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## Risks and benefits of systematic lymphadenectomy during interval debulking surgery for advanced high grade serous ovarian cancer

Louise Benoit, Meriem Koual, Marie-Aude Le Frère-Belda, Jonathan Zerbib, Laure Fournier, Huyên-Thu Nguyen-Xuan, Nicolas Delanoy, Enrica Bentivegna, Anne-Sophie Bats, Henri Azaïs

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1 **Risks and benefits of systematic lymphadenectomy during interval debulking surgery**  
2 **for advanced high grade serous ovarian cancer**

3 Running head: Lymphadenectomy in ovarian cancer

4

5 Benoit Louise <sup>1,2,3</sup>, Koual Meriem <sup>1,2,3</sup>, Le Frère-Belda Marie-Aude <sup>4</sup>, Zerbib Jonathan <sup>5</sup>,

6 Fournier Laure <sup>5</sup>, Nguyen-Xuan Huyen-Thu <sup>1,2</sup>, Delanoy Nicolas <sup>6</sup>,

7 Bentivegna Enrica <sup>1,2</sup>, Bats Anne-Sophie <sup>1,2,7</sup>, Azaïs Henri <sup>1,2,7</sup>

8

9 1. Gynecologic and Breast Oncologic Surgery Department, Georges Pompidou European Hospital, APHP.  
10 Centre, Paris, France

11 2. Paris University, Faculty of Medicine, Paris, France

12 3. INSERM UMR-S 1124, Université de Paris, Centre Universitaire des Saint-Père, Paris

13 4. Pathology Department, Georges Pompidou European Hospital, APHP. Centre, Paris, France

14 5. Radiology Department, Georges Pompidou European Hospital, APHP. Centre, Paris, France

15 6. Oncology Department, Georges Pompidou European Hospital, APHP. Centre, Paris, France

16 7. INSERM UMR-S 1147, Université de Paris, Centre de Recherche des Cordeliers, Paris

17

18 **Corresponding author:**

19 Dr Louise BENOIT

20 Gynecologic and Breast Oncologic Surgery Department

21 European Georges Pompidou Hospital

22 20, rue Leblanc 75908 Paris Cedex 15 France

23 E-mail: [louise.am.benoit@gmail.com](mailto:louise.am.benoit@gmail.com)

24 Tel : +33679169971

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29

30

31 **Synopsis**

32 The impact of lymphadenectomy in patients with ovarian cancer undergoing neoadjuvant chemotherapy  
33 with interval debulking surgery is debated. We found that lymphadenectomy did not enhance  
34 recurrence-free and overall survival at the cost of increased post-operative complications.

35 **Abstract (200 words)**

36 *Background:* Lymphadenectomy is debated in patients with ovarian cancer. The aim of our study was  
37 to evaluate the impact of lymphadenectomy in patients with high-grade serous ovarian cancer receiving  
38 neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS).

39 *Methods:* A retrospective, unicentric study including all patients undergoing NACT and IDS was  
40 carried out from 2005-2018. Patients with and without lymphadenectomy were compared in terms of  
41 recurrence free survival (RFS), overall survival (OS), and complication rates.

42 *Results:* We included 203 patients. Of these, 133 had a lymphadenectomy (65.5%) and 77 had involved  
43 nodes (57.9%). Patients without a lymphadenectomy were older, had a more extensive disease and less  
44 complete CRS. No differences were noted between the lymphadenectomy and no lymphadenectomy  
45 group concerning 2-year RFS (47.4% and 48.6%,  $p=0.87$ , respectively) and 5-year OS (63.2% versus  
46 58.6%,  $p=0.41$ , respectively). Post-operative complications tended to be more frequent in the  
47 lymphadenectomy group (18.57% versus 31.58%,  $p=0.09$ ). In patients with a lymphadenectomy,  
48 survival was significantly altered if the nodes were involved (positive nodes: 2-year RFS 42.5% and 5-  
49 year OS 49.4%, negative nodes: 2-year RFS 60.7% and 5-year OS 82.2%,  $p=0.03$  and  $p<0.001$ ,  
50 respectively).

51 *Conclusion:* Lymphadenectomy during IDS does not improve survival and increases post-operative  
52 complications.

53

54

55 **Key words:**

56

57 Epithelial ovarian cancer; lymphadenectomy; interval debulking surgery; neo-adjuvant chemotherapy.

58 **Introduction**

59 Epithelial ovarian cancer (EOC) is a gynecologic malignancy responsible of 313 959 new cases and is  
60 the 7<sup>th</sup> cause of death by cancer in women in 2019 worldwide [1]. The standard of care is defined by  
61 surgery followed by platinum-based chemotherapy [2,3]. The main prognostic factor is the completion  
62 of a complete macroscopic cytoreductive surgery (CRS), i.e. with no residual disease [4,5]. However,  
63 a large proportion of EOCs are discovered at an advanced stage where primary CRS is deemed  
64 impossible. These patients benefit from a neoadjuvant chemotherapy (NACT) followed by an interval  
65 debulking surgery (IDS) depending on the therapeutic response [4].

