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Review Article

Defining and mitigating the challenges of an older and obese population in minimally invasive gynecologic cancer surgery

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HIGHLIGHTS

- Despite physiologic challenges, older and obese patients can be offered minimally-invasive surgery
- Pre-, Peri- and Post-operative team work and communication are essential for MIS success
- Complications of MIS may be avoided with understanding of physiologic changes due to positioning and pneumoperitoneum

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ABSTRACT

The incidence of endometrial cancer (EC) is steadily increasing due in large part to an aging world population and rise in rates of obesity. Patients with obesity and advancing age can be seen as vulnerable populations, as they are both often subject to physician bias regarding surgical choices and assumptions regarding long-term outcomes. As we operate on an older and/or obese patient population, it is increasingly important that we adopt peri-operative management strategies and surgical techniques to best serve this complex patient population. Careful orchestration pre-, intra- and postoperatively is key to successful outcomes in robotic and laparoscopic surgery. Here, we review existing literature regarding EC in women with older age and/or obesity, outline recommendations for peri-operative management and common intra-operative issues—specifically common anesthetic issues surrounding cardiovascular, respiratory and neuromuscular systems—that are of heightened importance in women with older age and/or obesity. The goal of this review is to help define and mitigate common complications for these vulnerable patients with an EC diagnosis who, in accordance with carefully assessed health risks, can and should be offered standard of care surgery and treatment.

1. Introduction

With an estimated 61,380 new diagnoses in 2017 [1], endometrial cancer (EC) is the fourth most common women's cancer in the United States. Unlike other solid tumors, the incidence of EC is steadily increasing due in large part to an aging world population and rise in rates of obesity [2]. The percentage of the world population over age 60 is expected to increase from 11% in 2010 to 21% in 2050 [3]. Furthermore, current trends of increasing obesity predict there may be as high as an estimated 42.13 incident cases of EC per 100,000 women by the year 2030, a 55% increase over 2010 rates (27.03 cases per 100,000 women) [4]. Gynecologic surgeons have increasingly utilized minimally invasive surgery (MIS), specifically robotic-assisted, to surgically treat endometrial cancer (EC) with hysterectomy, helping to achieve excellent postoperative outcomes. For example, Gynecologic Oncology Protocol LAP2 showed decreased hospitalization and no inferior outcomes for patients who underwent laparoscopic hysterectomy and staging versus open surgery [5,6], paving the way for continued utilization of MIS approaches for women with EC. In that same trial, increasing body mass index (BMI) was shown to increase risk of surgical morbidity in both open and laparoscopic groups but the incidence of events in the laparoscopic group was significantly lower [7]. In addition, an ancillary data analysis of older patients treated on LAP2 demonstrated that the difference in all cause morbidity between open and laparoscopic approaches starts to separate at age 60 and continues to separate indicating the older the patient, the more they benefit from a MIS approach [8,9]. Robotic surgery, approved for use in gynecologic surgery in 2005, has allowed for MIS to emerge as the treatment of choice for EC in consensus guidelines over exploratory laparotomy. Due to the rapid rise in robotic surgery, ACOG published a Committee Opinion on robotic surgery in gynecology in 2015, reaffirmed in 2017 [9]. Cohort studies have indicated

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benefits from robotic surgery over laparoscopic surgery specific to women who are obese, such as decreased operative time, decreased blood loss and increased retrieval of lymph nodes [10].

As obesity rates rise, and the population becomes more aged, we continue to push limits on feasibility while maintaining the goals of adequate cancer staging, uncompromised patient safety, and successful training of future gynecologic surgeons. While helpful guidelines exist [11] and large case series of robotic surgery have been published [12–14], points along the learning curve differ for each member of the surgical team [15,16].

2. Outcomes among older and obese EC patients

Physician bias towards the elderly as well as the obese population may lead to fewer women within these groups being offered standard therapies and clinical trials. Distinction between chronological age and biologic age, performance status irrespective of age or BMI, and careful assessment of comorbidities are important factors in understanding the physiologic reserve of each specific patient and their ability to tolerate surgery.

