

Optimal Anesthesia Scheme for Transfer to Emergency Cesarean Section in Failed Labor Analgesia Trial Delivery

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Optimal anesthesia scheme for transfer to emergency cesarean section in failed labor analgesia trial delivery

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Abstract

Objective: To explore the optimal anesthetic method of transferring to emergency cesarean section after the failure of labor analgesia.

Methods: A retrospective study included 1154 patients who underwent cesarean section in Hubei Maternal and Child Health Hospital from January 2019 to January 2020, of which 586 patients were transferred to cesarean section after labor analgesia. They were divided into two groups according to the method of anesthesia: Epidural labor analgesia / Epidural anesthesia (ELA/EA) group : After the failure of natural labor during labor analgesia, local anesthetics continue to be added to the epidural(n=282);Epidural labor analgesia/Combined spinal and epidural anesthesia(ELA/CSEA) group: Combined spinal-epidural anesthesia was performed after spontaneous labor failure during epidural labor analgesia(n=304); Combined spinal and epidural anesthesia(CSEA) group: Patients who undergo emergency cesarean section without labor analgesia(n=568). The case data were reviewed and the

anesthetic methods, basic vital signs, medication, time, maternal and infant outcome of the three groups were descriptively analyzed.

Results: There was a difference in the time of admission to neonatal delivery, the maximum decrease of diastolic blood pressure and the difference of neonatal 1min apgar score between ELA/EA group and ELA/CSEA group. There was a difference in the dosage of spinal anesthesia between ELA/CSEA group and CSEA group.

Conclusion: When the obstetrician anesthesiologist fails during labor analgesia and needs to be transferred to cesarean section, they can choose to re-perform combined spinal-epidural anesthesia, which is beneficial to the early outcome of newborns, but the long-term effect on newborns needs to be further studied.

Key words: anesthetic mode; CSEA; emergency cesarean section; EA; Labor analgesia

Introduction

Labor analgesia can relieve the pain in the process of delivery, prevent the parturient from refusing natural delivery because of pain, and require cesarean section. Painless delivery reduces the proportion of cesarean section in China, which is widely carried out in China. Among them, epidural labor analgesia is the most commonly used and safe method of labor analgesia. However, due to the need for emergency cesarean section in the process of delivery, it is a dilemma to choose which anesthetic method can effectively and quickly complete the cesarean section. Epidural anesthesia can be used when the function of epidural catheter is good, but epidural anesthesia may lead to poor anesthetic effect and need to change to other anesthetic methods, resulting in a

series of adverse consequences¹. When emergency cesarean section is performed after the failure of labor analgesia, Whether it is more beneficial to re-use spinal anesthesia is the subject of our discussion in this article. This study retrospectively analyzed the emergency cesarean section after the failure of vaginal trial of labor analgesia in our hospital from January 2019 to January 2020 and the anesthetic implementation process and maternal and infant outcome of emergency cesarean section after vaginal trial delivery without labor analgesia, and summarize the experience in order to provide reference for the choice of anesthesia for this kind of cesarean section.

Data and Methods

- 1.Approved by the Ethics Committee.
- 2.From January 2020 to January 2021, a total of 705 people underwent emergency cesarean section after failed vaginal delivery after intravertebral delivery analgesia in Maternal and Child Health Hospital of Hubei province. A total of 783 people were transferred to cesarean section after vaginal trial labor without intraspinal labor analgesia. Among them, a total of 586 patients who were transferred to cesarean section after labor analgesia were included in the group. They were divided into two groups according to the method of anesthesia: ELA/EA group : After the failure of natural labor during labor analgesia, local anesthetics continue to be added to the epidural(n=282); ELA/CSEA group: Combined spinal-epidural anesthesia was performed after spontaneous labor failure during epidural labor analgesia(n=304); CSEA group: Patients who undergo emergency cesarean section without labor analgesia(n=568). Exclusion criteria: Direct

general anesthesia for emergency cesarean section, poor labor analgesia, twin pregnancy, placental abruption, placenta previa, umbilical cord prolapse, lack of case records, patients with serious cardio-cerebrovascular complications.

