

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

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

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- 46
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- 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.

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/m2). The secondary objectives 69 were the impact on overall survival and recurrence free survival.

Methods: All the patients who were treated for an EC in the 11 cancer institutes of the Francogyn group were included and classified into 3 weight groups: morbid (MG) (BMI over 40kg/m2), obese (OG) (BMI between 30 and 40kg/m2) and normal or overweight (NOG) (with a BMI under 30kg/m2). Adherence to guidelines was evaluated for surgical management, lymph node staging and adjuvant therapies.

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

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:

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	significatively 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

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 mass index (BMI) over 25 kg/m<sup>2</sup> may represent two billions of people, or 30% of the world 105 106 population(3). In this population, the relative risk to developpe an endometrial cancer is 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 107 higher than 35 kg/m<sup>2</sup>(2). 108

Surgery and adjuvant therapy for EC are determined according to ESGO-ESMO-ESTRO guidelines(4). Many reports previously described the surgical complexity of managing obese patients, usually at increased risk of post operative complications(5). Vargiu and al. recently showed that obese patients were under-staged in 9.4% of cases (p=0.017) because of sentinel lymph node (SLN) failure(6). Wissing M and al. showed that successful SLN or pelvic lymphadenectomy (LND) correlated negatively with BMI levels (adjusted OR 0.86 CI95% [0.76–0.97] for SNL and 0.76 CI95% [0.59–0.96] for LND, per 1 kg/m2 increment)(7).

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

In this context, clinicians always balance the need to offer obese patients the most
 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/m2). Our secondary objective included survival 125 analysis stratified by BMI categories.

#### 127 Methods

#### 128 Population included

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

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

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

141

142 Data collection

The following data were abstracted from patients' chart: socio-demographic, BMI (calculated as the weight in kilograms divided by the square of the height in meters, both measured at the time of diagnosis, and expressed in kg/m2), parity, menopausal status, high blood pressure, diabetes, hormone replacement therapy, history of breast cancer, FIGO stage, final pathologic analysis and adjuvant therapy. The date of surgery, recurrence and death were also reported.

150 *Patients' management* 

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

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

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

165 Tumors were classified according to the FIGO 2018 classification after final pathologic166 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).

Patients were retrospectively divided into three groups according to their BMI: normal, obese and morbid. "Normal or Overweight group" (NOG) included patients with a BMI greater or equal than 18 and less or equal than 30. "Obese group" (OG) included patients with a BMI higher than 30 but lower than 40. Eventually, "morbid group" (MG) 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 significatively 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)).

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

219

220 Adherence to guidelines according to BMI group.

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).

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

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

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

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

Pelvic LND was less often performed in MG patients at low and intermediate group risk. 24
(7%) MG patients versus 111 (57%) OG patients and 211 (65%) NOG patients had a pelvic
LDN in intermediate group (p-value=0.002 for intermediate and p-value < 0.001 for low risk).</li>
In high group risk, there was no significant difference between weight groups for surgical
approach or pelvic lymph node staging. MG patients had less para-aortic lymphadenectomy
(16 (23%) MG patients, 90 (35%) OG patients and 197 (41%) NOG patients, p = 0.011).

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.</li>

248

## 249 Survival analysis

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

#### 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

Severe obesity is associated with surgical complexity, especially for lymph node 267 268 staging. Vargiu et al. reported that obese patients (BMI>35kg/m2) were under-staged during 269 EC management in 9.4% versus 5% of non-obese patients (p-value=0.017). Moreover, there 270 was an empty package dissection in 8.2% of cases versus 3.9% for non-obese patients (p-271 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-value<0.0001) and 273 it was associated with a poorest RFS (HR=12.5 CI95%[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).

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

disease of 97.2% (Cl95% [85.0-100]), and a negative predictive value of 99.6% (Cl95% [97.9– 100]) even for high group risk(13). This procedure has been especially studied for obese patient by Matanes et al. who showed that performing a SLN instead of a pelvic LDN for obese patients is associated with a shorter operative time (p <0.001) and less blood loss (p = 0.03) without impact on OS and RFS (p 0.7 and 0.4 respectively)(14). SLN procedures in highrisk obese patients could increase the proportion of patients benefitting from the 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.

The development of quality indicators by ESGO and the certification of care centers might improve the adherence of international guidelines (16). Adherence to guidelines was more important regarding the choice of adjuvant therapy in obese patients, without significative difference after further stratification. The recent inclusion of the molecular analysis including immunohistochemistry for p53, mismatch repair proteins, and DNA 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.

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

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

338

Adherence to international guidelines for surgical management but not adjuvant
therapies, is significantly lower in morbid obese patients, especially the procedures of lymph
node staging.
Recent implementation of sentinel lymph node procedure even in high-risk patients as well
as the use of robotic procedures could increase the proportion of patients benefitting from

344 recommended therapies.

346 **References** 

347

3481.Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global349Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36350Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209–49.

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

3543.Caballero B. Humans against Obesity: Who Will Win? Adv Nutr Bethesda Md. 2019355Jan 1;10(suppl\_1):S4–9.

