

Original Article

Cardiac hemodynamic changes during spinal anesthesia for C-section in parturients with twin pregnancy

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Abstract: Background: Hypotension during spinal anesthesia (SA) is common. Twin gestation causes additional changes in maternal cardiac output (CO) compared to singleton gestation during pregnancy. The dynamic CO changes in parturients with twins after SA remain unclear. The first aim of this study was to compare the changes of CO and other hemodynamic parameters at different time after SA versus baseline. The second aim is to determine whether spinal anesthesia-induced hypotension could be predicted by baseline CO and other parameters derived from noninvasive cardiac output monitor (NICOM). Methods: CO, stroke volume (SV), heart rate (HR), mean arterial pressure (MAP), and total peripheral vascular resistance (TPR) of parturients with twins were continuously measured by NICOM technology. Changes of each parameter at predefined time points (in right lateral position, after SA, at incision, and after delivery) as compared to the baseline values were analyzed. The predictability of these baseline parameters for detecting SA induced hypotension was assessed using logistic regression. The effects of phenylephrine on hemodynamic profiles were also analyzed. Results: Five minutes after SA, CO decreased by about 17.5%, and was maintained at a lower level than the baseline value until fetal delivery ($p < 0.05$). After delivery and administration of oxytocin, CO significantly increased. At the end of the surgery, CO gradually returned to the baseline. Changes of SV were similar to CO, while HR increased after spinal anesthesia. The decrease in TPR was not significant after spinal anesthesia, but it decreased significantly after delivery ($p < 0.05$). Administration of phenylephrine significantly decreased HR and CO ($p < 0.05$). After SA, 32 parturients developed hypotension and 31 did not experience hypotension before delivery. No significant differences of baseline cardiac hemodynamic parameters were seen between hypotension group and normotension group. Conclusion: CO decreased significantly in parturients with twins after spinal anesthesia, and the occurrence of hypotension after spinal anesthesia may be mainly related to the reduction of CO. The baseline cardiac hemodynamic parameters were not predictive of spinal anesthesia induced hypotension during C-section.

Keywords: Twin pregnancies, spinal anesthesia, cardiac output, hypotension

Introduction

Twin pregnancies have significantly increased in China due to the rapid development of assisted reproductive technology. As compared to single pregnancy, twin pregnancies constitute a higher risk to both mother and fetuses, such as hypertensive disorders, gestational diabetes, preterm labor, intrauterine growth restriction, etc. [1, 2]. Twins would further exacerbate physiological changes in the mother during pregnancy, such as increase in blood volume, cardiac output (CO) and body oxygen consumption than a single fetus [3, 4]. There is a high rate of C-section for twins [2]. Spinal anesthesia is a

popular technique for C-section. Hemodynamic changes are usually associated with spinal anesthesia and delivery. Traditionally, noninvasive blood pressure (BP) and heart rate (HR) monitoring was used to assess maternal hemodynamics in obstetric anesthesia. Maternal status and placental perfusion are evaluated through BP. However, it is currently believed that CO is more relevant to placental perfusion [5, 6]. Although BP and HR can partially reflect CO, the correlation between BP and CO decreases after spinal anesthesia due to changes of peripheral vascular resistance, and BP cannot fully reflect changes of CO [7]. The correlation between HR and CO is also affected by stroke

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volume (SV). Classic textbook warns that hypotension is more common and severe after neuraxial anesthesia in multiple gestation than in single pregnancy [8]. Therefore, it is necessary to continuously monitor CO in pregnant women with multi-fetal pregnancies to help anesthesiologists to provide optimal and timely clinical management.

A noninvasive cardiac output monitoring (NICOM) system (Cheetah Medical, USA) can continuously monitor SV and CO based upon bioimpedance technology, which analyzes phase changes during cardiac ejection in thoracic impedance. NICOM also can calculate total peripheral vascular resistance (TPR) based on CO and BP. NICOM is a noninvasive, convenient, and reliable device for continuously measuring CO, and has acceptable accuracy and precision when compared to pulmonary artery catheter measurement of CO [9]. NICOM is also used during obstetric anesthesia [10, 11], and can effectively track hemodynamic changes [12].

