

## OBSTETRICS

# Transabdominal cervical cerclage in triplet pregnancies and risk of extreme prematurity and neonatal loss

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### Summary

There are no reports indicating the effect of prophylactic transabdominal cerclage (TAC) on the prolongation of multifetal pregnancies. We report the use of TAC in triplets, which evolved over 20 years in one practice. A retrospective cohort study of triplet pregnancies was conducted. Obstetric and neonatal outcomes were compared among women who underwent a prophylactic TAC or transvaginal cerclage and no cerclage. Of the 141 women who delivered triplets, prophylactic TAC was associated with reduced incidence of extreme prematurity and improved incidence of neonatal/postnatal survival. With the exception of mode of conception, prepregnancy weight, and the use of home monitoring uterine activity monitor, procardia and terbutaline, no major differences were found in terms of patient characteristics and pregnancy and delivery management among the three groups. It was concluded that in triplet pregnancies, prophylactic placement of a TAC appears to lower the incidence of delivery before 28 weeks.

**Keywords:** Multifetal pregnancy, transabdominal cerclage, transvaginal cerclage, triplet pregnancy

### Introduction

Premature birth (<37 weeks' gestation) is the most common cause of infant death and morbidity in the first months of life (March of Dimes 2008). Overall, the percentage of pre-term births has increased in the USA since the mid-1980s, despite the national goal set by the US Public Health Service to reduce the rate to 7.6% by 2010 (MacDorman and Mathews 2008). In 2005, 68.6% of all deaths occurred in pre-term infants, with a majority being extremely premature (<28 weeks' gestation). Even although extreme pre-term infants account for only 0.8% of all live births, they comprise nearly one-half (46.4%) of all infant deaths in the USA (Mathews and MacDorman 2008). Because of the high risk of death and damage in this group, a reduction in extreme pre-term deliveries could have an enormous impact (MacDorman and Mathews 2008).

Triplets and higher order multiples have increased by more than 400% since 1980 and contributed significantly to the overall prematurity rate (Martin et al. 2007). In the USA, over 93% of triplets are born pre-term, with a mean gestational age at delivery of 32–33 weeks. Almost 13% of triplet births are classified as extremely premature (Martin et al. 2007). Triplets are nearly 15 times more likely than singletons to die within 1 month of birth (Mathews and MacDorman 2007; Mathews and MacDorman 2008) and the infant mortality rate is 10 times the rate for singletons due, in part, to the high rate of pre-term delivery (Mathews and MacDorman 2008).

Several retrospective studies have evaluated the use of elective transvaginal cerclage (TVC) to prolong triplet pregnancy, with conflicting results (Bernasko et al. 2006; Elimian et al. 1999; Goldman et al. 1989; Itzkowic 1979; Lipitz et al. 1989; Mordel et al. 1993; Rebarber et al. 2005; Strauss et al. 2002; Zakut et al. 1977). However, no studies have evaluated

the use of prophylactic transabdominal cerclage (TAC) in this population. The purpose of this study was to compare gestational age and incidence of extreme pre-term delivery among triplet pregnancies who underwent a prophylactic TAC to those who underwent a prophylactic TVC and those that did not have a cerclage.

### Materials and methods

This study was a retrospective cohort of triplet pregnancies referred to one maternal–fetal medicine practice between 1989 and 2009. All three fetuses had to be alive on the 18th week ultrasound, to be included in the study. Triplet pregnancies that underwent planned fetal reduction or were not followed after 24 weeks' gestational age were excluded. This study was approved by the St. Vincent Hospital Institutional Review Board.

General management of patients included an aggressive approach to detect and manage pre-term contractions/labour. Surveillance included serial transvaginal ultrasound images of the cervix, selectively applied manual palpation and electronic uterine contraction monitoring. At the initial consultation, risks were discussed and the type of cerclage procedure offered depended on the clinical judgement of the principal author. Prior to 2002, TAC was recommended when only classical indications (history indicative of cervical incompetence with either a failed prophylactic TVC or deep cervical laceration or extreme cervical shortening) or non-classical indications (uterine anomaly, UA) or an extremely shortened cervix or deep cervical laceration without cervical incompetence) coexisted with the triplet pregnancy. Beginning in 2002, prophylactic TAC was offered to patients with triplets, as a treatment option, after detailed discussion of the operative risks.

