



HAL
open science

Impact of age on surgical staging and approaches (laparotomy, laparoscopy and robotic surgery) in endometrial cancer management

C. Bourgin, E. Lambaudie, G. Houvenaeghel, F. Foucher, Jérémy Lévêque, V. Lavoue

► To cite this version:

C. Bourgin, E. Lambaudie, G. Houvenaeghel, F. Foucher, Jérémy Lévêque, et al.. Impact of age on surgical staging and approaches (laparotomy, laparoscopy and robotic surgery) in endometrial cancer management. *EJSO - European Journal of Surgical Oncology*, 2017, 43 (4), pp.703–709. 10.1016/j.ejso.2016.10.022 . hal-01543369

HAL Id: hal-01543369

<https://univ-rennes.hal.science/hal-01543369>

Submitted on 20 Jun 2017

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 **Impact of age on surgical staging and approaches (laparotomy,**
2 **laparoscopy and robotic surgery) in endometrial cancer**
3 **management**

4 Charlotte Bourgin ^{a,b}, Eric Lambaudie ^c, Gilles Houvenaeghel ^c, Fabrice Foucher ^a,
5 Jean Levêque ^{a,b,d}, Vincent Lavoué ^{a,b,d}

6
7 a: Rennes University Hospital, Department of Gynaecology, Hôpital Sud, 16 boulevard de
8 Bulgarie, 35000 RENNES, France.

9 b: University of Rennes 1, Faculty of Medicine, 2 rue Henri le Guilloux, 35000 Rennes,
10 France.

11 c: Comprehensive Cancer Centre, Department of Surgical Oncology, Institut Paoli Calmette,
12 223 Boulevard Ste Marguerite, 13009 Marseille, France.

13 d: INSERM, ER440, Oncogenesis, Stress and Signaling (OSS), Eugène Marquis
14 Comprehensive Cancer Centre, Rennes, France.

15
16 **Corresponding author:** Vincent Lavoué, MD, PhD, Centre Hospitalier Universitaire de
17 Rennes, Service de gynécologie, Rennes, France. INSERM, ER 440, Oncogenesis, Stress and
18 Signaling, Centre Régional de lutte contre le Cancer Eugène Marquis, Rennes, France.
19 Université de Rennes 1, Faculté de Médecine, Rennes, France. Vincent.lavoue@chu-
20 rennes.fr. 02 99 26 59 71

24 **ABSTRACT**

25 **Objective:** This study aims to evaluate the different surgical approaches, perioperative
26 morbidity and surgical staging according to age in patients with endometrial cancer.

27 **Methods:** Multicentre retrospective study. Cancer characteristics and perioperative data were
28 collected for patients surgically treated for endometrial cancer. The patients were divided into
29 2 groups according to their age: younger or older than 75 years.

30 **Results:** Surgery was performed on 270 women < 75 years old and on $74 \geq 75$ years old.
31 Minimally invasive surgery was performed less often in the elderly compared with their
32 younger counterparts (58.2% vs. 74.8%; $p=0.006$). Independently of the surgical approach,
33 the rate of pelvic and para-aortic lymphadenectomy was lower in women older than 75 years
34 old than their younger counterparts (52.7% vs. 74.8%; $p < 0.001$; 8.1% vs. 21.8%; $p = 0.007$
35 respectively). According to the guidelines, more frequent surgical understaging was seen in
36 the elderly compared with the younger (37% vs. 15.2%; $p=0.002$). In the comparison of
37 complications for each surgical approach, there was no statistical difference in the ≥ 75 -year-
38 old age group in terms of intra- or postoperative complications between the laparotomy,
39 laparoscopy or robotic surgery group. We found a shorter length of hospital stay for the
40 women who underwent laparoscopy or robotic surgery compared with laparotomy
41 ($p < 0.0001$).

42 **Conclusion:** Elderly women with endometrial cancer are often surgically understaged
43 whereas there is no evidence of greater perioperative complications than for their younger
44 counterparts. They should benefit from minimally invasive surgery and optimal surgical
45 staging to the same extent as younger women.

46 **Keywords:** endometrial cancer, surgical approach, elderly, surgical staging

47 INTRODUCTION

48 Endometrial cancer is the fourth leading cancer among women in Western countries
49 with 54,870 new cases per year responsible for 10,170 annual deaths in the United States of
50 America (USA) and 7,200 new cases per year in France, making it the fifth leading cause of
51 death from cancer in women. It occurs mostly after the menopause with an average age at
52 diagnosis of 68 years. With the ageing population, an increased incidence of endometrial
53 cancer is observed (1). Interestingly, the National Institute of Aging predicts that there will be
54 more than 150 million people over 65 in 2050, corresponding to 16% of the overall
55 population with a strong trend towards an increasing percentage of female in the USA (2).
56 Surgical management of endometrial cancer is therefore set to increase in the coming years.
57 The International Federation of Gynaecology and Obstetrics (FIGO) (3), the European
58 Society of Gynaecological Oncology (ESGO) and the European Society of Medical Oncology
59 (ESMO) (4) support surgical staging for patients with endometrial cancer, particularly those
60 with high-risk types for which they recommend a surgical lymphadenectomy. Laparotomy is
61 the traditional surgical approach but minimally invasive techniques have played an increasing
62 role in this indication and we now know that laparoscopic surgical staging of endometrial
63 cancer is entirely feasible for a well-trained surgeon (5). However, few data are available in
64 the elderly population especially as they are under-represented in clinical trials (6). This lack
65 of participation has hampered the development of standardised treatment guidelines for the
66 elderly based on the best available evidence. Surgeons and anaesthesiologists are often
67 reluctant to perform minimally invasive surgery (laparoscopy or robotic surgery) on the
68 elderly because of the effects of Trendelenburg positioning and hypercapnia due to
69 pneumoperitoneum in a population with severe cardiopulmonary and respiratory
70 comorbidities.

