Is Cervical Length a Useful Predictor of Antepartum Hemorrhage in Patients with Placenta Previa?

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Objective: Placenta previa complicates 0.3-0.5% of pregnancies and can cause sudden antepartum massive hemorrhage (APH). Previous studies have indicated that cervical length (CL) measured by transvaginal ultrasonography may be a predicting parameter for APH in patients with placenta previa; however, conflicting data exist. Thus, we investigated the association between CL and APH in patients with placenta previa.
Methods: In total, 129 singleton pregnant women with placenta previa, who delivered at our institution from January 2010 to December 2016, were included in this study. The shortest CL measured throughout gestation was used for analysis, and we defined CL less or more than 30 mm as short or normal CL, respectively. We performed univariate and multivariate analyses, and a receiver-operating characteristics (ROC) curve was plotted to determine the cut-off CL value to predict APH.
Results: APH occurred in 26 patients. The adjusted odds ratio for APH was 3.80 (95% CI, 1.36-10.65) in patients with short CL. ROC analysis was performed to determine a cut-off CL value of 35 mm to predict APH, with a sensitivity of 80.7% and a specificity of 60.2%.
Conclusions: Our data indicated that CL measurements may be useful in determining patients at high risk of APH.

Key words: placenta previa, cervical length, antepartum hemorrhage, ultrasonography

INTRODUCTION

Placenta previa complicates 0.3-0.5% of pregnancies and can cause antepartum and intrapartum massive hemorrhage, which often necessitates allogenic blood transfusion and hysterectomy, rarely leading to maternal death [1]. Perinatal practice regarding placental previa has improved through efforts in referral of patients to advanced facilities, well-managed hospitalization during the 2nd and/or 3rd trimester, and countermeasure for hemorrhage during delivery. There is need for a useful clinical predictor for identifying patients at a high risk of antepartum massive hemorrhage (APH). Several recent retrospective studies have indicated that cervical length (CL) measured by transvaginal ultrasonography may be a predicting parameter for APH in patients with placenta previa [2-10]. However, conflicting data exist. Here, we report a retrospective chart review of patients with placenta previa and evaluated the relationship between the CL and the eventual occurrence of APH.

METHODS

Pregnant women with placenta previa, who delivered at our institution from January 2010 to December 2016, were retrospectively reviewed. This study was approved by the local Institutional Review Board for Clinical Research, and written informed consent was waived because of the retrospective design. The gestational age was confirmed in all patients on first-trimester ultrasonography. We excluded patients with multiple pregnancies and fetal anomalies. Placenta previa was diagnosed at 20 weeks of gestation based on transvaginal ultrasonography findings. CL was measured bi-weekly between 20 weeks and 35 weeks of gestation. Before CL measurement, patients were asked to empty their bladder. A sagittal view of the cervical carnal was obtained to visualize the straight line from the internal cervical os to the external cervical os. At least three measurements were obtained, and the shortest value was recorded. The shortest CL measured throughout gestation in each patient was used for analysis. Placenta previa was classified into the following types: complete, partial, and marginal previa. Patients with low-lying placenta were excluded. Selective cesarean section (CS) was scheduled around 37 weeks of gestation. In the case of ongoing active bleeding, emergency CS was performed regardless of gestational age. We defined CL less than 30 mm as short CL and that more than 30 mm as normal CL. APH was defined as uncontrollable, massive hemorrhage during antepartum phase that necessitated an emergency.

Statistical analysis was performed using with the Mann-Whitney U test, $\chi 2$ test, statistical and Fisher's exact tests in JMP Version 13 (SAS Institute Inc., Cary NC, US). Statistical significance was defined as a P-value < 0.05. A receiver-operating characteristics (ROC) curve was plotted to determine the cut-off

Table 1 Maternal characteristics of patients with placenta previa according to cervical length

	Normal CL (CL ≧ 30 mm) n = 102	Short CL (CL < 30 mm) n = 27	*P*-value
Maternal age (years)	35 (30.75–38)	33 (30–36)	0.128
Gravidity	1 (0–2)	1 (0–2)	0.630
Parity	0 (0–1)	1 (0–1)	0.291
Prior CS	12 (11.8%)	4 (14.8%)	0.743
ART	20 (19.6%)	5 (18.5%)	0.900

