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Mode of delivery of preterm twins $\leq 33+0$ weeks of gestation with first twin in breech presentation

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DE GYNECOLOGIE-OBSTETRIQUE

par

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Mode of delivery of preterm twins $\leq 33^{+0}$ weeks of gestation
with first twin in breech presentation.

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Summary

Introduction	5
Morbi-mortality of preterm birth	5
The delivery of twins, a story of controverse	6
Methods	8
Patients	8
Inclusion criteria	8
Outcomes	8
Statistics	10
Result	11
Discussion	19
Conclusion	24
Bibliography	25
Appendix	29

List of acronyms

ART : Assisted Reproductive Technology

BPD : BronchoPulmonary Dysplasia

BMI : Body Mass Index

CHU: Center Hospital University

IHV: Intraventricular Haemorrhages

IUGR: IntraUterine Growth Restriction

NEC: Necrotizing Enterocolitis

PPROM: Preterm Premature Rupture of Membrane

PVD : Planned Vaginal Delivery

PC: Planned Caesarean

RCT's: Randomized Controlled Trials

Introduction

The incidence of twin gestations has increased during the past forty years, and it represents today about 3.2% of all births in France in 2021.¹ This is due to the increased of maternal age at first pregnancy and due to the growing use of assisted reproductive technologies.²

Twin pregnancies have a higher risk of complications such as preterm birth, intrauterine growth restriction, and perinatal mortality and morbidity.² The risk of preterm birth is 10 times higher in the case of multiple as compared to single pregnancies (in France 5.5% of births < 37 SA among singletons versus 52,6% among multiple pregnancies in 2021)¹. Spontaneous prematurity in twin gestation is favoured by uterine distension or premature rupture of membranes and induced prematurity is mainly related to placental and vascular complications, that are more frequent in twin pregnancies.²

Morbi-mortality of preterm birth

According to a global epidemiological study, complications from preterm birth was in 2016 the leading cause of death of children before five years of age, accounting for about 16% of all children's death before five years and 35% of new-born's death.³

Currently, there is a lack of data on survival rate after extreme prematurity. In the French study EPIPAGE 2 started in 2011, which prospectively followed a cohort of preterm infants resulting from single or twin pregnancies, the survival at discharge rate was 31% at 24 weeks of gestation, 59% at 25 weeks of gestation, 75% at 26 weeks of gestation, 82% at 27 weeks of gestation, 90-95% at 28-31 weeks of gestation and after 32 weeks of gestation survival rate is superior to 97%.⁴

Morbi-mortality related to neonatal complications of prematurity are mainly neurological in relation with periventricular leukomalacia, intraventricular (IVH) and intraparenchymal haemorrhages. In the cohort EPIPAGE 2, the rate of severe to moderate neurodevelopmental disabilities at 5^{1/2}years, was 28% at 24-26 weeks of gestation, 19% at 27-31 weeks of gestation and 12% at 32-34 weeks of gestation.⁵ The CSEP (Surveillance of Cerebral Palsy) estimated the incidence of cerebral palsy in Europe at 2.08 per 1000 live births, but the incidence among premature infants with a weight of below 1500g was 70 times higher than those with a weight

> 2500g. ⁶ There are also more behavioural problems, emotional difficulties in premature infants and lower school enrolment, as well as more repetition at school.⁴ Other serious complications of prematurity include respiratory pathologies such as hyaline membrane disease or bronchopulmonary dysplasia (BPD) but also digestive complications such as digestive perforations or necrotizing enterocolitis (NEC) (whose mortality reaches 15-30%), neonatal sepsis and ophthalmological complications (retinopathy). The main risk factor for all these neonatal complications is demonstrate to be the gestational age. ⁴

The choice of an optimal mode of delivery may be an important part of the management of preterm birth in twin pregnancy.

The delivery of twins, a story of controversy

Determining the safest mode of delivery for twin pregnancy is more complex than in singletons, since beyond gestational age, birth order, various presentation combinations, estimate foetal weight, chorionicity and experience of the clinician performing the delivery need to be considered.

The delivery of twin pregnancy has been subject to controversy since several years. French guideline's date from 2009, concluded that there was no reason to recommend one type of delivery rather than another in twin pregnancies, regardless of gestational age at birth, because of the lack of solid evidence.⁷

For twin pregnancies, at or after 32 weeks of gestation when the first twin is in cephalic presentation, recent studies favour vaginal delivery, after thorough information to the patient about the risks of vaginal and caesarean delivery. Firstly, a large international randomized study, published in 2011, found no difference of morbimortality between the planned caesarean and planned vaginal delivery, with a cephalic first twin between 32 and 39 weeks of gestation. ⁸ Subsequently, JUMODA a French prospective cohort of nearly 6000 patients, including the first twin in cephalic presentation (at or after 32 weeks of gestation), using a consistent methodology, concluded that planned vaginal delivery for twin pregnancies was significantly associated with low neonatal morbi-mortality. In addition, planned caesarean compared to planned vaginal delivery before 37 weeks of gestation appeared to be associated with increased composite neonatal mortality and morbidity.⁹

For twin pregnancies where the first twin in breech presentation after 32 weeks of gestation, there are no randomized study to our knowledge. In this situation, British guidelines recommend delivery by planned caesarean section.¹⁰

However, a French study using the JUMODA cohort comparing neonatal mortality and morbidity by route of delivery for twin pregnancies with a first breech twin at 32 weeks of gestation or more, with a large sample of 1467 women, published in 2020, found in favour of vaginal delivery. Planned vaginal delivery was not associated with higher neonatal morbidity and mortality for either twin.¹¹ This finding supports the conclusions of several retrospective studies.¹²⁻¹⁴

For twins pregnancy, from 24 to 27 weeks of gestation, in 37% of cases, the first twin is in non-cephalic presentation, then from 28 to 31 weeks of gestation, the first twin is in non-cephalic presentation in 27.6% of cases and finally from 32 to 35 weeks of gestation, the first twin is in non-cephalic presentation in 19.7 % of case.¹⁵ Most of recent retrospective studies about the mode of delivery of pre-term twins excluded the first twin in breech presentation. There are several studies which approaches about the first twin in cephalic presentation. The majority of them, didn't find superiority of caesarean for first twin in cephalic presentation for the perinatal morbimortality.¹⁶⁻²⁰ Attempted vaginal delivery seems safe for this situation, although there is randomized studies to our knowledge.