71 The aim of this study was to evaluate the different surgical approaches, perioperative
72 complications and surgical staging according to age in patients with endometrial cancer.

73

74 MATERIALS AND METHODS

75 Patients

76 A retrospective data collection was carried out on patients with endometrial carcinoma
77 surgically treated by laparotomy, laparoscopy and robot-assisted laparoscopy in two tertiary
78 centres (Rennes teaching hospital and Institut Paoli Calmettes in Marseille, France) between
79 January 2006 and December 2014. Patients were divided into 2 cohorts: 1) women < 75 years
80 old, 2) women \geq 75 years old.

81 The endpoints were surgical staging compliance with French National guidelines (7) and
82 perioperative outcomes, including complications and length of postoperative hospital stay.

83

84 Data collection

85

86 Demographic and clinical data including age, body mass index (BMI), previous
87 abdominal or pelvic surgery, American Society of Anesthesiologists (ASA) score and
88 comorbidities were collected. We also recorded the tumour histological subtype, grade and
89 stage based on the 2009 International Federation of Gynecology and Obstetrics (FIGO)
90 classification (for patients treated from 2009 onwards) (3). Operative data including surgical
91 approach, operative time (from first skin incision to skin closure), estimated blood loss
92 (difference between pre- and postoperative haemoglobin levels) and operative procedure
93 (lymphadenectomy, omentectomy) were collected. Other procedures corresponded to surgical
94 procedures that were necessary but unrelated to surgical management of the endometrial

95 cancer such as colectomy, appendectomy, splenectomy, cholecystectomy or adhesiolysis. We
96 also recorded the length of hospital stay and peri- and postoperative complications according
97 to the Clavien-Dindo classification (8). We defined minor complications as grade I and II
98 complications from this classification and major complications as grade III or IV. A
99 congruent surgical staging system was defined according to the French National Cancer
100 Institute guidelines based on FIGO stage and histological subtype. When patients did not
101 undergo the recommended surgery (no lymphadenectomy or omentectomy performed) they
102 were considered as “understaged”. If they underwent more surgical procedures than
103 recommended they were considered as “overstaged”.

104

105 Surgical technique

106 Open surgery, laparoscopic and robotic procedures were performed by 5 primary
107 surgeons (E.L., G.H., F.F., J.L. and V.L.). All patients received per-operative prophylactic
108 antibiotics and post-operative prophylactic thromboprophylaxis in the form of subcutaneous
109 heparin 5000 UI.

110 The combination of FIGO 2009 stage, type and grade enabled stratification of the tumours
111 into recurrence risk groups as determined by the definition of the European Society for
112 Medical Oncology (ESMO) (9) (10). Low risk was defined as stage IA, grade 1 or 2,
113 histological type 1; intermediate risk consisted of stage IA, grade 3 and stage IB grade 1 or 2,
114 histological type 1; high risk encompassed stage IB, grade 3 and by extension stage \geq II
115 histological type 1, all type 2 tumours irrespective of stage and also all those with
116 lymphovascular emboli irrespective of type or stage (consistent with the policy of the French
117 gynaecologic oncology tumour board). All patients underwent a total hysterectomy and
118 bilateral salpingo-oophorectomy. Intermediate-risk patients also underwent bilateral pelvic
119 lymphadenectomy (iliac and obturator nodes). High-risk patients underwent bilateral pelvic

120 lymphadenectomy (iliac and obturator nodes), a para-aortic lymphadenectomy up to the left
121 renal vessels and infracolic omentectomy.

122

123 Statistical analysis

124

125 Descriptive parameters were expressed as a mean (\pm standard deviation [SD]) (and
126 median [range] when indicated). We compared the demographic and medical characteristics
127 of patients in the open surgery cohort, laparoscopic cohort and robotic surgery cohort using
128 Chi-square or Fisher's exact tests, as appropriate, for categorical or ordinal variables, and
129 unpaired *t*-test analysis for continuous variables. Only *p* values <0.05 were considered as
130 statistically significant. Multivariate analysis was performed using logistic regression with
131 SEM[®] (Statistics Epidemiology Medicine) software.

132

133 RESULTS

134

135 Between January 2006 and December 2014, 344 patients were surgically treated for
136 endometrial cancer: 270 women were <75 years old and 74 were ≥ 75 years old. The
137 demographic and clinical data are shown in Table 1. The older women were thinner than the
138 younger ones (BMI = 27 ± 6.5 vs. 29.9 ± 8.3 ; $p=0.001$). The number of medications,
139 comorbidities and ASA grade ≥ 3 rates were significantly higher in the older group ($p=0.03$;
140 $p=0.001$ and $p< 0.001$ respectively) (table 1). The histological and pathological features of
141 endometrial cancer are shown in Figure S1. Tumour stage, grade and histological subtype
142 were not statistically different between the 2 age groups.

