Pintarič et al.: Labour analgesia and anaesthesia in intrapartum C-sections

Relationship between labour analgesia modalities and types of anaesthetic techniques in categories 2 and 3 intrapartum caesarean deliveries

Tatjana Stopar Pintarič1,2, Maja Pavlica3, Mirjam Druškovič3, Gorazd Kavšek3, Ivan Verdenik3, Polona Pečlin3

1Department of Anaesthesiology and Intensive Therapy, University Medical Centre Ljubljana, Ljubljana, Slovenia
2Institute of Anatomy, Medical Faculty, University of Ljubljana, Ljubljana, Slovenia
3Department of Perinatology, Division of Obstetrics and Gynaecology, University Medical Centre Ljubljana, Ljubljana, Slovenia

*Corresponding author: Tatjana Stopar Pintarič; Email: tatjanas38@gmail.com

DOI: https://doi.org/10.17305/bb.2024.10186

Submitted: 18 December 2023/ Accepted: 04 March 2024/ Published online: 13 March 2024

Conflicts of interest: Authors declare no conflicts of interest.

Funding: This work was supported by the Slovenian Research Agency (grant number: P3-0043) and Department of Perinatology, Division of Obstetrics and Gynaecology research grant for tertiary projects (grant number: TP 20200159), University Clinical Centre, Ljubljana, Slovenia.

Data availability: The data reported in this study are available upon reasonable request to the corresponding author.
ABSTRACT

General anaesthesia is typically recommended for category 1 emergency caesarean delivery (CD). For categories 2-4 emergencies, either regional and general anaesthesia could be used. However, the factors influencing the choice of anaesthetic technique in these categories remain poorly understood. We analysed the association between the type of labour analgesia and subsequent anaesthetic techniques employed for intrapartum categories 2 and 3 CD. A prospective longitudinal cohort study was conducted at the University Medical Centre Ljubljana. A total of 300 women who underwent emergency CD between March and October 2021 were consecutively enrolled and categorised according to Lucas's classification of CD urgency. Parturients with category 1 and category 4 emergency CD were excluded from the analysis. Demographic, obstetric, and anaesthetic data were recorded. The techniques of anaesthesia (general, spinal, and epidural anaesthesia) employed for CD were analysed with respect to labour analgesia methods (remifentanil patient-controlled analgesia [remifentanil-PCA], epidural analgesia, and nitrous oxide). Of the participants, 124 (41.3%) had category 2, and 96 (32%) had category 3 emergency CD. Epidural analgesia was the most frequent analgesic option (43.8%), followed by remifentanil-PCA (20.7%) and nitrous oxide (5.1%), while 30.4% of parturient women received no analgesia. All anaesthetic methods showed a significant relationship with analgesic modalities ($P < 0.001$). Remifentanil-PCA was associated with a higher incidence of general anaesthesia. Contraindication to epidural analgesia was the primary factor related to the transition from remifentanil-PCA to general anaesthesia. Most parturients who received epidural analgesia were successfully converted to epidural anaesthesia. Spinal anaesthesia was the most common technique in women using $\text{N}_2\text{O}$ and those without labour analgesia. General anaesthesia was associated with lower 5 min Apgar scores. The method of labour analgesia is associated with the anaesthesia technique employed for categories 2 and 3 CD. This finding may guide patient counselling.
and intrapartum anaesthetic planning. However, the analysis should be cautiously interpreted as the selection of anaesthesia is a complex decision influenced by several clinical considerations.

**KEYWORDS:** Emergency caesarean delivery, labour analgesia, remifentanil-PCA, epidural analgesia, regional anaesthesia, general anaesthesia, obstetric anaesthesia, neonatal outcome
INTRODUCTION

Data collected from 169 countries, representing 98.4% of all global births, reveals that in 2015, an estimated 29.7 million deliveries (21.1%) were performed through caesarean delivery (CD) [1]. This proportion is expected to increase to 28.5% by the year 2030 [2]. Approximately 60% of women require anaesthetic intervention during labour [3], and the appropriate anaesthetic technique for CD is highly dependent on its urgency. The most widely used classification system for CD urgency is the four-scale category established by Lucas et al., which uses clinical criteria to determine the level of urgency based on potential maternal and/or foetal complications and whether it poses a life-threatening situation [4,5].

The National Institute for Health and Clinical Excellence (NICE) guidelines recommend performing unplanned category 1 and 2 CDs quickly after making the decision. They suggest using a decision-to-delivery interval of 30 minutes for category 1 CDs and 30 to 75 minutes for category 2 CDs as an audit metric for obstetric units [6,7]. However, there is ongoing debate about objective time limits for decision-to-delivery intervals, and no robust evidence exists linking this interval to outcomes [5]. For category 1 or "crash" CD, it is recommended that the time taken to achieve surgical anaesthesia should be kept as short as possible. Unless there are contraindications, rapid sequence induction of general anaesthesia is typically preferred for category 1 CDs because it consistently results in a shorter decision-to-delivery interval compared to spinal anesthesia [8,9].

