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Schmitt JJ, Baker MV, Occhino JA, et al. Prospective implementation and evaluation of a decision-tree algorithm for route of hysterectomy. Obstet Gynecol 2020;135:761–9.

Summary: A prospective algorithm was developed and implemented at the Mayo Clinic between November 2015 and December 2017 to determine the optimal route of hysterectomy using history of laparotomy, estimated uterine size, and vaginal access. The expected route of surgery was compared with the actual route to identify compliance and deviation, and surgical outcomes were analyzed. A total of 365 patients with benign disease met the inclusion criteria. Exclusion criteria included a wide variety of conditions such as endometriosis, adnexal disease, and concomitant pelvic organ prolapse.

Three-dimensional pelvic models were developed for outpatient evaluation by clinicians to represent 100-g, 280-g (12-week-sized), and 500-g (16-week-sized) uteri. The algorithm was developed to include examination under anesthesia for patients with uteri measuring between 13 and 16 weeks and with a history of laparotomy, based on the known higher historical conversion risk from a previously developed retrospective algorithm published by the same authors. Patients with uteri measuring >17 weeks were directed to laparoscopic, robotic, or abdominal hysterectomy. Most patients with uteri measuring ≤12 weeks, a history of ≤1 laparotomy, and adequate vaginal caliber, mobility, and descent on outpatient examination were directed by the algorithm to undergo vaginal hysterectomy. Overall, 55% of patients in this study met the criteria for vaginal hysterectomy. Of the 202 hysterectomies expected by the algorithm to be performed vaginally, 170 (84%) were performed vaginally. Demographically, these women had a mean age of 44.5 years, a mean body mass index (BMI) of 28, and a median uterine weight of 116 g. There were no intraoperative conversions in this group, and 94% were discharged within 24 hours of surgery. The success rate of vaginal surgery in those patients who required examination under anesthesia was lower (72%), with two conversions. These patients had a greater average age, BMI, and uterine weight. Forty-six patients (12.6%) deviated from the algorithm to a more invasive route: 44 to a robotic approach and two to laparotomy. Postoperative complications included a 3% rate of blood transfusion and reoperation in two patients.

Comment: The first thought that comes to mind when reading this paper is generalizability. There is no doubt that the skilled, high-volume surgeons at the Mayo Clinic are master technicians working in an environment with a rich pedigree of talented vaginal surgeons. The patient population they serve is also unique; here is a study published in the United States in which over 90% of the patients were white and had relatively normal BMIs. This is clearly not representative of the nation’s usual demographics. Many of us who care for a more ethnically diverse population of patients among whom uterine fibroids are the most common indication for hysterectomy can be forgiven for looking at these data and being somewhat skeptical about the relevance to our practices. Studies like this are a good reminder of what is possible in skilled, experienced, and motivated hands, inasmuch as it forces us to reflect and consider how a simple approach to surgery can be safe, efficient, and cost-effective. That is a good thing. But the genie is out of the bottle, and the numbers tell the story: There is an ongoing decline in vaginal hysterectomy in favour of laparoscopic and robotic approaches. The reasons for this involve more than just the seduction of technology; vaginal surgery is difficult ergonomically, particularly for the assistants, and surgical missteps are
difficult to correct because of limited exposure to upper vascular pedicles. A paper previously published in the February volume of the same journal (“Hysterectomy Route and Numbers Reported by Graduating Residents in Obstetrics and Gynecology Programs” by G. Gressel et al.) attests to the exact same trend among trainees. My sense is that this well-done study will do little to stem the tide moving away from vaginal and towards laparoscopic and robotic hysterectomy.

Mikos T, Lioupis M, Anthoulakis C, et al. The outcome of fertility-sparing and non-fertility-sparing surgery for the treatment of adenomyosis. A systematic review and meta-analysis. J Minim Invasive Gynecol 2020;27:309–31.e3.

