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MEchanical DIlatation of the Cervix in a Scarred uterus (MEDICS): the study protocol of a randomised controlled trial comparing a single cervical catheter balloon and prostaglandin PGE2 for cervical ripening and labour induction following caesarean delivery

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ABSTRACT

Introduction Labour induction in women with a previous caesarean delivery currently uses vaginal prostaglandin E2 (PGE2), which carries the risks of uterine hyperstimulation and scar rupture. We aim to compare the efficacy of mechanical labour induction using a transcervically applied Foley catheter balloon (FCB) with PGE2 in affected women attempting trial of labour after caesarean (TOLAC).

Methods and analysis This single-centre non-inferiority prospective, randomised, open, blinded-endpoint study conducted at an academic maternity unit in Singapore will recruit a total of 100 women with one previous uncomplicated caesarean section and no contraindications to vaginal delivery. Eligible consented participants with term singleton pregnancies and unfavourable cervical scores (≤5) requiring labour induction undergo stratified randomisation based on parity and are assigned either FCB (n=50) or PGE2 (n=50). Treatments are applied for up to 12 hours with serial monitoring of the mother and the fetus and serial assessment for improved cervical scores. If the cervix is still unfavourable, participants are allowed a further 12 hours' observation for cervical ripening. Active labour is initiated by amniotomy at cervical scores of ≥6. The primary outcome is the rate of change in the cervical score, and secondary outcomes include active labour within 24 hours of induction, vaginal delivery, time-to-delivery interval and uterine hyperstimulation. All analyses will be intention-to-treat. The data generated in this trial may guide a change in practice towards mechanical labour induction if this proves efficient and safer for women attempting TOLAC compared with PGE2, to improve labour management in this high-risk population.

Ethics and dissemination Ethical approval is granted by the Domain Specific Review Board (Domain D) of the National Healthcare Group, Singapore. All adverse events will be reported within 24 hours of notification for assessment of causality. Data will be published and will be available for future meta-analyses.

Strengths and limitations of this study

- This is a prospective randomised trial with randomisation into one of two interventions.
- This is a prospective randomised open, blinded endpoint study, and although participants and proceduralists applying the priming agent are aware of the intervention, the data analyst is blinded to the intervention.
- This is a direct comparison of two accepted methods of labour induction in women with one previous caesarean section.
- The study has a clear primary endpoint of the rate of change in cervical Bishop score, which is the main determinant of labour success prior to initiating induction with amniotomy with or without oxytocin.
- This study is not powered to determine the differences in rates of rare adverse events, including uterine scar rupture.

Trial registration number NCT03471858; Pre-results.

INTRODUCTION

The steady increase in caesarean section rates (CSR) and the associated rise in surgical and obstetric morbidity and healthcare costs are of growing concern globally.[1] The 2015 WHO statement on surgical delivery described the optimal CSR as between 10% and 15% by international healthcare consensus.[1 2] However CSR across heterogeneous populations has seen steady inflation from ~20% in the 1990s to ~30% by the 2000s, attributed largely to the rising CSR in nulliparous women in spontaneous labour and women

with a previous caesarean section (CS).[1 3–5] Although the overall incidence of complications due to CS[6] in high-resource nations is low,[7] avoidance of repeated CS and their associated surgical risks is a desirable although challenging goal. Successful vaginal births after caesarean section (VBAC) are associated with fewer maternal and neonatal complications, a higher chance of successful future vaginal delivery and the avoidance of risks associated with multiple repeat CS.[8] Numerous studies and systematic reviews have reported successful VBAC rates of 72%–76% after a single CS.[9] Thus, encouraging suitable pregnant women to attempt VBAC is important in labour management to maintain a reasonable caesarean delivery rate in keeping with international consensus.[7 9–15] Nevertheless, there is sufficient concern over the risks of uterine scar rupture (incidence ~0.4%–0.5%),[16] leading to fewer trials of labour after caesarean delivery (TOLAC) in the USA, from 62% pre-1996 to 44% after 1996.[17]

