Placenta and Reproductive Medicine

COMMENTARY

Reassessing the Bishop score in clinical practice for induction of labor leading to vaginal delivery and for evaluation of cervix ripening

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EMPIRICAL EVIDENCE GUIDES CLINICAL PRACTICE

Some 60 years ago, obstetrician and clinical researcher Edward H. Bishop first proposed a pelvic score to guide "selection of those patients most suitable for induction" of labor.[1] This original Bishop score is the summation of a numerical estimate for each of five criteria that included cervix dilation, effacement, consistency, position, and station. Notably, only multigravida women at term with prior vaginal delivery were studied, and induction of labor (IOL) methods at the time consisted of oxytocin, membrane stripping, and amniotomy. Empirical evidence by Bishop indicated that "induction may be successfully and safely performed when the pelvic score totals 9 or more. Under such circumstances, we have had no failures in induction, and the average duration of labor has been less than 4 hr" to achieve vaginal birth. IOL has since become more commonplace. Moreover, major advances in management of labor and new approaches to cervical ripening and IOL have improved maternal and newborn outcomes.[2] The simplicity and ease to implement popularized the use of what became known as the Bishop score in clinical practice and for research applications. Since then, the Bishop score has also been modified and more widely applied to include nulliparous and preterm women, as well as in research studies of cervical ripening. Contemporary convention indicates that beginning IOL with a lower Bishop score has increased risk for Cesarean deliver while a higher Bishop score increases the chance of a successful vaginal delivery. The current concern is whether use of the Bishop score predicts vaginal delivery following IOL in clinical practice, among nulliparas and preterm pregnancies, and is a valid research endpoint to evaluate cervical remodeling. With the intent to promote discussion, there are 3 reasons to reconsider the expanded use of the Bishop score for pre-induction cervical evaluation.

REASON #1: TODAY'S PATIENTS DIFFER FROM THE DEMOGRAPHIC USED TO DEVELOP THE BISHOP SCORE

Nearly 60 years ago, Bishop's original study focused on an outcome of vaginal delivery, which on average, occurred within 4 hours of IOL in a study population of multiparous women who had previous term vaginal birth(s). Importantly, the Bishop score was developed for elective IOL at term when the alternative of expectant management was not unreasonable. In modern obstetrics, IOL is generally pursued for maternal or fetal indications (*i.e.* hypertension, fetal growth restriction, *etc.*), when continuation of pregnancy is not recommended. Current

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rates of IOL exceed 20% of overall pregnancies in many countries.[3] Although specifically excluded by Bishop, his original or a modified scoring system has been extended to nulliparous women and, irrespective of past pregnancy history, IOL of pre-term pregnancies when medically indicated. In both circumstances, however, labor would be induced regardless of the Bishop score. Moreover, contemporary studies of IOL report delivery outcomes within 24 hours, not 4 hours, and methods of induction have advanced since 1964. Despite these significant differences, the original or modified Bishop score is commonly used with sparse empirical evidence for its predictive value in the current expanded, more diverse, and more medically complex patient population.

REASON #2: WITH NEW IOL APPROACHES, LOW BISHOP SCORES ARE NOT ALWAYS PREDICTIVE OF CESAREAN DELIVERY

The expanded use of the Bishop score in obstetrical practice mentioned above may also result from an increase in IOL based upon recent findings in the *ARRIVE* trial.[4] In this well-designed, large, randomized trial, IOL at 39 weeks decreased risk for cesarean delivery compared to expectant management. The trial found that "subgroup analyses of the primary perinatal outcome and of the secondary outcome of cesarean delivery showed no significant differences". The Discussion concludes that the "finding may seem unexpected, given the consistent evidence that women with an unfavorable Bishop score have a higher chance of cesarean delivery when labor is induced than women with a favorable score". Indeed, the rate of cesarean deliveries were higher among those randomized to IOL with a lower modified Bishop score (< 5, compared to ≥ 5). The authors note, however, that "labor induction in women with an unfavorable score still resulted in fewer cesarean deliveries than expectant management". This unexpected though not surprising result may reflect the explicit inclusion criteria in the trial of only nulliparous women. Conceivably, the basis for expecting that a modified Bishop score may be correlated with preparedness for vaginal delivery following IOL in nulliparous patients as empirically demonstrated in the original multiparous population is worthy of further investigation and discussion.

