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Incidence of Early Neonatal Mortality and Morbidity After Late-Preterm and Term Cesarean Delivery

Roberta De Luca, MD, Michel Boulvain, MD, PhD, Olivier Iiron, MD, Michel Berner, MD, Riccardo Erennio Pfister, MD, PhD

OBJECTIVE. To determine the age-stratified risk of intrapartum and neonatal mortality as well as morbidities of clinical relevance after elective cesarean delivery (ECD).

METHODS. This work was a cohort study including 56,549 prospectively recorded late-preterm and term deliveries. We analyzed the effect of cesarean delivery (CD) before the onset of labor on the following multiple neonatal outcomes before hospital discharge, compared with planned vaginal delivery (PVD) and emergency CD: mortality, birth depression, special care admission, and respiratory morbidity. We adjusted for confounders by multivariate analysis and stratified the risk according to gestational age (GA).

RESULTS. Mortality and morbidities had a strong GA-related trend with the lowest incidences consistently found between 38 and 40 weeks of gestation independent of delivery mode. Compared with infants delivered via PVD, infants delivered via ECD had significantly higher rates of mortality (adjusted risk ratio [aRR]: 2.1), risk of special care admission (aRR: 1.4), and respiratory morbidity (aRR: 1.8) but not of depression at birth (aRR: 1.1). Compared with emergency CD, newborns delivered via ECD had less depression at birth (aRR: 0.6) and admission to special care (aRR: 0.8), but mortality (aRR: 0.8) and respiratory morbidity (aRR: 1.0) rates were similar.

CONCLUSIONS. Gestational age–specific risk estimates are lowest between 38 and 40 weeks and should be included in the informed-consent process. The information should also be used to allow for appropriate preparation with respect to adequate staff and equipment. ECD is consistently associated with increased intrapartum and neonatal mortality, risk of admission, and respiratory morbidity compared with PVD and has no advantage over emergency CD in terms of mortality. Neonatal morbidities are lower after ECD than emergency CD only with term births. Our data provide evidence that ECD should not be performed before term.

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of spontaneous delivery, thus increasing prematurity, and second, CD likely reduces the beneficial effect of labor on lung adaptation.14–16

A limited number of studies, mostly of small size, have been conducted to compare neonatal morbidity particularly between ECD and vaginal delivery (VD).17,18

A recent systematic review of respiratory morbidity after ECD19 identified 8 observational studies,12,20–27 of which only 2 were stratified by GA.12,27 Because of heterogeneous study designs, varying selection criteria, and outcome definitions, no clear-cut conclusion was possible.19

Two subsequent, large population-based studies confirmed increased mortality28 and morbidities9 after CD at term with poorer outcomes for respiratory diseases, special care admission, and breastfeeding, but also reduced neonatal traumatic injuries. However, these studies excluded late-preterm neonates and did not stratify for GA, thus denying the clinician a parameter for decision in a GA frame where mortality and morbidities change abruptly.

We designed this study to compare mortality and incidence of clinically significant morbidities in the late-preterm and term neonate according to delivery mode by intention-to-treat. We used 20 years of data on 59,626 mother-infant pairs prospectively recorded in our database. The objective was to determine GA-stratified intrapartum and neonatal mortality and morbidity associated with ECD.

METHODS

The current study was performed at Geneva University Hospital, a tertiary care facility with ~4000 births and 100 neonates born of <32 weeks’ gestation yearly, serving mainly an urban white population. Clinical databases include prospectively collected data on obstetric and neonatal outcomes of all the deliveries performed between January 1982 and September 2004 (Fig 1). The current analysis included all live-born neonates of ≥34 weeks’ gestation, including infants who died intrapartum or in the delivery room. The hospital ethics committee approved the study.

A single electronic database (FilemakerPro7 [FileMaker, Inc, Santa Clara, CA]) was obtained by standardizing formats and merging the obstetric and neonatal databases when special care admission was required, using surname, date of birth, and birth weight as matching criteria; 98.1% of maternal files were electronically matched and 1.9% (typos, different surname or birth weight) were manually identified. Maternal data were duplicated for multiple pregnancies (2.3%), and subsequent pregnancies were treated as independent. All variables were checked for consistency manually and with computerized routines.

We defined ECD as a CD before the onset of labor and before rupture of membranes; this is in agreement with most other authors.7,9,12,19,22,24,25,27,28 We compared the outcome of newborns after ECD with emergency CD (ie, after the onset of labor or rupture of membranes) and with planned VD (PVd). Following the suggestions of the American National Institutes of Health,26–30 PVd included neonates born by emergency CD who presumably were intended for VD in addition to neonates actually born by VD.

