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Prospective cohort study comparing quality of life and sexual health outcomes between women undergoing robotic, laparoscopic and open surgery for endometrial cancer☆,☆☆

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HIGHLIGHTS

- No difference in patient-reported outcomes between laparoscopy and robotic surgery
- Improved quality of life up to 3 months following minimally invasive surgery
- Improved Functional Well-Being up to 6 months following minimally invasive surgery
- Type of surgical intervention does not demonstrate an impact on sexual health.
- Responders to sexual health questionnaires have low sexual functioning scores.

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ABSTRACT

Objective. To evaluate patient-reported outcomes (PROs) between women treated by laparoscopic, robotic and open approaches for endometrial cancer.

Methods. Prospective cohort study comparing PRO at baseline, short- (1 and 3 weeks) and long-term (12 and 24 weeks) follow-up postoperatively. Quality of life (QOL) measures were the Functional Assessment of Cancer Therapy (FACT-G), EuroQol Five Dimensions (EQ-5D), and Brief Pain Inventory (BPI). Sexual health measures were the Female Sexual Function Index (FSFI) and the Sexual Adjustment and Body Image Scale for Gynecologic Cancer (SABIS-G).

Results. 468 eligible patients (laparotomy = 92, laparoscopy = 152, robotic = 224) were recruited. There were no significant differences between the laparoscopy and robotic groups for any PRO ($P > 0.05$). At short-term follow-up, patients who underwent minimally invasive surgery (robotic or laparoscopy) had significantly higher FACT-G ($P < 0.0001$) and EQ-5D ($P < 0.0001$) scores, with less pain ($P = 0.02$) and improved pain interference ($P = 0.0008$), than patients undergoing laparotomy. At long-term follow-up, there were sustained improvements in the FACT-G ($P = 0.035$) and the health state EQ-5D visual analogue scale ($P = 0.022$). Surgical approach had no impact on sexual health ($P > 0.05$); however the mean FSFI score for the entire cohort met clinical cut-offs for sexual dysfunction.

Conclusion. Minimally invasive approaches result in improved QOL beyond the short-term postoperative

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period, with benefits noted up to 12 weeks after surgery. This prolonged QOL advantage provides further evidence that MIS should be the standard surgical approach for women with early stage endometrial cancer.

1. Introduction

Endometrial cancer is the most common gynecologic cancer in developed countries and has been increasing at a rate of over 2.5% per year in North America for the last decade [1]. Most women are diagnosed at an early stage and surgery is the primary treatment, including total hysterectomy, bilateral salpingo-oophorectomy and surgical staging, which can include pelvic and para-aortic lymph node assessment [2].

Historically, the preferred surgical approach for treatment of endometrial cancer has been laparotomy. However, multiple randomized controlled trials (RCTs) comparing laparoscopy to laparotomy have reported decreases in postoperative complication rates and length of hospital stay in women undergoing laparoscopy [3–6]. Importantly, there appears to be no difference in disease-free and overall survival in those women treated by a minimally invasive approach [6,7]. Based on these findings, laparoscopy, and more recently robotic surgeries, have become standard surgical approaches for endometrial cancer [2].

The impact of surgical approach on patient reported outcomes (PROs), such as overall health-related quality of life (QOL), is less clear [4,5,8]. The largest RCT did not show a minimally important difference in QOL between laparoscopy and laparotomy [8]. There has been limited assessment of sexual health using validated questionnaires in women with endometrial cancer and most studies have focused on body image alone [4,8,9]. In addition, there has been no direct prospective comparison of the PROs including QOL and sexual health between women treated by laparoscopic, robotic or open approaches.

Although there has been an increase in the use of minimally invasive surgery (MIS) in the management of endometrial cancer over the last 10 years, primarily due to the rapid uptake of robotic surgery, the majority of women are still managed by an open technique [10]. With increasing value placed on personalized cancer care, it is important to evaluate all outcomes, including PROs, between these surgical groups. The primary objective of this study was to evaluate the perioperative outcomes, PROs and cost-effectiveness of laparoscopic, robotic and open approaches for the treatment of early stage endometrial cancer [11]. Here we report the PRO component of the study, including QOL, pain, and sexual health in the early and late postoperative periods for each surgical group.