In fact, in case of preterm breech presentation, vaginal delivery have potential complications, such as head entrapment, that may increase perinatal mortality.²¹ Birth can induce traumatism during extraction manoeuvres. In rare cases, foetal interlocking may occur. On the other side caesarean sections with potential technical difficulties when performed at low gestational age, could lead to short- and long-term maternal morbidity.²² This is particularly, due to the frequent need for a vertical uterine incision (classic caesarean) with significant implications for her reproductive future²³.

Thus, scientific literature about de mode of delivery of preterm twin gestation with the first twin in breech presentation is even more scarce. The purpose of our study was to analyse the association between the intended mode of delivery and survival and normal neurodevelopment at 2 years corrected age in preterm twin pregnancies when the first twin is in breech presentation. We also, evaluate the association between the exposure and neonatal outcomes: survival at discharge and survival without morbidity.

Methods

Patients

Data came from birth register of Center Hospital University (CHU) of Nantes, a tertiary centre, between 2008 to 2019. All deliveries ≤ 33 weeks⁺⁰ of gestation of twin pregnancies was recorded. We excluded all twin pregnancies with foetal pathology (twins to twins syndrome, malformation, intrauterine death, medical termination...) or intervention during pregnancy (embryo reduction for triplets' pregnancy, laser...). We also excluded all women where the vaginal delivery was not possible because of emergency (placenta abruption, cord prolapse, metrorrhagia, pre-eclampsia...), or because the vaginal delivery seemed unreasonable (intrauterine growth retardation (IUGR) with pathologic Doppler, foetal heart rate abnormalities...), or because of recommended policies of our maternity (systematic caesarean for monochorial monoamniotic).

Inclusion criteria

We included all the women in preterm labour, who did not meet the exclusion criteria, for whom the planned mode of delivery depended on the decision of the obstetrician. The cephalic presentation of the second twin was not an exclusion criterion. All foetuses were alive at the beginning of the labour.

We compared two groups of women: Planned Vaginal Delivery (PVD) and Planned Caesarean (PC), even if the final mode of delivery differed from the plan (e.g., caesarean section during labour for the PVD group). Among PVD and PC groups, first twin in breech presentation and first twin in cephalic presentation was distinguished. This study refers to data collected when the first twin was in breech presentation.

Outcomes

All information about the woman, pregnancy and new-born was found in shared electronic medical record available since 2014 or using a mixed source (digital and paper medical file) for the cases that occurred before 2014.

For all women, we recorded the following demographics: age, Body Mass Index (BMI), parity, history of uterine scare, of Assisted Reproductive Technology (ART). Regarding the history of the pregnancy important parameters were recorded: chorionicity, antenatal steroids, magnesium sulfate perfusion before give birth, IUGR suspected, history of preterm premature rupture of membranes (PPROM), gestational age of the delivery, presentation of the second twin.

Delivery data were the actual mode of delivery, the need an instrumental extraction in case of vaginal delivery, the type of uterine scare in case of caesarean section (vertical incision or not), and the occurrence of a head entrapment, perineal tears, postpartum haemorrhage, and the need for particular therapy such as sulprostone, Bakri balloon tamponade, embolization or emergency surgery.

Neonatal outcomes recorded at birth were birthweight, Apgar at 1 and 5 minutes, blood gas value: arterial pH, venous pH, Lactates (the highest) and Base Excess (the lowest) measured on umbilical cord blood. For neonatal outcome, we recorded the survival rate at the end of the hospital stay. We also recorded survival without morbidity. We used data recorded during the hospitalisation. We considered the following pathologies as morbidities: bronchopulmonary dysplasia (oxygen therapy required after 36 weeks of gestation) or a necrotizing enterocolitis moderate or severe (stage II or III) or a severe intraventricular haemorrhage (grade III or IV) occurring during hospitalisation.

Finally, for the data concerning children, we used the “Grandir Ensemble” cohort. This is paediatric cohort, which include among others, all preterm new-born’s $\leq 33^{+0}$ weeks of gestation of Pays De La Loire, region of France. Preterm were classified into two groups according to gestational age (Group A and Group B). The inclusion criteria were for Group A: prematurity ≤ 30 SA and a birthweight < 1250 g and for Group B : prematurity between 31-33 weeks of gestation and a birthweight ≥ 1250 et ≤ 1500 g. The follow up for Group A was at 3 and 9 months, 1 and 2 years corrected age and for the Groupe B: 3 months, 1 and 2 years corrected age. For the two groups A and B the follow up was continued at 4-5-7 years.

To assess neurodevelopment at 2 years of age, we used data from the paediatric follow-up consultation at the 2 years corrected age. We defined 3 levels of neurodevelopment: normal, intermediate, and abnormal. Intermediate status meant mild difficulty (language, comprehension, etc.). Abnormal status was assigned in case of significant neurodevelopmental impairment. Each child was assigned to one of this three levels of neurodevelopment by a

paediatrician based on data from the 2-year corrected age follow-up consultation, blinded of the inclusion groups (PVD and PC). We excluded from our neurologic status assessment 3 children with genetics syndrome discovered retrospectively.

Statistics

First, we analysed the association between exposure (PVD) to both maternal and obstetrical characteristics using univariate analysis. Then, using a generalized estimating equation (GEE) to consider the correlation of the twin data, we calculated a propensity score. We defined it as the probability of being in the planned caesarean section group according to the following characteristics: Maternal age, maternal body mass index, nulliparous or not, assisted reproduction, gestational age, and birth weight Z-score of the child.

Secondly, we analysed the association between the exposure and the neonatal outcome (survival at discharge) without adjustment, then with adjustment for gestational age and female sex, and with adjustment for propensity score and gestational age. Thirdly we also analysed the association between exposure and survival without morbidities (i.e., severe IVH, NEC or BPD) without and with adjustment for gestational age and sex, then with adjustment for propensity score and gestational age. Finally, we analysed the association between the exposure and 2-years outcome (normal neurodevelopment compared to intermediate, abnormal neurodevelopment or death) without and with adjustment for gestational age and sex, and with adjustment for propensity score and gestational age.

Two sensitivity analyses were performed using multiple imputations of missing data of 2-years outcome, one in the general population and one in children born at 26 weeks of gestation and above. All tests were 2-sided, and $p < .05$ was considered statistically significant. All analyses were performed using SPSS 29.0.

Result

From 2008 to 2019, there were 48 475 births in the CHU of Nantes. The total number of preterm twin pregnancy $\leq 33^{+0}$ weeks of gestation was 413 (Figure 1). After excluding, 196 twin pairs (foetal pathology, intervention during pregnancy, vaginal delivery not possible because of emergency situation etc.), there were 217 women in preterm labour. There were 155 twin pairs (71,4%) in the PVD group and 62 twin pairs (28,6%) in the PC group. Of these, 61 women had the first breech twin, making 122 twins available for analysis. In the end, for the breech first delivery study: the PVD group included 15 women and the PC group included 46 women.

