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Cardiac output-guided maternal positioning in pregnancy-- can it improve outcomes?☆

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ABSTRACT

Chronic and recurrent obstruction of the inferior vena cava by the uterus during the second half of pregnancy are theorized to contribute to the causation of preeclampsia, fetal growth restriction, preterm birth, dysfunctional labor and postpartum uterine atony. Such obstruction is hypothesized to be asymptomatic for the mother but can be detected and minimized by non-invasive continuous trending of maternal cardiac output, because positional decreases in cardiac output can serve as a ***warning signal*** of obstruction of venous return. Injury may be caused by 1) decreased cardiac output, 2) increased uterine venous and intervillous pressures and 3) decreased intervillous perfusion. Wide variations in intervillous oxygen tension may be more harmful than low but stable oxygen tension. Clinical examples of asymptomatic but dramatic positional changes in maternal cardiac output in hospitalized patients are shown. Further research should begin with laboring patients, since cardiac output changes dramatically over time and with position during labor.

1. Introduction

Obstruction of the inferior vena cava by the gravid uterus has been understood as a problem in pregnancy since at least 1953 when the term “supine hypotensive syndrome of pregnancy” was introduced [1]. The syndrome is well known and widely understood as having three characteristics: 1) it is an acute and time-limited event, 2) it primarily affects the mother, and 3) it occurs late in pregnancy. But clinicians and researchers have paid much less attention to the possibility that such obstruction might occur much earlier in pregnancy and might insidiously cause fetal, placental and myometrial injury without the mother being aware that anything was wrong.

☆ My clinical research work which inspired this article was performed when I was Clinical Professor of Anesthesiology at the University of California San Diego School of Medicine. The article itself was written at my Permanent Address after my retirement.

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Obstruction of the inferior vena cava has also been generally understood as being a problem because it decreases maternal blood pressure. More sophisticated discussions recognize the fact that the decrease in blood pressure is caused by a decrease in cardiac output, but it is possible that this idea—although completely correct – has focused excessive attention on the arterial side of the maternal and uterine circulations.

As Gyselaers and others have emphasized [2–7], there has been a general neglect of the importance of the venous side of the maternal circulation in the pathogenesis of disorders of pregnancy. Two aspects of the venous circulation which have been neglected are venous return to the heart and uterine venous pressure.

2. Venous return equals cardiac output

In a steady state, cardiac output equals venous return. Fig. 1 shows this principle within an unobstructed maternal circulation. Fig. 2 shows how significant obstruction of the inferior vena cava reduces both venous return from the lower body and maternal cardiac output. Hence, a positional decrease of maternal cardiac output might serve as a ***warning signal*** that positional obstruction of the inferior vena cava has occurred. A reduction in venous return cannot be observed easily by itself, but a reduction in cardiac output can be detected by trending maternal cardiac output, and the fact that cardiac output equals venous return allows us to infer from a reproducible positional decrease in cardiac output that positional obstruction of venous return has occurred. It may be of great practical importance to both research and clinical care that *the **trending** of maternal cardiac output should be sufficient to detect positional obstruction of venous return.* Specifically, ***correct absolute values*** for maternal cardiac output are probably irrelevant for this limited but important purpose. This practical consideration may greatly facilitate both research and clinical care, since it is much easier to reliably identify trends of cardiac output than it is to obtain "correct" absolute values [8].

It must be noted, however, that although the trending of maternal cardiac output appears to be sufficient for the identification of maternal positions which cause positional obstruction of the inferior vena cava, correct absolute values for cardiac output and systemic vascular resistance appear to be essential for other research and clinical purposes, such as the prediction, prevention and treatment of preeclampsia and fetal growth restriction [9–14].

3. Increased uterine venous pressure—an under-recognized danger in pregnancy?

Fig. 2also shows how hemodynamically significant obstruction of the inferior vena cava increases uterine venous and intervillous space pressure– to 25 mm Hg in one case [15], and it is well known that—in general– increased venous pressure can cause severe organ dysfunction. When the organ in question is the uterus, the potential for fetal, placental or myometrial injury seems clear. But except for the introduction of the concept of "sluice flow" in 1973 [16], this possible harmful effect of increased uterine venous pressure on the health of a pregnancy seems to have been neglected.

4. Which is more dangerous in pregnancy—decreased cardiac output or increased uterine venous pressure?

Except for cases of hemorrhage and severe cardiac disease, increased uterine venous pressure may be a greater threat to fetal, placental and myometrial well-being than decreased cardiac output per se. I make this statement because the cardiovascular and autonomic nervous systems function to maintain blood pressure, rather than cardiac output. Transient changes in cardiac output are easy for the healthy cardiovascular and nervous systems to manage. A moderate decrease in cardiac output due to obstruction of the inferior vena cava may be compensated by the sympathetic nervous system with an increase in systemic vascular resistance which

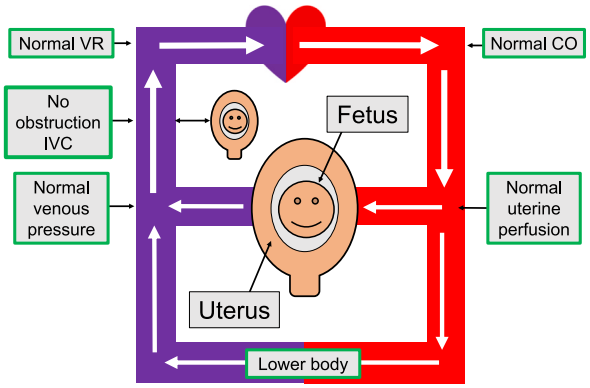


Fig. 1. The non-obstructed uterine circulation in pregnancy
Note that in a steady state, cardiac output always equals venous return—*whether lower body and uterine venous return are obstructed or not.* In this Figure, a) the uterus is not obstructing its own venous return or that of the rest of the lower body, b) maternal cardiac output and blood pressure are adequate, and c) uterine and lower body venous pressures are low.
Abbreviations: CO cardiac output, IVC inferior vena cava, VR venous return.

