

Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery

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ABSTRACT

Objective To examine the potential value of routine measurement of cervical length in singleton pregnancies at 23 weeks of gestation in the prediction of the risk for early spontaneous preterm delivery.

Methods Cervical length was measured by sonography at 23 weeks in 2567 singleton pregnancies in women attending for routine antenatal care. In 43 women, the length was ≤ 15 mm and 21 of these were managed expectantly, whereas in 22 cases a cervical cerclage was placed. In the pregnancies that were managed expectantly, the relation between cervical length and preterm delivery was examined and the risk of spontaneous delivery at ≤ 32 weeks was estimated.

Results Cervical length at 23 weeks was ≤ 15 mm in 1.7% of cases; this group contained 86%, 58% and 20% of pregnancies that delivered spontaneously at ≤ 28 , ≤ 32 and ≤ 36 weeks, respectively. The risk for delivery at ≤ 32 weeks decreased from 78% at a cervical length of 5 mm to 4% at 15 mm and 0.5% at 50 mm.

Conclusions Cervical length at 23 weeks is ≤ 15 mm in $< 2\%$ of the population; this group contains about 90% and 60% of the women delivering at ≤ 28 and ≤ 32 weeks, respectively. Measurement of cervical length provides accurate prediction of risk for early preterm delivery.

INTRODUCTION

Delivery before 37 weeks occurs in less than 10% of pregnancies but accounts for more than 75% of all neonatal deaths¹. In about one-third of cases, delivery is iatrogenic and in the other two-thirds it is spontaneous. Survival of preterm infants is mainly dependent on gestational age at delivery and survival increases from less than 5% for those born at 23 weeks to more than 95% by 32 weeks^{2,3}. The risk of severe handicap in survivors decreases from more than 60% for those born at 23 weeks to less than 5% by 32 weeks^{2,4}. Consequently, prediction of the high-risk group

for preterm delivery, especially at ≤ 32 weeks, and useful intervention to prevent this complication of pregnancy constitute major challenges in obstetrics.

Recently, several studies in pregnancies considered at high risk, because of a history of previous mid-trimester miscarriage or early preterm delivery, and those presenting with preterm labor, have reported that cervical assessment may provide useful prediction of preterm delivery⁵. Furthermore, in a screening study involving measurement of cervical length by transvaginal sonography at 24 weeks of gestation in a routine population of 2915 pregnancies, a cervical length of 20 mm or less identified 23% of those delivering before 35 weeks with a false-positive rate of 3% and a positive predictive value of 26%⁶.

The aim of this study was to establish the relation between cervical length in a routine population of singleton pregnancies at 23 weeks of gestation and risk of spontaneous preterm delivery.

SUBJECTS AND METHODS

During a 14-month period (January 1997 to March 1998), women attending King's College Hospital, London for routine antenatal care were offered the option of having transvaginal sonographic assessment of the cervix at 23 weeks of gestation. Patient recruitment, method of cervical assessment, acceptability and reproducibility of cervical length measurement and the relation of cervical length to demographic characteristics and previous obstetric history have been described previously⁷. Immediately before the scan, a speculum examination was carried out and a dry swab was taken from the posterior vaginal fornix for detection of bacterial vaginosis, as described by Nugent and colleagues⁸. Written informed consent was obtained from those agreeing to participate in the study, which was approved by the hospital ethics committee.

Patient characteristics, including demographic data and previous obstetric and medical history, were obtained from

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the patients at their first antenatal visit to the hospital by midwives and were entered into a computer database. Similarly, the ultrasound and Gram stain results were recorded in the database at the time of the scan. Gestational age was determined from the menstrual history and confirmed from the measurement of fetal crown–rump length at the first-trimester scan. Data on pregnancy outcome were obtained from the computerized system in the delivery ward, and, in those that delivered at home or in other hospitals, from the patients themselves or their general medical practitioners.

The information recorded in the patient notes was whether the cervical length was more than 15 mm or ≤ 15 mm. This cut-off was selected at the onset of the study, which was essentially an observational one. However, on the basis of existing data^{5,6}, the risk for preterm delivery associated with a cervical length of ≤ 15 mm was considered to be substantially increased and justified informing both the patient and her obstetrician. Patients with a cervical length above 15 mm had normal antenatal care. Those with a length of ≤ 15 mm were either managed expectantly or they had a Shirodkar cerclage; the main determinant in favor of or against placement of a cerclage was the preference of the individual obstetrician and there was no significant difference between the two groups in demographic characteristics, previous obstetric history, prevalence of bacterial vaginosis or median cervical length⁹.

