

Alma Mater Studiorum Università di Bologna
Archivio istituzionale della ricerca

Practice patterns and 90-day treatment-related morbidity in early-stage cervical cancer

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

Published Version:

Giorgio Bogani, V.D.D. (2022). Practice patterns and 90-day treatment-related morbidity in early-stage cervical cancer. GYNECOLOGIC ONCOLOGY, 166(3), 561-566 [10.1016/j.ygyno.2022.07.022].

Availability:

This version is available at: <https://hdl.handle.net/11585/902507> since: 2024-07-22

Published:

DOI: <http://doi.org/10.1016/j.ygyno.2022.07.022>

Terms of use:

Some rights reserved. The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

This item was downloaded from IRIS Università di Bologna (<https://cris.unibo.it/>).
When citing, please refer to the published version.

(Article begins on next page)

1 Title: **Practice patterns and 90-day treatment-related morbidity in early-stage cervical cancer**

2 Authors: Giorgio Bogani ^{1*}, Violante Di Donato ^{1*}, Giovanni Scambia ², Fabio Landoni ³, Fabio
3 Ghezzi ⁴, Ludovico Muzii ¹, Pierluigi Benedetti Panici ¹, Francesco Raspagliesi ⁵, The investigator
4 of the Italian Gynecological Cancer Study Group

5
6 * Co-first author

7
8 **Affiliations:**

- 9 1. Department of Maternal and Child Health and Urological Sciences, Sapienza University of
10 Rome, Policlinico Umberto I, Rome, Italy
- 11 2. Gynecologic Oncology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome,
12 Italy
- 13 3. Department of Obstetrics and Gynaecology, San Gerardo Hospital, Monza, Italy
- 14 4. Department of Obstetrics and Gynaecology, University of Insubria, F. Del Ponte Hospital,
15 Varese, Italy.
- 16 5. Gynecologic Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano,
17 Milan, Italy

18
19 **Corresponding authors:**

20 Giorgio Bogani, M.D., Ph.D.,

21 Department of Maternal and Child Health and Urological Sciences, Sapienza University of Rome,
22 Policlinico Umberto I, Viale del Policlinico 155, Roma, Italy

23 Phone: 00393803933116

24 Email: giorgiobogani@yahoo.it

25 Word Count: 2,305

27 **Highlights:**

- 28 - The publication of the LACC trial determined a shift from the use of minimally invasive to
- 29 open surgery.
- 30 - Overall and severe 90-day complication rates were not influenced by the surgical approach
- 31 - The paradigm shift from minimally invasive to open radical hysterectomy does not increase
- 32 the complication rate.

33 **Abstract**

34 **Background:** To evaluate the impact of the Laparoscopic Approach to Cervical Cancer (LACC) Trial
35 on patterns of care and surgery-related morbidity in early-stage cervical cancer.

36 **Methods:** This is a retrospective, a multi-institutional study evaluating 90-day surgery-related
37 outcomes of patients undergoing treatment for early-stage cervical cancer before (period I:
38 01/01/2016-06/01/2018) and after (period II: 01/01/2019-06/01/2021) the publication of the results
39 of the LACC trial.

40 **Results:** Charts of 1,295 patients were evaluated: 581 (44.9%) and 714 (55.1%) before and after the
41 publication of the LACC trial, respectively. After the publication of the LACC trial, the number of
42 patients treated with minimally invasive radical hysterectomy decreased from 64.9% to 30.4%
43 ($p<0.001$). Overall, 90-day complications occurred in 110 (18.9%) and 119 (16.6%) patients in the
44 period I and period II, respectively ($p=0.795$). Similarly, the number of severe (grade 3 or worse)
45 complications did not differ between the two periods (38 (6.5%) vs. 37 (5.1%); $p=0.297$). Overall and
46 severe 90-day complications were consistent between periods even evaluating stage IA ($p=0.471$),
47 IB1 ($p=0.929$), and IB2 ($p=0.074$), separately.

48 **Conclusions:** The present investigation highlighted that in referral centers the shift from minimally
49 invasive to open radical hysterectomy does not influence 90-day surgery-related morbidity.

50

51 **Keywords:** Laparoscopy; Radical hysterectomy; Morbidity; Complications

52 **Introduction**

53 Over recent years, the minimally invasive approach has revolutionized surgical care [1].
54 Accumulating evidence highlighted that minimally invasive surgery correlated with better
55 perioperative outcomes than open surgery [2, 3]. In comparison to open surgery, minimally-invasive
56 surgery is associated with lower postoperative pain, recovery time, hospital stays, and marked
57 improvements in cosmetic outcome and overall cost-effectiveness either in benign or malignant
58 disease. Level A evidence supports the adoption of minimally invasive surgery in endometrial cancer
59 [2]. Minimally invasive approach correlates with improved short-term postoperative course and
60 morbidity than open surgery without affecting oncologic outcomes. Similarly, retrospective data
61 highlighted the feasibility of laparoscopic radical hysterectomy in patients with early-stage cervical
62 cancer [4-6].

