

Hysterotomy size in fetal spina bifida repair determines prematurity risks: a matched-controlled study

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Background

Spina bifida aperta (SBA) is a congenital defect associated with progressive deterioration in utero. Prenatal repair by hysterotomy, compared to postnatal repair, has been shown to improve neurological outcomes at the expense of an increased prematurity risk and significant maternal morbidity. Several teams proposed to reduce the dimension of the uterine incision. In a large cohort of repairs by mini-hysterotomy (≤ 3.5 cm), prematurity was less than what was reported in the benchmark Management of Myelomeningocele Study (MOMS), and reported comparable rates of reversal of hindbrain herniation. This comparison, however, did not take into account potential confounders.

Objective

We aimed to investigate whether prenatal SBA repair through mini-hysterotomy results in **less prematurity** when compared to standard hysterotomy, but **adjusting for confounding factors**.

Material and methods

Study population

This is a retrospective analysis of prospectively collected data at two fetal surgery centers (University Hospitals Leuven, Leuven, Belgium and The Heart Hospital of Sao Paulo, Brazil). Both provided data from consecutive patients from their first case onwards (Leuven, March 2012; n=118; Sao Paulo, November 2014, n=405; both until May 2022). From these cohorts were excluded all patients who did not have either a standard (UZ Leuven) or mini-hysterotomy (The Heart Hospital), those who did not meet the MOMS criteria (operation before 26 weeks, BMI ≤ 35 kg/m², or no previous uterine surgery other than cesarean section) and patients with missing exact data for the primary outcome (gestational age at birth)