### Cerclage procedure

All cerclage procedures were performed by the primary author (JES) between 7.7 and 18.4 weeks' gestational age. All women were counselled on the risks and benefits before undergoing the prophylactic procedure. Intravenous broad-spectrum antibiotics (e.g. cefoxitin, cefotetan, or Unasyn – Ampicillin plus sulbactam) were administered in the operating room and perioperative treatment with indomethacin (450 mg total dose) over 2 days was used for uterine relaxation.

Vaginal cerclages were performed as an outpatient procedure, while patients who underwent a TAC were discharged within 3 days of the procedure. Prophylactic TVC procedures were performed under spinal anaesthesia, using a modified McDonald technique (McDonald 1957) with one or more large, nonabsorbable braided sutures (e.g. No. 2 Ethibond, Ethicon Inc.). All prophylactic TAC procedures were performed by laparotomy as described by Novy (1991) with modifications by the principal author as follows: fenestrations were created by careful dissection among the venous plexus medial to the uterine arteries on either side of the cervix at the level of the internal os. Opposite ends of a 5 mm Mersilene band were drawn through and tied anteriorly.

Patients who did not undergo a cerclage were treated during their pregnancy similar to the cerclage patients, including tocolytic agents, broad-spectrum antibiotics and indomethacin, at the discretion of the physician.

### Data

Data were collected prospectively and reviewed by practice staff, as an ongoing measure of quality of care. For this study, data were compared between three groups: patients who had a TVC procedure (TVC), patients who had a TAC procedure (TAC), and patients who did not have a cerclage (NC). Because this study focused on the effect of prophylactic cerclage, patients were grouped by the prophylactic procedure they received regardless if a rescue procedure was performed at a later time. For example, patients who did not receive a prophylactic cerclage, but had a rescue cerclage were designated as NC.

Gestational age at delivery, being the major determinant of morbidity and mortality, was the central outcome measured. Gestational age was determined in a standardised manner based on the best obstetric estimate using first trimester crown-rump length for the majority, who presented in the 1st trimester, and the earliest 2nd trimester multiple parameter measurements for those presenting later.

Relevant demographic information, medical history and obstetric complications, such as pre-eclampsia, gestational diabetes, and premature rupture of membranes, were abstracted from maternal medical records. Information on cerclage including indications, gestational age at procedure, and postoperative complications were also collected. Obstetric data collected included gestational age at delivery, incidence of very pre-term (<32 weeks' gestation) and extremely pre-term (<28 weeks' gestation) birth, mode of delivery, and peripartum complications. The following information was collected from the neonatal medical records: birth weight, days in the neonatal intensive care unit (NICU), ventilation days and incidence of small for gestational age (SGA: <5th percentile), very low birth weight (VLBW: <1500 g), extremely low birth weight (ELBW: <1000 g), and grade III or IV intraventricular haemorrhage (IVH III/IV).

### Statistical analysis

The primary outcomes were gestational age at delivery and the incidence of pre-term delivery at <28 weeks' gestation. Univariate analysis was performed using Fisher's exact test or Pearson  $\chi^2$ -test for categorical variables, and Student *t*-test or non-parametric Mann-Whitney *U* test, as appropriate, for continuous variables. A two-sided type one error (alpha) of <0.05 was considered statistically significant. Analyses were performed using SPSS statistical software, version 16.0 (SPSS Inc., Chicago, IL) or SAS statistical software, version 9.1 (SAS, Inc., Cary, NC). Kaplan-Meier survival analysis was used to estimate triplet gestational age at delivery. Treatment groups gestational age distributions were compared using the Log Rank test. Cox regression was used to determine if cerclage and other maternal factors were significant predictors of gestational age. To determine if cerclage and other maternal factors predicted triplet delivery prior to 28 weeks' gestation, a binary logistic regression model was developed. Neonatal outcomes were analysed using conditional logistic regression to adjust for the correlated nature of the individual triplets and their mother.