63 The Laparoscopic Approach to Cervical Cancer (LACC) Trial was designed to assess the non-
64 inferiority of a minimally invasive approach in comparison to open surgery [7]. However, the
65 unexpected results of the LACC trial showed that a minimally invasive approach is associated with
66 lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy
67 among women with early-stage cervical cancer [7]. Moreover, two secondary analyses of the
68 randomized LACC trial suggested that minimally invasive and open approaches correlated with
69 similar morbidity rates and postoperative quality of life (QoL) [8, 9]. The publication of the LACC
70 trial impacted clinical practice, dramatically. We assisted in a rapid paradigm shift, with a decrease
71 in the adoption of minimally invasive radical hysterectomy [10, 11]. Lewicki PJ et al., assessed the
72 use of minimally invasive surgery as compared with open radical hysterectomy for cervical cancer
73 before and after the publication of the LACC Trial. Using data from the Premier Healthcare Database,
74 the authors highlighted that the minimally invasive approach decreased from 58.0% (pre-LACC) to
75 42.9% (post-LACC) [10]. Other studies reported similar findings [11]. Interestingly, they observed
76 that the increased adoption of open radical hysterectomy resulted in an increased surgery-related

morbidity rate. In order to assess patterns of utilization of minimally invasive and open radical hysterectomy as well as surgery-related morbidity, we designed the present investigation.

Methods:

This is a multi-institutional retrospective study coordinated by the Fondazione IRCCS Istituto Nazionale dei Tumori. As coordinator center the Institutional Review Board of the Fondazione IRCCS Istituto Nazionale dei Tumori approved this investigation (#572020). Charts of patients affected by early-stage cervical cancer (stage IA- IB2) were collected in 24 referral centers in Italy. The primary endpoint measure was to evaluate how the publication of the LACC trial impacted patterns of care and surgery-related morbidity of patients affected by early-stage cervical cancer. For the purpose present study, we collected medical records of consecutive patients with newly diagnosed early-stage cervical cancer treated in Italy before (period I: 01/01/2016-06/01/2018) and after (period II: 01/01/2019-06/01/2021) the publication of the results of the LACC trial [7]. Supplemental material 1 displays the centers participating in the study.

We included consecutive patients receiving treatment (i.e., conservative approach, radical hysterectomy, and radiotherapy) in period I and period II. We included patients aged ≥ 18 years old, with a confirmed histological diagnosis of early-stage cervical cancer. In all included centers, data concerning surgical procedures, peri-operative details, as well as 90-day follow-up evaluations were recorded in computerized databases, updated by trained residents and nurses on a regular basis.

Exclusion criteria were: (i) stage II endometrial cancer receiving radical hysterectomy; (ii) administration of neoadjuvant chemotherapy; (iii) lack of data of 90-day postoperative course; (iv) consent withdrawal. During the two study periods, there were no significant differences in the facilities available for patient care and in the referral patterns of our services. Other features of patient management remained consistent in the two periods. The TNM classification was applied in order to categorize patients *per* stage [12]. Postoperative complications included any deviation of normal postoperative course, within 90 days. To improve quality of complication reporting complications

were graded per a severity system [13, 14]. The Clavien-Dindo classification was adopted to grade postoperative complications [13]. For the purpose of this study only severe complications, occurring within 90-day, are reported. They included events requiring surgical, endoscopic, or radiological intervention (with or without general anesthesia). Additionally, life threatening complications (including intensive care unit (ICU) admission as well as single or multi organ dysfunction) and postoperative death are registered [13]. Martin criteria were applied to improve quality of complications reporting [14]. Intraoperative complications were abstracted as well.

Statistical methods:

Basic descriptive statistics were used to describe the study populations. Differences in categorical variables were analyzed using the Fisher exact and Chi-square test when comparing two and three (or more) groups, respectively. When indicated odds ratio (OR) and 95% confidence intervals (95%CI) were calculated. T-test and Mann-Whitney tests were used to compare continuous variables as appropriate. P values <0.05 were considered statistically significant. Statistical analysis was performed with GraphPad Prism version 6.0 (GraphPad Software, San Diego CA) and IBM-Microsoft SPSS version 20.0 (SPSS Statistics. International Business Machines Corporation IBM 2013 Armonk, USA) for Mac.