Induction of labour (IOL) is a common obstetric intervention proposed for numerous indications such as medical disorders in pregnancy and intrauterine growth restriction, with the aim of achieving vaginal birth.[6 14 18] The key predictor to successful labour induction and vaginal delivery is the modified Bishop score (BS),[19 20] reflecting the architectural changes in the cervix that lead to effacement and dilatation, an indicator of how 'favourable' the cervix is for labour. A modified BS of more than 5 out of 10 points indicates a favourable cervix and a higher likelihood of vaginal delivery.[21–24] Consequently, before active labour is initiated by amniotomy and/or oxytocin infusion, an unfavourable cervix may require ripening or priming to improve the BS and likelihood of vaginal delivery.[25 26] IOL rates have increased over the last 20 years, from 9.5% in the 1990s to 22.5% in 2006 in the USA,[27–29] with up to 25%–35% of nulliparous women being induced at term.[30–32] Cervical priming and IOL can be achieved via mechanical or pharmacological methods.[25 33] There is concern, however, that IOL with prostaglandins may increase scar rupture rates up to fivefold in women with previous CS compared with spontaneous labour, leading to various professional bodies discouraging prostaglandin induction in the presence of a uterine scar.[6 14 16] More recent cohort studies and meta-analyses have shown that these increased rates are seen only with prostaglandin E1 and not with prostaglandin E2 (PGE2).[34–37] Several mechanical devices have been evaluated for priming and IOL, of which transcervical balloons such as the Foley catheter balloon (FCB) are the most widely used.[38–40] In women with an unscarred uterus, mechanical induction demonstrates a lower incidence of uterine hyperstimulation and similar CSR compared with locally applied prostaglandins.[34 38 41–47] Similarly, women with a previous CS induced with FCB showed no differences in uterine scar rupture rates when compared with spontaneous labour or IOL with amniotomy or oxytocin.[48–53]

A strong incentive to restrain healthcare costs and reduce surgical morbidity has increased interest in promoting VBAC, and therefore in a safe and effective induction agent for TOLAC.[54] The majority of available evidence attesting to the safety of mechanical induction in VBAC however is derived from retrospective cohort studies, and data from randomised controlled trials (RCTs) are limited. Most studies in a recent Cochrane review were underpowered and limited by the quality of evidence presented.[55] Only one RCT compared the efficiency of a double-balloon cervical catheter (DBC) with vaginal PGE2 for VBAC, demonstrating higher rates of induction failure and oxytocin augmentation in the mechanical group and similar rates of induction interval, birth within 24 hours of initiation, CS and neonatal outcomes.[42] Although FCB is used with increasing frequency in women attempting TOLAC due to its wide availability and low cost, and is a recommended alternative to prostaglandins,[9 56 57] vaginal PGE2 is still the standard priming agent for TOLAC in women with unfavourable BS at our institution. Thus, there is a need to objectively evaluate the efficacy of cervical priming with FCB against the standard vaginal PGE2. We propose a prospective, randomised, open, blinded-endpoint (PROBE) study entitled the 'MEchanical DIlation of the Cervix in a Scarred uterus' (MEDICS) to interrogate the hypothesis that FCB is the more effective and safer cervical priming method for women with one previous CS.[58] Because a favourable cervical score is the best predictor of successful labour prior to IOL, and as there are other reasons that TOLAC can be terminated, including the suspicion of scar rupture or fetal intolerance, the objective of this trial is to determine the rate of change in cervical BS (from unfavourable to favourable), as well as successful labour induction, vaginal delivery, adverse events and patient satisfaction.

METHODS AND ANALYSIS

Trial design

This single-centre, open-label PROBE trial will be conducted at the maternity unit of the National University Hospital of Singapore (NUH), an academic teaching hospital. The trial has been registered with ClinicalTrials.gov, and is designed in accordance with the Consolidated Standards of Reporting Trials guidelines, the Standard Protocol Items: Recommendations for Interventional Trials 2013 guidelines[59] and the Declaration of Helsinki.[60] Neither the patient nor the proceduralist will be blinded to the intervention, but data collectors and analysts will be blinded to the intervention during data analysis.[58] Recruitment commenced in February 2019 and this trial will run over a period of 2 years.