Numerous studies have observed hemodynamic changes after anesthesia, such as continuous measurement of CO in parturients with single pregnancy by means of noninvasive or invasive cardiac monitoring [13-15], but the exact changes in CO during spinal anesthesia in parturients with twins have not been reported. Therefore, the first aim of our study was to use NICOM to evaluate the characteristics of CO changes in parturients with twins during SA for C-section in this study. The predictive ability of non-invasive haemodynamic parameters for SA induced hypotension were studied in singleton pregnancies. So the second aim of our study was to investigate whether CO, HR, SV and TPR measured before the induction of SA could predict hypotension in parturients with twins.

Materials and methods

General information

The study was approved by the hospital Ethics Committee (Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai, China), and written informed consent was provided by all participants. A total of 72 ASA physical status I-II parturients with twin pregnancies of >35 weeks' gestation scheduled for elective C-section were recruited into this prospective, observational study between

October 2016 and July 2017. Cardiac hemodynamic parameters of parturients including CO, HR, SV, TPR and MAP were measured before and after SA. Exclusion criteria included age <18 years, height <155 cm, body mass index (BMI) >35 kg/m², hypertension, preeclampsia, diabetes mellitus, and bleeding disorders. All women fasted for at least eight hours.

Anesthesia

The parturients were in supine position with 15° left lateral tilt. An 18-gauge cannula was inserted into the vein of right hand, and 500 mL of Lactated Ringer's solution was infused before CSEA. Two dual-electrode skin sensors of NICOM were bilaterally placed on the upper thorax and lateral subcostal regions for continuous monitoring of HR, CO, TPR and SV. The noninvasive blood pressure (NBP) of left upper arm and pulse oxygen saturation (SPO₂) were monitored. A baseline CO, HR, SV, TPR and MAP were derived from the mean of three recordings after 5 min in supine position.

An assistant helped the parturients to be in the full right lateral position with knees bent and head down. CSEA was performed after 3 min in right lateral position. At the L3-4 interspace, epidural space was identified with a 17G Tuohy needle by loss of resistance to air. A 25G Whitacre spinal needle (B Braun) was introduced with the distal aperture facing cephalad. After clear flow of cerebrospinal fluid, 0.5% ropivacaine 2.5 ml (12.5 mg) was injected over 15-20 s. After spinal injection, an epidural catheter was placed 3 cm into the epidural space and secured. Then the parturients returned immediately to the supine position with 15° left lateral tilt. Oxygen was administered at 4 L/min via nasal catheter.

The parturients retained lateral position for a maximum of 3 min after spinal injection. Cases in which the maximal interval exceeded 3 min due to difficulty in insertion of the epidural catheter were excluded. NBP was recorded every min and changed to 3 min intervals after the second newborn delivery. Hypotension was defined as >25% fall in MAP below the baseline value, and was treated with 80 µg intravenous phenylephrine.

The level of anesthesia was measured every 2-min using loss-of-cold sensation to an alco-

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hol cotton wool. If maximal anesthesia level was below T6 at 15 min after the subarachnoid injection, 4 ml boluses of 2% lidocaine was given via the epidural catheter, and additional 4 ml after 5 min, if necessary. The surgery was started when the sensory block level was above T6. The parturients who received epidural supplement were excluded from analysis.

The oxytocin infusion (20 Units in 500 mL Lactated Ringer's solution) was infused at 10 U/h and carbetocin 100 µg was intravenously injected after clamping the second neonate's umbilical cord.