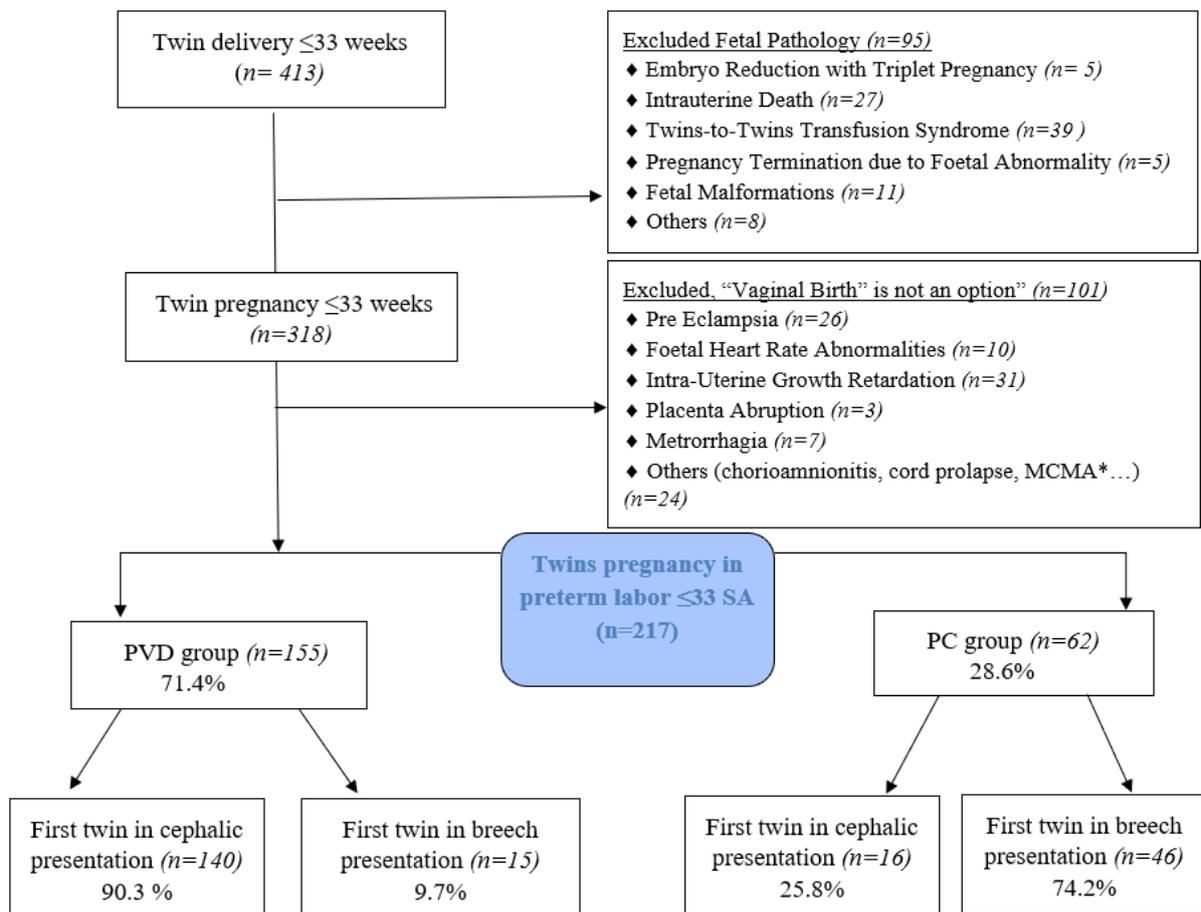


Figure 1. Flowchart of the maternal population. MCMA : MonoChronic MonoAmniotic twins.
PVD : Planned Vaginal Delivery; PC: Planned Caesarean.

Maternal and obstetrical characteristics according to the mode of delivery, did not differ between the 2 groups except for BMI ($p = 0.009$) (Table 1). Presentation of the second twin was not significantly different between the PVD group and PC group.

Table 1. Demographic Characteristics.

Maternal & Obstetrical Characteristics	Planned Mode of Delivery		
	PVD (n=15)	PC (n=46)	p
Age (y)	34 ± 5	31 ± 5	0.051
<25 y	1 (6)	7 (15)	
25-35 y	7 (47)	30 (65)	
>35	7 (47)	9 (20)	
BMI	22± 7	24± 5	0.009
<25	13 (87)	32 (70)	
≥25	2 (13)	14 (30)	
Nulliparous	8 (53)	30 (65)	0.54
Previous caesarean delivery	0 (0)	6 (13)	0.31
Assisted procreation	5 (33)	21 (46)	0.09
Dichorionic	15 (100)	40 (87)	0.52
Antenatal steroids	8 (53)	36 (78)	0.57
Magnesium Sulfate	6 (40)	13 (28)	0.56
Gestational age	28±3	30±2	0.052
<26 weeks	7 (47)	2 (4)	
26-27 weeks	0	6 (13)	
28-39 weeks	1 (6)	11 (24)	
30-33 weeks	7 (47)	27 (58)	
Cephalic presentation (2 nd twin)	5 (33)	11 (24)	0.51
Breech presentation (2 nd twin)	8 (53)	20 (43)	0.56
Transverse presentation (2 nd twin)	2 (13)	15 (32)	0.19

BMI: Body Mass Index; PC: Planned Caesarean; PVD: Planned Vaginal Delivery. Values are Numbers (%) or Means ± Standard Deviation.

The propensity score was used as a covariate to adjust the outcome (Table 2). It estimates the risk of being in the PC group for each woman. After measuring confounding variables, 3 maternal characteristics was significantly different between the two groups: maternal age, which decreased the risk of caesarean section (C-section), and ART and gestational age, which increases the risk of C-section.

Table 2. Propensity Score.

Maternal and Obstetrical Characteristic associated to caesarean risk

	OR	p
Gestational age	1,3 [1,0 ; 1,7]	0,02
ART	6,6 [1,3 ; 34,5]	0,02
Birth weight ZScore	1 [0,5 ; 1,8]	0,98
Maternal age	0,8 [0,7 ; 0,98]	0,03
BMI	0,9 [0,8 ; 1,2]	0,84
Nulliparous	1,1 [0,3 ; 4,9]	0,85

BMI : Body Mass Index; ART : Assisted Reproductive Procreation ; Birth Weight Z Score : Z Score of the Birth Weight.