Target population

Our target population consists of women ≥21 years of age (legal age of consent in Singapore) with one previous uncomplicated CS who are potential TOLAC candidates, with current singleton pregnancies of gestational age ≥37 weeks and with no contraindications to vaginal delivery. Exclusion criteria include, but are not limited

Table 1 Inclusion, exclusion and discontinuation criteria

Inclusion criteria	Exclusion criteria	Discontinuation criteria
► Aiming for TOLAC. ► Written informed consent. ► Singleton pregnancy. ► Gestational age ≥37 weeks. ► Understands the risks of TOLAC. ► Reactive CTG pre-induction. ► Unfavourable Bishop score ≤5 requiring cervical priming. ► Female 21 years of age and above at time of trial participation. ► One previous uncomplicated transverse lower segment caesarean section. ► Eligible for IOL for standard obstetric indications (postdate/post-term pregnancies at 40–41 completed weeks of gestation).	► Refusal to participate or to be randomized. ► Multifetal pregnancy. ► Latex allergy or poorly controlled asthma. ► Congenital uterine abnormality. ► Women with ≥2 caesarean sections. ► Previous classical or lower segment vertical incision, or inverted T or J incision in previous caesarean delivery. ► Previous uterine surgery with contraindication to vaginal delivery. ► Fetal contraindication to vaginal delivery (including major fetal abnormalities). ► Malpresentation or cord presentation. ► Placenta praevia <20 mm from internal cervical os. ► Maternal contraindication to vaginal delivery. ► Chorioamnionitis at presentation. ► Antepartum haemorrhage of undetermined origin deemed a contraindication to TOLAC. ► Suspected fetal macrosomia (estimated weight on ultrasound >4 kg) and deemed a contraindication to TOLAC.	► Failure to insert FCB. ► Suspicion of scar dehiscence or rupture. ► Maternal request to withdraw from trial. ► Severe unexplained bleeding per vaginum. ► Sepsis or chorioamnionitis necessitating expedited delivery. ► Maternal need to expedite delivery, for example, acute fetal distress.

CTG, cardiotocogram; FCB, Foley catheter balloon; IOL, induction of labour; TOLAC, trial of labour after caesarean.

to, refusal to be randomised; opting for elective repeat CS; ≥2 previous CS; a previous classical or lower segment vertical incision; inverted T or J incision in the previous CS; any structural abnormality of the uterus; multifetal pregnancy; placenta praevia or accreta; clinical suspicion of chorioamnionitis at presentation; and other fetal contraindications to vaginal delivery (table 1).

Patient involvement and recruitment

All candidates are thoroughly counselled during antenatal consultations on adverse outcomes of VBAC, including, but not limited to, uterine scar rupture, anorectal trauma, hypoxic-ischaemic encephalopathy, caesarean hysterectomy, and maternal or perinatal death.[9 61] On identification of medical indications for IOL, women will be informed of the trial and provided with a patient information sheet describing the processes and risks of the study. Standardised counselling will be performed using a checklist enumerating VBAC risks. Informed written consent will be taken in the clinic if the patient desires TOLAC, meets the eligibility criteria and agrees to participate in this trial (table 1). If eligible patients have not been counselled for trial participation at the clinic, they will be screened, consented and recruited on admission to the labour ward (table 2). Consent will be taken by a study investigator in accordance with good research practice. Confidentiality is also strictly maintained in accordance with the Personal Data Protection Act in Singapore. This research was designed without patient or public involvement. Neither patients nor the public were invited to comment on the study design, consulted to develop patient-relevant outcomes or interpret the results. Neither patients nor the public were invited to contribute to the writing or editing of this document for readability or accuracy. Results will not be disseminated to study participants.

Stratified randomisation and blinding/unblinding

Randomisation will be performed by a secure, computer-generated, online, centralised, web-based system from Sealed Envelope Ltd. 2019 (https://www.sealedenvelope.com/simple-randomiser/v1/lists) in a 1:1 ratio between