Existing literature on the anaesthetic management of emergency CD focuses mainly on category 1 CD or emergency CD as a whole failing to address the unique challenges posed by categories 2 and 3 emergencies. Although regional anaesthesia is generally recommended for non-crash CD, as it offers several benefits over general anaesthesia, the choice of anaesthetic modality is often not as straightforward as in category 1 CD [10]. This is particularly true regarding categories 2 and 3 CD, where general anaesthesia may be considered in addition to...
spinal or epidural anaesthesia, with the predictors of optimal anaesthetic modality often poorly defined or understood [5,11]. In both immediate- and intermediate-urgency intrapartum CD, maternal and foetal outcomes hinge on the obstetric anaesthetist's vigilance and coordinated effort due to time constraints and heightened risk, underscoring the critical significance of selecting the appropriate anaesthetic technique [12]. While several anaesthetic and obstetric factors and considerations may influence the choice of anaesthetic technique in categories 2 and 3 CD, the association between the applied labour analgesic modality and the selection of subsequent caesarean anaesthetic options has been scarcely investigated.

Several studies have shown that the choice of anaesthetic technique used for caesarean delivery can impact the newborn's outcome [13–15]. General anaesthesia is usually associated with lower Apgar scores at one and 5 minutes, while umbilical cord artery pH values does not differ. In general, all types of anaesthesia appear to be safe, but regional techniques provide certain advantages for the well-being of the newborns.

In cases where CD is required for a parturient with an existing labour epidural, it is customary to convert or 'top-up' the epidural catheter by administering a more concentrated local anaesthetic (LA) solution, typically in conjunction with a lipid-soluble opioid, to achieve surgical anaesthesia. [16]. Since existing considerations of the conversion of labour analgesia to anaesthesia have primarily focused on neuraxial analgesia techniques, very little is known regarding the principles and practice associated with the effective and safe transition from other non-neuraxial labour analgesia modalities (e.g., nitrous oxide and intravenous opioids) to surgical anaesthesia.

In parturients with remifentanil intravenous-patient controlled analgesia (remifentanil-PCA) who require CD, the selection of anesthetic technique for emergency CD is frequently unpredictable due to various factors, including individual patient preferences, obstetric
considerations, potential contraindications to specific techniques, and the presence of labor
pain, which can complicate the performance of neuraxial anesthesia. No previous studies
have specifically examined the anesthetic and obstetric implications of remifentanil-PCA or
other non-neuraxial analgesic methods on the subsequent approach to anesthesia for
intrapartum CD. To facilitate informed counseling regarding the relationship between labour
analgesia and subsequent anaesthetic choices in emergency CD, we aimed to analyse the
anaesthesia techniques employed in categories 2 and 3 emergency CD with respect to
different modalities of labour analgesia used in labours in our delivery unit.

MATERIALS AND METHODS

Study design and patient selection

The study was designed as a prospective longitudinal cohort study and received ethical
approval from the Republic of Slovenia National Medical Ethics Committee (approval
number: 0120-219/2021/3). The research was conducted at the labour and delivery unit of the
Perinatology Department, Division of Obstetrics and Gynaecology, at the University Medical
Centre Ljubljana. This unit handles approximately 5,000 deliveries annually, featuring a 70%
utilisation rate of neuraxial and remifentanil analgesia with a 1:1 ratio and a CD rate of 21%.
The study included women who underwent categories 2 and 3 emergency CD between March
and October 2021. We excluded cases of category 1 CD (obligatory general anesthesia) and
category 4 CD (without prior labor analgesia). Women with planned (‘elective’) CD were
also excluded from the analysis. A CD was classified as ‘elective’ if it was planned in
advance, allowing for careful preparation and scheduling, rather than waiting for labour to
begin naturally, or ‘emergency’ if it was performed after the onset of labour or in response to
a sudden medical condition that makes a vaginal delivery risky for the mother or baby.
Per institutional standard operative protocol, crash CD (category 1) is performed under general anaesthesia in the absence of known absolute contraindication, whereas regional anaesthesia is recommended for cases classified under urgency levels 2 - 4.

**Categorisation into urgency groups**

The indication for the intrapartum CD was carefully documented at the time of the decision, and the classifications adhered to the urgency-level categorisation system proposed by Lucas et al. [4]. The proposed indications for the categorization of patients into specific groups are as follows:

**Group 1** (‘crash’ CD: an immediate threat to maternal or foetal life): severe pathological cardiotocography (CTG) readings, such as sustained foetal bradycardia; massive haemorrhage from placenta previa or abruption accompanied by hemodynamic instability or pathological CTG patterns; uterine rupture; failed extraction of the second twin due to complications like a neglected transverse position; maternal cardiac arrest; and instances of failed instrumental delivery with evidence of severe foetal distress.

**Group 2** (maternal or foetal compromise not immediately life-threatening): failed instrumental delivery due to prolonged second stage of labour, foetal distress, as indicated by non-life threatening pathological CTG or a foetal scalp pH measurement below 7.20; foetal malposition during advanced labour; and placental abruption cases with mild bleeding and foetal compromise.

**Group 3** (need for early delivery without maternal or foetal compromise): bleeding placenta previa without concurrent hemodynamic instability; cephalo-pelvic disproportion (CPD), poor progress of labour; and cases of pathological CTG mandating completion of delivery in approximately 60 minutes; and foetal malposition at the outset of labour.
Group 4 (delivery at a suitable time for the patient and maternity team): failed induction, planned caesarean delivery with initial signs of labour; medical indications necessitating CD due to maternal conditions requiring stabilization, such as preeclampsia, appendicitis, or pancreatitis in the third trimester or foetal conditions such as intrauterine growth restriction.