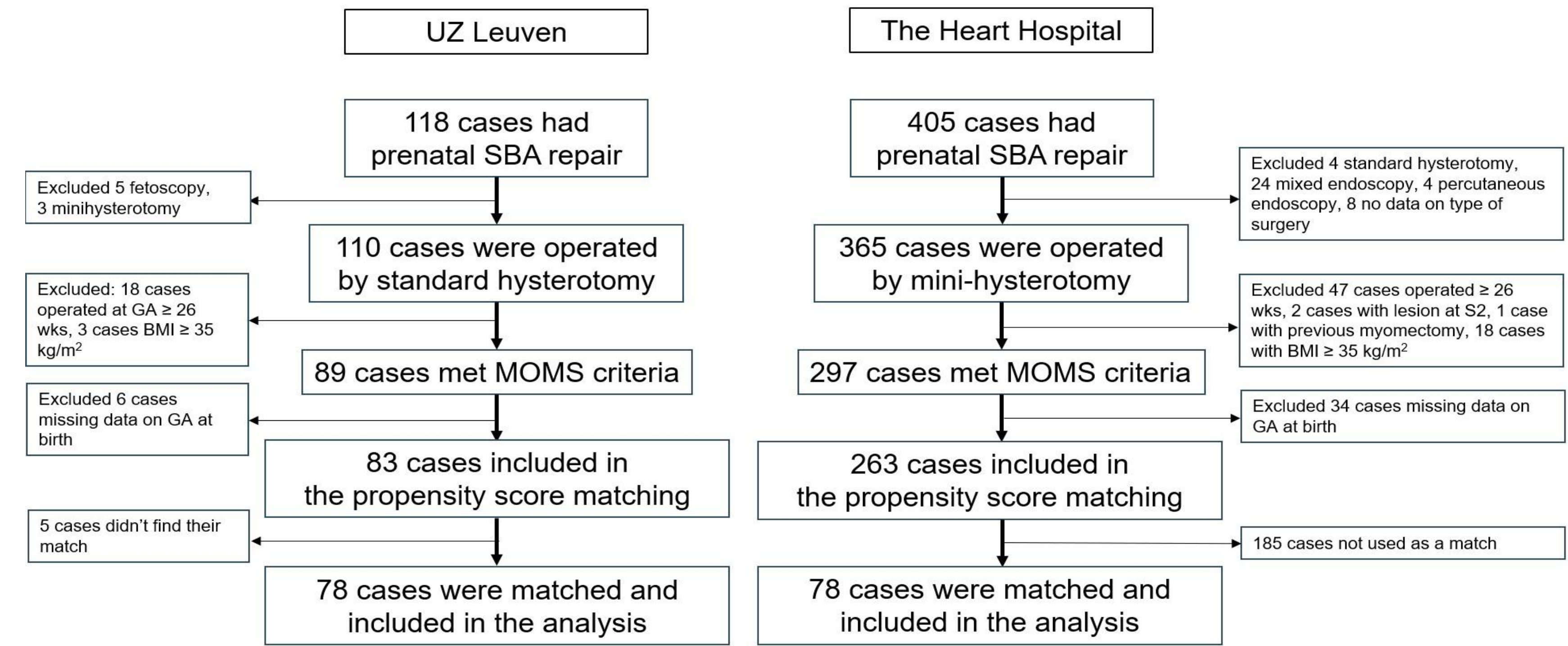


Figure 1: Study population flow chart

Material and methods

Procedure

Standard hysterotomy was defined as a uterine incision >3.5 cm as initially practiced at UZ Leuven whereas mini-hysterotomy was an incision ≤ 3.5 cm as introduced by the Heart Hospital (Figure 2)

Statistical analysis

This is a **matched-controlled study**, using the propensity score matching method. The propensity score used herein is calculated using a logistic regression model in which treatment type (mini-hysterotomy vs standard hysterotomy) is regressed versus baseline characteristics which were earlier reported to impact gestational age at delivery or membrane rupture, i.e. gestational age at operation, parity, lesion type&level as a proxy for complexity of fetal repair hance associated with operative time. We matched patients on a 1:1 basis, without replacement. For the matched pairs, continuous variables are displayed as median, interquartile range and are compared using non-parametric paired tests.

Since standard hysterotomy patients were per protocol scheduled to deliver at the latest at 37 weeks, while patients operated by mini-hysterotomy were allowed to continue further, the **time point at delivery was for both groups recategorized as prior to, or at or beyond 37 weeks**. We used Cox-regression analysis, censoring patients delivering prior to 37 weeks, to investigate the effect of hysterotomy type on gestational age at delivery.

Results

Table 1: Pre-operative characteristics of patients in both cohorts (left columns) and of matched pairs (right columns).

	Without propensity score matching			With propensity score matching		
	Standard hysterotomy (n=83)	Mini-hysterotomy (n=263)	P-value	Standard hysterotomy (n=78)	Mini-hysterotomy (n=78)	P-value
Age (years)	32.0 (28.0 – 36.0)	30.0 (25.0 – 34.0)	0.002	32.0 (27.8 – 36.0)	29.0 (25.0 – 33.0)	0.001
Parity			0.017			0.874
Nulliparous	35/83 (42.2)	136/237 (51.7) ^a		35/78 (44.9)	37/78 (47.4)	
Para 1 or more	48/83 (57.8)	101/237 (38.4) ^a		43/78 (55.1)	41/78 (52.6)	
BMI (kg/m ²)	24.7(22.2 – 28.2)	26.1 (23.9 – 28.7) ^b	0.035	24.8 (22.2 – 28.2)	26.9 (24.6 – 30.1) ^c	0.035
Lesion type			0.060			0.584
Myelomeningocele	55/83 (66.3)	191/249 (72.6) ^d		52/78 (66.7)	56/78 (71.8)	
Myeloschisis	28/83 (33.7)	58/249 (22.1) ^d		26/78 (33.3)	22/78 (28.2)	
Lesion level			0.783			0.199
Thoracic	5/83 (6.0)	17/260 (6.5) ^e		5/78 (6.4)	5/78 (6.4)	
L1-L2	12/83 (14.5)	50/260 (19.0) ^e		12/78 (15.4)	19/78 (24.4)	
L3-L4	40/83 (48.2)	115/260 (43.7) ^e		36/78 (46.2)	33/78 (42.3)	
L5-S1	26/83 (31.3)	78/260 (29.7) ^e		25/78 (32.1)	21/78 (26.9)	
Ventricular size (mm)	12.0 (9.5 – 14.0)	10.7 [8.9 – 13.0] ^f	0.032	12.0 (9.6 – 14.0)	11.0 (9.5 – 14.0) ^g	0.529
GA at operation (weeks)	25.3 (24.7-25.4)	23.8 (22.4 – 25.0)	<0.001	25.1 (24.7 – 25.4)	25.3 (24.6 – 25.7)	0.353

