

Excerpts from the World Medical Literature



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Verbakel JY, Heremans R, Wynants L, et al. Risk assessment for endometrial cancer in women with abnormal uterine bleeding: results from the prospective IETA-1 cohort study. *Int J Gynecol Obstet* 2022;159:103–10.

Summary: A prospective observational multicentre cohort study of 2417 pre- and postmenopausal women with abnormal uterine bleeding (AUB) to investigate the association between personal history, anthropometric features, lifestyle characteristics, and endometrial cancer (EC). The inclusion criteria included a variety of nonpregnancy-related AUB: postmenopausal bleeding (PMB), heavy menstrual bleeding, intermenstrual bleeding, and bleeding on hormone therapy. All patients underwent transvaginal ultrasound to determine endometrial thickness (ET) in the sagittal plane and endometrial sampling. The median age of the patients was 50, mean ET was 8.8 mm, mean BMI was 25 kg/m²; 41% were postmenopausal. The baseline risk assessment involved the use of a multivariable logistic regression model using age, BMI, and parity. In the subgroup of postmenopausal women, additional variables were added, including the presence of diabetes or hypertension, physical exercise, waist circumference, bra cup size, smoking, alcohol consumption, and family history. Of the 2417 patients, only 88% had a final histological diagnosis; the remaining 11% were assumed to be benign after 1 year of follow-up without further bleeding. Sampling was obtained by office biopsy in 31.5%, dilatation and curettage in 2.5%, hysteroscopically directed biopsy in 43.6%, and hysterectomy in 10.5%. The final diagnosis was atrophy in 9.3%, polyp or fibroid in 40.2%, benign endometrium in 32.2%, and malignancy or atypical hyperplasia in 6.4%. A greater percentage of those women with malignancy presented with light bleeding or spotting (60.4%) than those with benign findings (40.2%). The mean age for

women with malignancy was 67 versus 49 for those with benign findings. The mean BMI of those with malignancy was 26 kg/m² versus 25 kg/m² for those with benign findings. Combining age, BMI, and parity into a baseline risk assessment for all patients generated an area under the curve (AUC) of 0.82; none of the other variables, when added individually, resulted in an increased AUC. Adding sonographic ET to the baseline model increased the AUC in postmenopausal women (AUC from 0.73 to 0.85) but not in premenopausal women.

Comment: One more effort from the literature to help us “fine tune” our approach in women with AUB and particularly PMB. Previous literature reviewed in these excerpts demonstrated a <1:1000 risk of EC in women with heavy menstrual bleeding, and another study showed a higher risk of EC in women >60 with repeated episodes of bleeding. The association between PMB and EC with ET >5 mm is also well established. So, how do we use this information in clinical practice? The conundrum in real life is that cancer can occur in postmenopausal women with thin endometrium and light bleeding—so, can we ever really let down our guard in any patient with PMB? The AUC for the model they have created in this study is not rigorous enough to use age, BMI, and parity alone. My own practice is to defer what would be a difficult attempt at sampling unless the bleeding is repetitive regardless of the ET; I believe this is a reasonable compromise that limits the number of biopsies in many patients but not at the expense of missing malignancy.

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Wright JD, Chen L, Melamed A, et al. Containment bag use among women who undergo hysterectomy with power morcellation. *Obstet Gynecol* 2022;140:371–80.

Summary: A database study to examine trends in the use of laparoscopic power morcellators and containment bag systems in women undergoing minimally invasive hysterectomy in the United States (U.S.). The Premier Healthcare Database is a deidentified, hospital-based data source that captures inpatient and outpatient services across the U.S. Only patients undergoing laparoscopic supracervical hysterectomy (LASH) between the period from January 2010 to June 2018 were evaluated. The hospital billing records were examined to determine the use of power morcellators and containment bags. Major perioperative complications (e.g., bladder, ureteral, gastrointestinal, vascular injuries, etc.) were also analyzed. Of the 1 037 718 patients who underwent hysterectomy during that time period, only 67 115 (6.5%) underwent LASH. The rate of LASH declined from 8.4% in 2010 to 3.6% in 2018. Use of the power morcellator declined from 66.7% to 13.8% during that time period. Containment bag use increased from 5.2% to 15.2%. Uterine cancer and sarcoma incidence were 0.17% before the Food and Drug Administration warning in 2014 and 0.12% after. Containment bags were used in 11.1% of patients with malignancy before 2014 and 14.3% after the Food and Drug Administration warning ($P = 0.12$). Women who had laparoscopic power morcellation with a containment bag had a 35% increased risk of complications (adjusted relative risk 1.35, 95% CI 1.12–1.64).

Comment: Just like the use of hormone therapy has never recovered from the Women's Health Initiative Study in 2002, I fear supracervical hysterectomy and power morcellation may never recover from the Amy Reed story in 2014. There are so many points and nuances to this saga, and it would be difficult for me to cover them all, but here are the key ones: there is always a risk of occult uterine malignancy in women operated on for presumed benign disease, the relationship between morcellation of any type and adverse prognosis is unclear, LASH was a safe technique that simplified minimally invasive hysterectomy and minimized urinary complications, power morcellation was safe in experienced hands, and containment bags are a pain in the butt. Oh yeah, the decrease in the use of minimally invasive hysterectomy translates into more surgical complications overall as open hysterectomy becomes the default procedure. There must be some re-set in thinking and practice guidelines to allow for the reintroduction of

LASH and power morcellation of well-selected cases where the risk of occult malignancy becomes close to zero (e.g., women <40 years old, negative endometrial biopsy, etc.). And somebody better develop a containment bag that is less of a pain to use. Containment bag morcellation is tricky, has not really caught on, and is associated with more complications.