Data are expressed as median and range or number and a percentage of the total number of cases. Comparisons were analyzed by Mann-Whitney U test, chi-square test, and Fisher's exact test, where appropriate. *Significant P < 0.05, ** Highly significant P < 0.001. CL: cervical Length, CS: cesarean section, ART: assisted reproductive technology

Table 2 Ultrasonographic findings in patients with placenta previa according to cervical length

	Normal CL (CL ≧ 30 mm) n = 102	Short CL (CL < 30 mm) n = 27	*P*-value
Minimal CL (mm)	37.5 (34–45)	24 (19–26)	<0.001**
GA at minimal CL (weeks)	33 (30–35)	31 (29–34)	0.161
Type of previa			
Complete	56 (54.9%)	21 (77.8%)	0.031*
Partial	20 (19.6%)	2 (7.4%)	0.161
Marginal	26 (25.5%)	4 (14.8%)	0.311
Dominant placental location			
Anterior	15 (14.7%)	6 (22.2%)	0.347
Posterior	73 (71.6%)	15 (55.6%)	0.112
Others	14 (13.7%)	6 (22.2%)	0.278

Data are expressed as median and range or number and a percentage of the total number of cases. Comparisons were analyzed by Mann-Whitney U test, chi-square test, and Fisher's exact test, where appropriate. *Significant P < 0.05, **Highly significant P < 0.001. CL: cervical Length, GA: gestational age

CL value to predict APH. Statistical evaluation also included univariate and multivariate analyses. We investigated a possible association of the CL with APH. Additionally, an ROC analysis for CL was carried out.

RESULTS

In total, 129 women with placenta previa were enrolled in this study. We excluded patients with multiple pregnancies and fetal anomalies. Maternal characteristics are shown in Table 1, with a comparison between those with normal CL (n = 102; 79.1%) and those with short CL (n = 27; 20.9%). There were no significant differences between the groups with regards to maternal age, gravidity, parity prior CS, and the use of assisted reproductive technology (ART). Comparison between those with normal CL and short CL according to ultrasonographic findings are provided in Table 2. The median CL values in the normal and short CL groups were 37.5 mm (range 34.0–45.0) and 24.0 mm (range 19.0–26.0), respectively. Minimal CL value (P < .001) and prevalence of complete previa (P < 0.05) were significantly different between the two groups. There was no difference between the groups regarding the GA at minimal CL and dominant placental location (anterior, posterior, or others). Maternal outcomes are presented

in Table 3. The prevalence of APH and emergency CS were significantly higher among patients with short CL than among those with normal CL: 11 (40.7%) vs 15 patients (14.7%) for the former, and 15 (55.6%) vs 26 patients (25.5%) for the later (P < 0.05). No significant difference was observed between both groups regarding GA at delivery, prevalence of minor hemorrhage, GA at minor hemorrhage, prevalence of hemorrhage at CS, incidences of placenta accrete and cesarean hysterectomy. On univariate analysis, the odds ratios for APH using short CL and incidence of minor hemorrhage were 3.99 (95% confidence interval (CI) 1.55–10.24) and 5.05 (95% CI, 1.94–13.15), respectively. A multivariate analysis using short CL and incidence of minor hemorrhage showed the adjusted odds ratios for APH as 3.80 (95% CI, 1.36–10.65) and 4.88 (95% CI, 1.79–13.33), respectively (Table 4). Based on the ROC curve at a cut-off point of 35 mm for CL, the sensitivity, specificity, positive predictive value, and negative predictive value were 80.7%, 60.2%, 33.9% and 92.5%, respectively for the prediction of APH, with the area under the curve of 0.74 (Fig. 1).