66 Pelvic and aortic lymphadenectomy have been part of the standard guidelines during primary CRS for  
67 many years. However, the recent LION study has shown that systematic lymphadenectomy was  
68 associated with an increase in post-operative complications with no benefit on recurrence-free survival  
69 (RFS) and overall survival (OS) in patients with advanced EOC undergoing primary CRS followed by  
70 chemotherapy, and without any preoperative or per-operative suspicion of nodal involvement, after  
71 appropriate imaging and clinical assessment [6].

72 Little data exists on the benefit of a systematic lymphadenectomy for patients undergoing NACT  
73 followed by IDS [7–13]. Current evidence is based on small retrospective studies. Moreover, due to the  
74 different inclusion criteria (optimal residual disease, histological subtype) and the lymphadenectomy  
75 modalities (systematic or selective), the results differ from one study to another. Indeed, two studies  
76 have found that a lymphadenectomy could enhance OS [9,10] whereas most have not found a survival  
77 benefit from a systematic lymphadenectomy[7,8,10–12]. In this specific setting, more information is  
78 needed to fuel the debate on the importance of a systematic lymphadenectomy.

79 The aim of this study was therefore to assess the impact of a systematic lymphadenectomy during IDS,  
80 in terms of survival and morbidity for patients with an advanced EOC.

81

82

## 83 **Material and methods**

### 84 *Population*

85 The data of all patients with advanced EOC were retrospectively collected in our department from 2005  
86 to 2018. Our department is accredited for the surgical management of advanced EOC by the European  
87 Society of Gynecologic Oncology (ESGO). We included all patients with an advanced EOC (stage IIB-  
88 IV according to the 2014 classification of the International Federation of Gynecology and Obstetrics  
89 (FIGO)) who underwent a NACT followed by IDS [14]. Others histological subtypes than high grade  
90 serous ovarian cancer (HGSOC) were excluded to strengthen the conclusion of our study for the most  
91 frequent histology. This study was conducted in accordance with our institutional ethic guidelines for  
92 retrospective studies and was approved by the ethics committee of the National College of French  
93 Gynecologists and Obstetricians (2021-GYN- 0305).

94 Data regarding patient characteristics (age, body mass index (BMI), American society of anesthesiology  
95 (ASA) score, identified genetic mutation), tumor attributes (FIGO stage, histological type and grade,  
96 CA 125 tumor marker), neoadjuvant and adjuvant treatment (chemotherapy) surgical management  
97 (surgical route, extent of surgery), oncologic outcomes (RFS and OS, death, location of recurrence) and  
98 adverse events after surgery (intra- and post-operative complications) were collected. Information  
99 regarding race / ethnicity is not available in our study because French directives do not authorize studies  
100 on these data.

101

### 102 *Surgery*

103 Therapeutic management was decided for each woman during multidisciplinary tumor boards that  
104 included surgeons, oncologists, radiation oncologists, radiologists, pathologists and nuclear medicine  
105 physicians. All patients had an initial evaluation (laparoscopy and computed tomography (CT)) with a  
106 histological confirmation of their advanced ovarian cancer. Their disease was considered too extensive  
107 to undergo primary CRS. Resectability was systematically assessed by an experienced senior surgeon.  
108 Patients then received a platinum-based NACT and underwent a second evaluation (laparoscopy and/or  
109 CT) after 3-6 cycles of chemotherapy. The choice of the number of NACT cycles was left to the medical

110 team. Patients who were considered operable with an objective of no post-operative residual disease  
111 underwent an IDS, that included at least peritoneal cytology, bilateral salpingo-oophorectomy, total  
112 hysterectomy, omentectomy, appendectomy (depending on histology) and eventually a pelvic/para-  
113 aortic lymphadenectomy. The extent of the surgery (digestive resection, splenectomy, diaphragmatic  
114 peritonectomy...) depended on the spread of the disease and was carried out with the goal of complete  
115 macroscopic cytoreduction. Lymphadenectomy was performed according to patient comorbidities,  
116 extent of surgery and depended on ongoing research protocols. After IDS, patients had platinum-based  
117 adjuvant chemotherapy and targeted therapies (bevacizumab, PARP inhibitors) if indicated by the  
118 tumor board.

119 Residual disease was defined according to the completeness of cytoreduction score (CC) at the end of  
120 the intervention and separated in CC0 (no residual tumor), CC1 (residual tumor less or equal to 2.5mm),  
121 CC2 (residual tumor superior to 2.5mm but inferior or equal to 2.5cm), and CC3 (strictly superior to  
122 2.5cm). Staging was assessed by the FIGO stage and the peritoneal carcinomatosis index (PCI) defined  
123 by Sugarbaker [15]. The PCI was evaluated at the initial laparoscopy and before the IDS.

