Excerpts from the World Medical Literature

C. Ziegler

Cleve Ziegler, MD

Department of Obstetrics and Gynecology, McGill University, Montréal, QC

Uccella S, Kho RM, Garzon S, et al. The large uterus classification system: a prospective observational study. BJOG 2021;128:1526–33.

Summary: This was a prospective observational study to investigate the large uterus classification system to predict surgical outcomes and complications in total laparoscopic hysterectomies (TLHs) involving large uteri. The study population included 392 consecutive women who underwent TLH for large uteri (defined as clinically extending to or above the umbilicus) between 2004 and 2019 at two centres in Italy by two surgeons. A classification system was developed based on displacement of the adnexal vascular and uterine pedicles: type 1 (both pedicles located at the same level of those of a normal-sized uterus), type 2 (cranially displaced adnexal pedicles and normally placed uterine vessels), and type 3 (displaced uterine vessels with or without displacement of the adnexal pedicles). A detailed description was made at initial laparoscopic entry, and, in many cases, videos of the surgery were reviewed by an independent internal evaluator who was not present at the initial surgery. Data regarding typical demographic factors, operative time, blood loss, intra- and postoperative complications, conversion to open surgery, length of stay, and uterine weight were recorded. The primary outcome was the total complication rate (Clavien-Dindo classification); secondary outcomes included conversion rates, operative time, blood loss, and length of stay. Most uteri were morcellated vaginally, and a minority were removed by mini-laparotomy. Surgery was successfully completed laparoscopically in 92.6% of patients, of whom 64% had type 1, 21% type 2, and 15% type 3 uteri. The three groups were similar with respect to age, body mass index, and parity; however, the three groups had statistically significant differences in clinical outcomes. Average uterine weight was lower in type 1 than in type 2 or 3 (1124 vs. 1418 and 1307 g, respectively; $P < 0.001$). Conversion to open surgery was 6% for type 1, 6% for type 2, and 15.3% for type 3 ($P = 0.03$). Operative time was 112, 127, and 147 minutes for types 1, 2, and 3, respectively ($P < 0.001$). Postoperative complication rates were 8.8%, 14.6%, and 18.6% for types 1, 2, and 3, respectively ($P = 0.018$); these included infected hematomas, cuff dehiscence, vaginal bleeding, and ureteral stricture. Hospital stay was the same across the three groups. On multivariate analysis, the classification of type 2 or 3 versus type 1 uterus was the only independent predictor of a higher rate of complications (odds ratio 2.00; 95% confidence interval [CI] 1.09–3.68, $P = 0.02$). Interestingly, uterine weight was not independently associated with total complications (odds ratio 1.64; 95% CI 0.81–3.31; $P = 0.17$).

Comment: A couple of thoughts emerge from this simple observational study, with information gleaned over a period of 15 years, which represents a significant period of the learning curve for these complex procedures in the life of any surgeon. There were also developments in energy sources, uterine manipulators, and colpotomy delineators over this period, and some of these details are missing from the paper, although three surgical videos were also included. The simple message is that the type rather than the size of the uterus may be more important in predicting complexity and complications in TLH. In terms of practical application, this information would be helpful in preparing both patients and surgeons for these procedures, particularly regarding informed consent. Because these details were only obtained once the patient was under anesthesia, meaningful discussions were not possible. The real value, as the authors admit, would be the ability to refine preoperative imaging to guide the

J Obstet Gynaecol Can 2022;44(2):123-126

https://doi.org/10.1016/j.jogc.2021.11.007

consent discussion. We all know a prepared patient is better than a surprised one; as surgeons, we have that all-too-human tendency to sugarcoat the truth when it comes to discussing potential risk, as we stretch the limits of minimally invasive surgery. The ability to be much more specific when quoting risk of conversion to open surgery and other complications when tackling the large uterus would be a welcome development, although I suspect many high-volume surgeons can accurately and reliably predict their own numbers. Size may matter, but morphology seems to matter more when it comes to TLH for the mega-uterus. We are all continually pushing the envelope, and cases that seemed impossible laparoscopically a decade ago can be accomplished with a mixture of patience, experience, and persistence—as well as the right amount of courage.

Uccella S, Garzon S, Lanzo G, et al. Uterine artery closure at the origin vs at the uterus level in total laparoscopic hysterectomy: a randomized controlled trial. Acta Obstet Gynecol Scand 2021;100:1840–8.

