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Laparoscopic hysterectomy with morcellation vs abdominal hysterectomy for presumed fibroids: an updated decision analysis following the 2014 Food and Drug Administration safety communications

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Abstract

Previous decision analyses demonstrate the safety of minimally invasive hysterectomy for presumed benign fibroids, accounting for the risk of occult leiomyosarcoma and the differential mortality risk associated with laparotomy. Studies published since the 2014 Food and Drug Administration safety communications offer updated leiomyosarcoma incidence estimates. Incorporating these studies suggests that mortality rates are low following hysterectomy for presumed benign fibroids overall, and a minimally invasive approach remains a safe option. Risk associated with morcellation, however, increases in women age >50 years due to increased leiomyosarcoma rates, an important finding for patient-centered discussions of treatment options for fibroids.

Keywords

decision-analysis; fibroid; hysterectomy; laparoscopy; leiomyoma; leiomyosarcoma; morcellation; mortality; myoma

Background

Following a highly publicized case of morcellation–the practice of cutting uterine tissue into pieces or strips in minimally invasive surgery–where the patient was postoperatively diagnosed with leiomyosarcoma (LMS), the US Food and Drug Administration (FDA) issued safety communications in April and November 2014[1] about the use of morcellator

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devices. These communications resulted in significant changes in practice patterns among gynecologic surgeons[2,3] and increasing rates of abdominal hysterectomy (AH),[4] possibly leading to more complications for patients.[5,6] We previously published a decision analysis that attempted to incorporate risks associated with AH and laparoscopic hysterectomy (LH) using estimates of LMS available to the FDA at the time of the initial communications.[7] Mortality and quality-adjusted life-years favored LH in our model. However, numerous limitations compromised the studies used in the analysis, including the disparate time frames that date back to when some of the cases would not have been classified as cancer and inclusion of cases that were identified preoperatively and thus should never have been subject to potential morcellation.

Objective

We sought to update our decision analysis using studies published since the FDA communications to provide newer, higher-quality estimates of risk. We also added to the original analysis by incorporating the effect of age, which recent data suggest has a significant impact on the risk of malignancy among women undergoing surgery for presumed benign fibroids.[8–12]

Study design

We constructed a decision-tree model comparing clinical outcomes of LH and AH. Our primary outcomes were sarcoma- and hysterectomy-related mortality over a 5-year period following surgical intervention. Model design and clinical event inputs are presented elsewhere.[7] Briefly, we simulated a hypothetical cohort of 100,000 women undergoing LH or AH for presumed benign leiomyomata. We examined the frequency of transfusion, wound infection, venous thromboembolism, incisional hernia, vaginal cuff dehiscence, overall mortality, and complications associated with occult LMS, including death.

In this updated model, we used a weighted average among studies published since the FDA safety communications to inform a new estimate of occult LMS incidence. Sensitivity analysis included the range of LMS incidence among the individual studies. As in our previous model, sarcoma-related mortality estimates were derived from Surveillance, Epidemiology, and End Results Program–based 5-year mortality reporting.[13] We assumed that occult LMS in AH would afford the prognosis of an International Federation of Gynecology and Obstetrics stage I or stage II diagnosis (confined to the pelvis, 5-year mortality of 0.59) and that occult LMS with morcellation in LH, that of stage III (extrapelvic disease, 5-year mortality of 0.72). Thus, all women with occult LMS who underwent LH were given a worse prognosis than those undergoing AH. For our base-case model, we identified studies published after the 2014 FDA statements to calculate a weighted average of occult LMS incidence. In addition to our base-case model, we also compared 5-year mortality outcomes of AH and LH in women age <50 years and ≥50 years. We used recent studies that categorized incidence by age to modify predicted rates of occult LMS according to age subgroup.

The study was considered exempt from institutional review board approval because it involved analysis of previously published data.