124

### 125 *Survival*

126 RFS and OS were compared between the patients who underwent a lymphadenectomy and those who  
127 did not. RFS and OS were respectively defined as the time from the date of the initial diagnosis to the  
128 date of the first tumor recurrence or the date of death, of any cause. 2-year RFS and 5-year OS were  
129 also assessed.

130 The location of the recurrences was separated into peritoneal, nodal (above or below the left renal vein  
131 or over the diaphragm) and metastatic.

132 Among the patients who underwent a lymphadenectomy, we also compared the survival rates between  
133 the patients who had a positive histological lymphadenectomy (N+) to those who did not (N-).

134

### 135 *Post- and per-operative complication*

136 Peri- and post-operative morbidities were assessed according to the Clavien-Dindo classification [16].  
137 Major complications were defined by a grade over 3. Grade 3 complications require a surgical,

138 endoscopic, or radiological intervention (with or without anesthesia) and grade 4 complication are  
139 considered life-threatening complication. Grade 5 complications result in patient demise.

140 The 30-day mortality was also assessed.

141

#### 142 *Statistical analysis*

143 Continuous variables were expressed using the mean +/- the standard deviation or using the median and  
144 range. They were compared with a student-t test or a Wilcoxon test in case of non-parametric  
145 distributions. Categorical values were expressed using an absolute number and a percentage. They were  
146 compared with a chi2 test or Fischer's exact test.

147 A Kaplan Mayer curve was used to graphically express the differences in RFS and OS. A log rank test  
148 compared the two curves. A multivariate analysis was performed using the Cox regression model and  
149 including the variables with a p-value <0.05 in univariate analysis for survival analysis.

150 All statistical tests were two-sided, and the significance level was 0.05. Data were analyzed using R  
151 studio version 1.1447 and an Excel database (Microsoft, Redmond, WA).

152

153 **Results**

154

155 ***Patient's characteristics***

156 A total of 631 patients were diagnosed with an EOC in our institution from 2005 to 2018. Only patients  
157 with high-grade serous ovarian cancer (HGSOC) were selected for further analysis as the number of  
158 patients with other histology were insufficient (n=28) to draw solid conclusion regarding the value of  
159 systematic lymphadenectomy in these populations. Of these, 203 had an initially non-operable advanced  
160 disease and underwent NACT followed by IDS. One hundred and thirty-three (65.5%) had a  
161 lymphadenectomy and 70 (34.5%) did not (Figure 1). Of these, 57.89% (77/133) had positive lymph  
162 nodes.

163 The populations did not differ in terms of BMI, menopausal status, ASA score and BRCA  
164 mutation. Patients in the no lymphadenectomy group were older (average 68.37 years old versus 62.33,  
165  $p<0.001$ ).

166 Patients had similar tumor marker CA 125 and FIGO stage. Patients who did not undergo a  
167 lymphadenectomy had a non-significant higher PCI score on initial exploratory laparoscopy (average  
168 19.72 versus 21.54,  $p=0.15$ ). The two groups did not differ concerning NACT treatment (type, number  
169 of cycles). The median follow-up was 32 (4-120 months) and 26 (5-103 months) in the  
170 lymphadenectomy and no lymphadenectomy group, respectively ( $p=0.41$ ).

171 Patient characteristics are summarized Table 1.

172

173 ***Surgery***

174 Of the 133 patients who received a lymphadenectomy, 122 had both a pelvic and para-aortic  
175 lymphadenectomy. Concerning the other patients : 3 only had a pelvic lymphadenectomy, and 8 only  
176 had a para-aortic lymphadenectomy.

177 The mean number of nodes removed for the entire population was 31.37 (+/- 17): 22.5 (+/- 12.9) and  
178 12.2 (+/- 7.7) for para-aortic and pelvic lymphadenectomy, respectively.

179 Patients in the no lymphadenectomy group had more extensive disease according to the PCI score  
180 (average 8.45 versus 12.12,  $p<0.001$ ) (Table 2). They also had a significantly higher residual disease  
181 score (CC2, 21.43% versus 0.75%,  $p<0.001$ ).

182

### 183 *Per and post-operative complications*

184 In the whole population, 27.09% (55/203) of the patients presented a post-operative complication. Post-  
185 operative complications tended to be more frequent in the group with a lymphadenectomy (18.57 versus  
186 31.58,  $p=0.09$ ). The Clavien Dindo classification was similar in both groups. Per-operative  
187 complications and the 30-day mortality did not differ (Table 2).

188

### 189 *Survival*

190 No differences were noted between the lymphadenectomy and no lymphadenectomy group concerning  
191 2-year RFS (47.4% and 48.6%,  $p=0.87$ , respectively) and 5-year OS (63.2% versus 58.6%,  $p=0.41$ ,  
192 respectively). Median RFS was 21 months in the lymphadenectomy group and 17 months in the no  
193 lymphadenectomy group. Median OS was 28 months in the lymphadenectomy group and 20 months in  
194 the no lymphadenectomy group. The Kaplan-Meier curves did not differ neither for RFS (log-rank test,  
195  $p=0.3$ ) nor for OS ( $p=0.6$ ) (Figure 2).

