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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS WORLD CONGRESS

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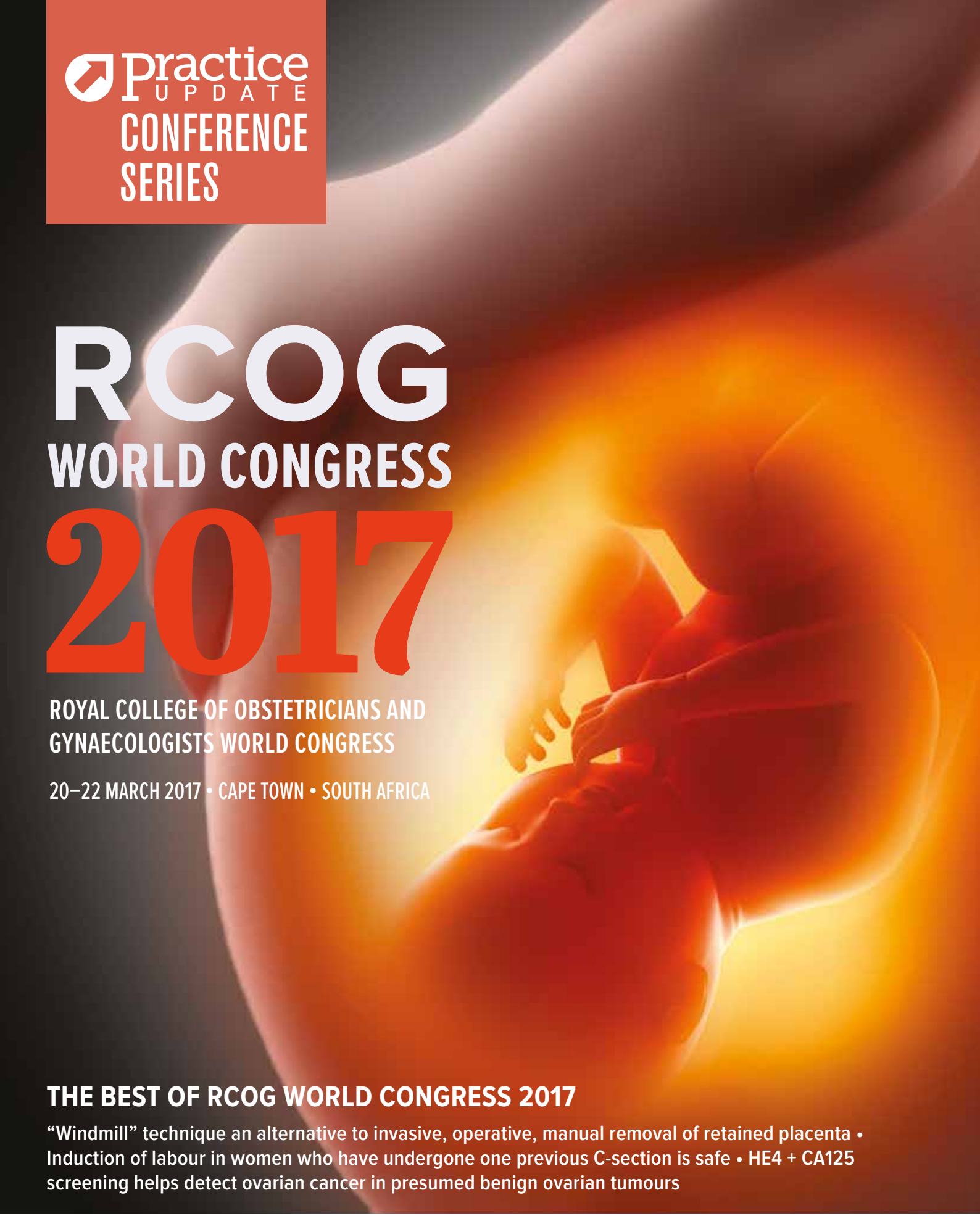

THE BEST OF RCOG WORLD CONGRESS 2017

"Windmill" technique an alternative to invasive, operative, manual removal of retained placenta • Induction of labour in women who have undergone one previous C-section is safe • HE4 + CA125 screening helps detect ovarian cancer in presumed benign ovarian tumours

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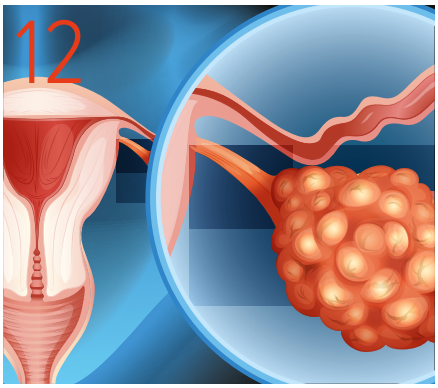

QUiPP app a safe alternative to treat-all strategy for threatened preterm labour

For women in threatened preterm labour, the QUiPP app can guide management accurately at risk thresholds of 1, 5 and 10%, allowing outpatient management for the vast majority, report a retrospective subanalysis of prospectively collected data from the EQuiPP and PETRA research databases.

Dr Helena Watson

Helena Watson, MB, BCHir, of Kings College London, UK, explained that triage of women in threatened preterm labour remains a common clinical challenge. Recent National Institute for Clinical Excellence (NICE) guidance advises a treat-all strategy prior to 30 weeks, based on concern about women with false-negative tests.

"The NICE guideline concerning threatened preterm labour has created a great deal of discussion among obstetricians, midwives and paediatricians, given its potential ramifications on services. As specialists in preterm birth, it was important for us to understand the reasoning behind this recommendation and whether we needed to alter our practice. For this reason, we modelled the impact of the NICE strategy vs our QUiPP app, which employs quantitative fetal fibronectin to predict preterm birth."

Neither the actual harm of false-negative tests nor the harms of overtreating the majority were evaluated. The QUiPP app predicts preterm birth accurately by combining prior history of spontaneous preterm birth, gestation, and quantitative fetal fibronectin.

Dr Watson and colleagues set out to evaluate the scale of false-negative and false-positive diagnoses using the QUiPP app relative to a treat-all strategy at 24–29 +6 weeks and to threatened preterm labour after 30 weeks.

The investigators identified all first episodes of suspected labour (abdominal pain or tightening) between 24 and 34 weeks, excluding women with vaginal bleeding or ruptured

> "Our findings demonstrate how rare false–negative tests are relative to the vast amount of inappropriate interventions and transfers across the UK that would be incurred by treating everyone with symptoms.

membranes. Each episode was retrospectively assigned a risk of birth within 7 days using the QUiPP app. A primary outcome of delivery within 7 days was used to model the accuracy of each approach.

Outcomes were available for 355 eligible women at the time of analysis. With a risk threshold of 5% (of delivery within 7 days) to treat, nine of nine women were treated correctly, for a sensitivity of 100% (one-sided 97.5% confidence interval 0.664) and a negative predictive value of 100% (CI 0.989).