During the study period, 3358 women with singleton pregnancies attended for a scan at 22–24 (median 23) weeks of gestation and 2702 (80%) of these agreed to participate in the study; in all cases the cervical length was measured successfully⁷. In 135 (5%) of the 2702 pregnancies there was no follow-up because the patients did not deliver in our hospital and they could not be contacted, since they had changed address and general practitioner. In

the 2567 pregnancies with known outcome, there were 62 cases of iatrogenic preterm delivery and these pregnancies were excluded from further analysis (Figure 1). In 43 women, the cervical length was ≤ 15 mm and these women were referred to their obstetricians for the further management of pregnancy. In 21 cases, the pregnancy was managed expectantly and in 22 a Shirodkar cerclage was placed under spinal anesthesia at 23–24 weeks. The 2462 women with cervical length more than 15 mm were managed expectantly and these pregnancies were randomly allocated into Group A and Group B of 1231 cases each (Figure 1).

Statistical analysis

The 21 cases with a short cervix that were managed expectantly were added to Group A and the sensitivity and false-positive rate for different cervical length cut-offs in the prediction of spontaneous preterm delivery were calculated. The normality of the distribution of cervical length was examined by the Kolmogorov–Smirnov test. The χ^2 test or Fisher's exact test was used to calculate the significance of differences in the percentage of spontaneous delivery at ≤ 32 weeks between subgroups, according to demographic characteristics, previous obstetric history and the presence or absence of bacterial vaginosis. Logistic regression analysis was used to determine those variables (from the demographic characteristics, past obstetric history, Gram stain result and cervical measurement) that provided a significant independent contribution in explaining the rate of spontaneous preterm delivery at ≤ 36 and ≤ 32 weeks. The likelihood ratio for delivery at ≤ 32 weeks was calculated from the frequency distribution of cervical lengths in the women delivering at ≤ 32 and ≥ 33 weeks. Regression analysis was then used to derive a curve describing the relation of likelihood ratios to cervical length. The

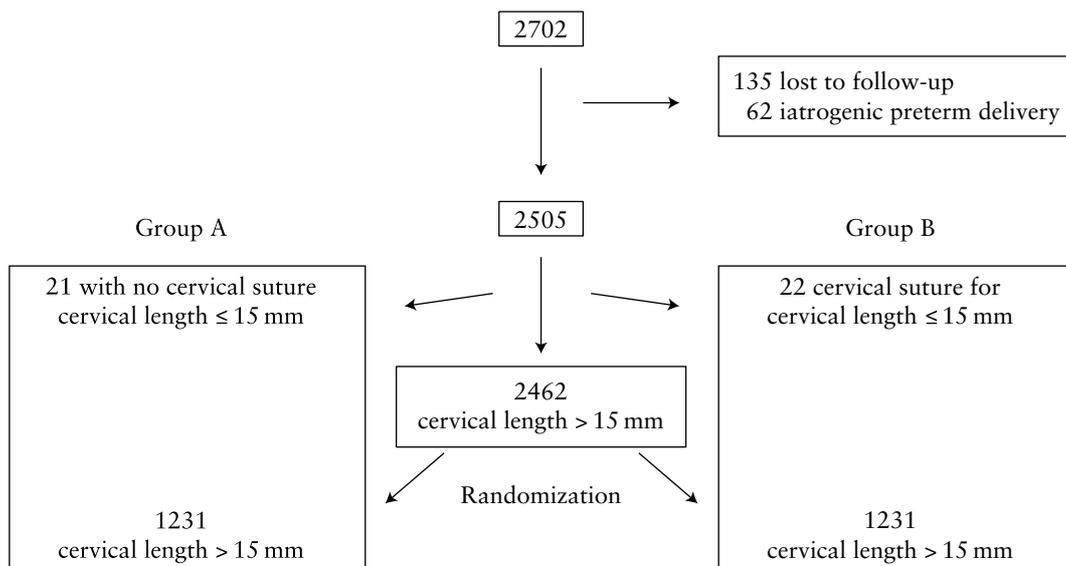


Figure 1 Study population. In this study, 2702 patients were recruited but 135 were lost to follow-up and 62 had iatrogenic preterm delivery. In the remaining 2505, there were 43 with cervical length of ≤ 15 mm and the 21 managed expectantly were allocated into Group A, whereas the 22 that had cervical cerclage were allocated into Group B. The 2462 patients with cervical length of > 15 mm were randomly allocated into Groups A and B