196 Lymphadenectomy was not associated with RFS (HR = 0.83 IC95%= 0.58-1.19,  $p=0.32$ ). Only PCI  
197 was associated with RFS after multivariate analysis (Table 3).

198 Likewise, lymphadenectomy was not associated with OS (HR= 0.89 IC95%= 0.57-1.41,  $p=0.64$ ). Only  
199 PCI was associated with OS after multivariate regression model (Table 3).

200 The location of recurrences was similar even though there was a non-significance increase of nodal  
201 recurrences in the no lymphadenectomy group (38.57% versus 34.59%,  $p=0.68$ ) (Table 2). In the  
202 lymphadenectomy group, nodal recurrences were mainly over the left renal vein (17/46, 36.9%) and  
203 over the diaphragm (25/46, 47.8%).

204

### 205 *Survival according to definitive lymph node status*

206 Of the 133 patients who benefitted from a lymphadenectomy, 59.4% had a positive lymphadenectomy  
207 on definitive analysis. Seventy-one patients (53.4%) had a positive para-aortic lymphadenectomy  
208 (average: 3 positive nodes) and 48 (36.1%) a positive pelvic lymphadenectomy (average: 2 nodes).  
209 The 2-year RFS and 5-year OS was significantly altered in the positive lymphadenectomy group  
210 (positive lymph nodes: 2-year RFS 42.5% and 5-year OS 49.4%, negative nodes: 2-year RFS 60.7%  
211 and 5-year OS 82.2%,  $p= 0.03$  and  $p<0.001$  , respectively)  
212 The survival curves were significantly different with an altered RFS ( $p<0.001$ ) and OS ( $p<0.001$ ) in the  
213 positive lymphadenectomy group (Figure 3). After multivariate analysis, positive pathological nodes  
214 were significantly associated with a worse OS and RFS (supplementary Table 1).

215 **Discussion**

216 In this study, we aimed to enrich the ongoing debate on the therapeutic value of systematic  
217 lymphadenectomy during IDS after NACT in patients with an advanced HGSOE (FIGO stage IIB-IV).  
218 We found that a systematic lymphadenectomy did not statistically improve RFS or OS, at the expense  
219 of higher post-operative complications. In the sub-group of patients benefitting from a systematic  
220 lymphadenectomy, patients with histological positive nodes presented an altered survival rate.

221  
222 The LION study, a randomized controlled trial comparing systematic lymphadenectomy to no  
223 lymphadenectomy, found that systematic lymphadenectomy did not impact RFS or OS and increased  
224 post-operative complications. However, this study only assessed patients who benefitted from primary  
225 CRS with FIGO stage IIB-IV EOC, and without any preoperative or per-operative suspicion of nodal  
226 involvement, after appropriate imaging and clinical assessment [6]. Several retrospective works are in  
227 accordance with our findings and have suggested that systematic lymphadenectomy during IDS after  
228 NACT does not improve survival of patients [7,11,12]. Two studies showed that lymphadenectomy  
229 enhanced OS. Indeed, Eoh et al. found an improved OS in patients with an optimal CRS undergoing  
230 systematic lymphadenectomy. However, in their work, they compared systematic lymphadenectomy to  
231 selective lymphadenectomy (suspicious nodes) [10]. Moreover, Eoh et al. had the highest rate of  
232 positive lymph nodes (54-66%) and of incomplete CRS (63-33%). Likewise, Song et al. suggested an  
233 altered OS in patients not undergoing a lymphadenectomy if complete CRS was achieved [9].

234  
235 Studies have found positive lymph nodes in 44-55.7% of patients undergoing primary CRS with  
236 systematic lymphadenectomy [6,17,18]. However, after NACT this rate drops to 11-54 % [7,8,19,20].  
237 In our work, 57.89% (77/133) of the 157 patients who benefitted from a lymphadenectomy had involved  
238 lymph nodes on definitive pathologic analysis. Despite the removal of these involved nodes, these  
239 patients did not present an improved OS, questioning the importance of the residual peritoneal tumor  
240 burden. Iwase et al. found the same results with a significant decrease in the 2-years RFS and 5-years  
241 OS in patients with a positive lymphadenectomy versus a negative lymphadenectomy (62% and 56%  
242 versus 26% and 24%, respectively  $p < 0.001$ ) [8]. Nodal metastasis could be more chemotherapy