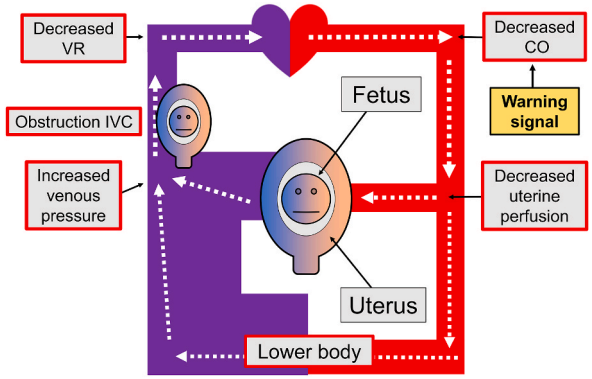


Fig. 2. Obstruction of venous return decreases cardiac output and increases uterine venous pressure
The decrease in cardiac output caused by obstruction of the inferior vena cava means that either maternal blood pressure must decrease or maternal systemic vascular resistance must increase. The increase in systemic vascular resistance would be carried out initially by the sympathetic nervous system and—if it occurs—would be part of the "cardiovascular compensation" referred to in subsequent Figures. *But this successful cardiovascular compensation may or may not occur.* This Figure also shows that uteroplacental perfusion decreases due to increased uterine venous pressure, decreased cardiac output and decreased blood pressure (if it does decrease). *But a very important aspect of this Figure is that* ***the decrease in cardiac output constitutes an actionable warning signal which is available for our use– whether successful cardiovascular compensation for the decreased cardiac output takes place or not.***
Abbreviations: CO cardiac output, IVC inferior vena cava, VR venous return.

maintains an adequate blood pressure, ***but the associated high uterine venous pressure cannot be corrected by cardiovascular and autonomic compensation, and this increased venous pressure may cause severe problems if it persists.***

5. The supine hypotensive syndrome of pregnancy—a failure of cardiovascular compensation for reduced cardiac output

Fig. 3 shows the results of a failure of cardiovascular compensation for a reduction in maternal cardiac output due to obstruction of the inferior vena cava. Positional obstruction of the inferior vena cava decreases venous return and cardiac output, and the cardiovascular and sympathetic nervous systems do not increase systemic vascular resistance sufficiently to maintain an adequate blood pressure. The pregnant woman suffers the "supine hypotensive syndrome of pregnancy" and—in one way or another—changes her position, relieves the obstruction and restores her venous return, cardiac output, blood pressure and sense of well-being.

In this scenario, cardiovascular compensation for positional obstruction of the inferior vena cava has failed. *But the fundamental immediate problem of inferior vena cava obstruction has been solved by a forced position change– after which the cardiac output increases and the uterine venous pressure decreases.* But what happens if cardiovascular compensation for positionally reduced cardiac output

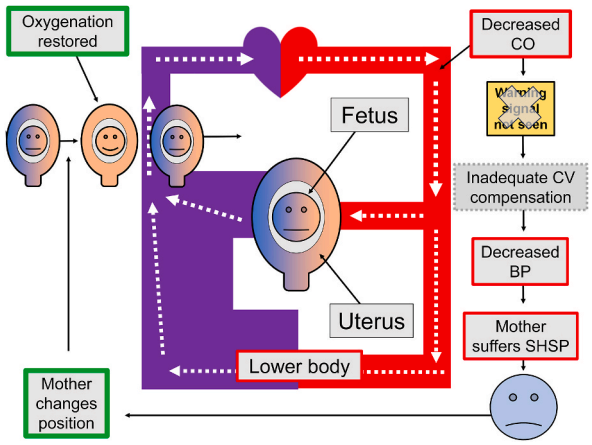


Fig. 3. The supine hypotensive syndrome of pregnancy occurs when cardiovascular compensation for decreased cardiac output is not adequate.
As can be seen in the Figure, the supine hypotensive syndrome of pregnancy is bad for the mother in the short term but may be good for the fetus in the long term. The reason for this is that the symptoms of the syndrome force the mother to change her position until her blood pressure is restored, at which time she will feel better. Her new and more acceptable body position relieves obstruction of the inferior vena cava, which increases the blood pressure and decreases uterine venous pressure—and the fetus is spared possible injury.
Abbreviations: BP blood pressure, CO cardiac output, CV cardiovascular, SHSP supine hypotensive syndrome of pregnancy

succeeds? That may turn out to be a long-term problem for the fetus, placenta and myometrium even though it is a short-term success for the mother, as shown in Fig. 4 and discussed in the next section.