Table 2 Timeline of recruitment of potential patients

Gestational age	Process	Information required/documents
Booking visit	Identification of potential patients. Education on mechanical IOL and the trial.	Flag patient in electronic records and study file. Patient information sheet (PIS) explaining the trial given to the patient.
>30 weeks	Identification of potential patients. VBAC counselling and consent. Discussion on methods of IOL if required. Education on mechanical IOL and the trial.	VBAC counselling. Addendum given to the patient explaining VBAC risks. PIS for the trial.
>36 to <40 weeks	Identification of potential patients who may require IOL <40 weeks for medically-indicated reasons. VBAC counselling and consent. Discussion on methods of IOL if required. Education on mechanical IOL and the trial. Trial consent.	VBAC counselling and addendum. PIS for the trial. Schedule date for IOL. Consent form signed for the trial.
≥40 weeks	Identification of potential patients who may require IOL for postdates/post-term pregnancies or other medical indications. Discussion on methods of IOL if required. Education on mechanical IOL and the trial. Trial consent.	VBAC counselling and addendum. PIS for the trial. Schedule date for IOL. Consent form signed for the trial (if not yet done).
Arrival to delivery suite	Identification of potential patients if not previously recruited for the trial. Discussion of methods of IOL. Trial consent.	VBAC counselling and addendum. PIS for the trial. Consent form signed for the trial (if not yet done). Randomisation.

IOL, induction of labour; PIS, patient information sheet; VBAC, vaginal birth after caesarean section.

each of the two treatment groups and will be stratified by the presence of previous vaginal deliveries to reduce prognostic imbalance. The stratification will result in population A with no previous vaginal births and population B with one or more previous vaginal deliveries. Thus, we will generate two series of sequentially numbered, sealed, opaque envelopes stratified as above. On admission to the labour ward, the separate consent forms for VBAC and trial participation will be checked and confirmed by the patient and the investigator to ensure continued eligibility for the trial. Admission cardiotocogram (CTG) will be performed to assess fetal well-being. The next sealed, opaque envelope in prelabelled series, selected from population A or B, will be opened and the intervention assigned to the patient. Women who decline participation after randomisation but before commencing induction will be managed according to existing labour protocols and will not be replaced in the trial; the reasons for their withdrawal will be recorded. Randomised participants will undergo cervical assessment (0-hour timepoint) performed by a study investigator who is a practising clinician in obstetrics and gynaecology. Cervical features will be recorded in the data collection proforma. Only three members of the study team will perform cervical assessments at the 0 hour, 6 hours and 24 hours timepoints to ensure consistency and minimise interobservational variability (figure 1). These three investigators have verified that their individual cervical measurements are similar. Labour providers who are not part of the study team will be blinded to the results of randomisation and the intervention the subject receives as far as possible. Unblinding may occur in the event of acute changes in status requiring additional vaginal examinations, for example, fetal distress, suspected abruption or uterine rupture. Data analysts will remain blinded to interventions.

Mechanical induction with a transvaginal cervical balloon catheter

A two-way 18 Fr single-balloon Foley catheter (Bardia, Bard Medical Division, Georgia) will be introduced transcervically into the extra-amniotic intrauterine space with aseptic technique using vaginal speculum and sponge-holding forceps. The balloon will be inflated with up to 50 mL of sterile water, barring maternal intolerance, and left in situ for 12 hours or until active labour if this commences first. For logistical reasons, the on-duty resident will perform the 12-hour cervical assessment, remove the balloon and document the findings in the electronic clinical records; these data will be extracted and entered into the data

