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History-indicated cerclage: the association between previous preterm history and cerclage outcome

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Objective
Our hospital's policy is to perform history-indicated cerclage (HIC) for pregnant patients with 1 or more second-trimester pregnancy losses. Recently, the American College of Obstetricians and Gynecologists (ACOG) guideline regarding indications for HIC was changed from 3 or more previous second-trimester fetal losses to one or more. In this study, we aimed to evaluate the efficacy of the revised guideline and to investigate the association between previous preterm history and cerclage outcome.

Methods
We conducted a retrospective observational study of cases of HIC in singleton pregnancies performed at our hospital between January 2007 and June 2016. We compared the perioperative complications and incidences of preterm delivery in patients with one previous second-trimester pregnancy loss against those in patients with ≥2 losses.

Results
The incidence of preterm delivery (<32 weeks) was significantly lower in patients with one previous second-trimester pregnancy loss than in those with ≥2 losses (15/194 [8%] vs. 28/205 [14%]). In the 1 loss and ≥2 losses groups, the rates of preterm premature rupture of membranes (PPROM) were 7% and 8%, the rates of PPROM at <32 weeks 2.1% and 3.4%, and the ratios of neonatal intensive care unit admission 10% and 17%, respectively.

Conclusion
Comparison of HIC in one previous second-trimester pregnancy loss group with HIC in the 2 or more previous second-trimester pregnancy loss group found no difference in pregnancy outcome. This finding supports the amended ACOG guideline for HIC indications. Based on our results, we also propose development of a new protocol for HIC-related complications.

Keywords: Cervix incompetence; Cervical cerclage; Preterm birth

Introduction

Classically, cervical insufficiency is a diagnosis based on an obstetric history of recurrent second- or early third-trimester fetal losses, following painless cervical dilation, prolapse or rupture of the membranes, and expulsion of a live fetus despite minimal uterine activity [1]. Cerclage is a treatment for women at risk of pregnancy loss due to cervical insufficiency. The risk of recurrent fetal loss without cerclage in women considered at high risk of cervical incompetence is not known exactly, due to the lack of properly designed studies. Uncontrolled studies suggest that infant viability is about 25% without cerclage, whereas it is 75%–90% with cerclage [2]. For this reason, prophylactic cerclage should be given serious consideration in

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women with histories of classic cervical insufficiency. Contemporary classifications include the history-indicated, ultrasound-indicated, and physical exam-indicated cervical cerclage [3]. History-indicated cerclage (HIC) is performed early in pregnancy, usually at between 12 and 14 weeks, based on poor obstetric or gynecologic history regardless of events in the current pregnancy. The effectiveness of HIC has been studied with mixed results [4-8]. Because of such discrepancies, indications for HIC vary across guidelines. Despite the necessity of achieving consensus on this issue, there are practical difficulties in performing randomized controlled trials (RCTs) targeting pregnant women [2,9,10].

Commonly reported complications of cervical cerclage include preterm premature rupture of membranes (PPROM), chorioamnionitis, preterm labor, cervical trauma, suture displacement, and bleeding. The reported rate of chorioamnionitis after HIC is 6.2%, while that of PPROM ranges from 18% up to 38% [11,12]. Thus, the recommended indications for HIC have been established based on stringent standards.

Recently, the American College of Obstetricians and Gynecologists (ACOG) guideline regarding indications for HIC has been changed, from 3 or more previous second-trimester fetal losses to 1 or more [2]. However, there is currently insufficient evidence to support this guideline. Additionally, there are no recommendations for the treatment of complications after HIC.

Our hospital's policy is to perform HIC in patients with histories of one or more previous second-trimester pregnancy losses. In this study, we compared HIC outcomes based on the number of previous preterm pregnancy losses(1 vs. 2 or more) in women at risk of preterm birth (PTB). Our goal was to investigate the association between previous preterm history and cerclage outcome, and to provide an evidence-based evaluation of the modified ACOG guideline.