We tested the following outcomes: (1) mortality including intrapartum death and death before discharge, a proxy for neonatal mortality; (2) depression at birth, defined by an arterial cord blood pH of ≤7.10 and/or a venous cord blood pH of ≤7.15 and/or an Apgar score at 5 minutes of <7; (3) admission to the special care unit; note that admission policy was based on clinical requirements, not on birth weight or GA; and (4) respiratory morbidity, defined as any respiratory disease requiring medical support for >30 minutes and special care admission (recorded since 1995).

GA was calculated by using the time elapsed between the first day of the last menstrual period and the day of delivery, confirmed by a first trimester ultrasound (performed routinely since 1980). We stratified GA in strata of 1 week, from 34 to 42 completed weeks, and grouped into late-preterm (<37 weeks) and term (≥37 weeks) neonates.

Differences in categorical data were tested by using the χ² test, whereas the Student’s t test was used for continuous variables. To adjust for the effect of potential confounders (gender, multiple birth, malformations, intrauterine growth retardation, macrosomia [≥4000 g], and year of birth), we performed a multivariate logistic regression analysis. All analyses were performed with SPSS 15.0 (SPSS Inc, Chicago, IL).

RESULTS

We retrieved the information on 59,626 mother-infant pairs between 1982 and 2004. Information from a consecutive period of 21 months from January 1996 (n = 5074) was not retrievable for informatics reasons; 1.3% (7427) of neonates were delivered by CD, of which 34.7% (n = 2574) were delivered by ECD and 65.3% (n = 4853) by emergency CD. PVd births

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CD</td>
<td>2574</td>
</tr>
<tr>
<td>Planned VD</td>
<td>53256</td>
</tr>
<tr>
<td>Emergency CD</td>
<td>4853</td>
</tr>
<tr>
<td>VD</td>
<td>48403</td>
</tr>
<tr>
<td>Missing values</td>
<td>719</td>
</tr>
</tbody>
</table>

TABLE 1

FIGURE 1

Cohort design deliveries from 1982 to 2004 (data 1996/1997 incomplete). Missing values for mode of delivery or major outcomes.
accounted for 95.4% (n = 53,256) of all births; 86.7% (n = 48,403) were delivered vaginally, and 8.7% (n = 4,853) had an emergency CD. Mean GA at delivery was 8 days younger after ECD than PVD (376/7 vs 390/7; 4853).

Outcomes
Intrapartum and neonatal mortality was 0.16% (n = 91); 20.3% (n = 11,612) of neonates had depression at birth, 7.0% (n = 3,936) were admitted to special care, and 2.3% (575 of 24,679; 1995–2004) had respiratory morbidity requiring special care admission. Univariate and multivariate comparison between delivery modes are given in Tables 1 and 2, and age-stratified incidences are shown in Figs 3 through 6.

Mortality
Mortality rates were higher after CD than VD (0.57% vs 0.10%; risk ratio [RR]: 5.7; P < .001). Adjusted mortality rates were also significantly higher when ECD was compared with PVD (Table 1). An increased mortality rate after ECD compared with PVD was found in the term group (0.41% vs 0.11%; RR: 3.72; P < .001) but not in the late-preterm group (1.34% vs 0.75%; RR: 1.79; P = .223). Mortality rates after ECD and emergency CD were similar in univariate or multivariate analysis (Table 2), in all strata (Fig 3), or when grouped into term (0.41% vs 0.42%; RR: 0.97; P = .999) and late-preterm (1.34% vs 1.89%; RR: 0.71; P = .605).

Depression at Birth
Depression at birth was similar after ECD and PVD (Table 1 and Fig 4). Depression was slightly less frequent after ECD than PVD in the term group (18.1% vs 20.3%; RR: 0.89; P = .01) but more frequent in the late-preterm group (41.1% vs 24.0%; RR: 1.7; P < .001).

Fewer neonates were depressed at birth after ECD compared with emergency CD (Table 2). The difference was significant in the term group (18.1% vs 29.6%; RR: 0.61; P < .001) but not in the late-preterm group (41.1% vs 41.6%; RR: 1.0; P = .945).

Special Care Admission
Admissions were more frequent after ECD than PVD (Table 1). The difference was significant in all strata <39 weeks and also more common after ECD in both the term (9.6% vs 5.6%; RR: 1.71; P = .001) and the late-preterm group (46.0% vs 25.0%; RR: 1.84; P < .001). The risk of admission decreased with increasing GA (Fig 4). The lowest incidence of admissions after ECD (6.6%) and PVD (4.7%) occurred in the 39-week stratum.

Admission rates were lower after ECD than emergency CD in the multivariate but not in the univariate analysis (Table 2); admissions after ECD were less common in the term group (9.6% vs 12.4%; RR: 0.77; P = .001) but similar in the late-preterm group (46.0% vs 40.3%; RR: 1.14; P = .098).

