Cesarean delivery and prematurity

Cesariana e prematuridade

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The Guidelines Project, an initiative of the Brazilian Medical Association, aims to combine information from the medical field in order to standardize procedures to assist the reasoning and decision-making of doctors.
The information provided through this project must be assessed and criticized by the physician responsible for the conduct that will be adopted, depending on the conditions and the clinical status of each patient.

Introduction

Preterm birth, defined as occurring before 37 weeks or 259 days of gestation, is the main determinant of neonatal morbidity and mortality, with severe short- and long-term consequences that deteriorate the quality of life, leading to physical, psychological and financial cost for both the individual and the family[1] (**C**).

The indication of cesarean delivery in preterm pregnancy can be based on three principles: a medically indicated cesarean section; C-section on the mother's request; and indication for convenience and preference of the physician[2] (**C**).

A planned cesarean delivery in cases of preterm labor can be protective, but can also be associated with high morbidity for both mother and fetus; therefore, the ideal mode of delivery for preterm singletons in cephalic or breech presentation remains controversial.

Objective

The objective of this review is to provide the best evidence available today on the indication of C-section in women presenting preterm labor and its relationship to maternal, peri- and neonatal morbidity and mortality.

Material and methods

The evidence used for analysis of maternal, perinatal and neonatal morbidity and mortality, according to mode of delivery chosen in cases of singleton preterm pregnancies in cephalic presentation, was obtained according to the following steps: preparation of the clinical question, structuring of the question, search for evidence, critical evaluation and selection of evidence.

Clinical question

Is the performance of a C-section in singleton preterm pregnancies in cephalic presentation related to lower maternal, perinatal and neonatal morbidity and mortality compared with vaginal delivery?

Structured question

The clinical question is structured according to the P.I.C.O. components (P [Patient]; I [Intervention]; C [Comparison]; O [Outcome]).

- **P:** preterm labor.
- **I:** cesarean-section.
- **C:** vaginal deliver.
- **O:** maternal, perinatal and neonatal morbidity and mortality.

Bases of scientific data consulted

The scientific databases consulted were: PubMed-Medline and Cochrane. Manual search from revisions references (narrative or systematic) was also performed.

Strategies for search of evidence

PubMed-Medline

Strategy: (cesarean section OR cesarean sections OR delivery, abdominal OR abdominal deliveries OR deliveries, abdominal OR caesarean section OR caesarean sections OR abdominal delivery OR C-section OR C section OR C-sections OR postcesarean section) AND (premature birth OR birth, premature OR births, premature OR premature births OR preterm birth OR birth, preterm OR births, preterm OR preterm births OR infant, premature OR infants, premature OR premature infant OR preterm infants OR infant, preterm OR infants, preterm OR preterm infant OR premature infants OR neonatal prematurity OR prematurity, neonatal OR obstetric labor, premature OR labor, premature obstetric OR premature labor OR preterm labor OR la-

bor, preterm OR labor, premature OR premature obstetric labor).

Cochrane

Strategy: cesarean section AND premature birth.

Studies retrieved (7/10/14)

TABLE 1 Number of studies retrieved with the search strategies used for each scientific database.

Database	Number of studies
Primary	
PubMed-Medline	4,816
Cochrane	124

Inclusion criteria for studies retrieved

Selection of studies, assessment of titles and abstracts obtained from the search strategy in the consulted databases was conducted by two researchers with skills in the preparation of systematic reviews, both independent and blinded, strictly observing the inclusion and exclusion criteria previously established. All potentially relevant studies were identified. Whenever the title and the summary were not enlightening, researchers sought the full article.

Study design

Narrative reviews, case reports, case series and studies presenting preliminary results were excluded from the assessment. Systematic reviews and meta-analyzes were used with the basic purpose of recovering references that perhaps had been lost at first, from the initial search strategy. Studies designed as cohort or controlled clinical trials (randomized or not) were included.

Cohort study was defined as those with follow-up of patients, the same history, and analysis of prognostic outcomes.

