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Review article

Risk of cesarean after induction of labor in twin compared to singleton pregnancies



C. Loscul^{a,b,*}, T. Schmitz^{b,c}, P. Blanc-Petitjean^{b,d}, F. Goffinet^{a,b}, C. Le Ray^{a,b}, for the JUMODA and MEDIP study groups

^aPort-Royal Maternity Unit, Cochin Hospital, Assistance Publique–Hôpitaux de Paris (APHP), DHU Risks in pregnancy, Paris-Descartes university, Paris, France

^bInserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Centre For Epidemiology and Statistics Sorbonne Paris Cité (CRESS), DHU Risks in pregnancy, Paris-Descartes university, Paris, France

^cDepartment of Obstetrics and Gynecology, Robert Debré Hospital, AP-HP, Paris Diderot university, Paris, France

^dDepartment of Obstetrics and Gynecology, Louis Mourier hospital, APHP, DHU Risks in pregnancy, Paris-Descartes university, Colombes, France

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ABSTRACT

Objective: To assess the risk of cesarean delivery after induction of labor in twin compared with singleton pregnancies.

Study design: This retrospective multicenter study compared data from two nationwide prospective cohorts: one of twin pregnancies established from February 2014 through March 2015 (JUMODA cohort), and the other of singleton pregnancies in November and December 2015 (MEDIP cohort). This study includes all women in both cohorts who had labor induced at ≥ 35 weeks of gestation, with a live fetus in cephalic presentation (Twin 1 for the twin pregnancies). Multivariate analyses with multilevel logistic regression models were used to study twin pregnancy as an independent risk factor for cesarean delivery, overall and stratified for parity and Bishop score.

Results: The outcomes of 1995 twin births after induction of labor were compared to those of 2771 induced singleton births. The cesarean rate differed significantly between the two populations and was higher in twins (23% in twins vs 19.4% in singletons, $P=0.002$). After adjustment for factors associated with cesareans, twin pregnancy was independently associated with it (aOR = 1.8, 95% CI 1.4–2.2).

Conclusion: Twin pregnancy appears to be an independent risk factor for cesarean births after induction of labor, but more than three-quarters of inductions culminated in vaginal delivery.

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Introduction

Twin pregnancies accounted for 3.6% of births in France in 2016 and 3.3% in the United States [1,2]. Compared with singleton pregnancies, they are associated with higher mortality and

* Corresponding author at: Maternité Port-Royal, 123 Bd Port-Royal, 75014 Paris, France.

E-mail address: closcul@gmail.com (C. Loscul).

morbidity for both women and babies [3–5]. After the publication of the Twin Birth Study [6], which found no clear difference in perinatal health status between the groups with planned cesarean compared with planned vaginal deliveries, the American College of Obstetricians and Gynecologists and the Society of Maternal-Fetal Medicine jointly issued guidelines encouraging trial of vaginal delivery in twin pregnancies [7]. Support for these has come recently from the results of the prospective French nationwide JUMODA study of twins, which showed higher neonatal morbidity between 32 and 37 weeks' gestation for planned cesareans than for trials of vaginal delivery [8].

Integrating the risk of stillbirth, the ideal term of birth for twin pregnancies, long set at 39 weeks, seems rather to be around 37 weeks when the pregnancy is dichorionic and 36 weeks when monochorionic; this discovery is likely to increase the rate of inductions for post-term among these women [9,10]. The outcome of induction of labor in twin pregnancies has been sparsely studied: only four studies specifically deal with this subject, and their conclusions diverge [11–14]. Nonetheless, the rate of induction among twin pregnancies is high, around one quarter of twin pregnancies were induced as in the JUMODA study and in the Twin Birth Study [8,15].

In view of this lack of data in the literature and of the substantial use of induction in these pregnancies, especially as this will very probably rise in the next few years, we sought to assess the risk of cesarean delivery after induction of labor in twin, compared with singleton, pregnancies.

Material and methods

We conducted an observational study comparing twin and singleton pregnancies from two separate French cohorts: the JUMODA and MEDIP cohorts.

JUMODA was a prospective, nationwide, observational study conducted in the general population between February 10, 2014, and March 1, 2015. Its objective was to study the neonatal mortality and morbidity of twins according to the planned mode of delivery. All French maternity units with more than 1500 deliveries per year were asked to participate. Overall, 176 maternity units, grouped around 20 regional coordinating centers, contributed to this cohort, which included 8823 women [8].