Data is presented in median (IQR) or n(%)
missing data: ^a 9.9%, ^b 6.8%, ^c 9.0%, ^d 5.3%, ^e 1.1%, ^f 5.7%, ^g 5.1%

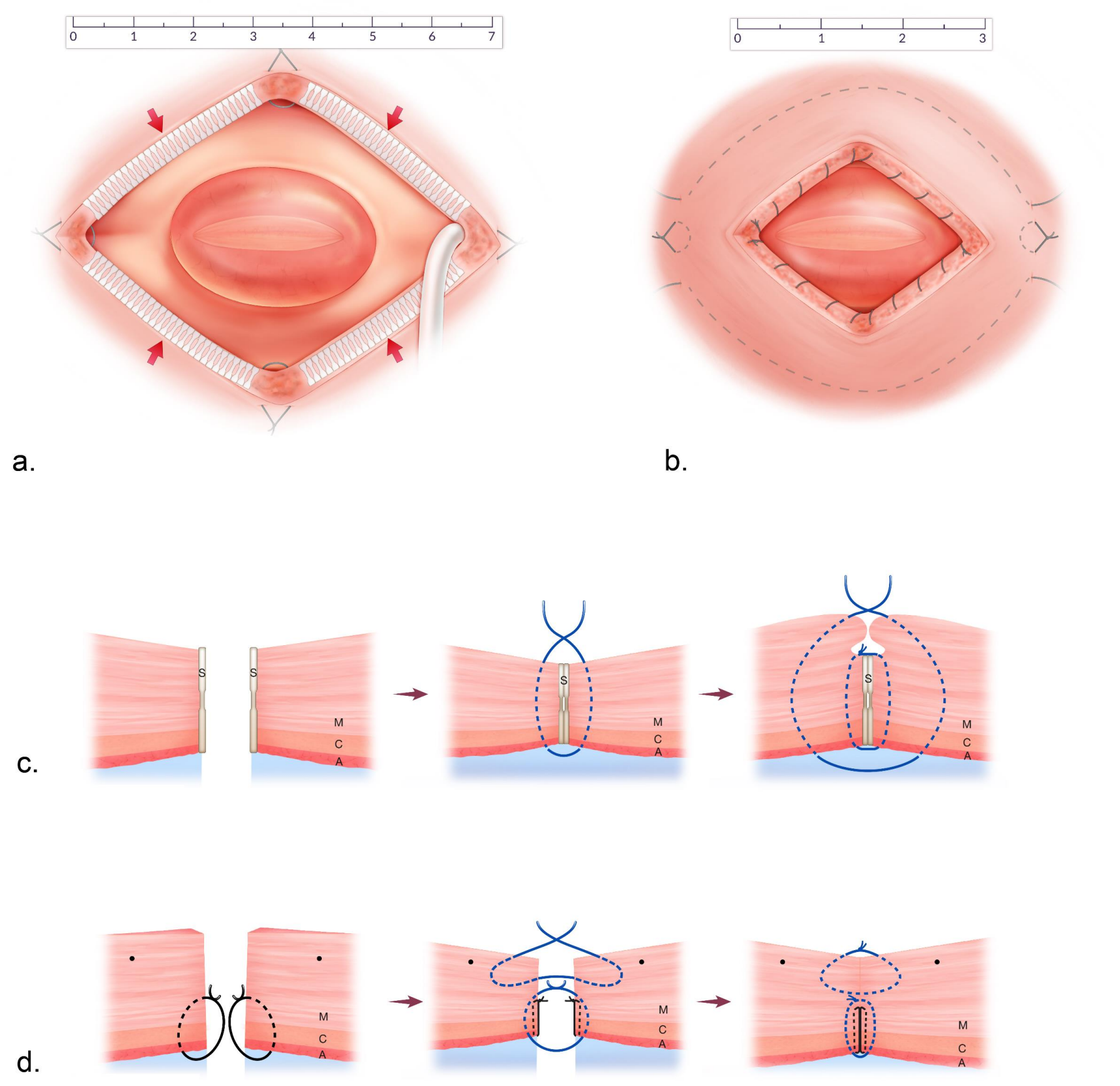


Figure 2:Schematic representation of surgical techniques in terms of uterine access