risk of spontaneous delivery at ≤ 32 weeks according to cervical length was then calculated by multiplying the overall rate by the appropriate likelihood ratio.

RESULTS

In the subgroup A of 1252 pregnancies that were managed expectantly (Figure 1), demographic characteristics and previous obstetric history (Table 1) were similar to those of the whole population⁷.

The cervical length was approximately normally distributed with some skewness at the lower end (Figure 2). The median value was 38 mm, and the 5th and 1st centiles were 23 mm and 11 mm, respectively. In 18.0%, 8.0%, 3.4% and 1.7% of cases, the cervical length was ≤ 30 mm,

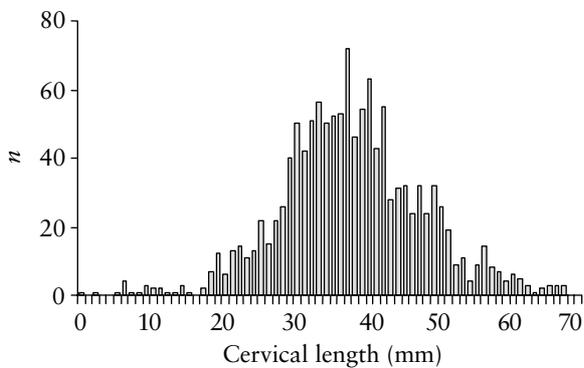


Figure 2 Distribution of cervical length at 23 weeks of gestation in 1252 singleton pregnancies managed expectantly (Group A)

≤ 25 mm, ≤ 20 mm and ≤ 15 mm, respectively. Bacterial vaginosis was present in 208 (16.6%) of the cases; there was no significant association between cervical length and the frequency of bacterial vaginosis (mean difference 0.66, 95% confidence interval -0.97 to 2.29).

In Group A, the spontaneous delivery rate at ≤ 36 , ≤ 34 , ≤ 32 , ≤ 30 , ≤ 28 and ≤ 26 weeks was 5.0%, 2.3%, 1.5%, 0.9%, 0.6% and 0.3%, respectively and the cervical length at 23 weeks was ≤ 15 mm in 20%, 38%, 58%, 82%, 86% and 100% of these cases (Figure 3).

The rate of spontaneous preterm delivery at ≤ 32 weeks was significantly higher in women of Afro-Caribbean origin compared to Caucasians but there were no significant differences between other subgroups (Table 1). Logistic regression analysis using demographic characteristics, past obstetric history, prevalence of bacterial vaginosis and cervical measurement demonstrated that, in explaining the rate of spontaneous preterm delivery at ≤ 36 weeks, there were significant independent contributions from cervical length and past obstetric history, whereas for delivery at ≤ 32 weeks only cervical length was significant.

The frequency distribution of cervical lengths in the women delivering at ≤ 32 and > 32 weeks and the likelihood ratio for delivery at ≤ 32 weeks are shown in Table 2. The relationship between likelihood ratio and cervical length is shown in Figure 4 ($\log_{10}(\text{likelihood ratio}) = 0.00005 \times \text{cervical length}^3 + 0.0058 \times \text{cervical length}^2 - 0.2284 \times \text{cervical length} + 2.7151$). The likelihood ratio for delivery at ≤ 32 weeks decreased from 51.5 at a cervical length of 5 mm to 2.7 at 15 mm and 0.4 at 50 mm and the corresponding estimated risks for severe preterm delivery were 78%, 4% and 0.5%, respectively (Figure 5).