Materials and methods

We conducted a retrospective observational study of cases of HIC in singleton pregnancies performed at Kangnam Sacred Heart Hospital of Hallym University between January 2007 and June 2016. The Institutional Review Board at Kangnam Sacred Heart Hospital approved this study (IRB file number 2017-05-031), and it was conducted according to the principles expressed in the Declaration of Helsinki. Patients who delivered at our hospital were included for further review. We compared patient groups based on the numbers of previous second-trimester pregnancy losses related to painless cervical dilation in the absence of labor or placenta abruption. The indications for HIC were one or more unexplained spontaneous second-trimester losses, a history of cerclage due to painless cervical dilation in the second-trimester, and a history of HIC. After reviewing the remaining charts, we excluded cases involving multiple pregnancies, fetal anomalies, or preeclampsia. We evaluated the perioperative complications and outcomes of the cases and conducted a subgroup analysis comparing patients with history of one prior preterm delivery and those with histories of 2 or more.

Cervical cerclages were performed using the McDonald Technique with one suture using 5 mm Mersilene tape placed in a purse-string fashion. Intraoperative ultrasound guidance and tocolytics were not used for the cerclage procedures. HIC was performed in the 12th–14th week of gestation. Serial transvaginal sonograms were performed in the outpatient ward, and if the cervical length (CL) was less than 25 mm we used vaginal progesterone. If, after use of progesterone, funneling occurred below the cerclage knot or membrane bulging was identified on physical examination, then we performed repeat cerclage. We did not repeat cerclage more than once, and did not perform repeat cerclage if funneling or bulging appeared after 26 weeks of gestation. The cerclage was removed in the 36th–37th week of gestation. It was removed a little earlier for preterm labor, PPROM, or if delivery was indicated.

We used SPSS Statistics software (IBM Corp., Armonk, NY, USA) for our statistical analyses. Variables were evaluated using the t-test and the χ^2 test, and a *P*-value <0.05 was considered statistically significant.

Results

We identified 1,214 patients who had had HIC performed at our hospital during the period studied. Of these, 418 who had delivered at our facility were included for further review. After applying our exclusion criteria, 399 cases remained and were analyzed. Among these patients there were no significant differences in age, mode of previous delivery, or previous history of cerclage. Moreover, there were no significant differences between the 2 groups in gestational age at delivery or

Table 1. Comparison of demographic characteristics and pregnancy outcomes of patients in 2 groups

Outcome	1 experience of second-trimester loss (n=194)	2 or more second-trimester losses (n=205)	*P*-value
Maternal age (yr)	33.2±3.6	33.7±3.4	0.114
Previous cervical cerclage			0.202
No	152 (78.4)	127 (62.0)	
Yes	42 (21.6)	78 (38.0)	
Delivery mode			0.147
NSD	126 (64.9)	113 (55.1)	
C/sec	68 (35.1)	91 (44.9)	
Gestational age at delivery (wk)	36.8±4.5	36.0±5.3	0.096
Birth weight (g)	2,949.7±807.6	2,837.1±966.9	0.206

Data are expressed as mean±standard deviation or number of subjects (%).
NSD, normal spontaneous delivery; C/sec, cesarean section.