The number needed to treat (NNT) and absolute risk reduction (ARR) were calculated for each treatment group. The ARR was considered significant if the 95% confidence interval (CI) did not include zero. A post-hoc power analysis indicated that this study attained 72% power at alpha = 0.05. A total of 12 more patients in the TAC group would have been required, at the same pre-term delivery rate, to achieve a statistically significant difference for delivery prior to 28 weeks between treatment groups.

### Results

A total of 151 triplet pregnancies were identified of which 141 (93.4%) met study inclusion criteria. Three patients had a fetal demise or planned reduction before 18 weeks' gestation and seven were lost to follow-up (due to seeking other care after initial consultation). Of the 141 triplet pregnancies, TAC was performed on 60 (42.5%) of the women, 31 (22.0%) underwent a prophylactic TVC and 50 (35.5%) did not have a prophylactic cerclage. Of the women who did not have a cerclage, five had placement of a rescue TVC. Two women who received a prophylactic TVC had subsequent failure of the cerclage; one underwent a rescue TVC and the other a rescue TAC.

Nearly all study participants were Caucasian (97.9%) and had a mean age of  $31.1 \pm 4.8$  years at delivery. While delivery occurred over a 21-year time span, as can be seen in Figure 1, the majority of patients (85.1%) delivered in the last 10 years.

### Indications for cerclage

The majority (83.5%) of women who underwent a prophylactic cerclage elected to do so because of their triplet pregnancy (Table I). Four women who underwent a TVC for non-classical indications had a uterine anomaly. Seven women elected to have a prophylactic TAC for non-classical indications; one had a deep cervical laceration without a history of cervical incompetence, one had a uterine anomaly, and five had an extremely shortened cervix without a history of cervical incompetence. The mean gestational age for prophylactic TVC placement was  $13.4 \pm 2.1$  weeks and ranged from 7.7 to 18.4 weeks and for prophylactic TAC

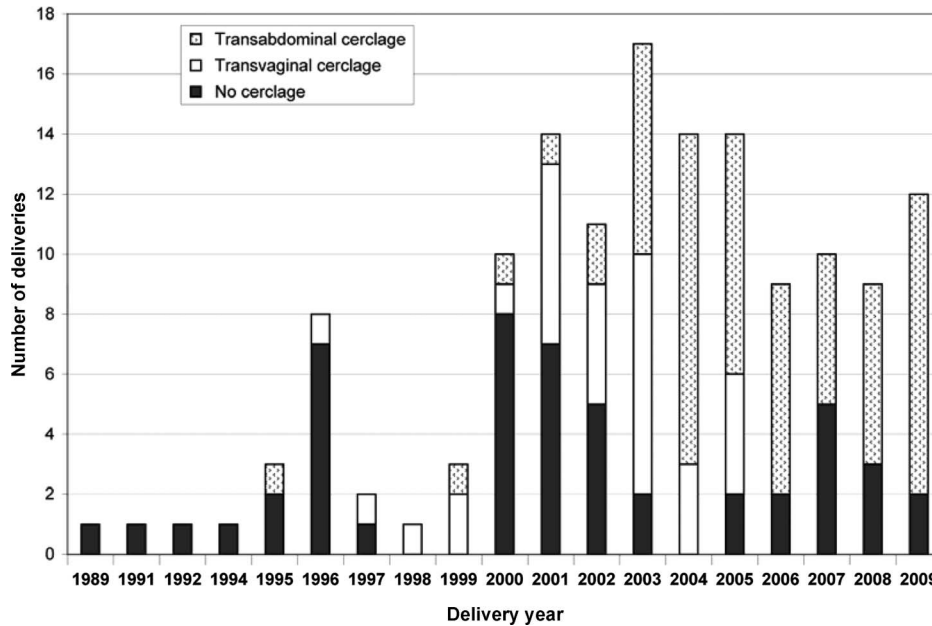


Figure 1. Triplet deliveries by year and treatment group.