Labour analgesia methods

The choice of labour analgesia method was made by women during labour, following consultations with anaesthesiologists, obstetricians, and midwives. The available modalities in our obstetric unit include remifentanil-PCA, epidural analgesia, nitrous oxide, and pethidine. All participants had the same analgesic options available to them.

Remifentanil-PCA

In our institution, labour epidural and remifentanil-PCA are equally represented as labour analgesic choices. Since its introduction in 2013, remifentanil-PCA has been widely used for medical, obstetrical, and patient-driven indications, with over 1300 cases of administration annually. Remifentanil-PCA administration adhered to the procedural guidelines of the Department of Anaesthesia and Intensive Therapy at the University Medical Centre Ljubljana. Remifentanil hydrochloride (Ultiva, GlaxoSmithKline, Oslo, Norway) was prepared in saline at a concentration of 40 µg mL⁻¹. The administration followed a stepwise approach, commencing at 20 µg and escalating to a maximum of 40 µg, with a bolus duration of 20 seconds and a lockout interval of 2 minutes, devoid of any background infusion. The anaesthesiology staff adjusted the dose based on the patient's request. Bolus dose increase occurred if pain intensity (assessed by an 11-point Numerical Rating Scale) rose and the patient's respiratory rate was > 9 breaths min⁻¹, with SpO₂ ≥ 94%, heart rate > 50 min⁻¹, and sedation score ≤ 2 on a five-point scale. Throughout the procedure, women received dedicated one-to-one midwifery care and underwent continuous monitoring utilising a
Capnostream® capnograph (Oridion®, Jerusalem, Israel) equipped with an oral-nasal cannula for sampling from the nose and mouth (Oridion®). All patients received supplemental oxygen at a rate of 2 litres per minute through a nasal catheter. The respiratory monitor continuously recorded waveform data for end-tidal CO₂, respiratory rate, SpO₂, and heart rate. Alarms were triggered in cases of oxygen desaturation (SpO₂ < 94%), bradypnea (respiratory rate < 8 min⁻¹), or apnoea exceeding 20 seconds. Staged interventions were initiated, commencing with verbal instruction to take a deep breath or a gentle tap if no response was elicited. Continuous foetal heart rate monitoring was performed with the Hewlett Packard Viridia Series 50IP® or Philips 50XM® cardiotocography (CTG) equipment. Remifentanil administration was halted in the event of pathological CTG changes, including reduced variability, bradycardia, tachycardia, or late decelerations. According to the institutional guidelines, contraindications for remifentanil-PCA use in labour include patient refusal, documented history of allergy to opioids, parenteral opioid medication administered within the previous two hours, opioid drug abuse, obstructive sleep apnoea, or unavailability of 1:1 midwife care [17–19].

**Epidural analgesia**

Epidural analgesia has been consistently administered around the clock in our institution since 2013, adhering to the established procedural guidelines of the Department of Anaesthesia and Intensive Therapy at the University Medical Centre Ljubljana. Catheter insertion was conducted with patients in a seated position. The epidural space was identified using an 18-gauge Tuohy needle (PORTEX® CSE cure® Combined Spinal Epidural System, Smiths Medical, Minnesota, USA) inserted in the midline, employing the loss of resistance technique with air or saline at the L3-L4 or L4-L5 intervertebral space. Subsequently, a 20-gauge multi-hole catheter was inserted. A test bolus of 3 ml of lidocaine 2% was administered to assess epidural placement, followed by an initial 20 ml infusion of a mixture containing
0.1% bupivacaine and 2 μg mL⁻¹ fentanyl. The epidural analgesia was delivered using the same local anaesthetic mixture via a combination of programmed intermittent epidural bolus (PIEB) and patient-controlled epidural analgesia (PCEA) techniques using a Rhythmic™ Evolution pump (Micrel Medical Devices, Athens, Greece). As per institutional protocol, contraindications for EA encompass patient refusal, localised sepsis at the puncture site, thrombocytopenia, coagulopathy or anticoagulant therapy, signs of cardiovascular instability, and significant lumbar deformity or prior major spinal surgery.

Nitrous oxide
Nitrous oxide (N₂O) was provided by midwives using an intermittent approach of 50%-70% N₂O in oxygen administered via a handheld facemask or mouthpiece. The parturient initiates inhalation, generating the flow of N₂O. The peak effect is achieved within 30 to 40 seconds, after which the parturient is instructed to exhale into the mask or mouthpiece to ensure complete elimination of respired particles through the system.

Pethidine
Per institutional protocol, eligible patients who opted for this modality received 50-100 mg intravenous pethidine injection. However, pethidine was used in only three parturients who were excluded from further analysis.

Anaesthetic techniques
General anaesthesia
General anaesthesia was provided via rapid sequence induction. Prior to induction, a pre-oxygenation regimen consisting of 4 to 5 vital-capacity breaths of pure oxygen was administered, followed by intravenous injection of 5 mg/kg of thiopental or 2 mg/kg of propofol and 1 mg/kg of succinylcholine chloride or rocuronium (1 mg/kg). Subsequently,
endotracheal intubation was performed, and anaesthesia was maintained with sevoflurane in a 60/40 nitrous oxide/oxygen mixture. For patients initially given suxamethonium, 0.5 mg/kg of rocuronium was administered for maintenance of neuromuscular blockade. After cord clamping, fentanyl 3–5 mg/kg was added intravenously.