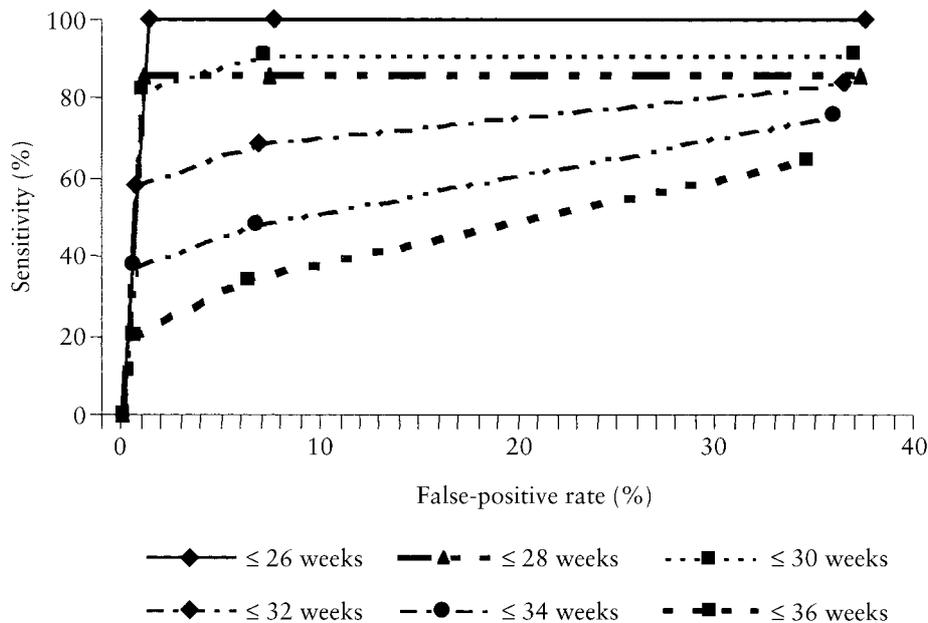


Figure 3 Receiver operator characteristic curves. The sensitivity and false-positive rate of cervical length of ≤ 15 mm, ≤ 25 mm and ≤ 35 mm at 23 weeks of gestation (the points on each curve represent the results when the cervical length was ≤ 15 mm, ≤ 25 mm and ≤ 35 mm) in the prediction of spontaneous delivery rate at ≤ 26 , ≤ 28 , ≤ 30 , ≤ 32 , ≤ 34 and ≤ 36 weeks of gestation

Table 1 Relation between rate of spontaneous delivery at ≤ 32 weeks of gestation and patient characteristics

Patient characteristics	Total (%)	Delivery ≤ 32 weeks (%)	RR	Comparison of subgroups	d.f.	p Value
<i>Age (years)</i>						
1 < 20	93 (7.4)	2 (2.2)	1.42		2	NS
2 20–35	919 (73.4)	13 (1.4)	0.93			
3 > 35	240 (19.2)	4 (1.7)	1.10			
<i>Ethnic group</i>						
1 Caucasian	596 (47.6)	4 (0.7)	0.44		2	< 0.05
2 Afro-Caribbean	594 (47.4)	15 (2.5)	1.66	1 vs. 2	1	< 0.05
3 Other	62 (5.0)	0		1 vs. 2	1	NS
<i>Ponderal index</i>						
1 < 19.8	88 (7.0)	1 (1.1)	0.75		2	NS
2 19.8–26	716 (57.2)	9 (1.3)	0.83			
3 > 26	448 (35.8)	9 (2.0)	1.32			
<i>Cigarette</i>						
1 Smoker	178 (14.2)	4 (2.2)	1.48		1	NS
2 Non-smoker	1074 (85.8)	15 (1.4)	0.92			
<i>Alcohol</i>						
1 Drinker	20 (1.6)	0			1	NS
2 Non-drinker	1232 (98.4)	19 (1.5)	1.00			
<i>Illicit drugs</i>						
1 User	7 (0.6)	0			1	NS
2 Non-user	1245 (99.4)	19 (1.5)	1.00			
<i>Cervical surgery</i>						
1 Cone biopsy	4 (0.3)	0			2	NS
2 Laser surgery	20 (1.6)	0				
3 None	1228 (98.1)	19 (1.5)	1.00			
<i>Obstetric history</i>						
1 Primigravidae	381 (30.4)	4 (1.0)	0.69		6	NS
2 Multigravidae	871 (69.6)	15 (1.7)	1.13	1 vs. 2	1	NS
3 Fetal loss at < 16 weeks	235 (18.8)	5 (2.1)	1.40	1 vs. 3	1	NS
4 Delivery at ≥ 37 weeks	566 (45.2)	8 (1.4)	0.93	1 vs. 4	1	NS
5 Delivery at 33–36 weeks	36 (2.9)	1 (2.8)	1.83	1 vs. 5	1	NS
6 Delivery at 24–32 weeks	12 (1.0)	1 (8.3)	5.49	1 vs. 6	1	NS
7 Termination at 16–23 weeks	16 (1.3)	0		1 vs. 7	1	NS
8 Miscarriage at 16–23 weeks	6 (0.5)	0		1 vs. 8	1	NS
<i>Bacterial vaginosis</i>						
1 Positive	208 (16.6)	5 (2.4)	1.58		1	NS
2 Negative	1044 (83.4)	14 (1.3)	0.88			