243 resistant such as Morice et al. suggested [20]. Moreover, it can be hypothesized that removing lymph  
244 nodes decreases the immunologic response thus promoting tumor proliferation [21]. One French  
245 multicentric study found that nodal status did not impact survival. This study found a small number of  
246 metastatic nodes (11%) compared to the high number in our study (57.89%) [7]. However, no hasty  
247 conclusion can be made concerning this subgroup as our work was not designed to analyze this. Indeed,  
248 in order to conclude on the necessity of a lymphadenectomy in histologically node positive patients, a  
249 study comparing lymphadenectomy versus no lymphadenectomy in node positive patients is needed.  
250 Defining this population pre-operatively is a major concern in ovarian cancer management as imaging  
251 and per-operative palpation cannot accurately predict lymph node involvement [22–25]. Likewise, our  
252 study did not evaluate the impact of a lymphadenectomy of an “unusual site” such as hepatoceliac nodes  
253 or omental nodes for too few patients underwent this procedure. These regions are systematically  
254 assessed yet rarely dissected in our work [26–28].

255

256 The two groups in our study presented different characteristics. Indeed, patients in the no  
257 lymphadenectomy group were older with a more extensive disease. These patients were therefore more  
258 likely to not undergo a complete CRS and a morbid lymphadenectomy. However, despite the inferior  
259 rate of complete cytoreduction (CC0) in the no lymphadenectomy group, these patients did not present  
260 an altered survival. On the contrary, patients who benefitted from a lymphadenectomy were initially  
261 fitter, and presented similar survival rates. It could be hypothesized that the lymphadenectomy itself  
262 generated a morbidity, altering their prognosis (31.58% post-operative complications versus 18.57%,  
263  $p=0.09$ ), even if the effective of our groups did not allow us to reach significant result.

264 More post-operative complications were noted in the lymphadenectomy group, yet this difference did  
265 not reach significance (31.58% versus 18.57%,  $p=0.09$ ). The Clavien Dindo classification, per-  
266 operative complications and the 30-day mortality were similar in both groups. It has been shown that a  
267 lymphadenectomy is a source of complications with notably longer operative times and transfusion  
268 rates [11,12]. Moreover, post-operative complications and extensive surgery can cause delay in  
269 adjuvant chemotherapy initiation [29].

270

271 In the no lymphadenectomy group, 28.57% of the patients had residual post-operative intraabdominal  
272 tumor versus 12.03% in the lymphadenectomy group. In this retrospective nonrandomized study, we  
273 chose to include patients who did not achieve complete cytoreduction. Excluding this population with  
274 the poorest prognosis would have resulted in a selection bias.

275

276 To our surprise, the patterns of recurrences did not differ between the two groups with 34.59% (46/133)  
277 and 38.57% (27/70) of nodal recurrences in the lymphadenectomy and no lymphadenectomy group  
278 ( $p=0.68$ ). This cannot be explained by the quality of the lymph node dissection as a satisfactory number  
279 of nodes were removed in our study (22.5 and 12.2 nodes for para-aortic and pelvic lymphadenectomy,  
280 respectively) [30–32]. Moreover, studies with more extensive lymphadenectomies found similar results  
281 [7,8,12]. Only Eoh et al. found more nodal recurrences in patients benefitting from a selective rather  
282 than from a systematic lymphadenectomy (45.5% vs 23.5%,  $p = 0.022$ ) [10]. Among the 27 patients  
283 with a nodal recurrence in the no lymphadenectomy, group only 3 had a salvage lymphadenectomy.  
284 Likewise, only 6 patients had a complementary adenectomy among the 46 patients with a nodal  
285 recurrence in the lymphadenectomy group. These patients did not have an isolated lymph node  
286 recurrence and had multiple lesions. It has been shown that patients with multiple lesions probably  
287 benefit less from a salvage lymphadenectomy [33].

288

289 Several limits must be noted. First, this was a retrospective, single site study. Since patients with more  
290 morbidities were more likely to not undergo a lymphadenectomy, a multivariate analysis was performed  
291 to limit confounding bias. Only patients with HGSOC were included in order to obtain a homogeneous  
292 population. Likewise, all patients were included regardless of their initial node status to avoid a selection  
293 bias. Indeed, accurately defining histologically positive patients pre-operatively is complex. Neither  
294 imaging nor per-operative palpation can precisely predict lymph node involvement<sup>20-23</sup>. In the LION  
295 trial, despite the selection of node negative patients by imaging and per-operative palpation, 55.7% had  
296 histologically positive nodes [6].