MEDIP was also a prospective, nationwide, observational study in the general population; it took place from November 17 through December 20, 2015. It sought to assess the frequency of use of different methods of induction, to analyze maternal and neonatal outcomes according to methods, and to assess women's satisfaction, also according to the method used. Seven perinatal networks

including 94 maternity units volunteered to participate in this study. The cohort included all women with labor induced for a live fetus: 3042 [16].

We selected our study population from these two cohorts according to the following inclusion criteria: women with labor induced ≥ 35 weeks, with no previous cesarean, with live fetuses, and in cephalic presentation (Twin 1 for the twins). The 35 weeks threshold was chosen to ensure that the duration of exposure of induction was the same in both groups: 35–40 weeks in twin pregnancies and 37–42 weeks in singleton pregnancies. Women with missing data for the mode of delivery or cervical dilation at the moment of the cesarean were excluded.

The primary outcome was cesarean delivery during labor. Cases of cesarean for the second twin when the first twin delivered vaginally, count as an intrapartum cesarean. We excluded women for whom this information was not reported. Factors relevant to explaining cesarean deliveries were selected for the analyses. The principal factor studied was twin pregnancy. The other factors were those found frequently in the literature and those for which we had a strong clinical hypothesis. They were classified in three categories: individual factors, including both mothers' preexisting characteristics (age, geographic origin, BMI, parity, and comorbidities) and obstetric factors (mode of conception, maternal disorders during pregnancy, fetal disorders); the factors associated with induction of labor (gestational age at induction, indication for induction, the method used, and the Bishop score at the start of induction); and organizational factors of the maternity units (level, annual number of deliveries, status – public, university-affiliation, or private). The indication of induction was classified into 5 categories: convenience, maternal indication, fetal indication, premature rupture of membranes (PROM) and post-term. Post-term had different definitions according to the type pregnancy: ≥ 39 weeks for twins and ≥ 41 weeks for singleton.

Statistical analyses

To assess the risk of cesarean deliveries after induction of labor in twin and singleton pregnancies, we first conducted a univariate analysis comparing the characteristics of the two groups. Next we analyzed the rates and characteristics of the cesareans. Cesarean rates were then calculated for the overall population and then within subgroups according to parity and to Bishop score. Two characteristics were evaluated to describe the cesareans: its indication and dilation at incision. Indications of cesarean were those reported by physicians, then failure to progress and fetal heart rate (FHR) abnormalities were classified according to the clinician's judgment.

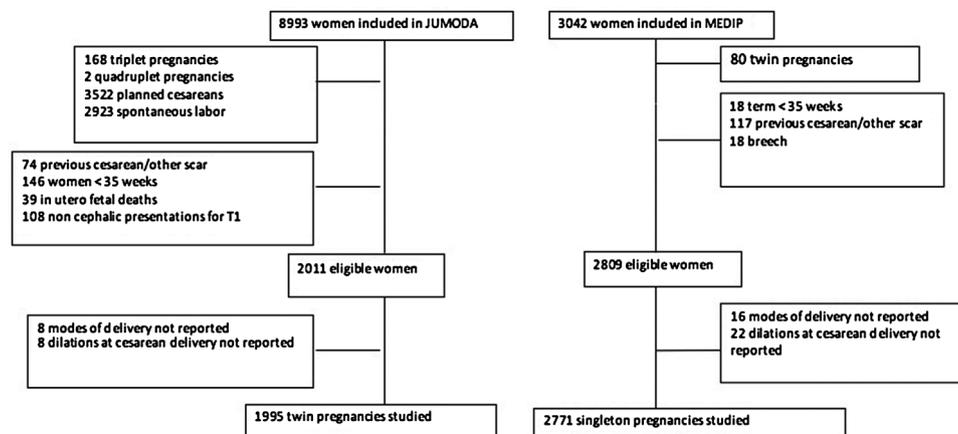


Fig. 1. Flow chart.

Finally we conducted univariate and multivariate analyses of the factors associated with cesarean delivery.

We then performed a sensitivity analysis by limiting the study population to women giving birth at centers that participated in both the JUMODA and MEDIP studies. Of the 94 centers participating in MEDIP, 42 also participated in JUMODA (45%) and included 1850 of the 2771 women with singleton pregnancies (66.8%). Of the 177 centers participating in JUMODA, 42 also participated in MEDIP (24%) and included 597 of the 1995 twin pregnancies included (29.9%). The purpose of this analysis was to ensure that the differences observed in the analysis of mode of delivery according to type of pregnancy were not explained by the different populations from different maternity units.

