



**HAL**  
open science

## **Adherence to ESGO guidelines and impact on survival in obese patients with endometrial cancer: a multicentric retrospective study**

Samia Ouasti, Johanna Ilic, Camille Mimoun, Sofiane Bendifallah, Cyrille Huchon, Lobna Ouldamer, Jerome Lorenzini, Vincent Lavoué, Emilie Raimond, Ludivine Dion, et al.

### ► To cite this version:

Samia Ouasti, Johanna Ilic, Camille Mimoun, Sofiane Bendifallah, Cyrille Huchon, et al.. Adherence to ESGO guidelines and impact on survival in obese patients with endometrial cancer: a multicentric retrospective study. *International Journal of Gynecological Cancer*, 2023, pp.ijgc-2023-004642. 10.1136/ijgc-2023-004642 . hal-04315009

**HAL Id: hal-04315009**

**<https://hal.sorbonne-universite.fr/hal-04315009v1>**

Submitted on 29 Nov 2023

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **Adherence to ESGO guidelines in obese patients with endometrial cancer and impact on**  
2 **survival: a multicentric retrospective study.**  
3

4 **Samia Ouasti<sup>1</sup>, Johanna Ilic<sup>1</sup>, Camille Mimoun<sup>2</sup>, Sofiane Bendifallah<sup>1,3</sup>, Cyrille Huchon<sup>2</sup>,**  
5 **Lobna Ouldamer<sup>4</sup>, Jerome Lorenzini<sup>4</sup>, Vincent Lavoué<sup>5</sup>, Emilie Raimond<sup>6</sup>, Ludivine Dion<sup>5</sup>,**  
6 **Helène Costaz<sup>7</sup>, Pierre Francois Dupré<sup>8</sup>, Olivier Graesslin<sup>6</sup>, Jennifer Uzan<sup>10</sup>, Yohan**  
7 **Kerbage<sup>11</sup>, Pauline Chauvet<sup>12</sup>, Geoffroy Canlorbe<sup>13</sup>, Cyril Touboul<sup>1,3</sup>, Yohann Dabi<sup>1,3</sup>**  
8

9 <sup>1</sup> Department of Obstetrics and Reproductive Medicine, Tenon Hospital, 4 Rue de la Chine,  
10 75020 Paris, France. samia.ouasti@gmail.com; ilicjohanna@yahoo.fr

11 <sup>2</sup> Department of Gynaecology, Lariboisière Hospital, 2 rue Ambroise Paré, 75010 Paris,  
12 France. camille.mimoun@aphp.fr, cyrillehuchon@yahoo.fr

13 <sup>3</sup> Clinical Research Group (GRC) Paris 6, Centre Expert Endométriose (C3E), Sorbonne  
14 University (GRC6 C3E SU), 4 Rue de la Chine, 75020 Paris, France.  
15 Sofiane.bendifallah@aphp.fr, cyrille.touboul@aphp.fr .

16 <sup>4</sup> Department of Gynaecology, Centre Hospitalier Universitaire De Tours, Hôpital  
17 Bretonneau, 2 Boulevard Tonnellé, 37000, Tours, France. lobna.ouldamer@univ-tours.fr,  
18 jerome.loranzini@univ-tours.fr

19 <sup>5</sup> Department of Obstetrics and Reproductive Medicine, CHU Anne de Bretagne, 16 Bd de  
20 Bulgarie BP 90347, F-35 203, Rennes Cedex 2, France. vincent.lavoue@gmail.com,  
21 ludivine.dion@chu-rennes.fr

22 <sup>6</sup> Department of Obstetrics and Gynecology, Maison Blanche Hospital, Reims-Champagne-  
23 Ardennes University, Reims, France. emilie\_raidmond@hotmail.com,  
24 olivier.graesslin@gmail.com

25 <sup>7</sup> Departement of oncology surgery, Centre de lutte contre le cancer Georges-François  
26 Leclerc, 21000 Dijon, France. hcostaz@cgfl.fr

27 <sup>8</sup> Department of Gynaecology, CHU de Brest, F-29200, Brest, France. pierre-  
28 francois.dupre@chu-brest.fr

29 <sup>10</sup> Department of Gynaecology and Obstetrics, Hôpital Foch, Suresnes, France.  
30 jennifer.uzan@aphp.fr

31 <sup>11</sup> Department of Gynaecology, CHU Lille, 1 Avenue Oscar Lambret, Lille F-59000, France;  
32 CHU Lille, University Lille, Lille F-59000. yohan.kerbage@gmail.com

33 <sup>12</sup> Department of Gynaecology, CHU de Clermont Ferrand, 1 Place Lucie Aubrac, 63 003  
34 Clermont Ferrand, France. po.chauvet@gmail.com

35 <sup>13</sup> Department of Gynecological and Breast Surgery and Oncology, Pitié-Salpêtrière,  
36 Assistance Publique des Hôpitaux de Paris (AP-HP), University Hospital, 75013 Paris, France.  
37 geoffroy.canlorbe@aphp.fr

38  
39  
40 *Corresponding author:* Yohann Dabi, yohann.dabi@aphp.fr, Department of Obstetrics and  
41 Reproductive Medicine, Tenon Hospital, 4 Rue de la Chine, 75020 Paris, France.  
42  
43  
44

45 *Conflict of interest:* Authors declare no conflict of interest for this work.