143 Concerning the surgical approach (Table 2), our data show significantly less
144 minimally invasive surgery in the elderly compared with their younger counterparts (58.2%
145 vs. 74.8%; $p=0.006$) although the number of conventional laparoscopy or robot-assisted
146 laparoscopy procedures was not statistically different between the 2 age groups. The elderly
147 women underwent more laparotomy procedures than the younger ones (35.1% vs. 22.3%;
148 $p=0.03$).

149 Surgical data and perioperative complications for all surgical approaches are shown in
150 Table 3 according to age. Mean operative time was significantly shorter in the elderly group
151 in comparison to the younger group (143 min \pm 70 vs. 195 min \pm 80; $p<0.001$). There was less
152 estimated blood loss in the older group (1.4 \pm 0.8 g/dL vs. 1.9 \pm 1.4; $p=0.008$). The rate of
153 pelvic and para-aortic lymphadenectomy was lower among women over 75 years compared
154 with their younger counterparts (52.7% vs. 74.8%; $p<0.001$; 8.1% vs. 21.8% $p=0.007$
155 respectively), but when lymphadenectomy was performed the mean number of removed or
156 positive lymph nodes was similar in the 2 groups. We found no statistical difference in the
157 rate of omentectomy or other surgical procedures in the 2 age groups. We also observed more
158 surgical understaging in the elderly group compared with the younger one (37% vs. 15.2%;
159 $p=0.002$) whereas there was no statistical difference in overstaging or congruent staging
160 between the 2 groups. Our data showed no statistical difference in terms of length of hospital
161 stay or transfusion between the 2 age groups. There was a higher rate of conversion
162 (laparoscopy to laparotomy) in the younger group than in the older one (10.5% vs. 4.6%;
163 $p=0.02$). Conversions are mainly due to respiratory intolerance or major adhesiolysis. No
164 statistical difference was observed in the rate of intra- or postoperative complications between
165 the elderly patients and their younger.

166 When comparing the data for each surgical approach according to age (Table 4), there
167 were fewer transfusions in the older group than in the younger group when women underwent

168 a laparotomy (7.6% vs. 31.6%; $p=0.02$). Concerning the laparoscopic surgical approach, we
169 observed a longer length of hospital stay for the older women than the younger ones (5.2 ± 2.2
170 vs. 7.2 ± 4.4 ; $p=0.02$) whereas there were fewer intraoperative complications in this group
171 (14.9% vs. 0%; $p=0.02$). These complications occurring in the younger group were mostly
172 classified as “other complications” meaning that 5 laparoscopic procedures were stopped due
173 to respiratory intolerance and 6 due to extensive adhesions. When we compared
174 complications for the robotic surgical approach, no statistical difference was observed
175 between the 2 age groups.

176 The comparison of complications according to surgical approach in the < 75-year-old
177 group is provided in Table 5. We observed a shorter length of hospital stay and less
178 transfusions for women who underwent laparoscopy or robotic surgery compared with
179 laparotomy (both $p<0.001$). The rate of vascular, urinary or other complications was higher in
180 the laparotomy group ($p=0.001$; $p=0.006$; $p=0.02$ respectively) whereas there was only a
181 statistical tendency to less overall intraoperative complications in the 3 surgical approach
182 groups ($p=0.07$). When we compared in pairs the laparotomic approach or the laparoscopic
183 approach to the robotic one, we found significantly less intraoperative complications for the
184 robotic approach ($p=0.04$, data not shown). Our data showed a higher rate of grade 2
185 postoperative complications in the laparotomy group compared with the other surgical
186 approaches ($p=0.004$).

187 The same comparison was done for the ≥ 75 -year-old group (Table 5) and no
188 statistical difference was observed for intra- or postoperative complications between the 3
189 groups. Our data merely showed a shorter length of hospital stay for women who underwent
190 laparoscopy or robotic surgery compared with laparotomy ($p<0.001$).

191 In multivariate analysis, only other surgical procedures (colectomy, splenectomy,
192 appendectomy, cholecystectomy, adhesiolysis) were significantly associated with

193 perioperative complications ($p < 0.001$) (Figure S2). Concerning postoperative complications,
194 in the multivariate analysis the laparotomy surgical approach was the primary complication
195 risk factor ($p = 0.002$) and the performance of pelvic lymphadenectomy was the second one
196 ($p = 0.03$). In the multivariate analysis, age over 75 years was not associated with postoperative
197 complications (Figure S3).

198

199 DISCUSSION

200

201 This study shows that elderly women with endometrial cancer do not receive the
202 recommended surgical staging and have less minimally invasive surgery than their younger
203 counterparts. They are more often understaged and not considered for lymphadenectomy
204 regardless of the surgical approach, whereas understaging could lead to incorrect adjuvant
205 treatment in these patients. However, elderly women want the same treatment as their younger
206 counterparts and are equally desirous of optimal surgery (11). But, elderly women are
207 surgically understaged. Yet despite significantly higher comorbidity rates consistent with
208 literature findings (12-15), our study showed no more intra- or postoperative complications in
209 the older group.