Results:

Charts of 1,327 patients were retrieved. Data of 32 patients were excluded since they did not match the inclusion criteria. The study included 1,295 patients: 581 (44.9%) and 714 (55.1%) before and after the publication of the LACC trial, respectively. The study population included 199 (34.2%), 211 (36.3%), and 171 (29.4%) patients with stage IA, stage IB1, and stage IB2 treated in the period I and 293 (41.1%), 219 (30.6%), and 202 (28.3%) patients with stage IA, stage IB1, and stage IB2 treated in the period II ($p=0.028$; p -for trend <0.001). The proportion of patients receiving conservative treatments increase over the study period (13.6% vs. 20.6%; p -for trend <0.001); while the proportion

129 of patients receiving radiotherapy (with or without chemotherapy) remained stable in the two periods
130 (5.8% vs. 7.3%; $p=0.303$). Figure 1 shows the flow of patients through the study design. Table 1
131 reports data of patients treated in the period I and period II. Data for patients affected by stage IA,
132 IB1, and IB2 are reported in Supplemental material 2, 3, and 4, respectively. After the publication of
133 the LACC trial, the number of patients treated with minimally-invasive radical hysterectomy
134 decreased from 64.9% (304 out of 468 radical hysterectomies) to 30.4% (157 out of 515 radical
135 hysterectomies) ($p<0.001$). The decrease of minimally-invasive radical hysterectomy rates was
136 observed for patients with stage IA (81.8% vs. 58.2% (-23.6%); $p<0.001$), stage IB1 (68.8% vs.
137 20.3% (-48.5%); $p<0.001$), and stage IB2 (45.3% vs. 14.5% (-30.8%); $p<0.001$). All participating
138 centers suggested that they adopted protective maneuvers with the aim to reduce the risk of disease
139 dissemination at the time of minimally invasive radical hysterectomy. Those maneuvers included: (i)
140 preoperative tumor removal thorough conization ($n=130$), the avoidance of the use of uterine
141 manipulator ($n=87$), vaginal closure before colpotomy ($n=37$). In most cases, surgeons adopted more
142 than one technique to reduce possible contamination of the abdominal cavity. These maneuvers were
143 used in 86% of patients with tumors <2 cm and 100% of tumors larger than 2 cm. Intraoperative
144 complication rates were similar between period I and period II (2.4% vs. 1.4%; $p=0.215$). Overall,
145 90-day complications occurred in 110 (18.9%) and 119 (16.6%) patients in the period I and period II,
146 respectively ($p=0.795$). Similarly, the number of severe (grade 3 or worse) complications were not
147 influenced by the publication of the LACC trial (38 (6.5%) vs. 37 (5.1%); $p=0.297$). Supplement
148 material 5 reports details of overall and severe complications in period I and period II. Overall and
149 severe 90-day complications were consistent between periods even evaluating stage IA, IB1, and IB2,
150 separately ($p>0.20$). Table 2 shows overall and severe complications that occurred in period I and
151 period II.

152 Considering available data on perioperative data, we observed that minimally invasive radical
153 hysterectomy correlated with similar operative time (235 vs. 244 minutes; $p=0.261$) and lower blood

154 loss (100 vs. 200; $p<0.001$) in comparison to open surgery. The mean (SD) postoperative recovery
155 time was 2 (1.1) and 4 (2.4) days after minimally-invasive and open radical hysterectomy ($p<0.001$).
156

157 **Discussion**

158 The present study evaluated changes in patterns of care and treatment-related morbidity in early-stage
159 cervical cancer patients after the publication of the LACC trial [7]. The present study reported a
160 number of noteworthy findings. First, we observed that the prevalence of minimally invasive radical
161 hysterectomy significantly decreased after the publication of the LACC trial [7]. Second, the burden
162 of intraoperative, 90-day postoperative complications, and 90-day severe postoperative complications
163 remained stable over the periods. This finding was confirmed after stratification per stage of the
164 disease. Third, we assisted an increased number of patients undergoing treatments in period II.

165 The LACC trial was designed to test the non-inferiority of minimally invasive radical hysterectomy
166 in comparison to open radical hysterectomy in early-stage cervical cancer [7]. The trial planned to
167 enroll 740 patients. However, the trial was suspended earlier (after the enrollment of 631 patients)
168 since the imbalance in deaths between the two groups [7]. Ramirez et al., observed that patients
169 undergoing minimally invasive radical hysterectomy had lower disease-free (91.2% vs. 97.1%) and
170 overall (93.8% vs. 99%) survival rates and a higher rate of locoregional recurrence (94.3% vs. 98.3%)
171 than patients who underwent open abdominal radical hysterectomy [7]. These findings were
172 corroborated by an epidemiological study published in the same issue of the NEJM [15]. Melamed et
173 al., reported data of patients with early-stage cervical cancer treated during the 2010-2013 period at
174 Commission on Cancer-accredited hospitals in the United States. They also conducted an interrupted
175 time-series analysis involving patients undergoing radical hysterectomy during the 2000-2010 period,
176 using the Surveillance, Epidemiology, and End Results (SEER) program database [15]. In this paper,
177 the authors observed that after a median follow-up of 45 months, the mortality rate was 9.1% and
178 5.3% after minimally invasive and open radical hysterectomy, respectively [15]. After the publication
179 of those two studies, accumulating evidence suggested the detrimental role of minimally invasive