46

47 No funding source was involved for this study.

48

49 *Authors contribution:* S.O. conducted the data extraction and wrote the manuscript. J.I.  
50 conducted the data extraction. C.M. conducted the original draft preparation. C.H.  
51 conducted the original draft preparation and the data extraction. L.O. conducted the original  
52 draft preparation and the data extraction. V.L. conducted the original draft preparation and  
53 the data extraction. E.R. conducted the original draft preparation and the data extraction.  
54 L.D. conducted the original draft preparation and the data extraction. H.C. conducted the  
55 original draft preparation and the data extraction. P.FD. conducted the original draft  
56 preparation and the data extraction. O.G. conducted the original draft preparation and the  
57 data extraction. J.U. conducted the original draft preparation and the data extraction. Y.K.  
58 conducted the original draft preparation and the data extraction. S.B. conducted the original  
59 draft preparation and supervised the project. C.T. conducted the original draft preparation  
60 and supervised the project. Y.D. conducted the data analysis and supervised the project. All  
61 the authors reviewed the manuscript and approved the final draft.

62

63 **Abstract**

64

65 **Objectives:** Obesity is known to be both a major risk factor for endometrial cancer and  
66 associated with surgical complexity. Therefore, the management of these patients is a  
67 challenge for surgeon and oncologist. The aim of this study is to assess the adherence to  
68 ESGO guidelines in patients morbidly obese (BMI > 40 kg/m<sup>2</sup>). The secondary objectives  
69 were the impact on overall survival and recurrence free survival.

70 **Methods:** All the patients who were treated for an EC in the 11 cancer institutes of the  
71 Francogyn group were included and classified into 3 weight groups: morbid (MG) (BMI over  
72 40kg/m<sup>2</sup>), obese (OG) (BMI between 30 and 40kg/m<sup>2</sup>) and normal or overweight (NOG)  
73 (with a BMI under 30kg/m<sup>2</sup>). Adherence to guidelines was evaluated for surgical  
74 management, lymph node staging and adjuvant therapies.

75 **Results:** 2375 patients were included: 1330 in NOG group, 763 OG group and 282 in MG  
76 group. The surgical management of MG was in according with the guidelines in only 30% of  
77 cases against 44% for OG and 48% for NOG (p< 0.001), especially because of a lack of lymph  
78 node staging. MG were more likely to receive the recommended adjuvant therapy (61% for  
79 MG, 52% for OG and 46% for NOG, p-value under 0.001).

80 Weight had no impact on OS (p-value=0.6) and MG patients had a better RFS (p =0.04).

81 **Conclusion:** Adherence to international guidelines for surgical management is significantly  
82 lower in MG patients, especially the procedures of lymph node staging. However, MG  
83 patients had more often the adequate adjuvant therapies. MG patients had a better RFS  
84 probably because of better prognosis tumors.

85 **Keys message:**

86

87 **What is already known on this topic:** Obesity is a risk factor of endometrial cancer. Its  
88 impact on the management of patients is however still debated.

89 **What this study adds:** The surgical management of patients with severe obesity is  
90 significantly different than the guidelines. However, severe obese patients have a better  
91 RFS and no impact was found on OS.

92 **How this study might affect research, practice or policy:** The development of robotic  
93 surgery, the extension of SLN indications and the study of new biological markers might  
94 improve the management of severe obese patients.

95

96 **Key words:** Endometrial cancer; severe obesity; clinical management; morbid obesity;  
97 sentinel lymph node; minimally invasive surgery

98

99 **Introduction**

100  
101 Endometrial cancer (EC) is the sixth most frequently diagnosed cancer in women,  
102 with 417.000 new cases and 97.000 new deaths in the world in 2020(1). The increasing  
103 number of cases in western countries could reflect the significant proportion of patients  
104 with risk factors such as obesity(2). According to the WHO, patients with excessive body  
105 mass index (BMI) over 25 kg/m<sup>2</sup> may represent two billions of people, or 30% of the world  
106 population(3). In this population, the relative risk to develop an endometrial cancer is  
107 ranging from 2.7 for patients with a BMI higher than 30 kg/m<sup>2</sup> to 4.7 for those with a BMI  
108 higher than 35 kg/m<sup>2</sup>(2).