Results

We identified 11 studies[10–12,14–21] published since the FDA safety communications of sufficient quality and pertaining to our target population of women undergoing hysterectomy who might be subject to morcellation (Table). The number of subjects ranged from 808–241,114 and LMS rates ranged from 0–0.0032 (1:314). In total, 539 cases of LMS were found among 318,006 surgeries for a weighted average of 0.0017. Using this LMS estimate and our base-case estimate for mortality from the procedure itself (LH 0.00012, AH 0.00032), overall mortality remained similar between groups, slightly favoring AH (2 fewer deaths overall). In sensitivity analyses, the number of incremental deaths ranged from 20 fewer in the LH group[21] to 21 fewer in the AH group,[14] with most scenarios favoring LH (Figure 1). We also identified 1 additional study published since our original decision analysis that provided new estimates of mortality from the procedure itself,[22] 0.00013 among 23,956 LH and 0.00034 among 14,616 AH. One-way sensitivity analyses using these estimates favor LH over AH in most scenarios (Figure 1).

Three studies categorized LMS incidence by age group.[10–12] Estimated LMS rates for women age <50 years ranged from 0.0011–0.0013. We selected 0.0012 as our <50-year-old base case. Estimated LMS rates for women age >50 years ranged from 0.0037–0.0081. Based on the number of observations in each study, we selected 0.007 as our ≥50-year-old base-case estimate. Thus, for the group aged <50 years, mortality favored the LH arm, with 16 more deaths secondary to LMS, but 21 fewer deaths due to the procedure itself, for an overall difference of 5 fewer deaths in the LH arm. The results were markedly different for the group age ≥50 years, with 91 more deaths secondary to LMS in the LH arm and a mortality difference of 70 fewer deaths with AH after accounting for differential procedural-related deaths (Figure 2).

Conclusions

Given the limitations of the studies used by the FDA to estimate the incidence of LMS for women undergoing surgery and the number of new estimates published since their 2014 safety communication, we thought it important to update our decision analysis with this latest, higher-quality information. Overall, we demonstrated consistency with our original findings, namely that mortality is not significantly different between AH and LH when accounting for a potentially higher death rate due to LMS morcellation in the LH group, counterbalanced by a higher procedural mortality rate in the AH group. Varying the rates of LMS incidence and hysterectomy mortality, most scenarios favored laparoscopy. Importantly, we were able to incorporate age as a risk factor into our model and propose that risk associated with morcellation is significantly higher in women age >50 years.

Strengths of the study include the more modern and diverse set of publications used to inform our model, the large number of subjects included in the series, and the use of a decision-analytic model, which is particularly helpful in situations where randomized trials

are not feasible, as in this case. That there was not a major swing in the conclusion of the model with integration of the expanded and improved data adds credibility to our original model. Mortality from the procedure itself (LH vs AH) was one of the most challenging clinical outcomes to assess in our original decision analysis, but we identified a newly published study[22] that provided very similar numbers to the original inputs,[23–25] again suggesting our model is robust.

Limitations of the study mirror those of the primary literature such as variation in LMS reporting strategies: some populations were those undergoing any fibroid surgery, some just hysterectomy, and some only those who underwent morcellation. Studies included in this updated decision analysis more closely mirrored our target population, although some did not limit their estimates to those undergoing surgery for fibroids, including a lower-risk population, such as women having a hysterectomy for pelvic organ prolapse. Further, there was variation in data collection strategies, with some studies using review of pathology reports to confirm LMS, for example, and others relying on billing records. Our broad inclusion criteria, use of sensitivity analyses, and the large sample size of many studies, however, may help address the influence of these differences in model outcomes.

Not all studies included an age-based analysis and thus were not included in that portion of the modeling. No studies stratified on menopausal status. We selected an age cut-off of 50 years, roughly corresponding to the average age of menopause, but are unable to account for factors such as the duration of fibroid presence or symptoms, or the impact of women of even more advanced age (eg, >60 years) who may be influencing LMS incidence estimates within this subpopulation. Additionally, we did not account for potential differences in mortality from the procedure itself based on age: older women may have a higher death rate after AH than younger women. However, such a difference in procedure mortality would further favor LH, making our model conservative in its estimations.