**Spinal anaesthesia**

Spinal anaesthesia was administered through a 25-gauge Sprotte needle, inserted in the midline and positioned at the L3–L4 intervertebral space with the injection of 7.5 to 11 mg of bupivacaine and 25 μg of fentanyl. Subsequently, the patient was positioned in a supine posture with a 15° left lateral tilt, and a 15° Trendelenburg position was adopted to enhance the cephalic distribution of the anaesthetic agents. We considered anaesthesia adequate if it resulted in an upper sensory block extending to the T4 level.

**Epidural anaesthesia**

In patients with existing epidural analgesia regimens, epidural anaesthesia for emergency intrapartum CD was established with an epidural top-up of 2% lidocaine to a total of 20 mL, commencing in the delivery room. We considered anaesthesia adequate if it resulted in an upper sensory block extending to the T4 level.

**Data analysis**

The following data were recorded for statistical analyses: demographic and obstetric data of parturients (age, body mass index (BMI), parity, CD history); the urgency level of CD graded from category 1 to 4; the type of labour analgesia employed (whether none, N2O, epidural, or remifentanil-PCA); the method of anaesthesia administered (such as general anaesthesia, spinal anaesthesia, or epidural anaesthesia); and the rate of conversions from regional anaesthesia to general anaesthesia. Additionally, we also recorded adverse neonatal outcomes, including mortality, Apgar scores below 7 at 5 minutes, umbilical cord artery pH levels below
7.0, and base excess values below 12. Descriptive statistics for parametric data are expressed as mean ± standard deviation (SD). The Student *t*-test and Chi-square test were employed for comparing continuous and categorical variables, respectively. A significance threshold was set at *p* < 0.05. All statistical analyses were performed with IBM SPSS Statistics for Windows Version 27.0 (Armonk, NY: IBM Corp).

**RESULTS**

A total of 300 women were prospectively enrolled in this study, with the distribution across urgency categories depicted in Table 1. Excluded from the analysis were women falling under category 1 CD, where timely delivery is imperative due to predominantly irreversible causes of foetal or maternal distress, such as umbilical cord prolapse, uterine scar dehiscence and placental abruption. Our centre utilizes general anaesthesia for category 1 CD to minimize the time from decision to delivery as much as possible. Women in category 4 CD were excluded because they had not received prior labour analgesia. During the study period, 49 potentially eligible CD were excluded from the analysis due to non-compliance with the study protocols. Additionally, data for two women were missing, and three cases involving pethidine labour analgesia were excluded from the final analysis. Of the remaining participants, 122 (41.3 %) were categorised under level 2 CD, while 95 (32%) were categorised as level 3 CD, forming the basis of our final analytical cohort. Figure 1 illustrates the patient screening and selection process.

The main indications for category 2 CD were foetal distress from non-immediately threatening pathological CTG (53 cases, 43%), foetal malposition during advanced labour (18 cases, 15 %), CPD (17 cases, 14%), and poor progress of labour (12 cases, 10%). The commonest indications for category 3 CD included poor progress of labour (39.6%), CPD (27.1%), and previously planned caesarean delivery with initial signs of labour (12.5%).
Table 2 presents a comprehensive overview of the demographic, obstetric, and anaesthetic data for participants in category 2 and 3 CD. These data are stratified based on the type of labour analgesia administered, namely, no analgesia, N₂O, epidural analgesia, and remifentanil-PCA. Epidural analgesia was the most frequent analgesic choice in this cohort (43.8%), followed by remifentanil-PCA (20.7%) and N₂O (5.1%), while about a third of the parturients (30.4%) required no labour analgesia. We observed no statistically significant differences in age, BMI, or previous CD history among the various labor analgesia groups. However, significant differences were noted in parity. Epidural analgesia was the most commonly used labor analgesic method among nulliparous women. The remifentanil-PCA group had the highest proportion of parturients with previous CD history. Among multiparous women without previous CD, the highest proportion was found in the no-analgesia group, followed by the remifentanil-PCA group.

Table 3 summarises the findings regarding the association of anaesthetic techniques with different analgesic modalities in category 2 and 3 CD. All anaesthetic methods showed a statistically significant relationship to analgesic modalities ($P < 0.001$). 69.5% of parturients who received epidural analgesia subsequently required conversion to epidural anesthesia for CD. Parturients utilizing other analgesic methods did not require epidural anesthesia. 53% of parturients who received no labour analgesia and 63.6% of those who received N₂O transitioned to spinal anaesthesia, while the rest had general anaesthesia. On the other hand, 60% of parturients who received labour remifentanil-PCA transitioned to general anaesthesia for intrapartum CD, while the rest utilised spinal anaesthesia. Further analysis of the selection of anaesthetic technique with respect to indications for remifentanil-PCA showed that among parturients receiving remifentanil-PCA, 'contraindication to epidural analgesia' due to patient refusal was significantly associated with the use of general anesthesia for CD (Table 4).
The association between neonatal outcome data and the different analgesic modalities and subsequent anaesthetic techniques is presented in Table 5. No differences in Apgar scores were observed between analgesic modalities when converted to neuraxial anaesthesia. However, in those converted to GA, significantly lower Apgar scores were observed only in the no-analgesia group \((P = 0.002)\). This finding appears to be associated with an elevated incidence of prematurity within this particular group. Upon further analysis of the subgroup with no analgesia in cases of prematurity, it was determined that most cases necessitated CD due to foetal malposition or foetal distress subsequent to the initiation of premature labour. In such cases, intrapartum analgesia was deemed unnecessary. Other neonatal parameters, including pH and base excess, showed no statistically significant relationship with the analgesic groups.