Table I. Cerclage indication.

Indication	TAC ( <i>n</i> = 60)		TVC ( <i>n</i> = 31)	
	<i>n</i>	(%)	<i>n</i>	(%)
Classical	4	6.7	0	
Non-classical	7	11.7	4	12.9
Triplets	49	81.7	27	87.1

TAC, transabdominal cerclage; TVC, transvaginal cerclage.

placement was  $13.0 \pm 1.1$  weeks and ranged from 10.7 to 17.6 weeks.

Table II shows population characteristics for the three treatment groups. While women who underwent a cerclage had a moderately significant lower pre-pregnancy weight (TVC 66 kg, TAC 67 kg, NC 77 kg;  $p = 0.042$ ), their pre-pregnancy body mass index (BMI) was not significantly different ( $p = 0.142$ ). The cerclage patients were more likely to be nulliparous ( $p = 0.037$ ), have an infertility intervention ( $p = 0.059$ ), and to use a home uterine activity monitor (HUAM) ( $p = 0.001$ ) compared with the no cerclage group. There were no significant differences among the three groups in the incidence of pregnancy comorbidities and pregnancy complications such as diabetes and hypertensive disorders (Table III). While not statistically significant, there was a trend toward fewer instances of premature rupture of membranes (PROM) in the TAC group ( $p = 0.077$ ). There were variations among the three groups in the use of tocolytic agents (Table III), with significant differences in the use of Procardia ( $p = 0.010$ ) and terbutaline ( $p = 0.019$ ).

Gestational age at delivery for the treatment groups are in Table IV. There were no significant differences in mean gestational age among the treatment groups. Kaplan–Meier analysis demonstrated there was no statistical difference in estimated mean gestational age at delivery among the three groups (Figure 2). Cox regression showed that maternal age at delivery ( $p = 0.002$ ) and parity ( $p = 0.016$ ) were the only

significant predictors of gestational age. Pre-pregnancy weight (0.056) was a near significant predictor of gestational age. Per the analysis, older, nulliparous women with a higher pre-pregnancy weight were more likely to deliver at an earlier gestational age.

There was a trend for fewer extreme pre-term deliveries in the TAC group; however, the difference was not statistically significant (Table IV). Binary logistic regression demonstrated that women with a history of a prior pre-term birth were significantly more likely to deliver prior to 28 weeks' gestation ( $p = 0.047$ ), as were pregnancies sharing chorion between two or more fetuses ( $p = 0.007$ ). Compared with triamnio/trichorion pregnancies, women with monoamnio/trichorion pregnancies were 43 times more likely to deliver before 28 weeks' gestation ( $p = 0.023$ ; OR: 43.2, 95% CI: 1.6, 1112.9) and women with a diamnio/trichorion pregnancy were more than five times more likely to deliver before 28 weeks ( $p = 0.009$ ; OR 5.5, 95% CI: 1.5, 20.1). There was a trend for women who did not undergo a prophylactic TAC to deliver before 28 weeks' gestation ( $p = 0.097$ ). Notably, the difference between TAC and TVC was significantly different ( $p = 0.032$ ) while the difference between TAC and no cerclage neared significance ( $p = 0.087$ ). Women who had a TVC were nearly eight times more likely to deliver before 28 weeks (OR: 7.9; 95% CI: 1.2, 52.6) and women that did not have a cerclage were nearly five times more likely to deliver at <28 weeks' gestation (OR: 4.8; 95% CI: 0.8, 29.5).