109 Surgery and adjuvant therapy for EC are determined according to ESGO-ESMO-ESTRO  
110 guidelines(4). Many reports previously described the surgical complexity of managing obese  
111 patients, usually at increased risk of post operative complications(5). Vargiu and al. recently  
112 showed that obese patients were under-staged in 9.4% of cases (p=0.017) because of  
113 sentinel lymph node (SLN) failure(6). Wissing M and al. showed that successful SLN or pelvic  
114 lymphadenectomy (LND) correlated negatively with BMI levels (adjusted OR 0.86 CI95%  
115 [0.76–0.97] for SNL and 0.76 CI95% [0.59–0.96] for LND, per 1 kg/m<sup>2</sup> increment)(7).

116 Likewise, dealing with severe obesity is a challenge for oncologists. Furlanetto et al.  
117 showed in a prospective randomized trial that obese patients who received the real dose  
118 dense chemotherapy according to their weight without adjustment had more severe  
119 toxicities without impact on survival(8). In the same time, ESGO guidelines clearly advise full  
120 dose chemotherapy to avoid under treated patients(9) .

121 In this context, clinicians always balance the need to offer obese patients the most  
122 appropriate therapies with the significant increase in morbidity in this population.

123           The primary objective of this study was to assess the adherence to ESGO guidelines in  
124 patients morbidly obese (BMI > 40 kg/m<sup>2</sup>). Our secondary objective included survival  
125 analysis stratified by BMI categories.

126

127 **Methods**

128 *Population included*

129 The research protocol was approved by the institutional review board of the French College  
130 of Obstetrics and Gynecology (2023 – GYN – 0108).

131 The inclusion was retrospective and multicentric, including 11 French tertiary cancer  
132 institutions of the FRANCOGYN group: Creteil University Hospital, Jean Verdier University  
133 Hospital, Lille University Hospital, Poissy University Hospital, Tenon University Hospital,  
134 Tours University Hospital, Rennes University Hospital, Reims University Hospital, Clermont-  
135 Ferrand University Hospital, Brest University Hospital, and Jean-Francois Leclerc Hospital.  
136 Patients treated for an EC histologically proven between 2000 and 2020 in one of the  
137 involved centers were selected.

138 Patients with BMI < 18 kg/m<sup>2</sup>, advanced metastatic disease never operated, rare  
139 tumors and incomplete anamnesis or follow up (lack of information on age, BMI or  
140 histology) were excluded.

141

142 *Data collection*

143 The following data were abstracted from patients' chart: socio-demographic, BMI  
144 (calculated as the weight in kilograms divided by the square of the height in meters, both  
145 measured at the time of diagnosis, and expressed in kg/m<sup>2</sup>), parity, menopausal status, high  
146 blood pressure, diabetes, hormone replacement therapy, history of breast cancer, FIGO  
147 stage, final pathologic analysis and adjuvant therapy. The date of surgery, recurrence and  
148 death were also reported.

149



150 *Patients' management*

151           Preoperative work-up included a digital vaginal and speculum examination,  
152 ultrasound, and pelvic MRI to assess preoperative risk group. All patients managed before  
153 the actualization of ESMO guidelines were re-evaluated to determine preoperative risk of  
154 lymph node invasion.

155           Patients' management were theoretically based on ESGO guidelines (4) and  
156 systematically validated in multidisciplinary committee including at least a radiologist, a  
157 onco-gynecological surgeon, a pathologist, and a medical oncologist.

158           The surgical treatment consisted of a hysterectomy with bilateral salpingo-  
159 oophorectomy(4,10). The lymph node staging of patients treated before 2016 was  
160 considered to be in adequation with guidelines if patients underwent a pelvic LND or a SLN  
161 for low-risk group and if it was associated with a lombo-aortic lymphadenectomy for  
162 intermediate and high group risk(10). After 2016, the lymph node staging was concordant  
163 only if a SLN was performed for low risk and a pelvic and lombo-aortic lymphadenectomy for  
164 intermediate and high group risk(4).

165           Tumors were classified according to the FIGO 2018 classification after final pathologic  
166 analysis(11).

167           Adjuvant therapy was assessed according to the postoperative group of risk of  
168 recurrence(4).

169

170 *Evaluation of the adherence to guidelines*

171           The concordance of the surgical procedure and the indication of adjuvant therapy  
172 was evaluated separately. The global management was considered to be concordant if the  
173 surgical and the adjuvant therapy was concordant to guidelines.

174 In all centers, for patient with stages I or II cancer, the follow up visit was conducted  
175 every six months for five years then every year with a simple clinical exam. For patients with  
176 stage III or IV cancer, follow-up visits were conducted every 3 months for the first 2 years,  
177 every 6 months for the following 3 years, and once a year thereafter.

178

#### 179 *Statistical analysis*

180 Data were managed with an Excel database (Microsoft Corporation, Redmond, WA,  
181 USA) and analyzed using SAS v9.4 (SAS Institute, Cary, NC, USA).