**DISCUSSION**

This study investigated the relationship between different methods of labour analgesia (neuraxial, remifentanil-PCA, and \(\text{N}_2\text{O}\)) and the type of anaesthesia technique (general, spinal, or epidural) employed for intrapartum CD of categories 2 and 3 urgencies. All anaesthetic techniques were found to have a statistically significant relationship with the type of labour analgesia priorly administered. The majority of women who received epidural analgesia transitioned to epidural anaesthesia. Conversely, among women who received remifentanil-PCA for labor analgesia, 60% transitioned to general anesthesia, with the remaining 40% undergoing spinal anesthesia. Patient refusal of epidural analgesia was the primary factor associated with the transition to general anesthesia in the remifentanil-PCA group. More than half of the women who received no labour analgesia and those who received \(\text{N}_2\text{O}\) transitioned to spinal anaesthesia. Overall, the analysis suggests that the modality of labour analgesia may be an important predictor of the subsequent anaesthetic
approach in the event of CD of intermediate urgency. The specific findings may be useful for patient counselling and can inform and guide anaesthetic and obstetric preparedness in intrapartum CD.

Currently, various pain relief options are accessible for labour, including neuraxial analgesia (e.g., epidural), parenteral opioids, and inhalational analgesia. The choice of labour pain management in women is shaped by factors such as health, demographics, and attitudes, with varying impacts depending on the specific technique employed [20]. Guidelines from both the American Society of Anaesthesiologists (ASA) and the American College of Obstetricians and Gynaecologists (ACOG) recommend epidural analgesia as the most adaptable, efficient, and least neurologically depressive analgesic method in obstetrics [21], with new techniques like programmed intermittent epidural bolus, dural puncture epidural, and ultrasound-guided neuraxial approaches offering improved precision [22]. Although neuraxial analgesia offers highly effective labour pain relief, its utilisation in labour can be influenced by factors like availability, contraindications, and individual preferences [23]. Severe conditions like deep vein thrombosis, pulmonary embolism, mechanical heart valve, arrhythmia, severe scoliosis, or post-surgical spine instrumentation may preclude optimal and timely administration of neuraxial labour analgesia [24]. Other analgesic strategies are indicated when central neuraxial analgesia is contraindicated, technically infeasible, or if the patient's preference dictates.

Epidural analgesia was the most frequently administered analgesic option in the analysed cohort, reflecting current clinical trends and recommendations. While epidural analgesia does not inherently elevate the risk of CD, approximately 10% of parturients utilising epidural analgesia during labour may require emergency CD [25,26]. To enable surgical anaesthesia in parturients with an existing labour epidural, it is standard practice to convert or 'top-up' the epidural catheter by administering a more concentrated local anaesthetic solution, often
combined with a lipid-soluble opioid when a CD is indicated. It was shown that lidocaine 2%, with or without fentanyl, provides the quickest onset of sensory blockade during conversion, and the inclusion of ropivacaine 0.75% in the epidural top-up solution diminishes the necessity for additional supplementation in surgery [16]. Efficient conversion of labour analgesia to surgical anaesthesia may serve as a valuable quality of care indicator in addition to affirming the prior efficacy of the labour analgesia modality [16].

The observation that epidural anaesthesia was solely associated with epidural analgesia suggests that this anaesthetic technique is primarily favoured in the context of priorly established neuraxial access with epidural analgesia. Accordingly, patients with labour epidural analgesia should be counselled about the overall likelihood of transitioning to anaesthesia via top-up of existing analgesia and that in the event of failed conversion of epidural analgesia to surgical anaesthesia, general but not spinal anaesthesia is typically likely. It was reported that the likelihood of unsuccessful conversion from labour epidural analgesia to anaesthesia rises with higher bolus administrations in labour, heightened urgency for CD, and care administered by a non-obstetric anaesthesiologist [27]. Our analysis also showed a low conversion rate from epidural to general anaesthesia. The Royal College of Anaesthetists guidelines recommend that the conversion rate from neuraxial to general anaesthesia for category 1 and categories 1–3 CD should be maintained at less than 15% and 5%, respectively [28]. Although we observed no association between spinal anaesthesia with previous epidural analgesia, a retrospective analysis of parturients who received epidural labour analgesia but needed subsequent CD under regional anaesthesia found that spinal anaesthesia resulted in reduced time from anaesthesia to surgical incision and total anaesthetic time, lower postoperative pain scores, and decreased morphine dosage when compared to epidural anaesthesia [26]. Similarly, rapid sequence spinal anaesthesia is increasingly preferred over general anaesthesia for many category 1 CD indications [11].
Nonetheless, administering spinal anaesthesia after epidural analgesia can lead to an unanticipated profound blockade, potentially reaching total sensory and motor spinal anaesthesia [29,30].