Other risk factors may allow for additional stratification, but data on these were too sparse to be included into this updated analysis. A case-control study indicates the presence of a solitary tumor of >7 cm, non-white race, and anemia as possible risk factors for LMS,[26] and a retrospective cohort demonstrates a more significant role of endometrial biopsy in detecting the disease.[27] Lastly, our model could not account for new specimen containment technologies or better preoperative screening before surgery involving morcellation, which may further shift the benefits of LH favorably.

Using newer, higher-quality, estimates of LMS incidence confirmed the main findings of our original decision analysis. Particularly for women age <50 years, minimally invasive hysterectomy remains a safe option for the informed patient to consider. Although overall risks of LMS and mortality in general are low, the elevated risk of LMS in older patients should be incorporated into patient-centered risk-benefit discussions regarding surgery for fibroids.

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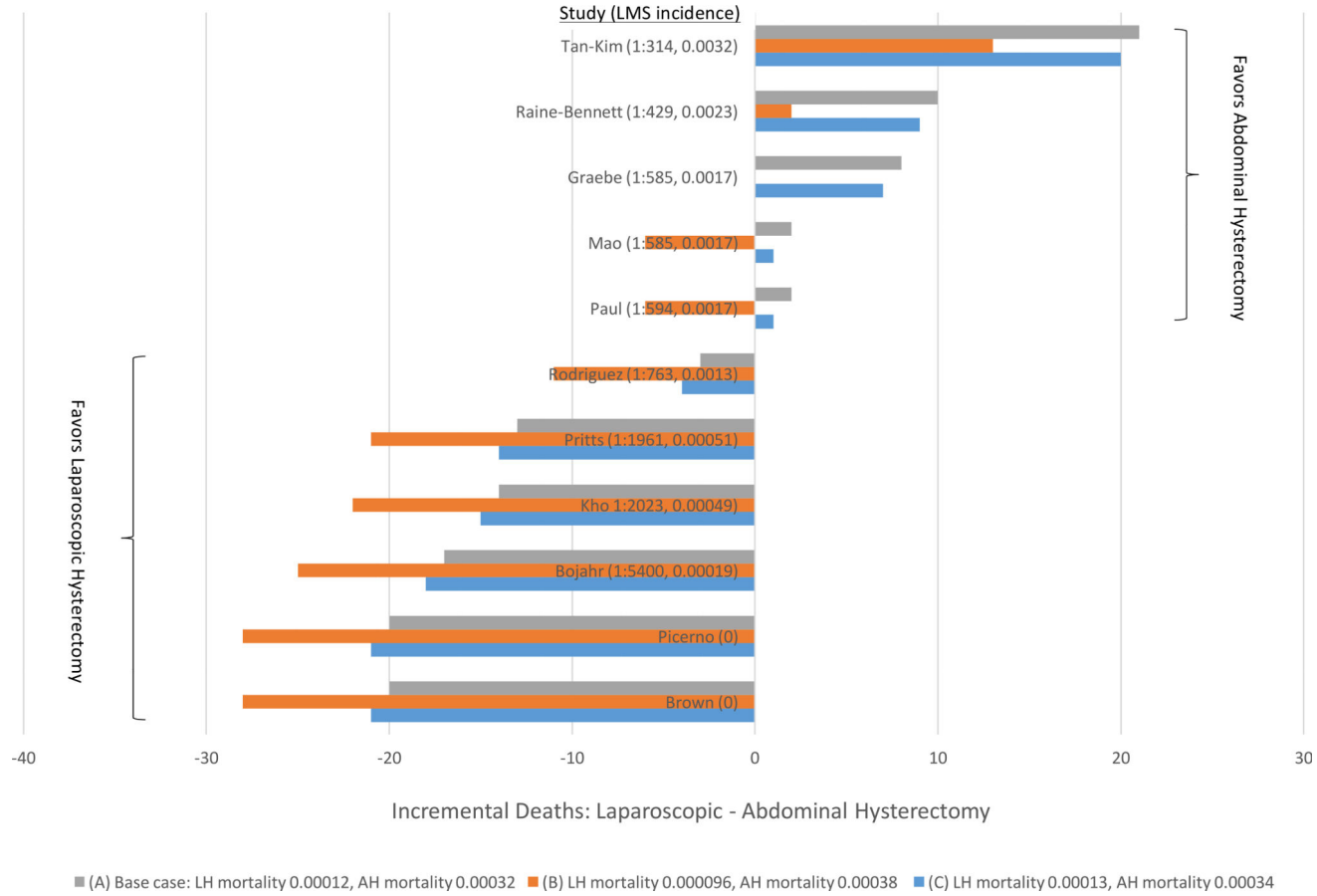