6. Successful cardiovascular compensation for decreased cardiac output—a long-term problem disguised as a success?

The problem with the cardiovascular compensation for reduced cardiac output as shown in Fig. 4 is that it does not decrease the elevated uterine venous pressure. It must be noted that whereas Fig. 3 appears to be based on substantial evidence, Fig. 4 is a theory which requires much further research, although the theory has high biological plausibility. In the theorized scenario of Fig. 4, obstruction of the inferior vena cava has occurred, cardiac output has decreased, and the sympathetic nervous system has increased the systemic vascular resistance sufficiently to maintain an adequate maternal blood pressure. The pregnant woman therefore feels well and feels no need to change her body position. ***But the uterine venous pressure continues to be elevated.*** This review presents the theory that this persistent and only partially compensated hemodynamic condition may lead to insidious fetal, placental and myometrial injury during the second half of pregnancy. ***The purpose of "cardiac output-guided maternal positioning" would be to prevent this "compensated" (but harmful) hemodynamic condition from persisting.***

7. Cardiac output-guided maternal positioning—detecting a warning signal and averting a bad outcome?

Figs. 3 and4 show that the warning signal of decreased cardiac output is present in both the scenario of the highly symptomatic supine hypotensive syndrome of pregnancy (Fig. 3) and in the scenario in which effective cardiovascular compensation results in an asymptomatic mother (Fig. 4). *But in both scenarios, no one detects the warning signal!* Fig. 5 shows how modern technology could detect the warning signal and encourage the mother to change her body position to one which provides more oxygen to her developing baby before any damage is done. This is the theory behind cardiac output-guided maternal positioning.

8. Clinical examples of positional changes in maternal cardiac output

Fig. 6 and Fig. 7 show clinical examples of positional decreases of cardiac output in patients who have been hospitalized preterm for pregnancy complications [5,6]. The maternal positions which cause obstruction of the inferior vena cava vary greatly from patient to patient and the ability of venous collaterals to compensate for inferior vena cava obstruction varies greatly as well [17–19]. Fig. 8 shows how a well-developed lumbar, vertebral venous and azygos collateral system might allow normal venous return, cardiac output and uterine venous pressure even when the inferior vena cava is obstructed.

This variability in the occurrence and consequences of inferior vena cava obstruction makes it impossible to predict with certainty what maternal recumbent positions obstruct blood flow from the lower body and uterus. It is known that a left-tilted maternal position is most likely to allow unobstructed venous return through the uterine veins and inferior vena cava, but this general rule cannot be relied upon either clinically or in research. The best way to ensure unobstructed uterine venous return during pregnancy may be to rely on maximizing the maternal cardiac output at rest, but this possibility remains to be investigated [20–22].

There is evidence that increased patient activity and movement during labor may benefit labor progress [23–25]. It may be that this

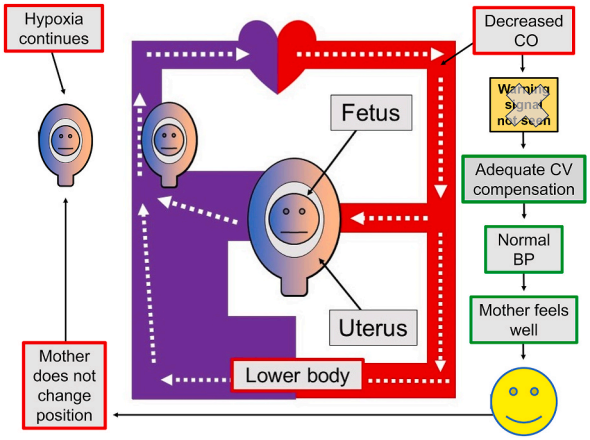


Fig. 4. Successful maternal cardiovascular compensation for decreased cardiac output may subject the fetus to insidious injury from prolonged high uterine venous pressure

At first, this may seem like a paradoxical result—that maternal cardiovascular "compensation" for obstruction of the inferior vena cava may turn out to be harmful for the developing fetus, but that is the theory of this Review. Despite lying in a position which impairs fetal, placental and myometrial oxygenation, the mother feels well and feels no need to change her position. Prolonged poor perfusion and oxygenation may thereby cause permanent injury.

Abbreviations: BP blood pressure, CO cardiac output, CV cardiovascular.