RR, relative risk; d.f., degrees of freedom; NS, not significant

The formula for cervical length-related risk for preterm delivery at ≤ 32 weeks was applied to the 1252 patients in Group A and 1230 patients in Group B (excluding the 22 cases of cervical cerclage) to calculate the expected number of spontaneous deliveries at ≤ 32 weeks; the observed and expected numbers were 19 and 18.9 for Group A and 10 and 8.9 for Group B, respectively.

DISCUSSION

This study has demonstrated that measurement of cervical length at 23 weeks of gestation provides sensitive prediction of severe preterm delivery. Cervical length at this gestation is ≤ 15 mm in less than 2% of the population and this group contains about 60% of women delivering spontaneously at ≤ 32 weeks, 80% of those delivering at ≤ 30 weeks and 100% of those delivering at ≤ 26 weeks. Furthermore, the study provides a model for the prediction of individual risk for spontaneous delivery at ≤ 32 weeks based on cervi-

cal length at 23 weeks. The estimated risk for severe preterm delivery increases exponentially with decreasing cervical length from about 0.2% at 60 mm, to 0.8% at 30 mm, 4.0% at 15 mm and 78% at 5 mm.

A previous study, on this group of patients, demonstrated that cervical length is associated with ethnic group, maternal age, ponderal index, drug abuse and past obstetric history⁷. We found that the only contributor in predicting early preterm delivery is cervical length. Consequently, the well-described associations between certain demographic characteristics and past obstetric history with preterm delivery may be mediated through cervical changes that are apparent as cervical shortening by 23 weeks of gestation.

In contrast to delivery at ≤ 32 weeks, in the prediction of delivery at ≤ 36 weeks there were significant independent contributions from past obstetric history, and the sensitivity of short cervix at 23 weeks was only 20%. Indeed, only one of the 43 women delivering spontaneously

Table 2 Frequency distribution of cervical lengths in the women delivering at > 32 and ≤ 32 weeks and the likelihood ratio (LR) (observed and regressed) and risk for delivery at ≤ 32 weeks

Cervical length (mm)	Delivery > 32 weeks		Delivery ≤ 32 weeks		Observed LR	Regressed LR	Risk %
	n	%	n	%			
0–10	10	0.81	8	42.11	51.92	51.51	78.2
11–20	77	6.24	3	15.79	2.53	2.66	4.0
21–30	371	30.09	2	10.53	0.35	0.71	1.1
31–40	494	40.06	5	26.32	0.66	0.48	0.7
41–50	213	17.27	1	5.26	0.30	0.42	0.6
51–60	59	4.79	0	0.00	—	0.24	0.4
61–70	9	0.73	0	0.00	—	0.04	0.1

