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Laparoscopic vs. open treatment of endometrial cancer in the elderly and very elderly: An age-stratified multicenter study on 1606 women kn, kn kn

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HIGHLIGHTS

- In elderly EC patients, laparoscopy has less complications than open surgery.
- The advantages of laparoscopy are maintained even among elderly/very elderly subjects.
- Elderly subjects with EC are more delicate and have a higher risk of complications.

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ABSTRACT

Objective

To investigate in depth the effect of increasing age on the peri-operative outcomes of laparoscopic treatment for endometrial cancer, compared to open surgery, with stratification of patients according to the different definitions of elderly age used in the literature.

Methods. Data of consecutive patients who underwent surgery for endometrial cancer staging at six centers were reviewed and analyzed according to surgical approach (laparoscopic or open), different definitions of elderly and very elderly age (\geq 65 years, \geq 75 years, \geq 80 years), and class of age (<65; \geq 65– <75; \geq 75–80; \geq 80 years). Multivariable analysis to correct for possible confounders and propensity-score matching to minimize selection bias were used.

Results. A total of 1606 patients were included: 938 and 668 patients received laparoscopic and open surgery, respectively. With increasing age, fewer patients received laparoscopy (P < 0.001 with ANOVA). The percentage of patients who received lymphadenectomy declined significantly in both groups for age ≥ 80 years. Blood transfusions, incidence and severity of post-operative complications, and hospital stay were significantly lower among patients who had laparoscopy both in younger (<65 years) and elderly (whether defined as ≥ 65 or ≥ 75 years) patients, with no effect of age on any of the characteristics analyzed (ANOVA: P > 0.05). The same tendency was observed among very-elderly patients (≥ 80 years). Multivariable and propensity score-matched analysis confirmed these findings.

Conclusions. Laparoscopy for staging endometrial cancer retains its advantages over open surgery even in

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[🌣] Condensation: Laparoscopy is an advantageous alternative to open surgery in elderly and very elderly women affected by endometrial cancer.

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elderly and very-elderly patients. Our data strongly suggest that minimally-invasive surgery is advantageous even among subjects \geq 80 years.

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1. Introduction

Endometrial cancer is the most common malignancy of the female genital tract in Western countries. It has been estimated that in the United States more than 54,870 cases will be diagnosed and 10,170 deaths related to this malignancy will occur in the year 2015 [1].

The incidence and biological aggressiveness of endometrial cancer increases with age [2–5]. Because of the world's population increasing longevity [6], the total number of patients affected by this malignancy is expected to grow in the next few years, as well as their age at diagnosis. The mainstay of treatment for endometrial cancer is represented by removal of the uterus, the adnexa and, if indicated, the pelvic/para-aortic nodes in a systematic fashion in order to obtain the removal of the primary tumor and to decide whether adjuvant treatment is needed to prevent possible disease relapses [7]. As a direct consequence of the aging of the population, the number of elderly women necessitating surgical treatment for endometrial cancer will inevitably increase.

It is now widely accepted that laparoscopic surgery is associated with better post-operative results and the same oncological outcomes compared with open surgical approach [8,9]. These benefits could be amplified just in elderly subjects since they represent a very vulnerable subpopulation. On the other hand, older age is still considered a potential contraindication to endoscopic treatment, mainly because of anesthesiological concerns.

To date, only few studies with a very limited number of patients included have investigated the safety of the laparoscopic approach in elderly patients affected by endometrial cancer [10-13]. In addition, available data are biased by the different definitions used of "older age" and "elderly". Some authors consider that older age is over 65 years, whereas others use more strict parameters such as an age ≥ 75 or ≥ 80 years [14].

In light of these considerations, the aim of the present large multicenter cohort study was to investigate the impact of age on perioperative outcomes in patients undergoing laparoscopic surgery for endometrial cancer staging.

2. Materials and methods

The present research is a large multi-institutional cohort study including patients with primary, histologically confirmed endometrial carcinoma.

