Evaluation of two alternative ablation treatments for cervical pre-cancer against standard gas-based cryotherapy: a randomized non-inferiority study.

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Abstract

INTRODUCTION: Gas-based cryotherapy is the conventional ablative treatment for cervical pre-cancer in low-income settings, but the use of gas poses significant challenges. We compared the depth of necrosis induced by gas-based cryotherapy with two gas-free alternatives: cryotherapy using CryoPen,and thermoablation. METHODS: We conducted a five-arm randomized non-inferiority trial: double-freeze carbon dioxide (CO2) cryotherapy (referent), single-freeze CO2 cryotherapy, double-freeze CryoPen, single-freeze CryoPen, and thermoablation. Subjects were 130 women scheduled for hysterectomy for indications other than cervical pathology, and thus with healthy cervical tissue available for histological evaluation of depth of necrosis post-surgery. The null hypothesis was rejected (ie, conclude non-inferiority) if the upper bound of the 90% confidence interval (90% CI) for the difference in mean depth of necrosis (referent minus each experimental method) was <1.14 mm. Patient pain during treatment was reported on a scale of 0 (no pain) to 10 (worst pain). RESULTS: A total of 133 patients were enrolled in the study. The slides from three women were deemed unreadable. One patient was excluded because her hysterectomy was postponed for reasons unrelated to the study, and two patients were excluded because treatment application did not follow the established protocol. For the remaining 127 women, mean depth of necrosis for double-freeze CO2 (referent) was 6.0±1.6 mm. Differences between this and other methods were: single-freeze CO2 = 0.4 mm (90% CI -0.4 to 1.2 mm), double-freeze CryoPen= 0.7 mm (90% CI 0.04 to 1.4 mm), single-freeze CryoPen= 0.5 mm (90% CI -0.2 to 1.2 mm), and thermoablation = 2.6 mm (90% CI 2.0 to 3.1 mm). Mean pain levels were 2.2±1.0 (double-freeze CO2 cryotherapy), 1.8±0.8 (single-freeze CO2 cryotherapy), 2.5±1.4 (double-freeze CryoPen), 2.6±1.4 (single-freeze CryoPen), and 4.1±2.3 (thermoablation). DISCUSSION: Compared with the referent, non-inferiority could not be concluded for other methods. Mean pain scores were low for all treatments. Depth of necrosis is a surrogate for treatment efficacy, but a randomized clinical trial is necessary to establish true cure rates.

Incidence of adverse events in minimally invasive versus open radical hysterectomy in early cervical cancer: Results of a randomized controlled trial.

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Abstract

BACKGROUND: Standard treatment of early cervical cancer involves a radical hysterectomy and retroperitoneal lymph node dissection. The existing evidence on the incidence of adverse events following minimally invasive versus open radical hysterectomy for early cervical cancer is either non-randomized or retrospective. OBJECTIVE: To compare the incidence of adverse events following minimally invasive versus open radical hysterectomy for early cervical cancer. STUDY DESIGN: The Laparoscopic Approach to Carcinoma of the Cervix (LACC) trial was a multinational, randomized non-inferiority trial conducted between 2008 and 2017, in which surgeons from 33 tertiary gynecological cancer centers in 24 countries randomized 631 women International Federation of Gynecology and Obstetrics 2009 stage IA1 with lymph-vascular invasion to IB1 cervical cancer to either minimally invasive versus open radical hysterectomy. Patients were randomly assigned to undergo minimally invasive (n = 319) or open radical hysterectomy (n = 312). The LACC trial was suspended for enrolment in September 2017 due to an increased risk of recurrence and death in the minimally invasive surgery group. Here we report on a adverse events within 6 months after surgery. RESULTS: Of 631 patients randomized, 536 (85%) (mean age, 46.0 years) met inclusion criteria for this analysis; 279 (52%) underwent minimally invasive radical hysterectomy, and 257 (48%) underwent open radical hysterectomy. Of those, 300 (56%), 91 (16.9%), 69 (12.8%) experienced at least one grade 2+, grade 3+, or a serious adverse event. The incidence of intraoperative grade 2+ adverse events was 12% (34/279 patients) in the minimally invasive versus 10% (26/257) in the open group (p=0.45). The overall incidence of postoperative grade 2+ adverse events was 54% (152/279 patients) in the minimally invasive versus 48% (124/257) in the open group (p=0.14). CONCLUSIONS: For early cervical cancer, the use of minimally invasive compared with open radical hysterectomy resulted in a similar overall incidence of intraoperative or postoperative adverse events.