Controlled clinical trials were evaluated according to the Jadad score.[3]

P.I.C.O. components

- **Patient:** nulliparous or multiparous women in labor of a preterm singleton live fetus in cephalic position.
- **Intervention:** cesarean-section.
- **Comparison:** vaginal delivery.
- **Outcome:** the outcomes were divided into maternal and newborn outcomes. The maternal outcomes include: maternal death or severe maternal morbidity (admission to ICU, sepsis and organ failure); bleeding complications (postpartum hemorrhage, anemia, need for blood transfusion after childbirth) and complications of surgical wound (wound infection, dehiscence or pain). Late maternal outcomes were also included, such as complications in breastfeeding, perineal pain, abdominal pain, dyspareunia, urinary incontinence, fecal incontinence, perineal trauma, and genital dystopia. Newborn outcomes, in turn, include: perinatal or neonatal death (excluding cases of death related to fatal fetal abnormalities), neonatal morbidity, such as seizures (occurring within the first 24 hours of birth or that require two or more drugs to control), Apgar score, birth asphyxia, respiratory complications, infection, need for admission into neonatal intensive care unit, neonatal encephalopathy, trauma at birth (bone fractures, subdural hematoma, cerebral or intraventricular hemorrhage), spinal cord injury, peripheral nerve injury (e.g., brachial plexus injury), disabilities in childhood, hypotonia, intubation or need for ventilation for at least 24 hours, and need for tube feeding for four days or longer.

Language

We included studies available in Portuguese, English, French or Spanish.

According to publication

Only studies with full text available were considered for critical assessment.

Studies selected in the first assessment

After entering the search strategy in the primary databases (PubMed-Medline and Cochrane), the assessment of titles and abstracts led to the selection of nine studies.

Evidence selected in critical evaluation and exhibition of results

The studies considered for full text reading were critically assessed according to inclusion and exclusion criteria, study design, P.I.C.O., language and availability of the full text.

Results pertaining clinical status will be displayed individually, showing the following items: clinical question, number of studies selected (according to inclusion criteria), description of the studies (Table 2), results and summary of the available evidence. References related to the studies included are shown in Table 4.

After applying the inclusion and exclusion criteria, the evidence selected in the search and defined as randomized controlled trials (RCT) were subjected to an appropriate checklist for critical assessment (Table 3). Critical assessment of RCTs allows to classify them according

to the Jadad score, so that Jadad < 3 trials are considered inconsistent (**B**), and those with scores ≥ 3, consistent (**A**). For critical analysis of non-randomized studies, among them prospective observational studies, we used the Newcastle-Ottawa scale.[4]

For results with available evidence, wherever possible the following specific items are defined: population, intervention, outcomes, the presence or absence of benefit and/or damage and controversies.

Cost issues will not be included in the results.

The results will be presented preferably in absolute data, absolute risk, number needed to treat (NNT), or number needed to harm (NNH), and occasionally in mean and standard deviation.

TABLE 2 Worksheet used for description of studies included, and exposure of the results.

Evidence included
Study design
Population selected
Time of follow-up
Outcomes considered
Expression of results: percentage, risk, odds, hazard ratio

TABLE 3 Critical assessment script for randomized controlled trials (Checklist).

Study data	**Sample size calculation**
Reference, study design, Jadad, strength of evidence	Estimated differences, power, significance level, total number of patients
Patient selection	**Patients**
Inclusion and exclusion criteria	Recruited, randomized, prognostic differences
Randomization	**Patient follow-up**
Description and blinded allocation	Time, losses, migration
Treatment protocol	**Analysis**
Intervention, control and blinding	Intention to treat, analyzes of intervention and control
Outcomes considered	**Result**
Primary, secondary, measuring instrument of the outcome of interest	Benefit or harm in absolute data, benefit or harm on average

Results

Clinical question

Is the performance of a C-section in singleton preterm pregnancies in cephalic presentation related to lower maternal, perinatal and neonatal morbidity and mortality compared with vaginal delivery?

Evidence selected

TABLE 4 Selection process.

Type of publication	Included
Non-concurrent cohort studies	9[5-15]

The main reasons for the exclusion of works were: the unavailability of the full text; a study design other than longitudinal observational (retrospective or prospective) or experimental (controlled clinical trials, randomized or not) studies.

Results of the evidence selected

Of the 4,940 articles initially retrieved, nine were selected to support the summary of evidence concerning maternal, perinatal and neonatal morbidity and mortality, according to mode of delivery chosen for labor resolution of preterm fetuses in cephalic presentation. Studies included are shown in Table 4.

