Caesarean Section in the Second Delivery to Prevent Anal Incontinence after Asymptomatic Obstetric Anal Sphincter Injury: The EPIC Multicentre Randomised Trial

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Cesarean section in the second delivery to prevent anal incontinence after asymptomatic obstetrical anal sphincter injury: the EPIC multicenter randomized trial

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Running head : Cesarean for prevention of anal incontinence

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ABSTRACT :

Objective: To determine whether planned cesarean section (CS) for a second delivery protects against anal continence in women with obstetrical anal sphincter lesions.

Design: Randomized trial.

Setting: 6 maternity units in the Paris area.

Sample : Women at high risk of sphincter lesions (first delivery with 3d degree laceration and/or forceps) but no symptomatic anal incontinence.

Methods : Endoanal ultrasound was performed in the third trimester of the second pregnancy. Women with sphincter lesions were randomized to planned CS or vaginal delivery (VD).

Main outcome measures : Anal continence at 6 months post-partum. Secondary outcomes were urinary continence, sexual morbidity, maternal and neonatal morbidities and worsening of external sphincter lesions.

Results : Anal sphincter lesions were detected by ultrasound in 264/434 women enrolled (60.8%) ; 112 were randomized to planned VD and 110 to planned CS. At 6-8 weeks after delivery, there was no significant difference in anal continence between the 2 groups. At 6 months after delivery, median Vaizey scores of anal continence were 1 [IQR 0-4] in the CS group and 1 [IQR 0-3] in the VD group (p = 0.34). There were no significant differences for urinary continence, sexual functions or for other maternal and neonatal morbidities.

Conclusions : In women with asymptomatic obstetrical anal sphincter lesions diagnosed by ultrasound, planning a CS had no significant impact on anal continence 6 months after the second delivery. These results do not support advising systematic CS for this indication.

Funding : French Ministry of Health National Program for Clinical Research Grant

Key words: obstetrical anal sphincter lesion, cesarean section, anal endosonography, anal incontinence

Tweetable abstract:

C-section for the 2d delivery did not protect against anal continence in women with asymptomatic obstetrical anal sphincter lesions.

Introduction

Anal incontinence is a source of distress for patients, with a major impact on sexual health [1] and quality of life [2, 3]. It is a frequent symptom [4], with a prevalence of 14.8% among women in a population-based study in the United States [5]. Obstetrical anal sphincter injuries (OASIS) are visible third or fourth-degree perineal lacerations, reported in 2 to 12% of vaginal deliveries [6, 7] associated with anal incontinence in up to 38% [1] or even 53% [8] of cases at long term. Occult anal sphincter lesions, which are not noticed at the time of delivery, can be detected by systematic endoanal ultrasonography in up to 27% of women after their first vaginal delivery [9]. These undiagnosed anal sphincter lesions may result in anal incontinence in 9% of women [7, 9]. Instrumental delivery is the most important risk factor for anal incontinence, with anal sphincter lesions reported in up to 63% to 82 % of forceps deliveries [9] and anal incontinence in 23 % [9]. Post-delivery anal incontinence decreases over time, but it contributes to anal incontinence in the long term [10].

In case of anal sphincter lesions at the first delivery, cesarean section (CS) is often discussed for subsequent deliveries, with the purpose of protecting anal function, but consensus is lacking. [11] [12] [13, 14]. Current RCOG guidelines state that in women who have suffered OASIS, elective caesarean section may be considered in case of symptoms or endoanal ultrasonographic defects[15]. To date there is no high-level evidence from a randomized trial to help make an informed decision [14]. The potential benefit needs to be proven, since CS is a major surgical procedure with risks for the mother and infant [16], including maternal morbidities and mortality at surgery and during subsequent pregnancies[17]. In recent retrospective cohort studies comparing CS versus repeat VD in women with a history of anal sphincter lesions, no significant difference was found in the incidence of anal incontinence [10,

[18]. However, indication bias could not be ruled out in such observational studies. The potential benefit of prophylactic CS on urinary incontinence, quality of life and sexual functions also must be addressed, as they deeply impact quality of life [2, 19]. Our objective was to evaluate whether anal incontinence could be prevented by planned CS for the second delivery, in women with asymptomatic anal sphincter disruption after the first delivery.

Methods

Study design

The multicenter, prospective, randomized, open EPIC (Etude de Prévention de l'Incontinence par Césarienne) trial compared planned CS to planned VD for the second delivery in women with a history of a traumatic first delivery with anal sphincter lesions on endosonography and no self-reported anal incontinence at baseline.

Women were recruited in 6 maternity units in the Paris area (5 academic centers and 1 general hospital), between 01/04/2008 and 29/12/2014, with their written, informed consent for each of the 2 steps of the study. Patients were not formally involved in the development of the research and no core outcome was used. The study was approved by an ethics committee (Comité de Protection des Personnes Ile de France V, Paris, France).