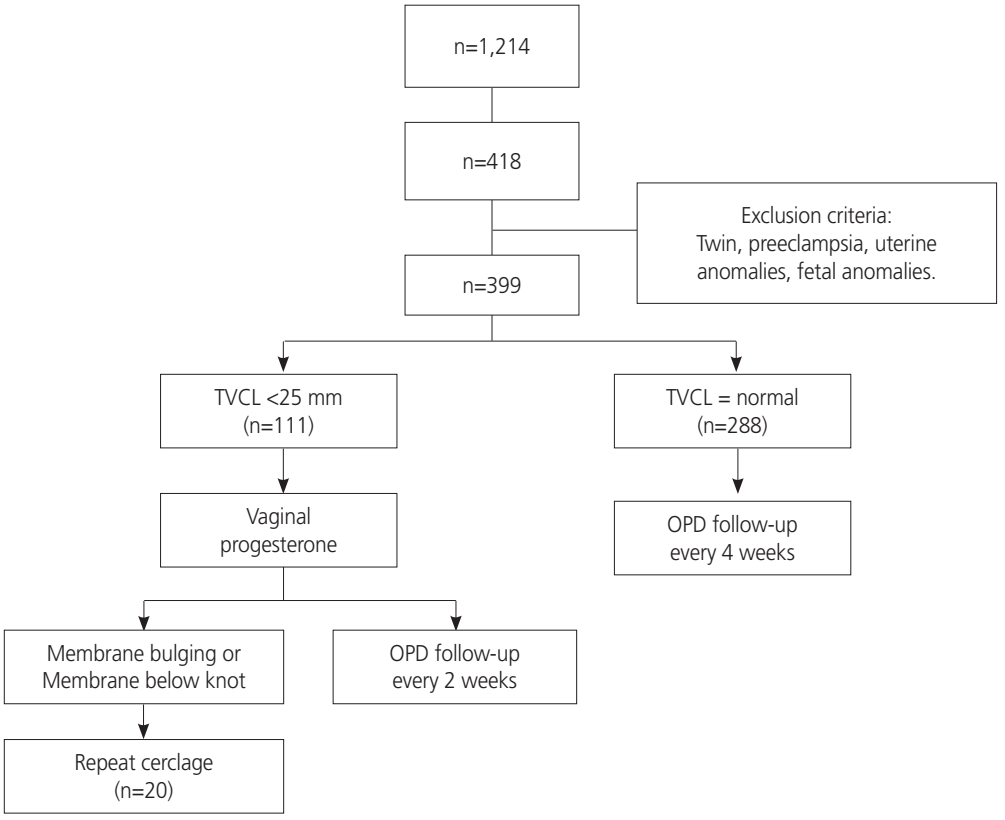

Fig. 1. Patient distribution and management of history-indicated cerclage. TVCL, transvaginal sonogram of cervical length; OPD, outpatient department.

in neonatal weight (Table 1).

There were no intraoperative complications or postoperative complications beyond the 2-week period. Vaginal progesterone was prescribed to 111 patients with follow-up CL less than 25 mm after cerclage. During the follow-up, repeat cerclage was performed in 16 patients due to membrane bulging, and in 4 because of funneling below the knots (Fig. 1).

Patients were admitted for the following reasons: preterm labor requiring tocolytic treatment (28 [7%]); CL shortening greater than 10 mm, with or without funneling, detected before 28 weeks of gestation on regular follow-up through transvaginal sonography (48 [12%]); PPROM (31 [8%]); and other diagnoses (19 [5%]). There were 4 cases of fetal demise (1%), 291 patients (73%) who delivered after 37 weeks of

Table 2. Comparison of clinical outcomes between cases of 1 and of 2 or more past second-trimester losses

Outcome	1 experience of second-trimester loss (n=194)	2 or more second-trimester losses (n=205)	*P*-value
Re-admission	54 (28)	72 (35)	0.261
Fetal demise	2 (1)	2 (1)	0.140
PPROM	14 (7)	17 (8)	0.416
Repeat cerclage	8 (4)	13 (6)	0.112
Delivery			
<37 wk	47 (24)	61 (30)	0.129
<32 wk	15 (8)	28 (14)	0.040
NICU admission	19 (10)	32 (17)	0.044
Use of progesterone	47 (24)	64 (31)	0.201

Data are expressed as mean±standard deviation or number of subjects (%).
PPROM, preterm premature rupture of membranes; NICU, neonatal intensive vare unit.

gestation, and 71 neonates (18%) who were admitted to the neonatal intensive care unit (NICU).

The incidence of delivery before 32 weeks of gestation was significantly lower in the group with one previous second-trimester pregnancy loss than in the group with 2 or more losses (15/194 [8%] vs. 28/205 [14%]; *P*=0.040). However, there was no difference between the 2 groups in the incidence of delivery before the 37th week (*P*=0.129). The rates of PPROM were 7% and 8% (*P*=0.416) in the 1 loss group and the 2 or more losses group, respectively, and the rates of PPROM before 32 weeks of gestation 2.1% and 3.4% (*P*=0.305), respectively. The rates of NICU admission were 10% in the 1 loss group vs. 17% in the 2 or more losses group (*P*=0.044) (Table 2).