Positive predictive value was 30% (95% CI 0.043 to 0.481) before 30 weeks and 20% (CI 0.119 to 0.543) between 30 and 34 weeks. If this 5% threshold had been used to triage women between 24 and 29 +6 weeks, 89% of admissions (n=168) could have been avoided safely vs 0% with a treat-all strategy. No true cases would have been missed as no women given a risk <10% who delivered within 7 days.

Dr Watson said that for women in threatened preterm labour, the QUiPP app can guide management accurately at risk thresholds of 1, 5, and 10%, allowing outpatient management for the vast majority.

A treat-all approach would have protected none, exposed 188 mothers and babies to unnecessary risk of hospitalisation and steroids, and increased the burden on networks and transport services due to unnecessary in utero transfers.

Prediction should be used before 30 weeks to determine management until evidence accrues that such high levels of unnecessary intervention do less harm than the rare false-negatives.

"Our findings demonstrate," Dr Watson said, "how rare false-negative tests are relative to the vast amount of inappropriate interventions and transfers across the UK that would be incurred by treating everyone with symptoms."

She added, "We would also like to stress that no evidence supports the view that a false-negative test incurs harm automatically. Most women would present again and receive timely intervention. A large multicentre study (EQuiPPT) is planned later this year to confirm these findings and evaluate the clinical impact of the QUiPP app as a tool to manage threatened preterm labour."

“Windmill” technique an alternative to invasive, operative, manual removal of retained placenta

The windmill technique for delivery of the retained placenta is a simple, safe, effective and easy to teach technique that reduces invasive operative manual removal of the placenta, reduces postpartum blood loss, reduces delay in the placenta delivery and may reduce cost, results of a 3-year, case-control study show.

Dr Larry Hinkson

Larry Hinkson, MD, of Charité University Hospital, Berlin, Germany, said, “The Royal College of Obstetricians and Gynaecologists World Congress in Cape Town provides the ideal forum for us to present results and set up networks in Africa to encourage further study and implementation of the technique.”

Dr Hinkson and colleagues set out to assess the reduction in the need for manual removal of the placenta with a new "windmill technique” of placenta delivery in patients with retained placenta after vaginal delivery.

Secondary outcomes included postpartum blood loss, postdelivery haemoglobin changes, duration of placenta delivery, intubation and general anaesthesia, antibiotic prophylaxis, and length of hospitalisation.

> "Using the windmill technique for retained placenta, 86% of patients avoided invasive operative manual removal of the placenta.

The windmill technique of placenta delivery was developed at Charité University Hospital for management of retained placenta and involves the application of continuous 360° umbilical cord traction and rotation in such a manner as to be perpendicular to the direction of the birth canal at the level of the introitus.

This rotation through 360° is repeated slowly and continuously with a movement akin to the motion of the blades of a windmill until the placenta is safely delivered.

Patients with retained placenta more than 30 minutes after vaginal delivery at term and following failed traditional interventions such as oxytocin infusion, bladder emptying and controlled cord

traction were consented and offered the windmill technique of placenta delivery.

Study cases were compared with controls where an operative manual removal of placenta was performed. Patients with suspected placenta implantation problems, uterine atony, severe vaginal tract injury and coagulopathies were excluded from the study.

Over the study period, 31 patients were recruited with 14 in the study arm and 17 in the control group. Using the windmill technique for retained placenta, 86% (12/14) of patients avoided invasive operative manual removal of the placenta.

A statistically significant reduction in mean blood loss (429 vs 724 mL, P = 0.02) and mean postoperative fall in haemoglobin values (1.3 vs 2.4 g/dL, P = 0.03) were observed. Time to delivery of the placenta, antibiotic prophylaxis, and general anaesthesia were reduced.

Dr Hinkson concluded that the windmill technique for delivery of the retained placenta is a simple, safe, effective and easy-to-teach technique that reduces invasive operative manual removal of the placenta, reduces postpartum blood loss, reduces delay in the placenta delivery and may reduce cost.

This is an innovative and new technique that can be life-saving, especially in low-resource areas with limited or no access to operative facilities. ■

Second stage of labour in primiparas more common than previously thought, and reduces spontaneous vaginal deliveries

Prolonged second stage of labour in primiparas has been shown to be more common than previously thought. The chance of spontaneous vaginal delivery decreases linearly with the duration of second stage, report results of a retrospective cohort study.


Dr Sophia Brismar-Wendel

> "The risk of sphincter injury was almost five times higher in operative vaginal delivery after a prolonged second stage.

Sophia Brismar-Wendel, PhD, of the Karolinska Institute, Stockholm, Sweden, explained that prolonged second stage (>3 h/2 h with/without epidural analgesia) may increase the risk of operative vaginal delivery, emergency caesarean section and obstetric anal sphincter injury.

The prevalence and effects of prolonged second stage has been scarcely reported in Sweden. Dr Brismar Wendel and colleagues set out to investigate the prevalence of prolonged second stage, mode of delivery, and risk of obstetric anal sphincter injury in primiparous women.

Dr Brismar-Wendel and coinvestigators used data from computerised hospital records at a large Swedish university hospital to review the cases of primiparas who gave birth in 2013. They included 2668 women with planned vaginal delivery, singleton cephalic birth at ≥34 weeks of gestation.

Of these, a fully dilated cervix was noted in the partograph of 2134. Risk of emergency caesarean section and operative vaginal delivery were calculated for women with a prolonged second stage vs those with women with a normal second stage.

Risk of obstetric anal sphincter injury was calculated in women who underwent operative vaginal delivery after a prolonged second stage (n=200) and a normal second stage (n=101), and in women with spontaneous vaginal delivery with a prolonged second stage (n=500). Women who gave birth via spontaneous vaginal delivery and normal second stage were used as reference (n=1250).

Multivariable logistic regression analyses with adjusted odds ratios and 95% confidence intervals were performed to control for potential confounding factors such as body mass index, epidural, gestational week and maternal age.

A total of 762 (28.6%) women experienced a prolonged second stage. The chance of spontaneous vaginal delivery decreased with every hour from 93.6% to 11.1% at >7 h (adjusted odds ratio 0.19, 95% CI 0.15–0.25).

Compared with women who experienced a normal second stage, the adjusted odds ratio for emergency caesarean section in women whose second stage was prolonged 4.80 (95% CI 2.85–8.08; 8.3% vs 1.5%) and for operative vaginal delivery was 4.32 (95% CI 3.31–5.64; 28.7% vs 7.4%).

Compared with women who gave birth via spontaneous vaginal delivery and a normal second stage, adjusted odds ratios for obstetric anal sphincter injury were 1.42 (95% CI 0.95–2.12; 9.4 vs 6.6%) for women who gave birth via spontaneous vaginal delivery with a prolonged second stage, 2.05 (95% CI 1.23–3.40; 15.8%) for women with operative vaginal delivery and a normal second stage, and 4.96 (95% CI 3.34–7.36; 28.5%) for women who underwent an operative vaginal delivery with a prolonged second stage.