Women having a history of a traumatic first delivery were first assessed for eligibility by the obstetrician at clinic visits in the third trimester of their second pregnancy. They were included if they had a first vaginal instrumental delivery with forceps (vacuum extractions were not considered) and/or with a diagnosis of a third-degree perineal tear, had no self-reported anal incontinence at inclusion (on a questionnaire with yes/no answers), were 18

113 years old or over, and signed informed consent. The main exclusion criteria were a history of
114 anal surgery, a fourth-degree perineal tear at the first delivery, self-reported AI, defined as
115 involuntary leakage of gas or stools and any other indication for planned CS for non-
116 proctologic reasons.

117 After inclusion, women had a proctological evaluation including the Vaizey score [20] and anal
118 endosonography with the same expert operator (LA). The Vaizey score was chosen for its
119 sensitivity by considering 24 components of AI, including loss of flatus with or without loss of
120 liquid and solid stool, pad use, stool urgency, medication use and quality of life.
121 Endosonography was performed with a 7-10 MHz rotating rectal probe and a hard sonolucent
122 plastic cone (Bruel and Kjaer,Naemm, Denmark). Three anal canal levels (upper,middle, and
123 lower) were studied and recorded (videorecorder, Sony, Tokyo, Japan). Anal sphincter lesions,
124 were characterized as defined by Law et al. [21]: a lesion of internal sphincter was identified as
125 a hyperechoic loss of continuity of the normal internal hypoechoic ring. A lesion of the external
126 anal sphincter was identified as a hypoechoic loss of continuity of the normal external
127 hyperechoic ring (figure S1); the angulation defect was quantified and defined as severe if
128 more than 90°.

129 *Trial procedures*

130 Women with all types of external anal sphincter lesions at ultrasound were offered to
131 participate in the randomized trial, and if they consented were assigned (1:1 ratio) to planned
132 CS at 39 weeks' gestation or vaginal delivery. Concealment was obtained with a computer-
133 generated randomization scheme, in various-sized blocks, stratified by center, transmitted in
134 separate sealed and opaque envelopes prepared by the sponsor. Blinding was not feasible,
135 but investigators were unaware of aggregate outcomes during the study, since the analysis

was performed only after the follow-up period was completed and the database was frozen. In the vaginal delivery group, the management of the delivery, including episiotomy, forceps or vacuum, was left to the appreciation of the clinician. In case of an emergent indication unrelated to the issue of anal sphincter protection, CS was allowed.

Outcomes

Standard obstetrical and perinatal outcomes were recorded after delivery. Study visits were planned with the proctologist and the obstetrician at 6-8 weeks post-partum and 6 months (up to 24 months). The 6-8 weeks and 6 months follow-up visit included the Vaizey, Wexner, and also the Female Sexual Function Index (FSFI)[22], physical and mental Short-Form Survey (SF12) and Measurement of Urinary Handicap (MUH) score [23]. In addition, the 6-months visit included an anal ultrasound examination. The primary outcome was anal incontinence at 6 months after delivery (M8), as measured by the Vaizey score [20]. Secondary endpoints were anal incontinence (Vaizey score) at 6 to 8 weeks after delivery (W6-8); post-partum transient anal incontinence (at least 1 stool and/or at least 2 gas leakages after delivery, which has disappeared at W6-8), maternal morbidities (hemorrhage, uterine rupture, placenta accreta, hematomas, cervico-vaginal lacerations, hemoperiteum, organ wounds, anesthesic complications, infections, deep vein thrombosis), fetal/neonatal morbidities (respiratory distress, infection, acidosis, trauma, neonatal intensive care), urinary continence meaured with the MUH score, quality of life with the 12-Item Short-Form Health Survey (SF12) score [24], women's sexuality with the FSFI and worsening of external sphincter lesions (defined as increase of angulation from baseline of more than 10 degrees) measured 6 months after delivery.

Statistical analysis

Assuming a mean (SD) Vaizey score at M8 of 5 (6) in the control group [9, 20], 86 women/group would provide 90% power at a 2-sided α-level of 0.05 to detect a clinically meaningful difference of mean Vaizey score of 3 between groups. The target for enrollment was increased to account for potential loss to follow-up.

Baseline characteristics are reported by trial group (CS and VD) as numbers (%) for categorical variables and means (± standard deviations, SD) or medians [interquartile range, IQR] for continuous variables, as appropriate.

All analyses were performed according to the intention-to-treat (ITT) principle. Missing data were handled using multiple imputations on principal and secondary endpoints except maternal and neonatal outcomes. Variables included in the imputation models were BMI, age, ethnic group, history of constipation, history of diarrhea, use of forceps, perineal tear, ruptured internal sphincter, components of Vaizey score, MUH score, SF12 score at baseline, W6-8 and M8, and FSFI score at M8. Procedures of multiple imputations used assume that the missing data are missing at random (MAR) and were adapted for data sets with arbitrary missing patterns. We used fully conditional specification (FCS) method with linear regression for continuous variables, and with discriminant function for categorical variables. We obtained analyses results by averaging results across 5 imputed datasets using Rubin's rules. The Vaizey score at M8 post-partum was compared between CS and VD groups using a permutation test, as this variable was not normally distributed and showed a floor effect. A post-hoc subgroup analysis of the primary outcome was conducted in the 27 women with Vaizey scores ≥5 (a cut-off usually defining anal incontinence [25]) at the prenatal visit, after testing positive for interaction with trial arm. Secondary outcomes were compared between VD and CS groups using Chi-square or Fisher exact test, Student, Wilcoxon or permutation test as appropriate.