210 Women over 65 years old account for almost two-thirds of new cancer diagnoses and three-
211 quarters of all cancer-related deaths (12) (13). Despite this trend, data focused on practice
212 with elderly populations in the context of endometrial carcinoma (the most common
213 gynaecological cancer in developed countries) remains scarce (11) (14-19). The majority of
214 elderly patients are treated with traditional open surgery and a smaller percentage with vaginal
215 or laparoscopic surgery. Despite the high rate of minimally invasive surgery in patients over
216 75 years old in this study (58%) because of our well-trained teams, we still observed a lower
217 rate of minimally invasive surgery in the elderly when compared with younger patients. Even

218 if minimally invasive surgery is performed less often in the elderly, elderly patients derive
219 similar benefits to those observed for younger patients. Like other authors (14-19), we
220 observed fewer intraoperative complications, a shorter length of hospital stay and fewer
221 transfusions with the laparoscopic approach and robotic surgery in the elderly group when
222 compared with those undergoing open surgery. This lower rate of complications in patients of
223 all ages should lead to consideration of minimally invasive surgery for all women, regardless
224 of their age.

225 Moreover, our study raises the issue of surgical understaging of elderly women in current
226 practice. This finding is not justified by surgical difficulties due to patient morphology as, like
227 other authors, we show that elderly endometrial cancer women are thinner than younger ones
228 (13) (14) (16) (17). Besides, our results do not show any statistical difference in terms of
229 endometrial cancer histological subtype, grade or FIGO stage between the 2 age groups. Some
230 literature data even report more aggressive endometrial cancer in elderly women, with more
231 serous tumours (12) (18), more advanced FIGO stages (12) (16) or higher histological grades
232 (11) (13) (16). The literature data also show that elderly women have poorer disease-free-
233 survival rates (19) (20) (21) (22) and higher 5-year recurrence rates compared with younger
234 patients (18) (22) (23). These poorer survival rates are related to cancer aggressiveness but
235 could also be related to surgical understaging or adjuvant treatments. Indeed, a question
236 remains unanswered in this study and in the literature: for an equal histology, is that survival
237 differs between elderly and young women? If it is, there is therefore a need for adequate
238 surgical staging for elderly patients with endometrial cancer, with lymphadenectomy
239 performed according to the established guidelines in order to regain a prognosis similar to that
240 of younger patients. This warrants more aggressive surgical staging in elderly endometrial
241 cancer patients with greater use of minimally invasive surgery in order to reduce perioperative
242 morbidity. In fact, it seems, the medico-surgical team is less likely to practice aggressive

243 treatments on elderly women. Maybe, this reluctance is due to a lack of an adequate definition
244 of an old person? Hence, better than age, the actual concept of frailty is adopted by
245 geriatricians and corresponds to a reduction in physiological reserves limiting the patient's
246 capacity to respond to a stress and predisposing him/her to adverse events (23). This
247 definition, adapted for surgery, could help anaesthesiologists and surgeons to take decision
248 about the kind of surgery to practice, thanks to the development of surgical specific
249 oncogeriatric scores. Thereby, in the surgical specific domain, it has been established that
250 preoperative frailty in elderly women, defined by the Fried's Frailty Criteria, is predictive of
251 postoperative morbidity (postoperative complications and rehospitalisation within the 30
252 days) (24). This tool is unfortunately too time-consuming (approximately 20 min) and is not
253 currently used. In order to improve the surgical management of elderly women, it is necessary
254 to develop better oncogeriatric scores than these currently available (25). Indeed, if medico-
255 surgical teams do not treat equally older women because of morbidities, this different
256 treatment must be based on objective criteria, which is not the case today.

257 Otherwise, we wonder if there is an interest to treat older women differently than younger
258 women? To date, any publication, except Benedetti's one (22), proves there is an interest to
259 understaged older women. In this way, we currently have no arguments to not treat elderly
260 women as younger women. If not, the guidelines should change. In this context, endometrial
261 cancer staging by sentinel lymph node detection may represent an interesting alternative,
262 particularly in this sub-population. In fact, this surgical technic is safe and provide less
263 morbidity compared with lymphadenectomy (26). However sentinel lymph node detection in
264 endometrial cancer remains controversial. The technic is not yet standardised because of a
265 lack of survival evidence. On the other hand, the therapeutic role of systematic
266 lymphadenectomy is controversial. Indeed, some recent trials negate the therapeutic role of
267 systematic lymphadenectomy (27) (28).

268 Nevertheless, known lymph node status remains crucial in order to tailor adjuvant treatment
269 especially in high-risk endometrial cancer, more frequent in elderly (29) (30). There is still a
270 need of randomised control trials but the literature data suggests it could be beneficial mostly
271 in a frailty population Sentinel lymph node biopsy could resolved the question of node status
272 in endometrial cancer because answers lymph node involvement with fewer morbidity (31)
273 (32).