In the PVD group, there was 13 vaginal deliveries and 2 caesareans during labour and in the PC group (one because foetal heart rate abnormalities of the first twin during labour, and the other because of cord prolaps during labour), there was 45 caesareans and 1 vaginal delivery because labour progress too rapidly to perform a caesarean delivery (Table 3). Only one pair of twin pair had no foetal heart rate monitoring during labour. This decision was made by the obstetrician, justified by an early gestational age (24 weeks of gestation). The first twin died in the delivery room and the second during the hospitalisation.

Table 3. Descriptive Analyse of Deliveries.

Characteristics of deliveries	Planned mode of delivery	
	PVD (n=15)	PC (n=46)
First twin		
Vaginal delivery	13 (87)	1 (2)
Caesarean low incision	2 (13)	42 (91)
Caesarean vertical incision	0 (0)	3 (7)
Second twin		
Vaginal delivery	13 (87)	1 (2)
Caesarean low incision	2 (13)	42 (91)
Caesarean vertical incision	0 (0)	3 (7)
Head entrapment first twin	0 (0)	0 (0)
Head entrapment second twin	2 (13)	1(2)
Postpartum Haemorrhages	1 (6)	7 (15)
Embolization	0 (0)	1 (2)
Hysterectomy	0 (0)	1 (2)
Vaginal Tears	2 (13)	0 (0)
OASI	0 (0)	0 (0)

OASI : Obstetrical Anal Sphincter Injury. Data are numbers (%).

On the PVD group, there was no emergency caesarean delivery on the second twin after a vaginal delivery for the first twin. In the PC group, 7 % of delivery had a caesarean with a vertical incision of uterus and 91% a caesarean with a low incision of uterus. There were 2 verticals incisions and another one was made in addition to a low incision to remove the second twin. There were 2 heads entrapments in the PVD group and 1 in the PC group. Both head entrapments on the PVD group occurred at 24 weeks of gestation, on the second twin, they were resolved with nitronal intravenous injections, and both new-borns died (one in the delivery room). On the PC group, the head entrapment occurred on the second twin at 29 weeks of gestation during the caesarean, it was resolved with nitronal intravenous injection and a vertical hysterotomy supplement, and the new-born survived. Also on the Table 3, shows that the rate of postpartum haemorrhages higher on the PC group. Among the 7 haemorrhages, 2 of them were severe: 1 required embolization, and 1 an emergency hysterectomy. In the case of

hysterectomy, the aetiology of the haemorrhage was atony favoured by twin pregnancies and polyhydramnios on the second twin. The posology of sulprostone had been decrease because of ventricular extrasystole maternal. There was no foetal interlocking in our study population.

The were 122 new-borns in our cohort population. For the analyse at 2 years, we excluded 3 of them for whom a genetic syndrome was diagnosed after birth. In the end, there were 108 children in the analysis at 2 years (11 missing data). One of them was transferred in another region during hospitalisation, 4 of them moved before 2 years, 2 children were not included in Grandir Ensemble because of social problems and there were 4 losses of follow up. Analysis with multiple imputations account considered the 11-missing data (Figure 2).

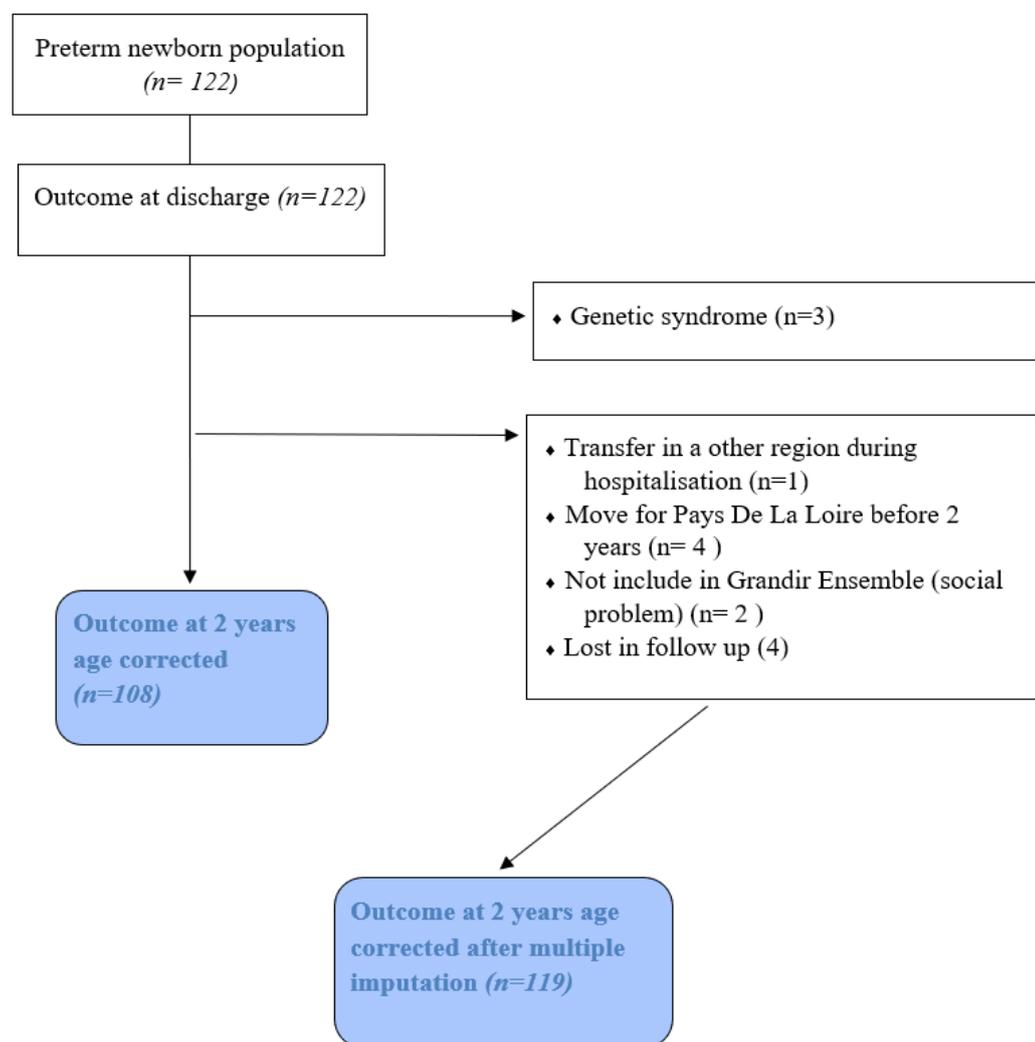


Figure 2. Flowchart of the children population.

Table 4. Descriptive analyse of neonatal outcomes at birth.