3. Details of each method of anesthesia.

3.1 Methods of labor analgesia: All parturients were in the left supine position, Percutaneous extradural lateral catheterization in lumbar 2-3 intervertebral space, All parturients were placed in left recumbent position with epidural lateral catheterization in lumbar 2-3 intervertebral space with a depth of 4cm, and continuous epidural labor analgesia (ELA) was performed with analgesia pump. Epidural regimen: 0.08% ropivacaine combined with 0.5 μ g/ml sufentanil, the first dose was 6-12 ml/h. When incomplete analgesia occurred during analgesia (visual analog score \geq 4), the patient-controlled dose was 9.9 ml and the limit was 35ml/h. 1500ml lactate Ringer's solution was infused intravenously during labor analgesia. During the process of labor analgesia, 1500ml lactate Ringer's solution was infused intravenously.

3.2 Anesthesia for cesarean section: If the epidural catheter function of the patient transferred to emergency cesarean section after labor analgesia is good, the anesthesiologist on duty can choose epidural anesthesia or re-puncture combined spinal-epidural anesthesia. If the function of the epidural catheter is not good, the epidural catheter will be removed and re-punctured for combined spinal-epidural anesthesia. General anesthesia in other special cases was not included in this study. The criteria for judging the good function of epidural catheters should meet the following three points:(1) The parturient reported that the analgesic effect was good

during labor analgesia, and there was no frequent medication.(2) No obvious exfoliation was found in the epidural catheter.(3) No blood and cerebrospinal fluid were drawn back.

3.3 Epidural anesthesia cesarean section (ELA/EA) was performed after labor analgesia: After entering the room, the epidural dose of 2% lidocaine was given 4 ml, and the mixture of 0.75% ropivacaine + 2% lidocaine was given 5-10 ml after observing the absence of total spinal anesthesia. the operation began after reaching above the anesthesia level of chest six. The patients who did not reach the anesthesia level of chest six for more than 10 minutes were regarded as the failure of epidural anesthesia and changed to general anesthesia. Hydroxyethyl Starch 130/0.4 and Sodium Chloride Injection and lactate Ringer's solution were infused during the perioperative period.

3.4 Cesarean section with combined spinal-epidural anesthesia (ELA/CSEA) was performed after labor analgesia: After entering the room, the pregnant woman was placed in a lateral recumbent position and the original epidural catheter was removed. Re-puncture at lumbar 3-4 for combined spinal-epidural anesthesia, See subarachnoid injection of 0.5% ropivacaine 12mg to 18mg after unobstructed cerebrospinal fluid drainage, The epidural tube was placed to the cephalic side, and the depth of the tube was 4cm. Hydroxyethyl Starch 130/0.4 and Sodium Chloride Injection and lactate Ringer's solution were infused during the perioperative period.

3.5 Method of combined spinal-epidural anesthesia(CSEA) for emergency cesarean section without labor analgesia: After entering the room, the pregnant woman was

placed in a lateral position and punctured at lumbar 3-4 for combined spinal-epidural anesthesia. See subarachnoid injection of 0.5% ropivacaine 12mg to 18mg after unobstructed cerebrospinal fluid drainage, The epidural tube was placed to the cephalic side, and the depth of the tube was 4cm. Hydroxyethyl Starch 130/0.4 and Sodium Chloride Injection and lactate Ringer's solution were infused during the perioperative period.

Determination of anesthetic level: The level of temperature block was tested with alcohol-stained cotton swabs every minute to evaluate whether T6 level block was achieved; The motor block level was evaluated with a modified Bromage score every 5 minutes. The operation can begin when the cold feeling of T6 disappears and there is no clamp pain in the skin. The failure of EA anesthesia block was defined as 10 minutes after epidural administration, there was still clamp pain on T6 plane. It needs to be converted to general anesthesia (GA) in the following situations : Anesthetic block failed or patchy block or clamp pain occurred at the operation site of the patient. We used visual analogue scale ((VAS)) to evaluate intraoperative pain, If VAS > 4, fentanyl 50-100ug was injected intravenously as a supplementary analgesic. If the VAS score is not less than 4 after the use of fentanyl, it is considered to have failed and should be changed to general anesthesia.

Data collection: The clinical data of 1154 parturients were collected retrospectively, including age, complications, history of delivery, causes of conversion to cesarean section, causes of emergency cesarean section, vital signs of labor analgesia and anesthesia during cesarean section, dosage of methoxamine, atropine or other

auxiliary analgesics, adverse reactions and maternal and infant outcomes.