All statistical analyses were performed using SAS V.9.4 (SAS Institute Inc., Cary, North Carolina, USA).

Results

A total of 549 women were included, of whom 434 had anal endosonography, which showed that 264 (60.8%) had anal sphincter lesions. Of these, 222 (84.1%) accepted to be randomized, 112 were assigned to planned VD and 110 to planned CS (Figure 1, Flowchart). Among the 222 randomized women, 20 (9.0%) had third-degree perineal tears during spontaneous VD and 202 (91.0%) had forceps at the first delivery including 140 (71.1%) without perineal tears and 29 (14.7%) with third-degree perineal lacerations (table 1). There were no significant differences at baseline between the 2 trial arms. The only medical history was neurological disease, diabetes and cholecystectomy in 2 patients (0.9%) each. The principal treatments used during the 2nd pregnancy were iron supplements in 133 (61.0%) and laxatives in 8 (3.7%). Although according to the eligibility criteria, none of the women self-reported any anal incontinence symptom at inclusion, the Vaizey score was calculated during the data analysis as being ≥5 in 27 women before the second delivery, corresponding to the definition of symptomatic anal incontinence. Women who did not complete the M8 visit did not differ from those who completed this visit except for age (Table S1).

For the second delivery, 17 (15.6%) women in the VD arm had CS for obstetrical indications, whereas 18 (16.5%) women in the CS arm delivered vaginally (Table 2). In the VD arm, 5 women had (5.5%) forceps delivery and 1 (1.9%) 3d degree lacerations during spontaneous VD.

Outcomes

Primary and secondary outcomes are reported in Table 3. At W6-8 after delivery, anal incontinence was not statistically different between trial arms, nor was post-partum transient anal incontinence (11.7% in the CS arm vs 25.0% in the VD arm (absolute risk difference [95% CI]: -13.3 [-25.1 to 0.0]).

At the M8 endpoint, the median [IQR] Vaizey score for anal incontinence was 1/24 [0-4] in the CS arm vs 1/24 [0-3] in the VD arm (p=0.34) (table 3). This primary outcome was actually measured at a median [IQR] time of 8.0 [6.8 – 11.2] months post-partum (call now M8), due to constraints in scheduling and if necessary re-scheduling appointments. When comparing Vaizey scores at inclusion and at the M8 visit, the results did not differ between the CS and VD groups (median (IQR) differences 0.0 [-1.5-2.0] and 0.0 [0.0-1.0], respectively, p = 0.9825) (Figure S2). The effect of trial arm on Vaizey score at M8 differed between women with Vaizey score at inclusion <5 and women with Vaizey score at inclusion ≥5 (significant interaction, p=0.008). Post-hoc subgroup analyses showed that in the subgroup of 27 women with a Vaizey score before delivery ≥5, Vaizey score at M8 were significantly lower in the CS than in the VD arm (median 3 IQR [0-7] vs 6 [3.5-8.5], p=0.026).

At M8, there was no statistically significant difference between groups for urinary incontinence (MUH score), sexual function (FSFI) and physical and mental quality of life assessed with SF12.

Similarly we found no difference between the 2 arms for maternal morbidity. Minor complications occurred in 4 (4.9%) patients in the VD arm and 8 (8.8%) in the CS arm, including 3 (3.3%) anesthetic complications (headaches) in the CS arm and none in the VD arm. After delivery, 21 (13.8%) received iron supplements and 8 (5.3) took laxatives. For neonatal

outcomes, 5 (6.1%) had at least one complication in the VD arm including 4 transfers to neonatal care units (2 for respiratory distress and 2 for infection) versus none in the CS arm.

Among the 222 randomized women, 125 (56.3%) had post-partum endosonography at the M8 visit, 61 (54.5%) in the VD arm and 64 (58.2%) in the CS arm. Baseline characteristics of these women did not differ from those without endosonography (Table S1). External sphincter lesions deteriorated more frequently in the VD arm than in the CS arm (11 (22.4%) women vs 1 (2.2%), absolute risk difference -20.2 [95% CI: -31.7 to -7.6]), but no additional internal sphincter lesions were observed.

Discussion

Main Findings : In this randomized trial of women with asymptomatic anal sphincter lesions from a first delivery, planned cesarean section in the second delivery was not protective against anal incontinence at 8 months post-partum. At 6-8 weeks post-partum, anal incontinence was less frequent in the cesarean section group, but the difference was not statistically significant. In addition, we found no benefit of cesarean section on urinary incontinence, sexual functions or quality of life.

Strengths/Limitations: To our knowledge, it is the first randomized controlled trial addressing this issue. Also, anal incontinence was assessed with the standardized, validated and widely used Vaizey score, and sphincter lesions were defined by endosonography. External validity was supported by the diversity of trial settings, including teaching hospitals and general hospitals in diverse populations ranging from poor to affluent, with no center effect.