a. Standard hysterotomy, front view

b. Mini-hysterotomy, front view

Consecutive steps for opening and closure of myometrium and membranes in:

c. Standard hysterotomy, transversal view

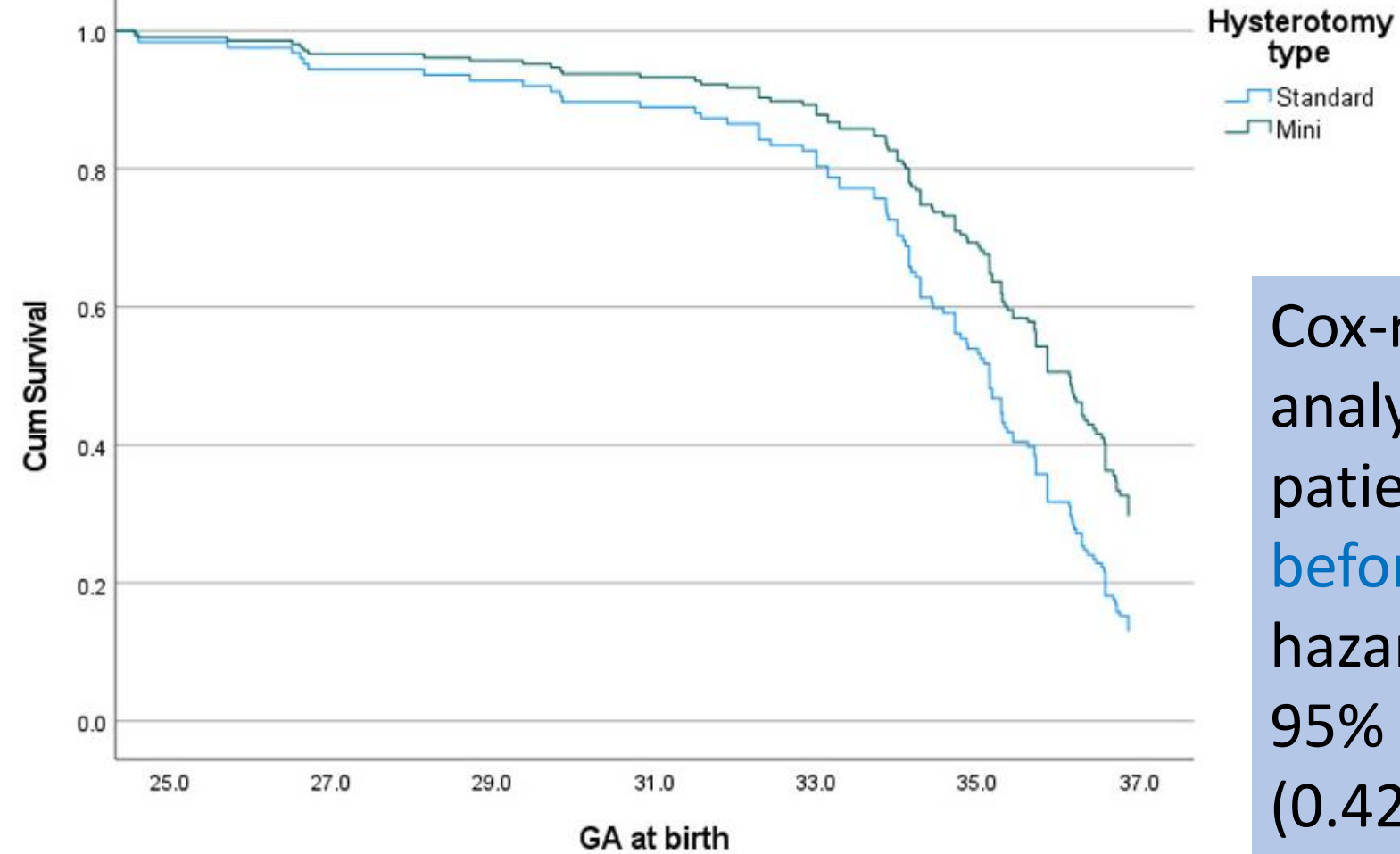
d. Mini-hysterotomy, transversal view

Results

Table 2: Perioperative and birth outcomes

	Standard hysterotomy (n=78)	Mini-hysterotomy (n=78)	P-value
Peri-operative outcomes			
Skin to skin operative time (min)	200 (173.5 – 225.5) ^a	180 (150.3 – 220.0) ^b	0.042
Duration of neurosurgical repair (min)	70.5 (59.3 – 94.0) ^c	55.0 (39.0 – 77.0) ^d	0.028
Neurulation	52/78 (66.7)	0/78 (0)	<0.001
Separate dural closure	37/78 (47.4)	78/78 (100)	<0.001
Myofascial flap closure	76/78 (97.4)	78/78 (100)	0.500
Skin closure			<0.001
Primary repair	59/78 (75.6)	77/78 (98.7)	
Patch augmentation	19/78 (24.4)	1/78 (1.3)	
In utero outcome			
Reversal of hindbrain herniation 1 wk post-operation	Reported in (n)	Reported in (n)	0.180
No	2/76 (2.6) ^e	8/72 (10.3) ^f	
Partially or complete reversal	74/76 (97.4) ^e	64/72 (82.1) ^f	
Outcomes at birth			
Membrane rupture <37 weeks	26/76 (33.3) ^g	29/76 (38.0) ^h	0.749
GA at membrane rupture(weeks)	34.7 (31.9 – 35.9)	34.6 (33.8 – 36.1)	0.176
