



Bariatric surgery as a means to decrease mortality in women with type I endometrial cancer — An intriguing option in a population at risk for dying of complications of metabolic syndrome☆



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HIGHLIGHTS

- Sustained weight loss may improve survival in obese endometrial cancer patients
- Weight loss surgery may be a cost effective way to improve survival in this cohort

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ABSTRACT

Objective. To estimate the cost-effectiveness and utility of a strategy of offering weight loss surgery (WLS) to women with low risk stage I endometrial cancer (EC) and BMI ≥ 40 kg/m².

Methods. A modified Markov state transition model was designed to compare routine care to WLS for women with low risk stage I endometrioid EC, age < 70 , with a mean BMI 40. A time horizon of 15 years was used to simulate the overall survival (OS) of 96,232 women treated from 1988–2010 from SEER*Stat data. To simulate the effects of WLS on OS, a hazard ratio (0.76, 95% CI 0.59–0.99) representing the OS improvement achieved from this intervention (derived from a prospective trial) was modeled. We assumed that 90% of women undergoing bariatric procedures would experience a reduction in BMI. We assumed that 5% of women not undergoing WLS would achieve weight loss to a BMI of 35. Costs of treatment for obesity-related chronic diseases and quality of life (QOL)-related utilities were modeled from published reports.

Results. The mean cost-effectiveness for each strategy was: \$69,295 and 8.10 quality-adjusted life years (QALYs) for routine care versus \$100,675 and 9.30 QALYs for WLS. WLS had an incremental cost-effectiveness ratio (ICER) of \$26,080/QALY compared to routine care. At a willingness to pay threshold of \$50,000/QALY, WLS was the strategy of choice in 100% of simulations.

Conclusions. WLS is a potentially cost-effective intervention in women with low risk, early stage EC, at least in part due to improved quality of life with weight reduction.

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1. Introduction

Endometrial cancer is the most common gynecologic cancer diagnosed in the United States, with an estimated 54,870 new cases in 2015 [1]. The vast majority of these will be endometrioid adenocarcinoma (Type I) tumors. Obesity has long been characterized as a risk factor for the development of Type 1 endometrial cancer. Obese women with endometrial cancer often have a less aggressive tumor and lower stage

at initial diagnosis [2], leading to a growing number of unhealthy cancer survivors who enter post-treatment surveillance each year. The economic impact of obesity on the healthcare system continues to rise. If current trends continue, the cost of obesity-related morbidity could reach 16–18% of all US healthcare expenditures in 2030 [3]. This strain on the system is a call to action for all providers to find new ways to reduce the obesity-related health impact to individuals and economic impact to society.

Obesity has been linked to an increased risk of early mortality regardless of cancer status [4]. In women with endometrial cancer, obesity has been shown to increase the risk of recurrence compared with normal weight [4]. While a separate report by von Gruenigen et al. did not find an association between obesity and rate of recurrence, they did find that a higher BMI was associated with higher all-cause

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mortality [5]. This is consistent with analysis of SEER data suggesting that women diagnosed with early-stage, low-grade endometrial cancer who survived >5 years were more likely to die from cardiovascular causes than their cancer [6]. Weight loss surgery (WLS) has been found to be an effective form of sustained weight loss for obese patients who have failed other weight loss strategies [19]. In more recent studies, it was shown to be effective at reducing all-cause mortality and risk of cardiovascular disease [7,8]. Additionally, WLS has most recently been shown to be associated with a decreased risk of developing endometrial cancer; a retrospective cohort of women with a history of bariatric surgery were shown to be at a 71% reduced risk for developing endometrial cancer compared to those women who had not had bariatric surgery [10].

For the treatment of morbid obesity in a patient who has failed other weight loss options, the cost-effectiveness of weight loss surgery has been explored. Multiple cost analyses have been performed on studies with various primary outcomes including reduction in Type-2 diabetes, reduced risk of heart disease, and overall weight loss in these studies [11–14]. A systematic cost-effectiveness analysis review completed in 2009 showed that WLS was cost-effective for these various outcomes across many of the studies analyzed [9].

Given the complex relationship between obesity, endometrial cancer and the intriguing relationship between bariatric surgery reducing metabolic syndrome and its complications (as well as potentially impacting the risk of developing endometrial cancer), we set out to assess the potential cost-effectiveness of weight loss surgery on overall mortality in a cohort of obese survivors with endometrial cancer.

2. Methods

2.1. Model

We constructed a modified Markov state transition model for cost–utility analysis from a third party payer perspective to compare two strategies for care in survivors of Type I endometrial cancer with low-risk disease: (1) weight loss surgery (WLS) and (2) routine/non-surgical weight loss care. We did not specify the type of weight loss surgery (i.e. sleeve gastrectomy or Roux-en-Y gastric bypass, etc.). The control arm was not assigned a specific alternative weight loss strategy. The time horizon of the model was 15 years. Cost estimates are in 2014 dollars and effectiveness was quantified using quality-adjusted life years (QALY). Costs and effects were discounted at an annual rate of 3%. The model was constructed using data from published reports. A representative decision tree is depicted in Fig. 1.

