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Cervical cerclage in twin pregnancies

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Abstract
Purpose To evaluate the outcomes of cervical cerclage (CC) in twin pregnancies.
Methods Retrospective analysis of twin pregnancies undergoing CC between January 2001 and December 2009 at our Institution. CC was offered in case of a cervical length measurement ≤20 mm (ultrasound-indicated CC) or in case of cervical dilatation with membranes at or beyond the external cervical os (physical examination-indicated CC). Cervicovaginal and rectal swabs were obtained preoperatively. Perioperative antibiotics and tocolysis were administered.
Results There were 28 cases of ultrasound-indicated and 14 of physical examination-indicated CC. Positive swab cultures were observed in 21 % of cases. The incidence of preterm delivery <34 weeks was 32 % [95 % confidence interval (CI) 16–52 %] and 50 % (95 % CI 23–77 %) in the ultrasound-indicated and physical examination-indicated CC group, respectively. The incidence of premature rupture of membranes <34 weeks was 21 % (95 % CI 8–41 %) and 29 % (95 % CI 8–58 %) in the ultrasound-indicated and physical examination-indicated CC group, respectively. Perinatal survival was 96 % (95 % CI 88–100 %) in the ultrasound-indicated CC group, and 86 % (95 % CI 67–96 %) in the physical examination-indicated CC group.
Conclusions We showed a high-risk of preterm delivery in both groups, but with a high overall perinatal survival. Our data stress the importance of re-evaluating the efficacy of CC in twin pregnancies by properly designed clinical trials, particularly if it is physical examination indicated.

Keywords Dichorionic · Monochorionic · Cervical length · McDonald · Preterm delivery

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Introduction

Twin pregnancies are a high-risk obstetric population and the largest part of adverse outcome excess in these pregnancies is related to preterm delivery (PTD) [1]. Although maternal–foetal complications and iatrogenic preterm delivery are more common in twin pregnancies, spontaneous labour and preterm premature rupture of the membranes (PPROM) are responsible for three out of four twin preterm deliveries [2]. In order to reduce perinatal complications, the identification of twin pregnancies at high risk of preterm delivery, and the prolongation of those pregnancies, must be obtained [1]. There is evidence of an association between decreasing second-trimester cervical length (CL), as measured by transvaginal ultrasound, and increasing risk of spontaneous PTD in twins [3]. However, an effective intervention to be applied once cervical shortening has been detected is yet to be identified. The use of cervical cerclage (CC) to prevent PTD is still controversial, particularly in multiple pregnancies. According to the systematic reviews available, CC in twin pregnancies seems to be associated with a significantly increased risk of preterm birth [4, 5].

The aim of this study was to evaluate the outcomes of CC performed in twin pregnancies at our Institution.

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Methods

We retrospectively analysed all twin pregnancies that underwent CC at our institution between January 2001 and December 2009. The study population consisted of consecutive twin pregnancies that received a CC at $\leq 26^{+2}$ weeks of gestation for an ultrasound CL $\leq$20 mm (ultrasound-indicated or therapeutic CC) or for cervical dilatation with membranes at or beyond the external cervical os (physical examination-indicated or clinically indicated or emergency CC). Patients who had a history-indicated CC placement were excluded.

Patient characteristics were obtained at the first visit and recorded into a twin clinic database. These data included demographic data, ethnicity, medical and obstetric history, parity, gravidity, assisted reproduction technology (ART), multifetal embryo reduction (MFER). The pregnancies were verified as being monochorionic or dichorionic according to the absence of presence of the lambda sign, respectively, at an ultrasound examination performed at 10–14 weeks of gestation.

Transvaginal ultrasonographic measurement of cervical length (CL) was performed between 18 and 25 weeks of gestation using a standardized technique previously described [6]. The majority of the CL measurements were obtained at the time of the foetal anatomic survey between 19 and 22 weeks of gestation. In brief, each examination was performed with the patient in the dorsal lithotomy position. The probe was inserted into the anterior vaginal fornix until the internal cervical os, the endocervical canal and the external os could all be visualized. Reduced pressure on the transducer was applied to avoid falsely elongated cervical measurements. CL was recorded as the distance in millimeters between the points at which the proximal and distal endocervical walls were juxtaposed. In cases of clinically indicated cerclage, where no closed endocervical canal was present, the length of the remaining cervix surrounding the protruding membranes was measured between internal and external os: a completely effaced cervix corresponded to a measurement of 0 mm. Each examination was continued for a few minutes to observe any dynamic cervical changes that may have occurred. The cervix was measured three times, also under Valsalva manoeuver; and the shortest measurement was recorded. The CL measurement was performed by obstetricians trained in this technique, and all the images were recorded in an ultrasound database and reviewed to confirm their adequacy.