In addition, current methods for IOL differ from those used during Bishops time (mostly oxytocin and amniotomy). New pharmacologic agents and mechanical approaches are intended to mimic cervical remodeling, presumed to precede spontaneous labor.[2,3] Contemporarily, induction may use misoprostol and a transcervical single or double-balloon catheter either individually, in succession, or simultaneously to facilitate cervical compliance, followed by oxytocin and amniotomy. The staged use of multiple ripening agents is inherently a slower process with delivery success often more than 24 hours after IOL initiation. However, this approach results in cesarean delivery in as much as 21.4% of women with lower pre-induction Bishop scores.[5] Two reviews exemplify the opposing conclusions for use of the modified Bishop score to accurately forecast vaginal birth,[6,7] a conflict that may in part be due to survey of different literature and analyses of data from nulliparous and multiparous women. Neither review disputed the conclusion of Bishop's original report that a high score was highly predictive of vaginal delivery in multiparous women. A more comprehensive perspective of the parturition process recognizes that prepartum term and preterm human tissues have not been or are not readily available for study. Moreover, given current understandings, birth may itself be a compound endpoint of biomechanical smooth muscle activity for uterine contractions during labor that is mechanistically distinct from cross-linked collagen breakdown and distensibility of the cervix for dilation.

REASON #3: BISHOP SCORE MAY REFLECT POST-RIPENED CERVICAL DILATABILITY

Commonly considered the lower portion of the uterus, evidence clearly indicates that the cervix is a unique connective tissue structure compared to the uterine endometrium or myometrium.[8] Distinct morphological, immunological, and embryological characteristics of the highly innervated cervix are common among mammals. Moreover, across species, the two basic functions of the cervix are as a barrier to the vaginal ecology and its virtual disappearance prior to birth. Over 50 years ago, Danforth *et al.* recognized that remodeling of the cervix begins well before the onset of labor.[9] Since then, research related to cervical remodeling has mainly focused on clinical outcomes, while histologic and biochemical studies have largely used animal models. It is important to acknowledge that studies of the cervix in animals and in vitro models may not easily translate into clinical practice, but such efforts are generally necessary owing to clinical and ethical considerations that limit the availability of cervical biopsy tissues in women during pregnancy. In nonhuman primates and other mammals, few studies of the lower reproductive tract during pregnancy have done a time-course survey or even used a Bishop score to assess readiness for labor.[10] These considerations do not discount the valuable contributions of studies in pregnant women that focus on available biopsies from the ectocervix subregion and lower uterine segment near or at term which collectively suggest that inflammation drives antepartum remodeling.[11]

Beyond the significant predictive value for vaginal birth following IOL in multipara women at term, the term "favorable" for a Bishop score, whether original or modified, lacks a clear definition based in a physiologic or tissue-specific process. Each criterion in the score, including estimates of dilation, effacement, consistency, position, and station, can

be attributed to cervix structure.[12] However, biomolecular markers of these structural features or their time course for prepartum changes remain to be understood given that the process or period of cervical "ripening" or remodeling is conceived to begin by 32 weeks of pregnancy.[13] During this early 3rd trimester, there is a paucity of studies about essential parts of the reproductive tract to define a start, progression, or conclusion of remodeling that distinguish phases of cervix ripening from softening to subsequent dilation, or a low (unfavorable) *versus* high (favorable) Bishop score in women. Understanding these parameters are important for discussions of whether the Bishop score is useful to assess preparedness of term or preterm women for successful IOL.

Mammalian models of the antepartum cervix have been informative of the remodeling process due to translationally relevant similarities in structure, function, and biomechanics.[8,14] Studies of the inflammatory process associated with cervix remodeling including biomolecular endpoints, cross-linked collagen structure, and correlation to tensile parameters in animal models are indicative of comparable processes in women where limitations prevent study during the antepartum period. In particular, some 3–5 days before labor in mice (days 15–18 of pregnancy), comparable to weeks 32–38 of pregnancy in women, an increase in inflammation in the cervical stroma is characterized by expansion of the extracellular space (decreased cell nuclei density), reduced cross-linked collagen, and increased residency of macrophages. These features of remodeling occur when progesterone in circulation is at or near peak concentrations in replicate studies in multiple strains of mice and rats well before labor or birth.[15] This finding is consistent with evidence from a biomolecular study of peripartum ectocervix biopsies from women at term or delivered by cesarean that suggest the cervix had already begun remodeling.[16] By contrast, the precipitous fall in systemic progesterone in some mammals, rodents in particular, is more coincident with labor than cervix remodeling. Conceptually, this may represent an actual withdrawal of progesterone to support pregnancy and block labor compared to the functional loss of response to sustained progesterone in circulation in women. For use of the Bishop score, assessments are typically antenatal at term or in women at risk for preterm delivery. This period can be deduced to reflect post-ripening dilation and a response to either uterine contractions or exogenous ripening agents. Danforth's recommendation to attend to the period well before labor appears clinically relevant to understanding cervical remodeling and is worth consideration.