Dr Brismar-Wendel concluded that prolonged second stage of labour in primiparas was shown to be more common than previously thought. The chance of spontaneous vaginal delivery decreased linearly with the duration of the second stage of labour.

The risk of sphincter injury was almost five times higher in operative vaginal delivery after a prolonged second stage. This information can be used in the management of the second stage and timing of operative vaginal delivery.

Future genomic mapping will help treat, delay, or reverse ovarian function loss

Selective predictive and diagnostic gene panels as well as novel treatment strategies to delay or reverse the loss of ovarian function in the future will benefit patients and their families, results of a characterisation of genomic mapping of premature ovarian insufficiency show.

Dr Eva Hoffmann

Eva Hoffmann, PhD, of the Centre for Genome Damage and Stability, University of Sussex, Falmer, UK, explained that idiopathic premature ovarian insufficiency is a life-long disorder affecting an estimated 226,000 women in the UK. Epidemiological, familial and cohort studies have demonstrated a genomic component, likely underestimated due to the reduced capacity of affected women to reproduce.

The only genetic tests performed routinely are FMR1 premutation and cytogenetics, the latter specifically for X chromosome abnormalities. A myriad of implicated genes has been identified, however, the majority of which act in a monogenic Mendelian fashion.

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The presence of multiple genes is hardly surprising since the embryological formation of the primordial oocyte pool, postnatal oogenesis and folliculogenesis are highly complex pathways.

Embryological expansion of the pool depends on meiosis, hence, disruption of genes that critically control meiosis result in premature ovarian insufficiency. Frz1 allows entry into meiosis and knockout mice demonstrate embryological germ cell loss. Mutations in human FRZ1 remain to be identified.

Targeted disruption of meiotic recombination through knockout of murine Psmc3ip, Dmc1, Msh5 and Hfm1 genes results in abnormal ovarian development and absent follicles. Mutations of the human homologues PSMC3IP, DMC1, MSH5 and HFM1 have been identified in families with ovarian dysgenesis.

Genes that disrupt chromatid pairing such as STAG3 and SYCE1 have been found to cause premature ovarian insufficiency in pedigrees. Mouse homologues, Stag3 and Syce1, likewise, exert a similar effect when knocked out. Mutations in critical oocyte-specific transcription factors FIGLA and NOBOX and their murine counterparts, Figla and Nobox, result in decreased oocyte numbers and increased oocyte degeneration.

Oogenesis occurs alongside folliculogenesis mediated through exceedingly coordinated and tightly regulated paracrine and endocrine mechanisms. Disrupted molecular signalling through mutations in FSHR, LHCGR, INHA, BMP15 in humans and mice, respectively, impair folliculogenesis and result in absent mature ovarian follicles.

FMR1 premutation and cytogenetic abnormalities account for only approximately 10% of idiopathic premature ovarian insufficiency, presenting a significant unmet diagnostic need. Thorough characterisation through large-scale whole genomic sequencing is being undertaken through the Genomics England 100,000 Genome Project and the Premature Ovarian insufficiency study Linking Limited Ovarian function with genomics (APOLLO).

Identification of novel genomic factors and an understanding of the incidence of rare pathogenic gene aberrations will be a step towards completing the genomic map of this condition. In the long term, selective predictive and diagnostic gene panels as well as novel treatment strategies to delay or reverse the loss of ovarian function will benefit patients and their families. ■

Induction of labour in women who have undergone one previous C-section is safe

Induction of labour in women who have undergone one previous caesarean section has been found to be a safe option, associated with a reasonable vaginal birth rate, provided they are assessed appropriately and counselled regarding potential risks, report results of a retrospective analysis.

Dr Mohsen El-Sayed

Mohsen El-Sayed, MD, of Darent Valley Hospital, Kent, UK, and colleagues set out to examine perinatal and maternal outcomes after induction of labour in women who had undergone one previous caesarean section.

The cases of all women who had undergone one previous lower-segment caesarean section and singleton delivery and underwent induction of labour at a single centre were reviewed. Data were collected from a computerised database from 2001 to 2012 in a district general hospital in the UK.

Four hundred and sixteen women fulfilled these criteria. The general policy was to properly assess women with one previous caesarean section. If deemed appropriate, they would be induced for obstetric reasons. Methods of induction included prostaglandin gel and artificial rupture of membranes with or without syntocinon.

Regarding the mode of delivery, 31% underwent caesarean section and 69% delivered vaginally. Vaginal delivery included both spontaneous and the operative vaginal delivery. In terms of maternal outcomes, no caesarean hysterectomies were reported, nor uterine rupture or maternal mortality in the two groups of vaginal and caesarean births.

In terms of perinatal outcomes, the Special Care Baby Unit admission rate was 1.5% in the caesarean section group vs 2.1% in the vaginal birth group. No intrapartum or neonatal deaths were reported in either group. In the vaginal birth group, seven women were induced for intrauterine death.

The caesarean section rate is rising with increasing numbers of pregnant women presenting to their obstetricians and midwives with one previous caesarean section. This rise represents a challenge because the evidence is conflicting regarding mode of delivery in this population.

Initial studies concluded that induction of labour in women with a history of one previous caesarean section was comparable to spontaneous onset of labour in terms of the caesarean section rate and uterine rupture.

On the other hand, studies challenged this conclusion. Others looked at factors associated with successful vaginal birth after one caesarean section, such as previous vaginal birth.

Dr El-Sayed concluded that induction of labour in women with one previous caesarean section has been found to be a safe option associated with a reasonable vaginal birth rate, provided they are assessed appropriately and counselled regarding potential risks.

Shock index closest to insult may be most useful tool to identify and triage obstetric hypovolaemic shock

Shock index proximate to insult is significantly associated with adverse outcome, and represents a useful tool for identification and triage of the sickest patients. Shock index may not, however, represent an optimal indicator of severity of status over time, report a retrospective study of 700 patients.

Dr Alison El Ayadi

> "The results suggest that a lower shock index threshold is required as a prognostic indicator if measured beyond the initial insult.

Alison El Ayadi, ScD, MPH, of the University of California, San Francisco, explained that shock index, the ratio of pulse to systolic blood pressure, has been identified as superior to conventional vital signs as an early marker of haemodynamic compromise across multiple clinical contexts, including in obstetric haemorrhage.

Little evidence exists, however, of the clinical utility of serial shock index tracking over time. Dr El Ayadi and colleagues sought to explore pretreatment trajectories of shock index following onset of hypovolaemic shock among a cohort of women in obstetric haemorrhage.

Dr El Ayadi and coinvestigators analysed data from 700 pregnant/postpartum women in hypovolaemic shock in low-resource settings who had undergone at least two vital sign measurements following study entry before treatment initiation (that is, intravenous fluid, blood transfusion, oxytocin or nonpneumatic antishock garment).