182 Patients were retrospectively divided into three groups according to their BMI:  
183 normal, obese and morbid. "Normal or Overweight group" (NOG) included patients with a  
184 BMI greater or equal than 18 and less or equal than 30. "Obese group" (OG) included  
185 patients with a BMI higher than 30 but lower than 40. Eventually, "morbid group" (MG)  
186 included grade 3 obesity, also known as severe obesity, defined as a BMI higher than forty.

187 Statistical analysis was based on Chi square and Fisher's exact tests for ordinal  
188 variables. For continuous variables, Student's t test or Mann-Whitney test were used (p  
189 values < 0.05 were considered significantly different). Recurrence free survival (RFS) was  
190 defined as the time between surgery and relapse or the last follow up if no event occurred.  
191 Overall survival (OS) was calculated from the date of surgery to death or the last follow up if  
192 no event occurred. Patients who were still alive or without recurrence were censored at the  
193 date of the last follow-up visit. The Kaplan-Meier method was used to estimate the survival  
194 distribution and the log-rank test was used to compare survival data (p values < 0.05 were  
195 considered significantly different).

196           In accordance with the journal’s guidelines, we will provide our data for independent  
197 analysis by a selected team by the Editorial Team for the purposes of additional data analysis  
198 or for the reproducibility of this study in other centers if such is requested.

199

200

201 **Results**

202 *Characteristics of the study population*

203           Between 2000 and 2020, 2852 patients were treated for an EC within one of the  
204 centers involved and 2375 were selected for analyses (Figure 1). NOG patients represented  
205 1330 patients, OG 763 patients and MG 282 patients.

206

207 The main characteristics of the patients are displayed in Table 1.

208           MG patients were significantly younger with a median age of 63 for MG, 66 for OG  
209 and 68 for NOG (p-value < 0.001) and had more comorbidities as high blood pressure (181  
210 (64%) MG patients, 392 (51%) OG patients, 445 (33%) NOG patients (p-value < 0.001)) or  
211 diabetes (109 (39%) MG patients, 188 (25%) OG patients and 131 (10%) NOG patients (p-  
212 value < 0.001)).

213 MG patients had less aggressive tumor than OG or NOG patients. Endometrioid carcinoma  
214 represented 238 (88%) MG tumors, 634 (85%) OG tumors and 1054 (81%) NOG tumors (p-  
215 value= 0.002). Among them 150 (63%) were grade 1 for MG, 359 (57%) for OG and 555  
216 (53%) for NOG tumors (p-value=0.005). Therefore, MG patients were more often classified in  
217 low ESMO group than OG or NOG patients (141 (52%), 296 (40%) and 496 (38%)  
218 respectively, p-value < 0.001).

219

220 *Adherence to guidelines according to BMI group.*

221           Adherence to guidelines according to BMI group are displayed in table 2.

222 MG patients were managed according to guidelines in 19% of cases (53 patients) against  
223 24% of NOG or OG patients (322 and 182 patients respectively) (p-value = 0.138).

224 The surgical management of MG patients was more likely different from guidelines for low  
225 and intermediate group risk than high group risk (Table 3).

226 The surgical route chose for low and intermediate group risk was more often laparoscopic  
227 for NOG and OG. For MG patients open surgery was more often elected (p-value < 0.001).

228 MG patients had significantly less lymph node staging when indicated. 85 (30%) MG  
229 patients had the recommended surgical management against 644 (48%) NOG patients and  
230 355 (44%) OG patients (p-value < 0.001).

231 MG patients had less often SLN biopsy when required. Only 16 (11%) MG patients versus 70  
232 (24%) OG patients and 153 (31%) NOG patients had a SLN in low group (p-value < 0.001 for  
233 low risk and p-value=0.005 for intermediate). Furthermore, when it was performed, only 10  
234 (63%) SLN was detected in MG patients versus 62 (89%) in OG and 137 (90%) in NOG (p-  
235 value=0.008).

236 Pelvic LND was less often performed in MG patients at low and intermediate group risk. 24  
237 (7%) MG patients versus 111 (57%) OG patients and 211 (65%) NOG patients had a pelvic  
238 LDN in intermediate group (p-value=0.002 for intermediate and p-value < 0.001 for low risk).

239 In high group risk, there was no significant difference between weight groups for surgical  
240 approach or pelvic lymph node staging. MG patients had less para-aortic lymphadenectomy  
241 (16 (23%) MG patients, 90 (35%) OG patients and 197 (41%) NOG patients, p = 0.011).

242 In all weight groups, the weight had not impact on lymph node invasion on final pathology.

243

#### 244 *Adjuvant therapy*

245 171 (61 %) MG patients were managed according to guidelines for adjuvant therapy  
246 while only 396 (52%) OG patient and 618 (46 %) NOG patients had the adjuvant therapy  
247 recommended (p < 0.001). In the sub-group analysis, no significative trend was observed.