This trial also has limits. Our study was necessarily unblinded, and the main outcomes were patient-reported, thus we cannot exclude reporting bias. However, all investigators were

unaware of aggregate outcomes during the study. Also, crossovers were observed (cesareans in the vaginal delivery group and vice versa), but the trial was analysed according to the intent to treat, as recommended, and thus compares the strategy of planned cesarean versus planned vaginal delivery. We observed a Vaisey score at M8 of only 1 in the VD group (as well as the CS group), whereas a score of 5 in VD group was used for sample size calculation because 5 points on the Vaisey score is recognized as reflecting clinically significant anal incontinence [25], which would justify an indication for CS. This decreased the power to demonstrate a difference between the two trial arms, however the point estimates are identical in both arms of the trial, which is in favor of an absence of difference rather than lack of power. Moreover, this does not weaken the main finding because it means that a second vaginal delivery was not a significant risk factor for developing clinically significant anal incontinence. The main endpoint planned at M6 after delivery was actually measured at a median of 8 months after delivery, but this longer follow-up may strengthen rather than weaken the evaluation. Lastly, one fifth of the randomized women did not complete the 6 months post-partum follow-up, which could lead to attrition bias; however their characteristics did not differ between the two study groups, and the analysis was perfomed according to the intent-to-treat principle, with multiple imputations performed for handling missing data.

Interpretation in light of other studies : Our findings are consistent with recent observational studies, including longer follow-up [18, 26]. In an observational cohort study, CS for women with anal sphincter disruption at the first delivery was associated with no benefit on anal incontinence 5 years after the second delivery [18]. However, most women sustaining obstetric injuries develop anal incontinence later, after their 50s. Nygaard et al [27] found that anal sphincter disruption following an index delivery was a risk factor for flatus incontinence 30

years later. Some large population-based cohort studies failed to show any difference in the incidence of flatus incontinence in women above 50, according to whether they delivered vaginally or by CS [19], but a recent population-based study from Sweden found that the risk of anal incontinence was lower after CS than after VD [28]. AI also was higher among women who delivered by CS compared with nulliparas and higher among nulliparas compared with men. In another study, an association was found between ultrasound diagnosis of anal sphincter lesions and long-term fecal incontinence after a first delivery [29]. Because anal incontinence is multifactorial, including neurological and gastro-intestinal as well as mechanical causes, this symptom can occur without sphincter lesions and vice versa. Anal sphincter lesions are observed by ultrasound in less than half of women with postpartum anal incontinence [9]. In an unselected primiparous population, anal sphincter disruption was detected by ultrasound screening after delivery in 27 % of women, most of whom had no symptoms [30]. Thus, although CS can be protective from anal sphincter lesions [8, 9], ultrasound evidence is one of many factors associated with anal continence. Besides, it has been shown that the severity of the anal sphincter lesion is an important risk factor for subsequent anal incontinence, particularly the depth of the disruption of both the external and internal sphincters [31]. In our trial, we did not observe a protective effect of CS in the subgroup with severe anal sphincter ruptures (defined as >90°)(data not shown). In another study, only 4th-degree tears were associated with an increased risk of anal incontinence at 10 months postpartum [32], but this was an exclusion criterion in our trial.

One important difference between our trial and most retrospective studies was the inclusion of women whose first delivery was by forceps, even in the absence of a diagnosis of a third-degree perineal laceration. We found 60% of with anal sphincter defects at ultrasound in this

group. It thus remains to be shown whether our findings can be replicated in different populations including only OASIs which are diagnosed at delivery.

Some observational studies have shown that a subsequent vaginal delivery following an obstetrical anal sphincter injury may result in additional or recurrent lesions [33], which may be apparent or occult, however without any significant change in the continence score according to the mode of delivery. In our trial, the incidence of repeated clinically apparent OASIS was low, since only one woman had a repeated 3rd degree tear.

Endosonographic aggravation of external sphincter lesions occurred significantly more often in the VD group than the CS group. These findings may indicate that CS avoids some occult sphincter disruptions, but on the other hand they signify that ultrasound evidence of anal sphincter lesions is not predictive of symptoms of anal incontinence.

Conclusion

Our findings are not in favor of recommending CS for subsequent deliveries in women with asymptomatic ultrasound anal sphincter lesions resulting from a first delivery. This should be useful for clinicians and women to avoid numerous unnecessary cesarean sections[13]. However, we cannot exclude a protective effect of prophylactic CS for women with symptomatic anal sphincter lesions. We did find a significant benefit of CS among women with mild clinical AI detected before the second delivery at the proctological visit. Since it is a post-hoc subgroup analysis, it must be interpreted with caution.

Because of taboos surrounding anal incontinence, it is difficult to reveal without meticulous questioning. In our trial, 27 women self-reported no anal incontinence at inclusion, but had a Vaizey score ≥5 measured by a proctologist. Comparatively to endosonography, clinical-based

diagnosis of IA is less expensive, more accessible and seems more predictive of functional outcome, as has been previously suggested in retrospective studies [18, 26]. Thus, our findings do not support performing anal endosonography for women with an overt OASI or forceps instrumentation for their first delivery in order to decide on the mode of delivery.