297

298 Our results issued from a large population treated at an expert center point out that a systematic  
299 lymphadenectomy during IDS after NACT in patients with an advanced HGSOC (FIGO stage IIB-IV)  
300 does not statistically improve RFS nor OS, at the expense of a non-significant higher post-operative  
301 complication rate. A large prospective randomized trial is needed to close this debate.  
302

303

304 **Conflict of interests**

305 **Funding:** None

306 **Conflicts of interest:** None

307

308 **Author contribution**

309 Louise Benoit : Conceptualization ; Data curation; Formal analysis ; Investigation; Methodology;

310 Roles/Writing - original draft

311 Koual Meriem : Conceptualization; Supervision; Validation ; Writing - review & editing.

312 Le Frère-Belda Marie-Aude: Conceptualization ; Supervision; Validation ; Writing - review & editing.

313 Zerbib Jonathan: Data curation; Formal analysis ; Investigation

314 Nguyen-Xuan Huyen-Thu: Conceptualization ; Supervision; Validation ; Writing - review & editing.

315 Delanoy Nicolas: Conceptualization ; Supervision; Validation ; Writing - review & editing.

316 Bentivegna Enrica: Conceptualization ; Supervision; Validation ; Writing - review & editing.

317 Fournier Laure: Conceptualization ; Supervision; Validation ; Writing - review & editing

318 Bats Anne-Sophie: Conceptualization ; Formal analysis ; Investigation; Methodology ; Supervision;

319 Validation ; Writing - review & editing.

320 Azaïs Henri: Conceptualization ; Formal analysis ; Investigation; Methodology ; Supervision;

321 Validation ; Writing - review & editing.

322

323 **Data availability**

324 The data that support the findings of this study are available upon reasonable request from the

325 corresponding author. The data are not publicly available due to privacy or ethical restrictions.

326

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328

329

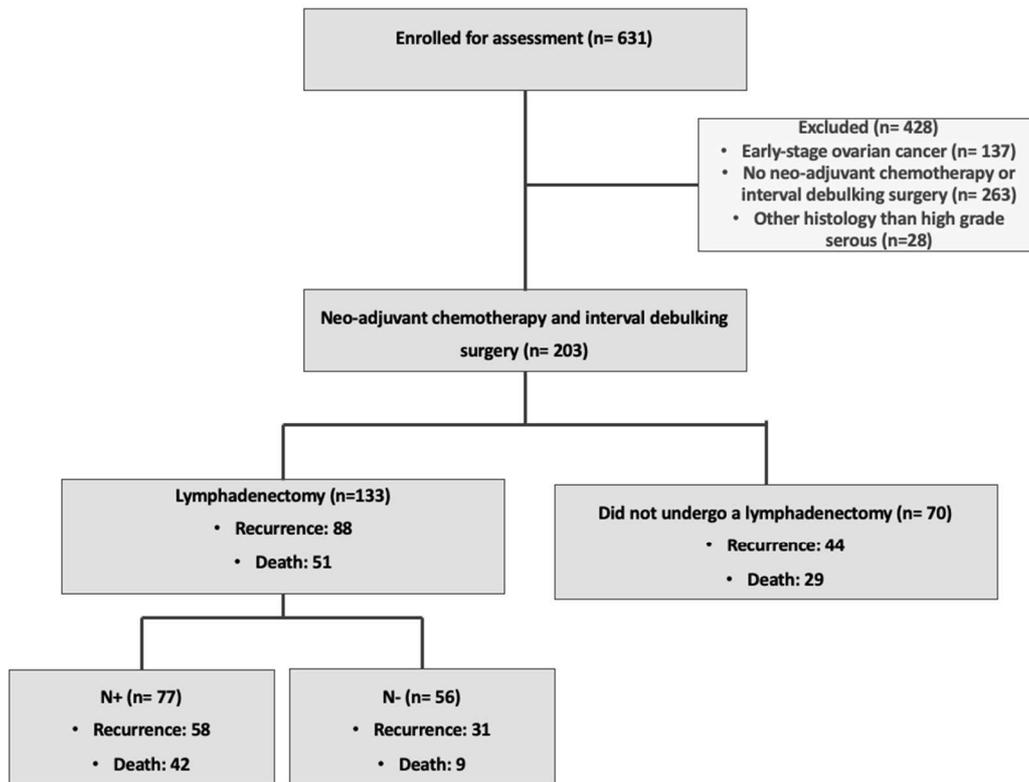
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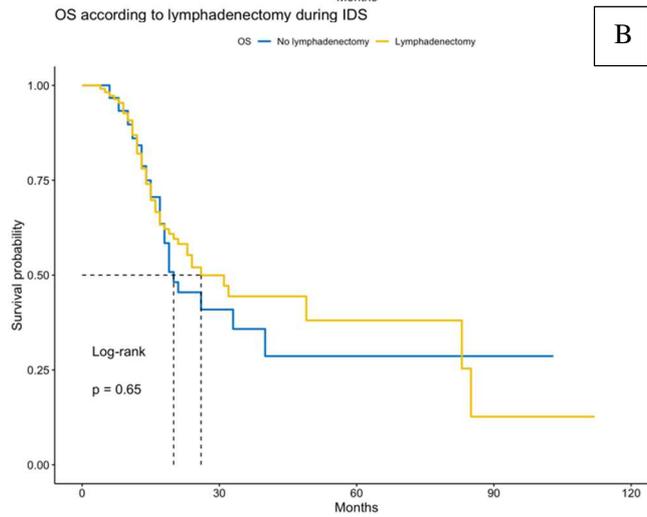
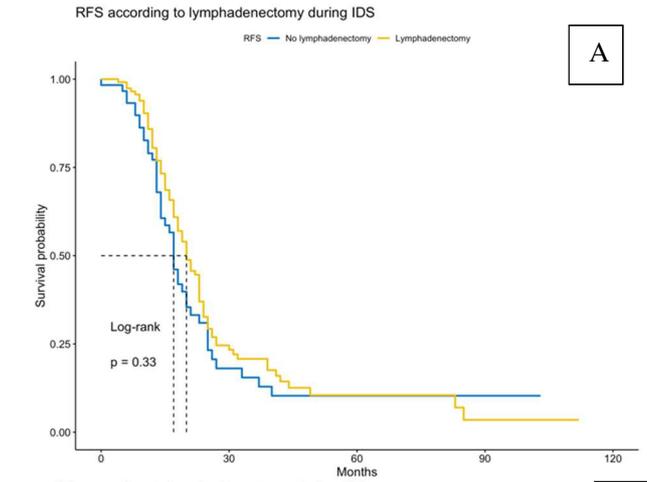
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**Figure 1.** Flow chart of patients with a stage IIB-IV epithelial ovarian cancer who underwent neo-adjuvant chemotherapy followed by interval debulking surgery