If a CL measurement of $\leq$20 mm was obtained or if cervical dilatation (at any stage) with membranes at or beyond external cervical os were diagnosed, a transvaginal CC was offered. In all cases vaginal and endocervical swabs were obtained before CC placement, to check for possible infection. If the swabs were positive for bacterial colonization, the patient received targeted antibiotic therapy and CC was performed after at least 5 days of therapy. All women with dilated cervix and/or prolapsed membranes were placed on prophylactic intravenous antibiotic treatment with either ceftazidime 1 g or clindamycin 600 mg three times per day before receiving the results of the swabs taken at admission.

Perioperative tocolytic agents were administered (indomethacin 200 mg/day per os for 1–2 days before and for 2–3 days after the CC). In those patients not receiving antibiotic treatment, a single prophylactic dose of ampicillin 2 g and sulbactam 1 g, or clindamycin 600 mg, was administered intravenously 30 min before the procedure. CC placement was performed using the McDonald technique under general anaesthesia. All the CC procedures were performed as an inpatient procedure, by one of two experienced operators only. A double monofilament prolene stitch n.0 was applied. In all cases the CC was placed only in the absence of regular uterine contractions, as assessed by tocography and clinical examination.

All patients were followed up periodically every 2 weeks during the pregnancy in a dedicated twin outpatient clinic. Recommendations for heavy physical activity restriction and warning for possible maternal symptoms (e.g. uterine contractions) were given to the patients. If preterm labour before 34 weeks of gestation was diagnosed, based on the presence of regular contractions with cervical changes detected by digital examination and/or ultrasound, the patient was admitted to start tocolytic therapy with intravenous atosiban.

Data on admission and follow-up, including CL ultrasound measurements, clinical examinations and gestational age at cerclage were recorded into the twin clinic database. Data on pregnancy outcome including gestational age at delivery, PPROM, spontaneous vs iatrogenic PTD, mode of delivery were obtained from the women's hospital records. Data on neonatal morbidity and mortality were obtained from the Neonatal Intensive Care Unit.

The Chi-square, Fisher, and Mann–Whitney test were applied for intergroup comparisons, as appropriate. All statistical calculations were performed with the SPSS statistical software (release 16, SPSS Inc., Chicago, IL, USA). Two-tailed p values <0.05 were considered statistically significant.

Results

A total of 42 twin pregnancies underwent CC: 28 with ultrasonographic indications (ultrasound-indicated CC group) and 14 with clinical indications (physical examination-indicated CC group).

Clinical characteristics of the two groups, including maternal age, parity, chorionicity, are described in Table 1. The overall incidence of vaginal and endocervical colonization was 21 % (9/42): 18 % (5/28) in the ultrasound-indicated CC group, and 29 % (4/14) in the physical examination-indicated CC group ($p = 0.26$). Cultures were positive for *Streptococcus agalactiae* in 7 % of cases (3/42), *Ureaplasma urealyticum* in 7 % (3/42), and multiple bacterial infection in 7 % (3/42). Pregnancy and neonatal outcomes are presented in Table 2. The median gestational age at delivery was 34^{+6} weeks in the ultrasound-indicated CC group and 32^{+0} in the physical examination-indicated CC group. The overall perinatal survival was 93 % (78/84) and the incidence of respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC) and interventricular haemorrhage (IVH) was 23 % (19/84), 1 % (1/84) and 2 % (2/84), respectively.