274 Finally, our study has limitations that should be recognised. First, this is a retrospective study,
275 but there is a paucity of prospective data on this subject in the literature. Despite its
276 retrospective nature, this study represent a large cohort on the subject, with 344 patients
277 included and 74 patients over 75 years old, which represents 21% of the whole population and
278 serves to support the reliability of our results. We also collected data from 2 recognised
279 centres, both of which perform a large number of gynaecologic oncology procedures
280 according to the established guidelines and implement similar practices, which contribute to
281 the power of our study. Nevertheless, one recent study published by Uccella et al (15) had
282 more power compare to the present study. Indeed, their cohort showed 1606 patients, 271 of
283 whom over 75 years and 113 over 80 years and showed that the risk of wound complications,
284 bowel lesions and overall perioperative complications are higher among elderly subjects
285 compared to younger one. Present study can note this point, probably because of lack of
286 power. Moreover, one interesting aspect of the study is the simultaneous comparison of the 3
287 surgical approaches, which is not often observed in the literature. Indeed, we showed better
288 outcome with robotic surgery when compared with laparoscopic: length stay is lower, less
289 post-operative complications but only for young patients and not for elderly, probably due to
290 lack of power.

291

292

293 **CONCLUSION**

294

295 The present study shows elderly women with endometrial cancer do not receive the
296 recommended surgical staging and have less minimally invasive surgery than their younger
297 counterparts. Adequate surgical staging is necessary for elderly patients with endometrial
298 cancer, with lymphadenectomy performed according to the established guidelines in order to
299 regain a prognosis similar to that of younger patients. This more aggressive surgical staging in
300 elderly endometrial cancer patients warrants greater use of minimally invasive surgery in
301 order to reduce perioperative morbidity. There is a huge need for guidelines according age to
302 manage correctly endometrial cancer patients.

303

304 Acknowledgments are due to Estelle Bauville as surgeons of patients and to Tracey Wescott
305 for editing the draft. VL obtains funding from La Vannetaise.

306 The authors have no conflict of interest to declare.

307 Contribution to authorships:

308 -Dr Bourgin: writer, statistical analysis, data collection

309 -Pr Houveneaghel, Dr Lambaudie: Surgeons at the Institut Paoli Calmettes, Marseille, France.

310 They have operated patients with endometrial cancer and they have accepted to give us their
311 database.

312 -Pr Levêque, Dr Foucher: Surgeons at CHU Rennes, France. They have operated patients with
313 endometrial cancer and they have accepted to give us their database

314 -Pr Lavoué: co-writer, designer of the study, surgeon at CHU Rennes, France.

315 All authors participated in the design of the study. VL and CB carried out the data analysis
316 and wrote the first draft of the manuscript. VL is a guarantor of the study. All authors (CB,

317 EL, GH, FF, JL,VL) contributed to the subsequent writing of the paper and gave substantial
318 input into the study. All authors approved final draft.

319 Details of ethics approval: Ethical approval was obtained from local institutional review
320 board.

321 Funding: none

322

323

324

ACCEPTED MANUSCRIPT

325 **References**

- 326 1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013
327 Jan;63(1):11–30.
- 328 2. nia-who_report_booklet_oct-2011_a4__1-12-12_5.pdf [Internet]. [cited 2014 Feb 27].
329 Available from: [http://www.nia.nih.gov/sites/default/files/nia-](http://www.nia.nih.gov/sites/default/files/nia-who_report_booklet_oct-2011_a4__1-12-12_5.pdf)
330 [who_report_booklet_oct-2011_a4__1-12-12_5.pdf](http://www.nia.nih.gov/sites/default/files/nia-who_report_booklet_oct-2011_a4__1-12-12_5.pdf)
- 331 3. Creasman W. Revised FIGO staging for carcinoma of the endometrium. *Int J Gynecol*
332 *Obstet.* 2009 May;105(2):109.
- 333 4. igj50159 2..30 - ESMO_ESGO_ESTRO_Consensus_Conference_on.2.pdf [Internet]. [cited
334 2016 Jan 10]. Available from: [http://www.esgo.org/wp-](http://www.esgo.org/wp-content/uploads/2015/12/ESMO_ESGO_ESTRO_Consensus_Conference_on.2.pdf)
335 [content/uploads/2015/12/ESMO_ESGO_ESTRO_Consensus_Conference_on.2.pdf](http://www.esgo.org/wp-content/uploads/2015/12/ESMO_ESGO_ESTRO_Consensus_Conference_on.2.pdf)
- 336 5. Holub Z, Jabor A, Bartos P, Hendl J, Urbánek S. Laparoscopic surgery in women with
337 endometrial cancer: the learning curve. *Eur J Obstet Gynecol Reprod Biol.* 2003 Apr
338 25;107(2):195–200.
- 339 6. Lewis JH, Kilgore ML, Goldman DP, Trimble EL, Kaplan R, Montello MJ, et al.
340 Participation of patients 65 years of age or older in cancer clinical trials. *J Clin Oncol Off*
341 *J Am Soc Clin Oncol.* 2003 Apr 1;21(7):1383–9.
- 342 7. 9595-cancer-de-lendometre-synthese-des-recommandations.pdf [Internet]. [cited 2014
343 Feb 27]. Available from: [http://www.e-](http://www.e-cancer.fr/component/docman/doc_download/9595-cancer-de-lendometre-synthese-des-recommandations)
344 [cancer.fr/component/docman/doc_download/9595-cancer-de-lendometre-synthese-](http://www.e-cancer.fr/component/docman/doc_download/9595-cancer-de-lendometre-synthese-des-recommandations)
345 [des-recommandations](http://www.e-cancer.fr/component/docman/doc_download/9595-cancer-de-lendometre-synthese-des-recommandations)
- 346 8. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new
347 proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.*
348 2004 Aug;240(2):205–13.
- 349 9. Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, et al. Endometrial
350 cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann*
351 *Oncol Off J Eur Soc Med Oncol ESMO.* 2013 Oct;24 Suppl 6:vi33–8.
- 352 10. Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, et al. Endometrial
353 cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann*
354 *Oncol Off J Eur Soc Med Oncol ESMO.* 2011 Sep;22 Suppl 6:vi35–9.
- 355 11. Nordin AJ, Chinn DJ, Moloney I, Naik R, de Barros Lopes A, Monaghan JM. Do elderly
356 cancer patients care about cure? Attitudes to radical gynecologic oncology surgery in
357 the elderly. *Gynecol Oncol.* 2001 Jun;81(3):447–55.
- 358 12. Lachance JA, Everett EN, Greer B, Mandel L, Swisher E, Tamimi H, et al. The effect of
359 age on clinical/pathologic features, surgical morbidity, and outcome in patients with
360 endometrial cancer. *Gynecol Oncol.* 2006 Jun;101(3):470–5.