Respiratory Morbidity
Respiratory morbidity was more than twice as frequent after ECD compared with PVD (Table 1) and was more common in both the term group (3.5% vs 1.7%; RR: 2.05; P = .001) and the late-preterm group (18.9% vs 8.8%; RR: 2.15; P < .001). Respiratory morbidity fell with progressing GA, and the lowest incidence was 1.4% in the 39-week stratum after PVD and 2.7% in the 38-week stratum after ECD (Fig 5).

Neonates delivered by ECD had a similar risk of respiratory morbidity to those delivered by emergency CD (Table 2), however, respiratory morbidity was lower in the term group (3.5% vs 5.2%; RR: 0.67; P = .013) and higher in the late-preterm group (18.9% vs 11.9%; RR: 1.59; P = .032).

DISCUSSION
This large cohort study on neonatal morbidities by intended mode of delivery shows a consistent association...
between ECD and mortality as well as with clinically relevant morbidities. The well-documented GA trend is confirmed, with the lowest mortality and morbidities between 38 and 40 weeks’ gestation. Compared with PVD (including emergency CD), ECD is associated with significantly higher mortality, admission rates, and respiratory morbidity. Compared with emergency CD, ECD is associated with less depression, admissions, and injuries.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ECD, % (n/N)</th>
<th>Emergency CD, % (n/N)</th>
<th>RR</th>
<th>95% CI</th>
<th>P</th>
<th>aRR*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0.54 (14/2574)</td>
<td>0.58 (28/4853)</td>
<td>0.94</td>
<td>0.50–1.79</td>
<td>.857</td>
<td>1.03</td>
<td>0.49–2.15</td>
<td>.938</td>
</tr>
<tr>
<td>Birth depression</td>
<td>21.4 (551/2574)</td>
<td>30.9 (1499/4852)</td>
<td>0.61</td>
<td>0.55–0.68</td>
<td>&lt;.001</td>
<td>0.60</td>
<td>0.52–0.68</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Admission</td>
<td>14.7 (377/2558)</td>
<td>15.4 (744/4629)</td>
<td>0.95</td>
<td>0.83–1.09</td>
<td>.446</td>
<td>0.77</td>
<td>0.65–0.90</td>
<td>.002</td>
</tr>
<tr>
<td>Respiratory morbidity</td>
<td>5.5 (88/1593)</td>
<td>5.9 (167/2618)</td>
<td>0.93</td>
<td>0.72–1.21</td>
<td>.583</td>
<td>0.83</td>
<td>0.61–1.13</td>
<td>.231</td>
</tr>
</tbody>
</table>

* Adjusted for GA, malformations, intrauterine growth retardation, twin/multiple births, macrosomia, gender, and year of birth.

* Includes intrapartum mortality and predischarge mortality.
respiratory morbidity in the term neonates but not the preterm neonates. Mortality rates with ECD and emergency CD are similar.

**Limitations and Strengths**

The general increase in CD rates is often attributed to ECD that is not performed for dystocia or fetal distress. CD rates at our perinatal center remained below the Swiss National figures (29.2% in 2004) as a result of a low proportion of CDs performed electively over the 20 years (Fig 2). This policy has limited the number of ECDs in this study. Nevertheless, our findings are based on a large population in the various delivery groups.

Published data on neonatal morbidities after CD remain limited, particularly after ECD where case control studies prevail. Population-based cohort studies remain rare or do not consider GA-specific morbidities and usually focus on single severe outcomes such as mortality. Cohort studies sampling on delivery mode have recruited only small numbers. A recent very large study analyzed the direct effect of CD on the neonate but limited the analysis to delivery at term. By excluding late-preterm delivery, important clinical information was lost on a high-risk population increasingly being delivered by ECD. We included late-preterm deliveries and stratified results by GA to provide generally available clinical data that could be presented to parents before deciding on the mode of delivery and inform the clinician on likely staff needs.

A policy of restricted indications for ECD, as in our center, possibly selected pregnancies with higher neonatal risk and thus may have led to an overestimation of...
unfavorable outcomes. Only a randomized, controlled trial comparing ECD with VD as intention-to-treat would overcome this weakness, but presently, no such study is available except in specific contexts such as in the term-breech or steroids-at-term trials. The outcomes reported are difficult to compare with our study except for respiratory morbidity of 5.1% and gross mortality of 0.3% that are similar or lower in our cohort. Our categorization of births into ECD and PVD resembles an intention-to-treat approach employed in a randomized, controlled trial and solves ethical and recruitment problems likely to be encountered in any attempt to do a truly randomized, controlled trial of ECD versus “planned” VD.