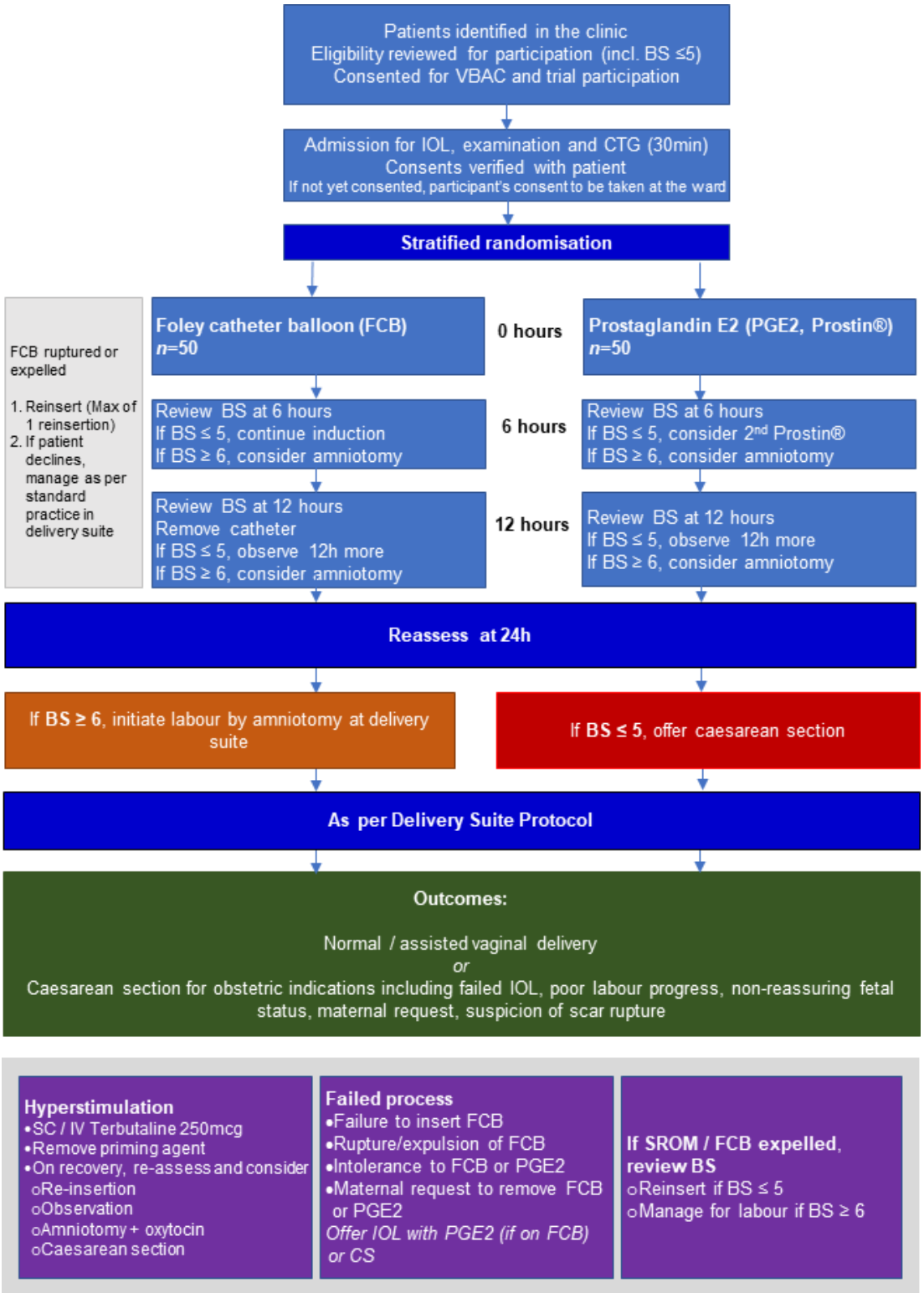

Figure 1 Intervention protocol showing recruitment, randomisation, monitoring and delivery. BS, Bishop score; CS, caesarean section; CTG, cardiotocogram; IOL, induction of labour; IV, intravenous; SC, subcutaneous; VBAC, vaginal births after caesarean section; SROM, Spontaneous Rupture of Membranes

collection proforma by the study investigators. If active labour does not occur within 12 hours and BS is still ≤5, the balloon will be removed, clinical assessment repeated and the participant observed for a further 12 hours if there is no need to expedite delivery. Clinical assessment by a trained resident will be repeated at the end of the surveillance period (24 hours from initiation). In the event of insertion failure or maternal intolerance, the participant will be offered the opportunity to discontinue the trial and proceed with PGE2

induction following labour ward protocol, or caesarean delivery. Outcomes will be analysed by intention-to-treat (figure 1).

Induction with dinoprostone (PGE2)

A single 3 mg dinoprostone tablet (Prostin E2, Pfizer, New York) will be applied vaginally. Clinical assessment by a trained resident will be performed 6 hours later (figure 1). If the BS is ≤5, a second tablet will be applied in the absence of active labour and clinical assessment repeated at the 12-hour timepoint. For logistical reasons, the on-duty resident will perform the 12-hour assessment and document the findings in the electronic clinical records; these data will be extracted and entered into the data collection proforma by the study investigators. Unless there is spontaneous progress into active labour or a need to expedite delivery, the participant will then be observed for up to a further 12 hours. Clinical assessment will be repeated at the end of the surveillance period (24-hour timepoint). Outcomes will be analysed by intention-to-treat.

