Different Hemodynamic Types of Preeclampsia Observed Under Ultrasonic Cardiac Output Monitor (USCOM): A Report of Two Cases

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Abstract: Preeclampsia is a serious and uncommon complication of pregnancy, which affects 5% to 7% of pregnancies and is associated with maternal and fetal adverse outcomes. Moreover, preeclampsia is a polymorphic disease with different hemodynamic types, thus requiring different therapeutic strategies. As a hemodynamic tool, the ultrasonic cardiac output monitor (USCOM) is useful in the detection of preeclampsia as early as the 5th to 16th week of gestation, with abnormal hemodynamic indicating preeclampsia. Although blood pressure (BP) rises in preeclamptic patients, it is not a sensitive indicator for the diagnosis of preeclampsia. However, hemodynamic may change in the 5th to 11th week of gestation. In this paper, the hemodynamic types of two cases were reported using USCOM. The SV, CO, and SVRI values were significantly different in both the cases, indicating the patients had different types of preeclampsia. The hemodynamic parameters were more useful than blood pressure for managing the two cases. Moreover, the mother and fetal were safe after treatment. If preeclampsia had been assessed only from the perspective of BP, the two cases would have been diagnosed as having mild hypertension, and we would not be able to determine the severity. USCOM allowed the identification of preeclampsia-associated hemodynamics and defined individualized therapeutic targets, which cannot be identified by BP alone.

Keywords: Preeclampsia; USCOM; Hemodynamic types

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1. Introduction

Preeclampsia is a serious and polymorphic complication that is unique to pregnancy, and it affects 5% to 7% of pregnancies [1-5]. It is defined as hypertension accompanied by proteinuria or other organ dysfunctions. This syndrome increases the risk of maternal and neonatal morbidity and mortality [6-9]. Effective prevention and treatment are required. One-third of cases presenting with gestational hypertension before the 34th week of gestation will develop preeclampsia [10-13]. Expectant management is usually considered during the perinatal period. The exact cause of preeclampsia is unknown, but there is a consensus that the placenta plays a crucial role in the pathogenesis of preeclampsia.

In normal pregnancy, the placenta undergoes remodeling, resulting in decreased resistance to the uterine spiral arteries and increased blood flow, which is defined by vessel recasting. In preeclampsia, vessel recasting is abnormal. There is no decrease in uterine spiral arteries’ resistance or increase in blood flow. Uterine spiral artery blood flow-perfusion deficiency leads to hypoxia of the placenta, thereby causing a persistent release of inflammatory cytokines into the maternal circulation, which act on vascular...
endothelial cells [14]. There are many types of cytokines, including hypoxia-inducible factor-1 alpha (HIF-1α), transforming growth factor-β3 (TGF-β3), soluble endoglin (sENG), vascular endothelial growth factor (VEGF), placental growth factor (PLGF), and so on [15], which causes various effects, such as vasoconstriction, vasodilation, oxidative stress, and immune inflammatory responses. To the best of our knowledge, no one mechanism is superior to the other in the heterogeneous syndrome of preeclampsia.

Preeclampsia is usually classified as mild, moderate, or severe based on blood pressure (BP), but this classification is relatively limited. Normal BP during pregnancy is maintained by various mechanisms, of which the autonomic nervous system (ANS) plays an important role [16]. According to the simplified form of Poiseuille-Hagen equation (cardiac output (CO) = pressure/resistance), it can be concluded that BP = CO × SVR or (SV × HR) × SVR, as confirmed by Guyton [17]. In the latent stage of circulatory dysfunction, despite small changes have occurred in CO, SV, and SVR, BP remains within the normal range through the compensating effect of the ANS. Moreover, BP also remains within the normal range in the compensating phase of preeclampsia. As the ANS adapts in a stepwise manner, the BP gradually changes from normal to abnormal [16]. Although preeclampsia is diagnosed only when the BP rises, BP is not a sensitive indicator for the diagnosis of preeclampsia [18], as it is impossible to detect anything abnormal in the early stage of pregnancy. Studies have shown that changes in hemodynamic can be detected in the 5th to 11th week of gestation [19,20]. Therefore, it may be beneficial for early detection and diagnosis of preeclampsia through hemodynamic monitoring in the clinic.