Summary: This was a single-blind randomized (1:1) controlled trial of 180 women undergoing TLH for benign indications between December 2019 and August 2020 at one centre in Italy. Patients were randomly assigned to either conventional bipolar ligation of the uterine vessels at the level of the uterus (UL) or ligation of both uterine arteries at origin (OR) with 5-mm permanent titanium clips. The primary outcome was intraoperative blood loss as measured in the suction device by the anesthesiologist at the time of surgery; secondary outcomes included operative times, conversion to laparotomy, hemoglobin drop, length of hospital stay, and major and minor complications (Clavien-Dindo classification). Mean patient age was 54.2 years, mean body mass index was 25 kg/m^2, 40% were postmenopausal, and the main indication for surgery was uterine fibroids (50.6%). Mean uterine weight was 301 g (range 30–2800 g). There were no conversions to open surgery in either group. All 90 patients assigned to OR had successful ligation of the uterine artery; conversely, there was a 12.2% failure rate for UL ($P < 0.001$). The most common explanation for failure was incidental endometriosis, found in 18% of those patients. Mean intraoperative blood loss was higher in the UL group than in the OR group (108.5 vs. 69.3 mL; $P = 0.003$). The mean difference in hemoglobin drop between groups was −0.04 g/dL (95% CI −0.29 to 0.22 g/dL; $P = 0.77$). The incidence of minor and major complications was similar between the groups (10% vs. 6.7%; $P = 0.37$). Intraoperative blood loss associated with ligation of the uterine vessels OR did not appear to change with uterine weight.

Comment: We stay in northern Italy, where butter reigns over olive oil and the surgeons seem to be latter-day Michelangelos—a reminder that volume and experience lead to good outcomes in surgery. Most gynaecologic surgeons looking to duplicate what they do in open surgery when they transition to laparoscopy must apply a hefty amount of energy to coagulate the uterine vessels—often repeatedly and well after they have been barbequed to beyond well done. Ligation of the uterine arteries at source requires retroperitoneal dissection and is a technique not commonly used by most surgeons. However, practice makes perfect, and expertise with this manoeuvre can be a game-changer when the going gets tough. I think the message from this study, which failed to show any clinically meaningful difference between the two groups, was the 12% failure rate of UL versus the 0% failure rate of OR; this is not a trivial difference and reminds us we need to be able to reach into our bag of tricks for a trick that will get us out of any jam—and that includes the not uncommon scenario of unexpected endometriosis or a nasty lower-segment fibroid. I was surprised, however, at the average age and significant postmenopausal status of this cohort of patients—about a decade older than in my experience.

Ali MK, Emam SM, Abdel-Aleem MA, et al. Misoprostol versus expectant management in women with incomplete first-trimester miscarriage after failed primary misoprostol treatment: a randomized clinical trial. Int J Gynaecol Obstet 2021;154:558–64.

Summary: This was an open-label randomized controlled trial to compare the effectiveness of repeat misoprostol versus expectant management in women with first-trimester incomplete miscarriage who had been previously treated with misoprostol. The primary outcome was the number of women with a complete miscarriage at 1 week (i.e., no bleeding, no symptoms, and a thin endometrium of <10 mm); secondary outcomes included the number of women with a complete miscarriage at 2 and 4 weeks, the number needing surgical intervention at 4 weeks, and mean hemoglobin at 1 week. A total of 90 women were evaluated, half randomly assigned to each group (800 μg misoprostol administered vaginally vs. placebo). Inclusion criteria were incomplete miscarriage after administration of misoprostol due to embryonic

death, defined as an endometrial thickness >10 mm. There were no significant differences in baseline characteristics between groups (i.e., average age 28 years; average gestational age 9 weeks; same number of parous women and prior cesarean deliveries). A total of 6 women were excluded from the final analysis for a variety of reasons. The rate of complete miscarriage at 1 week was significantly higher in the misoprostol group than in the expectant management group (69.0% vs. 16.7%; $P < 0.001$). Similarly, the complete miscarriage rate at 2 weeks was significantly higher in the misoprostol group ($P = 0.000$). However, at 4 weeks, both groups had a similar rate of complete miscarriage ($P = 0.433$). No statistically significant differences were found between the groups regarding the need for surgical evacuation at 4 weeks (4.8% vs. 11.9%; $P = 0.433$). Women in the misoprostol group were more satisfied but reported more pain than those in the expectant group ($P < 0.001$). Kaplan-Meier analysis of "survival" until the occurrence of complete miscarriage revealed a significantly shorter length of time in the misoprostol group ($P < 0.001$). Multiple logistic regression revealed that previous cesarean delivery (odds ratio 5.15; 95% CI 1.15–23.05; $P = 0.032$) and larger uterine contents (odds ratio 1.17; 95% CI 1.00–1.36, $P = 0.042$) were significant predictors for incomplete miscarriage at 1 week.