The team reviewed running-mean, smoothed mean and median band trajectories of shock index overall and by subgroups: country, severity of condition at study entry, definitive diagnosis and maternal outcome, over 5 h following shock onset. They also estimated more complex statistical models of shock index trajectory, and accounted for within-individual differences and different follow-up times.

Median untreated follow-up time was 35 minutes (interquartile range 25–85). Haemorrhage aetiology was:

- 19.3% complications of abortion
- 15.9% uterine atony
- 15.3% retained placenta
- 13.3% ectopic pregnancy
- 13.0% placental abruption
- 23.2% other diagnoses.

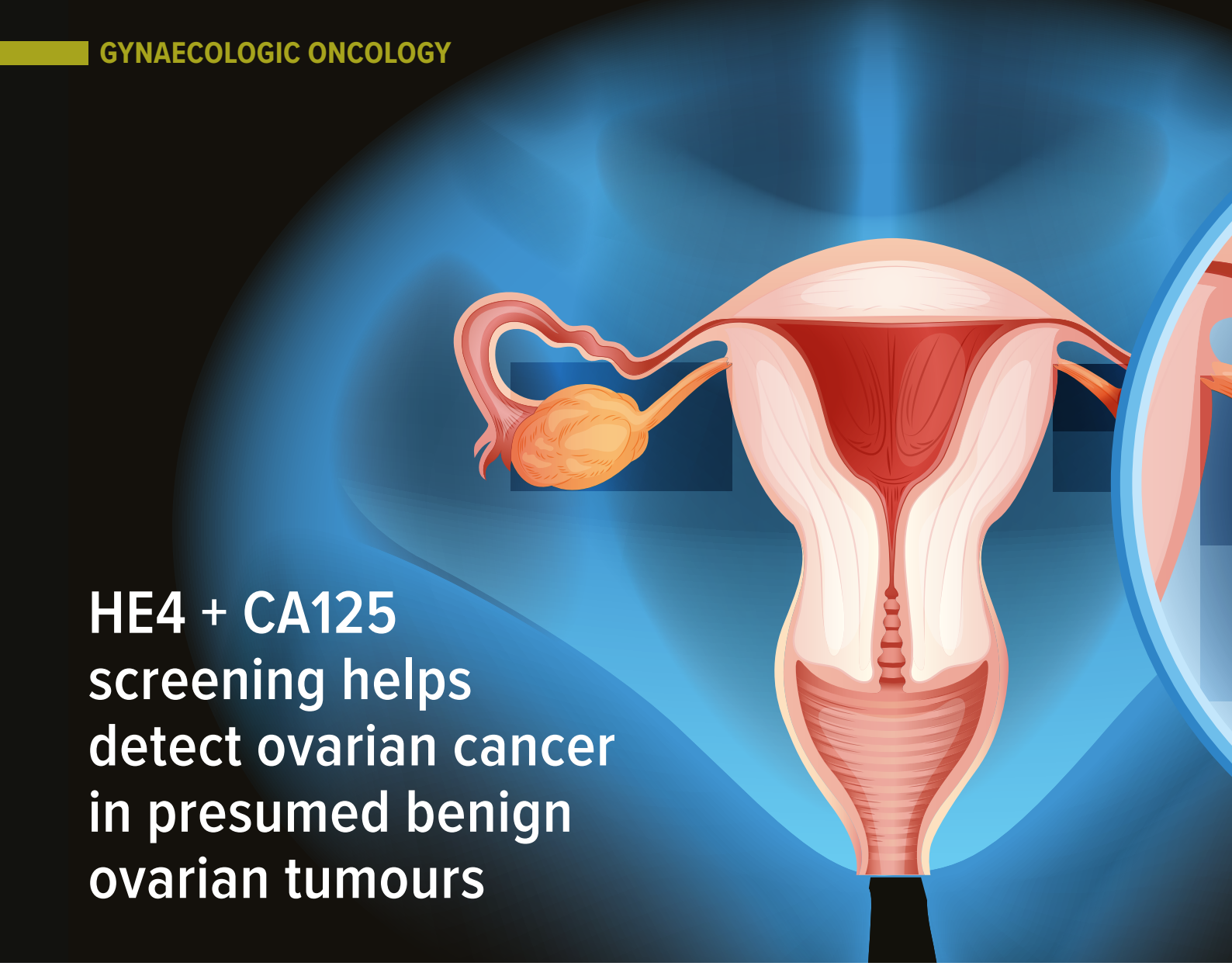
Shock indices were abnormal (≥0.9) for 90.1% of participants at study entry: 63.5% between 0.9 and 1.4, 19.1% between 1.4 and 1.69 and 7.5% at ≥1.7. Outcomes included 14 deaths (2.0%) and 11 severe maternal morbidities (1.6%).

All groups experienced improvement in shock index over time, despite not receiving treatment. Overall, shock index improved by 7.5% in the first hour after study entry, and by 18.3% through the second hour.

This improvement was observed across most subgroups, including women who died eventually or suffered severe morbidity. Median time to normal obstetric shock index (<0.9) was 240 minutes (95% confidence interval 180–270) overall and ranged by country (105–295 minutes), severity of status at study entry (15–420 minutes), and definitive diagnosis (140–815 minutes).

Dr El Ayadi concluded that observed improvements in shock index over time before treatment, even in those who suffered death or severe morbidity, may carry significant implications for the clinical utility of the shock index over time. Shock index proximate to insult is significantly associated with adverse outcome, and represents a useful tool for identification and triage of the sickest patients.

The results suggest that a lower shock index threshold is required as a prognostic indicator if measured beyond the initial insult. Improvements in shock index over time in the absence of treatment may be biologically plausible and attributable to the body's compensatory mechanisms. The pathophysiology of this phenomenon merits further evaluation. ■



HE4 + CA125 screening helps detect ovarian cancer in presumed benign ovarian tumours

The combination of human epididymis protein 4 (HE4) and carbohydrate antigen 125 (CA125) has been found to perform better than Risk of Malignancy Index and Risk of Ovarian Malignancy Index scores to predict ovarian cancer risk in patients with a presumed benign ovarian tumour, an open prospective, multicentre research study of biomarkers show.