248

249 *Survival analysis*

250           The survival curves are displayed in figure 2. Mean follow up was 40 months. MG  
251 patients had a better RFS than OG and NOG ( $p = 0.04$ ). No difference was observed in OS ( $p$   
252  $= 0.6$ ). Survival curves comparing morbid obese patients to the obese and non-  
253 obese or overweight patients are displayed in Supplementary Figure 1.

254

255 **Discussion**

256 *Summary of main results*

257 In our retrospective multicentric cohort, we found that MG patients were more likely  
258 to have an incomplete or inappropriate lymph node staging, even in low and intermediate  
259 risk situations. Indeed, 70% of MG patients didn't have the recommended staging when only  
260 56% of OG patients and 52% of NOG patients' staging were not in accordance to guidelines  
261 ( $p < 0.001$ ). However, the choice of adjuvant therapy was more often in accordance with  
262 guidelines: 61% of MG patients and only 52% of OG patients and 46% of NOG patients ( $p <$   
263  $0.001$ ). MG patients had increased RFS when compared to OG or NOG ( $p=0.04$ ), but without  
264 significant impact on OS ( $p=0.6$ ).

265

266 *Results in the context of published literature*

267 Severe obesity is associated with surgical complexity, especially for lymph node  
268 staging. Vargiu et al. reported that obese patients ( $BMI > 35 \text{ kg/m}^2$ ) were under-staged during  
269 EC management in 9.4% versus 5% of non-obese patients ( $p\text{-value}=0.017$ ). Moreover, there  
270 was an empty package dissection in 8.2% of cases versus 3.9% for non-obese patients ( $p\text{-}$   
271  $\text{value}=0.022$ )(6). Canlorbe et al. highlighted that nodal staging was performed for only 70%  
272 of obese patient in high group risk against 90% of non-obese patients ( $p\text{-value}<0.0001$ ) and  
273 it was associated with a poorest RFS ( $HR=12.5 \text{ CI}95\%[3.1-51.3]$ )(12). In our cohort, MG  
274 patients had significantly less lymph node staging, and this was even significant for pelvic  
275 lymph nodes in the low and intermediate group risk. For high group risk, the difference was  
276 observed on para-aortic staging ( $p = 0.011$ ).

277 The generalization of SLN, especially for high-risk patients, might improve the lymph  
278 node staging in patients with EC. The FIRES trial showed a sensitivity to detect node-positive

279 disease of 97.2% (CI95% [85.0-100]), and a negative predictive value of 99.6% (CI95% [97.9–  
280 100]) even for high group risk(13). This procedure has been especially studied for obese  
281 patient by Matanes et al. who showed that performing a SLN instead of a pelvic LDN for  
282 obese patients is associated with a shorter operative time ( $p < 0.001$ ) and less blood loss ( $p =$   
283 0.03) without impact on OS and RFS ( $p = 0.7$  and  $0.4$  respectively)(14). SLN procedures in high-  
284 risk obese patients could increase the proportion of patients benefitting from the  
285 appropriate surgical and adjuvant therapies according to ESGO guidelines.

286         Regarding survival, the impact of obesity remains unclear. In a meta-analysis by  
287 Kokts-Porietis RL and al, the increase of the BMI is associated with a higher cancer  
288 recurrence and all-cause mortality but no impact was found on cancer specific mortality(15).  
289 In our cohort, MG patients had a better RFS ( $p = 0.04$ ) but without difference in OS between  
290 weight group ( $p = 0.6$ ). This difference in RFS could be explained by the fact that morbid  
291 obesity seems to be associated with better prognostic tumors: more endometrioid  
292 carcinoma, lower FIGO stage and therefore more low-risk group ( $p$ -value under 0.001). In  
293 this group risk, the probability of lymph node invasion is lower so the lack of lymph node  
294 staging had probably less impact on RFS.

295 MG patients were also younger than OG or NOG patients (median of 63, 66 and 68 years old  
296 respectively,  $p$ -value under 0.001) which could impact positively OS.

297         The development of quality indicators by ESGO and the certification of care centers  
298 might improve the adherence of international guidelines (16). Adherence to guidelines was  
299 more important regarding the choice of adjuvant therapy in obese patients, without  
300 significative difference after further stratification. The recent inclusion of the molecular  
301 analysis including immunohistochemistry for p53, mismatch repair proteins, and DNA  
302 sequencing for POLE exonuclease domain aim to tailor adjuvant therapies according to



303 specific subgroups. For example, simple clinical surveillance can be decided in POLE-mutated  
304 patients(4). Vanessa M López-Ozuna and al. has already been working on finding molecular  
305 predictive biomarkers for obese patients(17). Finding the molecular marker that enables to  
306 avoid the surgical difficulties in this population seems to be the next big thing. In the present  
307 cohort, the impact of molecular classification couldn't be evaluated because of the lack of  
308 information for all patients due to our inclusion period.