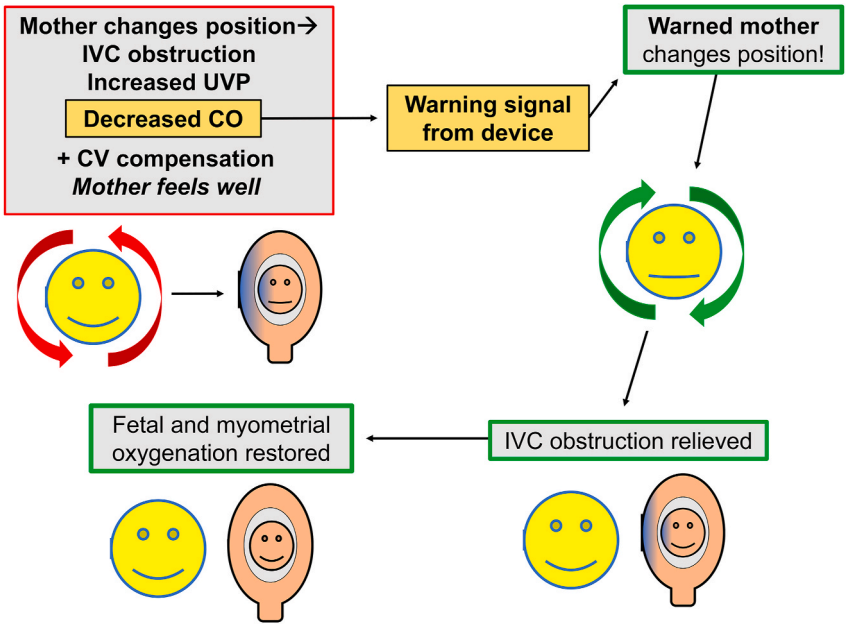


Fig. 5. This Figure shows an alternative to the situation portrayed in Fig. 4. A wearable device which continuously trends maternal cardiac output and the orientation of the mother's body could inform the mother when a new body position reduces her cardiac output. The mother would receive the message and would change her body position so that her cardiac output returns to normal. In this way, optimal perfusion and oxygenation of the fetus, placenta and myometrium would be restored.
Abbreviations: BP blood pressure, CO cardiac output, CV cardiovascular, IVC inferior vena cava, UVP uterine venous pressure.

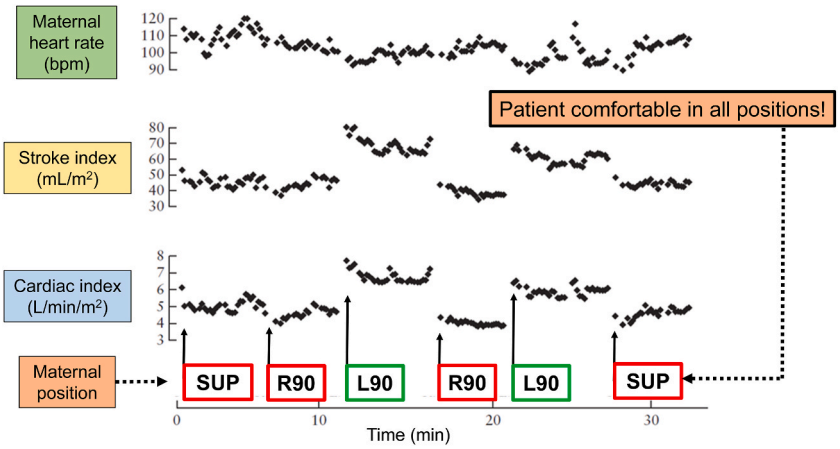


Fig. 6. Cardiac output varies dramatically with maternal position in a 34-year-old woman admitted for preterm labor at 26 + 3/7 weeks estimated gestational age
Maternal cardiac output is lowest in the full right lateral decubitus position and slightly higher in the supine position. The cardiac output is much higher in the full left lateral decubitus position. Could unrecognized hypoxia or wide variation in uteroplacental oxygenation have contributed to premature labor in this patient?
Abbreviations: L/R left/right tilting of patient; SUP supine; "90" refers to degrees of patient tilt (full lateral position)
Figure has been used from Refs. [5,22] with permission.

effect is due to improved uteroplacental perfusion, and for most of human history labor has been associated with discomfort and movement on the part of the parturient. Modern methods of labor analgesia often relieve or remove a great deal of labor pain, but this lack of pain may allow the parturient to maintain body positions in labor which are not optimal for uteroplacental perfusion. Cardiac output-guided maternal positioning in labor might allow parturients to have the "best of both worlds"—adequate labor analgesia combined with optimum uteroplacental perfusion.

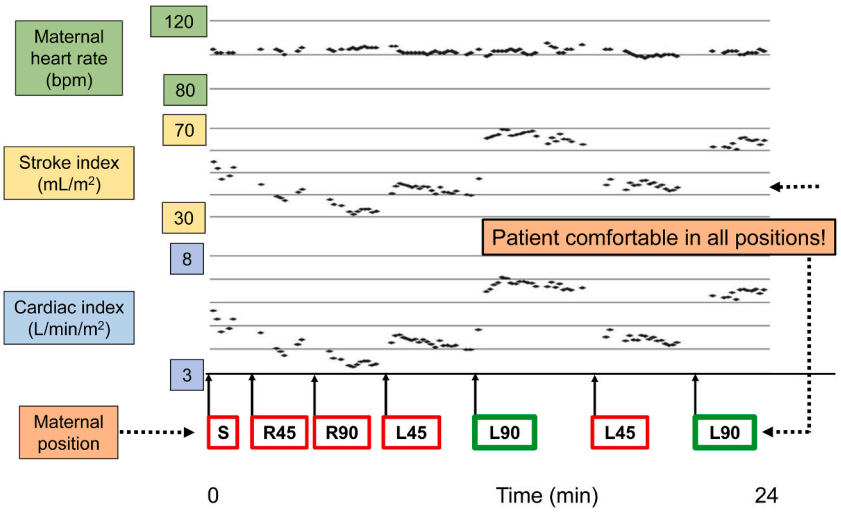


Fig. 7. Cardiac output varies dramatically with maternal position in a woman admitted for fetal growth restriction at 30 weeks estimated gestational age
This patient shows decreased cardiac output in all positions except for the full left lateral decubitus position. Could unrecognized hypoxia or wide variation in uteroplacental oxygenation have contributed to fetal growth restriction in this patient?
Abbreviations: L/R left/right tilting of patient; S supine; "45" or "90" refers to degrees of patient tilt
Figure has been used from Refs. [6,22] with permission.