Neonatal outcomes	Planned mode of delivery		
	PVD (n=30)	PC (n=92)	p
First twin			
Weight (g)	1130±468	1383 ± 374	0.07
Apgar 1'	5±3	7±3	0.04
Apgar 5'	8±2	9±2	0.13
pH veinous	7,33± 0,06	7,32±0,06	0.75
pH arterial	7,23±0,08	7,27±0,05	0.15
Lactate	4.33± 4,43	3,14± 1,24	0.01
Base Excess	-5.17±3,91	-3,42±2,93	0.09
Second twin			
Weight (g)	1113 ±457	1386± 368	0.04
Apgar 1'	5 ±3	6 ±3	0.21
Apgar 5'	8 ±2	8 ±2	0.07
pH veinous	7,31 ±0,07	7,31 ±0,05	0.95
pH arterial	7,24 ±0,05	7,26 ±0,06	0.21
Lactate	4,17 ±1,59	2,58 ±2,2	0.02
Base Excess	-4,01 ±4,25	-3,58 ±3,1	0.9

Data are mean± standard derivation.

Base Excess is the lowest Value; Lactate is the highest Value

For neonatal outcomes at birth, no significant result was found between the two groups for the Apgar at 5 minutes, it as above 7 for both (Table 4). Birthweight was significantly different for the second twins between the two groups ($p= 0.04$), it was lower on the PVD group. Lactates were significantly different between the two groups, for both twins with a higher level in the PVD group. Apgar at 1 minute for the first twin was significantly lower in the PVD group.

On the PVD group, there were 67% of survival at discharge (versus 93% on the PC group), 43% of survival without morbidity (versus 78% on the PC group) and 39 % of survival and normal neurodevelopment at 2 years (versus 79% on the PC group) (Table 5). In the PVD group all deaths occurred before 26 weeks of gestation (Table 5 complement). Deaths concerned 33% of the PVD group, and 6 % of the PC group.

Table 5. Descriptive analyse of outcomes.

Neonatal outcomes	Planned mode of delivery		
	PVD (n=30)	PC (n=92)	p
Survival at discharge	20 (67)	86 (93)	<0,001
Survival without morbidity	13 (43)	72 (78)	<0,001
Survival and normal neurodevelopment at 2 years corrected age	10 (39)	65 (79)	<0,001

Data are numbers (%).

Table 5 (complement). Descriptive analyse of death classified by gestational age.

	PVD (n=30)	PC (n=92)
Death <26 weeks/ total number of <26 weeks	10 /14 (33)	3/4 (3)
Death ≥ 26 weeks/ total number of ≥ 26 weeks	0/16 (0)	3/88 (3)

Data are numbers (% of death on the whole group).

The univariate analyses revealed significant differences between the two groups for survival at discharge, survival without morbidity and survival and good development at age 2 years corrected (Table 6). After adjustment on gestational age and the sex foetal, the first outcome

which was survival at discharge, was not significantly different between the two group (1,7 [0,2;14,7], p= 0.63) either for the survival without morbidity (0,32 [0,05;1,94], p=0.21) or for the survival and a good development at 2 years corrected age (0,28 [0,08;1,02, p=0.055). Similarly, after adjustment for propensity score and gestational age, there were no significant differences for neonatal outcomes.

Table 6. Univariate and adjusted analyse of neonatal outcomes.

PVD	OR	p	OR ^a	p ^a	OR ^b	p ^b
Survival at discharge	0,14 [0,36;0,54]	0,005	1,7 [0,2;14,7]	0,63	1,9 [0,28;12,7]	0,51
Survival without morbidity	0,21 [0,06;0,68]	0,009	0,32 [0,05;1,94]	0,21	0,3 [0,06;2,21]	0,27
Survival and normal neurodevelopment at 2 years age corrected	0,16 [0,05;0,48]	0,001	0,28 [0,08;1,02]	0,055	0,3 [0,07;1,22]	0,09

PVD: Planned Vaginal Delivery.

OR and p : Univariate Analyse.

OR^a and p^a :Analyse Adjusted on Gestational Age and Gender (Female).

OR^b and p^b : Adjusted on Propensity Score and Gestational Age

In relation to sensitivity analyses, when multiple imputations were used in all cohort, the adjusted OR for the association between the exposure and survival with an optimal examination at 2 years was 0.34 [0.08 – 1.39], p=0.13 and in children born at 26⁺⁰ weeks of gestation and above was 0.21 (95% CI, 0.04 – 1.26, p=0.08).

Discussion

Our study did not find a significant difference of survival and normal neurodevelopment at 2 years for preterm twin $\leq 33^{+0}$ weeks of gestation when the first twin is in breech presentation, between the PVD and the PC groups after adjustment on the confounding variable. Survival at discharge and survival without morbidity were also not significantly different.

Among the results, some elements can be put forward in favour of PC and others in favour of PVD. In support of planned caesarean, for survival and neurological status at 2 years, the results showed a borderline significant trend towards poorer neurological status in the PVD group (0,28 [0,08;1,02], $p^a = 0.055$, 0,3 [0,07;1,22] $p^b : 0,09$). We made sensitive analyse, with multiple imputation to avoid the bias of loss of follow-up, which remained consistent with this trend (0.34 (0.08–1.39), $p=0.13$). Finally, we performed an analysis that excludes all twin pregnancies where the delivery was $<26^{+0}$ weeks (as many deaths occurred before 26 weeks in the PVD group, which could have explained this trend) and despite this, the neurological prognosis appears to be poorer in the PVD group, without reaching significantly 0.21 (95% CI, 0.04 – 1.26, $p=0.08$). A larger study would be necessary to confirm or not this trend.

However, in support of the planned vaginal delivery which is mainly criticised because of the risk of head entrapment, our study showed that caesarean section does not avoid this complication (one case on the PC group). Maternal morbidity was also lower on the PVD group, with 2 severe post-partum haemorrhages on the PC group (one embolization and one emergency hysterectomy), no one in the PVD group and 7% of vertical incision of uterus on the PC group (which affects the maternal obstetrical prognosis). These results are consistent with what has already been described in the literature in the context of extreme prematurity.²⁴ In view of this element, a study on the maternal morbidity and obstetrical prognosis in subsequent pregnancies of these patients might also be of interest.