180 radical hysterectomy [16, 17]. Reasons, why the execution of minimally invasive hysterectomy
181 correlates with poor outcomes, are still unknown. The most imputable reasons are the possible
182 contamination of the pelvic cavity at the time of colpotomy and the flow of CO₂ that might spread
183 the cells into the abdominal cavity [16, 18]. We must note that the CO₂ pressure might cause the
184 penetration of the cells into the superficial mesothelial layer of the peritoneum. Moreover, the CO₂
185 might promote the spread of the cells in mechanical and biochemical ways. Interestingly, research
186 from our study group evaluated patterns of recurrence in patients undergoing laparoscopic and open
187 radical hysterectomy [19]. Applying a propensity-matched comparison, the findings of this study
188 highlighted that patients undergoing laparoscopic radical hysterectomy are at higher risk of
189 developing intrapelvic recurrences and peritoneal carcinomatosis in comparison to patients
190 undergoing open radical hysterectomy [19]. We assisted in a paradigm shift from minimally invasive
191 to open radical hysterectomy [20].

192 The LACC trial is one of the most impacting studies in the field of gynecologic oncology, being a
193 game-changer. Even the NEJM classified the LACC trial as one of the most impacting studies for the
194 year 2018 [7]. Accumulating data from the U.S. suggested that after the publication of the LACC
195 trial, a dramatic decrease in the adoption of minimally invasive radical hysterectomy was observed
196 [10, 11]. Interestingly, Matsuo K et al., evaluating the National Inpatient Sample from October 2015
197 to December 2018, evaluated data of 5,120 and 1,645 patients undergoing surgery before and after
198 the publication of the LACC. In the post LACC period patients were less likely to have a minimally
199 invasive radical hysterectomy (-63%), but more likely to develop perioperative complications (+23%)
200 and longer length of hospital stay (3 vs. 2 days) [11]. The present study provides similar findings, we
201 observed an important (statistically significant) decrease in the adoption of minimally invasive radical
202 hysterectomy that was more evident in patients with stage IB1 (-48.5%), than for stage IB2 (-30.8%),
203 and stage IA (-23.6%). However, we have to highlight that the reduction of minimally invasive radical
204 hysterectomy rates was less pronounced than those expected. In our series, the shift from minimally
205 invasive to open hysterectomy did not correlate with an increased morbidity rate. This data

206 corroborated the secondary analysis of the LACC trial suggesting that surgery-related morbidity does
207 not differ significantly between the two approaches [8]. The inherent biases related to the
208 retrospective nature of the study design are the main weaknesses of the present paper. Additionally,
209 four points of the present paper have to be addressed: (i) due to the absence of follow-up, we are not
210 able to evaluate the impact of this paradigm shift on oncologic outcomes of early-stage cervical cancer
211 patients involved in this study. (ii) we observed an increased number of patients treated in period II;
212 this feature might be related both to the improvement in patients' workflow and due to COVID-19.
213 After the onset of the COVID-19 outbreak, we assisted to centralization of oncologic cases in referral
214 - highly specialized centers (like those included in our series) [21]. (iii) We collected a huge amount
215 of data (more than 1,300 patients) from the whole Italian territory, with a potential missing of cervical
216 cancer cases diagnosed and treated in low volume centers. (iv) We were not able to correct our results
217 on the basis of patients demographic characteristics. The main merit of the present study is the
218 inclusion of a large sample size of consecutive patients treated before and after the publication of the
219 LACC trial [7]. Moreover, this paper investigated the impact of the LACC trial in a European country
220 for the first time. Interestingly, the inclusion of patients who had not radical surgery (i.e., conservative
221 treatment and radiotherapy) would help to avoid possible allocation biases and to better understand
222 the changes in patterns of care in cervical cancer management.

223 In conclusion, the present study evaluated changes in the pattern of care in patients treated before and
224 after the publication of the LACC trial [7]. We assisted in an important decrease in minimally invasive
225 radical hysterectomy, over time. The increased prevalence of open surgery did not correlate with
226 worse perioperative outcomes. Intraoperative, postoperative, and severe postoperative complication
227 rates were similar between groups. Further evidence is warranted to assess peri-operative and long-
228 term changes in early-stage cervical cancer, provided by the LACC trial [7].

229

230 **Authors contribution:**

231 Conceptualization: All authors., Methodology: All authors.; Data extraction: All authors; Project
232 administration: GB, VDD.; Supervision: GS, FR.; writing – original draft: All authors; writing –
233 review & editing: All authors.