FIGURE 1. Incremental deaths: laparoscopic–abdominal hysterectomy

Number of incremental deaths per 100,000 associated with laparoscopic hysterectomy (LH) by varying candidates for leiomyosarcoma (LMS) incidence and mortality from procedure itself used in sensitivity analysis. At incidence of 0.0032, 0.0023, 0.0022, and 0.0017, there were fewer deaths per 100,000 associated with abdominal hysterectomy (AH). At incidence of 0.0013, 0.00051, 0.00049, and 0.00019, there were fewer deaths per 100,000 associated with LH. **A**, Base-case estimate: LH mortality 0.00012, AH mortality 0.00032.[25] **B**, Sensitivity analysis 1: LH mortality 0.0.00096, AH mortality 0.00038.[23–24] **C**, Sensitivity analysis 2: LH mortality 0.00013, AH mortality 0.00034.[22]

Siedhoff. Updated laparoscopic vs abdominal hysterectomy decision analysis. Am J Obstet Gynecol 2017.

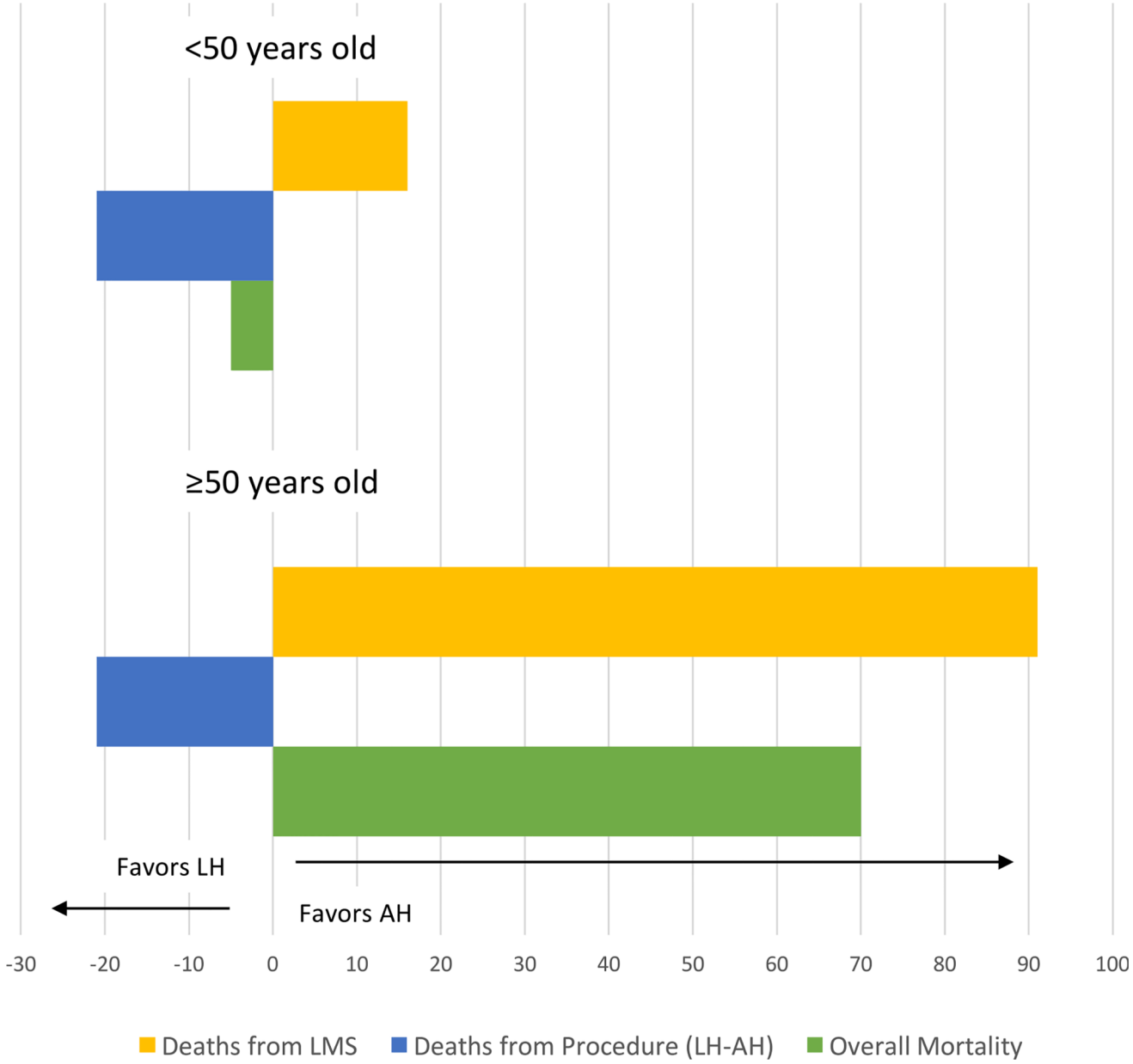

FIGURE 2. Mortality estimates stratified by age

Number of incremental deaths per 100,000 in laparoscopic hysterectomy (LH) and abdominal hysterectomy (AH), stratified by age.

LMS, leiomyosarcoma.

Siedhoff. Updated laparoscopic vs abdominal hysterectomy decision analysis. Am J Obstet Gynecol 2017.

TABLE

Studies published following 2014 Food and Drug Administration safety communications included in updated decision analysis

Publication year	Author	Location	Study period	No. of subjects	Study characteristics	Observed leiomyosarcoma incidence
2015	Tan-Kim et al[14]	United States	2001 through 2012	941	Laparoscopic hysterectomy patients with morcellation	1:314 (0.0032)