Madhvani K, Garcia S, Fernandez-Felix B, et al. Predicting major complications in patients undergoing laparoscopic and open hysterectomy for benign indications. *CMAJ* 2022;194:E1306–17.

Summary: The authors developed and validated a multivariable logistic prediction model for risk of complications in laparoscopic (LH) and open hysterectomy (AH) for benign disease using routinely collected data in a retrospective cohort study in England. They identified all patients undergoing these 2 procedures between 2011 and 2018 and used data from the Hospital Episode Statistics database to identify 11 predictors for inclusion and all Clavien-Dindo class 3 and 4 complications. The predictors included age, ethnicity, obesity, diabetes, gynaecological diagnosis, and the presence of adhesions. There was a model development and validation process that used a multivariable logistic regression approach with prespecified predictors without a selection strategy. In the LH group, the rate of major complications was 4.4% (3307 out of 68 559 patients) and 4.9% in the AH group (6201 of 125 971). The number of LH increased over the 7-year period. In the univariate analysis of both LH and AH, adhesions had the strongest association with major complications (OR 2.03, 95% CI 1.87–2.20 for LH, OR 2.50, 95% CI 2.35–2.65 for AH). In the AH group, Asian race and diabetes were also associated with risk of complications. The C-statistic (discriminatory ability) for the laparoscopic model was 0.60 (CI 0.60–0.62) and 0.67 (CI 0.65–0.69) for the abdominal model across the various areas in England that were evaluated. An online calculator can be found at www.evencio.com.

Comment: I may sound like a broken record (does that analogy still mean anything in 2022?!), but patients do not like surprises, particularly surgical complications. This study—like one I recently reviewed from Denmark a few issues back—is a reality check for surgeons; based on data from hundreds of thousands of cases, there is an irreducible risk of about 5% for major complications in benign hysterectomy, both LH and AH. I believe we all have the very natural and human tendency to underestimate our own complications and “shield” the patient from the worry of the risks associated with surgery. As the

authors pointed out, this information is essential for patients to make a truly informed decision, as there are often less risky alternatives for the treatment of benign gynaecological disease. The important message in this study is the risk conferred by previous surgery (they used adhesions as a proxy for previous surgery, though they may occur spontaneously in endometriosis); I have also previously reviewed a *JAMA* paper that demonstrated a significantly increased risk of hemorrhage in patients undergoing LH after prior cesarean delivery. The evidence is building that despite better training, better tools, and more minimally invasive surgeries, the risk of major complications always remains; though an honest and candid discussion before surgery is not a guarantee you will not be sued, we should be forthcoming about the potential complications of benign gynaecological surgery and take care to document these discussions clearly—particularly in patients who have had prior surgery.

Hamade S, Alshiek J, Javadian P, et al. Evaluation of the American College of Surgeons National Surgical Quality Improvement Program risk improvement calculator to predict outcomes after hysterectomy. *Int J Gynecol Obstet* 2022;158:714–21.

Summary: The objective of this study was to evaluate the American College of Surgeons (ACS) surgical risk calculator reliability in predicting adverse outcomes within 30 days after hysterectomy. This was a single-site prospective cohort study of 634 patients undergoing hysterectomy over a 4-month period in a major U.S. hospital. Surgery was performed by the benign gynaecology service in 341/634 (54%) hysterectomies; the remainder had surgery by gynaecological oncologists or urogynaecologists, but most surgeries were for benign disease. A total of 21 de-identified surgical variables were abstracted from the hospital electronic medical records and were entered into the ACS National Surgical Quality Improvement Program (ACS-NISQUIP) calculator. The 30-day complications included a long list of mostly serious medical complications but did include return to the operating room, surgical

site infection, and serious surgical complications. Three metrics were used to predict the validity of the ACS-NISQUIP calculator, including the C-statistic, the Hosmer-Lemeshow statistic, and the Brier score. Fifty-four of the 634 patients (8.5%) had serious complications; neither type of hysterectomy, American Society of Anesthesiology score, BMI, race, or age were significantly different between the group of patients who had complications and those who did not ($P > 0.05$). The ACS-NISQUIP overestimated the rates of complications in all categories. The AUCs for predicting return to the operating room, renal failure, readmission, and surgical-site infection were 0.607 (95% C-statistic index CI 0.37–0.85), 0.882 (95% CI 0.80–0.96), 0.637 (95% CI 0.52–0.75), and 0.553 (95% CI 0.40–0.71). The calculator had generally poor predictive capability.

Comment: The authors provided several explanations for the poor predictive ability of this calculator. Foremost, though the ACS-NISQUIP calculator was developed with data from 4.3 million operations in 780 hospitals (our own included!), gynaecological surgeries accounted for only 5.3%. It seems to have been implemented in certain surgical subspecialties with more success (colorectal, bariatric, and pediatric) than others (head and neck, spine, and urology). I briefly introduced the notion of the C-statistic in my discussion of the previous paper, and these authors used 2 other predictive scores in this analysis with similarly poor results. Interestingly, they also refer to previous research that shows >90% of patients wanted to use this calculator as part of an informed consent process. So what is the take home message? Clearly, the ACS-NISQUIP tool is not ready for primetime in gynaecology, and, in fact it, may do a disservice to patients by “scaring them away” from surgery. My own sense is there is an “X-factor” underlying it all: the skill of the surgeon. Unless the track record of an experienced surgeon is factored into the equation, we will never have a purely objective tool that accurately predicts outcome. As I have mentioned before: “It ain’t the size of the wand, it’s the magic of the magician.”