Data collection

a. Maternal demographics: age, height, weight, body mass index (BMI), fetal gestational age, preoperative hematocrit and conception method.

b. Perioperative data: anesthesia and surgery time, total volume of fluid administration, highest sensory block level, and episodes of hypertension.

c. Hemodynamic data: CO, HR, SV, TPR and MAP were recorded at predefined time points: baseline after 5 min in supine position (T0), at 3 min in the right lateral position (T1), 2 min after spinal anesthesia (T2), 5 and 10 min after spinal anesthesia while supine (T3, T4), at skin incision (T5), immediately after the first newborn delivery (T6), immediately after the second newborn delivery (T7), 3 min after the second newborn delivery (T8), 10 min after the second newborn delivery (T9), and at the end of surgery (T10).

d. Effect of phenylephrine bolus given before delivery on hemodynamics, including CO, HR, SV and MAP.

Statistical analysis

The normality of data distribution was assessed by the Kolmogorov-Smirnov test. Demographic data and baseline measurements are presented as mean ± SD or median (range) for continuous variables and categorical data are presented as number and frequency. We used unpaired t-test, Mann-Whitney test and Fisher's exact test to compare parturient characteristics between parturients who developed hypoten-

sion and those who didn't and Perioperative data. We used logistic regression to examine associations between hypotension and CO, HR, MAP, SVR, SV, age, height, weight, BMI, gestational age, parity, conception, preoperative hematocrit, fluid administration and highest sensory block level. All these parameters were checked multicollinearity. We excluded one of them from logistic regression model if there was a correlation between any pair of parameters. We used a backward stepwise selection to develop the final regression model, selecting the model with Hosmer and Lemeshow test at each step. Analysis of variance with repeated-measures was used to compare the hemodynamic variables from pre-defined time-points to baseline.

Statistical analysis was performed using GraphPad Prism Software (Version 5.0) and using statistical software SPSS 23 software (IBM Corp.). The α level for all analyses was set as $p < 0.05$.

Results

Seventy-two parturients participated in this study. Four cases with poor signal acquisition were excluded after the amniotic fluid and blood entered the contact surface between the NICOM electrode chip and the skin. Three cases were excluded due to difficulty in epidural catheter placement with the catheterization time >3 min after spinal anesthesia. Two cases were excluded because of incomplete block and administration of epidural supplement. A total of 63 cases were included in this study. The anesthesia time was 60.1 ± 10.1 min, and surgery time was 40 (35-47) min.

In this study, 42 cases (66.7%) developed hypotension. Among them, 10 cases developed hypotension after delivery and administration of oxytocin. Therefore, there were 32 cases with spinal anesthesia-induced hypotension before delivery. The age, height, weight, BMI, Gestational age, parity and conception methods were similar in those parturients who developed predelivery hypotension and those who did not after spinal anesthesia. There were no significant differences in fluid administration and the level of the sensory block (**Table 1**).

Table 2 demonstrated the baseline hemodynamic data before spinal anesthesia in parturi-

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Table 1. Characteristics of parturients who developed hypotension and those who did not after spinal anesthesia before delivery. Values are mean \pm SD, median (range), or number

	Normotension (n=31)	Hypotension (n=32)	p value
Age (yr)	32.32 \pm 3.80	31.31 \pm 3.97	0.307
Height (cm)	161.03 \pm 4.45	162.56 \pm 5.75	0.243
Weight (kg)	73.96 \pm 9.15	76.15 \pm 10.72	0.385
BMI (kg/m ²)	28.49 \pm 3.08	28.82 \pm 3.87	0.709
Gestational age (weeks)	36.38 \pm 1.07	36.53 \pm 0.93	0.261
Parity (Nulliparity/Multiparity)	27/4	28/4	1.000
Conception (IVF/non-IVF)	22/9	19/13	0.335
Preoperative hematocrit (%)	34.38 \pm 2.90	34.30 \pm 3.16	0.923
Fluid administration (ml)	874.19 \pm 208.91	906.25 \pm 188.27	0.279
Highest sensory block level	T5 (T4-T6)	T5 (T4-T5)	0.885

IVF-ET: in vitro fertilization-embryo transfer, BMI: body mass index.