Table 3 Clinical outcomes in patients with placenta previa according to cervical length

	Normal CL (CL ≧ 30 mm) n = 102	Short CL (CL < 30 mm) n = 27	*P*-value
GA at delivery (weeks)	36.0 (35.0–37.0)	36.0 (32.0–37.0)	0.017
Minor hemorrhage	41 (40.2%)	14 (51.9%)	0.276
GA at minor hemorrhage (weeks)	31.0 (28.8–34.0)	28.0 (27.5–34.3)	0.453
APH	15 (14.7%)	11 (40.7%)	0.003*
Emergency CS	26 (25.5%)	15 (55.6%)	0.003*
Hemorrhage at CS (ml)	1652 (1225.8–2172.3)	1845 (1100–2228)	0.567
Placenta accreta	5 (4.9%)	1 (3.7%)	0.793
Cesarean hysterectomy	6 (5.9%)	1 (3.7%)	0.657

Data are expressed as median and range or number and a percentage of the total number of cases. Comparisons were analyzed by Mann-Whitney U test, chi-square test, and Fisher's exact test, where appropriate. *Significant P < 0.05, **Highly significant P < 0.001. CL: Cervical Length, GA: gestational age, APH: antepartum hemorrhage, CS: cesarean section

Table 4 Correlated risk factors for APH in univariate and multivariable logistic regression analysis

Variables	Univariate odds ratio (95% CI: lower-upper)	*P*-value	Multivariate odds ratio (95% CI: lower-upper)	*P*-value
Short cervix	3.99 (1.55–10.24)	0.004*	3.80 (1.36–10.65)	0.011*
Minor hemorrhage	5.05 (1.94–13.15)	< 0.001**	4.88 (1.79–13.33)	0.002*

Risk factors for antepartum hemorrhage, on the basis of univariate and multivariate analysis, were introduced into a logistic regression analysis. Data are expressed odds ratio and 95% confidence intervals (CI). *Significant P < 0.05, **Highly significant P < 0.001. CL: cervical length, NA = not applicable
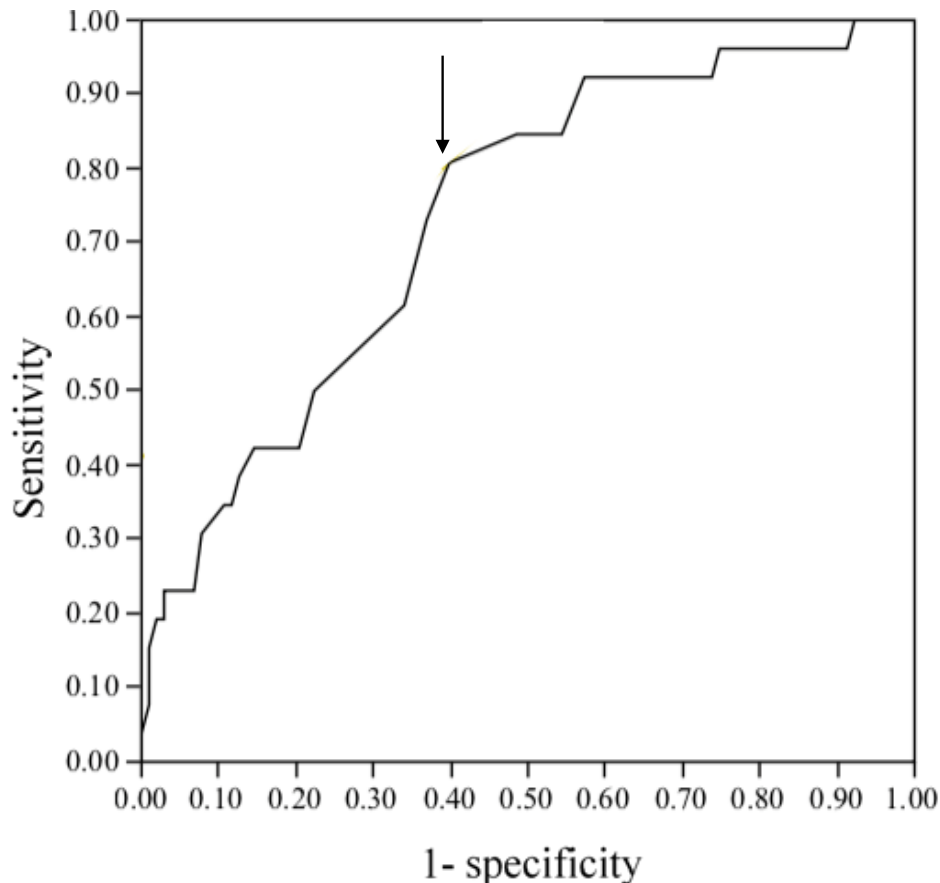