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

5. Bouwman F, Smits A, Lopes A, Das N, Pollard A, Massuger L, et al. The impact of BMI on surgical complications and outcomes in endometrial cancer surgery--an institutional 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.

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

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

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

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

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

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

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

39115.Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality392among endometrial cancer survivors: A systematic review and meta-analysis. Obes Rev Off J

393 Int Assoc Study Obes. 2021 Dec;22(12):e13337.

Concin N, Planchamp F, Abu-Rustum NR, Ataseven B, Cibula D, Fagotti A, et al.
European Society of Gynaecological Oncology quality indicators for the surgical treatment of
endometrial carcinoma. Int J Gynecol Cancer Off J Int Gynecol Cancer Soc. 2021
Dec;31(12):1508–29.

17. López-Ozuna VM, Kogan L, Hachim MY, Matanes E, Hachim IY, Mitric C, et al.
Identification of Predictive Biomarkers for Lymph Node Involvement in Obese Women With
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

## 410 Table 1: Epidemiological and pre operative histological characteristics by body mass index

## 411 in the whole population.

412

			NOG	OG		MG	p-value
		N=1330	) N:	=763	N=282	2	
Epidemiological charecteristic	s:						
Age, mean (median)		(68)	67 (6		(63)	63	< 0.001
Body mass index, mean (mediar	n)	(24)	24 (3	34 3)	(46)	46	0.001
Menopause, n (%)		) 1223 (92%)		, 702 2%)	25 (89%)		0.169
Menopausal hormone replaceme	ent therapy, n (%)	292 (22%)		87 1%)		13	0.001
High blood pressure, n (%)		( <u>445</u> (33%)		392 1%)	(67,6) 18 (64%)		0.001
Diabete, n (%)		131 (10%)		188 5%)	(39%)	9	0.001
Breast cancer history, n (%)		(10%) 12( (9%)	0	52 %)		10	0.004
Nulligravida, n (%)		(378) 402 (30%)		226 0%)	(4 %) 89 (32%)		0.831
Histological charecteristics :		(30 %)	(5	0 78)	(32 /0)		
Histological type, n (%	<b>(</b> )						0.002
Endometrioid carcine	oma	1054 (81%)		634 5%)	23 (88%)		
Other t	Vpe	254	·	114	Ś	1	
outor (		(19%)	(1	5%)	(12%)		
	NA	22	15	5	13		
Histological grade, n	%)	555		359	15	0	0.005
	1	(53%)	(5	7%)	(63%)		
	2	361 (34%)		187 0%)	7. (30%)		
	3	138		881		16	
		(13%)	(1	4%)	(7%)		
	NA	276	12	29	44		0.440
FIGO stage, n (%)		661		368	157	,	0.149
	ΙΑ	(51%)		9%)	(58%)		
	IB	376 (29%)		28 9%)	70 (26%)		
	11	84	4	40	1		
		(6%) 5		i%) 23	(5%)	6	
	IIIA	(4%)	(3	%)	(2%)	_	
	IIIB	7 (1%)		10 %)	(0%)	0	
	IIIC	85 (7%)		57 %)	1 (6%)	5	
	IV	(170) 45 (3%)	5	32 %)	(3%)	7	
	NA	22	15		13		
ESMO group, n (%)							< 0.001
	Low	496 (38%)		296 0%)	14 (52%)		
	Intermediate	486		257	7	0	
		(37%) 326		4%) 195	(26%) 5		
	High	(25%)		6%)	(22%)		
	NA	22	15	5	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

	NOG		OG	MG p-value
	N=1330	N=763	_N=282	
Surgical procedure concordance, n (%) :				
	644 (48%)	355 (44%)	85 (30%)	< 0.001
Adjuvant therapy concordance, n (%) :				
	618 (46%)	396 (52%)	171 (61%)	< 0.001
Global adherence, n (%) :				
	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.

## 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 :	group risk : <u>Low</u>		Intermediate				 High					
	NOG	OG	MG		NOG	OG	MG		NOG	OG	MG	
	N = 496	N = 296	N = 141	p-value	N = 326	N = 195	N = 58	p-value	N = 486	N = 257	N = 70	p-value
Surgery												
Surgical route				< 0.001				< 0.001				0.121
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%)	
Sentinel lymph node procedure												
Performed, n (%)	153 (31%)	70 (24%)	16 (11%)	< 0.001	113 (35%)	56 (29%)	8 (14%)	0.005	69 (14%)	25 (10%)	6 (9%)	0.129
Detected, n (%)	137 (90%)	62 (89%)	10 (63%)	0.008	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
Pelvic Lymphadenectomy												
Performed, n (%)	271 (55%)	144 (49%)	31 (22%)	< 0.001	211 (65%)	111(57%)	24 (7%)	0.002	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
Pelvic staging												
Performed, n (%)	327 (66%)	175 (59%)	45 (32%)	< 0.001	251 (77%)	130 (32%)	27 (47%)	< 0.001	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
Lombo-aortic lymphadenectomy												
Performed, n (%)	39 (8%)	19 (6%)	1 (1%)	0.009	61 (68%)	27 (14%)	2 (3%)	0.009	197 (41%)	90 (35%)	16 (23%)	0.011
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.