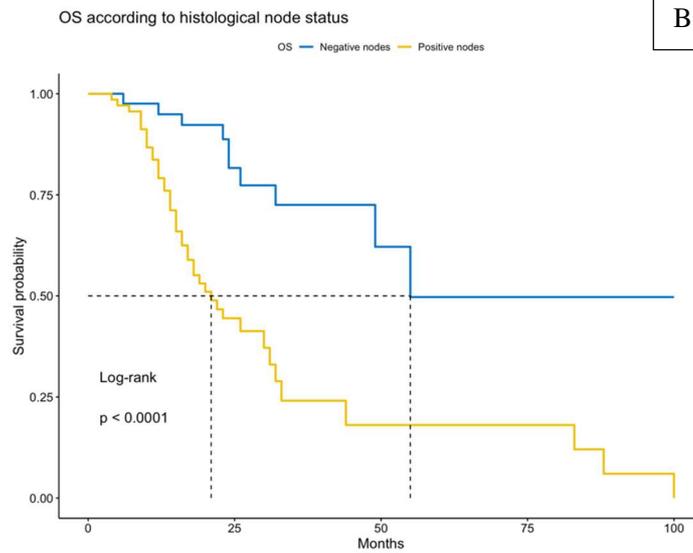
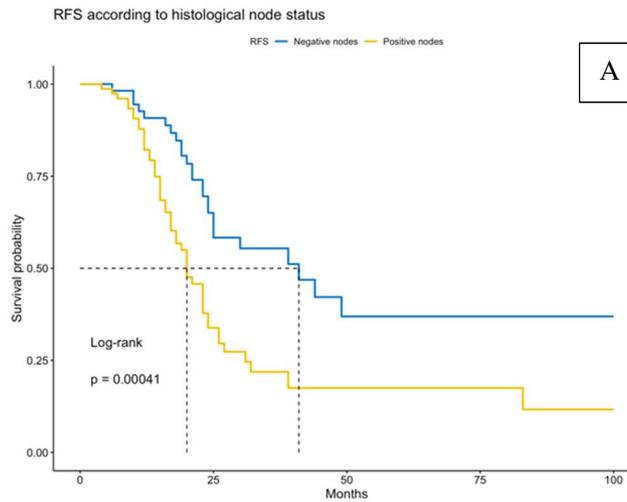


**Figure 2:** Patients with a stage IIB-IV high grade serous ovarian cancer who underwent neo-adjuvant chemotherapy followed by interval debulking surgery either with or without systematic lymphadenectomy (LND)

- A. Recurrence free survival (RFS) of patients with a stage IIB-IV ovarian cancer who underwent neo-adjuvant chemotherapy followed by interval debulking surgery (p=0.3)
- B. Overall survival (OS) of patients with a stage IIB-IV ovarian cancer who underwent neo-adjuvant chemotherapy followed by interval debulking surgery (p=0.6)



**Figure 3.** Patients with a stage IIB-IV high-grade serous ovarian cancer who underwent neoadjuvant chemotherapy followed by interval debulking surgery with a systematic lymphadenectomy  
A. Recurrence free survival (RFS) according to node status after neo-adjuvant chemotherapy ( $p < 0.001$ )  
B. Overall survival (OS) according to node status after neo-adjuvant chemotherapy ( $p < 0.001$ )