309

### 310 *Strengths and weaknesses*

311 Some of the limits deserve to be mentioned. The retrospective nature of our work  
312 could have biased the results. However, the large multicentric inclusion reflect the  
313 difference of management of EC in several French cancer institutions.

314 Furthermore, due to the large time of inclusion (2000 to 2020), few patients have  
315 been operated by robotic access. E. Kawai and al. showed that obese patients can safely  
316 undergo robotic access surgery compared to non-obese patients with no more laparotomy  
317 conversion (5% vs 3% p-value 0.619) or post operative complications (5% vs 9%, p-value  
318 0.738). However, despite the use of robotic assisted laparoscopy, less obese patients  
319 underwent pelvic lymphadenectomy (5 vs 12%, p-value=0.005)(18). Moreover, indications  
320 for lymph node surgical staging evolved over the years with more patients eligible to less  
321 morbid procedures such as SLN. However, a strength of this work was that the adherence to  
322 guidelines was evaluated according to the year of management for each patient included.

323 Another lack of this study is the absence of information regarding post operative  
324 complications. It remains possible that the occurrence of some complications had impact on  
325 the decision to propose adjuvant therapies. Laparotomy surgical access is significantly  
326 more chosen in MG population (22% of MG patients against 17% of NOG patients in low

327 group risk (p-value of 0.001); 45% of MG patients against 22% of NOG patients in  
328 intermediate group risk (p-value of 0.001). Bouwman and al. showed that obese women had  
329 significantly more postoperative surgical complication mainly if the access is open  
330 surgery(5). Reijntjes et al. showed in a randomized trial that there were no significant  
331 difference between laparoscopy or laparotomy surgical access on RFS (90.3% vs 84.1%  
332 CI95% [0.31-1.52]) or OS (89.2% vs 82.8% CI95%0.30-1.19))(19).

333

334

335

336

337 **Conclusion**

338

339 Adherence to international guidelines for surgical management but not adjuvant  
340 therapies, is significantly lower in morbid obese patients, especially the procedures of lymph  
341 node staging.

342 Recent implementation of sentinel lymph node procedure even in high-risk patients as well

343 as the use of robotic procedures could increase the proportion of patients benefitting from

344 recommended therapies.

345

346 **References**

347

348 1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global  
349 Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36  
350 Cancers in 185 Countries. *CA Cancer J Clin*. 2021 May;71(3):209–49.

351 2. Shaw E, Farris M, McNeil J, Friedenreich C. Obesity and Endometrial Cancer. *Recent  
352 Results Cancer Res Fortschritte Krebsforsch Progres Dans Rech Sur Cancer*. 2016;208:107–  
353 36.

354 3. Caballero B. Humans against Obesity: Who Will Win? *Adv Nutr Bethesda Md*. 2019  
355 Jan 1;10(suppl\_1):S4–9.

356 4. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al.  
357 ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma.  
358 *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc*. 2021 Jan;31(1):12–39.

359 5. Bouwman F, Smits A, Lopes A, Das N, Pollard A, Massuger L, et al. The impact of BMI  
360 on surgical complications and outcomes in endometrial cancer surgery--an institutional  
361 study and systematic review of the literature. *Gynecol Oncol*. 2015 Nov;139(2):369–76.

362 6. Vargiu V, Rosati A, Capozzi VA, Sozzi G, Gioè A, Berretta R, et al. Impact of Obesity on  
363 Sentinel Lymph Node Mapping in Patients with apparent Early-Stage Endometrial Cancer:  
364 The ObelyX study. *Gynecol Oncol*. 2022 May;165(2):215–22.

365 7. Wissing M, Mitric C, Amajoud Z, Abitbol J, Yasmeen A, López-Ozuna V, et al. Risk  
366 factors for lymph nodes involvement in obese women with endometrial carcinomas. *Gynecol  
367 Oncol*. 2019 Oct;155(1):27–33.

368 8. Furlanetto J, Eiermann W, Marmé F, Reimer T, Reinisch M, Schmatloch S, et al. Higher  
369 rate of severe toxicities in obese patients receiving dose-dense (dd) chemotherapy according  
370 to unadjusted body surface area: results of the prospectively randomized GAIN study. *Ann  
371 Oncol Off J Eur Soc Med Oncol*. 2016 Nov;27(11):2053–9.

372 9. Griggs JJ, Mangu PB, Anderson H, Balaban EP, Dignam JJ, Hryniuk WM, et al.  
373 Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of  
374 Clinical Oncology clinical practice guideline. *J Clin Oncol Off J Am Soc Clin Oncol*. 2012 May  
375 1;30(13):1553–61.

376 10. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, et al.  
377 ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and  
378 follow-up. *Ann Oncol Off J Eur Soc Med Oncol*. 2016 Jan;27(1):16–41.