Statistical analysis: The data were analyzed by SPSS20.0 software. The variables are analyzed by descriptive statistical analysis. The summary statistics of all variables are expressed by mean \bar{x} and minimum-maximum values, and the classified data are summarized as numbers (%) percentage. P1 is the comparison between ELA/EA and ELA/CSEA, P2 is the comparison between ELA/CSEA and CSEA, and the data between groups are compared by t-test, The difference was statistically significant ($P < 0.05$).

Results

Basic information data

Table 1:

	ELA/EA (282)	ELA/CSEA (304)	CSEA (568)
Age (y)	29 (22–36)	30 (21–37)	28 (24–39)
Days of pregnancy (d)	281 (271–289)	282 (276–290)	279 (253–286)
Puerpera/parturient	233 (82.6%)	260(85.5%)	426 (75%)
Complications(diabetes or hypertension)	152 (53.9%)	157 (51.6%)	300 (52.8)
Reasons for conversion to cesarean section			
Abnormal fetal position and stagnant stage of labor	30 (10.6%)	32 (10.5%)	89(15.7%)
Fetal distress	173 (61.3%)	196(64.5%)	351(61.8%)
Fever	27 (9.6%)	35(11.5%)	89 (15.7%)
Other factors	52 (18.4%)	41(13.5%)	39 (6.9%)

The stage of labor when transferring to cesarean section

Incubation period	63 (22.3)	73 (24.0)	114 (20.1)
Active phase	102 (36.2)	107 (35.2)	196 (34.5)
The second stage of labor	117 (41.5)	124 (40.8)	258 (45.4)

Table 2:

	ELA/EA (282)	ELA/CS (304)	CSEA (568)	P value
Admission-fetal delivery time (min)	24 (19-27)	19 (16-23)	18 (15-23)	P1=0.01; P2=0.52
Admission-fetal delivery time (mmHg)	25 (15-30)	25 (15-30)	30 (20-50)	P1=0.17; P2=0.06
Maximum diastolic blood pressure drop (mmHg)	20 (15-25)	30 (20-40)	30 (20-40)	P1=0.02; P2=0.18
Maximum heart rate increase (Times\ minute)	15 (10-20)	20 (15-25)	20 (15-25)	P1=0.31; P2=0.51
Lactic acid Ringer's solution volume (ml)	650 (500-750)	650 (500-750)	800 (500-1000)	P1=0.95; P2=0.03
Hydroxyethyl Starch 130/0.4 and Sodium Chloride	300 (100-500)	250 (100-500)	450 (100-500)	P1=0.65; P2=0.12
Injection amount (ml)				
Total amount of epidural lidocaine and ropivacain (ml)	10 (8-15)			
Total amount of ropivacaine injection in subarachnoid space (mg)		12.0 (11.3-13.5)	15.8 (14.25-18)	P2= 0.01
Intraoperative methoxamine dosage (mg)	1.5 (0-4)	2 (0-4)	2 (0-4)	P1=0.21; P2=0.32
Intraoperative atropine dosage (mg)	0.1 (0-0.2)	0.1 (0-0.2)	0.1 (0-0.2)	P1=0.35; P2=0.41
Intraoperative bleeding volume	300(150-350)	300(150-300)	300(150-300)	P1=0.45; P2=0.36
Intraoperative urine volume	450(100-600)	400(150-650)	350(150-600)	P1=0.55; P2=0.43
Nausea and vomiting occurred during the operation	9(3.2%)	15(5.5%)	27(4.7%)	

Assist other analgesics / No other analgesics were used	466(16.3%)	7(2.3%)	12(2.1%)
Other factors	52 (18.4%)	41(13.5%)	39 (6.9%)
The stage of labor when transferring to cesarean section			
Incubation period	63 (22.3)	73 (24.0)	114 (20.1)
Active phase	102 (36.2)	107 (35.2)	196 (34.5)
The second stage of labor	117 (41.5)	124 (40.8)	258 (45.4)