Further studies are needed to determine whether CS may be useful in the long term, among women with mildly symptomatic anal lesions, and if so whether women with third- or fourth-degree perineal tears and/or forceps at their first delivery can benefit from a proctological examination in order to make a decision regarding their subsequent deliveries.[9]

Acknowledgments

We thank Coralie Gernez, Amandine Fauquembergue, Aline Dechanet and Marion Schneider from the Unité de Recherche Clinique of Hôpital Bichat–Claude-Bernard for their efforts in project management, enrollment, data collection, monitoring and data management of the trial, all the staff members of the participating maternities, the women who participated.

We also thank Drs Anabela RODRIGUES, Amélie BENBARA and Guillaume GIRARD for her contribution to inclusions.

All the authors report no conflict of interest.

Contribution to authorship

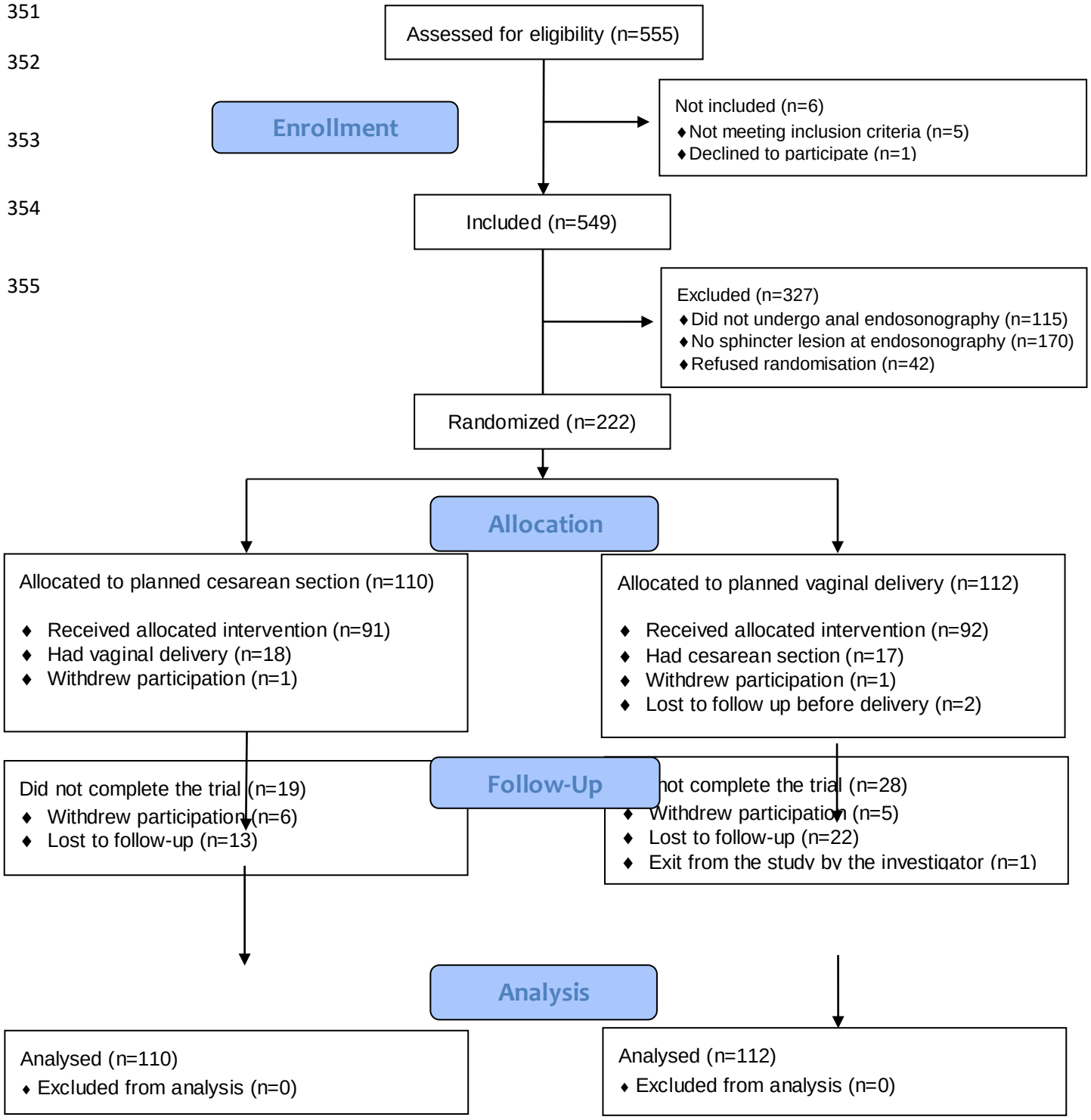
LA, FT and ABM contributed to the design of this study. LA, ALT, CCC, OP included most of the patients. CR and FT conducted the analyses and LA, LM, ABM, ALT, CCC, OP, CR and FT contributed to the interpretation of data. LA, LM and FT drafted the manuscript and all the authors critically revised the manuscript and approved the version to published.