379 11. Lewin SN. Revised FIGO staging system for endometrial cancer. *Clin Obstet Gynecol*.  
380 2011 Jun;54(2):215–8.

381 12. Canlorbe G, Bendifallah S, Raimond E, Graesslin O, Hudry D, Coutant C, et al. Severe  
382 Obesity Impacts Recurrence-Free Survival of Women with High-Risk Endometrial Cancer:  
383 Results of a French Multicenter Study. *Ann Surg Oncol*. 2015 Aug;22(8):2714–21.

384 13. Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, Hanna RK, et al. A comparison of  
385 sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES  
386 trial): a multicentre, prospective, cohort study. *Lancet Oncol*. 2017 Mar;18(3):384–92.

387 14. Matanes E, Eisenberg N, Amajoud Z, Gupta V, Yasmeen A, Ismail S, et al. Sentinel  
388 Lymph Node Sampling as an Alternative to Lymphadenectomy in Patients With Endometrial  
389 Cancer and Obesity. *J Obstet Gynaecol Can JOGC J Obstet Gynecol Can JOGC*. 2021  
390 Oct;43(10):1136-1144.e1.

391 15. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality  
392 among endometrial cancer survivors: A systematic review and meta-analysis. *Obes Rev Off J*

- 393 Int Assoc Study Obes. 2021 Dec;22(12):e13337.
- 394 16. Concin N, Planchamp F, Abu-Rustum NR, Ataseven B, Cibula D, Fagotti A, et al.  
395 European Society of Gynaecological Oncology quality indicators for the surgical treatment of  
396 endometrial carcinoma. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc.* 2021  
397 Dec;31(12):1508–29.
- 398 17. López-Ozuna VM, Kogan L, Hachim MY, Matanes E, Hachim IY, Mitric C, et al.  
399 Identification of Predictive Biomarkers for Lymph Node Involvement in Obese Women With  
400 Endometrial Cancer. *Front Oncol.* 2021;11:695404.
- 401 18. Kawai E, Benoit L, Hotton J, Rance B, Bonsang-Kitzis H, Lécuru F, et al. Impact of  
402 obesity on surgical and oncologic outcomes in patients with endometrial cancer treated with  
403 a robotic approach. *J Obstet Gynaecol Res.* 2021 Jan;47(1):128–36.
- 404 19. Reijntjes B, van Suijlichem M, Woolderink JM, Bongers MY, Reesink-Peters N, Paulsen  
405 L, et al. Recurrence and survival after laparoscopy versus laparotomy without  
406 lymphadenectomy in early-stage endometrial cancer: Long-term outcomes of a randomised  
407 trial. *Gynecol Oncol.* 2022 Feb;164(2):265–70.
- 408
- 409

410  
411  
412

**Table 1: Epidemiological and pre operative histological characteristics by body mass index in the whole population.**

	NOG N=1330	OG N=763	MG N=282	p-value
<b>Epidemiological charecteristics :</b>				
Age, mean (median)	67 (68)	66 (66)	63 (63)	< 0.001
Body mass index, mean (median)	24 (24)	34 (33)	46 (46)	0.001
Menopause, n (%)	1223 (92%)	702 (92%)	250 (89%)	0.169
Menopausal hormone replacement therapy, n (%)	292 (22%)	87 (11%)	13 (5%)	0.001
High blood pressure, n (%)	445 (33%)	392 (51%)	181 (64%)	0.001
Diabete, n (%)	131 (10%)	188 (25%)	109 (39%)	0.001
Breast cancer history, n (%)	120 (9%)	52 (7%)	10 (4%)	0.004
Nulligravida, n (%)	402 (30%)	226 (30%)	89 (32%)	0.831
<b>Histological charecteristics :</b>				
<b>Histological type, n (%)</b>				<b>0.002</b>
<i>Endometrioid carcinoma</i>	1054 (81%)	634 (85%)	238 (88%)	
<i>Other type</i>	254 (19%)	114 (15%)	31 (12%)	
NA	22	15	13	
<b>Histological grade, n (%)</b>				<b>0.005</b>
1	555 (53%)	359 (57%)	150 (63%)	
2	361 (34%)	187 (30%)	72 (30%)	
3	138 (13%)	881 (14%)	16 (7%)	
NA	276	129	44	
<b>FIGO stage, n (%)</b>				0.149
IA	661 (51%)	368 (49%)	157 (58%)	
IB	376 (29%)	28 (29%)	70 (26%)	
II	84 (6%)	40 (5%)	14 (5%)	
IIIA	50 (4%)	23 (3%)	6 (2%)	
IIIB	7 (1%)	10 (1%)	0 (0%)	
IIIC	85 (7%)	57 (8%)	15 (6%)	
IV	45 (3%)	32 (4%)	7 (3%)	
NA	22	15	13	
<b>ESMO group, n (%)</b>				<b>&lt; 0.001</b>
Low	496 (38%)	296 (40%)	141 (52%)	
Intermediate	486 (37%)	257 (34%)	70 (26%)	
High	326 (25%)	195 (26%)	58 (22%)	
NA	22	15	13	

**Table 1: Epidemiological and pre operative histological characteristics by body mass index in the whole population.**

MG, morbid group; NOG, non-obese overweight group; OG, obese group.