- 361 13. Zeng XZ, Lavoue V, Lau S, Press JZ, Abitbol J, Gotlieb R, et al. Outcome of Robotic
362 Surgery for Endometrial Cancer as a Function of Patient Age. *Int J Gynecol Cancer Off J*
363 *Int Gynecol Cancer Soc.* 2015 Feb 26;
- 364 14. Siesto G, Uccella S, Ghezzi F, Cromi A, Zefiro F, Serati M, et al. Surgical and survival
365 outcomes in older women with endometrial cancer treated by laparoscopy.
366 *Menopause N Y N.* 2010 Jun;17(3):539–44.
- 367 15. Uccella S, Bonzini M, Palomba S, Fanfani F, Malzoni M, Ceccaroni M, et al. Laparoscopic
368 vs. open treatment of endometrial cancer in the elderly and very elderly: An age-
369 stratified multicenter study on 1606 women. *Gynecol Oncol.* 2016 May;141(2):211–7.
- 370 16. Vaknin Z, Perri T, Lau S, Deland C, Drummond N, Rosberger Z, et al. Outcome and
371 quality of life in a prospective cohort of the first 100 robotic surgeries for endometrial
372 cancer, with focus on elderly patients. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc.*
373 2010 Nov;20(8):1367–73.
- 374 17. Jolly S, Vargas CE, Kumar T, Weiner SA, Brabbins DS, Chen PY, et al. The impact of age
375 on long-term outcome in patients with endometrial cancer treated with postoperative
376 radiation. *Gynecol Oncol.* 2006 Oct;103(1):87–93.
- 377 18. Bogani G, Cromi A, Uccella S, Serati M, Casarin J, Mariani A, et al. Laparoscopic staging
378 in women older than 75 years with early-stage endometrial cancer: comparison with
379 open surgical operation. *Menopause N Y N.* 2014 Jan 27;
- 380 19. Vaknin Z, Ben-Ami I, Schneider D, Pansky M, Halperin R. A comparison of perioperative
381 morbidity, perioperative mortality, and disease-specific survival in elderly women
382 (≥ 70 years) versus younger women (< 70 years) with endometrioid endometrial
383 cancer. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc.* 2009 Jul;19(5):879–83.
- 384 20. Lavoue V, Zeng X, Lau S, Press JZ, Abitbol J, Gotlieb R, et al. Impact of robotics on the
385 outcome of elderly patients with endometrial cancer. *Gynecol Oncol.* 2014
386 Jun;133(3):556–62.
- 387 21. Alektiar KM, Venkatraman E, Abu-Rustum N, Barakat RR. Is endometrial carcinoma
388 intrinsically more aggressive in elderly patients? *Cancer.* 2003 Dec 1;98(11):2368–77.
- 389 22. Benedetti Panici P, Basile S, Salerno MG, Di Donato V, Marchetti C, Perniola G, et al.
390 Secondary analyses from a randomized clinical trial: age as the key prognostic factor in
391 endometrial carcinoma. *Am J Obstet Gynecol.* 2014 Apr;210(4):363.e1–363.e10.
- 392 23. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in
393 older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001
394 Mar;56(3):M146–56.
- 395 24. Courtney-Brooks M, Tellawi AR, Scalici J, Duska LR, Jazaeri AA, Modesitt SC, et al.
396 Frailty: an outcome predictor for elderly gynecologic oncology patients. *Gynecol Oncol.*
397 2012 Jul;126(1):20–4.