Table 1 Clinical characteristics

	Ultrasound indicated ($n = 28$)	Clinically indicated ($n = 14$)
Maternal age (years)	33 [23–41]	32 [21–40]
Nulliparous	14 (50 %)	13 (87 %)
Previous uterine surgery	0 (0 %)	2 (13 %)
Previous preterm delivery	1 (4 %)	0 (0 %)
Dichorionic placenta	25 (89 %)	13 (93 %)
Monochorionic placenta	3 (11 %)	1 (7 %)
Gestational age at cerclage (weeks)	23^{+0} [20^{+5}–26^{+2}]	22^{+3} [19^{+1}–_24^{+4}]
Cervical length at cerclage (mm)	14 [4–20]	Not applicable
Cervical dilatation at cerclage (cm)	0 [0–1]	1 [1–3]
Residual cervical length around protruding membranes (mm)	Not applicable	10 [0–18]
Positive cultures	5 (18 %)	4 (29 %)
Antibiotic treatment	5 (18 %)	4 (29 %)

Data are shown as *n* (%) or median [range]

The incidence of PTD and PPROM was compared between monochorionic (4/42) and dichorionic (38/42) pregnancies, but no significant difference was observed: PTD <34 weeks was observed in 75 % (3/4) versus 34 % (13/38; $p = 0.28$); PPROM in 25 % (1/4) versus 24 % (9/38; $p = 1$) in monochorionic and dichorionic twins pregnancies, respectively.

The incidence of PTD and PPROM was analysed in the group of ultrasound-indicated CC comparing the cases with negative (82 %; $n = 23/28$) and positive (18 %, $n = 5/28$) swab cultures. Cases with negative swabs showed a non-statistically significant trend for better outcome (reduced PPROM risk) than the group with positive swabs: the incidence of PTD was 26 % (6/23) and 40 % (2/5), respectively ($p = 0.35$); the incidence of PPROM was 13 % (3/23) and 20 % (1/5), respectively ($p = 0.43$).

Table 2 Pregnancy and neonatal outcomes

	Ultrasound indicated ($n = 28$)	Physical examination indicated ($n = 14$)
Gestational age at delivery, weeks	34^{+6} [25^{+0}–37^{+3}]	32^{+0} [23^{+2}–38^{+6}]
Delivery		
<34 weeks	9 (32 %; 95 % CI 16–52 %)	7 (50 %; 95 % CI 23–77 %)
<32 weeks	6 (21 %; 95 % CI 8–41 %)	7 (50 %; 95 % CI 23–77 %)
<28 weeks	2 (7 %; 95 % CI 1–24 %)	3 (21 %; 95 % CI 5–51 %)
Cerclage to delivery interval, weeks	12^{+3} [2^{+0}–15^{+0}]	9^{+6} [0^{+3}–17^{+6}]
Preterm premature rupture of membranes	6 (21 %; 95 % CI 8–41 %)	4 (29 %; 95 % CI 8–58 %)
Birth weight (g)	2,076 [680–2980]	1,841 [500–3,020]
Admission to NICU	30/56 (54 %; 95 % CI 40–67 %)	15/28 (54 %; 95 % CI 31–72 %)
Length of NICU stay, days	32 [1–270]	39 [4–98]
Perinatal survival	54/56 (96 %; 95 % CI 88–100 %)	24/28 (86 %; 95 % CI 67–96 %)
Respiratory distress syndrome	12/56 (21 %; 95 % CI 12–34 %)	7/28 (25 %; 95 % CI 11–45 %)
Intraventricular haemorrhage	1/56 (2 %; 95 % CI 0–10 %)	1/28 (4 %; 95 % CI 0–18 %)
Retinopathy	1/56 (2 %; 95 % CI 0–10 %)	1/28 (4 %; 95 % CI 0–18 %)
Necrotising enterocholitis	1/56 (2 %; 95 % CI 0–10 %)	0/28 (0 %; 95 % CI 0–12 %)
Sepsis	2/56 (4 %; 95 % CI 0–12 %)	0/28 (0 %; 95 % CI 0–12 %)

Data are shown as *n* (%) or median [range]. 95 % confidence intervals (CI) are shown where appropriate

Discussion

This study evaluated the outcomes of CC performed in twin pregnancies, showing a high risk of preterm delivery <34 weeks in both the ultrasound-indicated and physical examination-indicated CC groups (32 and 50 %, respectively), but with an overall perinatal survival rate of 93 %.

These preliminary results are in contrast with the systematic reviews available [4, 5]. In particular, Berghella et al. concluded that ultrasound-indicated CC in twin pregnancies is associated with a higher risk of PTD (75 % before 35 weeks) and a higher incidence of perinatal mortality (23 %). However, these data are related to a relatively small population of 49 pregnancies from three randomized controlled trials, each of which had different inclusion criteria and management protocols, and none of which was intended to specifically evaluate the role of CC in twin pregnancies [4]. Our data show better results compared to the meta-analysis data [4] for therapeutic CC, with a lower rate of PTD <34 weeks (32 %) and lower perinatal mortality (4 %).