413

**Table 2: Adherence to guidelines according to weight group**

414

	NOG N=1330	OG N=763	MG N=282	p-value
<b>Surgical procedure concordance, n (%) :</b>				
	644 (48%)	355 (44%)	85 (30%)	< 0.001
<b>Adjuvant therapy concordance, n (%) :</b>				
	618 (46%)	396 (52%)	171 (61%)	< 0.001
<b>Global adherence, n (%) :</b>				
	322 (24%)	182 (24%)	53 (19%)	0.138

**Table 2: Adherence to guidelines according to weight groups.**

MG, morbid group; NOG, non-obese overweight group; OG, obese group.

415

416

417 **Table 3: Surgical procedure by ESMO pre operative group risk of lymph node invasion and**  
 418 **by body mass index.**  
 419

ESMO group risk :	Low			p-value	Intermediate			p-value	High			p-value
	NOG N = 496	OG N = 296	MG N = 141		NOG N = 326	OG N = 195	MG N = 58		NOG N = 486	OG N = 257	MG N = 70	
<b>Surgery</b>												
<b>Surgical route</b>				<b>&lt; 0.001</b>				<b>&lt; 0.001</b>				<b>0.121</b>
Laparoscopy, n (%)	394 (79%)	226 (76%)	92 (65%)		247 (76%)	145 (74%)	24 (41%)		255 (52%)	118 (46%)	33 (47%)	
Open surgery, n (%)	86 (17%)	56 (19%)	31 (22%)		73 (22%)	36 (18%)	26 (45%)		211 (43%)	127 (49%)	29 (41%)	
Vaginal surgery, n (%)	11 (2%)	10 (3%)	15 (11%)		2 (1%)	8 (4%)	4(7%)		10 (2%)	5 (2%)	4 (6%)	
Robotic laparoscopy, n (%)	5 (1%)	4 (1%)	3 (2%)		4 (1%)	6 (3%)	4 (7%)		10 (2%)	7 (3%)	4 (6%)	
<b>Sentinel lymph node procedure</b>												
Performed, n (%)	153 (31%)	70 (24%)	16 (11%)	<b>&lt; 0.001</b>	113 (35%)	56 (29%)	8 (14%)	<b>0.005</b>	69 (14%)	25 (10%)	6 (9%)	0.129
Detected, n (%)	137 (90%)	62 (89%)	10 (63%)	<b>0.008</b>	109 (96%)	51 (91%)	7 (88%)	0.249	56 (81%)	23 (92%)	6 (100%)	0.244
Positive, n (%)	10 (7%)	6 (10%)	2 (20%)	0.361	21 (19%)	8 (16%)	1 (14%)	0.831	15 (27%)	9 (39%)	1 (17%)	0.427
<b>Pelvic Lymphadenectomy</b>												
Performed, n (%)	271 (55%)	144 (49%)	31 (22%)	<b>&lt; 0.001</b>	211 (65%)	111(57%)	24 (7%)	<b>0.002</b>	350 (77%)	179 (70%)	41 (59%)	0.07
Positive, n (%)	9 (3%)	2 (1%)	0 (0%)	0.316	15 (7%)	9 (8%)	2 (8%)	0.937	350 (77%)	179 (70%)	41 (59%)	0.07
<b>Pelvic staging</b>												
Performed, n (%)	327 (66%)	175 (59%)	45 (32%)	<b>&lt; 0.001</b>	251 (77%)	130 (32%)	27 (47%)	<b>&lt; 0.001</b>	359 (74%)	188 (73%)	45 (64%)	0.239
Positive, n (%)	15 (3%)	8 (3%)	2 (1%)	0.581	33 (10%)	16 (31%)	3 (5%)	0.429	99 (20%)	59 (23%)	13 (19%)	0.620
<b>Lombo-aortic lymphadenectomy</b>												
Performed, n (%)	39 (8%)	19 (6%)	1 (1%)	<b>0.009</b>	61 (68%)	27 (14%)	2 (3%)	<b>0.009</b>	197 (41%)	90 (35%)	16 (23%)	<b>0.011</b>
Positive, n (%)	5 (13%)	3 (16%)	0 (0%)	0.880	9 (15%)	2 (7%)	1 (50%)	0.197	56 (28%)	23 (26%)	6 (38%)	0.607

**Table 3: Surgical procedure by ESMO pre operative group risk of lymph node invasion and by body mass index.**

MG, morbid group; NOG, non-obese overweight group; OG, obese group.

420