2. Patients and methods

This was a multi-center prospective cohort study approved by research ethics boards of participating centers. All participants provided written informed consent prior to enrollment. Patients were recruited from one of eight gynecologic oncology centers in Canada between February 2012 and May 2014. Women were eligible if they met the following criteria: (1) aged 18 years or older; (2) undergoing primary surgery for a histologically-confirmed endometrial cancer of any histologic subtype or grade; (3) clinically confined to the uterus (International Federation of Gynecology and Obstetrics (FIGO) stage 1); Eastern Cooperative Oncology Group (ECOG) performance status of less than two; (4) English or French speaking; and (5) able to complete questionnaires independently. Patients were ineligible if they had preoperative radiation or chemotherapy, evidence of disease beyond the uterus on preoperative imaging or clinical exam, or were medically unfit to undergo surgery. Surgical approach was determined by the treating gynecologic oncologist. Only four participating centers had access to a robotic platform during this study. All patients were to undergo a hysterectomy and bilateral salpingo-oophorectomy and the decision to perform more extensive surgery including pelvic and/or para-aortic lymphadenectomy was made by the surgeon. Postoperative pain management and sexual counselling was determined by each center. Patients were seen in clinic at 3, 12, and 24 weeks postoperatively for routine surveillance. Clinical and demographic data were collected at baseline before surgical intervention.

2.1. Data collection

Patients completed PROs before surgery (baseline) and at 1, 3, 12, and 24 weeks postoperatively. Quality of life (QOL) was assessed at all time points, whereas sexual health was assessed at baseline, 12, and 24 weeks only, as patients were instructed to withhold from sexual activity in the early postoperative period. QOL measures were the Functional Assessment of Cancer Therapy (FACT-G), EuroQol Five Dimensions (EQ-5D), and Brief Pain Inventory (BPI). Sexual health measures were the Female Sexual Function Index (FSFI) and the Sexual Adjustment and Body Image Scale for Gynecologic Cancer (SABIS-G). Questionnaires were either completed in the outpatient clinic or returned in pre-paid envelopes by mail. Reminder phone calls were made to participants if they had not returned the questionnaire within 1 week.

2.2. Validated measures

The FACT-G (version 4) is a 27-item validated cancer-specific questionnaire assessing overall quality of life (QOL) [12]. Patients completed its four core subscales for physical (PWB), social/family (SWB), emotional (EWB) and functional (FWB) well-being, as well as an endometrial cancer-specific subscale (EnWB). The FACT-G has high internal consistency, internal validity, and test-retest reliability. It has been shown to successfully differentiate patients based on stage and performance status, and is sensitive to clinical changes over time.

The EQ-5D is a QOL measure that assesses patients' preference-based overall health status [13]. It covers five domains including mobility, self-care, usual activities, pain/discomfort and anxiety/depression with three levels of severity. Index-based scores are calculated and vary along a continuum of 0 (dead) to 1 (best possible health) using population-based weighted preferences [14,15]. The EQ-5D also contains a 20 cm visual analogue scale (VAS) for participants to mark their health state today ranging from 0 (worst imaginable) to 100 (best imaginable) [13].

The BPI measures two domains of pain including severity (4 items) and interference with activity and emotions [16]. Both domains have excellent internal consistency and have been validated in cancer and postoperative patients [17,18].

The FSFI is a 19-item questionnaire assessing six domains of sexual function. Validation studies have demonstrated excellent internal consistency and test-retest reliability [19]. High scores indicate better functioning. The SABIS-G is a seven-item measure to assess changes in sexuality and body image after a diagnosis of gynecologic cancer [20]. This measure has demonstrated high internal consistency for both factors and has excellent test-retest reliability and discriminant validity.

2.3. Statistical analyses

The sample size of this study was based on the 15% reduction in complication rate between MIS and open surgical group [11]. For the

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