Summary: This paper is a systematic review of 19 studies published between 2009 and 2018 with a total of 1843 patients who underwent a variety of conservative surgical procedures for adenomyosis. It examined outcomes of pain, bleeding, and reduction in uterine volume 12 months after surgery. Inclusion criteria included a clear preoperative diagnosis by ultrasound and/or magnetic resonance imaging, postoperative conformation by histology, use of standardized scores to report pain and bleeding, measurement of uterine volume, and full description of the operative technique. Exclusion criteria included small studies (<20 patients), no clear description of primary and secondary outcomes, and studies not published in English. Outcomes were evaluated based on whether there had been full or partial excision of adenomyosis. Surgical techniques included classical “wedge” resection, “flap” techniques, and hysteroscopic resection. Approaches included open, laparoscopic, and robotic surgery. Visual analogue scores (VASs) were used primarily to evaluate pain/dysmenorrhea, a variety of scales were used to evaluate bleeding, and ultrasound was used to calculate uterine volume.

After complete excision of adenomyosis, postoperative pain measurement improved by 70% to 90%, menorrhagia improved by 70% to 92%, and uterine volume was reduced by 65%; after partial excision, pain improved by 41% to 90%, bleeding improved by 48% to 89%, and uterine volume decreased by 25% to 89%. After meta-analysis of the available studies, complete excision was associated with an improvement in pain and menorrhagia and a reduction in volume by a factor of 6.2, 3.9, and 2.3, respectively; for partial excision, these improved by a factor of 5.9, 3.0 and 2.9, respectively. Interestingly, hysterectomy was associated with an improvement in pain of only 2.2. Recurrences (2%–3%) and serious complications were rare in both groups. Comment: This is an intriguing paper that evaluates a surgical technique that is very rarely used in North America or Europe. In fact, even though all papers reviewed and included in this study were published in English, all except two were either retrospective or prospective cohort studies performed in China, Korea, or Taiwan. Moreover, preoperative uterine volumes were in the 200-cm³ range, indicative of rather small uteri. I have had one personal experience of “debulking” an unexpected adenomyosis in my career; it was stressful, and although the patient had over a decade of improvement in her quality of life, she ultimately required hysterectomy. Most surgeons would not intentionally advise or perform this surgery, but maybe we should consider it in selective cases, given the feasibility and good outcomes reported in this paper.

Amiri M, Nahidi F, Biddendi-Yarandi R, et al. A comparison of the effects of oral contraceptives on the clinical and biochemical markers of polycystic ovarian syndrome: a crossover randomized controlled trial. Hum Reprod 2020;35:175–86.

Summary: This study was a crossover, randomized controlled, six-arm trial. All six arms included two 6-month treatment periods; one period involved treatment with oral contraceptives (OCs) containing levonorgestrel (LNG), and the other involved OCs containing desogestrel (DSG), cyproterone acetate (CPA), or drospirenone (DRS). The trial was conducted in Iran between 2016 and 2018 and enrolled 200 patients who met clinical and biochemical criteria for polycystic ovarian syndrome (PCOS). The primary outcome was free-androgen index, calculated using serum sex-hormone-binding globulin and testosterone; secondary outcomes included the modified Ferriman-Gallway score, anthropomorphic measurements (height, weight, waist circumference, and BMI), and other metabolic parameters including fasting blood sugar, fasting insulin, and lipid profile. Outcome measurements were collected at months 3 and 6 in both 6-month treatment periods, with a wash-out period of 6–8 weeks between treatment periods. Ultrasound evaluation of the uterus and ovaries was also performed.
A total of 88 patients completed the study. The results of the hormonal assays showed a greater decrease in free-androgen index levels in addition to a higher increase in sex-hormone-binding globulin levels \( (P < 0.001) \) after 3 and 6 months of treatment with OCs containing DSG, CPA, and DRS than after treatment with OCs containing LNG \( (P < 0.001) \). Patients taking OCs containing DRS and DSG had nonsignificantly greater decreases in body weight at 3 and 6 months than those on LNG-containing OCs. DRS-containing OCs were associated with a greater clinical improvement in acne at 6 months than those containing LNG \( (P = 0.007) \). DRS-, DSG-, and CPA-containing OCs were associated with improved lipid profiles in 3 and 6 months compared with LNG OCs \( (P < 0.05 \text{ and } P = 0.001) \).