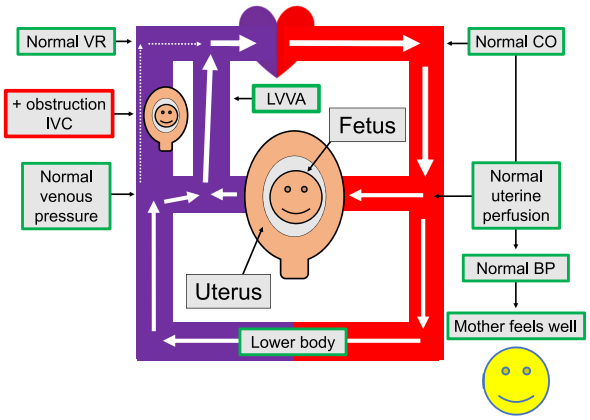


Fig. 8. The lumbar, vertebral venous and azygos collateral system can compensate for inferior vena cava obstruction
Partial or even complete obstruction of the inferior vena cava may not necessarily increase uterine venous pressure to harmful levels because venous collaterals may sufficiently decompress uterine venous pressure to avoid injury. This last statement is a theory, since the importance of the collateral system is not fully understood and varies greatly between patients.
Abbreviations: BP blood pressure, CO cardiac output, IVC inferior vena cava, LVVA lumbar, vertebral venous and azygos collaterals, VR venous return.

9. "Autotransfusion waves" of increased cardiac output during labor

Fig. 9 shows another example of how trending maternal cardiac output may be useful to patient care during labor. This patient hemodynamic record shows the dramatic improvement in maternal hemodynamics produced by a maternal position change after the administration of epidural analgesia [6,7,22]. Turning the patient into full left lateral decubitus position produces two dramatic results: 1) increased baseline cardiac output between uterine contractions and 2) the appearance of increases in cardiac output coinciding with uterine contractions. We have called these periodic increases in cardiac output during labor "autotransfusion waves" since they appear to be caused by autotransfusion in the presence of an unobstructed uterine venous return system.Table 1 (see Appendix A) summarizes the hemodynamic consequences of obstruction of the inferior vena cava in the absence of adequate collateral venous pathways and Fig. 10 summarizes proposed interactions between these factors.

It is important to note in Fig. 10 that impairment of fetal oxygenation is theorized to be due to impairments of both uteroplacental and fetoplacental perfusion. Uteroplacental perfusion decreases because of increased intervillous space pressure and reduced cardiac

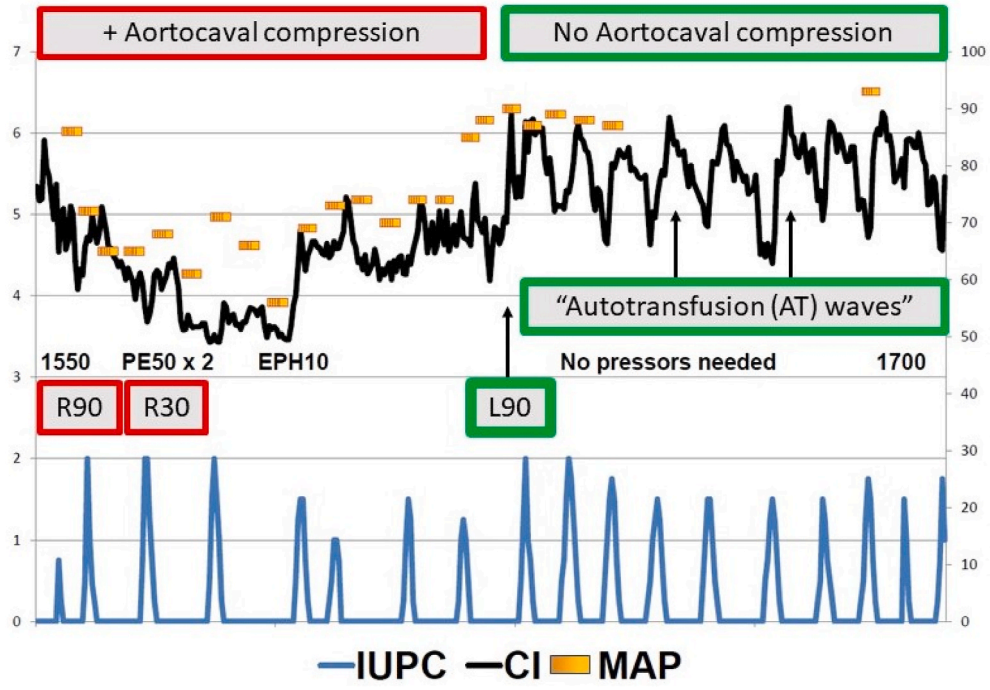


Fig. 9. Dramatic positional changes in maternal cardiac output during labor under epidural analgesia.
During the first half of this 70-min patient hemodynamic record, blood pressure and cardiac output decrease dramatically after epidural administration. During this period the patient is positioned on her right side and vasopressors are required to maintain blood pressure. When the patient is turned into the full left lateral decubitus position ("L90" in the Figure) her average cardiac output increases dramatically and we see "autotransfusion waves"— periodic increases in maternal cardiac output coinciding with uterine contractions [6, 22, 69, 70]. Turning the patient onto her left side appears to relieve obstruction of the inferior vena cava since the baseline cardiac output between contractions increases and autotransfusion waves now accompany each uterine contraction.
Abbreviations: AT autotransfusion; CI cardiac index, liters/min/m^2, left axis; EPH10 ephedrine vasopressor 10 mg intravenous bolus, IUPC intrauterine pressure measured by catheter, arbitrary units; L/R left/right tilting of the patient; MAP mean arterial pressure, mm Hg, right axis; PE50 phenylephrine vasopressor 50 μg intravenous bolus; "30" or "90" refers to degrees of patient tilt; "+" means aortocaval compression is presumed to be present.

output, but the possible explanation for the impairment of fetoplacental perfusion is more complicated since it may occur via two separate mechanisms: increased intervillous pressure and decreased intervillous oxygen tension, as will be explained in the next section.

