantly improved outcomes for patients treated in relatively high-volume (semi-)specialized hospitals (cohort 1996–2003) [8,9]. Following these studies, centralization was initiated. The 5-year age-standardized overall survival (all stages) improved from 31% to 40% between 1990 and 2019 in the Netherlands; however, 10-year overall survival remained poor (25–28%, all stages) [23]. According to the definitions used by Vernooij et al., all patients analyzed in the current study were treated in high-volume (semi-)specialized centers. Compared to the historical cohorts of Vernooij et al., the current study showed improved complete CRS rates.

In 2019, Timmermans et al. reported on the outcomes of Dutch patients with advanced-stage (FIGO IIIC-IVB) ovarian cancer between 2008 and 2015 based on the Dutch Cancer Registry [17]. Comparing the complete CRS rates, the present study shows improved results: complete iCRS 50% vs. 70.0%, and complete pCRS 41% vs. 73.3%. These findings show that concentration of surgical volume and the requirements set by the Dutch Gynecological Oncology Society potentially led to improved rates of complete CRS. However, our study does not unequivocally support a further concentration of care, because no associations were observed between surgical volume and outcomes for patients undergoing iCRS. The improved rates of complete CRS may also be partially influenced by the increased utilization of neoadjuvant chemotherapy. Timmermans et al. reported varying rates of pCRS FIGO-stage IIIC-IVB ranging from 24% to 48% (regional variation) [17]. In our study, the proportion of pCRS for FIGO-stage IIIC-IVB was substantially lower, ranging from 15 to 23% across surgical volume groups.

Similar analyses were performed by Nasioudis et al. on data from the United States [2]. Nasioudis et al. analyzed patients undergoing pCRS for FIGO III-IV ovarian cancer. Patients were stratified by annual surgical volume (low <6.8, medium 6.8–17.2, and high >17.2. Complete CRS was only 42.2% compared to 73.3% in our study. The authors observed that 90-day mortality was significantly higher in low-volume hospitals compared to medium- and high-volume hospitals, whereas the current data did not reveal differences in 30-day mortality between volume groups.

Like the OVHIPEC-trial, our findings indicate that adding HIPEC to iCRS was associated with increased length of stay [22]. In contrast to the trial, however, we observed an association between the addition of HIPEC and an increase in severe complications. This discrepancy may be explained by the fact that patients undergoing HIPEC are more frequently admitted to the ICU immediately after surgery compared to those undergoing regular iCRS. In our classification, patients admitted to the ICU for more than two days who experienced any complication were considered to have severe complications.

Strengths of the current study include the sample size, the fact that the population-based, reliable, detailed clinical data of the DGOA registry were used, the adjustment of outcomes for case-mix factors, and the limited missing values. There are also certain limitations. First, the retrospective analysis of the prospectively registered data. However, these data are currently the best available data to assess associations between surgical volume and outcomes in a real-world setting. Second, case-mix variables not included in the models, such as race, ethnicity, and socioeconomic factors, could have impacted the outcomes. We chose to include the most important available case-mix factors with limited missing values. Third, whether the result of CRS was complete remains a subjective finding. However, Dutch gynecologic oncologists reported the result of CRS including residual disease scoring. Therefore, inter-observer bias was minimalized. Fourth, surgeon volume was not analyzed in the current study as the DGOA reports quality of care at the institutional level. Analyzing the results of a single surgeon was not possible, because surgical teams consist of either two gynecologic oncologists, one gynecologic oncologist and one fellow, or one gynecologic oncologist and a surgical oncologist in the Netherlands. Last, overall survival was not analyzed. In this study we focused on short-term outcomes such as result of CRS and other postoperative outcomes. Since complete CRS is strongly related to overall survival, we used the result of CRS as outcome measure.

The data from the current study suggest that improving the quality of care for patients undergoing CRS for advanced-stage ovarian cancer does not solely depend on increasing surgical volumes, as we observed no associations between surgical volume and outcomes in the iCRS cohort. To enhance the quality of care, it is crucial to identify best practices and outliers to ultimately establish the optimal standard of care. During this process of clinical auditing, it is also essential to discuss the clinical data transparently in roundtable discussions to eventually enhance the quality of care. It should be noted that the centralization of care initiated in 2012 led to the improvement of the ability to identify best practices and outliers and establish optimal standards of care.

Policy makers should also acknowledge the access to care from the patients' perspective. When the minimum is set at fifty CRS per center per year, a maximum of twelve hospitals will perform CRS for advanced-stage ovarian cancer in the Netherlands (based on the current data). Recently, a study described that elder patients with malignancies in the Netherlands are less willingly to travel further to specialized hospitals for optimal treatment [24]. While most patients with ovarian cancer are elderly, policy makers should consider the consequences of further centralization for the optimal treatment of these patients. Additionally, surgical capacities should be considered when volumes are increased.

Besides its impact on regionally organized and centralized healthcare in resource-rich countries, the current results could furthermore impact the global gynecologic oncology community: governments in countries lacking centralized ovarian cancer care may find motivation in our results to establish regional networks, centralize care, and implement clinical auditing. However, significant global disparities in care

organization exist, and particularly resource-poor countries may face challenges in implementing such changes to their care organization [25].

The current study analyzed the quality of care for advanced-stage ovarian cancer within the centralized healthcare system in the Netherlands. Future research should focus on international comparisons of outcomes of patients in centralized vs. non-centralized healthcare systems. Such comparisons would facilitate a more comprehensive analysis of the impact of hospital volume (and centralization) on outcomes of patients undergoing CRS for advanced-stage ovarian cancer, potentially allowing to define an optimal minimum annual volume for CRS. Furthermore, these future analyses should also incorporate case-mix adjustment.

5. Conclusions

Although centralization of surgical care has significantly improved short-term outcomes for patients with advanced-stage ovarian cancer in the Netherlands, our results do not support further centralization in the current centralized Dutch healthcare system for patients undergoing iCRS. For patients undergoing pCRS (FIGO-stage IIB-IVB) high-volume was associated with increased rates of complete CRS (similar association of medium- and high-volume and increased complete pCRS in FIGO IIIC-IVB). These findings could suggest a more accurate patient selection process for pCRS in (medium and) high-volume hospitals, supporting the case for additional centralization. However, patients treated in high-volume hospitals had a prolonged length of stay and increased severe complications after pCRS, possibly explained by more aggressive, radical approach to achieve complete CRS. Moreover, completeness rates differed substantially across hospitals in the various volume groups. Therefore, the current results emphasize that enhancing the quality of care is multifactorial and not solely accomplished by increasing surgical volumes.

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Author contribution

MA was the principal author and performed the analyses. BS, WD, MW, and RK all performed the interpretation of data and performed revision of the manuscript. The participants of the Dutch Gynecological Oncology Audit Collaborators Group collected data for the registry and read and approved the manuscript.

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CRediT authorship contribution statement

M.D. Algera: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **W.J. van Driel:** Writing – review & editing, Supervision, Methodology, Conceptualization. **B.F.M. Slangen:** Writing – review & editing, Supervision, Methodology, Conceptualization. **M.W.J.M. Wouters:** Writing – review & editing, Supervision, Methodology, Conceptualization. **R.F.P.M. Kruitwagen:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

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