Monitoring after intervention

Participants will be managed according to labour ward protocols regarding fetal and maternal monitoring after commencing induction. Continuous CTG is applied for 2 hours postapplication to monitor for hyperstimulation, followed by intermittent fetal and maternal monitoring every 6 hours over the 24-hour study period in the ambulatory ward. Further clinical assessment is performed following spontaneous labour onset, amniorrhexis, intolerable maternal pain or a non-reassuring CTG. In the event of spontaneous membrane rupture and BS ≥6, oxytocin infusion may be started if the participant is not in active labour. If the BS is ≤5 and there is no requirement to expedite delivery, the induction agent may be left in situ and the participant reassessed at the next timepoint (figure 1). Clinical assessment will be performed at the end of the surveillance period (24 hours from application). When the cervix becomes favourable (BS ≥6 at any timepoint) or on progress into the active phase of labour (cervical dilation of ≥2 cm, significant effacement of >50% and regular contractions at 2–3 min intervals), amniotomy will be performed followed by oxytocin infusion if required according to labour ward protocols. Labour progress is recorded on a traditional partogram, and labour arrest is defined as a lack of progressive cervical dilation or lack of fetal descent over at least two clinical reviews (when alert and action lines are crossed).[62] The labour ward team will make the diagnosis of labour arrest and the patient will be offered an option for caesarean section as per protocol. Management can be individualised for patients who request more time to labour depending on the risk assessment at that time. Participants may abandon TOLAC at any time and opt for caesarean delivery. Outcomes will be included in intention-to-treat analyses.

Outcome measures

The objective of this study is to evaluate the effectiveness of mechanical cervical ripening with FCB leading to successful labour induction in VBAC. The primary endpoint (table 3) is the rate of change in the modified BS over the 24-hour surveillance period, allowing an objective assessment on the efficacy of this process. The secondary endpoints include the rates of active labour and vaginal delivery within 24 hours of initiating priming and within 12 hours of active labour onset, induction-to-vaginal delivery interval, uterine hyperstimulation with abnormal fetal heart rate, caesarean delivery, serious maternal morbidity (eg, uterine rupture, admission to intensive care unit, septicaemia) or death, and serious neonatal morbidity (Apgar ≤7 at 1 min, cord pH ≤7.1 at birth[63]) or death, as defined by Cochrane reviewers using the Grading of Recommendations Assessment, Development and Evaluation framework for quality evidence.[55] Other outcomes include oxytocin augmentation, analgesia use in labour, and other labour complications such as obstetric anal sphincter injuries, conversion to malpresentation and postpartum haemorrhage.

Data collection

Patients will be managed by a team of obstetricians, residents, midwives and nurse clinicians. Demographical data, indication for IOL, baseline and interval physical assessments, and other trial-relevant clinical data will be collected in study proforma by the attending clinical staff. Patient identifiers (name, national registration identification numbers) will be stored separately on a master recruitment form, and only trial participation numbers will be used to identify participants on the study proforma, which will be stored in a safe for at least 1 year from the time of recruitment of the last patient. All data will be entered into a password-protected electronic database accessible only to investigators. Data entry and analyses will be performed by study team members not directly involved in the recruitment, randomisation and clinical management of the participants (ie, blinded to interventions).

Statistical analysis plan and sample size estimation

We deliver ~4000 pregnancies annually, of which 10%–15% are of patients with a single previous CS. Of these, ~60% attempt TOLAC (20 per month) and 20%–25% undergo IOL (5 per month). At our centre, the current VBAC success rate is ~40%–55%, with the remaining patients undergoing emergency CS. The variance applied to our population is derived from a retrospective cohort study from Hong Kong using the DBC in 24 women with one previous CS in which the median improvement in BS was 3 units with an IQR of 2.[50] Assuming a normal distribution we derive a variability of δ=1.5. Postulating that the difference in modified BS between the two groups at 12–24 hours is 1 point with a range of 2–8 points (SD=1.5),[64] using α=0.05% and 80% power we calculate that we require 40 patients in