When women who underwent a cerclage for reasons other than triplet pregnancy were excluded ( $n = 15$ ), the association between TAC and delivering after 28 weeks' gestation became stronger. Instead of a trend, women who had a TAC were significantly more likely to deliver after 28 weeks compared with those that had a TVC or no cerclage ( $p = 0.027$ ). For all other maternal and obstetric variables, the results did not change appreciably with the exclusion of these women. The results of the Cox regression remained the same; only maternal age and parity were significant predictors of gestational age at delivery ( $p = 0.001$ ,  $p = 0.025$ , respectively)

Table II. Population characteristics by group.

	TAC ( <i>n</i> = 60)		TVC ( <i>n</i> = 31)		NC ( <i>n</i> = 50)		<i>p</i> value
	Median	IQR	Median	IQR	Median	IQR	
Maternal age at delivery (years)*	31.1	4.9	30.2	4.4	31.6	5.0	0.453
Pre-pregnancy weight (kg)	67.1	20.4	66.2	14.1	77.1	27.2	0.042
Pre-pregnancy body mass index (kg/m <sup>2</sup> )	25.6	8.2	25.3	7.1	27.3	11.5	0.142
Length of post-delivery hospital stay (days)	7.0	20.0	7.0	17.0	7.0	20.0	0.900
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Nullipara	37	61.7	23	74.2	23	46.0	0.037
Prior pre-term birth (20–37 weeks' gestation)	7	11.7	2	6.5	4	8.0	0.806
Tobacco use	4	6.7	1	3.2	5	10.0	0.590
Infertility intervention	54	90.0	30	96.8	38	76.0	0.020
Ovulation induction	26	43.3	18	58.1	18	36.0	
<i>In vitro</i> fertilisation	28	46.7	12	38.7	20	40.0	
Home uterine activity monitor	41	68.3	23	74.2	19	38.0	0.001
Caesarean section delivery	60	100.0	29	93.5	46	92.0	0.093
Received antenatal steroids	40	67.8	20	64.5	27	54.0	0.319

TAC, transabdominal; cerclage; TVC, transvaginal cerclage; NC, no cerclage; IQR, interquartile range. \*Reported as mean (standard deviation, SD).

Table III. Pregnancy comorbidities and complications and tocolytic use.

	TAC ( <i>n</i> = 60)		TVC ( <i>n</i> = 31)		NC ( <i>n</i> = 50)		<i>p</i> value
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Pre-term labour	51	85.0	27	87.1	40	80.	0.731
Chorioamnionitis	2	3.3	2	6.5	3	6.0	0.689
Premature rupture of membranes	7	11.7	8	25.8	14	28.0	0.077
Pre-eclampsia	21	35.0	9	29.0	10	20.0	0.220
Chronic hypertension	5	8.3	0		5	10.0	0.209
Gestational hypertension	13	21.7	8	25.8	9	18.0	0.703
Diabetes mellitus	2	3.3	1	3.2	1	2.0	1.000
Gestational diabetes mellitus	6	10.0	4	12.9	4	8.0	0.670
Tocolytic agents							
Indocin	39	65.0	14	46.7	24	48.0	0.119
Magnesium sulfate	37	62.7	16	51.6	29	58.0	0.594
Procordia	50	83.3	24	77.4	29	58.0	0.010
Terbutaline	36	60.0	23	74.2	21	42.9	0.019

TAC, transabdominal cerclage; TVC, transvaginal cerclage; NC, no cerclage.

Table IV. Gestational age at delivery.

	TAC ( <i>n</i> = 60)		TVC ( <i>n</i> = 31)		NC ( <i>n</i> = 50)		<i>p</i> value
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Gestational age (median/IQR)	33.1/2.7		32.6/3.6		33.6/4.0		0.299
Extremely pre-term (<28 weeks)	2	3.6	5	16.1	6	12.2	0.072
Very pre-term (<32 weeks)	16	28.6	14	45.2	16	32.7	0.202
Pre-term (<37 weeks)	60	100.0	30	96.8	50	100.0	0.334

TAC, transabdominal cerclage; TVC, transvaginal cerclage; NC, no cerclage; IQR, interquartile range.