The main purpose of hemodynamic monitoring is to measure the oxygen delivery (DO₂) and the oxygen consumption (VO₂). VO₂ is elevated in normal pregnancy, along with an increase in DO₂ to maintain adequate placental perfusion to support fetal growth. This hemodynamic change mainly includes the increase in CO and the decrease in peripheral vascular resistance, especially the resistance of uterine spiral arteries. Traditionally, the hemodynamics of preeclampsia is characterized by higher peripheral vascular resistance and lower CO accompanied by decreased DO₂. The ultrasonic cardiac output monitor (USCOM) is a non-invasive, continuous Doppler monitor that can be used for monitoring CO, basing on a continuous-wave (CW) Doppler principle with a transportable touchscreen monitor and a 2.2 MHz ultrasound probe [21]. In this study, the hemodynamics and BP of two women with singleton pregnancy were monitored using USCOM.

2. Method
This study was approved by the Ethics Committee of Shandong Maternal and Child Health Hospital. The data of preeclamptic patients admitted to the intensive care unit (ICU) in Shandong Maternal and Child Health Hospital were monitored after the patients had signed an informed consent. Hemodynamics were measured using USCOM 1A maternal monitor (USCOM Limited, Sydney, Australia), and BP was measured using a conventional arm device (Omron, Japan). All measurements were taken with the patients in a supine position. The hemodynamic indices and BP measurements were compared and analyzed. The normal hemodynamic values for pregnancy were determined based on those described by Vinayagam, et al. [22]. Grading of maternal hypertension was performed based on NICE guidelines: mild hypertension (140-149/90-99 mmHg), moderate hypertension (150-159/100-109 mmHg), and severe hypertension (> 160/110 mmHg) [23]. The antepartum and postpartum clinical observations and maternal outcomes were then assessed.

3. Findings
3.1. Case 1
The first patient was a 28-year-old woman with a singleton pregnancy. She had no previous history of hypertension. All tests were normal until the 34th week of pregnancy. Although her BP was normal, her
urine protein was positive at the 35th week. At the 38th week, the patient was transferred to Shandong Maternal and Child Health Hospital when her BP rose to 149/90 mmHg. She was then diagnosed with preeclampsia. Hemodynamic monitoring was conducted using USCOM, and the data are shown in Figure 1.

![Figure 1](image)

**Figure 1.** Results of hemodynamic monitoring; A: Aortic USCOM demonstrating a severely elevated SV of 123 ml (normal: > 79 ml), a CO of 3.5 L/min (normal: 7-8 L/min), and a normal SVR of 913 dyne.s/cm² (normal: 800-1000 dyne.s/cm²), whereas DO₂ was above normal (1339 versus 900 ml/m²); B: The input and output of the patient in the ICU; C: NT-pro BNP rose and then fell between March 1 and March 5.

Her hemodynamic type was high CO and low peripheral vascular resistance. BP was the major reason for the increased CO. The N-terminal-pro B-type natriuretic peptide (NT-pro BNP) of the patient was also monitored since a high NT-pro BNP level indicates increased cardiac stress. Besides, CO is also positively correlated with the stroke volume. Based on the above analysis, furosemide was used to promote negative fluid balance after cesarean section. As a result, the baby had a perfect Apgar score and a normal weight at birth, while the mother had to stay in ICU for 5 days of observation.

### 3.2. Case 2

The second patient was a 31-year-old woman with a singleton pregnancy. Her BP was normal until the 19th week of pregnancy (128/94 mmHg). Although her BP was significantly elevated at the 27th week of pregnancy, no antihypertensives were prescribed. Her BP reached 150/95 mmHg at the 26th week, with no observable blood flow in the umbilical artery based on ultrasound examination. The patient was then hospitalized, and antihypertensive therapy was initiated. The USCOM was utilized before and after antihypertensive therapy. The results demonstrated that this case had low CO and high peripheral vascular resistance, which is completely different from that of the first patient. After antihypertensive therapy, her BP dropped to approximately 130/80 mmHg, and the blood flow in the umbilical artery improved. The
pregnancy was terminated by cesarean section at the 29th week, and the baby survived. By comparing the USCOM data before and after antihypertensive therapy, peripheral vascular resistance was found to have decreased significantly after the therapy, and the umbilical cord blood flow also improved (Figure 2). The NT-pro BNP value of 15 pg/ml revealed that the patient’s heart capacity was normal.