To our knowledge this is the first specific study about preterm twins $\leq 33^{+0}$ weeks of gestation with the first twin in breech presentation. Several studies about twin pregnancies in breech presentation, include preterm twins in their population. Published in 2000, a multicentre retrospective study, was regarding delivery of breech first twins. It concerned 12 European and Israeli centres. The result showed that the neonatal mortality was significantly increase among vaginal births of pairs in whom first twins weighed less than 1500 g.²⁵ Conversely, a Netherland

based cohort study, from 2018 compare in intended mode of delivery the mortality and neonatal morbidity in very preterm twin pregnancy (26-32 weeks of gestation) for singleton and twin for woman in preterm labour. In the subgroup analyse (414 women), for the breech/cephalic, there were not statistically difference of mortality and for the breech/breech or transverse presentation, mortality was not significantly different and the neonatal morbidity of the first twin was significantly higher for planned caesarean section as compared to planned vaginal delivery. The maternal morbidity was higher for planned caesarean.¹⁶ Some other studies compared the route of delivery of first breech twins, including preterm deliveries, probably to maintain power, but no subgroup analysis by gestational age was performed. None of these studies found evidence of excess mortality for vaginal delivery.^{13,14,26,27}

The scientific literature on the delivery of breech preterm in singletons case is richer but equally contradictory. There is few RCT's. A review from 2012, including randomized trial (116 patients), with cephalic and breech presentation for woman in pre term labour before 37 weeks of gestation, didn't found any superiority between vaginal delivery and caesarean for the perinatal morbidity et mortality even in the subgroup in breech presentation.²⁸

Given that, there is a several number of observational studies which debate about the optimal way of delivery with contradictory results. In a Netherland study's, from 2015, with a large cohort of 8356 women's with analyse outcomes by intended mode of delivery, the subgroup of women delivering at 28–32 weeks of gestation, intended caesarean delivery was associated significantly to a decrease of composite mortality and severe morbidity, compared with intended vaginal delivery²⁹. This paper was criticised, because of failure on the methodology.³⁰ Quite contrary, French studies well conducted with strong method suggest that a policy of planned vaginal delivery for pre-term breech was not associated with a detectable increased risk of new-born death or severe morbidity. The head entrapment was the principal risk of the vaginal delivery, and was rare^{21,22,31}.

On the one hand, due to the lack of equivocal results but also since publication of the Term Breech Trial in the year 2000 (whose results were extrapolated to the preterm pregnancy), caesarean has become the preferred mode of delivery in many centres for preterm breech presentation, despite the lack of evidence^{32,33}.

Although there are several French studies that encourage planned vaginal delivery in twin pregnancy, with reassuring results, in France, planned caesarean concerned 37% of twin

pregnancies in 2021 (4 times more than singleton), and the final mode of delivery was caesarean in 58% of cases (20 % for singleton).¹ A part of this caesarean is probably explained, by the fact that the optimal mode of delivery of pre-term twins is not clearly determined.

However, maternal morbidity must be considered when choosing the route of delivery, particularly in the case of preterm delivery, as it may result in severe maternal morbidity²⁴. Some studies suggest an association between low gestational age and increased maternal morbidity in caesarean section³⁴. In addition to the increased risk of postpartum haemorrhage, surgical wound and thromboembolic risk, the risk of vertical incision carried out in case of early preterm, affects the patient's obstetrical prognosis for future pregnancies (uterine rupture, placenta accreta spectrum disorder ...). An Australian observational study published in 1997, covering a period of 9 years, showed that at 24 weeks' gestation, 20% of caesarean sections were vertical. This incidence fell to less than 5% at 30 weeks' gestation and to less than 1% from 34 weeks' gestation³⁵. This study is interesting because Australian obstetricians had a similar caesarean rate to France (18%).

Caesarean section is also a source of neonatal complications, as there are sometimes extraction difficulties that can cause anoxia and trauma, but also long-term complications, with recent research suggesting that it can lead to impaired immune development, with increased risk of allergy, asthma, reduced diversity of the gut microbiome, more obesity in childhood compared to vaginal births.³⁶

Neonatal outcomes at birth were similar between the two groups, although lactate levels were higher in the PVD group, this did not appear to have any clinical impact as the 5-minute Apgar was similar between the two groups. The birth weight of the second twin was lower in the PVD group, related to the lower gestational age in the PVD group. These data are reassuring about the planned vaginal delivery since the clinical condition at birth was not significantly different between the two groups.

There was no significant difference of maternal and obstetrical characteristics between our two groups except for the BMI which was lower on the PVD group. However, trends can be observed in our study, which is interesting because these data had influenced the decision of the mode of delivery. In the PVD group, maternal age was higher (34 vs. 31 years), there were fewer nulliparous (53% in the PVD group vs. 65% in the CP group), fewer ART (33% in the

PVD group vs. 46% in the CP group), and gestational age was lower in the PVD group (28 weeks vs. 30 weeks of gestation in the CP group).

In the French study of Bourtembourg *and al.*, which compare twin delivery between 26 to 37 weeks of gestation, with the first twin in breech position, maternal characteristics are comparable to our study. In the PVD group, maternal age was also higher, this can be explained by the fact that they are more often multiparous, and the vaginal delivery seems safer in this situation. In the PC group there were significantly fewer nulliparous women, and fewer ART¹³. Indeed, when twin pregnancies are the result of infertility treatment, they are often considered more "valuable" pregnancies. Clinicians therefore prefer a caesarean section, which they consider safer than a vaginal delivery, which seems riskier. Conversely, in cases of extreme prematurity, the opposite reasoning is generally applied: considering the significant maternal morbidity of a very early caesarean section, and the poor prognosis of new-borns in relation of their prematurity, vaginal delivery is often preferred by clinicians, which is why the gestational age was lower in the PVD group.

The delivery characteristics were comparable to the other studies, except that there was no emergency caesarean section on the second twin. The rate of head entrapment was 13% (2/15) in the PVD group, occurring both times at 24 weeks of gestation for the second twins. One of these foetuses died in the delivery room, the other died during hospitalisation. This rate varies from studies. In the French study of Lorthé *and al.*, which compare neonatal outcome and 2 years' outcome according to planned delivery route of preterm breech singleton from 26 weeks of gestation, there was 143 new-borns on the PVD group and only one died following a head entrapment.²² In another French study from 2021, which aimed to assess whether vaginal delivery of a foetus in breech presentation at extremely preterm gestational age was safe (included foetus at 25 to 27⁺⁶ weeks of gestation), the rate of head entrapment was 27.4% (31/113) and 29% of them were followed by neonatal death in the delivery room. In half of the case, foetus was aged of 25 weeks of gestation.³⁷ Head entrapment's incidence seems highest before 28 weeks of gestation. Bodmer *et al.* in a study published in 1986, reported 7 deaths caused by head entrapment among 55 breech presentations before 28 weeks of gestation, compared with 2 of 211 after 28 weeks of gestation³⁸

The results of our study are therefore comparable to other studies, although there are limitations to consider. The main limitation was the fact that we made an observational retrospective study

where a randomized study would have been desirable. Other limitations are the lack of power of our study due to the rarity of the situation and due to the fact, that is a monocentric study. Monocentric study induces a lack of variation in medical practices. There are 3 tertiary cents in the region Pays De La Loire, which include preterm birth in the cohort “Grandir Ensemble”. In one of these tertiary centres, preterm twins whose first twin in breech have systematically a routine caesarean. The other centre has no predefined policy but has not been contacted.