Six Italian institutions were involved in the study protocol. Institutional review board (IRB) approval for this study was obtained at all the six participating institutions. Each gynecologic service prospectively collected data concerning demographics, surgical procedures, intra- and postoperative details, pathology reports, as well as follow-up evaluations. The protocol of the present study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [15].

All consecutive patients who underwent surgical treatment for histologically-proven endometrial cancer by laparoscopy in the time period January 2000 to March 2013 were considered. As comparator arm, we identified all patients treated by open surgery during the same time period at the same Institutions. The same inclusion and exclusion criteria were used for the study group and the controls. A part of the patients included in the current analysis was included in a previous smaller multicenter study [16].

All patients received peritoneal washing and total hysterectomy with bilateral salpingo-oophorectomy with or without pelvic/para-aortic lymphadenectomy. The decision to perform or not pelvic/para-

aortic lymphadenectomy was based on preoperative and intraoperative uterine risk factors and the expected anesthesia risk. Details of the surgical technique used for both laparoscopic and open approach have been published previously [17,18].

All the procedures were performed by surgeons with extensive background in gynecologic oncology and advanced experience in minimally invasive surgery.

Patients with stage IV disease according to the International Federation of Gynecology and Obstetrics (FIGO) classification [19], those with <12 months follow-up, those with incomplete clinical/histological data, and those who did not undergo hysterectomy as primary treatment were excluded. In the laparoscopic group, only patients undergoing total laparoscopic hysterectomy (defined as complete laparoscopic detachment of the uterus, including uterine pedicle division and colpotomy) were included.

Patients were divided according to the intended initial surgical (whether laparoscopic or open) approach. The analysis of perioperative outcomes was then performed dividing patients as follows: <65 years; \geq 65 years; \geq 75 years; \geq 80 years. The reason for this subdivision of groups was the intent to cover all the possible definitions of elderly age and very elderly age. We also performed an analysis of outcomes stratifying subjects in the different classes of chronological age (*i.e.* <65 years; \geq 65 and <75 years; \geq 75 and <80 years; \geq 80 years), in order to obtain also information as to whether different categories of increasing age may have a different response to minimally invasive treatment.

Pre-operative assessment of the expected anesthesiological risk was based on the American Society of Anesthesiology (ASA) score [20]. Moreover, the presence and relevance of comorbidities was assessed using the Charlson comorbidity index (CCI), which predicts the 10-year mortality due to comorbid conditions [21].

For the purposes of the present analysis, laparoscopy and open approach were compared with respect to baseline characteristics, perioperative data, and surgical and long-term outcomes. The management and outcome of each post-operative complication were recorded in order to grade their severity based on the Clavien-Dindo scoring system, a widely-recognized surgical complication scoring system [22]. FIGO surgical stage [19], tumor grade and histopathological type were recorded for each patient. Following surgery, patients were examined every 3 months for 2 years, then every 6 months for the next 3 years, and yearly thereafter.

2.1. Statistical analysis

Statistical analysis was performed with GraphPad version 5.00 for Windows (GraphPad Software, San Diego, CA, USA) and STATA version 11.2 (StataCorp, College Station, TX, USA). Statistical significance was considered achieved for P < 0.05 (two-tailed). Normality testing (D'Agostino and Pearson test) was performed to determine whether continuous variables were sampled from a Gaussian distribution. Afterwards, comparisons between two groups of continuous variables were accomplished using independent-samples t-test or Mann–Whitney U test, as appropriate. When more than two groups had to be compared, the one-way analysis of variance (ANOVA) was used. Post-hoc analysis was performed with Bonferroni post-test. Categorical covariates were compared with chi-square test.

Univariate analysis and multiple logistic regression were performed to identify factors associated with peri-operative outcomes. As potentially related to the surgical outcome of the two different approaches we tested the following variables: body mass index (BMI), obesity,

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