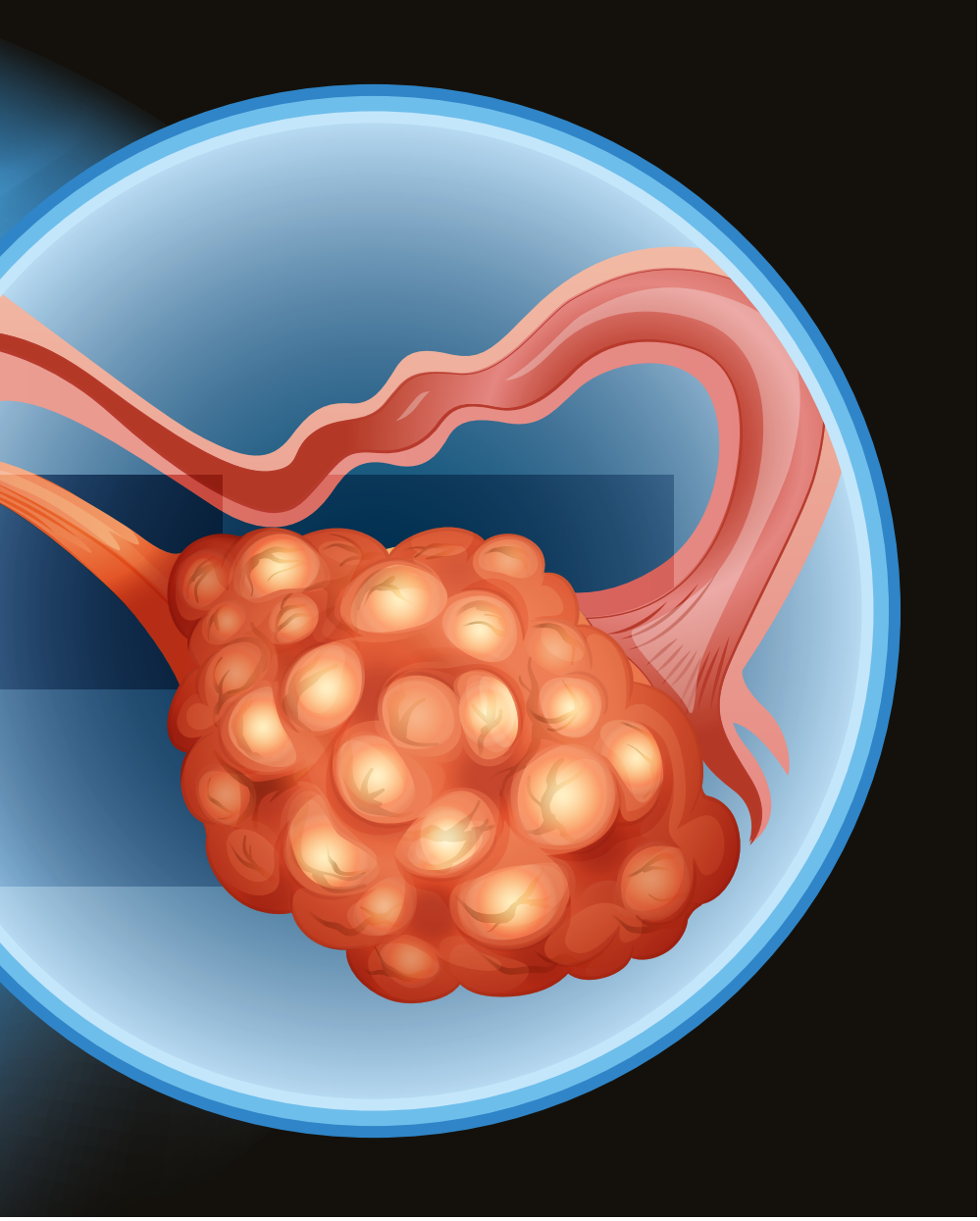
Dr Vincent Dochez

Vincent Dochez, MD, of the University Hospital of Nantes, France, said, "Ovarian cancer is the fifth leading cause of death for women with cancer worldwide. In more than 70% of cases, it is diagnosed at an advanced phase. Mean survival duration is only 5 years, (30%). More than 90% of ovarian lesions are detected before menopause, and over 60% of those detected after menopause are found to be benign."

He continued, "It seems essential to identify early malignant ovarian tumours from benign ovarian tumours. New clinical practice recommendations were published recently in France. The term presumed benign ovarian tumours has been introduced in relation to the more usual term of ovarian lesion or ovarian cyst."

Dr Dochez's objective was to evaluate the diagnostic performance of HE4, carbohydrate antigen 125 (CA125), the Risk of Malignancy Index and the Risk of Ovarian Malignancy Index in discriminating ovarian cancer from benign ovarian diseases.

The investigators evaluated several tumour markers. Dr Dochez explained, "CA125 was first described in the early 1980s. In ovarian cancer, serum CA125 levels may be elevated, but CA125 sensitivity is low in the early phases. Increased CA125 levels are also reported in other physiological or



pathological conditions (menstruation, pregnancy, endometriosis, inflammatory pleural and peritoneal diseases)."

He continued, "The diagnostic efficiency of CA125 serum monitoring is insufficient to diagnose malignancy in presumed benign ovarian tumours. Other biomarkers were developed to improve specificity for ovarian carcinomas, such as HE4. This biomarker has been reported to be overexpressed in ovarian cancer."

"Guidelines and the literature are based on studies of patients with ovarian tumours with or without presumed underlying ovarian cancer. Indeed, these studies included all patients presenting for an ovarian lesion including suspected malignant masses, in the presence or absence of evidence of invasion or metastasis (ultrasound or pelvic magnetic resonance imaging). For example, in a patient with peritoneal carcinoma, surgery is necessarily indicated in cases of pathology and diagnosis. Diagnostic markers in this situation are unnecessary because they do not alter management. A recruitment bias, therefore, is in evidence in relation to this population."

"Patients admitted for surgery with a presumed benign ovarian tumour, with no suspected sonographic criteria of polycystic ovary or cancer, nor ascites or metastasis."

The primary endpoint was specificity of CA125 and HE4 for the diagnosis of ovarian cancer. Secondary endpoints were specificity of the Risk of Malignancy Index and Risk of Ovarian Malignancy Index values and area under the curve of receiver operating characteristic curves of these markers and algorithms.

Two hundred and fifty patients were included initially in four centres and 221 patients were finally analysed:

- 209 benign ovarian lesions (94.6%)
- 12 malignant tumours (5.4%) (two adenocarcinomas and ten borderline tumours.

Mean values of the HE4, CA125, Risk of Malignancy Index and Risk of Ovarian Malignancy Index were significantly higher in the malignant group than in the benign group ($P < 0.001$). Specificity was significantly higher using a combination of HE4 and CA125 (99.5%) than using HE4 and CA125 individually (90.4% and 91.4%, respectively, $P < 0.001$).

Specificity of Risk of the Malignancy Index algorithm was significantly higher than the Risk of Ovarian Malignancy Index (99.0% and 83.3%, respectively, $P < 0.001$), but did not differ significantly vs a combination of HE4 and CA125.

Areas under the curve of CA125 (0.83), HE4 (0.91), combination of HE4 and CA125 (0.92), Risk of Malignancy Index (0.88) and Risk of Ovarian Malignancy Index (0.92) values did not differ significantly.

Moreover, the positive likelihood ratio was significantly higher for the combination of HE4 and CA125 (104.5) than for HE4 (5.81, $P = 0.004$), CA125 (6.97, $P = 0.006$) or Risk of Ovarian Malignancy Index values (4.48, $P = 0.002$).