Trial Registration : EPIC trial. ClinicalTrials.gov number, NCT00632567

This study (N° ID-RCB 2006-A00518-43) was approved by the Comité de Protection des Personnes (Ethical Human Subjects Protection Review) Paris-Ile-de-France V of Saint Antoine Hospital PARIS 12 on the 02 October 2007 (n°07709) and French Health Authority on 22 October 2007 (Ref: DGS2007-0188).

349

Figure 1 : Enrollment, Randomization, and Follow-up of the Study Participants



356 **Table 1. Baseline characteristics of women randomized.***

	Total (N=222)	Vaginal delivery group (N=112)	Cesarean section group (N=110)
Age (years), mean ± SD	32.7 ± 4.5	32.8 ± 4.6	32.7 ± 4.5
Body Mass Index (kg/m)^2, mean ± SD	26.6 ± 4.4	26.2 ± 4.2	27.1 ± 4.6
Geographical origin, N (%)			
Europe	134 (61.2)	64 (58.2)	70 (64.2)
North Africa	50 (22.8)	26 (23.6)	24 (22.0)
Sub-Saharan Africa	16 (7.3)	11 (10.0)	5 (4.6)
Other	19 (8.7)	9 (8.2)	10 (9.1)
Missing data	*3 (1.4)*	*2 (1.8)*	*1 (0.9)*
First delivery, N (%)			
Spontaneous with 3d degree perineal laceration	20 (9.0)	11 (9.8)	9 (8.2)
Episiotomy	6 (35.3)	4 (44.4)	2 (25.0)
Missing data	*3 (15.0)*	*2 (18.2)*	*1 (11.1)*
Forceps	202 (91.0)	101 (91.8)	101 (92.7)
no perineal laceration	140 (71.1)	71 (71.7)	69 (70.4)
1st degree perineal laceration	20 (10.2)	12 (12.1)	8 (8.2)
2nd degree perineal laceration	8 (4.1)	1 (1.0)	7 (7.1)
3rd degree perineal laceration	29 (14.7)	15 (15.2)	14 (14.3)
Missing data	*5 (2.5)*	*2 (2.0*	*3 (3.0)*
Episiotomy	180 (90.5)	88 (88.0)	92 (92.9)
Missing data	*3 (1.5)*	*1 (1.0)*	*2 (2.0)*
Birthweight (g), mean ± SD	3388 ± 444	3444 ± 444	3332 ± 438
Care and outcome after first delivery, N (%)			
Pelvic Floor Physical Therapy performed	143 (66.5)	75 (69.4)	68 (63.6)
Anal incontinence before 2 months post-partum	27 (12.4)	10 (9.2)	17 (15.7)
Urinary incontinence^2 after first delivery	72 (33.3)	40 (36.7)	32 (29.9)
Continence and health scores during 2nd pregnancy and before 2nd delivery			
- Vaizey score, median [IQR]	1.0 [0.0-2.0]	0.0 [0.0-2.0]	1.0 [0.0-3.0]
- Vaizey score≥5, no. (%)	27 (12.3)	12 (10.9)	15 (13.8)
- Measurement of Urinary Handicap (MUH) score, median [IQR]	4.0 [1.0-8.0]	5.0 [1.0-8.0]	4.0 [1.0-8.0]
- Physical Short-Form Health Survey (SF12) score, mean ± SD	42.0 ± 8.6	41.7 ± 8.4	42.3 ± 8.7
- Mental SF12 score, mean ± SD	48.8 ± 9.1	48.9 ± 9.1	48.7 ± 9.2

357 *no significant differences ($p<0.05$) between the trial arms

Table 2. Description of the second deliveries.*

	Total (N=222)	Vaginal delivery group (N=112)	Cesarean section group (N=110)
Lost to follow-up	4	3	1
Birthweight (g), mean ± SD	3357 ± 443	3438 ± 443	3234 ± 417
Actual mode of delivery	110 (50.5)		
- Vaginal, no. (%)	108 (49.5)	92 (84.4)	18 (16.5)
- Cesarean, no. (%)		17 (15.6)	91 (83.5)
In case of vaginal delivery			
- Vacuum, no. (%)	4 (3.7)	3 (3.3)	1 (5.6)
- Forceps, no. (%)	5 (4.6)	5 (5.5)	0 (0.0)
- Anterior presentation, no. (%)	100 (96.2)	84 (95.5)	16 (100.0)
- *Missing data*	*6 (5.5)*	*4 (4.5)*	*2 (11.1)*
- Posterior presentation, no. (%)	2 (1.9)	2 (2.3)	0 (0.0)
- Episiotomy, no. (%)	34 (31.2)	28 (30.4)	6 (35.3)
- Perineal laceration, no. (%)	57 (52.3)	52 (56.5)	5 (29.4)
- 1st degree	47 (82.5)	42 (80.8)	5 (100.0)
- 2nd degree	9 (15.8)	9 (17.3)	0 (0.0)
- 3d degree	1 (1.8)	1 (1.9)	0 (0.0)
- Shoulder dystocia, no. (%)	2 (2.5)	2 (2.8)	0 (0.0)
- Duration of labor (hours), median [IQR]	4.0 [3.0 - 5.0]	4.0 [3.0 - 5.0]	3.0 [1.5 - 4.5]
- Active pushing (min), median [IQR]	11.0 [5.0 -15.0]	12.0 [5.0 - 16.0]	9.5 [7.0 - 10.0]

Data are mean ± SD or median [inter-quartile range] or n (%)

*There was no significant differences between the trial arms ($p<0.05$), except for the occurrence of perineal laceration among women who delivered vaginally (absolute difference risk [CI 95%]: -27.1 [-49.7 to -1.4]).