ALTERNATIVE APPROACHES TO PRE-INDUCTION CERVICAL EVALUATION

Bishop's scoring system has stood the test of time to forecast vaginal birth in multiparas at term undergoing IOL. While we acknowledge its overall simplicity and ease of use, perhaps the time has now come to revisit the utility of Bishop score assessment for the prediction of vaginal delivery in modern practice, particularly with regard to its expanded application to nulliparous and preterm patients. The current challenge is to identify markers, biomolecular, imaging, or others that collectively forecast readiness of the cervix for vaginal birth following IOL. Conceivably, multiple factors may correlate indices of relevance to inflammatory processes that are associated with the progression of structural remodeling of the cervix throughout pregnancy. In this regard, efforts to synthesize existing data with more recent findings may improve existing algorithms for IOL and validate an expanded use of the Bishop score.[17,18] The ultimate goal would be to individualize the timing of IOL procedures to optimize outcomes for each pregnancy.

Advances in several current technologies provide multiple novel approaches to assess the remodeling process and readiness of the cervix for birth in contemporary patient populations. In reconsideration of individual elements of Bishop's scoring system, cervical length (CL) represents effacement, an integral component of the Bishop score. Recently, transvaginal ultrasound can identify women with a short CL, a known risk for second trimester spontaneous preterm birth, and predict vaginal delivery after IOL at term.[19] However, the value of CL measurements by ultrasound alone or in conjunction with a specific Bishop score would need to be standardized and generally accepted to identify readiness for IOL. Moreover, varying pre-induction CL among individuals may lead to different delivery outcomes in response to standard induction methods.[19,20] Second, addition of multiple markers of cervical morphometry with, by example, elastography holds promise to evaluate critical features of antepartum cervix remodeling.[21] A third approach, distinct from sonography, is Raman spectroscopy for in vivo interrogation of the ectocervix.[22] This method can create a unique fingerprint of specific molecules during a routine exam which assesses specific biomolecular structure, concentrations, and water content – factors known to change during cervical remodeling. This approach has proven useful to diagnose cervical dysplasia, and in a longitudinal study, remodeling changes as pregnancy progressed to term, during labor, and postpartum. Lastly, correlation of increased proinflammatory cytokines in cervicovaginal fluid and circulation during pregnancy in association with preterm labor,[23] with structural remodeling of the cervix, may ultimately bridge the gap to improve assessment of IOL readiness or risk for spontaneous preterm birth. Novel approaches to assess the readiness of the cervix for birth, especially with respect to analyses of images acquired by minimally-invasive methods, will depend upon validation and clinical consensus.

The development of therapeutic approaches to regulate

inflammatory processes that forestall or promote remodeling in a case-dependent manner may optimize the efficacy of IOL for vaginal delivery and have implications to predict and prevent preterm birth. Ultimately, evaluation of the current continued use of the Bishop score in practice and research is needed to improve the prospect that a therapeutic intervention, whether systemic or local, could be administered at the appropriate time during pregnancy to regulate the timing and course of inflammatory remodeling processes in the cervix to reduce morbidity, as well as improve maternal and newborn IOL outcomes.

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Author contributions

Kuba K: conceptualized relevance for practice and multiple revisions of manuscript drafts, critically evaluated and interpreted literature for clinical relevance. Kirby MA: wrote original basic science portions, edited, proofed, and helped critically evaluate past publications to reference manuscript. Hughes F: corroborated and refined relevance for clinical practice, reviewed and helped critically evaluate literature for clinical portions of manuscript. Yellon SM: conceived, wrote, and revised sections to integrate basic and clinical science components. Analyzed and interpreted, referenced, revised and approved final manuscript.

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Conflict of interest

None declared.

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