Serum HE4 concentrations were significantly lower in patients using combined oral contraceptives than other contraceptive mode (40.6 and 48.1 pmoL/L, respectively, $P = 0.02$) and significantly higher in smokers (61.5 and 49.3 pmoL/L, respectively, $P < 0.001$), but unaffected by body mass index.

Dr Dochez concluded that the combination of HE4 and CA125 performed better than Risk of Malignancy Index and Risk of Ovarian Malignancy Index values to predict ovarian cancer risk in patients with a presumed benign ovarian tumour. While oral contraceptives and smoking appeared to influence HE4 levels, it might be beneficial to establish an algorithm including these parameters.

He said, "Our study was the first to evaluate CA125 and HE4 as well as Risk of Malignancy Index and Risk of Ovarian Malignancy Index algorithms to discriminate ovarian cancer from benign ovarian diseases, that is, presumed benign ovarian tumours." ■

"One stop" endometrial screening for Lynch syndrome effective in detecting early-stage endometrial cancer

One-stop endometrial screening for women with Lynch syndrome has been shown to be effective in detecting early-stage endometrial cancer, report a single-centre, retrospective review.

Mourad W. Seif, MD, of St. Mary's Hospital, UK, explained that Lynch syndrome, otherwise known as hereditary nonpolyposis colorectal cancer (HNPCC), is autosomal dominant, and predisposes patients to a variety of cancers, including endometrial cancer, with substantial lifetime risk and at a younger age.

In many cases, the cancer can present before menopause as the first or sentinel cancer. In view of the increased lifetime risk of endometrial cancer and its insidious mode of presentation, surveillance strategies are being unveiled across a number of institutions worldwide for early detection of atypical hyperplasia and endometrial cancer.

"Over the years," Dr Seif said, "strategies for screening of gynaecological cancers have been developed, following the success of cervical cancer screening. Screening for endometrial cancer in generally low-risk populations has not been recommended.

Strategies are needed, however, to screen high-risk women such as those with Lynch syndrome because lifetime risk of endometrial cancer has been rising. This cancer can also develop in much younger women. Endometrial cancer usually develops postmenopausally. Hence the consensus is to start screening women with Lynch syndrome at age of 35 years."

At St. Mary's Hospital in Manchester, UK, a one-stop endometrial surveillance service was installed in 1999. "In fact," Dr Seif noted, "we began this screening service almost 20 years ago." The service uses a combination of transvaginal ultrasound scanning, outpatient hysteroscopy and endometrial biopsy.

A total of 176 patients were referred to the endometrial screening service over a 17-year period. Fifty-two patients are currently undergoing active annual screening. Screening commences at age of 35 years. Inclusion criteria are family history suggestive of Lynch syndrome, 50% risk of pathogenic familial mutation and women with a pathogenic mutation for MLH1, MSH2 and MSH6.

Fourteen patients in the service were diagnosed with endometrial cancer or atypical endometrial hyperplasia as a direct result of screening. Patients were in screening an average of 4 years before diagnosis of the abnormality, and all are still living. A further 15 women chose total laparoscopic or abdominal hysterectomy and bilateral salpingo-oophorectomy to reduce risk.

A satisfaction survey was recently administered and included patients with Lynch syndrome (n=6). Of those questioned, 100% understood the explanation of the procedure, felt they had the opportunity to ask questions and found staff friendly and supportive.

During hysteroscopy, 67% of patients felt some pain, but all felt this was acceptable. Overall satisfaction rates ranged between 8 and 10 of 10, where 10 was the best possible, and 50% of patients rated the service 10.

Dr Seif concluded that the one-stop endometrial screening service for women with Lynch syndrome was shown to be effective in detecting atypical hyperplasia and early-stage endometrial cancer.

The screening program provides an opportunity for women to choose between risk reduction surgery and the conservative screening approach, and is well accepted. "Of note," he said, "our data revealed women who had hyperplasia in their 30s and cancer in their early 40s."

"The data we presented are not results of a particular study, but rather are results of a service which we felt necessary to cover the large gap in health care for this population of high-risk women. The data will inform our local health care policy. In fact, we have organised an upcoming meeting of international experts to formulate consensus guidance with respect to endometrial surveillance for women with Lynch syndrome."

Patients with abnormal uterine bleeding should proceed straight to hysteroscopy

It is cost- and time-efficient to assess patients presenting with abnormal uterine bleeding directly in the hysteroscopy clinic to avoid additional delay and patient anxiety, report results of a multicentre histological study.

Dr Shirin Irani

Shirin Irani, MD, of the Heart of England Foundation Trust, Birmingham, UK, explained that abnormal uterine bleeding encompasses a range of presenting problems including postmenopausal bleed.

No standardised pathway for investigation has been established, but patients commonly undergo transvaginal ultrasound followed by endometrial sampling, often performed initially by Pipelle biopsy. Biopsy is performed frequently in clinic or after outpatient hysteroscopy. A common problem with Pipelle biopsy as a blind procedure is attaining an inadequate sample.

Dr Irani and colleagues set out to investigate the rate of inadequate Pipelle samples performed in the setting of the outpatient gynaecology clinic and after outpatient hysteroscopy. The also attempted to assess for a difference in the significance of an inadequate sample in the management of patients who undergo hysteroscopy vs. those who do not.

Histological results from 389 consecutive endometrial samples obtained over 1 month in from 2015 from three hospital sites in the Heart of England Foundation Trust were collated.

Rates of inadequate samples were calculated for samples taken in clinic and after hysteroscopy. Electronic case notes of patients with inadequate samples were reviewed to determine whether they underwent further investigation before discharge or a management decision was reached.

Overall, 8.2% of samples from outpatient clinics were inadequate vs 7.9% of samples performed after hysteroscopy. None of the patients who underwent hysteroscopy proceeded to further investigation vs 91.2% of those with inadequate samples from clinics.

In patients presenting with postmenopausal bleed, the rate of inadequate samples was comparable between those performed in clinics (13.0%) and after hysteroscopy (13.1%). Eighty percent, however, of patients with inadequate samples from clinics required further investigation.

Of the 11 patients who went on to further investigation, eight underwent hysteroscopy and repeat Pipelle biopsy, one underwent dilatation and curettage, and two, magnetic resonance imaging. These patients attended an average of two more outpatient appointments before a management or discharge decision was reached.

Dr Irani concluded that patients whose sample taken in outpatient clinics was inadequate required further investigation and appointments. This was not necessary in patients whose uterine cavity was assessed hysteroscopically.