GA at delivery (weeks)	35.1 (33.8 – 36.6)	36.0 (34.2 – 37.2)	0.048
GA at delivery, no. (%)			0.029
< 30 ^{g/i} weeks	6/78 (7.7)	7/78 (9.0)	
30 ^{g/i} – 34 ^{h/i} weeks	31/78 (39.7)	16/78 (20.5)	
35 ^{g/i} – 36 ^{h/i} weeks	33/78 (42.3)	31/78 (39.7)	
≥ 37 ^{g/i} weeks	8/78 (10.3)	24/78 (30.8)	
Birthweight (g)	2,495.0 (2,141.3 – 2,906.5) ^j	2,578.0 (2,090.0 – 2,860.0) ^j	Not calculated
Uterine scar status	n=73	n=76	0.025
Intact	66/73 (84.6) ^k	75/76 (96.2) ^l	
Dehiscence	7/73 (9.0) ^k	1/76 (1.3) ^l	
Uterine rupture	0/73 (0) ^k	0/76(0) ^l	
Neonatal CSF leakage	2/73 (2.6) ^m	0/74 (0) ⁿ	0.500

Data is presented in median (IQR) or n(%)
missing data: ^a 1.3%, ^b 2.6%, ^c 7.7%, ^d 3.8%, ^e 2.6%, ^f 7.7%, ^g 2.6%, ^h 2.6%, ⁱ 3.8%, ^k 6.4%, ^l 2.6%, ^m 6.4%, ⁿ 5.1%



No. at risk	25w	27w	29w	31w	33w	35w	37w
Standard	77	75	74	72	67	41	8
Mini	77	74	73	70	67	55	24

Cox-regression analysis censoring patient delivery **before 37 weeks'**: hazard ratio 0.60, 95% CI (0.42 – 0.85), p=0.004

Conclusion

Prenatal open SBA repair through mini-hysterotomy resulted in a higher gestational age at delivery. This coincided with a lower uterine dehiscence rate and no difference in rate of reversal of hindbrain herniation or cerebro-spinal fluid leakage at birth.