Table 3: situation of pregnant women and newborns

	ELA/EA (282)	ELA/CSE (304)	CSEA (568)	P value
Before operation, the sensory level is higher than the level of chest 4.	2 (0.7%)	2 (0.7%)	3(0.5%)	
After operation, the feeling level is higher than the level of chest 4.	1 (0.4%)	2 (0.7%)	5 (0.9%)	
Need respiratory support or general spinal anesthesia	0	0	0	
The puerpera is enrolled in icu.	2(0.7%)	3(0.7%)	6(1.1%)	
Failure of anesthesia to general anesthesia	6 (2.1%)	1(0.3%)	1 (0.2)	
1min Apgar score	8 (7-10)	9 (8-10)	9 (8-10)	P1=0.02 P2=0.21
5min Apgar score	10 (9-10)	10 (9-10)	10 (9-10)	P1=0.56 P2=0.61
Neonatal NICU entry rate	16(5.7%)	14(4.6%)	28(4.9%)	

Results

1. General information : A total of 586 parturients were included in labor analgesia and transferred to cesarean section during the study period, 568 cases of emergency cesarean section without labor analgesia, a total of 1154 cases. The average age of pregnant women was 29 years old (22-39 years old), The body mass index (BMI) before delivery was 19.6-31.6 kg/m². The average time of vaginal trial labor under epidural analgesia was 8.9 h (1.5-25.0 h). The general situation of parturients and the reasons for conversion to cesarean section are shown in Table 1.

2. Results of anesthesia for cesarean section: In the data of the time(min) of admission to fetal delivery, the ELA/EA group was 24min, Higher than the other two groups, It is statistically significant. The total of subarachnoid ropivacaine(mg) injection in ELA/CSEA group was 12.0 mg, which was higher than that in CSEA group (15.8mg). The diastolic blood pressure drop of 30 (20-40) mmHg in ELA/CSEA group was higher than that of 20 (15-25) mmHg in ELA/ESA group. The details are shown in Table 2.

Maternal and newborn status: Among the 282 cases in ELA/EA group, 2 cases had sensation level to chest 2 level after anesthesia, and the patients complained of chest tightness, but did not receive respiratory support and only inhaled oxygen routinely. 0.5-1 hour after operation, the sensory level dropped to chest 10 and returned to the ward. 6 cases were changed to general anesthesia: among them, 4 cases did not reach the level of chest 6 10 minutes after epidural injection, and then changed to general

anesthesia; One case was changed to general anesthesia because the surgeon thought that the muscle was too tight to take out the fetus or suture; One patient developed limb anesthesia on one side and weak anesthesia on the other side, so it was changed to general anesthesia. In 2 cases of ELA/CSEA group, the sensory plane was higher than the level of chest 4, and one patient complained of hand numbness and weakness of swallowing saliva, but could breathe on his own and did not need additional respiratory support. In one case, there was no sensory plane block 5 minutes after CSEA. The analysis may be due to the failure of the operation. The local anesthetic was not injected into the subarachnoid space and was changed to general anesthesia. In CSEA group, there were 3 cases whose sensory plane was above the level of chest 2, but no respiratory support was needed; There was a case of anesthetic failure converted to general anesthesia due to insufficient spinal anesthesia and epidural bleeding, and finally transferred to general anesthesia. There was no need for respiratory support or general spinal anesthesia in the three groups. The parturients with postoperative anesthesia level above chest 4 or low blood pressure were transferred to PACU for further observation. There were 1 case (0.4%) in ELA/EA group, 2 cases (0.7%) in ELA/CSEA group and 5 cases (0.9%) in CSEA group. Among the three groups, 11 cases were treated with ligation of uterine double arteries because of perioperative blood loss, and the parturients were transferred to intensive care unit (ICU) for observation after operation. There was significant difference in neonatal 1min apgar score between ELA/EA group and ELA/CSEA group ; There was no difference in 5min apgar score and neonatal in neonatal intensive care

unit(NICU) among the three groups. The details are shown in Table 3.

Discussion

Parturient women in vaginal delivery due to uterine contraction, fetal head drop and other factors can lead to severe pain, the body secretes a large amount of catecholamines, if not treated in time, it can lead to prolonged labor or delayed labor, and even lead to dystocia or postpartum hemorrhage, seriously affecting the health of mothers and infants, so safe, reliable and quick analgesia in the process of delivery can not only ensure the smooth progress of delivery. It can also further improve the fertility quality. At present, many scholars believe that epidural labor analgesia is an ideal way of labor analgesia, which has the following characteristics: (1) it has a slight impact on mothers and infants; (2) the drug administration is convenient, effective and accurate, and can meet the needs of analgesia in the whole process of labor;(3) there is no motor block, which will not affect uterine contraction and maternal movement; (4) keep the parturient awake and take an active part in the delivery process; (5) if necessary, it can meet the needs of operation; (6) the analgesic effect is definite.