- 398 25. Bourgin C, Saidani M, Poupon C, Cauchois A, Foucher F, Leveque J, et al. Endometrial
399 cancer in elderly women: Which disease, which surgical management? A systematic
400 review of the literature. *Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol*. 2015
401 Nov 11;
- 402 26. Tschernichovsky R, Diver EJ, Schorge JO, Goodman A. The Role of Lymphadenectomy
403 Versus Sentinel Lymph Node Biopsy in Early-stage Endometrial Cancer: A Review of the
404 Literature. *Am J Clin Oncol*. 2016 Jun 8;
- 405 27. Clark LH, Soper JT. Endometrial Cancer and the Role of Lymphadenectomy. *Obstet
406 Gynecol Surv*. 2016 Jun;71(6):353–60.
- 407 28. Bogani G, Ditto A, Martinelli F, Signorelli M, Perotto S, Lorusso D, et al. A critical
408 assessment on the role of sentinel node mapping in endometrial cancer. *J Gynecol
409 Oncol*. 2015 Oct;26(4):252–4.
- 410 29. Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. *Lancet
411 Lond Engl*. 2016 Mar 12;387(10023):1094–108.
- 412 30. Koskas M, Rouzier R, Amant F. Staging for endometrial cancer: The controversy around
413 lymphadenectomy - Can this be resolved? *Best Pract Res Clin Obstet Gynaecol*. 2015
414 Aug;29(6):845–57.
- 415 31. Ballester M, Dubernard G, Lécuru F, Heitz D, Mathevet P, Marret H, et al. Detection rate
416 and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: a
417 prospective multicentre study (SENTI-ENDO). *Lancet Oncol*. 2011 May;12(5):469–76.
- 418 32. Kang S, Yoo HJ, Hwang JH, Lim M-C, Seo S-S, Park S-Y. Sentinel lymph node biopsy in
419 endometrial cancer: meta-analysis of 26 studies. *Gynecol Oncol*. 2011 Dec;123(3):522–
420 7.

421

422

423 **Tables and Supplementary figures list**

424 **Table 1:** *Demographic and clinical characteristics*

425 **Table 2:** *Surgical approaches*

426 **Table 3:** *Surgical procedures and complications*

427 **Table 4:** *Surgical complications*

428 **Table 5:** *Surgical complications according to surgical approach*

429 **Figure S1:** *Tumour characteristics*

430 **Figure S2:** *Multivariate analysis for perioperative complications*

431 **Figure S3:** *Multivariate analysis for postoperative complications*

Table 1: Demographic and clinical characteristics

	< 75 y N = 270	≥ 75 y N = 74	p value
Age	63.5 [22-74]	80 [75-89]	< 0.001
BMI	29.9 ± 8.3	27 ± 6.5	0.001
Parity	2.2 ± 1.8	2.5 ± 2.5	NS
No. of medications	2.7 ± 2.5	4.2 ± 2.4	0.003
No. of diseases	1.3 ± 1.3	1.8 ± 1.6	0.05
Previous abdominal or pelvic surgery	165 (61.1%)	41 (55.4%)	NS
ASA score ≥3	39 (14.4%)	25 (33.8%)	< 0.001
Comorbidities *	174 (64.4%)	62 (83.8%)	0.001
Hypertension	117 (43.3%)	49 (66.2%)	
CVD/strokes	58 (21.5%)	29 (39.2%)	
Diabetes	40 (14.8%)	11 (14.8%)	
CLD/CGD	37 (13.7%)	4 (5.4%)	
2 nd malignancy	40 (14.8%)	15 (20.3%)	

y: years old; BMI: Body Mass Index (kg/m^2); ASA: American Society of Anesthesiologists; NS: Not Significant; * Comorbidities including: Cardiovascular Diseases (CVD), Chronic Lung Diseases (CLD), Chronic Gastrointestinal Diseases (CGD)

Table 2: *Surgical approaches*

	< 75 y N = 270	≥ 75 y N= 74	p value
Minimally invasive surgery	202 (74.8%)	43 (58.2%)	0.006
Laparoscopy	127 (47%)	27 (36.5%)	NS
Robotic surgery	75 (27.8%)	16 (21.7%)	NS
Laparotomy	60 (22.3%)	26 (35.1%)	0.03
Vaginal	8 (2.9%)	5 (6.7%)	NS

Table 3: *Surgical procedures and complications*

	< 75 y N = 270	≥ 75 y N = 74	p value
Operative time (min)	195 (± 80)	143 (± 70)	< 0.001
Estimated blood loss (≠ Hb in g/dL)	1.9 (± 1.4)	1.4 (± 0.8)	0.008
No. of lymphadenectomies			
Pelvic	202 (74.8%)	39 (52.7%)	< 0.001
Para-aortic	59 (21.8%)	6 (8.1%)	0.007
No. of omentectomies	55 (20.4%)	8 (10.8%)	NS
Other procedures	75 (27.8%)	16 (21.6%)	NS
Total no. of lymph nodes	19.4 (± 10.2)	16.4 (± 10.8)	NS
No. of positive lymph nodes	0.8 (± 3.3)	0.2 (± 0.7)	NS
Surgical staging			
Understaging	24 (15.2%)	17 (37%)	0.002
Congruent staging	96 (60.8%)	22 (47.8%)	NS
Overstaging	38 (24%)	7 (15.2%)	NS
Hospital stay (d)	5.8 (± 3.5)	7.7 (± 6)	NS
Transfusions	28 (10.3%)	6 (8.1%)	NS
Conversion	21 (10.5%)	2 (4.6%)	0.02
Intraoperative complications	23 (8.5%)	4 (5.3%)	NS
Vascular	9 (3.4%)	3 (4%)	NS
Digestive	1 (0.3%)	0 (0%)	NS
Urinary	3 (1.1%)	0 (0%)	NS
Other*	10 (3.7%)	1 (1.3%)	NS
Postoperative complications**			
Minor	48 (17.8%)	10 (13.5%)	NS
Major	11 (4.1%)	6 (8.1%)	NS