Table 3 : Outcomes following the second delivery in women with anal sphincter lesions randomized to cesarean *vs.* vaginal delivery

Endpoint	Vaginal delivery arm (N=112)	Cesarean section arm (N=110)	Median or mean difference or Absolute Risk Difference (95% CI)	P Value
Primary endpoint				
Vaizey score at M8, median [IQR]	1.0 [0.0-3.0]	1.0 [0.0-4.0]	0.0 (0.0 to 2.0)	0.34
Secondary endpoints				
Vaizey score at W6-8, median [IQR]	0.0 [0.0-3.0]	0.0 [0.0-3.0]	0.0 (-2.0 to 1.0)	0.62
Post-partum transient anal incontinence at W6-8, no. (%)	18 (25.0)	9 (11.7)	-13.3 (-25.1 to 0.0)	0.32
MUH score at M8, median [IQR]	0.0 [0.0-4.0]	1.0 [0.0-4.0]	1.0 (-1.0 to 2.0)	0.72
FSFI score at M8, median [IQR]	28.1 [23.5-31.2]	27.1 [22.1-31.4]	-1.0 (-4.0 to 1.9)	0.61
Physical SF12 score at M8, mean ± SD	52.1 (6.7)	51.7 (7.0)	-0.4 (-2.5 to 1.6)	0.62
Mental SF12 score at M8, mean ± SD	46.2 (9.2)	46.6 (9.5)	0.4 (-2.3 to 3.2)	0.39
Maternal morbidities, no. (%)	4 (4.9)	8 (8.8)	3.9 (-2.7 to 11.2)	0.31
Neonatal morbidities, no. (%)	5 (6.1)	0 (0.0)	-6.1 (-11.7 to -1.3)	0.023
Worsening of external sphincter lesions at ultrasound, no. (%)	11 (22.4)	1 (2.2)	-20.2 (-31.7 to -7.6)	0.003

All the analyses were conducted in the intent-to-treat population except maternal and neonatal morbidities (completers), and are superiority analyses. For secondary endpoints, the confidence intervals have not been adjusted and inferences drawn from the intervals may not be reproducible.

References

1. Mous M, Muller SA, de Leeuw JW. Long-term effects of anal sphincter rupture during vaginal delivery: faecal incontinence and sexual complaints. BJOG : an international journal of obstetrics and gynaecology. 2008 Jan;115(2):234-8.
2. Otero M, Boulvain M, Bianchi-Demicheli F, Floris LA, Sangalli MR, Weil A, et al. Women's health 18 years after rupture of the anal sphincter during childbirth: II. Urinary incontinence, sexual function, and physical and mental health. Am J Obstet Gynecol. 2006 May;194(5):1260-5.
3. Desseauve D, Proust S, Carlier-Guerin C, Rutten C, Pierre F, Fritel X. Evaluation of long-term pelvic floor symptoms after an obstetric anal sphincter injury (OASI) at least one year after delivery: A retrospective cohort study of 159 cases. Gynecol Obstet Fertil. 2016 Jul-Aug;44(7-8):385-90.
4. Sharma A, Yuan L, Marshall RJ, Merrie AE, Bissett IP. Systematic review of the prevalence of faecal incontinence. Br J Surg. 2016 Nov;103(12):1589-97.
5. Menees SB, Almario CV, Spiegel BMR, Chey WD. Prevalence of and Factors Associated With Fecal Incontinence: Results From a Population-Based Survey. Gastroenterology. 2018 May;154(6):1672-81 e3.
6. Gurol-Urganci I, Cromwell DA, Edozien LC, Mahmood TA, Adams EJ, Richmond DH, et al. Third- and fourth-degree perineal tears among primiparous women in England between 2000 and 2012: time trends and risk factors. BJOG : an international journal of obstetrics and gynaecology. 2013 Nov;120(12):1516-25.
7. Oberwalder M, Connor J, Wexner SD. Meta-analysis to determine the incidence of obstetric anal sphincter damage. Br J Surg. 2003 Nov;90(11):1333-7.
8. Samarasekera DN, Bekhit MT, Wright Y, Lowndes RH, Stanley KP, Preston JP, et al. Long-term anal continence and quality of life following postpartum anal sphincter injury. Colorectal Dis. 2008 Oct;10(8):793-9.
9. Abramowitz L, Sobhani I, Ganansia R, Vuagnat A, Benifla JL, Darai E, et al. Are sphincter defects the cause of anal incontinence after vaginal delivery? Results of a prospective study. Dis Colon Rectum. 2000 May;43(5):590-6; discussion 6-8.
10. Jango H, Langhoff-Roos J, Rosthoj S, Saske A. Long-term anal incontinence after obstetric anal sphincter injury-does grade of tear matter? Am J Obstet Gynecol. 2018 Feb;218(2):232 e1- e10.
11. McKenna DS, Ester JB, Fischer JR. Elective cesarean delivery for women with a previous anal sphincter rupture. Am J Obstet Gynecol. 2003 Nov;189(5):1251-6.
12. Farrar D, Tuffnell DJ, Ramage C. Interventions for women in subsequent pregnancies following obstetric anal sphincter injury to reduce the risk of recurrent injury and associated harms. The Cochrane database of systematic reviews. 2014 Nov 6(11):CD010374.
13. Long E, Jha S. Factors that influence patient preference for mode of delivery following an obstetric anal sphincter injury. Eur J Obstet Gynecol Reprod Biol. 2018 Feb;221:28-33.
14. Waldman R. ACOG Practice Bulletin No. 198: Prevention and Management of Obstetric Lacerations at Vaginal Delivery. Obstet Gynecol. 2019 Jan;133(1):185.
15. RCOG RCoOaG. Management of third and fourth degree perineal tears. RCOG Press. 2015;Green top guideline 29.
16. Lumbiganon P, Laopaiboon M, Gulmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, et al. Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. Lancet. 2010 Feb 6;375(9713):490-9.
17. Ducarme G, Pizzoferrato AC, de Tayrac R, Schantz C, Thubert T, Le Ray C, et al. Perineal prevention and protection in obstetrics: CNGOF clinical practice guidelines. J Gynecol Obstet Hum Reprod. 2019 Sep;48(7):455-60.
18. Jango H, Langhoff-Roos J, Rosthoj S, Sakse A. Mode of delivery after obstetric anal sphincter injury and the risk of long-term anal incontinence. Am J Obstet Gynecol. 2016 Jun;214(6):733 e1-e13.