Due to the complexity of the delivery process, a considerable number of patients need to be converted to cesarean section, so a common challenge faced by obstetrical anesthesiologists is how to deal with epidural catheters during natural delivery conversion to cesarean section. Some authors suggest that parturients undergoing epidural labor analgesia can be directly anesthetized under epidural anesthesia when they need to transfer to cesarean section. However, in some cases, the use of epidural

catheters placed during delivery may not be reliable in surgical anesthesia. A retrospective meta analysis showed that during conversion to cesarean section after epidural labor analgesia, the reasons for the failure of epidural anesthesia include the increase in the number of punctures during epidural catheterization and the urgency of caesarean section²; In addition, some studies believe that the risk factors include the type of epidural labor analgesia (simple epidural analgesia and combined spinal-epidural analgesia), epidural infusion during labor analgesia, increased injection times due to explosive pain during trial labor, maternal height, epidural medication during surgical anesthesia, whether or not to be a full-time obstetrician anesthesiologist, etc, due to the different definition of failure, the conclusions are not consistent³, It can be seen that there are many factors affecting the effect of epidural anesthesia. The best management of patients with failed epidural anesthesia is also controversial. The anesthesia choices of parturients after the failure of epidural anesthesia include: replacement of epidural catheter by re-puncture, spinal anesthesia by re-puncture, and switching to general anesthesia⁴. However, after the failure of epidural administration, the dose of spinal anesthesia is difficult to control, and the risk of high spinal cord block increases⁵, In fact, the study found that for parturients who need to transfer to emergency cesarean section for epidural labor analgesia, high nerve block often occurs in patients with epidural local anesthesia but failed anesthesia and then re-puncture for spinal anesthesia. the probability of high nerve block in patients with direct spinal anesthesia is very low⁶. General anesthesia after the failure of epidural anesthesia also has potential problems such as satiety, difficult

airway and hypotension⁷. The Royal College of Anesthesia recommends that the rate of general anesthesia for parturients undergoing epidural anesthesia should not exceed 3%, the proportion of conversion from intraspinal anesthesia to general anesthesia for elective cesarean section is less than 1%, the proportion of general anesthesia for emergency cesarean section is less than 5%⁸. However, studies have found that patients who fail to perform epidural anesthesia after labor analgesia are as likely to switch to general anesthesia as high as 21%⁹.

The biggest disadvantage of anesthetic failure is to prolong the interval between the decision of emergency cesarean section and fetal delivery. However, it is generally believed that shortening the interval between decision-to-delivery interval(DDI) is related to the improvement of early neonatal outcome, Neonatal Apgar score and umbilical blood pH value were lower when DDI was prolonged¹⁰. Therefore, in epidural labor analgesia, how to choose anesthesia for emergency cesarean section due to changes in maternal or fetal conditions is a great challenge.

A total of 586 patients who were transferred to cesarean section during labor analgesia were included in this study. In ELA/EA group, 6 cases (2.1%) were converted to general anesthesia because of incomplete block; In ELA/CSEA group, 1 case (0.3%) was transferred to general anesthesia due to the failure of anesthesia puncture. Therefore, the success rate of anesthesia in ELA/CSEA group was significantly higher than that in ELA/EA group. At the same time, our study showed that there was no significant increase in the incidence of hypotension in ELA/CSEA group, and there was no occurrence of total spinal anesthesia. This may be related to