234

235 **Conflicts of interest:**

236 The Authors declare no conflicts of interest.

237 No funding sources supported this investigation.

238

239 **Legend to Figure:**

240 Figure 1: Study design

241 **References**

- 242 1- Orlando MS, Greenberg CC, Pavuluri Quamme SR, Yee A, Faerber AE, King CR. Surgical
243 coaching in Obstetrics and Gynecology: an evidence-based strategy to elevate surgical education and
244 promote lifelong learning. *Am J Obstet Gynecol*. 2022 Feb 14:S0002-9378(22)00105-3. doi:
245 10.1016/j.ajog.2022.02.006. Epub ahead of print. PMID: 35176285.
- 246 2- Walker JL, Piedmonte MR, Spirtos NM, Eisenkop SM, Schlaerth JB, Mannel RS, et al. Recurrence
247 and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical
248 staging of uterine cancer: Gynecologic Oncology Group LAP2 Study. *J Clin Oncol*. 2012 Mar
249 1;30(7):695-700. doi: 10.1200/JCO.2011.38.8645. Epub 2012 Jan 30. Erratum in: *J Clin Oncol*. 2012
250 May 1;30(13):1570. PMID: 22291074; PMCID: PMC3295548.
- 251 3- Yin S, Gao W, Shi P, Xi M, Tang W, Zhang J. Primary Laparoscopic Surgery Does Not Affect the
252 Prognosis of Early-Stage Ovarian Clear Cell Cancer. *Cancer Manag Res*. 2021 Aug 14;13:6403-6409.
253 doi: 10.2147/CMAR.S321173. PMID: 34421313; PMCID: PMC8372305.
- 254 4- Hao X, Han S, Wang Y. Comparison of conventional laparoscopy and robotic radical hysterectomy
255 for early-stage cervical cancer: A meta-analysis. *J Cancer Res Ther*. 2015 Nov;11 Suppl:C258-64.
256 doi: 10.4103/0973-1482.170533. PMID: 26612449.
- 257 5- Wang YZ, Deng L, Xu HC, Zhang Y, Liang ZQ. Laparoscopy versus laparotomy for the
258 management of early stage cervical cancer. *BMC Cancer*. 2015 Nov 24;15:928. doi: 10.1186/s12885-
259 015-1818-4. PMID: 26596955; PMCID: PMC4657298.
- 260 6- Cai J, Yang L, Dong W, Wang H, Xiong Z, Wang Z. Retrospective comparison of laparoscopic
261 versus open radical hysterectomy after neoadjuvant chemotherapy for locally advanced cervical
262 cancer. *Int J Gynaecol Obstet*. 2016 Jan;132(1):29-33. doi: 10.1016/j.ijgo.2015.06.042. Epub 2015
263 Sep 25. PMID: 26434669.
- 264 7- Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally Invasive
265 versus Abdominal Radical Hysterectomy for Cervical Cancer. *N Engl J Med*. 2018 Nov
266 15;379(20):1895-1904. doi: 10.1056/NEJMoa1806395. Epub 2018 Oct 31. PMID: 30380365.

267 8- Obermair A, Asher R, Pareja R, Frumovitz M, Lopez A, Moretti-Marques R, et al. Incidence of
 268 adverse events in minimally invasive vs open radical hysterectomy in early cervical cancer: results
 269 of a randomized controlled trial. *Am J Obstet Gynecol.* 2020 Mar;222(3):249.e1-249.e10. doi:
 270 10.1016/j.ajog.2019.09.036. Epub 2019 Oct 3. Erratum in: *Am J Obstet Gynecol.* 2020
 271 Nov;223(5):757. PMID: 31586602; PMCID: PMC7181470.

272 9- Frumovitz M, Obermair A, Coleman RL, Pareja R, Lopez A, Ribero R, et al. Quality of life in
 273 patients with cervical cancer after open versus minimally invasive radical hysterectomy (LACC): a
 274 secondary outcome of a multicentre, randomised, open-label, phase 3, non-inferiority trial. *Lancet*
 275 *Oncol.* 2020 Jun;21(6):851-860. doi: 10.1016/S1470-2045(20)30081-4. Erratum in: *Lancet Oncol.*
 276 2020 Jul;21(7):e341. PMID: 32502445.

277 10- Lewicki PJ, Basourakos SP, Qiu Y, Hu JC, Sheyn D, Hijaz A, et al. Effect of a Randomized,
 278 Controlled Trial on Surgery for Cervical Cancer. *N Engl J Med.* 2021 Apr 29;384(17):1669-1671.
 279 doi: 10.1056/NEJMc2035819. PMID: 33913646.

280 11- Matsuo K, Mandelbaum RS, Klar M, Ciesielski KM, Matsushima K, Matsuzaki S, et al.
 281 Decreasing utilization of minimally invasive hysterectomy for cervical cancer in the United States.
 282 *Gynecol Oncol.* 2021 Jul;162(1):43-49. doi: 10.1016/j.ygyno.2021.05.005. Epub 2021 May 13.
 283 PMID: 33992450.

284 12- Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K, et al. Revised
 285 FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet.* 2019 Apr;145(1):129-135.
 286 doi: 10.1002/ijgo.12749. Epub 2019 Jan 17. Erratum in: *Int J Gynaecol Obstet.* 2019 Nov;147(2):279-
 287 280. PMID: 30656645.

288 13- Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-
 289 Dindo classification of surgical complications: five-year experience. *Ann Surg.* 2009
 290 Aug;250(2):187-96. doi: 10.1097/SLA.0b013e3181b13ca2. PMID: 19638912.