The univariate analysis used the Chi-2 and the Student t-tests. To determine the variables to be included in the logistic regression models, we first compared all of the factors selected for our analyses according to mode of delivery in a univariate analysis. Then we included the factors significantly associated with cesarean delivery in the univariate analysis. Because the Bishop score and method of induction were closely correlated, we did not include them simultaneously in the models, but instead used two separate models.

To construct these models, we analyzed the log-linearity of the continuous variables by comparing the linear model to a fractional polynomial. We then tested the clinically relevant interactions, i.e. between gestational age and type of pregnancy, between the Bishop score and type of pregnancy, and between parity and type of pregnancy.

Because this was a multicenter study, we also tested for a center-effect. We used a two-level logistic regression models for this purpose, with the women as the first level and the maternity units as the second. A random effect was also included, and the multilevel model was tested with a random intercept (STATA software, version 12.1).

Data for the Bishop score were missing in 10.5% of cases. Because of the strong clinical interest of this variable, we performed multiple imputations by chained equations, and then we conducted the logistic regression for the imputed cases.

Ethical approval

The National Data Protection Authority (DR-2013-528), the consultative committee on the treatment of information on personal health data for research purposes (13- 298), and the committee for the protection of people participating in biomedical research (PP-13-014) approved JUMODA. The MEDIP protocol was registered in the US NIH Clinical trials database (n° AAP-2014-030) and approved by the Ile de France 1 Patient Protection Committee in May 2015 (n°CPPIDF1-2015-May - DAP 21bis). The advisory committee on treatment of data from health research (CCTIRS, n°15.609) and the National Data Protection Authority (CNIL, n° MMS/VCS/AR1510301) approved the data collection for MEDIP.

Results

Fig. 1 presents the selection of women for our study. Overall, we studied 1995 twin pregnancies and 2771 singleton pregnancies for which labor was induced.

Baseline characteristics of women were compared between twin and singleton pregnancies. (Table 1).

The mean gestational age at induction was lower for the twin pregnancies (37.6 weeks vs 39.8 for the singleton pregnancies, $P < 0.001$).

Twin pregnancies had a favorable cervix at the beginning of induction more often, with a higher mean Bishop score than among singleton pregnancies (5.7 vs 4.0, $P < 0.001$). Thus, the

method of induction also differed significantly; more oxytocin for the twin pregnancies by oxytocin and more prostaglandins for singleton pregnancies.

In the overall population, the cesarean rate was higher for twin than singleton pregnancies (23% vs 19.4%, $P = 0.002$) (Table 2). This difference was also found among both nulliparous (35.9% vs 30.5%, $P = 0.006$) and parous women (10% vs 7.3%, $P = 0.02$). After stratification for the Bishop score, it was also found in the groups with a Bishop score ≤ 3 (39.3% vs 27.2%, $P < 0.001$), of 4–5 (25.3% vs 16.2%, $P < 0.001$), and of 6–7 (18.2% vs 10.1%, $P < 0.001$). For Bishop

Table 1

Comparison of general an induction-related characteristics according to type of pregnancy.