At birth, the newborn only weighed one kilogram, which was far below the normal weight, and had a extremely low 1-point and 5-point APGAR scores in the first and fifth minute, respectively. It was not until the tenth minute that the baby’s Apgar score barely reached 7 points. The mother required a day of ICU care after cesarean section.

Figure 2. Peripheral vascular resistance and umbilical cord blood flow after antihypertensive therapy; A: Pre-treatment pulmonary USCOM 1A demonstrating an impaired SV of 59 ml (normal: > 79 ml), a CO of 4.8 L/min (normal: 7-8 L/min), an elevated SVR of 4303 dyne.s/cm² (normal: 800-1000 dyne.s/cm²), and a low DO₂ (594 versus 900 ml/m²); B: Post-treatment pulmonary USCOM 1A demonstrating no significant improvement in CO, SV, or DO₂, but showing a significant decrease in SVR of 1598 dyne.s/cm² (normal: 800-1000 dyne.s/cm²)

3.3. Comparative analysis of the hemodynamics in the two cases
The treatments used were reviewed, and the hemodynamic values were compared between the two cases. Their hemodynamic characteristics, including MAP, CO, SV, SVR, and DO₂, were completely different (Figure 3), thus leading to varied maternal and fetal outcomes. The maternal volume status determined the length and intensity of the mother’s treatment in ICU, whereas DO₂ was found to be closely associated with the birth weight of the newborn. This is consistent with previous studies [24].
Figure 3. Hemodynamic characteristics of the two cases; A: MAP of the first and second patient; B: CO of the first and second patient; C: SV of the first and second patient; D: SVR of the first and second patient; E: DO$_2$ of the first and second patient