**Table 1.** Patient characteristics

Patient characteristics		Lymphadenectomy N=133 (%)	No lymphadenectomy N=70 (%)	p
Age (years)	Mean+/- SD	62.33 +/- 10.65	68.37 +/-10.95	<b>&lt;0.001</b>
BMI (kg/m <sup>2</sup> )	Mean+/- SD	23.62 +/- 4.71	24.07 +/- 5.35	0.57
Menopause	Yes	107 (80.45)	60 (85.71)	0.44
	No	22 (16.54)	8 (11.43)	
	NA	4 (3.01)	2 (2.86)	
BRCA mutation	Yes	22 (16.54)	6 (8.57)	0.43
ASA score	1	32 (24.06)	8 (11.43)	0.06
	2	44 (33.08)	32 (45.71)	
	3	12 (9.02)	11 (15.71)	
	4	0	1 (1.43)	
	NA	45 (33.83)	18 (25.71)	
CA125 (U/ml)	Mean +/- SD	1976 +/-3504	2587 +/- 3865	0.28
PCI score on initial exploratory laparoscopy	Mean +/- SD	19.72 +/- 7.78	21.54 +/- 6.46	0.15
FIGO stage	IIIA	2 (1.5)	2 (2.86)	0.30
	IIIB	2 (1.5)	4 (5.71)	
	IIIC	79 (59.4)	38 (54.29)	
	IV	42 (31.58)	19 (27.14)	
	NA	8 (6.02)	7 (10)	
NACT by Carboplatin and Paclitaxel		128 (96.24)	68 (97.14)	1
Number of NACT cycles	Mean +/- SD	4.39 +/-1.42	4.6 +/-1.55	0.34
Adjuvant chemotherapy	Yes	198 (81.2)	51 (72.86)	0.23
	No	25 (18.8)	19 (27.14)	

*Abbreviations:* PCI = peritoneal carcinomatosis index, NACT= neo-adjuvant chemotherapy, ASA= American society of anesthesiology, BMI= body mass index, FIGO = International Federation of Gynecology and Obstetrics, SD= standard deviation

**Table 2.** Surgical characteristics and post-operative and per operative complications

Surgical and post-operative characteristics		Lymphadenectomy N=133 (%)	No lymphadenectomy N=70 (%)	p
<b>Interval debulking surgery</b>				
PCI	Mean +/- SD	8.45 +/- 5.91	12.12 +/- 8.12	<b>&lt;0.001</b>
Completeness of Cytoreduction score (CC)	CC0	116 (87.22)	48 (68.57)	<b>&lt;0.001</b>
	CC1	15 (11.28)	5 (7.14)	
	CC2	1 (0.75)	15 (21.43)	
	NA	1 (0.75)	2 (2.86)	
<b>Survival</b>				
Recurrence		87 (65.41)	44 (62.86)	1
Death		51 (38.35)	29 (41.43)	1
Location of recurrence	Peritoneal	65 (48.87)	32 (45.71)	0.77
	Nodal	46 (34.59)	27 (38.57)	0.68
	Metastasis	25 (18.8)	19 (27.14)	0.23
<b>Per and post-operative complications</b>				
Peri-operative complications	Yes	33 (24.81)	10 (14.29)	0.14
	No	97 (72.93)	56 (80)	
	NA	3 (2.26)	4 (5.71)	
Post-operative complications	Yes	42 (31.58)	13 (18.57)	0.09
	No	88 (66.17)	53 (75.71)	
	NA	3 (2.26)	4 (5.71)	
Clavien Dindo grade of post-operative complications	1-2	25 (59.52)	9 (69.23)	0.48
	3	12 (28.57)	4 (30.76)	
	4-5	5 (11.91)	0	
30-day mortality	Yes	1 (0.75)	0	1
	No	132 (99.25)	68 (97.14)	
	NA		2 (2.86)	

*Abbreviations:* SD= standard deviation, PCI = peritoneal carcinomatosis index

**Table 3.** Cox regression model of univariate and multivariate analysis of variables associated with recurrence free survival (A) or overall survival (B)

A.

Variables associated with recurrence-free survival		Univariate			Multivariate		
		HR	IC	p	HR	IC	p
Peritoneal Carcinomatosis index		1.05	1.03-1.08	<0.001	1.05	1.02-1.09	<0.001
Completeness of Cytoreduction score (CC)	Reference = CC0			<0.001			0.60
	CC1	1.9	1.03-3.45		0.79	1.02- 1.08	
	CC2	3.4	1.63-7.09		1.56	0.60- 4.01	

B.

Variables associated with overall survival		Univariate			Multivariate		
		HR	IC	p	HR	IC	p
Peritoneal Carcinomatosis index		1.05	1.02-1.09	<0.001	1.04	1.01-1.08	<b>0.02</b>
Completeness of Cytoreduction score (CC)	Reference = CC0			<0.001			0.28
	CC1	3.18	1.7-5.81		1.59	0.70- 3.60	
	CC2	2.4	1.17-4.89		0.85	0.30- 2.43	

Abbreviations: HR= hazards ratio, IC= confidence interval 95%