Type of pregnancy (N total = 4766)	Twin (N=1995) n (%)	Singleton (N=2771) n (%)	P
Maternal Age (Years)			
mean(+/-SD)	31.7 (5.2)	30.7 (5.3)	<0.001
≤ 20	20 (1.0)	71 (2.6)	
[20–35]	1533 (76.8)	2176 (78.5)	<0.001
>35	442 (22.2)	524 (18.9)	
Geographic origin			
France	1366 (75.8)	1606 (69.7)	
French overseas departments and territories	19 (1.0)	25 (1.1)	
Europe	59 (3.3)	87 (3.8)	<0.001
North Africa	205 (11.4)	367 (15.9)	
Africa	93 (5.2)	129 (5.6)	
Asia	27 (1.5)	67 (2.9)	
Other	37 (1.8)	24 (1.0)	
BMI before the pregnancy (kg/m²)			
mean (+/-SD)	23.7 (4.8)	24.6 (5.7)	0.0001
<18.5	114 (5.9)	167 (6.3)	
[18.5–25[1248 (64.4)	1481 (55.9)	<0.001
[25–30[373 (19.3)	579 (21.9)	
≥ 30	201 (10.4)	422 (15.9)	
Nulliparas	1001 (50.3)	1439 (52.0)	0.27
Preexisting diseases			
Hypertension	13 (0.7)	23 (0.8)	0.5
Diabetes	10 (0.5)	31 (1.1)	0.02
Assisted reproductive technologies	685 (34.5)	117 (4.3)	<0.001
Maternal disorder during pregnancy			
Hypertension	121 (6.1)	189 (6.8)	0,3
Preeclampsia	249 (12.5)	88 (4.9)	<0.001
Diabetes	239 (11,8)	419 (15,1)	<0.001
Threatened preterm delivery	480 (24,1)	94 (3,4)	<0.001
Fetal growth restriction	308 (15,4)	174 (6,3)	<0.001
Gestational age at induction			
(Weeks of gestation)			
mean (+/-SD)	37,6 (1,1)	39,8 (1,5)	<0.001
<37	497 (25,0)	114 (4,1)	
[37-39[1247 (62,7)	692 (25,0)	<0.001
[39-41[246 (12,3)	1002 (36,3)	
≥ 41	0 (0,0)	958 (34,6)	
Indication for induction			
Convenience/compassion	410 (20,6)	191 (6,9)	
Maternal indication	508 (25,6)	510 (18,5)	
Fetal indication	403 (20,3)	702 (25,4)	<0.001
PROM	127 (6,4)	705 (25,5)	
Post-term	539 (27,1)	654 (23,7)	
Bishop score at the start of induction			
mean (+/-SD)	5,7 (2,0)	4,0 (1,9)	<0.001
≤ 3	224 (13,8)	1108 (41,9)	
[4–5]	490 (30,3)	964 (36,5)	<0.001
[6–7]	605 (37,4)	485 (18,3)	
≥ 8	299 (18,5)	87 (3,3)	
Method of induction			
Oxytocin	1314 (65,9)	1015 (36,7)	<0.001
Prostaglandin	609 (30,5)	1656 (59,9)	
Balloon catheter	71 (3,6)	95 (3,4)	

Table 2
Comparison of cesarean rates according to type of pregnancy.

Type of pregnancy (N Total = 4766)	Twin (N=1995) n/N (%)	Singleton (N=2771) n/N (%)	P
Cesarean	459 (23.0)	537 (19.4)	0.002
Cesarean according to parity			
- Among nulliparas (N=2440)	359/ 1001 (35.9)	439/1439 (30.5)	0.006
- Among parous women (N=2316)	99/987 (10.0)	97/1329 (7.3)	0.02
Cesarean according to the Bishop score			
- ≤ 3 (N=1332)	88/224 (39.3)	301/1108 (27.2)	< 0.001
- [4-5] (N= 1454)	124/490 (25.3)	156/964 (16.2)	< 0.001
- [6-7] (N= 1090)	110/605 (18.2)	49/485 (10.1)	< 0.001
- ≥ 8 (N= 386)	37/299 (12.4)	10/87 (11.5)	0.82

Table 3
Descriptive analysis of cesareans according to type of pregnancy.

Among women who had a cesarean (N Total = 996)	Twin (N=459) n (%)	Singleton (N=537) n (%)	P
Indication for cesarean			
- Failure to progress	260 (56.6)	136 (25.3)	
- FHR abnormalities	145 (34.6)	311 (57.9)	<0.001
- Non-engagement at full dilation	39 (8.5)	50 (9.3)	
- Other	15 (3.3)	40 (7.4)	
Dilation at cesarean delivery			
- < 3cm	114 (24.8)	156 (29.0)	
- [3cm-6cm]	183 (39.9)	195 (36.3)	0.29
- ≥ 6cm	162 (35.3)	186 (34.6)	

scores ≥ 8 , however, the cesarean rates did not differ significantly between twin and singleton pregnancies (12.4% vs 11.5%, $P=0.8$). The indications for cesareans differed significantly between the two groups (Table 3).

In the first model adjusting on the Bishop score at induction, the association between twin pregnancy and cesarean delivery persisted after adjustment; the odds ratio of the twin pregnancy for the risk of cesarean was 1.8 (95% CI 1.4–2.2). In the second model adjusting on the method of induction, the excess risk of a cesarean for the twin pregnancies also persisted, with an odds ratio of 1.5 [1.2–1.8] (Table 4).