4. Discussion

There are different types of preeclampsia. Scholars have classified preeclampsia as early onset and late onset. The former usually occurs before the 34th week, while the latter usually occurs after the 34th week [25,26]. Early onset preeclampsia (before 34 weeks) is commonly associated with increased peripheral vascular resistance, fetal growth restriction (FGR), and adverse maternal factors. In contrast, late onset preeclampsia (after 34 weeks) is often related to decreased peripheral vascular resistance, a low rate of fetal involvement, and more favorable perinatal outcomes [25,26]. DO$_2$ is closely associated with FGR. From the perspective of the fetus, early onset preeclampsia requires more hemodynamic monitoring, especially DO$_2$, whereas hemodynamic monitoring for late onset preeclampsia is extremely important from a maternal perspective. The increased CO in late onset preeclampsia outweighs the reduced vascular resistance, leading to high BP. Therefore, compared to early onset preeclampsia, the volume burden in late onset preeclampsia is extremely high, causing a higher probability of heart failure and pulmonary edema. Late onset preeclampsia requires more rigorous volume management during pregnancy. Diuretics are commonly prescribed in essential hypertension before conception and are used during pregnancy for treating hypertension and cardiac disease [27]. The use of diuretics during pregnancy is controversial. Guidelines for preeclampsia state that diuretics can be used for heart failure. However, it has also been reported that for low-resistance preeclampsia with CO, the rational use of diuretics can effectively reduce CO without increasing peripheral vascular resistance [10,13]. The hemodynamic parameters of USCOM provide useful information to reasonably guide women during their pregnancies.
The hemodynamic characteristics of the two cases were completely different from each other. The first patient had mild hypertension, and her pregnancy was continued after antihypertensive therapy. However, the USCOM results, NT-pro BNP levels, and severe edema suggested that her condition was serious. Due to severe hemodynamic abnormalities, the first patient underwent cesarean section and was monitored in ICU after delivery. Based on the USCOM data, the patient’s hemodynamics were characterized by high CO and low peripheral vascular resistance. This was in contrast to the more common combination of low CO and high peripheral vascular resistance. Heart failure is widely recognized to cause a rise in NT-pro BNP. However, this patient had elevated NT-pro BNP without any signs of heart failure. Her NT-pro BNP level reflected an increase in ventricular wall tension caused by increased volume \[28\]. The treatment approach of maintaining negative fluid balance was implemented \[29-32\]. However, the decline in NT-pro BNP reached a turning point on March 3. Before March 3, there was negative fluid balance although NT-pro BNP levels were rising. The fluid that caused the rise in BNP was from the interstitial space. It has been reported that the main pathophysiology of preeclampsia is the uncontrolled inflammatory response. A large number of inflammatory factors enter the maternal blood circulation and damage the maternal endothelial glycocalyx layer, resulting in capillary leak syndrome \[33\]. The existence of capillary leak syndrome in preeclampsia was confirmed via animal experiments \[34\]. This syndrome leads to increased vascular permeability, further causing numerous vascular components including albumin to enter the interstitial space. After delivery, the levels of inflammatory factors decrease, the glycocalyx layer and vascular permeability return to normal, and the excess interstitial fluid passes through the lymphatic circulation back into the blood. This is the reason that the negative fluid balance in the early postoperative period of this patient was accompanied by a transient increase in NT-pro BNP. High CO-type preeclampsia with increased CO and large amounts of interstitial fluid are risk factors for heart failure. Besides, high CO-type preeclampsia requires a reduction in cardiac preload before delivery and a short-term control of fluid intake after delivery. BP cannot provide the information that we want, but the USCOM can provide precise information to guide treatment. The second patient had preeclampsia with low CO and high peripheral vascular resistance, which might be related to absent umbilical artery blood flow. Although there was no significant improvement in DO\(_2\), the peripheral vascular resistance decreased, and the umbilical artery blood flow was restored after treatment. The decrease of peripheral vascular resistance was found to be associated with blood flow in the umbilical artery. The elevation of BP in the second patient occurred at the 19th week, which was much earlier than the first patient. Previous studies have proven that an abnormal hemodynamic status could be detected by USCOM as early as the 16th week of pregnancy. If this patient had undergone monitoring with USCOM at the 16th week of gestation, advanced treatment could have been initiated. In fact, her BP rose slightly at the 19th week, but the attending doctor did not treat her because the doctor thought that the interference had affected her BP. Her blood pressure and USCOM data both suggested that the patient’s condition was serious when she was brought to the hospital, but treatment was delayed prior to the transfer. Fortunately, after she received treatment and was monitored using USCOM, both the mother and child were safe. All in all, if preeclampsia had been assessed only on the basis of BP, the two cases would have been diagnosed as mild hypertension, and the severity of these cases would have been missed.

5. Limitations
The hemodynamic values of pregnancy in these two cases were far from the normal values, which were reported by Vinayagam, et al. \[22\]. The first patient was diagnosed as preeclampsia with high CO and low peripheral vascular resistance, while the second patient was diagnosed as preeclampsia with low CO and peripheral vascular resistance. To date, many studies have reported the hemodynamic types of preeclampsia, but no statistical analyses have been performed on the hemodynamic parameters of the two types of
preeclampsia. This study preliminarily detected the hemodynamic parameters of different types of preeclampsia using USCOM. This study investigated the use of USCOM in preeclampsia to provide a new diagnostic method for preeclampsia. Further studies in this field are still required in the future.

6. Conclusion
Preeclampsia often results in adverse maternal and fetal outcomes. Therefore, early detection and treatment are required. It is essential to have effective detection methods or biomarkers. Hemodynamic improvement is vital for achieving healthy pregnancy outcomes for both the mother and fetus in pregnancy. According to the analysis of two preeclamptic cases, we found that monitoring using USCOM allows the identification of preeclampsia-associated hemodynamics and defined individualized therapeutic targets, which cannot be identified by BP alone.

Disclosure statement
The author declares no conflict of interest.

References


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