with pre-pregnancy weight trending towards significance ( $p = 0.057$ ). Binary logistic regression results were similar to the results presented above. The only difference was that a history of a prior preterm delivery was no longer statistically significant. Pregnancies in which two or more fetuses shared a chorion were still significantly more likely to deliver before 28 weeks' gestation ( $p = 0.026$ ,  $p = 0.003$ , respectively) as were women that had a TVC ( $p = 0.030$ ). The trend for women who did not have a cerclage to delivery at <28 weeks' gestation ( $p = 0.083$ ) also remained. Our results suggest that

undergoing a prophylactic TAC reduced the risk of delivery before 28 weeks' gestation by 10% (ARR: 10.2, 95% CI: 1.5, 19.0). The number needed to treat (NNT) was 9.8 (95% CI: 5.3, 66.1). Alternatively, for every 10 patients who underwent a TAC, one less triplet set was delivered before 28 weeks compared to TVC and no cerclage.

Of a total of 423 infants, 416 (98.3%) were live born. Of the live born, 391 (94.0%) were alive at the time of NICU discharge. Table V shows neonatal outcomes for the three groups. The incidence of IUFD was similar among the three

groups; however, the incidence of neonatal demise prior to NICU discharge was significantly higher in the TVC and no cerclage groups ( $p=0.023$ ). In general, the neonatal outcomes of live born infants were similar among the groups with the exception of birth weight and NICU and ventilation days. There was a trend for infants in the TAC group to be smaller ( $p=0.061$ ) and have significantly less median ventilation days ( $p=0.046$ ), while the median NICU days was significantly less for the no cerclage group ( $p < 0.001$ ). However, when maternal and obstetric factors were adjusted for, and infants were clustered in the regression as a triplet set, there were no significant differences in the outcomes between the three treatments groups.

For TAC patients, complications were rare. In one instance, surgery had to be abandoned (at 13 weeks) due to unfavourable anatomical circumstances. For this study, she was classified as NC. She delivered at 24 weeks after non-responsive progressive cervical dilatation that began at 20

weeks' gestation. The largest estimated blood loss (estimated by the attending anaesthesiologist) was one of 350 ml, with the remainder of cases estimated at or below 150 ml. No fetuses died during surgery or in the postoperative period in the TAC group. One patient had an erosion of cerclage tape through the lateral upper cervical wall occurring with labour at 33 weeks followed by an uneventful caesarean delivery and defect repair, with survival of all babies.

## Discussion

Neonatal intensive care has made major advances in recent decades by improving outcomes and increasing neonatal survival. However, mortality and damage in babies born extremely prematurely remain. If the fetal environment remains favourable, obstetric efforts to prolong pregnancy, for even modest increments under 28 weeks, are likely to reduce death and suffering. Triplets and higher order births present such an opportunity with the risk of delivery at <28 weeks at 127/1,000 as opposed to 8/1,000 in singletons (Martin et al. 2007). The potential of good outcomes in the majority of triplets may make physicians complacent. However, extreme premature birth in nearly one in seven triplet sets is a potentially devastating prospect.

To date, reports have been pessimistic with regard to prophylactic vaginal cerclage in reducing extreme prematurity in multifetal pregnancies (Berg et al. 1983; Bernasko et al. 2006; Dor et al. 1982; Itzkowic 1979; Lipitz et al. 1989; Mordel et al. 1993; Rebarber et al. 2005; Roman et al. 2005; Ron-El et al. 1981; Ron-El et al. 1992; Strauss et al. 2002; Zakut et al. 1977). Only Goldman et al. (1989) and Elimian et al. (1999) reported improved pregnancy outcomes in triplet pregnancies undergoing vaginal cerclage. Unlike many of the TVC studies (Elimian et al. 1999; Lipitz et al. 1989; Mordel et al. 1993; Strauss et al. 2002), our study had a larger sample size.