Our analysis has shown that remifentanil-PCA is associated with a higher incidence of general anaesthesia in categories 2 and 3 emergency CD. Several factors potentially influence this observed association. Firstly, women opting for remifentanil-PCA often present with contraindications for epidural analgesia. Additionally, certain obstetric conditions, such as a history of previous CD, twin gestation, or a breech presentation, may pose heightened risks with epidural analgesia, prompting a preference for alternative analgesic approaches [31–34].

A recent study by Parissetti et al. demonstrated that EA constitutes a significant risk factor for the failure of vaginal breech delivery, leading to an increased likelihood of intrapartum CD [35]. Jaschevatzky et al. reported higher rates of operative vaginal deliveries and higher pre-term perinatal mortality in twin deliveries with EA, despite similar neonatal status (as assessed by the Apgar score at one minute) in both the EA and control groups [33]. Similarly, in a case series of parturients with multiple gestation who delivered vaginally, a higher incidence of low Apgar-minus-colour scores at one minute among the second twins of at least 36 weeks gestation was reported in the EA group [32]. Our analysis of the selection of anaesthetic technique with respect to indications for remifentanil-PCA shows that EA refusal was the only statistically significant factor related to the increased transition to general anaesthesia for CD. Given the higher likelihood of encountering general anaesthesia in labouring women who received remifentanil-PCA, it is imperative that parturients are counselled beforehand regarding the potential need for transition to general anaesthesia and the associated complications thereof (especially a higher likely hood of gastric paresis with the consequent risk of regurgitation and aspiration) [36], should intrapartum CD become necessary. Despite many controversies regarding remifentanil efficacy and safety,
remifentanil-PCA shows comparable delivery and neonatal outcomes to epidural analgesia within any of the Ten Groups Classification System (TGCD) labour types [17,19]. In the present analysis, remifentanil-PCA and epidural anaesthesia also demonstrated comparable neonatal outcomes. As previously shown in other studies [13–15], general anaesthesia typically correlated with a higher incidence of neonates having low Apgar scores at the fifth minute, with no significant difference in umbilical cord artery pH and base excess values.

Furthermore, our analysis shows that women who received no labour analgesia and those who received N₂O mainly transitioned to spinal anaesthesia, suggesting that this anaesthetic option is associated with parturients who are naïve to invasive analgesic modalities. A retrospective analysis found that only a small proportion of labouring women (mostly nulliparous women with an initial preference for non-medical birth) chose nitrous oxide for analgesia during labour and delivery, with the majority ultimately converting to neuraxial analgesia, suggesting the minimal analgesic effect of nitrous oxide and the need to counsel parturients on the potential of analgesia conversion [37]. Nevertheless, women using N₂O experience enhanced maternal satisfaction and coping compared to those without analgesia, despite its lower analgesic effectiveness compared to neuraxial labour analgesia [38], suggesting that pain relief is not the only contributor to maternal satisfaction with labour analgesia [39].

Our cohort demonstrated no adverse neonatal outcomes attributable to hypoxia. Neonatal parameters (including pH and base excess) revealed no statistically significant differences among groups. Furthermore, Apgar scores showed no variation between analgesic modalities when transitioning to neuraxial anaesthesia. Conversely, conversion to GA was associated with significantly lower Apgar scores within the no-analgesia group (P = 0.002). Further analysis revealed a significantly higher incidence of preterm birth (before the 37th week of gestation) in the no-analgesia group (66%) compared to those receiving EA or remifentanil-
PCA (<1%). In the no-analgesia group, most CDs were performed due to abnormal fetal positioning early in labor, often involving presentations such as breech, footling, or transverse lie. These laboring mothers had not yet requested intrapartum analgesia. The disparity in the gestational age notably affected the Apgar score assessment of the newborn, especially when using general anaesthesia to perform CD. The effects of general anaesthesia on the newborn are multifactorial and can vary depending on the specific circumstances of the CD and the individual responses of both the mother and the baby. General anesthesia medications readily cross the placenta, potentially causing neonatal central nervous system depression that manifests as respiratory difficulties and may lead to lower Apgar scores [40].

Although the results of our analysis indicate that the type of labour analgesia used could be a significant factor in predicting the subsequent anaesthetic approach for intrapartum CD, it is crucial to interpret our findings with caution. First, the study's observational, non-randomized design inherently limits causal inference due to the potential for uncontrolled confounding variables. Variations in patient characteristics or clinical practices across groups may bias the observed results. Nevertheless, as randomized controlled trials (RCTs) on the effects of labor analgesia and anesthetic choice in category 2 and 3 emergency CD are unlikely in the near future, patient counseling regarding potential associations between anesthetic methods in these scenarios will continue to rely primarily on observational data. Second, our analysis has primarily examined the association between the chosen analgesic modality and the subsequent anaesthetic transition. We did not consider the specific indications and rationale guiding the labour analgesic/anaesthetic choice. The choice of analgesic technique during labor and subsequent anesthetic management for intrapartum cesarean delivery (CD) is a complex decision influenced by diverse factors. These include patient preferences (e.g., prior experience, pain perception, concerns about nerve damage), anesthesia-related considerations
(e.g., indications and contraindications), obstetric circumstances, fetal well-being, and other clinical factors [41]. Thus, it is imperative to recognize that the choice of anaesthesia is not solely a consequence of preexisting labour analgesia but rather a complex and carefully considered decision aimed at optimising the outcome for both the parturient and the neonate.