1. Malloy MH, et al. (**B**).[5]
   - Design: non-concurrent observational longitudinal study.
   - Population: Women who gave birth (through C-section or vaginally) to fetuses (n=1,765) weighing less than 1,550 g in seven neonatal intensive care centers.
   - Outcome: neonatal morbidity and mortality.
   - Result: the cesarean delivery rate for newborns weighing 501-750 g was 32.5% and for those weighing between 751 to 1.000 g, 52.4%. With respect to neonatal mortality in cases of C-section, there was a 53% rate for newborns weighing 501-750 g, compared to 64% among those born vaginally. However, analyzing the newborns weighing between 751 to 1,000 g, the mortality rate for those born by C-section was 14.4% compared to 7.8% for births that occurred vaginally. The incidence of intraventricular hemorrhage was significantly lower among newborns weighing between 1,251 and 1,500 g born by cesarean delivery compared to vaginal births (11.8 *versus* 18.9%, respectively). After adjustment performed using logistic regression (considering gestational age, breech presentation, presence or absence of labor), no difference was found in neonatal mortality and intraventricular hemorrhage between the two modes of delivery; OR=1

(95CI: 0.71 to 1.41) and OR=0.85 (95CI: 0.61 to 1.19), respectively.

2. Malloy MH, et al. (**B**).[6]
   - Design: non-concurrent observational longitudinal study.
   - Population: retrospective analysis of all births by C-section between the years 2000 and 2003 (maternal demographics, chosen mode of delivery and neonatal morbidity and mortality were crossed).
   - Outcome: neonatal morbidity and mortality.
   - Result: information of a total of 422,001 live births was available for analysis. After adjustment by logistic regression conducted for length, weight, gender, Apgar score at 5 minutes, breech presentation, and presence of any medical complications of the mother or during labor, the authors found an *odds ratio* for neonatal mortality at gestational ages 32, 33, 34, 35 and 36 weeks of 1.69 (95CI: 1.31 to 2.20); 1.79 (95CI: 1.40 to 2.29); 1.08 (95CI: 0.83 to 1.40); 2.31 (95CI: 1.78 to 3) and 1.98 (95CI: 1.50 to 2.62), respectively.

3. Högberg U, et al. (**B**).[7]
   - Design: non-concurrent observational longitudinal study including data from seven Swedish centers.
   - Population: retrospective analysis of all births occurred from 1990 to 2000 (data on 2,094 children with gestational ages from 23 to 27 +6/7 weeks were analyzed).
   - Outcome: neonatal morbidity and mortality.
   - Result: at a gestational age from 23 to 25 weeks, 38% of births were by C-section, while at a gestational age of 26 to 27 weeks, 66% of births occurred by this mode of delivery. After excluding the cases of preeclampsia/eclampsia, the authors observed that the birth of fetuses in cephalic presentation occurred vaginally showed no significant difference with respect to neonatal mortality compared with those born by C-section.

4. Arpino C, et al. (**B**).[8]
   - Design: non-concurrent observational longitudinal study.
   - Population: retrospective analysis of all preterm births.
   - Outcome: neonatal morbidity and mortality.
   - Result: in newborns with gestational age <32 weeks, C-section did not determine a protective effect on abnormalities identified using cranial ultrasonography (birth trauma). Likewise, in newborns aged 32 weeks or more, after controlling for confounding factors, no protective effect was identified with the indication of C-section.

5. Ahmeti F, et al. (**B**).[9]
   - Design: non-concurrent observational longitudinal study.
   - Population: cohort included 12,466 births, and was studied retrospectively. Analysis of neonatal mortality associated with mode of delivery (vaginal or C-section) was conducted according to birth weight (500 to 999 g; 1,000 to 1,499 g; 1,500 to 1,999 g; and 2,000 to 2,499 g).
   - Outcome: neonatal mortality.
   - Result: 1,135 premature births resulting in 1,189 premature infants were identified. The global rate of C-section was 32%. Among preterm infants with birth weights between 500 and 999 g, 5.7% were born vaginally, compared with 0.4% born by C-section. As for the other groups, a higher percentage of C-sections (3.2% for weight between 1,000 and 1,499 g; 8.8% from 1,500 to 1,999 g; and 19.8% for those weighing 2,000 to 2,499 g) was identified. The authors observed lower mortality associated with C-section in infants with birth weights of 1,000 to 1,499 g ($p < 0.01$).