19. Fritel X, Ringa V, Varnoux N, Zins M, Breart G. Mode of delivery and fecal incontinence at midlife: a study of 2,640 women in the Gazel cohort. Obstet Gynecol. 2007 Jul;110(1):31-8.
20. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut. 1999 Jan;44(1):77-80.
21. Law PJ, Bartram CI. Anal endosonography: technique and normal anatomy. Gastrointest Radiol. 1989 Fall;14(4):349-53.
22. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000 Apr-Jun;26(2):191-208.
23. Marquis P, Amarenco G, Sapede C, Josserand F, McCarthy C, Zerbib M, et al. [Elaboration and validation of a specific quality of life questionnaire for urination urgency in women]. Prog Urol. 1997 Feb;7(1):56-63.
24. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996 Mar;34(3):220-33.
25. Perry S, Shaw C, McGrother C, Matthews RJ, Assassa RP, Dallosso H, et al. Prevalence of faecal incontinence in adults aged 40 years or more living in the community. Gut. 2002 Apr;50(4):480-4.
26. Fradet-Menard C, Deparis J, Gachon B, Sichitiu J, Pierre F, Fritel X, et al. Obstetrical anal sphincter injuries and symptoms after subsequent deliveries: A 60 patient study. Eur J Obstet Gynecol Reprod Biol. 2018 Jul;226:40-6.
27. Nygaard IE, Rao SS, Dawson JD. Anal incontinence after anal sphincter disruption: a 30-year retrospective cohort study. Obstet Gynecol. 1997 Jun;89(6):896-901.
28. Larsson C, Hedberg CL, Lundgren E, Soderstrom L, TunOn K, Nordin P. Anal incontinence after caesarean and vaginal delivery in Sweden: a national population-based study. Lancet. 2019 Mar 23;393(10177):1233-9.
29. Guzman Rojas RA, Salvesen KA, Volloyhaug I. Anal sphincter defects and fecal incontinence 15-24 years after first delivery: a cross-sectional study. Ultrasound Obstet Gynecol. 2018 May;51(5):677-83.
30. Faltin DL, Boulvain M, Irion O, Bretones S, Stan C, Weil A. Diagnosis of anal sphincter tears by postpartum endosonography to predict fecal incontinence. Obstet Gynecol. 2000 May;95(5):643-7.
31. Roos AM, Thakar R, Sultan AH. Outcome of primary repair of obstetric anal sphincter injuries (OASIS): does the grade of tear matter? Ultrasound Obstet Gynecol. 2010 Sep;36(3):368-74.
32. Laine K, Skjeldestad FE, Sanda B, Horne H, Spydslaug A, Staff AC. Prevalence and risk factors for anal incontinence after obstetric anal sphincter rupture. Acta Obstet Gynecol Scand. 2011 Apr;90(4):319-24.
33. Fitzpatrick M, Cassidy M, Barassaud ML, Hehir MP, Hanly AM, O'Connell PR, et al. Does anal sphincter injury preclude subsequent vaginal delivery? Eur J Obstet Gynecol Reprod Biol. 2016 Mar;198:30-4.