In order to reduce the impact of these biases on our results, we used a strong methodology, which is our strength. We made two group classified by intention of treat and not actual mode which can lead to classification bias. We decided to compare only preterm labour and excluded all preterm deliveries for another reason (pre-eclampsia, etc.). We assessed the evaluation neurologic at 2 years which have a real clinical impact. We made a propensity score, to try to avoid confounding factors and two sensitive analyses, to support our results. Finally, we had good internal and external validity, as our population was comparable and consistent with other studies.

Conclusion

Our study found no significant difference between PVD and PC for survival and neurologic development at 2 years of corrected age of preterm twin when the first twin is in breech presentation after adjustment for confounding variables. Although there may be a poorer neurological status in the PVD group, this result needs to be confirmed or not with significant outcome. Maternal morbidity appears to be higher in the planned caesarean group and should be taken into account in the choice of delivery route. Aware of the limitations of our study, we propose that, as with breech delivery at term, each situation requires consideration in order to provide the most appropriate care for each woman in an individualized practice.

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Appendix

Figure 3, 4 and 5. Propensity score distribution in the non-exposed and exposed groups

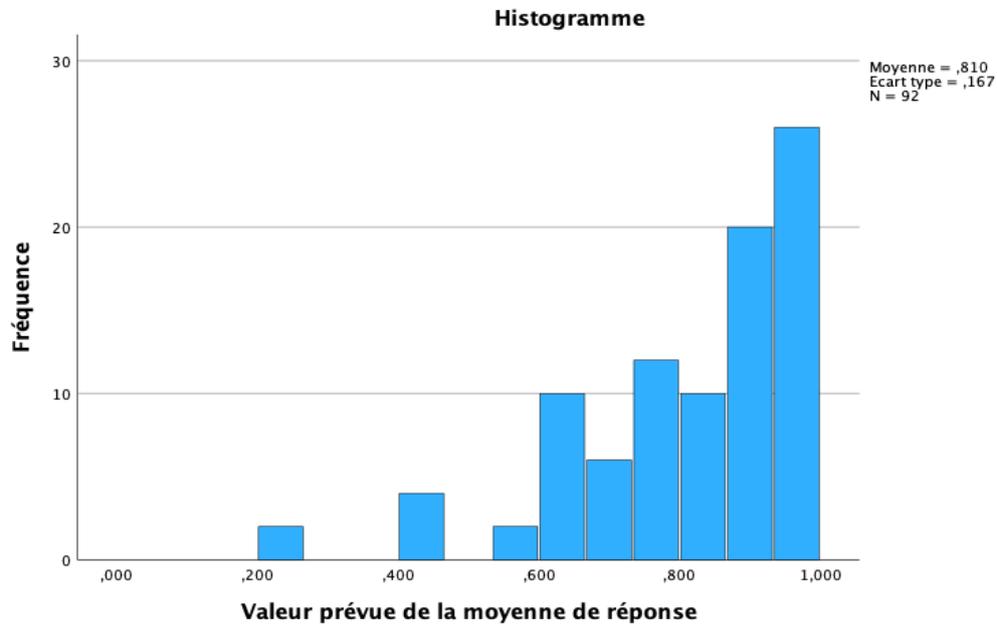


Figure 3. Propensity score distribution in the exposed group

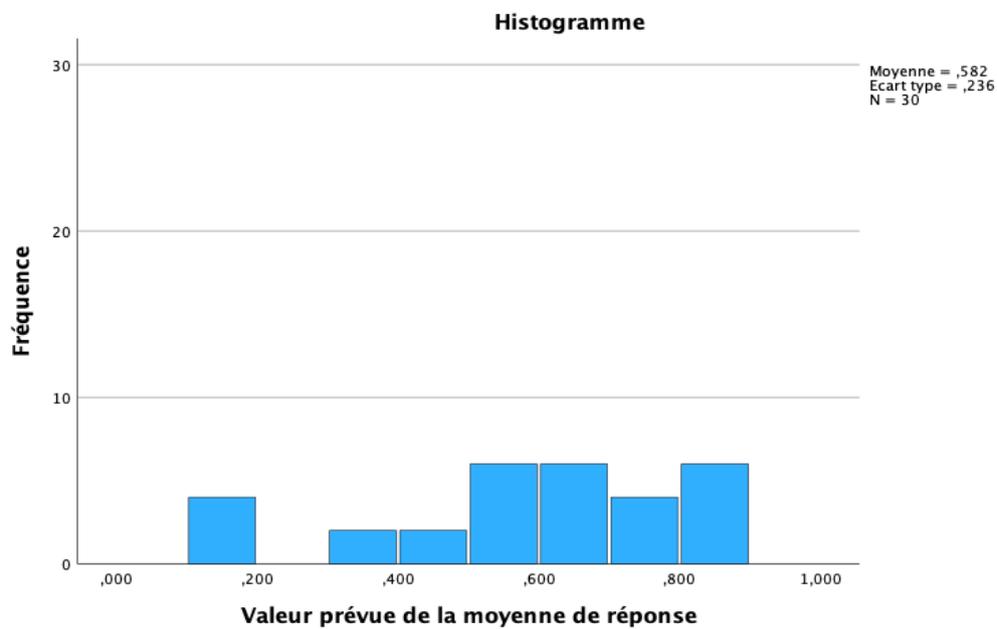


Figure 4. Propensity score distribution in the non-exposed group

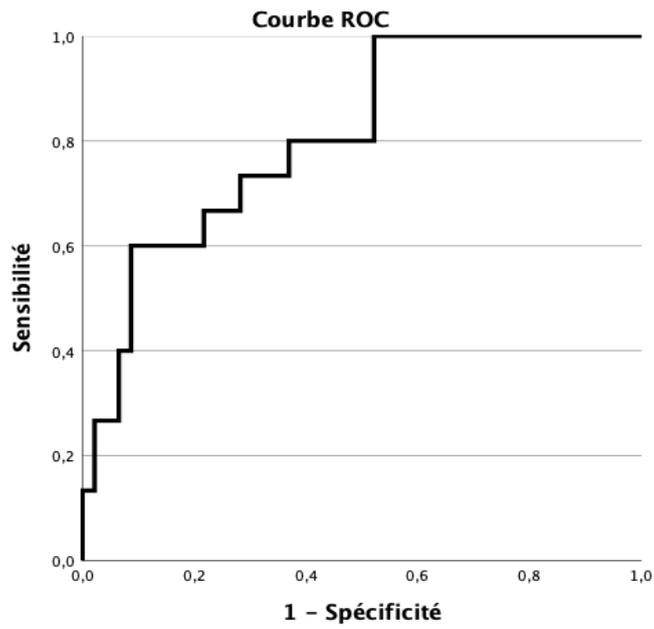
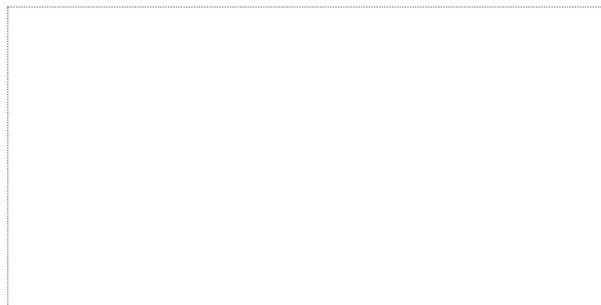


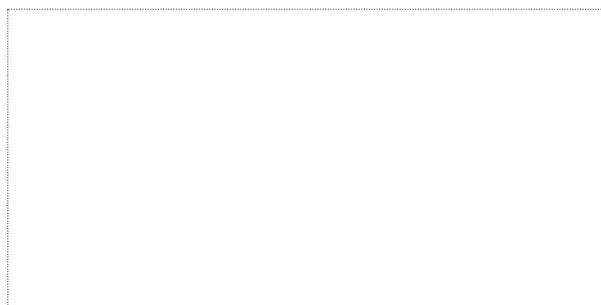
Figure 5. Roc curve of the propensity score.

Vu, le Président du Jury,



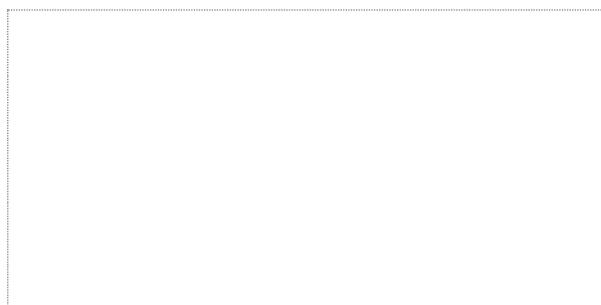
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MODE OF DELIVERY OF PRETERM TWINS WITH BREECH PRESENTATION

Which route of delivery for preterm labour in twin pregnancies with the first twin in breech?

Objective: First, to compare survival and neurodevelopment outcomes at 2 years for preterm twin $\leq 33^{+0}$ weeks of gestation, with the first twin in breech presentation according to the planned mode of delivery: Planned Vaginal Delivery (PVD) or Planned Caesarean (PC). Second, to compare in this situation survival at discharge and survival without morbidity, neonatal outcomes at birth and maternal morbidity.

Methods: Retrospective cohort of women with preterm breech first twins delivered after preterm labour before $\leq 33^{+0}$ weeks of gestation at Nantes University Hospital from 2008 to 2019. We used a propensity score to estimate the risk of having a caesarean. An adjusted analysis was used to compare outcomes (survival at discharge, survival without morbidity and survival and normal neurodevelopment at 2 years). First, outcomes were adjusted for gestational age and female sex and a second, on propensity score and gestational age. Two sensitivity analyses were used to support our results. An analyse with multiple imputation for the first outcome after adjustment on propensity score, and the same analysis excluding $< 26^{+0}$ weeks of gestation.