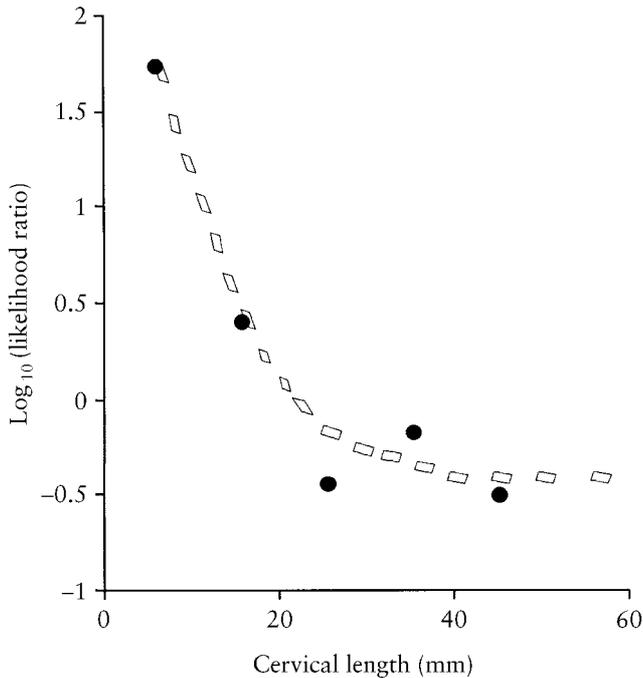


Figure 4 Likelihood ratios for spontaneous delivery at ≤ 32 weeks according to cervical length at 23 weeks of gestation (\log_{10} (likelihood ratio) = $0.00005 \times \text{cervical length}^3 + 0.0058 \times \text{cervical length}^2 - 0.2284 \times \text{cervical length} + 2.7151$)

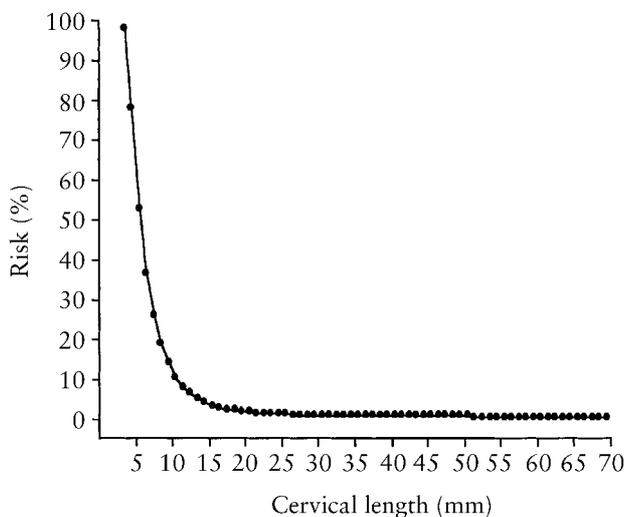


Figure 5 Risk for spontaneous delivery at ≤ 32 weeks according to cervical length at 23 weeks of gestation

at 33–36 weeks was from the group with a cervix of ≤ 15 mm. Consequently, cervical assessment provides sensitive prediction of spontaneous delivery within the next 10 weeks. This is the likely explanation for the much lower sensitivity (23%) in the prediction of preterm delivery that was reported in a previous major screening study of cervical assessment at 24 weeks; in that study only delivery before 35 weeks was considered⁶.

There is extensive evidence suggesting that, in a high proportion of pregnancies complicated by preterm labor, the underlying cause may be ascending infection from the lower genital tract; intrauterine infection, either directly or through the host response with the release of cytokines, may stimulate the production of prostaglandins that induce uterine contractions^{10,11}. In our study, there was no significant association between the presence of bacterial vaginosis and either cervical length or the incidence of spontaneous severe preterm delivery. Although these findings suggest that factors other than mere colonization of the lower genital tract are implicated in preterm delivery, they do not preclude a role for intrauterine infection. Indeed, it could be postulated that cervical shortening, with a concomitant loss of cervical mucus, may promote intrauterine infection; the mucus, through its physical properties and intrinsic antibacterial activity, normally acts as a barrier to ascending infection.

In our inner-city mixed population, the overall incidence of preterm delivery at ≤ 32 weeks was about 2%, which is similar to the incidence in all singleton pregnancies in the USA¹². In two-thirds of the cases (1.5%), delivery was spontaneous and in the other one-third it was iatrogenic. The likelihood ratio for spontaneous early preterm delivery when the cervical length was 20 mm was about 1 and the risk decreased linearly with cervical length from about 1.5% at 20 mm to 0.2% at 60 mm. For cervical length below 20 mm, there was an exponential increase in risk to about 15% at 10 mm and 80% at 5 mm. These findings demonstrate that the cervix maintains its physiological role as an effective barrier to early preterm delivery until its length is shortened to below one-third of the average.

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