There are no reports indicating the effect of prophylactic TAC on the prolongation of multifetal pregnancies. We report the use of TAC in triplets, which evolved over 20 years in one practice. In our study of 141 women who delivered triplets, we found prophylactic TAC was associated with reduced

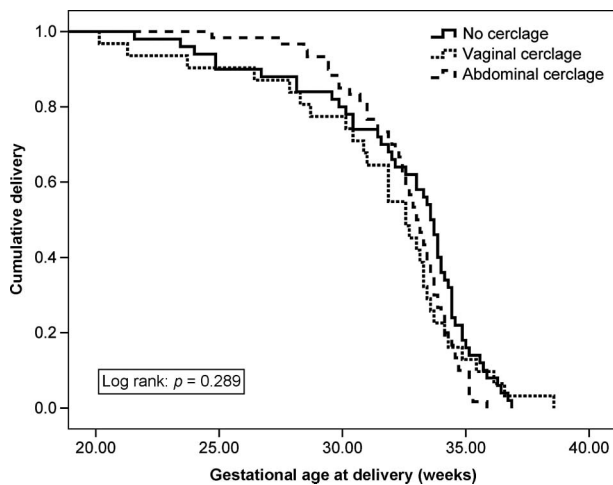


Figure 2. Kaplan-Meier survival curve for gestation age at delivery by treatment group (Log rank test,  $p=0.357$ ). NC, no cerclage; TVC, transvaginal cerclage; TAC, transabdominal cerclage.

Table V. Neonatal outcomes.

	TAC ( $n=180$ )		TVC ( $n=93$ )		NC ( $n=150$ )		$p$ value
	$n$	(%)	$n$	(%)	$n$	(%)	
Intrauterine fetal demise							
<24 gestational weeks	2	1.1	0		2	1.3	
$\geq 24$ gestational weeks	0		3	3.2	0		
Live birth	178	98.9	90	96.8	148	98.7	0.488
Discharged from NICU alive	173	97.2	81	90.0	137	92.6	0.023
Neonatal demise <24 gestational weeks	0		9	10.0	6	4.0	
Neonatal demise $\geq 24$ gestational weeks	5	2.8	0		5	3.4	
Following are based on live births > 24 weeks' gestation							
Birth weight (mean $\pm$ SD)	1664.6 $\pm$ 450.6		1745.9 $\pm$ 561.5		1804.6 $\pm$ 589.6		0.061
NICU days* (median/IQR)	23.0/18.0		20.0/20.0		15.0/18.5		<0.001
Ventilation days* (median/IQR)	0/0		0/1.5		0/1.0		0.046
Small for gestational age (<5th percentile)	15	8.4	2	2.5	8	5.6	0.172
Extremely low birth weight (<1,000 g)	12	6.7	6	7.4	17	12.0	0.231
Very low birth weight (<1,500 g)	63	35.4	27	33.3	38	26.8	0.246
Required ventilation	36	20.2	24	29.6	42	29.6	0.101
Intraventricular haemorrhage III/IV	4	2.2	2	2.5	9	6.3	0.174

TAC, transabdominal cerclage; TVC, transvaginal cerclage; NC, No cerclage; SD, standard deviation; IQR, interquartile range. \*Based on infants discharged alive.

incidence of extreme prematurity and improved incidence of neonatal/postnatal survival. This association was even stronger when women that had a cerclage for reasons other than triplet pregnancy were excluded. In our study, with the exception of mode of conception, parity, prepregnancy weight, use of home uterine activity monitoring, and use of procordial, and terbutaline, no major differences were found in terms of patient characteristics and pregnancy and delivery management. Although the data do not offer a method to select patients most at risk for application of this modality, and thus eight of nine patients undergoing the procedure may have had limited benefit, the procedural risk seems small. In our study, the lower neonatal/postnatal deaths in the TAC group were likely related to fewer extreme pre-term deliveries. The lower neonatal deaths prior to NICU discharge in the TAC group would be expected to result in more NICU and ventilation days. When maternal and obstetric factors were considered, whether or not the mother received a cerclage (TAC or TVC) did not predict selected neonatal outcomes.