6. Sonkusare S, et al. (**B**).[10]
   - Design: non-concurrent observational longitudinal study.
   - Population: in all, 124 preterm newborns (gestational age between 30 and 35 weeks) were analyzed. Outcomes related to 70 neonates born vaginally were compared to the outcomes of 54 infants born by C-section (indication mainly due to maternal hypertension and oligohydramnios).
   - Outcome: perinatal morbidity and mortality.
   - Result: as for mortality, it was higher among those born by C-section compared to vaginal birth (20 *versus* 10%, respectively), despite the difference being non significant. Regarding neonatal morbidity, no significant differences between the delivery modes were identified.

7. Ghi T, et al. (**B**).[11]
   - Design: non-concurrent observational longitudinal study (1990 to 2007).
   - Population: births of singletons with gestational age between 25 and 32 +/-6/7 weeks (n=109) were

analyzed, and the outcomes of those born vaginally were compared to the cases of C-section.
- Outcome: maternal and neonatal morbidity and mortality.
- Result: using logistic regression, the authors found that birth weight less than 1,100 g presented as the sole predictor of neonatal adverse outcomes, which were not related to mode of delivery. Regarding maternal morbidity, the authors found that C-sections, compared with vaginal deliveries, led to more morbidity (46 *versus* 10%, respectively).

8. Riskin A, et al. (**B**).[14]
   - Design: non-concurrent observational longitudinal study (1995 to 2000).
   - Population: births of singletons in cephalic presentation with gestational age from 24 to 34 weeks (n=2,955) and weight ≤1,500 g were analyzed.
   - Outcome: neonatal morbidity and mortality.
   - Result: in this study, the authors found a cesarean section rate of approximately 51.7% indicated mainly due to maternal hypertensive disorders or prepartum hemorrhage. The rate of mortality previous to hospital discharge was lower after indication of C-section (13 *versus* 22%); however, using multivariate analysis with adjustments for other risk factors related to mortality, the authors found that the mode of delivery did not have an effect on the survival of the newborns (OR=1 with 95CI: 0.74 to 1.33).

9. Wylie BJ, et al. (**B**).[15]
   - Design: non-concurrent observational longitudinal study (1994 to 2003).
   - Population: live births of singletons in cephalic presentation and with a very low birth weight (500 to 1,500 g) were analyzed.
   - Outcome: neonatal morbidity and mortality.
   - Result: from a sample of 1,216 cesarean births and 1,250 vaginal births, it was not possible to conclude that C-sections offer an advantage in terms of lower neonatal morbidity compared to vaginal deliveries.

Discussion

C-sections are known to be associated with an increased risk of respiratory morbidity in the newborn, caused by hormones and physiological changes associated with labor and necessary for lung maturation[12] (**B**). C-section in preterm pregnancies is also particularly problematic regarding surgical technique, given that the lower segment may not be formed and, thus, a vertical incision in the upper part of the uterus may be required. In this situation, further complications may occur, including increased blood loss and increased risk of uterine rupture in subsequent pregnancies[11,13] (**B**).

The concept of planned C-section in preterm deliveries implies the possibility of accurately diagnosing and performing a C-section early in the period of labor, or right before it, and, therefore, as explained above, the risk of preterm birth is increased.

The studies in this review should be viewed with caution on account of their distinct populations, which makes it difficult to compare data. In a retrospective study, the assessment of preterm fetuses, especially those with very low birth weight (weighing less than 1,500 g) did not allow to identify evidence that C-section could provide protection with regard to the reduction of neonatal morbidity and mortality[5] (**B**). In addition, subsequent analysis conducted by the same author found that for newborns considered intermediate and late preterm, that is, with gestational age between 32-36 weeks, an indication of C--section, weighing logistic regression analysis, showed increase in the risk of neonatal morbidity and mortality[6] (**B**). However, other retrospective studies failed to identify significant differences between the delivery routes in the mortality analysis of preterm infants (gestational age between 30 to 35 weeks and 24 to 34 weeks)[10,14] (**B**).

With respect to fetal birth trauma, no significant differences between preterm births by C-section or vaginal delivery were identified[8] (**B**). After assessing maternal outcomes, the authors were able to identify higher morbidity for women undergoing C-section compared to vaginal delivery[11] (**B**).

Final recommendations

In the absence of other obstetrical indications that make it necessary to perform the delivery by upper route, planned C-section for the birth of preterm fetuses in cephalic presentation should not be indicated with the purpose of fetal protection.

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