the fact that the local anesthetic dosage of ELA/CSEA in our study is 12.0mg, which is significantly lower than that of CSEA in 15.8mg. Therefore, it is suggested that during spinal anesthesia after labor analgesia, when the demand for local anesthesia is about 3.8mg less than that of cesarean section, It can achieve good analgesic effect and the incidence of high nerve block is low. In this study, the decrease of systolic blood pressure was not obvious in ELA/CSEA group, but the decrease of diastolic blood pressure was more obvious than that of systolic blood pressure, which was related to the supplement of lactate Ringer's solution 1500ml during labor analgesia. Another result of this study was that the time of admission to fetal delivery(min) in ELA/CSEA group was 19 (16-23) min, Lower than ELA/EA (98) group 24 (19-27) min; There was no significant difference in neonatal birth weight, 5min Apgar score and neonatal NICU entry between the two groups ($P>0.05$); However, there was significant difference in 1minApgar score between the two groups ($P<0.05$). This shows that the ELA/CSEA group has an advantage over ELA/EA in shortening DDI, and it is related to the improvement of early neonatal outcome, and whether the long-term neonatal outcome is related to this needs further study. It is suggested that in order to strive for relatively sufficient anesthesia time, once a decision is made for cesarean section, the conversion process from epidural analgesia to epidural anesthesia should begin in the delivery room¹¹⁻¹². However, our hospital did not do this, because we considered that during maternal transport, it was still possible to cause the epidural tube to shift to the subarachnoid space or prolapse. The epidural anesthesia for parturients who needed emergency cesarean section in our hospital

began after entering the operating room, which is also the reason why the ELA/EA group had a longer time to enter the room and deliver the fetus. It increases the risk of EA failure after ELA and increases the conversion rate of general anesthesia. In this study, the probability of requiring additional analgesics in the ELA/EA group is higher, and some studies have also found that EA after ELA is more prone to intraoperative pain than spinal anesthesia (SA) (15.3% vs 2.5%)¹³, which further shows that EA is prone to insufficient analgesia. Insufficient maternal analgesia not only causes harm to the body and mind of the parturient, but also affects the operation of the surgeon, which may further lead to an increase in the amount of bleeding and poor long-term wound healing. Considering the onset time of anesthesia and the degree of muscle relaxation, CSEA after ELA has more advantages¹⁴. At the same time, compared with women who underwent elective cesarean section under regional anesthesia, parturients who underwent cesarean section after vaginal trial delivery may experience more serious anxiety during operation, and increased anxiety may aggravate intraoperative pain and increase the need for anesthesia. In addition, tissue injury and pain during delivery can reduce the pain threshold of CS during delivery through central sensitization mechanism. therefore, CSEA with dense sensory block may be more effective in inhibiting intraoperative pain than EA¹⁵.

However, re-puncture of CSEA after ELA is more difficult than that of ordinary emergency cesarean section. In this study, one case failed to re-puncture and was transferred to general anesthesia. In practice, we found that if the dura mater is more elastic when re-punctured in the same space as the labor analgesia puncture, it is not

easy to be punctured by the spinal anesthesia needle, we consider that this may be related to the accumulation of a large number of local anesthetics in the epidural for a long time. At the same time, the accumulation of a certain amount of local anesthetic fluid in the epidural space may affect the judgment of cerebrospinal fluid reflux, which makes it difficult for the operator to judge whether to reach the subarachnoid space, which can lead to the failure of spinal anesthesia. But we have an experience that usually if we reach the subarachnoid space, there will be continuous spinal anesthesia fluid and the spinal anesthesia fluid will be unobstructed. If there is transparent fluid with air bubbles in the spinal anesthesia needle and the return is not smooth, and there is no sense of breakthrough through the epidural space, it should still be in the epidural space; At the same time, whether the re-puncture of CSEA after EA will increase the probability of nerve injury, this study did not observe the relevant indicators.

To sum up, in this retrospective cohort analysis, In this study, we use a small dose of spinal anesthesia to make the advantages of CSEA after ELA more reflected. We believe that spinal anesthesia has more advantages than epidural anesthesia when labor analgesia needs to be transferred to emergency cesarean section, which is mainly reflected in:(1).Faster delivery of the fetus can lead to a better early outcome of the newborn.(2). The success rate of anesthesia is higher, and the anesthesia satisfaction of parturients and surgeons is improved.

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Authors' contributions

Wen-hao Bu and Wei Wu designed the study. Na Li 、 Lin Chen and Lin-li Yue Zhang retrieved the data and performed the data analysis. Wen-hao Bu and Wei Wu drafted the manuscript. All the authors participated in the discussion of the results and critically revised the manuscript. The authors read and approved the final manuscript.

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None

Availability of data and materials

The datasets used and/or analyses performed during the study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the medical ethics committee of Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. The ethics committee approved this

procedure as the study only involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, and these sources are publicly available.

Consent for publication

Not applicable.

Conflict of Interest

The authors declared that they have no conflicts of interest.

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