Results: Among 413 twin delivery $\leq 33^{+0}$ weeks of gestation, we included 61 women, 15 in the PVD group (30 new-borns) and 46 in the PC group (92 new-borns). After both adjusted analysis, there was no significant difference of survival at discharge ([0,28; 12,7] p :0.51), no significant difference of survival without morbidity (0,3 [0,06;2,21], p :0,27), and no significant difference of survival and normal neurodevelopment at 2 years corrected age (0,3 [0,07;1,22] p :0,09). The two sensitivity analysis didn't found either significant result: in the general population : 0.34 [0.08 – 1.39], p=0.13 and after $< 26^{+0}$ weeks of gestation exclusion : 0.21 [0.04 – 1.26], p=0.08.

Conclusion: Taking into account the limitations of our study, we found no significant difference in survival and neurodevelopment at two years. A trend against planned vaginal delivery for the first outcome should be noted with caution. Maternal morbidity appears to be higher in the planned caesarean group and should be taken into consideration in the choice of delivery route. As with breech births at term, there is probably a need for individualized thinking in each situation.

Keywords : twin pregnancy; mode of delivery; preterm; breech presentation

NOM : DHONNEUR

PRENOM : Camille

Titre de Thèse : Quelle voie d'accouchement pour les jumeaux prématurés ≤ 33 SA avec le premier jumeau en siège ?

RESUME

Les grossesses gémellaires sont à risque de mise en travail prématuré. Dans cette situation, la voie d'accouchement est débattue, notamment quand le premier jumeau en siège. Nous avons recueilli l'ensemble des accouchements de grossesse gémellaire, après mise en travail spontanée ≤ 33 SA avec le premier jumeau en siège au CHU de Nantes de 2008 à 2019. Nous avons comparé deux groupes de patiente selon la voie d'accouchement prévue : tentative d'accouchement voie basse (TAVB) ou césarienne d'emblée. Le critère de jugement principal était de comparer la survie et l'état de développement neurologique à 2 ans entre les enfants nés dans le groupe TAVB et ceux nés dans le groupe césarienne d'emblée. Les critères de jugement secondaires étaient la survie à la sortie d'hospitalisation, la survie sans morbidité sévère pendant l'hospitalisation, l'état néonatal immédiat, la morbidité maternelle. Parmi les 61 grossesses gémellaires répondant aux critères d'inclusion, il y avait 15 TAVB et 46 césariennes d'emblée. Après ajustement sur les facteurs confondant, il n'y avait pas de différence significative sur la survie et le développement neurologique à 2 ans, ni sur les critères de jugements secondaires. La morbidité maternelle semblait plus élevée dans le groupe césarienne d'emblée.

MOTS-CLES

Grossesse Gémellaire ; Prématurité ; Voie d'accouchement ; Siège