Third, as a single-center study, the generalizability of our results to a broader population may be limited. However, our position as Slovenia's largest tertiary center, handling one-third of the nation's births and diverse pregnancy referrals, suggests that our findings may have relevance for other major obstetric centers. While a larger, multi-center retrospective study could offer more definitive insights, our study provides valuable initial data on this important topic.

**CONCLUSION**

This prospective cohort study investigated the relationship between various labour analgesia methods (neuraxial, remifentanil-PCA, and N₂O) and the anaesthesia technique (general, spinal, or epidural) for intrapartum CD of categories 2 and 3 urgencies. Our analysis shows that more than half of women utilising remifentanil-PCA for labour analgesia transitioned to general anaesthesia for intrapartum CD, with a smaller proportion undergoing spinal anaesthesia. Contraindications to epidural analgesia were significantly associated with transitioning from remifentanil-PCA to general anaesthesia. On the other hand, most women who received epidural analgesia continued with epidural anaesthesia, while those in other analgesic groups seldom underwent this approach. Additionally, more than half of women who received no labour analgesia or N₂O underwent spinal anaesthesia, suggesting a preference for this option among parturients without prior invasive analgesia. Our observations may be useful for counselling patients and guiding anaesthetic preparedness in categories 2 and 3 intrapartum CD. Nevertheless, it is imperative to approach these findings.
with caution, as our analysis primarily explored the association between the types of analgesic modality and subsequent anaesthetic transitions without consideration of specific factors that impact the selection of anaesthetic techniques. The decision regarding anaesthesia technique during intrapartum CD is complex, influenced by a spectrum of factors extending beyond preexisting labour analgesia.

**Author Contributions**

Conceptualisation: PP, MD, GK, TSP; methodology TSP, MP, MD, GK, IV, PP; data curation: MP, IV, PP; statistical analysis: IV; writing — original draft preparation: PP, TSP, writing, review and editing TSP, MP, MD, GK, IV, PP; supervision PP. All authors have read and approved the submitted version of the manuscript.

**Acknowledgments**

We are grateful to Chiedozie Kenneth Ugwoke, MD, for assistance with manuscript proofreading.

**Institutional Review Board Statement**

The study was approved by the National Medical Ethics Committee of the Republic of Slovenia (approval No: 0120-219/2021/3).

**Informed Consent Statement**

Written informed consent was obtained from all study participants prior to their enrollment.
References


8. Palmer, E.; Ciechanowicz, S.; Reeve, A.; Harris, S.; Wong, D.J.N.; Sultan, P. Operating Room-to-Incision Interval and Neonatal Outcome in Emergency Caesarean Section: A


15. Bidon, C.; Desgranges, F.P.; Riegel, A.C.; Allaouchiche, B.; Chassard, D.; Bouvet, L. Retrospective Cohort Study of Decision-to-Delivery Interval and Neonatal Outcomes According to the Type of Anaesthesia for Code-Red Emergency Caesarean Sections in


Deliveries between 1.3.2021 and 18.10.2021 (n = 3433) \[\rightarrow\] Vaginal deliveries excluded (n = 2718)

Caesarean deliveries (CD) (n = 715) \[\rightarrow\] Elective CD excluded (n = 366)

Urgent CD (n = 349) \[\rightarrow\] Excluded due to poor adherence to categorisation protocol (n = 49)

Included in the parent study (n = 300) \[\rightarrow\] Urgency Category 1 and Category 4 excluded (n = 80)

Urgency Category 2 (n = 124) and Category 3 (n = 96) \[\rightarrow\] Pethidine labour analgesia recipients excluded (n = 3)

Final analysis Urgency Category 2 (n = 122) and Category 3 (n = 95)

Figure 1. Flowchart of the patient enrolment process.
Table 1. Distribution of parturients according to the level of urgency of intrapartum caesarean delivery

<table>
<thead>
<tr>
<th>Level of urgency*</th>
<th>Interpretation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Immediate threat to maternal/foetal life</td>
<td>50 (16.7%)</td>
</tr>
<tr>
<td>2</td>
<td>Maternal or foetal compromise that is not immediately life-threatening</td>
<td>124 (41.3%)</td>
</tr>
<tr>
<td>3</td>
<td>Need for early delivery without maternal or foetal compromise</td>
<td>96 (32.0%)</td>
</tr>
<tr>
<td>4</td>
<td>Delivery at a suitable time for the patient and maternity team</td>
<td>27 (9.0%)</td>
</tr>
</tbody>
</table>

Note: *Per the categorisation of urgency of caesarean delivery proposed by Lucas et al. [4]. The green highlight indicates the categories of interest in the present study.
Table 2. Maternal demographic and obstetric data with respect to different labour analgesic methods