Key assumptions of the model included: 1) All patients who underwent weight loss surgery and experienced a response also achieved an improvement in QOL; 2) Among patients who achieved meaningful weight loss following WLS (90% of patients): 2/3 of patients would have a drop in BMI of 5 points, while 1/3 would drop by 10 points; 3) 5% of patients in the control group would experience a 5 point drop in BMI; 4) Survival advantages observed in prior studies of WLS are achievable by women with a history of endometrial cancer;

and 5) All patients who experienced a nonfatal complication of surgery were still eligible for a drop in BMI following surgery.

2.2. Clinical estimates

2.2.1. Survival

We queried SEER*Stat data for 96,232 women treated for endometrial cancer from 1988–2010 [30]. We used the SEER*Stat data for baseline survival estimates of women with stage 1 endometrial adenocarcinoma (including grades 1–3). We excluded high-risk histologic subtypes including clear cell, papillary-serous, and sarcomas. In the surgery arm, we then applied to this survival data a hazard ratio (HR) derived from an existing large, non-randomized controlled trial on the survival benefit of weight loss surgery [7]. The HR from this large prospective cohort was 0.76 (95% confidence interval, 0.59–0.99). Follow up in the RCT cohort was over a 10-year period. In our model, overall survival was modeled over a 15 year timespan.

2.2.2. Quality of life

In the model, quality of life (QOL) was assumed to improve following WLS as reflected in the utility score. A utility is a number between 1 and 0 where 1 is equal to perfect health and 0 is death. We modeled a baseline utility score of 0.73 (± 0.21) and a post-surgical improvement to 0.88 (± 0.14), based on a prospective published report of the effects of WLS on QOL in obese subjects without malignancy [24].

2.2.3. Weight-loss surgery outcomes

Baseline BMI of the modeled cohort was 40. We estimated that of those who underwent weight loss surgery, 90% would achieve some amount of weight loss, with the remaining 10% not experiencing clinically significant weight loss. We further stratified weight loss by change in BMI. We estimated, based on prospective trials [8,9,18], that two-thirds of patients who lost weight would experience a drop in BMI to 35. The remaining one-third would experience a drop to 30.

The control arm of the model used the same survivor cohort, but without a specified weight-loss intervention. This is consistent with other published studies that compare WLS to non-surgical weight loss. Despite not specifying types of non-surgical weight loss, we did assume that counseling would be provided to this group. We estimated that 5% of this group would see a reduction in BMI to 35.

Outcomes for perioperative mortality, major/minor surgical complications and re-operation were obtained from published literature (Table 1) [7,15–19]. In the WLS cohort, we assumed a perioperative mortality rate of 0.3% within 30 days of surgery. The major and minor complication rates are 2.6% (CI 95%: 2.3–2.8) and 4.7% (CI 95%: 4.4–5.1) respectively [16].

2.3. Cost estimates

2.3.1. Weight-loss surgery

A large systematic review and cost-effectiveness analysis of surgical weight loss was used as a reference to estimate the costs of surgical

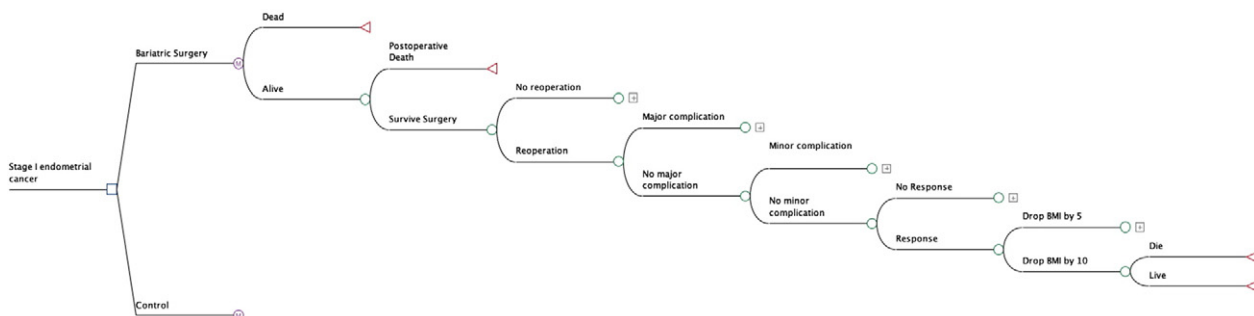


Fig. 1. Markov model decision tree.

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