Table 2. Baseline hemodynamic data before spinal anesthesia. Values are mean \pm SD

	Normotension (n=31)	Hypotension (n=32)	p value
CO (L/min)	6.35 \pm 0.68	6.08 \pm 0.81	0.163
HR (beats/min)	88.36 \pm 11.23	86.53 \pm 14.54	0.580
MAP (mmHg)	99.10 \pm 8.04	96.81 \pm 8.71	0.284
TPR (dynes sec/m ⁵)	1274.07 \pm 254.20	1313.31 \pm 233.56	0.526
SV (ml)	73.28 \pm 12.84	71.77 \pm 13.37	0.648

CO: cardiac output, HR: heart rate, MAP: mean arterial blood pressure, TPR total peripheral vascular resistance, SV: stroke volume.

Table 3. Results of logistic regression analysis to predict spinal anesthesia-induced hypotension

	OR	95% CI	p value
CO	0.485	0.224-1.053	0.067
Height	1.101	0.984-1.232	0.092

ents who became hypotensive after anesthesia, and those who did not. The HR, MAP, TPR and SV were not different between the groups. There was a tendency to a lower CO for those who developed hypotension ($p=0.163$), but the difference did not reach statistical significance.

Table 3 showed the results of the logistic regression analysis. Logistic regression analysis identified no independent factor to predict spinal anesthesia-induced hypotension.

The hemodynamic changes of parturients with twin pregnancies are shown in **Figure 1**. The baseline values of hemodynamics were as follows: MAP was 98 \pm 8 mmHg, CO was 6.2 \pm 0.7 L/min, HR was 87 \pm 13 beats/min, SV was

73 \pm 13 ml and TPR was 1294 \pm 243 dynes-sec/m⁵. MAP decreased significantly as compared to the baseline value ($p<0.05$) from 2 min after spinal anesthesia to the end of the surgery (**Figure 1A**). As compared to the baseline value, a significant reduction in CO occurred at 3 min after the parturients were in the full right lateral position with knees bent ($p<0.05$). At 5 minutes after spinal anesthesia, CO decreased about 17.5% from the baseline value. CO remained at a lower level than the baseline value until the first newborn delivery ($p<0.05$). After delivery of both newborns, and administration of oxytocin and carbetocin, CO significantly increased. At the end of the surgery, CO gradually returned to the baseline level (**Figure 1B**). HR increased significantly in the early stage after spinal anesthesia ($p<0.05$), while there was no significant change at 10 min and later time points (**Figure 1C**). SV and CO showed similar changes. SV also decreased significantly at 3 min after the parturients were in the full right lateral position with knees bent ($p<0.05$). SV was significantly lower than the baseline value after anesthesia and until newborn delivery. After delivery, SV was significantly elevated ($p<0.05$) (**Figure 1D**).