Location where the sample was taken did not affect the chance of the sample being inadequate. It could therefore be argued that, especially in the context of postmenopausal bleed that poses additional technical challenge of sampling a thin and atrophic endometrium, it is cost- and time-efficient to assess patients presenting with abnormal uterine bleeding directly in the hysteroscopy clinic to avoid additional delay and patient anxiety. ■

Pelvic vein incompetence and chronic pelvic pain are strongly associated

The frequency of pelvic vein incompetence in both chronic pelvic pain patients and healthy women has been shown to be very much higher than expected, with a strong statistical association between chronic pelvic pain and pelvic venous incompetence, a case-control study shows.

Dr David Riding

> "Though chronic pelvic pain was clearly associated with reduced self-perception of health, patients were often discharged from clinical services before pelvic vein incompetence has been excluded.

David Riding, MSc, MBChB, MRCS, of the University of Manchester and University Hospital of South Manchester, UK, explained that chronic pelvic pain affects 24% of premenopausal women, accounts for 20–30% of gynaecology outpatient appointments, and costs €3.8 billion per year.

Despite extensive investigation including laparoscopy, 55% of women fail to receive a diagnosis and endure persistent symptoms. Women with pelvic vein incompetence describe a dull pelvic ache throughout the day that is worse on standing and sitting.

Dr Riding and colleagues set out to explore the frequency of pelvic vein incompetence in women with chronic pelvic pain vs matched healthy controls.

Women with chronic pelvic pain with no gynaecological cause despite diagnostic laparoscopy investigation were invited to participate. Age- and parity-matched healthy volunteers were recruited as controls.

A validated transvaginal Duplex ultrasound technique was used to detect pelvic vein incompetence, defined as reflux >0.7 s throughout the ovarian or internal iliac veins in the semistanding position with reflux into second-order veins, pelvic varices, or the thigh. All participants completed validated symptom and generic health status questionnaires.

An interim analysis was conducted after recruiting 100 subjects, including 44 matched case-control pairs. Pelvic vein incompetence was found in 15 (34.1%) women with chronic pelvic pain and in seven (15.9%) healthy controls ($P = 0.046$).

Pelvic varices were found in 12 (27.3%) women with CPP and only one (2.3%) control ($P = 0.002$). 'Dull' pain was experienced by 54.5% of women with pelvic vein incompetence (case or control) vs 22.7% of those without pelvic vein incompetence ($P = 0.005$).

Women with pelvic vein incompetence were more likely to experience pain throughout the day. Mean EuroQol-5D 3L quality of life scores were significantly lower in cases than controls for overall health evaluation (72.6% vs 86.9%, $P < 0.001$) and health state description (69% vs 98%, $P < 0.001$).

Dr Riding concluded that the frequency of pelvic vein incompetence in both chronic pelvic pain patients and healthy women was very much higher than expected, with a strong statistical association between pelvic vein incompetence and chronic pelvic pain. Pelvic vein incompetence was also associated with a characteristic symptom profile of dull lower abdominal, pelvic and thigh pain that lasts throughout the day.

Though chronic pelvic pain was clearly associated with reduced self-perception of health, patients were often discharged from clinical services before pelvic vein incompetence has been excluded. A randomised controlled trial of coil/foam occlusion of incompetent pelvic veins in women with chronic pelvic pain is underway to explore the efficacy of treatment. ■

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Patient age and size/weight of endometrial polyps in postmenopausal women predictive of malignancy

Patient age and size/weight of endometrial polyps in postmenopausal women have been found to be predictive of malignancy, results of a 5-year, prospective histological study suggest.

Lidia Ewa Krasnicka, MD, of the University Hospital of Wales, Cardiff, UK, explained that she and her colleagues set out to predict the probability of malignancy or hyperplasia in endometrial polyps of postmenopausal women undergoing outpatient hysteroscopic resection.

They studied symptomatic postmenopausal women undergoing outpatient hysteroscopic resection for known endometrial polyp(s) at a purpose-built outpatient hysteroscopic suite in a large university hospital.

Dr Ewa Krasnicka said, "I wanted to be able to give patients with a polyp a more accurate risk of cancer. Patients could then give more informed consent."

The women presented with vaginal bleeding to the gynaecology outpatient department and were subsequently found to harbour endometrial polyp(s) on transvaginal ultrasound scan or diagnostic hysteroscopy.

All polyps were removed using a traditional 8- or 10-mm resectoscope. Resection was carried out with monopolar diathermy and glycine following an intracervical block. All specimens were volumetrically assessed and weighed before formal histological assessment.

Data were analysed with IBM SPSS Statistics version 20 and multinomial logistic regression analysis was carried out to assess the relationship between patient age, volume and weight of the polyp and the dependent variable of hyperplasia or malignancy.

In all, 269 patients were included. Of the 269 polyps included in the data set, 21 (7.8%) were endometrial cancer and 33 (12.3%) were hyperplastic. The best-fit regression model generated can be used to estimate the probability of hyperplasia or malignancy in the polyp.

Dr Ewa Krasnicka concluded that patient age and the size or weight of the polyp can be predictive of cancer or hyperplasia in the polyp. Preoperative ultrasound assessment of polyp volume combined with patient age allows for a better estimate of the chance of hyperplasia or malignancy. This information is beneficial for preoperative patient counselling, as well as prioritisation of surgical urgency.

She said, "We are looking at other patient factors, such as body mass index, to add to the predictive model. The model could be easily implemented in a smartphone application."

Two trials of uterine artery embolisation confirm high success, with caveats

Two UK trials of uterine artery embolisation performed at National Health Service centres point to success of the procedure, with larger fibroids more likely to need further surgical intervention, report two 3-year retrospective reviews.

Brian P. Dromey, MD, of Leeds Teaching Hospitals National Health Service Trust, and D. Balachandran Nair, MD, of Barnet General Hospital, London, both conducted 3-year retrospective studies of uterine artery embolisation.

Dr Dromey introduced his work by explaining that uterine artery embolisation was first reported for symptomatic uterine fibroids in 1991. The safety of the procedure has been established in the literature. Thirty-two percent of women have been reported to undergo further intervention for fibroid symptoms or procedure-related complications after 5 years, vs 4% for hysterectomy.

Dr Dromey reviewed data collected from 2012–2014. Eighty-one of the studied patients were followed subsequent to uterine artery embolisation.

A high rate of technical success was observed, with only a single abandoned procedure. Of the 81 cases, 52 women (67%) underwent uterine artery embolisation for heavy or painful periods, 21 for pressure symptoms, and four for chronic pelvic pain.

The Royal College of Obstetricians and Gynaecologists recommends that women be examined between 3 and 6 months post uterine artery embolisation. Sixty-eight women were scheduled for radiological follow-up. Over 3 years, 61 women (76%) were seen by the gynaecology department after uterine artery embolisation.

Of these, 20 women were seen on a nonscheduled basis. Sixteen were seen with a clinical description of vaginal discharge, three were seen with infection directly attributable to uterine artery embolisation and one was seen following prolapse of the uterine fibroid.