<table>
<thead>
<tr>
<th></th>
<th>No analgesia</th>
<th>Nitric oxide</th>
<th>Epidural analgesia</th>
<th>Remifentanil-PCA</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>66</td>
<td>11</td>
<td>95</td>
<td>45</td>
<td>217</td>
<td></td>
</tr>
<tr>
<td>(30.4%)</td>
<td>(5.1%)</td>
<td>(43.8%)</td>
<td>(20.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>32.6 ± 5.9</td>
<td>31.3 ± 4.9</td>
<td>31.5 ± 4.6</td>
<td>32.0 ± 5.6</td>
<td>31.9 ± 5.2</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.641)</td>
<td></td>
</tr>
<tr>
<td>BMI (mean ± SD)</td>
<td>24.5 ± 5.2</td>
<td>22.3 ± 3.6</td>
<td>24.7 ± 3.9</td>
<td>26.2 ± 5.5</td>
<td>24.8 ± 4.8</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.060)</td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>33/66</td>
<td>6/11</td>
<td>93/95</td>
<td>24/45</td>
<td>156</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(50.0%)</td>
<td>(54.0%)</td>
<td>(98.0%)</td>
<td>(53.3%)</td>
<td></td>
<td>(70.7%)</td>
<td></td>
</tr>
<tr>
<td>Multiparous with previous CD</td>
<td>15/33</td>
<td>3/5</td>
<td>½</td>
<td>11/21</td>
<td>30/61</td>
<td>ns</td>
</tr>
<tr>
<td>(45.5%)</td>
<td>(60%)</td>
<td>(50%)</td>
<td>(52%)</td>
<td></td>
<td>(49.0%)</td>
<td>(0.918)</td>
</tr>
<tr>
<td>Multiparous without previous CD</td>
<td>18/33</td>
<td>2/5</td>
<td>½</td>
<td>10/21</td>
<td>31/61</td>
<td>ns</td>
</tr>
<tr>
<td>(54.5%)</td>
<td>(40.0%)</td>
<td>(50.0%)</td>
<td>(48.0%)</td>
<td></td>
<td>(51.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean (standard deviation) or n (%) and with a significance threshold at P < 0.05. CD: Caeserean delivery; Remifentanil-PCA: Remifentanil intravenous-patient controlled analgesia; SD: Standard deviation; ns: Not significant.
Table 3. Selection of anaesthetic techniques with respect to labour analgesic modalities

<table>
<thead>
<tr>
<th>No analgesia</th>
<th>N₂O</th>
<th>EA</th>
<th>Remifentanil-PCA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>General anaesthesia</td>
<td>31 (47%)</td>
<td>4 (36.4%)</td>
<td>28 (29.5%)</td>
<td>27 (60%)</td>
</tr>
<tr>
<td>Epidural anaesthesia</td>
<td>0</td>
<td>0</td>
<td>66 (69.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Spinal anaesthesia</td>
<td>35 (53%)</td>
<td>7 (63.6%)</td>
<td>1 (1.0%)</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>Conversion from epidural anaesthesia to general anaesthesia</td>
<td>0</td>
<td>0</td>
<td>3 (3.3%)</td>
<td>0</td>
</tr>
</tbody>
</table>

P is significant at < 0.05. EA: Epidural analgesia; Remifentanil-PCA: Remifentanil intravenous-patient controlled analgesia; GA: General anaesthesia; N₂O: Nitrous oxide.

Table 4. Mode of anaesthetic transition with respect to indications for remifentanil-PCA

<table>
<thead>
<tr>
<th>GA</th>
<th>RA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraindications for EA</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Failed EA</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Obesity&gt;35 BMI</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Previous CD</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Twin and breech vaginal deliveries</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Others (patient preferences)</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

P is significant at < 0.05. BMI: Body mass index; CD: Caeserean delivery; EA: Epidural analgesia; GA: General anaesthesia; RA: Regional anaesthesia; Remifentanil-PCA: Remifentanil intravenous-patient controlled analgesia; ns: Not significant.
Table 5: Relationship between neonatal outcome data and analgesic/anaesthetic modalities

<table>
<thead>
<tr>
<th></th>
<th>No analgesia</th>
<th>N2O</th>
<th>EA</th>
<th>Remifentanil-PCA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-min Apgar &lt; 7 after RA (spinal + EA)</td>
<td>1/35 (2.9%)</td>
<td>0/7</td>
<td>1/70</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>5-min Apgar &lt; 7 after GA</td>
<td>5/31 (16.1%)</td>
<td>0/4</td>
<td>0/25</td>
<td>0/27</td>
<td>0.022</td>
</tr>
<tr>
<td>pH umbilical artery &lt; 7 after RA( spinal + EA)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>pH umbilical artery &lt; 7 after GA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Base excess umbilical artery &lt; -12 after RA</td>
<td>1/35 (2.9%)</td>
<td>0</td>
<td>3/70</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Base excess umbilical artery &lt; -12 after GA</td>
<td>2/31 (6.5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Preterm birth &lt; 37 weeks, n (%)</td>
<td>38 (66%)</td>
<td>2</td>
<td>0</td>
<td>2 (0.4%)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

P is significant at < 0.05. NICU: Neonatal intensive care unit; EA: Epidural analgesia; GA: General anaesthesia; RA: Regional anaesthesia; Remifentanil-PCA: Remifentanil intravenous-patient controlled analgesia; N2O: Nitrous oxide; ns: Not significant.