y: years old ; Min: minutes; Hb: haemoglobin; No.: number; Other procedures: cholecystectomy, appendectomy, colectomy, splenectomy, adhesiolysis d: days; * Other: respiratory complications and morphological (obesity-related) surgical complications; ** postoperative complications according to the Clavien-Dindo classification

Table 4: *Surgical complications*

	< 75 y	≥ 75 y	<i>p</i> value
Laparotomy	N=60	N=26	
Hospital stay (d)	9.8 (± 4.3)	10.7 (± 7.9)	NS
Transfusions	19 (31.6%)	2 (7.6%)	0.02
Intraoperative complications	10 (16.7%)	2 (7.6%)	NS
Vascular	5 (8.3%)	1 (3.8%)	NS
Digestive	1 (1.7%)	0 (0%)	NS
Urinary	3 (5%)	0 (0%)	NS
Other*	1 (1.7%)	1 (3.8%)	NS
Postoperative complications**			
Minor	16 (26.7%)	5 (19.2%)	NS
Major	5 (8.3%)	1 (3.8%)	NS
Laparoscopy	N=127	N=27	
Hospital stay (d)	5.2 (± 2.2)	7.2 (± 4.4)	0.02
Transfusions	6 (4.7%)	1 (3.7%)	NS
Conversion	16 (12.6%)	0	NS
Intraoperative complications	19 (14.9%)	0	0.02
Vascular	1 (0.75%)	0	NS
Digestive	1 (0.75%)	0	NS
Urinary	0	0	NS
Other*	17 (13.4%)	0	0.04
Postoperative complications**			
Minor	15 (11.8%)	1 (3.7%)	NS
Major	4 (3.1%)	1 (3.7%)	NS
Robotic surgery	N=75	N=16	
Hospital stay (d)	3.7 (± 1.5)	4.5 (± 3.3)	NS
Transfusions	0 (0%)	0 (0%)	NS
Conversion	4 (5.3%)	0 (0%)	NS
Intraoperative complications	4 (5.3%)	0 (0%)	NS
Vascular	0 (0%)	0 (0%)	NS
Digestive	0 (0%)	0 (0%)	NS
Urinary	0 (0%)	0 (0%)	NS
Other*	4 (5.3%)	0 (0%)	NS
Postoperative complications**			
Minor	6 (8%)	1 (6.2%)	NS
Major	2 (2.6%)	0 (0%)	NS

y: years old ; d: days; *Other: respiratory complications and morphological (obesity-related) surgical complications; ** postoperative complications according to the Clavien-Dindo classification

Table 5: *Surgical complications according to surgical approach*

	Laparotomy	Laparoscopy	Robotic	<i>p</i> value
Patients < 75 years old	N=60	N=127	N=75	
Hospital stay (d)	9.8 (± 4.3)	5.2 (± 2.2)	3.7 (± 1.5)	<0.001
Transfusions	19 (31.7%)	6 (4.7%)	0 (0%)	<0.001
Intraoperative complications	10 (16.7%)	19 (15%)	4 (5.3%)	NS
Vascular	5 (8.3%)	1 (0.8%)	0 (0%)	0.001
Digestive	1 (1.7%)	1 (0.8%)	0 (0%)	NS
Urinary	3 (5%)	0	0 (0%)	0.006
Other*	1 (1.7%)	17 (13.4%)	4 (5.3%)	0.02
Postoperative complications**				
Minor	16 (26.7%)	15 (11.8%)	6 (8%)	0.004
Major	5 (8.3%)	4 (3.1%)	2 (2.7%)	NS
Patients ≥ 75 years old	N=26	N=27	N=16	
Hospital stay (d)	10.7 (± 7.9)	7.2 (± 4.4)	4.5 (± 3.3)	<0.001
Transfusions	2 (7.7%)	1 (3.7%)	0 (0%)	NS
Intraoperative complications	2 (7.7%)	0	0 (0%)	NS
Vascular	1 (3.8%)	0	0 (0%)	NS
Digestive	0 (0%)	0	0 (0%)	NS
Urinary	0 (0%)	0	0 (0%)	NS
Other*	1 (3.8%)	0	0 (0%)	NS
Postoperative complications**				
Minor	5 (19.2%)	1 (3.7%)	1 (6.2%)	NS
Major	1 (3.8%)	1 (3.7%)	0 (0%)	NS

d: days; *Other: respiratory complications and morphological (obesity-related) surgical complications; **postoperative complications according to the Clavien-Dindo classification