

## Prediction and prevention of preterm birth after cervical conization

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The introduction of the cervical cancer screening strategy has substantially reduced the incidence of and mortality from invasive cervical cancer.<sup>1</sup> This trend has been attributed to early detection and following treatment of pre-invasive cervical lesions, and cervical intraepithelial neoplasia (CIN) is commonly diagnosed in women of reproductive age. Although the fact that the conservative treatment for CIN (including cold knife conization, large loop excision of the transformation zone (LLETZ)/loop electrosurgical excision procedure (LEEP), laser conization, or ablative therapy) should be effective is the most important issue, subsequent impact of these treatment modalities on future fertility and pregnancy outcome is also a major concerning point in younger women.

Substantial evidence indicates that cervical conization is associated with preterm birth. Earlier studies on the relationship between cervical conization and subsequent pregnancy complications were hindered by small sample size, poor study design, or failure to control confounding factors. However, recent studies with larger sample size, systematic review, or meta-analysis have generally found an increased risk of preterm birth after cold-knife conization and LLETZ or LEEP, although the data on obstetric risk after ablative therapy such as cryotherapy or laser vaporization are contradictory.<sup>2,3</sup>

In this issue of Journal of Gynecology Oncology, there are two articles<sup>4,5</sup> dealing with the association between cervical conization and preterm delivery. Both studies showed a higher rate of preterm delivery after cervical conization (27.7% and 32.1%) than that in low risk pregnancies. The study of Nam et al.<sup>4</sup> focused on the prediction of preterm birth by identifying risk factors, and Shin et al.<sup>5</sup> tried to evaluate the efficacy of cerclage as a preventive strategy for preterm birth.

In the study of Nam et al.,<sup>4</sup> the type of conization, the volume of specimen, and second trimester cervical length were the

possible risk factors for preterm birth, but only the second trimester cervical length was the significant risk factor after adjusting for confounding variables in multivariate analysis. Several other researchers also tried to identify subgroups of women who are at higher risk for preterm birth after conization. Suggested risk factors include a shorter procedure-to-pregnancy interval,<sup>6</sup> the depth of cervical excision,<sup>2</sup> and short cervical length,<sup>3,7</sup> etc. In terms of cervical length, cervical conization does not seem to shorten the cervical length in all patients. Berghella et al.<sup>7</sup> reported that only 28% had a short cervix in pregnant women at between 16 and 24 weeks after cervical conization. Considering that cervical length is not always shortened after conization, measuring cervical length may be also useful in predicting preterm delivery in pregnant women after conization, as suggested by the study of Nam et al.<sup>4</sup> and other recent evidences.<sup>3,7</sup>

The preventive strategies for preterm birth after these procedures are a more challenging issue. There are several possible mechanisms by which cervical conization increase the risk of preterm delivery. Decreased mechanical support or increased susceptibility to infection after the loss of cervical mucus production may contribute to preterm delivery.<sup>8</sup> Prophylactic cerclage does not seem to prevent preterm delivery,<sup>9</sup> and even in patients who present with a short cervix, rescue cerclage had failed to show efficacy.<sup>10</sup> Shin et al.<sup>5</sup> also failed to see the efficacy of cerclage as a preventive method for preterm birth, even after confining analysis to those with short cervix (cervical length of less than 25 mm). In the study of Nam et al.,<sup>4</sup> the rate of preterm birth after cerclage was not lower in patients who had undergone prophylactic cerclage than those without.

There are several points to be considered in these two articles. First, both studies are retrospective studies, and therefore the confounders were not controlled adequately. The physician bias in the management might significantly influence the study result. In fact, women who underwent cerclage had significantly shorter cervical length and higher rate of nulliparity, and had lower specimen weight with marginal significance than those in the expectant group.<sup>5</sup> Relatively small number of cases is also the major weak point. Second, both studies did not clarify the urgency of the cerclage. The pregnancy outcome and complica-

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tion rates after cerclage differs according to the type of the cerclage: elective cerclage (history indicated cerclage) vs. urgent cerclage (ultrasound indicated cerclage) vs. emergency cerclage (cerclage after definite cervical dilatation).<sup>11</sup> But none of these studies stated the type of cerclage employed.

But Nam et al.<sup>4</sup> tried to focus on the risk factors for preterm birth, and integrated all associated factors together rather than a single factor, in the largest numbers of Korean patients ever published on this subject. The study of Shin et al.<sup>5</sup> has the strength that almost all patients were followed up for antenatal care and delivery after conization in a single institution.

What issues should be evaluated in further studies? In spite of the suggestions on the association between the risk of preterm birth and increased susceptibility to infection after the loss of cervical mucus production after cervical conization, there is a paucity of information regarding the risk of preterm birth according to the inflammatory milieu in the vagina or cervix in pregnant women after cervical conization. Recent evidence suggests that a cervical inflammatory milieu in early or mid-trimester pregnancy is associated with preterm birth in pregnant women.<sup>12</sup> For prevention, the efficacy of progesterone in women after cervical conization needs to be evaluated. If a patient's obstetric history is consistent with a spontaneous preterm birth, prophylactic administration of progesterone may be an option, because some reports showed progesterone supplementation was effective in decreasing the recurrent preterm birth in women with previous preterm delivery.<sup>13,14</sup> However, whether progesterone should be offered to all patients who have underwent cervical conization, regardless of a history of preterm birth, needs to be proven in future studies.

#### CONFLICT OF INTEREST

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

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