10. Two possible causes of decreased fetoplacental perfusion: increased intervillous pressure and global hypoxic fetoplacental vasoconstriction

The first possible cause of decreased fetoplacental perfusion is *compression of chorionic villi and their fetal vessels by increased intervillous space pressure* [16,26]. This effect has been termed "sluice flow" [16] and refers to the fact that when organ tissue pressure exceeds downstream venous pressure outside the organ in question, tissue perfusion is limited by tissue pressure and not by downstream venous pressure. The existence of this phenomenon is well-accepted in pulmonary physiology and critical care [27] and can also be understood in the context of "compartment syndromes," when tissue perfusion is curtailed by increased pressure in a tissue compartment.

The second possible cause of decreased fetoplacental perfusion is *hypoxic fetoplacental vasoconstriction throughout the placenta caused by globally decreased intervillous oxygen tension.* As its name suggests, hypoxic fetoplacental vasoconstriction—whether local or generalized– occurs when intervillous hypoxia causes the primary stem villus arteries of the chorionic villi to constrict [28–31].

Hypoxic fetoplacental vasoconstriction is usually thought of as a beneficial response which functions *locally* to match fetoplacental perfusion with uteroplacental perfusion. When one intervillous space and its corresponding chorionic villus become hypoxic due to a lack of maternal perfusion, this localized hypoxia triggers vasoconstriction of the primary stem villus artery of that specific hypoxic chorionic villus. The result is that fetal cardiac output is re-directed away from the hypoxic intervillous space and towards other spaces which contain more oxygen.

But hypoxic fetoplacental vasoconstriction may be profoundly harmful if it restricts the perfusion of all chorionic villi at once, as might occur when globally decreased intervillous perfusion creates generalized intervillous hypoxia. This generalized restriction of all fetoplacental perfusion would deprive the fetus of even the small amount of oxygen which remains within all the hypoxic intervillous

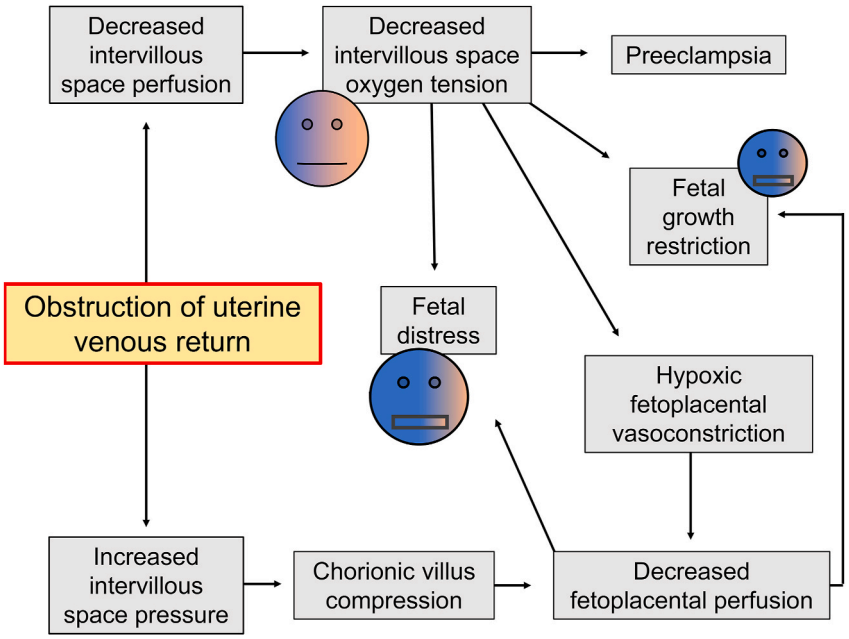


Fig. 10. Obstruction of uterine venous return may exacerbate preeclampsia and fetal growth by multiple interrelated mechanisms involving decreased perfusion and increased pressure.
Obstruction of uterine venous return decreases intervillous perfusion and increases intervillous pressure. Decreased intervillous perfusion may cause intervillous hypoxia sufficient to cause any of the four following conditions: 1) preeclampsia, 2) fetal growth restriction, 3) hypoxic fetoplacental vasoconstriction, or 4) fetal distress. It is also possible that it is not the *absolute level of oxygen tension* which causes fetal, placental and myometrial injury in some cases. Rather, it may be the *wide variation of intervillous oxygen tension* which causes injury, as suggested in Fig. 11.
Obstruction of uterine venous return also increases intervillous space pressure, which may mechanically compress chorionic villi [26], resulting in decreased fetoplacental perfusion, decreased fetal oxygen uptake and increased umbilical artery pulsatility indices. Decreased fetoplacental perfusion may precipitate "fetal distress" in the short term or fetal growth restriction in the long term.

spaces.