Table 3 Primary and secondary outcomes

Primary outcome	► The increase in BS from a baseline of ≤5 (immediately before intervention) to ≥6 at the predetermined timepoints at 12 and 24 hours postapplication.
Secondary outcomes	► Active labour (with or without delivery) within 24 and 48 hours from cervical balloon/PGE2 insertion. ► Induction-to-labour, induction-to-delivery, FCB application-to-displacement, FCB removal-to-delivery intervals, oxytocin augmentation, analgesia use in labour. ► Number of PGE2 tablets required in total or FCB readjustments/reinsertions. ► Mode of delivery, that is, caesarean section, normal vaginal delivery, instrumental delivery, caesarean section rate, successful VBAC rate. ► Labour complications: uterine hyperstimulation (ie, >5 contractions/10 min with abnormal CTG), placental abruption, cord prolapse, postpartum haemorrhage, third-degree/fourth-degree perineal tears, uterine rupture, conversion to malpresentation. ► Maternal complications: failed device insertion, inability to void urine following insertion, intolerance of device and early removal, vaginal bleeding after insertion of device. ► Neonatal complications: fetal distress, meconium-stained liquor, neonatal Apgar score of <7 at 5 min, cord blood pH of ≤7.0, admission to NICU, neonatal hypoxic-ischaemic encephalopathy, neonatal death. ► Infectious complications: intrauterine infection, maternal sepsis (eg, endometritis, UTI), neonatal sepsis, maternal fever, onset of antibiotics.

BS, Bishop score; CTG, cardiotocogram; FCB, Foley catheter balloon; NICU, neonatal intensive care unit; PGE2, prostaglandin E2; UTI, urinary tract infection; VBAC, vaginal births after caesarean section.

each arm. Anticipating an attrition rate of 20%, a total of 100 subjects will be randomised equally into the two groups. A general linear model will be used to compare numerical outcome variables between both groups, while Poisson regression will be used to compare binary outcomes and derive relative estimates. All analyses will be performed using SPSS V.25.0 and GraphPad Prism V.6.07.

Safety monitoring and interim analysis

All adverse events in the MEDICS trial will be reported within 24 hours of notification by the study team. Serious adverse events will be logged and reported by the principal investigator; these are defined as any adverse event occurring at any time during the study that may result in death, life-threatening experiences, inpatient hospitalisation or prolongation of existing hospitalisation, persistent or significant disability, congenital anomalies, birth defects, or other medical events that jeopardise the well-being of the mother or the fetus. Anonymised details will be sent to the Domain Specific Review Board for assessment of causality; details will be input into the trial's database. Notable adverse reactions to either intervention, uterine scar rupture, severe neonatal or maternal morbidities, and perinatal or maternal death will be reported. No interim analysis is planned. Trial monitoring will be performed by an independent research monitor.

Follow-up

Data will be collected during routine outpatient clinic reviews at 2 and 6–8 postnatal weeks to assess for delayed complications, including endometritis or maternal sepsis.

DISCUSSION, ETHICS AND DISSEMINATION

To our knowledge this study will be the first RCT comparing transcervical FCB with vaginal PGE2 in women attempting VBAC, and will address the knowledge gap regarding the optimal method for cervical ripening and labour induction in this patient population, where current data are derived mainly from retrospective analyses and observational studies with small patient numbers and protocol heterogeneity.[65] By comparison, the ongoing PROBAAT-S trial (http://www.studies-obsgyn.nl/probaats/page.asp?page_id=1048) is a large prospective observational study designed to compare IOL by prostaglandins, FCB or amniotomy in women with at least one previous CS, in which the primary outcome is neonatal and maternal morbidity rather than mode of delivery. The PROBE design used here compensates for the inability to blind the patient and the proceduralist applying the priming agent by maintaining blinded analysis. Stratified randomisation of participants based on parity is important as prior vaginal deliveries improve the likelihood of a successful VBAC; not accounting for this

introduces a type 1 error if a greater proportion of such women are inadvertently randomised into either arm. Caesarean deliveries comprise ~30% of all deliveries at NUH; 25% of TOLAC candidates require medically indicated IOL similar to published rates,[66] and only 40%–50% of women achieve successful VBAC, considerably lower than international success rates of 60%–80%.[54 67–70] As the number of local women with previous CS has increased from 7.7% (2000–2002) to 10.9% (2009–2010), assessing the efficacy of mechanical IOL is timely.[3 71] Our goal is to efficiently prime women for labour and increase the likelihood of VBAC without increasing complications. Thus, our primary outcome is successful cervical ripening. As multiple factors influence the likelihood of successful VBAC or labour complications (eg, hyperstimulation, cephalopelvic disproportion), induction-to-delivery interval and uterine scar rupture are secondary outcomes. This trial is not powered for uterine rupture as this is a rare event, and much larger numbers are required to study this.