Fig. 1 Receiver operating characteristics curve for cervical length in the prediction of antepartum hemorrhage

Table 5 Review of previous studies for cervical length association with antepartum hemorrhage or emergency cesarean section in patients with placenta previa

Author(year)	Study Design	Short CL association with APH	Definition of a short SL
Ghi(2009)	retrospective	Positive	Not specified
Stanfford(2010)	retrospective	Positive	CL ≦ 30 mm
Hasegawa(2011)	retrospective	Negative	CL < 25 mm
Zaitoun(2011)	retrospective	Positive	CL ≦ 30 mm
Fukushima(2012)	retrospective	Positive	CL ≦ 30 mm
Urmila(2013)	retrospective	Positive	CL ≦ 30 mm
Sekiguchi(2015)	retrospective	Positive	CL ≦ 35 mm
Shin(2016)	retrospective	Negative	CL < 25 mm
Altralgey(2019)	cohort	Positive	CL < 30 mm

CL: cervical length, APH: antepartum hemorrhage

DISCUSSION

Our study showed that short CL and minor hemorrhage are risk factors for APH in pregnant women with placenta previa. CL measurements may be useful, and a CL of 35 mm was the most appropriate cutoff value for predicting the risk of APH.

Cases of placenta previa generally present with painless vaginal bleeding in the 2nd and 3rd trimesters. Sudden, uncontrollable, massive hemorrhage requiring emergency CS sometimes occurs and leads to maternal and neonatal morbidity and mortality. The effacement and dilatation of the cervix is thought to be one of the reasons for placental vessel tearing, which causes massive hemorrhage [11]. It is difficult to predict accurately which individuals are at risk of APH. Assessment of the risk factors for APH is one of the important issues in the management of the patients with placenta previa.

Ultrasonography is a useful and minimally invasive examination. Previous studies have reported the associations of CL measured by transvaginal ultrasonography with APH or emergency CS in women with placenta previa (Table 5) [2-10]. Ghi *et al.* reported that CL measured by transvaginal ultrasonography predicts the risk of emergency CS before 34 weeks of gestation in patients with complete placenta previa compared with those who underwent elective cesarean section [2]. Other studies also reported that CL < 35 or 30 mm at any gestational age was associated with increased risk of APH or emergency CS [3, 5-8, 10]. Our study suggested that a CL of 35 mm was the most appropriate cutoff value for predicting the risk of APH. However, some reports have shown no correlation between short CL and massive hemorrhage [4, 9]. The association between short CL and APH remains controversial.

Some previous studies have reported that serial CL measurements are more informative than a single measurement. Sekiguchi *et al.* also used serial CL measurements in complete placenta previa and reported that a decrease in CL after 26 gestational weeks is a risk factor for preterm CS due to massive hemorrhage [8]. Shin *et al.* also reported that a single CL measurement is not adequate to predict the outcome. They focused on the change in CL and suggested that a change in CL greater than 6 mm from the second to third trimester provides useful clinical information on emergency CS [9]. Zaitoun *et al.* reported that CL < 30 mm combined with thick lower placental edge predicts the risk of emergency CS in women with complete placenta previa [5]. In our study, CL was also measured bi-weekly, and the shortest measurement was recorded. We focused only on the shortest CL measured throughout the gestation period in each patient. Considering that not only CL but also other ultrasonographic changes might enable the accurate evaluation of patients with placenta previa at a high risk for APH.

One of the main limitations of this study is its retrospective design. Another limitation is the small number of patients with short CL. Therefore, a prospective study on a large number of patients is required to confirm the usefulness of CL as a predicting parameter for APH in patients with placenta previa.

In conclusion, our findings showed that CL measurement by transvaginal ultrasonography may be useful in determining high-risk patients for APH.

CONFLICT OF INTEREST

We have no conflict of interest to declare.

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