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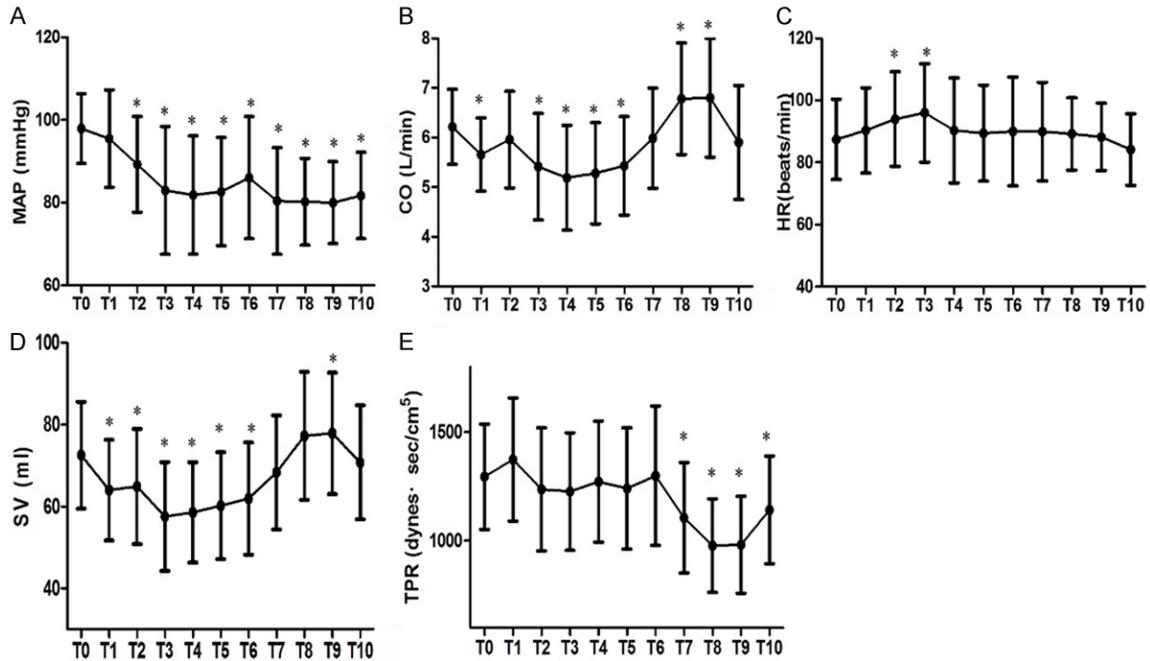


Figure 1. Changes in hemodynamic variables at pre-defined time points during C-section under spinal anesthesia. Data are presented as mean (SD). * $p < 0.05$ as compared to the baseline values. Time points: baseline after 5 min in supine position (T0), at 3 min in the right lateral position (T1), 2 min after spinal anesthesia (T2), 5 and 10 min after spinal anesthesia while supine (T3, T4), at skin incision (T5), immediately after the first newborn delivery (T6), immediately after the second newborn delivery (T7), 3 min after the second newborn delivery (T8), 10 min after the second newborn delivery (T9) and at the end of surgery (T10). (n=63). (A) Mean arterial blood pressure (MAP), (B) Cardiac output (CO), (C) Heart rate (HR), (D) Stroke volume (SV), and (E) Total peripheral vascular resistance (TPR).

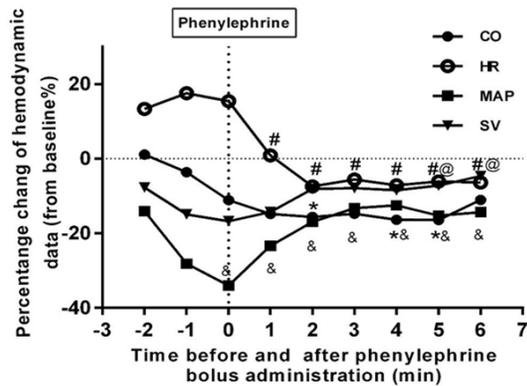


Figure 2. Changes in hemodynamic variables before and after the administration of the first bolus of phenylephrine. Data are presented as the mean percentage change in mean arterial pressure (MAP), cardiac output (CO), heart rate (HR) and stroke volume (SV). *, #, &, @ $p < 0.05$ compared to data at 1 min before the administration of phenylephrine in CO, HR, MAP and SV, respectively (n=32).

TPR decreased after spinal anesthesia but the difference was not significant. TPR decreased significantly after the administration of oxytocin and carbetocin ($p < 0.05$) (Figure 1E).

32 cases with pre-delivery hypotension after spinal anesthesia were enrolled to compare the effects of phenylephrine on hemodynamic profiles. The hemodynamic data at different time points are presented as the percentage of the changes from baseline. As compared to the data at 1 min before the administration of phenylephrine, CO and HR decreased significantly, and MAP increased significantly after phenylephrine administration. SV increased significantly at 5 min and 6 min after phenylephrine administration ($p < 0.05$) (Figure 2).