291 14- Martin RC 2nd, Brennan MF, Jaques DP. Quality of complication reporting in the surgical
 292 literature. *Ann Surg.* 2002;235:803-13.

293 15- Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, et al. Survival after
 294 Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer. *N Engl J Med*. 2018 Nov
 295 15;379(20):1905-1914. doi: 10.1056/NEJMoa1804923. Epub 2018 Oct 31. PMID: 30379613;
 296 PMCID: PMC6464372.

297 16- Chiva L, Zanagnolo V, Querleu D, Martin-Calvo N, Arévalo-Serrano J, Căpîlna ME, et al.
 298 SUCCOR study: an international European cohort observational study comparing minimally invasive
 299 surgery versus open abdominal radical hysterectomy in patients with stage IB1 cervical cancer. *Int J*
 300 *Gynecol Cancer*. 2020 Sep;30(9):1269-1277. doi: 10.1136/ijgc-2020-001506. Epub 2020 Aug 11.
 301 PMID: 32788262.

302 17- Bogani G, Di Donato V, Muzii L, Casarin J, Ghezzi F, Malzoni M, et al. Assessing the role of
 303 minimally invasive radical hysterectomy for early-stage cervical cancer. *Eur J Obstet Gynecol*
 304 *Reprod Biol*. 2022 Aug;275:64-69. doi: 10.1016/j.ejogrb.2022.06.004. Epub 2022 Jun 8. PMID:
 305 35753229.

306 18- Chacon E, Manzour N, Zanagnolo V, Querleu D, Núñez-Córdoba JM, Martin-Calvo N, et al.
 307 SUCCOR cone study: conization before radical hysterectomy. *Int J Gynecol Cancer*. 2022 Jan
 308 17:ijgc-2021-002544. doi: 10.1136/ijgc-2021-002544. Epub ahead of print. PMID: 35039455.

309 19- Bogani G, Ghezzi F, Chiva L, Gisone B, Pinelli C, Dell'Acqua A, et al. Patterns of recurrence
 310 after laparoscopic versus open abdominal radical hysterectomy in patients with cervical cancer: a
 311 propensity-matched analysis. *Int J Gynecol Cancer*. 2020 Jul;30(7):987-992. doi: 10.1136/ijgc-2020-
 312 001381. Epub 2020 May 23. PMID: 32448809.

313 20- Casarin J, Bogani G, Multinu F, Mariani A, Abu-Rustum NR, Ghezzi F, et al. Paradigm shifts in
 314 gynecologic oncology. *Int J Gynecol Cancer*. 2021 Dec;31(12):1617. doi: 10.1136/ijgc-2021-003108.
 315 Epub 2021 Oct 29. PMID: 34716176.

316 21- Bogani G, Scambia G, Cimmino C, Fanfani F, Costantini B, Loverro M, et al. Characteristics and
 317 patterns of care of endometrial cancer before and during COVID-19 pandemic. *J Gynecol Oncol*.

318 2022 Jan;33(1):e10. doi: 10.3802/jgo.2022.33.e10. Epub 2021 Nov 12. PMID: 34910391; PMCID:
319 PMC8728669.