Discussion

Patient selection for HIC, also known as prophylactic cerclage, is based on a history of classic features of cervical insufficiency. HIC is performed electively as a preventative measure in asymptomatic women at 12–14 weeks of gestation. Vaginal progesterone is administered on an outpatient basis when the CL shortens to less than 25 mm. While the recommendations concerning the timing of cerclage do not differ, the indications for HIC vary.

According to the Royal College and the Canadian guidelines, the indication for HIC is 3 or more previous PTBs and/or second-trimester losses [9,10]. In contrast, under the ACOG guideline the indication for HIC is a "History of one or more second-trimester pregnancy losses related to painless cervical dilation and in the absence of labor or placenta abruption; or Prior cerclage due to painless cervical dilation in the second-trimester." The ACOG guideline was revised in 2013, and the indication for HIC was changed from that given by the previous guideline (2003), which was identical to those of the Royal College and the Canadian guidelines [9,10]. This change to the ACOG guideline was not explained, however [2]. There have been only 3 RCTs that have investigated the efficacy of HIC. Two trials compared cerclage with no cerclage in women with a history of PTB and found no significant improvement in outcome in those treated with cerclage [4,5]. The third trial, an intent-to-treat study of 1,292 women with singleton pregnancies at risk of preterm delivery, reported that there were fewer deliveries before 33 weeks of gestation in the cerclage group (83 [13%]) than in the no-cerclage group (110 [17%]; *P*=0.030) [6].The ACOG cited these 3 studies in both 2003 and 2013. The results of a questionnaire released by the Society for Maternal Fetal Medicine in 2008 had, however, found that 96% of doctors preferred to perform cerclage after one pregnancy loss [13].

We routinely perform HIC in patients with one or more second-trimester pregnancy losses. We favor HIC because it causes fewer complications than ultrasound-indicated cerclage and physical exam-indicated cerclage [11,14,15]. Our comparison of the outcomes of patients with one previous second-trimester pregnancy loss and those with 2 or more losses correspond with and supports the newly revised ACOG guideline.

PPROM is considered the most common complication fol-

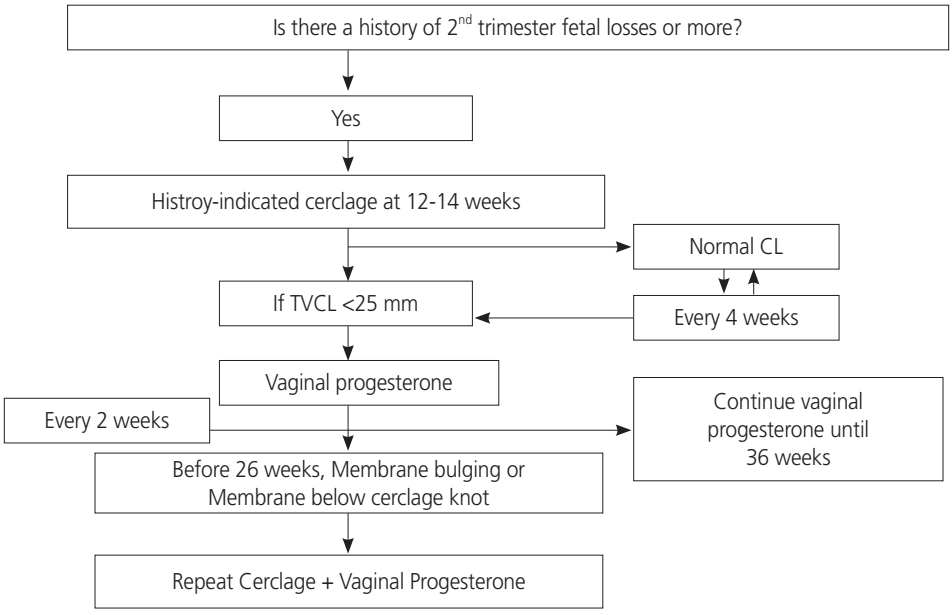

Fig. 2. Algorithm for history-indicated cerclage. TVCL, transvaginal sonogram of cervical length; CL, cervical length.