11. Hypoxic fetoplacental vasoconstriction may occur slowly

Hypoxic fetoplacental vasoconstriction appears to be a relatively slow process which requires approximately 12–15 min to begin and 30 min or more to develop fully [29]. This gradual response to intervillous space hypoxia may be beneficial by preventing the fetoplacental circulation from over-reacting to transient reductions in intervillous space oxygen tension due to transient obstruction of uterine venous return. It may also explain why some fetuses appear to "tolerate" the supine position for some time—perhaps approximately 23 min [32] – but then "decompensate" and develop "fetal distress." *If we were able to avoid positional intervillous hypoxia in the first place it might avoid some episodes of "fetal distress" due to global activation of hypoxic fetoplacental vasoconstriction.*

12. Nitric oxide donors, hypoxic fetoplacental vasoconstriction, venodilation and the global maternal circulation

As we have already mentioned, hypoxic fetoplacental vasoconstriction may have both a beneficial and a counterproductive aspect—beneficial when it occurs locally, but counterproductive and harmful when it acts simultaneously throughout the entire placenta. Hypoxic fetoplacental vasoconstriction has an analog in the lung– hypoxic *pulmonary* vasoconstriction– which matches pulmonary blood flow with alveolar ventilation, and which serves the function of preventing the perfusion of hypoxic alveoli. Nitric oxide donors such as nitroglycerin interfere with both hypoxic fetoplacental vasoconstriction and hypoxic pulmonary vasoconstriction [33–39], and they also appear to have beneficial effects in preventing or mitigating preeclampsia and fetal growth restriction [11–14]. *It is therefore conceivable that these agents may produce their benefits during pregnancy by preventing the generalized occurrence of hypoxic fetoplacental vasoconstriction when obstruction of uterine venous return globally decreases intervillous oxygen tension.*

Despite this potentially beneficial vasodilatory effect of nitroglycerin within the placenta, the peripheral venodilation which it causes will promote pooling of maternal blood in the capacitance veins of the legs, abdomen and pelvis– and this reduction of venous return will be greatly exacerbated if there is concurrent obstruction of the inferior vena cava. In other words, nitroglycerin might *help* fetal oxygenation by preventing hypoxic fetoplacental vasoconstriction, but it might *hurt* fetal oxygenation by reducing maternal cardiac output.

An alternative explanation for the beneficial effect of nitric oxide donors might be that it dilates collaterals to the inferior vena cava,

thereby promoting an increase in venous return and a reduction in uterine venous pressure. All of these are speculations, of course, but I believe that these considerations support the thesis that further research with nitric oxide donors in pregnancy should be undertaken with full awareness of the hemodynamic complexity of the situation– involving possible peripheral venodilation, inferior vena cava obstruction, increased uterine venous pressure, intervillous hypoxia and hypoxic fetoplacental vasoconstriction.

13. Obstruction of uterine venous return acts within a larger uterine perfusion system

As shown in Fig. 12, obstruction of uterine venous return occurs within a larger four-component uterine perfusion system. The three other components of the system are 1) the heart, 2) the spiral arteries and 3) myometrial tissue pressure. The fact that the four components are in series suggests that deficiencies in the four components may act in an additive or even synergistic manner to impair fetal oxygenation, and a possible implication of this fact is that obstruction of the inferior vena cava may be particularly dangerous in patients who already have problems in the other three components of the system, such as patients with obesity [40–49], short maternal stature [50,51], a large ("overdistended") uterus, diabetes, chronic hypertension, history of preeclampsia or limited cardiac output due to cardiac disease. It should be noted as well that patients with these conditions do appear to be at higher risk for preeclampsia, fetal growth restriction, non-indicated preterm birth, dysfunctional labor and postpartum uterine atony, and if we allow obstruction of uterine venous return to occur in these patients it may increase their risk even further. We now consider specific syndromes to which obstruction of uterine venous return may contribute.

14. Preeclampsia and fetal growth restriction

The dominant current explanation for both preeclampsia and fetal growth restriction is that defective spiral artery remodeling causes chronic intervillous hypoxia by decreasing intervillous perfusion [52–54], but inadequate maternal cardiac output, elevated myometrial tissue pressure and obstruction of uterine venous return can also be expected to decrease intervillous perfusion and thereby cause intervillous hypoxia.

Recurrent obstruction of uterine venous return– alternating with the relief of that obstruction– may also injure chorionic villi because the variation in intervillous oxygen tension which this alternation causes may be more harmful than a low intervillous oxygen tension per se, as shown in Figure 11 [55–59].

15. Preterm labor and birth

The pathogenesis of non-indicated preterm birth is probably multifactorial since the known risk factors are diverse. Obstruction of the inferior vena cava and uterine venous return might contribute to spontaneous preterm birth by four mechanisms: 1) "subclinical" placental abruption due to increased uterine venous pressure [60]; 2) premature production of myometrial inflammation by recurrent cycles of ischemia and reperfusion [22,61,62]; 3) production of fetal hypoxic stress which activates the fetal hypothalamic-pituitary-adrenal axis; and 4) changes in the vaginal microbiome which promote ascending infectious chorioamnionitis