The individual characteristics independently associated with cesarean delivery were: maternal age > 35 years (adjusted OR 2.5, 95% CI 1.8–3.6), birth in French overseas departments and territories or in Africa (aOR = 2.5 [1.2–5.4] and aOR = 2.1 [1.4–3.1]), BMI > 25 kg/m² (aOR = 1.2 [1.1–1.4]) and BMI ≥ 30 kg/m [2] (aOR = 2.5 [1.7–3.6]) and primiparity (aOR = 6.3 [5.1–7.8]). The Bishop score was an independent risk factor for cesareans after induction. The lower the Bishop score at the start of induction, the stronger the association (aOR = 1.7 [1.4–3.1] for a Bishop score between 4 and 5, aOR = 3.6 [2.3–5.1] for a Bishop score ≤ 3).

The analyses conducted for women at the 42 centers common to two cohorts (N = 2447) showed results similar to those for the analysis of the entire population. The cesarean rate in twin

pregnancies was 24% versus 19% in singletons ($P=0.008$), the crude OR of the association between twin pregnancy and cesarean delivery was 1.3 [1.1–1.6], and the OR adjusted for the variables of the final model was 1.7 [1.2–2.5]. These results are thus identical to those of our principal analysis (Table 5).

Discussion

Our study shows that although the risk of a cesarean after induction was higher in twin than singleton pregnancies, more than three-quarters of the induced twin pregnancies had vaginal deliveries. The more favorable the cervix at the start of induction, the less marked the difference in the cesarean rate between twin and singleton pregnancies. Because our study was performed with data from two prospective cohorts from the general population, we were able to analyze exhaustive, validated data from a large number of women. To ensure the comparability of the two populations and to limit the bias engendered by our methodology, we conducted a sensitivity analysis limiting the analyses to maternity units that participated in both cohorts. The results obtained were identical to those in the overall population because the Bishop score was essential for our analyses, we used models with multiple imputations. The results for the cases with imputation were stable compared with those for complete cases and thus leads us to suggest that the availability of the missing data would not have modified the strength of the association. Our rate of 23% cesarean delivery among twin is close to frequencies reported in observational studies in France and in other countries [14,17,18]. In a secondary analysis of the multicenter international Twin Birth Study, the rate of cesarean among induction was significantly higher (40.5%), but a selection bias cannot be excluded, limiting extrapolation of its results [15].

Consideration of the Bishop score is an important strength of our study. Only two of the four previous studies in the literature on this subject [11–14] had collected this information, and then for only a small number of women, while this variable was analyzed for 4262 women in our study. The Bishop score, which is decisive in the choice of method of induction and a recognized risk factor for cesareans, is a highly relevant clinical indicator for studying induction [19]. Adjustment for this score thus appears essential in assessing the risk of cesareans in induced twin pregnancies. We included in our analyses all of the factors known to be likely to influence the risk of cesareans, including center; this limited the likelihood of confounding biases.

The difference in cesarean rates between twin and singleton pregnancies has previously been reported. Nonetheless, the analysis of the various risk factors for cesareans in our study shows that the odds ratio associated with twin pregnancy is substantially lower than that of other risk factors, such as maternal age older than 35 years, obesity, nulliparity, or an unfavorable cervix. Ghassani et al. reported a 27% cesarean rate in twins compared with 17% in singletons [14], and the study by Okby et al. found 31% of twins were delivered by cesareans compared with 17% of singletons [11]. In our study, the absolute risk of cesarean in induced twin pregnancies was only 23%, comparatively low in relation to other obstetric situations in which induction of labor is routinely proposed. The cesarean rate is higher, for example, for nulliparous women with post-term singleton pregnancies in France (27%) [20]. Nonetheless, induction is internationally accepted for these women [21,22]. Given that three quarters of the inductions of labor for these twin pregnancies resulted in vaginal delivery and that cesarean delivery before labor is known to result in greater morbidity than attempted vaginal delivery [8,23], there does not appear to be any medical justification for an initial cesarean of women pregnant with twins.

This higher risk of cesarean after induction for twin than singleton pregnancies could be explained by difference in the

Table 4

Analysis of factors associated with cesarean delivery : adjustment for the Bishop score (model 1) and for the method of induction (model 2).