Cervical balloons promote ripening and active labour directly by exerting continuous pressure on the cervix, and indirectly by promoting local prostaglandin secretion, local inflammation (with production of interleukins IL-6, IL-8 and metalloproteinase-8) and neuroendocrine stimulation.[72] Recently, however, prostaglandin induction has become standard treatment for TOLAC despite the lack of good evidence of clinical superiority and concerns over safety, with the main advantage being ease of application. Compared with prostaglandins, the advantages of cervical balloons are their wide availability, low cost and easier preservation, with comparable or improved patient satisfaction and pain scores, while the main disadvantage is a higher likelihood for labour augmentation with oxytocin as the transition to active labour occurs later.[73] This in turn elevates the potential risk for uterine rupture during TOLAC. Concerns regarding increased maternal or neonatal infectious morbidity were not borne out in recent systematic reviews and meta-analysis.[38 74 75]

Recently Tan *et al*[76] showed equivalent efficacy of the DBC and PGE2 for labour induction in a cohort of Singaporean women with unscarred uteruses. Cheuk *et al*[50] reported successful cervical ripening and vaginal delivery with no serious maternal and perinatal morbidity using DBC in 75% of women with previous caesarean deliveries in a retrospective review.[50] Cervicovaginal application of a DBC, such as the Cook or Atad balloons, applies pressure within the lower uterine segment in addition to bidirectional pressure on the cervix, increasing local prostaglandin production. Studies comparing single cervical balloons with DBC show no differences in mode of delivery, patient satisfaction or complication rates.[77 78] We have selected FCB as the trial intervention rather than DBC as it is significantly cheaper and more readily obtained; furthermore, mechanical induction is uncommon in our institution and this represents an opportunity to improve local VBAC management. Extra-amniotic saline infusion does not enhance vaginal delivery rates and carries a similar risk of hyperstimulation, and so has not been included as a trial intervention.[38]

We will compare mechanical induction with vaginal Prostin pessaries rather than dinoprostone gel or slow-release inserts as this is the current standard of care for TOLAC at our institution.[12] Labour induction agents are used with caution as the balance of evidence suggests that prostaglandins and oxytocin do increase uterine rupture rates.[35 37] Higher balloon filling volumes (60 mL vs 30 mL) produced a greater likelihood of delivery within 12 hours of induction.[79] A shorter duration of balloon insertion (12 hours) resulted in higher vaginal delivery rates and similar CSR compared with a longer duration of use (24 hours).[80] Thus in our protocol we will maintain a 30–50 mL-filled FCB for a maximum of 12 hours. While prelabour rupture of membranes (PROM) at term is a relative contraindication to mechanical induction, this condition accounts for ~30% of inductions at our institution. Retrospective studies and randomised trials show no differences in the incidence of chorioamnionitis with transcervical balloons in the presence of ruptured membranes compared with oxytocin or vaginal misoprostol.[81–83] Thus we will recruit women who meet eligibility criteria even if they are diagnosed with PROM, as detailed in table 2.

Dissemination

The evidence from this randomised trial enables determination of the more efficient and safer method of labour induction in TOLAC. It may improve the local incidence of successful VBAC and may encourage a change in local practice to improve the management of these high-risk labours. The authors aim to publish the data in peer-reviewed journals following conclusion of the trial.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval for collection and use of human data was awarded by the National Healthcare Group (Singapore) Domain Specific Review Board (DSRB, domain D) for Obstetrics and Gynaecology following a full review (DSRB/2018/00248). The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional

committees on human experimentation and with the Helsinki Declaration of 1975 as revised in 2008.

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