2016	Raine-Bennett et al[10]	United States	2006 through 2013	34,728	Hysterectomies for presumed benign fibroids	1:429 (0.0023)
2015	Graebe et al[15]	United States	2005 through 2013	1361	Laparoscopic hysterectomy patients with power morcellation	1:454 (0.0022)
2015	Mao et al[11]	United States	2008 through 2011	241,114	Patients undergoing hysterectomy or myomectomy, SEER California registries	1:585 (0.0017)
2016	Paul et al[16]	India	2004 through 2014	1781	Laparoscopic hysterectomy patients with vaginal morcellation	1:594 (0.0017)
2016	Rodriguez et al[12]	United States	2002 through 2011	12,226	Laparoscopic supracervical hysterectomy for fibroids among US insurance claims	1:763 (0.0013)
2015	Pritts et al[17]	Various	1984 through 2014	30,193	Meta-analysis of 133 studies on myomectomy or hysterectomy for fibroids; required histopathology to be explicitly reported; included studies where cancer was not found	1:1961 (0.00051)
2016	Kho et al[18]	United States	2010 through 2014	10,119	Hysterectomies at single institution	1:2023 (0.00049)
2015	Bojahr et al[19]	Germany	1998 through 2014	10,731	Laparoscopic supracervical hysterectomy patients with morcellation	1:5400 (0.00019)
2016	Picerno et al[20]	United States	2004 through 2015	1004	Laparoscopic hysterectomy or laparoscopic myomectomy with morcellation	0
2015	Brown et al[21]	United States	2002 through 2008	808	Laparoscopic supracervical hysterectomy with morcellation	0

SEER, Surveillance, Epidemiology, and End Results Program.

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