At present, few studies have been conducted on the efficacy of CC to prevent PTD in twin pregnancies [1, 7–11]; most of them are focused on ultrasound-indicated CC, have analysed a small number of cases and are controversial on the role of CC. Most of the studies on CC in twin pregnancies did not exclude the presence of cervicovaginal colonization before performing a CC, although infections are reported as one of the major causes of preterm delivery, at least in singleton pregnancies [12–14]. In our series, ultrasound-indicated CC with negative swabs showed a non-statistically significant trend for better outcome than the group of CC with positive swabs and the group with physical exam-indicated CC, confirming previous considerations on singleton pregnancies [8, 15] and emphasizing the importance of detecting microbial colonization.

In our study, the incidence of vaginal colonisations was 18 % in ultrasound-indicated CC group and 29 % in the physical examination-indicated group, but CC was only performed after antibiotic treatment. A positive culture for *Ureaplasma* was not considered an absolute indication for antibiotics, which explains the two cases in the ultrasound-indicated CC group with a positive culture which were not given antibiotics. In the physical examination-indicated CC group, antibiotic therapy was often started empirically before getting the swab results (Table 1).

Even if in singleton pregnancies cerclage to delivery interval is shorter with physical examination-indicated cerclage than with ultrasound-indicated cerclage [9, 16], our series of twin pregnancies was not large enough to allow us to investigate differences in cerclage to delivery interval between these two groups. However, the results reported by Daskalakis and colleagues [17] in singleton pregnancies with physical examination-indicated CC seem to indicate a lower risk of neonatal mortality and PTD <32 weeks than in our series, confirming an overall worse outcome in twin pregnancies. Monochorionic pregnancies showed a trend towards a higher incidence of PTD before 34 weeks; however, the small absolute number of cases was again too small to allow any further analyses.

The main limitations of the present study are its retrospective nature, and the lack of an appropriate control group with no CC. In some pregnancies with a particularly bad prognosis (e.g. short or dilated cervix <20 weeks) CC may not have been performed, and this might have biased the results towards a more favourable outcome for CC. We think that this is unlikely to have affected our results for ultrasound-indicated CC, as we had a strict protocol requiring CL measurement at the second-trimester scan, and offering of CC in cases with a CL ≤20 mm. In our database, we could not retrieve any patient with a CL ≤20 mm who declined CC placement. This bias could be more likely with physical examination-indicated CC, where pregnancy loss could have happened between presentation (e.g. emergency admission) and the time scheduled for CC placement.

The results reported by PECEP Trial Group [18] show the potential benefits of the Arabin cervical pessary for prevention of preterm birth in a high-risk population, and there are ongoing randomized clinical trials specifically assessing the role of the Arabin pessary in twin pregnancies. Should these trials demonstrate a beneficial effect of the Arabin pessary in twins pregnancies, this would exploit its use given its potential advantages over CC: the pessary is not invasive, and it does not require anaesthesia for placement. However, the pessary cannot be applied on a significantly dilated or effaced cervix, and may have a limited effect on very short cervices. Moreover, as outlined above, the CC has never been assessed in properly designed clinical trials in twin pregnancies, making use of homogenous definitions for stratifying the risk for PTD (previous PTD, CL measurement). Such high-quality data are absolutely needed to define the role of CC, and to avoid wiping out from clinical practice.

Overall, if we consider all CC, the outcomes in our study are better than those presented in the available meta-analyses [4, 5], even if the comparison with better designed or larger papers would not be easy. Moreover, outcomes in the physical examination-indicated CC group in our study are somewhat encouraging, given how extreme this clinical presentation is. A management protocol including infection screening and a liberal use of antibiotics and indomethacin might partly explain these differences. Despite the limitations of our study design, our data stress the importance of re-evaluating the efficacy of CC in twin pregnancies by properly designed clinical trials. Particularly, they might

well inform clinical practice for the rare but extremely risky cases of emergency cerclage, which may often be abandoned because of the currently available twin cerclage data.

Conflict of interest We declare that we have no conflict of interest.

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