**Comment:** As a surgically inclined gynaecologist, I rarely read (and even more rarely review) papers on endocrine and metabolic disorders. This paper caught my attention because of where it was written, its rigorous study design, and, most importantly, the fact that it was not sponsored by any pharmaceutical company: “This study was supported by the Shahid Beheshti University of Medical Sciences with no conflicts of interest described.” Pharmaceutical companies have pitched their OCs with claims of the beneficial metabolic effects of their “unique progestin.” OCs are all equally effective for contraception and differ very little in terms of associated thromboembolic risks. Very few head-to-head studies have looked at biochemical and clinical outcomes over a 1-year period, and even fewer studies have been limited to patients with PCOS. This carefully done study supports the greater anti-androgenic properties of the newer progestins both in terms of biochemical parameters (serum androgens and lipid profile) and clinical outcomes such as acne and weight gain. The key message is the time it takes to see these results, specifically improvements in acne. We need to reinforce this with patients, who often abandon OCs after the first few months of use.Clinicians should carefully consider the more modern progestins when prescribing an OC for a patient with PCOS.

**Fava M, Peloggia A, Baccaro LF, et al.** A randomized controlled pilot study of ulipristal acetate for abnormal bleeding among women using the 52-mg levonorgestrel intrauterine system. Int J Gynaecol Obstet 2020;149:10–5.

**Summary:** This is a randomized, double-blind, placebo-controlled pilot study conducted in Brazil between September 2016 and 2018. Users of the levonorgestrel-releasing intrauterine system who reported prolonged or frequent uterine bleeding for at least 1 year were randomly assigned to receive 5 mg ulipristal acetate (UPA) or placebo for 5 days. Bleeding was recorded for 90 days after treatment began and was compared between groups. Eligible patients were between the ages of 18 and 45 with an intrauterine system in place for between 1 and 4 years. Ultrasound was performed to rule out associated uterine pathology. Exclusion criteria included use of other medication, hematological abnormalities, or use of anticoagulants.

Of 94 eligible women, 64 declined treatment. Thirty patients were enrolled in this pilot study, and five were lost to follow-up. There was no difference between groups with respect to age, BMI, parity, or previous cesarean delivery. Patients in each group were equally likely to describe frequent, prolonged, and irregular bleeding. The number of days before bleeding stopped and the days free of bleeding were statistically similar between the groups \( (P > 0.05) \), although there was a trend towards fewer days before bleeding stopped \( (3.3 \pm 4.5 \text{ vs. } 6.6 \pm 8.5 \text{ days}; P = 0.399) \) and more days free of bleeding \( (19.6 \pm 14.0 \text{ vs. } 11.7 \pm 9.5d; P = 0.177) \) among users of UPA than users of placebo. At 30, 60, and 90 days after treatment, the mean number of bleeding days was not statistically significantly different between the groups \( (P > 0.05) \).

**Comment:** The quest for an effective drug to control progestin-associated breakthrough bleeding reminds me of one my favorite U2 songs: “I Still Haven’t Found What I’m Looking For.” Researchers have tried almost everything—non-steroidal anti-inflammatory drugs, tranexamic acid, mifepristone, estrogens, and metalloproteinase inhibitors—to find the “magic bullet” to treat this bothersome side effect of progestin-only contraception. I would have predicted that a selective progesterin receptor modulator such as ulipristal, with its known antiproliferative effect on the endometrium, would not have been a good choice; Mirena itself is already associated with endometrial atrophy, and the choice of UPA would simply exacerbate that effect. Counselling and reassurance seem to be the only tools we have so far—like handwashing and social distancing for SARS-CoV-2, to make a contemporary analogy. My hope is that some clever researchers find solutions to both of these problems soon. I predict an effective vaccine will be discovered before we have a “cure” for breakthrough bleeding.