Discussion

In this study, we demonstrated a marked decrease in MAP, CO and SV without significant TPR change after spinal anesthesia. Half of the parturients with twins experienced hypotension before delivery. The pre-anesthetic CO and other hemodynamic parameters were not predictive for hypotension.

Right-lateral position is a common maternal position during induction of CSEA [16, 17]. When the parturient was placed in the full right

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lateral position with her thighs flexed onto abdomen and chin flexed onto chest, CO and SV decreased significantly at 3 min. In another study, 40 term parturients were randomized to the left lateral decubitus or sitting position for induction of epidural analgesia. Maternal CO measured by a thoracic electrical bioimpedance monitor was significantly lower in left lateral position than in the sitting position [18]. In the lateral position, aortocaval compression may be aggravated by the flexion of the spine and the thighs exerting a backward force on the uterus. Compression of femoral vessel also contributes to reduced venous return. As compared to parturients with single fetus, parturients with twins have a larger and heavier uterus, and flexed lateral position may place more pressure on the uterus to increase aortocaval compression and reduce venous return. Therefore, parturients with twins should not be kept in lateral flex position for a long time while performing SCEA.

After spinal anesthesia, MAP decreased significantly and was maintained at a lower level than the baseline value until fetal delivery. Like MAP, CO decreased significantly at 5 min after spinal anesthesia until delivery. Although TPR also decreased after spinal anesthesia, it was not significant. Similarly, other study showed that total vascular resistance was maintained in parturients with single fetus in postspinal period [19], and Liu and co-workers [13] reported no significant reduction of systemic vascular resistance (SVR) except at 5 min after spinal anesthesia. Since we used phenylephrine to treat hypotension after spinal anesthesia, we could not exclude the effect of phenylephrine on TPR. As $MAP=CO \times TPR$ [7], MAP is proportional to CO when TPR is constant. In this study, the decrease in MAP after spinal anesthesia may be mainly affected by the decrease in CO rather than TPR. HR increased significantly at the early stage and reverted to near baseline level at the late stage in postspinal period, while SV decreased significantly after spinal anesthesia. Because $CO=SV \times HR$ [7], the decrease of SV mainly contributed to the reduction of maternal CO. Generally, SV reflects the amount of venous return (preload) [20]. A review on hemodynamic changes after spinal anesthesia demonstrated that CO typically dropped due to a decrease in venous return [21].

The most frequent response to spinal anesthesia for C-section is a marked decrease in MAP and partial compensation from increased CO in Singleton Pregnancy [7, 14]. Langesaeter and co-workers [14] observed a profound and rapid decrease of SVR with a compensatory increase of CO after spinal anesthesia in parturients with single fetus during C-section. This study did not find significant increases in CO during postspinal period, although the MAP decreased and HR increased significantly.

We concluded that continuous decrease of CO secondary to venous return reduction may be the main cause of hypotension after spinal anesthesia, which is consistent with traditional views on maternal hypotension mechanism [22]. Since parturients with twins have a larger and heavier gravid uterus as compared to parturients with single fetus [23], their CO can be more reduced due to the greater compression of inferior vena cava (IVC) by gravid uterus after spinal anesthesia.

After fetal delivery, MPA was maintained at a lower level than the baseline value, while CO and SV were significantly elevated, TPR decreased significantly, and there was no significant change in HR. Maternal hemodynamic changes after delivery by C-section have many potential mechanisms including removal of aortocaval compression, blood loss, auto transfusion from uterine contraction, vasopressors, uterotonic drugs, etc. [20, 24]. Just after the twins were delivered, CO and SV increased simultaneously, which may be related to removal of IVC compression and increase in venous return.