Of the 16 women seen with a noninfectious discharge, five underwent elective hysterectomy. All patients seen with pelvic infection or prolapse of the fibroid underwent hysterectomy. At the time of data collection, 33 of the 81 women (41%) had undergone additional treatments, were pregnant, or were in the care of reproductive medicine specialists.

The incidence of further intervention was noted to be greater in women with two or more types of fibroid. When compared to women with radiological findings of either subserosal, intramural or submucosal uterine fibroids, the intervention rate for women with multiple fibroid types was 39.3%, whereas the rate for further intervention in women with a single fibroid type was 13.7%.

> "The findings reiterate the importance of individualisation with regard to patient counselling and options offered to treat large fibroids.

Dr Dromey concluded that uterine artery embolisation was shown to be safe, requires a mean hospital stay of one night and can be effective for treating uterine fibroid symptoms. During the follow-up period, 15% of women who underwent uterine artery embolisation progressed to hysterectomy.

The data suggest that further interventions are more likely in women with multiple fibroid types. Women with a single fibroid type were half as likely as the quoted Royal College of Obstetricians and Gynaecologists incidence to undergo further interventions. Women with well described fibroids of a single type benefited most from uterine artery embolisation and were less likely to undergo additional interventions.

D. Balachandran Nair, MD, of Barnet General Hospital, London, explained that widespread interventional procedures over the last 2 decades has been accompanied by less stringent case selection and the possible need for further intervention.

Dr Nair and colleagues set out to examine all women undergoing uterine artery embolisation for symptomatic fibroids from 2012 through 2015 in a district general hospital, to assess those requiring further surgical intervention and to characterise these women with the goal of establishing possible risk factors, which, in turn will aid in case selection and patient counselling.

All patients undergoing surgical intervention following uterine artery embolisation were characterised with regard to presenting symptoms, size and site of fibroid (based on preprocedure magnetic resonance imaging), coexisting adenomyosis, reason for further intervention, type of intervention, and interval between the primary procedure and further intervention.

All patients underwent MRI scanning to assess suitability prior to the procedure. Patients were followed for a minimum of 8 (range 8–44) months post procedure.

Two hundred and ten women underwent uterine artery embolisation for fibroid uterus over the 3-year period. Of these, 15 required further surgical intervention in the form of total or subtotal hysterectomy (n=12), open myomectomy (n=1) or hysteroscopic resection of degenerated fibroid (n=2). Two of 15 required hysterectomy as an emergency procedure due to acute presentation within the first 3 months.

The remaining women underwent an elective procedure for persisting/recurring symptoms during the second and third years post uterine artery embolisation. Heavy periods were the predominant presenting symptom. Most patients who required further intervention harboured intramural fibroids >9 cm (66%). Only one of the 15 women exhibited coexisting adenomyosis confirmed by MRI.

Emergency hysterectomies were performed for suspected sepsis. Ongoing/recurrent heavy periods and persisting pressure symptoms were common indications for further elective intervention.

Dr Nair concluded that rates of surgical intervention following uterine artery embolisation for symptomatic fibroids were comparable to those previously reported in large studies.

Results of this study show that risk of requiring further intervention is higher for larger fibroids. No increased prevalence of adenomyosis was observed in patients requiring further intervention.

The findings reiterate the importance of individualisation with regard to patient counselling and options offered to treat large fibroids. ■

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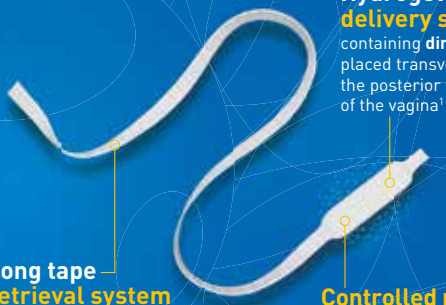

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MINIMUM PRODUCT INFORMATION CERVIDIL® [10 mg dinoprostone (Prostaglandin E2)] VAGINAL INSERT. **INDICATION:** Cervical ripening in patients, at or near term, who have favourable induction features and in whom there is a medical or obstetrical indication for induction of labour. **CONTRAINDICATIONS:** hypersensitivity to dinoprostone or other constituents of the vaginal insert; patient carrying more than one fetus or fetus is in non-vertex presentation; commenced labour; when oxytocic drugs are being given or to be given intravenously within 30 minutes; when strong prolonged uterine contractions are inappropriate e.g. previous major uterine surgery, cephalopelvic disproportion, fetal malpresentation, suspicion or evidence of fetal distress, more than three full term deliveries, previous cervical surgery or cervical rupture; current pelvic inflammatory disease unless prior treatment; where vaginal delivery is not indicated; unexplained vaginal bleeding; abnormal cardiotocography; suspected fetal compromise; ruptured membranes; post-amniotomy; uterine hyperstimulation; hypertonic uterine contractions. **PRECAUTIONS:** For hospital use only by trained obstetrical personnel with appropriate facilities; caution if cervical (Bishop) Score ≥ 8; incorrect positioning of CERVIDIL insert; use only if facilities for continuous fetal and uterine monitoring are available; remove if maternal or fetal complications or adverse effects occur or if labour commences; remove prior to amniotomy and oxytocin administration; previous uterine hypertony, glaucoma, epilepsy or asthma; cease NSAIDs prior to administration; second dose not recommended; women > 35 years, with complications during pregnancy and women at gestational age > 40 weeks – monitor immediately post-partum for early signs of a developing disseminated intravascular coagulation (DIC); cardiovascular, renal or hepatic impairment. Pregnancy Category C. Not for use during lactation. **INTERACTIONS:** Concurrent use of CERVIDIL in patients receiving oxytocics not recommended. Following the removal of CERVIDIL, a waiting period of at least 30 minutes is recommended before sequential use of oxytocin. **ADVERSE EFFECTS:** Common (1% to <10%): uterine hyperstimulation, uterine tachysystole, fetal distress. **POST MARKETING:** fever, nausea, vomiting, diarrhoea, abdominal pain, uterine rupture, genital oedema and anaphylactic reaction. Increased risk of post-partum DIC has been reported in patients whose labour was induced by pharmacological means, either with dinoprostone or oxytocin. **DOSAGE AND ADMINISTRATION:** Remove from freezer immediately before use. Remove CERVIDIL from packaging by tearing along the foil, do not use scissors or sharp instruments as this may damage the product. Use the retrieval tape to gently pull the product out of the sachet. Insert one pessary (vaginal insert) high into the posterior fornix using small amounts of water-soluble lubricant if required. Ensure enough withdrawal tape for removal. Patient to remain recumbent for 30 minutes after insertion. Refer to the full PI for instructions and recommendations on removal. CERVIDIL should not be used beyond 12 hours. After removal ensure that entire product, pessary (vaginal insert) and retrieval system, has been removed from the vagina. **STORAGE:** Freezer below -18 ºC. Controlled periods of time of up to one month at 2 to 8 ºC can be allowed within the shelf life of the product.(#37592-v4A)

References: 1. CERVIDIL® approved Product Information.

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