The strength of our study lies in its large number, nearly 60,000 mother-infant pairs, prospectively and electronically recorded. Presently, it is the largest GA-stratified cohort on neonatal outcomes comparing ECD with PVD. To account for potential confounders commonly associated with the reported neonatal morbidities, we adjusted our results in a multivariate analysis including year of birth to account for uneven variable definition over a long study period. Indeed, confounders may have been present, because adjusted estimates are different from the crude estimates.

Methodology
An effect of nonindependence resulting from duplicated maternal data for twins may tend to reduce the variability of the estimates thus slightly narrowing confidence intervals without influence on trends. Its contribution in this analysis is small given the small percentage of twins. By linking maternal and neonatal data into 1 single cohort, our study allowed the analysis of several outcomes, an advantage over case-control studies that usually sample on 1 single and severe outcome. We chose neonatal outcomes in terms of clinical relevance for the patient and the caregiver and not on the basis of specific diagnoses. Intrapartum and neonatal mortality, depression at birth, special care admission, and respiratory morbidity translate into risk management, support of parental anxiety, and requirements for resuscitation facilities and hospital beds, with a direct impact on economic issues.

Effect of GA
Depression at birth, admission to special care, and respiratory morbidity showed an expected strong age-related trend independent of delivery mode. This was particularly marked for respiratory morbidity with a >10-fold decrease from 34 weeks’ gestation to term after PVD and ECD and a fourfold decrease after emergency CD. Clearly, late-preterm infants do not behave as term infants. A CD anticipates delivery by definition. Mean GA for the neonates after ECD was indeed significantly younger than after PVD. An excess mortality and morbidity resulting from an anticipated delivery, however, would not have been fully accounted for in our GA stratification, because it compares within a stratum. In addition, by stratifying into completed weeks, we have artificially underestimated the mean GA of the stratum by at least 3.5 days.

To plan equipment and staffing, hospitals need be aware that in the 34th week, up to 54% of neonates after ECD (38% after PVD) are depressed at birth. Resuscitation requirements are easily underestimated, because depression at birth is most often benign when appropriate care is given. Moreover, in the 34th week, special care admission is required in up to 69% of neonates after ECD (47% after PVD), leading to separation from their mother during the essential early bonding period.

For all neonatal outcomes tested, a nadir of morbidities was found between 38 and 40 weeks’ gestation. The lowest incidence of the combined adverse outcomes (mortality, depression at birth, respiratory distress, and special care admission) is indicative of the best time to be born. The lowest incidence of combined neonatal complications was in the 39-week stratum after PVD and ECD and 41-weeks stratum after emergency CD. Thereafter was an increasing trend in complications.

Effect of Delivery Mode
Because CD may be life-saving, it is often assumed by the public opinion that ECD avoids neonatal risks. Rare traumatic complications are indeed reduced in the absence of labor and VD. However, our data show a significant excess mortality (adjusted risk ratio [aRR]: 2.09) after emergency CD compared with PVD. Although this was not statistically significant throughout all GA strata and in the late-preterm group because of small numbers, it was significant in the larger term group and overall in the cohort. Admission rates and respiratory morbidities were consistently higher after ECD than PVD including all strata except at 39 and 40 weeks’ gestation, making the finding very robust. The similarity in outcomes at 39 to 40 weeks’ gestation is coincident with the lowest mortality and rate of individual or combined morbidities.

Neonates born by emergency CD are delivered because of an imminent risk and are therefore expected to have a poorer outcome. Indeed, in mature infants, depression at birth, special care admission, and even respiratory morbidity were higher after emergency CD than ECD, but mortality was similar. In late-preterm infants, ECD had no better outcome than emergency CD, and a negative association was confirmed for respiratory morbidity.

The association between ECD and respiratory morbidity compared with PVD was reported and we confirmed it. Although compared with emergency CD we did not substantiate an overall difference for respiratory morbidity, an inverse interaction between preterm (RR: 1.59) and term (RR: 0.67) neonates is noteworthy. The use of steroids before ECD at term may further improve lung condition, an effect attributable to enhanced maturity of surfactant production and lung liquid clearance.
CONCLUSIONS
Our age-stratified cohort confirms that adverse neonatal outcomes decrease with increasing GA independent of delivery mode, with the lowest risk between 38 and 40 weeks’ gestation. This provides epidemiologic confirmation of “term,” the age at birth that is supposed to have the lowest neonatal risk. We provide GA-specific risk estimates that allow informed consent for the mode of delivery as well as planning for resources. Our study also shows that CD, whether before or after the onset of labor, is associated with increased mortality and clinically relevant morbidities (except in term neonates). ECD carries a higher risk for the neonate than PVD and has no advantage over emergency CD in terms of mortality, except at term, where ECD has a lower morbidity than emergency CD. Our data provide evidence that ECD should not be performed before term. We believe that the worldwide escalating CD rate urgently calls for health care policy makers and professionals to prospectively investigate and monitor its medical and social outcomes.

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