Echocardiographic measurements showed that uterine contractions increase maternal SV and CO through auto transfusion of 300-500 ml of uterine blood into the maternal circulation at each contraction [20, 25]. Uterotonic drugs are regarded as dominant factors affecting hemodynamics. In our hospital, oxytocin and carbetocin are routinely co-administrated in parturients with twin pregnancies during C-section. Oxytocin and carbetocin have similar hemodynamic side-effects, such as peripheral vasodilation, dose-related decrease in arterial pressure with a compensatory increase in HR and CO [24]. Effect of oxytocin and carbetocin on hemodynamics were compared after cesarean delivery by Rosseland and co-workers [20].

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They observed a decrease in arterial pressure, and increase in HR, SV and CO after intravenous oxytocin or carbetocin. HR increased to a maximum at 90 s after intervention. In another study, the maximum increase of HR occurred within 1 min after the oxytocin bolus [26]. We did not find significant increase in HR, which may be because we only recorded the data at 3 min after administration of oxytocin and carbetocin. In our study, 10 cases developed hypotension and received bolus of phenylephrine after delivery, so phenylephrine also impacted the hemodynamics in the post-delivery period.

Phenylephrine is commonly used as the first-line vasopressor to treat spinal hypotension for C-section. However, its use can cause a dose-related reflexive slowing of maternal HR, and a corresponding reduction in maternal CO [6]. In this study, we also observed that phenylephrine significantly decreased CO of parturients with twins by decreasing the HR. The duration of effect on CO lasted for about 5 minutes. These results were consistent with those of study in parturients with single fetus [13]. In the case of continuous decrease in maternal CO in parturients with twins after spinal anesthesia, the potential harm to fetuses due to further drop in CO caused by phenylephrine remains uncertain.

Hypotension after spinal anesthesia for C-section is common and is a risk factor for adverse maternal and fetal events. An ability to identify those who would suffer from hypotension following spinal anesthesia would give clinicians an opportunity to take preventative measures. The predictive ability of non-invasive haemodynamic parameters for hypotension have been investigated in parturients with single fetus undergoing C-section [27, 28]. Yokose and co-workers [27] demonstrated that pre-anesthetic HR may be a prognostic factor for hypotension associated with spinal anesthesia. In this study, we found a tendency to a lower baseline CO for parturients with twins who developed hypotension, but the difference had not statistical significance. The baseline HR, MAP, SV and TPR were also not predictive for spinal anesthesia-induced hypotension.

The current study had three limitations. First, all participants were healthy women with a gestational age of >35 weeks. In fact, twin gestations have high rates of complications including

preterm delivery and hypertensive disorders. It is unknown whether our results can be extrapolated to twin gestations with comorbid conditions such as preeclampsia or <35 weeks gestation. Second, we did not compare the hemodynamic changes after spinal anesthesia in parturients with single fetus and those with twin pregnancies. This study aimed to describe characteristics of hemodynamic changes in parturients with twin pregnancies at different stages after spinal anesthesia. Comparison of cardiac hemodynamic changes in parturients with twins versus single pregnancy will be studied in the future. Third, We did not compare the cardiac hemodynamics during spinal anesthesia in parturients with twins and those with single fetus. Data regarding CO and blood pressure in parturients with twins during spinal anesthesia are lacking. The aim of this study was to assess the change at different time point after anesthesia and delivery. Therefore, parturients with single fetus were not enrolled in our study.

In summary, our results in parturients with twins showed that maternal CO decreased steadily after spinal anesthesia until delivery, which was mainly related to the reduction of venous return. The decrease of BP presumably resulted from a drop in CO after spinal anesthesia. During the post-delivery period, CO increased significantly, which may be related to the increase in venous return after release of IVC compression and the administration of uterotonic drugs. The pre-anesthetic non-invasive haemodynamic parameters including CO, HR, SV, MAP and TPR were not predictive for spinal anesthesia-induced hypotension.

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Disclosure of conflict of interest

None.

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