320 *** The Italian Gynecological Cancer study group**

321 Giorgio Bogani ¹, Violante Di Donato ¹, Giovanni Scambia ², Fabio Ghezzi ³, Jvan Casarin ³, Fabio
322 Landoni ^{4, 5}, Giampaolo Di Martino ⁴, Tommaso Grassi ⁴, Anna Myriam Perrone ⁶, Pierandrea De
323 Iaco ⁶, Francesco Multinu ⁷, Roberto Berretta ⁸, Vito A Capozzi ⁸, Errico Zupi ⁹, Gabriele Centini ⁹,
324 Antonio Pellegrino ¹⁰, Silvia Corso ¹⁰, Guido Stevenazzi ¹¹, Anna Chiara Boschi ¹², Giuseppe Commerci
325 ¹², Pantaleo Greco ¹³, Gennaro Scutiero ¹³, Francesco Sopracordevole ¹⁴, Giorgio Giorda ¹⁴, Mariasole
326 Fichera ¹⁴, Tommaso Simoncini ¹⁵, Marta Caretto ¹⁵, Enrico Sartori ¹⁶, Federico Ferrari ¹⁶, Antonio
327 Cianci ¹⁷, Giuseppe Sarpietro ¹⁷, Maria Grazia Matarazzo ¹⁷, Pierluigi Giampaolino ¹⁸, Giuseppe
328 Bifulco ¹⁸, Michele Morelli ¹⁹, Michele Di Dio ¹⁹, Annamaria Ferrero ²⁰, Nicoletta Biglia ²⁰, Fabio
329 Barra ²¹, Simone Ferrero ²¹, Stefano Cianci ²², Vito Chiantera ²³, Alfredo Ercoli ²², Sergio Schettini
330 ²⁴, Teresa Orlando ²⁴, Francesco G Cannone ²⁵, Giuseppe Ettore ²⁵, Andrea Puppo ²⁶, Elena Olearo ²⁶,
331 Umberto Leone Roberti Maggiore ²⁷, Valeria Artuso ²⁷, Innocenza Palaia ¹, Giorgia Perniola ¹,
332 Rossana Tripodi ¹, Tullio Golia D'Augè ¹, Iaria Cuccu ¹, Margherita Fischetti ¹, Giusi Santangelo ¹,
333 Assunta Casorelli ¹, Andrea Giannini ¹, Ottavia D'Oria ¹, Giuseppe Vizzielli ²⁸, Stefano Restaino ²⁸,
334 Alice Bergamini ²⁹, Luca Boccione ²⁹, Francesco Plotti ³⁰, Roberto Angioli ³⁰, Giulia Mantovani ³¹,
335 Marcello Ceccaroni ³¹, Chiara Cassini ³², Mattia Dominoni ³², Laura Giambanco ³³, Silvia Amodeo
336 ³³, Livio Leo ³⁴, Raphaël Thommaset ³⁴, Diego Raimondo ³⁵, Renato Serrachioli ³⁵, Mario Malzoni
337 ³⁶, Francesca Falcone ³⁶, Franco Gorlero ³⁷, Martina Di Luca ³⁷, Enrico Busato ³⁸, Sami Kilzie ³⁸,
338 Andrea Dell'Acqua ³⁹, Giovanna Scarfone ³⁹, Paolo Vercellini ³⁹, Marco Petrillo ⁴⁰, Giampiero
339 Capobianco ⁴⁰, Andrea Ciavattini ⁴¹, Liliana Mereu ⁴², Paolo Scollo ⁴², Flavia Sorbi ⁴³, Massimiliano
340 Fambrini ⁴³, Federico Romano ⁴⁴, Giuseppe Ricci ^{44, 45}, Giuseppe Trojano ⁴⁶, Gianluca Raffaello
341 Damiani ⁴⁶, Roberto Consonni ⁴⁷, Nadia Di Lorenzo ⁴⁷, Antonio Lippolis ⁴⁸, Raffaele Tinelli ⁴⁸,
342 Lorenzo Aguzzoli ⁴⁹, Vincenzo D Mandato ⁴⁹, Stefano Palomba ⁵⁰, Marcello Tripodi ⁵⁰, Davide
343 Calandra ⁵¹, Franco Pellegrini ^{51, 52}, Fulvio Zullo ⁵³, Daniela Surico ⁵⁴, Valentino Remorgida ⁵⁴,
344 Francesco Ruscitto ⁵⁵, Paolo Beretta ⁵⁵, Enrico Vizza ⁵⁶, Ludovico Muzii ¹, Pierluigi Benedetti Panici
345 ¹ and Francesco Raspagliesi ²⁷

346

347 **Affiliations:**

- 348 1. Department of Maternal and Child Health and Urological Sciences, Sapienza University of
349 Rome, Policlinico Umberto I, Rome, Italy
- 350 2. Gynecologic Oncology Unit, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome,
351 Italy
- 352 3. Department of Obstetrics and Gynaecology, University of Insubria, F. Del Ponte Hospital,
353 Varese, Italy.
- 354 4. Department of Obstetrics and Gynaecology, San Gerardo Hospital, Monza, Italy
- 355 5. University Milano - Bicocca, Milano, Italy
- 356 6. Unit of Gynecology, AOU S. Orsola - Malpighi – Bologna, Italy
- 357 7. Department of Gynecologic Oncology, IEO, European Institute of Oncology IRCCS, Milan,
358 Italy
- 359 8. Department of Obstetrics and Gynaecology, University of Parma, Parma, Italy
- 360 9. Department of Obstetrics and Gynaecology, University of Siena, Siena, Italy
- 361 10. Department of Obstetrics and Gynaecology, ASST Lecco – Ospedale Alessandro Manzoni,
362 Lecco, Italy
- 363 11. Department of Obstetrics and Gynaecology, ASST OVEST MI, Legnano (Milan) Hospital,
364 Legnano, Italy
- 365 12. Department of Obstetrics and Gynaecology, AUSL Romagna, Ospedale “Santa Maria delle
366 Croci”, Ravenna, Italy
- 367 13. Clinica Ostetrica e Ginecologica – Dipartimento Scienze Mediche – Università di Ferrara,
368 Ferrara, Italy
- 369 14. Gynecological Oncology Unit, Centro di Riferimento Oncologico - National Cancer Institute,
370 Aviano, Italy.