lowing cerclage, and reportedly occurs in up to 38% of cases [10]. Our data, however, showed only an 8% rate of PPROM. Given that the rate of PROM in all pregnancies is 3%, a rate of 8% may not be excessive in a subgroup of high-risk patients. Thus, cerclage itself should not be considered to increase the rate of PPROM significantly. Detailed patient histories and co-morbidities were not considered in our subgroup analysis. We identified 4 cases of intrauterine fetal death after 20 weeks of gestation through local clinic follow-up. Although it was difficult to determine exact causes, 2 patients were diagnosed with overt diabetes mellitus, and one showed placental abruption.

Several studies have proven that the use of either cervical cerclage or vaginal progesterone is effective in the prevention of preterm delivery [16-21]. Regarding progesterone, the exact mechanism of action in preventing PTB is unknown, although several mechanisms are proposed. In general, the evidence seems to favor 2 mechanisms: an anti-inflammatory effect that counteracts the inflammatory process leading to PTB, and a local increase in progesterone in gestational tissues that counteracts the functional decrease in progesterone leading to PTB [21]. In contrast, one study has reported that vaginal progesterone is not associated with a reduced risk of preterm delivery or of composite neonatal adverse outcomes, and has no long-term beneficial or harmful effect on outcomes in children at 2 years of age [18]. Regarding cervical cerclage, meanwhile, compared to the case of no intervention it is associated with reductions in the rate of PTB at 37 weeks of gestation and in perinatal mortality. However, indirect comparisons between vaginal progesterone and cerclage indicate that there are no significant differences between the 2 interventions [17]. Currently, there are no evidence-based guidelines for the management of complications after HIC. Several studies have investigated the use of vaginal progesterone after cerclage and pessary. Among the various routes of progesterone delivery, including intramuscular, vaginal, and oral, vaginal progesterone has the advantages of easy accessibility and satisfactory patient compliance. Although expectant management is an alternative to using vaginal progesterone after cerclage for a short CL, randomized studies and long-term safety data are needed to establish consensus guidelines [22-27]. In a retrospective study of 53 singleton pregnancies affected by acute cervical insufficiency treated with cerclage, Jung et al. [22] concluded that vaginal progesterone with physical exam-indicated cerclage was associated with a reduction in spontaneous PTBs. Although the study was limited to physical exam-indicated cerclage, the result contributes significantly to our ability to prevent PTBs. Based on these considerations, our hospital has modified its policies for cerclage and the use of progesterone [21,28,29]. If there is a short cervix with or without funneling after HIC, we use vaginal progesterone and perform serial transvaginal sonograms every 2 weeks. Although sufficient evidence supporting this treatment is lacking, more studies are underway. If there is

funneling below the surgical knot or membrane bulging during follow-up, we perform repeat cerclage [30].

HIC cannot be considered a cure-all procedure, and for this reason, we suggest guidelines for the management of complications after HIC. Performing an RCT to evaluate policies for the management of HIC-related complications is difficult. Therefore, we propose a policy based on our interpretation of our findings (Fig. 2).

Our study has some limitations. First, it was a retrospective review, and we may have achieved a more precise conclusion if we had compared the outcomes of HIC and no treatment in women with histories of one previous preterm delivery in the second-trimester. Second, not all pregnancy results could be confirmed. We believe our complication rate would be even lower if we could include the patients who delivered our clinic in our study. As to the strengths of our study, they include the facts that it was performed in a single institution, that many patients were followed to delivery, and that our patient cohort was large. However, additional research and RCTs are still needed in the future.

In conclusion, the outcome of HIC among the one second-trimester pregnancy loss group was better than that among the 2 or more previous pregnancy losses group. This finding supports the amended ACOG guideline for HIC indications. Based on the results of this study, we also propose development of a supplemental guideline for HIC that includes policies for complications following HIC.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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