Outcomes for women with EC worsen as age increases, with higher prevalence of high-grade disease, lymph vascular invasion and increased depth of invasion [17]. Among patients with early-stage EC, age ≥ 70 years and tumor characteristics independently predict recurrence, even when controlled for surgical staging [17]. Increasing age is associated with higher American Society of Anesthesiologists (ASA) class, co-dependence with activities of daily living (ADLs), diabetes, hypertension requiring medications, cardiac and neurologic diagnosis as well as a higher prevalence of pre-operative anemia and hypoalbuminemia [18]. Intraoperative complications do not appear to vary with age for laparotomy or MIS approaches. However, despite no difference in surgical complexity among age groups, data from 4000 women in the National Surgery Quality Improvement Program (NSQIP) showed that octogenarians ($n = 328$) were less likely than younger patients to undergo laparoscopic surgery [18]. Postoperative morbidity (inclusive of surgical and medical complications) is higher for open compared to MIS approach, but increases with age for both. For example, medical complications increase from 15.5% to 27% among patients <65 to >85 undergoing open procedures as compared to 6.7 to 20.8% in the same age range for those patients undergoing MIS approach [17]. In multivariate analysis, age by each decade >60 were not associated with increased mortality compared to age ≤ 60 years. Significant predictors of mortality were respiratory or renal disease, dependent functional status, and hypo-albuminemia. Octogenarians were more likely to have non-surgical complications (8% vs. 3–5%, $p = 0.001$) but there was no difference in surgical complications ($p = 0.89$). Significant predictors of complications were higher ASA Scoring System class, anemia, and thrombocytosis [18]. In another review, specific geriatric-associated factors such as functional dependency, fatigue, depression, frailty and cognitive impairment were associated with increased post-operative complications [19]. Frailty, functional dependency, and depression predicted discharge to a non-home institution. Emphasis should thus be focused on perioperative control of nutritional status and comorbidities in older women [19] Taken together, the literature suggests that an increased effort should be made to perform MIS in appropriately-triaged older patients.

Obesity is a medical term that can evoke negative emotions, and an initial visit can be a difficult time to start this conversation. EC is a teachable moment for providers to encourage behavior change that might ultimately reduce obesity-related morbidity. Further study of how strategies such as those outlined in the Society of Gynecologic Oncology's Obesity Toolkit [20] can be efficiently implemented into perioperative care must be pursued. However, many patients are comfortable with the terms “excess weight” or “weight issues,” and an open discussion of known complications related to their weight can help set realistic expectations for postoperative recovery. This may also help set the stage for further postoperative counseling regarding lifestyle after cancer.

Case series of robotic hysterectomies in obese patients describe a complication rate range between 7.5% (mean BMI 33 kg/m^2) [21] to 20% (mean BMI 40.9 kg/m^2) [22]. Cohort studies have also indicated it is *not* necessarily obesity that drives complication rates in MIS, but rather the number of associated comorbidities. In one series, 70% (300 out of 543 of patients) had a BMI ≥ 30 kg/m^2, with the upper range of 69 kg/m^2. Increasing number of comorbidities had the highest impact on complication rate, and patients with renal or cardiac co-morbidities had the highest rate of complications [13]. Another cohort (mean BMI 40.9 kg/m^2; 56 women with BMI ≥ 50 kg/m^2) found increasing BMI was associated with increasing risk of conversion to open surgery [22], but otherwise not significantly associated with increased number of complications. Morbid obesity did not adversely affect the operative outcomes for patients with EC who were operated on using the robotic system [23]. In these cohort studies, all authors argue for careful discussion of peri-operative risks, but all positively conclude that robotic surgery should remain an acceptable, and perhaps preferable, option over laparoscopy for women who are obese. Successful robotic hysterectomies have been reported for women with body mass indices (BMI) of as high as 75 kg/m^2 [24].

3. Pre-operative assessments

Optimal surgical management of vulnerable populations with cancer starts pre-operatively with thorough assessment of the patient's baseline function and comorbidities. Selection of patients and procedures, optimization of their functional status prior to surgery, and appropriate management of perioperative expectations are all key to decreasing complications. Prehabilitation and anesthesiologist assessment should therefore be mandatory in these high-risk patients. Table 1 may provide a roadmap for consideration of the medically complex patient with EC.

Risk prediction tools and scoring systems can help predict morbidity and mortality, but have not easily been validated in gynecologic surgery, and have been especially difficult to predict MIS complications due to the overall low rate of events. Commonly-used tools in general surgery

Table 1
Preoperative assessment of risk and predictors of mortality in vulnerable populations.

High-risk category	Highest predictors of morbidity	Strategies for improving outcomes
Age > 65	Frailty Cognitive Impairment Functional Dependency Depression Anemia Thrombocytosis Hypoalbuminemia (< 3 g/dL)	Maximizing nutritional status perioperatively
Age > 65 and BMI > 30 kg/m^2	High ASA class # of Medical comorbidities • Renal disease • Congestive heart failure • Cardiovascular disease • Diabetes	Concept of prehabilitation Optimization of comorbidities Identify possible intensive care unit needs
BMI > 30 kg/m^2	Obstructive sleep apnea Obesity hypoventilation	Preoperative polysomnography Intraoperative ventilation strategies Attention to ERAS Need for postoperative counseling of weight-related long-term outcomes Possibility of delayed surgery until weight loss

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