- 371 15. Department of Clinical and Experimental Medicine, Division of Obstetrics and Gynecology,
372 University of Pisa, Pisa, Italy
- 373 16. Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
- 374 17. Department of General Surgery and Medical-Surgical Specialties, Gynecological Clinic,
375 University of Catania, Catania, Italy
- 376 18. Department of Obstetrics and Gynaecology, AOU Federico II – Naples, Italy
- 377 19. Department of Obstetrics and Gynaecology, AO "S.S. Annunziata" – Cosenza, Italy
- 378 20. Academic Department of Obstetrics and Gynecology, Mauriziano Hospital, Torino, Italy
- 379 21. Academic Unit of Obstetrics and Gynecology, IRCCS Ospedale Policlinico San Martino,
380 Genova, Italy
- 381 22. Department of Human Pathology of Adult and Childhood "G. Barresi", Unit of Gynecology
382 and Obstetrics University of Messina, Italy
- 383 23. Department of Gynecologic Oncology, University of Palermo, Italy
- 384 24. Department of Obstetrics and Gynaecology, AOR San Carlo, Potenza, Italy
- 385 25. Department of Obstetrics and Gynaecology, ARNAS Garibaldi Catania, Catania, Italy
- 386 26. Department of Obstetrics and Gynaecology, ASO Santa Croce e Carle, Cuneo, Italy
- 387 27. Gynecologic Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano,
388 Milan, Italy
- 389 28. Department of Maternal and Child Health, University-Hospital of Udine, Udine, Italy
- 390 29. Department of Obstetrics and Gynaecology, IRCCS San Raffaele Hospital, Milan, Italy
- 391 30. Department of Obstetrics and Gynecology, Campus Bio-Medico University of Rome, Rome,
392 Italy
- 393 31. Department of Obstetrics and Gynecology, Gynecology Oncology and Minimally-Invasive
394 Pelvic Surgery, International School of Surgical Anatomy, Sacred Heart Hospital Negrar,
395 Verona, Italy

- 396 32. Department of Obstetrics and Gynecology, IRCCS Foundation Policlinico San Matteo and
397 University of Pavia, Pavia, Italy
- 398 33. Department of Obstetrics and Gynecology, S. Antonio Abate Hospital, Trapani, Italy and
399 Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical
400 Specialties (PROMISE), University of Palermo, Palermo, Italy
- 401 34. Departments of Gynecology & Obstetrics- Hopital Beauregard- AUSL Valleè d'Aoste, Aosta,
402 Italy
- 403 35. Division of Gynaecology and Human Reproduction Physiopathology, Department of Medical
404 and Surgical Sciences (DIMEC). IRCCS Azienda Ospedaliero-Universitaria di Bologna. S.
405 Orsola Hospital. University of Bologna, Bologna, Italy
- 406 36. Endoscopica Malzoni, Center for Advanced Endoscopic Gynecologic Surgery, Avellino,
407 Italy.
- 408 37. Department of Obstetrics and Gynaecology, Ente Ospedaliero Ospedali Galliera, Genova,
409 Italy
- 410 38. Department of Obstetrics and Gynaecology, Ospedale di Treviso, Treviso, Italy
- 411 39. Gynaecology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan,
412 Italy
- 413 40. Gynecologic and Obstetric Unit, Department of Medical, Surgical and Experimental Sciences,
414 University of Sassari, Sassari, Italy
- 415 41. Gynecologic Section, Department of Odontostomatologic and Specialized Clinical Sciences,
416 Università Politecnica delle Marche, Ancona, Italy
- 417 42. Department of Obstetrics and Gynecology, Oncological Gynecology Unit, Ospedale
418 Cannizaro, Catania, Italy
- 419 43. Gynecology Unit, Careggi University Hospital, Department of Biomedical, Experimental and
420 Clinical Sciences "Mario Serio," University of Florence, Florence, Italy

- 421 44. Department of Obstetrics and Gynaecology, Institute for Maternal and Child Health, IRCCS
422 'Burlo Garofolo', Trieste, Italy
- 423 45. Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy.
- 424 46. Department of Obstetrics and Gynaecology, Madonna delle Grazie Hospital ASM Matera,
425 Italy
- 426 47. Gynecology Unit, Ospedale Valduce, Como, Italy
- 427 48. Unit of Obstetrics and Gynaecology, Valle D'Itra Hospital, Martina Franca, Taranto, Italy
- 428 49. Unit of Obstetrics and Gynecology, Azienda Unità Sanitaria Locale -IRCCS, Reggio Emilia,
429 Italy
- 430 50. Unit of Obstetrics and Gynecology, GOM of Reggio Calabria & University 'Magna Graecia'
431 of Catanzaro, Italy
- 432 51. Unit of Obstetrics and Gynecology, University G. D'Annunzio of Chieti-Pescara, Italy
- 433 52. Unit of Obstetrics and Gynecology, Santo Spirito Hospital. Pescara, Italy
- 434 53. Unit of Obstetrics and Gynecology, Università "Magna Graecia" di Catanzaro, Catanzaro,
435 Italy
- 436 54. Unit of Obstetrics and Gynecology, University of Eastern Piedmont, Novara, Italy
- 437 55. Gynecology Unit, Ospedale Valduce, Como– ASST Lariana, S. Anna, Como, Italy
- 438 56. Gynecologic Oncology Unit, Department of Experimental Clinical Oncology, IRCCS
439 "Regina Elena" National Cancer Institute, 00144 Rome, Italy