Comment: We move to the land of the pharaohs. I love studies that look at common clinical problems and refine management so that it is optimal and predictable for patients and clinicians. First-trimester miscarriage certainly meets the bill, and the ongoing literature on the subject enables us to target the right treatment to the right patient at the right time. Some first-trimester miscarriages (specifically, early embryonic death) can drag on for weeks, require multiple visits and ultrasounds, and often "medicalize" an event that would have eventually happened on its own. But we live in an impatient world, are both blessed and cursed with technology that provides ultra-high-resolution imaging, and often feel compelled to do something rather than wait. This study confirms the effectiveness of repeat misoprostol treatment when the first dose did not do the trick, but it reminds us that sooner or later the tissue will be passed, and life will go on. My only criticism is the stringent definition of "incomplete" in this study; others have used a more liberal definition of 15- or up to 30-mm endometrial thickness, which would minimize the number of patients labelled as having retained tissue. Nevertheless, women were more satisfied with repeat misoprostol, despite the slight increase in pain associated with its use. The other message is that dilation and curettage may be preferable in women who have had a cesarean delivery.

Dioun S, Wu J, Chen L, et al. Intraoperative rupture of the ovarian capsule in early-stage ovarian cancer: a meta-analysis. Obstet Gynecol 2021;138:261–71.

Summary: This study is a systematic review and meta-analysis of high-quality observational studies to examine the effects of intraoperative ovarian capsule rupture on progression-free survival and overall survival in women undergoing surgery for early ovarian cancer. The Newcastle-Ottawa scale was used to determine the quality of the studies, and only 17 of 2354 studies identified in the initial search were deemed appropriate. These 17 studies included in the meta-analysis comprised data from 20 366 patients, of whom 12 756 (62.6%) did not have intraoperative or preoperative capsule rupture and 6532 (33.2%) had capsule rupture of an otherwise intact early-stage ovarian cancer. A total of 1078 patients (5.3%) had preoperative capsule rupture, invasion through the serosa, or positive peritoneal fluid. In the entire cohort, 9939 patients (51.3%) underwent an open surgical procedure and 2676 (13.8%) underwent a minimally invasive procedure; route of surgery could not be determined for 34.9% of patients. Clear cell cancers were the histological subtype most associated with rupture (57%), followed by endometrioid, serous, and mucinous tumours. Patients with intraoperative capsule rupture had worse progression-free survival (hazard ratio [HR] 1.92; 95% CI 1.34–2.76; $P < 0.001$). There was also worse overall survival (HR 1.48; 95% CI 1.51–1.91; $P = 0.003$); this represents an almost 50% reduction in overall survival. Interestingly, patients with preoperative rupture did not have worse survival than those with intraoperative rupture (HR 1.39; 95% CI 0.96–2.20; $P = 0.08$). The main limitations of the study (because of its retrospective nature) include the normal biases and the inability to control for surgical approach or staging, use of adjuvant chemotherapy, and tumour size or histology.

Comment: This is a debate that has raged on since the murky past of my residency and one that has yet to be conclusively answered based on this latest publication. Rupture of adnexal masses is the exception rather than the rule in benign gynaecology; although we try our best to remove cysts intact, this is technically impossible for endometriomas, and dermoid cysts are ruptured about half the time by laparoscopy. The ability to predict whether an adnexal mass is malignant by imaging, tumour markers, and age also remains imprecise, despite attempts to quantify this probability with Ovarian-Adnexal Imaging-Reporting-Data System scores and other indices by

ultrasound and magnetic resonance imaging; masses thought to have a low probability of malignancy will continue to be operated on by both generalists and oncologists, and in these cases, this paper demonstrates a strong association between cyst rupture and survival for unexpected cancers. Studies show a 25% rupture rate for minimally invasive surgery overall, so this is a relevant and clinically important matter. As we all continue to push the envelope in minimally invasive surgery—laparoscopic or robotic—good judgement is necessary. A little incision and a few weeks of pain may be preferable to fewer years of life overall.