As in many medical endeavours, clinicians and researchers sometimes need to focus on treatments to reduce death and suffering in a small, selected group of patients in order to achieve dramatic benefit. Effective incremental improvements to current neonatal care are difficult to achieve when delivery occurs before 28 weeks. Therefore, it is imperative that obstetricians find ways to prolong gestation beyond this point. Just increasing gestational age at delivery from 26 weeks to 28 weeks can result in a mean savings of over US\$60,000 per surviving infant (Gilbert et al. 2003). In 2005, there were 6,208 triplet births in the USA (Martin et al. 2007). Assuming none of these pregnancies had a TAC, and based on our calculated ARR of 10.2, undergoing a prophylactic TAC has the potential to reduce extreme prematurity by 633 babies per year. Even modest prolongation in triplet pregnancy duration may have a substantial financial impact on neonatal costs. Although cost does not adequately express suffering, it is a relative index of it.

These findings also offer us insight into the evolution of pre-term birth which results from the cervical insufficiency/pre-term labour complex. We may assume the difference in effect of vaginal and transabdominal cerclage to be the level of closure of the cervix, with closure at the level of the internal os effected by the transabdominal approach as opposed to the variable level along the cervical structure in the vaginal approach. It is unlikely that the massive expansion of the uterine contents in triplets or the power of the uterine muscle would be physically contained by a simple band without altering the physiological milieu. This, along with the trend towards a reduced incidence of PROM in the current report, leads us to postulate that opening, or 'funneling' of the internal os may be an evolving component of the cervical insufficiency/pre-term labour pathophysiology.

Given that our study was retrospective and the deliveries took place over a 20-year period, there are several potential limitations including selection bias, change in obstetric and NICU practices over time, and inaccuracy of records. In addition, the study did not achieve adequate statistical power. There are many potential sources of selection bias including the fact that prior to 2002, only women with a possible worse prognosis (e.g. previous failed TVC) were offered a TAC. In an attempt to reduce this bias and to limit the heterogeneity of the women in the cerclage groups, those who had a cerclage

for reasons other than a triplet pregnancy were removed from the analysis. However, this actually strengthens rather than reduces the effect of prophylactic TAC. Another possible selection bias includes recognised and unrecognised differences between the groups. To limit this bias, data were collected on many maternal and obstetric variables that had the potential to affect our results and we attempted to control for the differences through statistical analysis. Finally, the patient's selection of whether or not to have a cerclage and type of cerclage selected and the patient referral pattern may have biased our sample.

This study is of a surgical innovation evolving over more than 10 years. During this time, the practice became more known for management of triplets, and for placement of TAC, particularly for higher order multiples. Direct referrals by infertility specialists, often after the TAC option was discussed with the patient, has increased over the years. For these reasons and because of the success of the TAC procedures without significant complications led to an increased use of prophylactic TAC and a decreased use of TVC.

A limitation of the study is that it occurred over a 20-year time period; however, during the time most triplet pregnancies were managed (the latter decade), there has been little dramatic change in obstetric practice relative to the extremely premature newborn. Specifically, use of antenatal steroid treatment to enhance fetal lung maturity, when delivery could be adequately anticipated, has been a policy of this practice since before 1989. There have been major changes in practice in the NICU; however, these have resulted in only modest changes in outcomes with most levelling off in the mid-1990s (Doyle and Saigal 2009). One change in NICU practice that significantly improved outcomes was the therapeutic administration of surfactant to reduce the effect of surfactant deficiency in symptomatic newborns. Throughout the time period of our study, surfactants and advanced ventilation methodologies (including oscillators) were utilised regularly for care at the institutions in which the infants were delivered.

One of the strengths of the study is the homogeneity between the study groups, with the exception of the use of prophylactic cerclage. The inability to identify a strategy for selection of highest risk triplet pregnancies is frustrating. The possibility remains that patient selection was affected by unconscious physician or patient bias. The ideal study would be a randomised multicentre clinical trial to evaluate the role of routine TAC in the management of triplet pregnancy.

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