Variables	Risk of cesarean		
	Crude OR [95% XI]	Model 1 N= 4079 ORa [95% CI]	Model 2 N= 4534 ORa [95% CI]
Twin	1.2 [1.1-1.4]	1.8 [1.4-2.2]	1.5 [1.2-1.8]
Maternal age (years)			
≤20	1.4 [1.2-1.8]	0.8 [0.6-1.1]	0.9 [0.7-1.1]
]20-35]	1	1	1
>35	2.3 [1.8-3.0]	2.5 [1.8-3.6]	2.7 [2.0-3.7]
Geographic origin			
France	1	1	1
French overseas departments and territories	2.2 [1.2-4.2]	2.5 [1.2-5.4]	2.6 [1.3-5.4]
Europe	0.9 [0.6-1.4]	0.9 [0.6-1.5]	0.8 [0.5-1.3]
North Africa	0.9 [0.7-1.1]	1.0 [0.7-1.3]	1.0 [0.8-1.3]
Africa	1.7 [1.2-2.3]	2.1 [1.4-3.1]	2.1 [1.5-3.0]
Asia	0.7 [0.4-1.3]	0.6 [0.3-1.1]	0.7 [0.4-1.3]
Other	2.1 [1.2-3.7]	1.6 [0.7-3.3]	2.4 [1.3-4.5]
BMI before pregnancy (kg/m²)			
<18,5	0.8 [0.7-0.9]	0.8 [0.7-0.9]	0.8 [0.7-0.9]
]18,5-25[1	1	1
]25-30[1.2 [1.1-1.3]	1.2 [1.1-1.4]	1.2 [1.1-1.3]
≥30	1.8 [1.3-2.5]	2.5 [1.7-3.6]	2.4 [1.7-3.4]
Assisted reproductive technologies	1.9 [1.6-2.2]	1.1 [0.8-1.3]	1.0 [0.8-1.3]
Nulliparas	5.4 [4.5-6.4]	6.3 [5.1-7.8]	6.1 [5.0-7.4]
Indication for induction			
Convenience	0.5 [0.4-0.6]	0.7 [0.5-0.9]	0.7 [0.5-0.9]
Maternal disorder	1.2 [1.0-1.5]	1.1 [0.8-1.3]	1.0 [0.8-1.3]
Fetal disease	1.0 [0.8-1.3]	1.2 [0.9-1.5]	1.1 [0.9-1.4]
PROM	0.8 [0.6-1.0]	0.8 [0.6-1.0]	0.8 [0.6-1.0]
Post-term	1	1	1
Bishop score			
≤3	3.1 [2.2-4.3]	3.4 [2.3-5.1]	
]4-5]	1.7 [1.2-2.4]	2.1 [1.4-3.1]	-
]6-7]	1.2 [0.9-1.8]	1.4 [1.0-2.1]	
≥ 8	1	1	
Method of induction			
Oxytocin	1		1
Prostaglandin	2.2 [1.9-2.6]	-	1.6 [1.3-1.9]
Balloon catheter	2.7 [1.8-4.0]		1.9 [1.2-2.9]

Table 5

Comparison of cesarean rates according to type of pregnancy in the maternity units participating in both cohorts.

Type of pregnancy (N Total = 2447)	Twin (N = 597) n (%)	Singleton (N = 1850) n (%)	P	Crude OR [95% CI]	Adjusted OR* [95% CI]
Vaginal delivery	453 (75.9)	1497 (80.9)	0.008	1.3 [1.1-1.6]	1.7 [1.2-2.5]
Cesarean	144 (24.1)	353 (19.1)			

* Adjustment for maternal age, geographic origin, BMI before pregnancy, ART, parity, indication for induction, Bishop score.

management of labor. Indeed, the management of lack of progress in dilation may differ between twin and singleton pregnancies, and professionals may tend to perform a cesarean more rapidly for a non-progressing twin than singleton pregnancy. It is also undeniable that the risk of dystocia during labor is greater in twin pregnancies, more mechanical dystocia and more labor dystocia with a more distended uterus less able to respond to oxytocin. Although the causes of cesareans (FHR abnormality and dystocia) are more frequent in twin pregnancies regardless of whether labor is spontaneous or induced and is not specific to induction itself, they most probably explain the differences we observed.

Conclusion

Twin pregnancy remains an independent risk factor for cesarean delivery after induction, regardless of parity. Nonetheless, more than three-quarters of twin pregnancies with induction of

labor have vaginal deliveries. This finding justifies a recommendation against starting with a cesarean delivery before labor when maternal and fetal conditions allow an induction to be considered.

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Key message

Although twin pregnancy is associated with the risk of cesarean delivery, more than three quarters of twin pregnancies with induced labor are delivered vaginally.

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