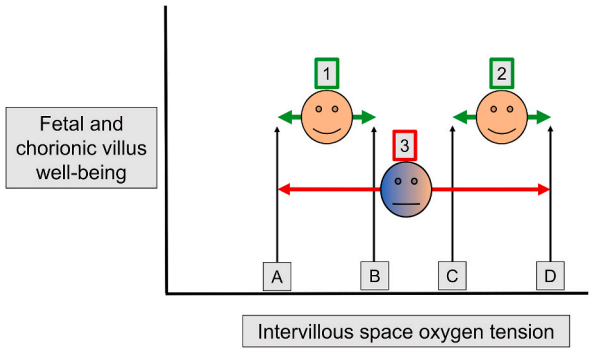


Fig. 11. Wide variations in intervillous oxygen tension may be more injurious to chorionic villi than lower oxygen tensions per se
Lower oxygen tensions per se (within limits) may not injure chorionic villi and the fetus as much as wide *variations* in intervillous space oxygen tension. In other words, the chorionic villi and fetus may be able to adapt to a relatively wide range of oxygen tension ***as long as that specific oxygen tension is held reasonably stable over time.*** This Figure is an attempt to convey that idea schematically: Both Fetus #1 and Fetus #2 are thriving, despite the fact that the average intervillous oxygen tension to which Fetus #1 is exposed is lower than that for Fetus #2. A corollary of this insight is that it might well be misleading to characterize the intervillous space of Fetus #1 as "hypoxic" compared to that of Fetus #2, since the word "hypoxia" often implies an absolute level of oxygenation which is harmful if maintained. The key to the probable good outcomes for both Fetus #1 and Fetus #2 is that the *variation* of intervillous oxygenation to which they are exposed during intrauterine life is minimal (the green double arrows are short). By contrast, Fetus #3 is not doing well because its exposure to oxygen varies widely throughout the day– perhaps as a result of intermittent obstruction of uterine venous return (the double red arrow is long).
Reference [22] used with permission. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

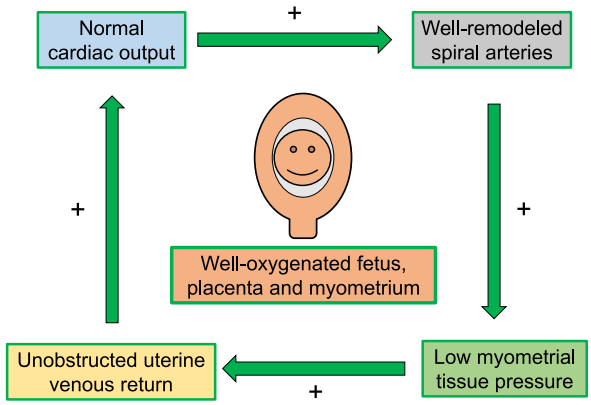


Fig. 12. Obstruction of uterine venous return is one of four potential obstacles to adequate fetal, placental and myometrial oxygenation
Obstruction of uterine venous return acts in series with three other components of the uterine perfusion system: 1) the heart, 2) the spiral arteries, and 3) myometrial tissue pressure. A defect in any one component will impair the results of the entire system and combinations of these barriers may function synergistically to harm the fetus.

[63]. These mechanisms are all speculative, but are biologically plausible, and deserve further investigation.

16. Dysfunctional labor and uterine atony

Myometrial hypoxia and acidosis are known to impair myometrial function [64–67], and obstruction of uterine venous return has been proposed as one possible cause of that hypoxia during labor [68]. When the myometrium does not contract adequately during labor, oxytocin is often administered. The implicit assumption seems to be that if the fetal heart rate is satisfactory, the myometrium is receiving adequate oxygen. But this may not be the case since during labor the contracting myometrium needs more oxygen– but receives less oxygen– than when it is not contracting. The fetus "announces" its hypoxic stress with bradycardia or loss of heart rate variability, but we have no way of knowing whether the myometrium is receiving adequate oxygen during labor, and hypoxic myometrium will not contract on its own or respond to oxytocin. *It may be that what the myometrium needs sometimes in labor is not oxytocin, but more oxygen* [68], and supplying that badly needed oxygen through optimal patient positioning might result in less oxytocin use, fewer cesarean deliveries and less postpartum uterine atony.

Summary

Obstruction of the inferior vena cava by the uterus during the second half of gestation decreases maternal venous return and cardiac output, and non-invasive technology for detecting these decreases is available. Inferior vena cava obstruction (when it obstructs uterine venous return) increases uterine venous pressure, decreases intervillous perfusion and decreases cardiac output, and all of these effects may contribute to the causation of preeclampsia, fetal growth restriction, preterm birth and dysfunctional labor.

Minimizing the time a woman spends in body positions which impair uteroplacental perfusion might prevent or mitigate these complications. This proposed therapy has been termed "cardiac output-guided maternal positioning," and is based on the fact that cardiac output equals venous return in a steady state.

It is important to emphasize that although the reduction in maternal cardiac output serves as an *actionable warning signal* for obstruction of the inferior vena cava, the reduction in cardiac output per se may not be the main cause of injury. Increased uterine venous pressure and decreased intervillous space perfusion may cause much of the injury by decreasing both uteroplacental and fetoplacental perfusion. This review presents a biologically plausible but unproven theory which needs further investigation.

Practice points

- Consider acquiring practical experience with non-invasive cardiac output trending in pregnant women, especially in labor when cardiac output changes are dramatic and highly educational.
- Anesthesiologists can help you get started.
- Increase your and others' awareness of possible injury from positionally increased uterine venous pressure in the second half of pregnancy.

Research agenda

- Use the USCOM Doppler system to confirm positional cardiac output trending results already obtained with impedance cardiography.
- Can impedance cardiography supplement USCOM for this purpose since it is less labor-intensive?

- Increase patient numbers to acquire meaningful series for detailed analysis.
- Start clinical trials of "cardiac output-guided maternal positioning" in labor to reduce "fetal distress," dysfunctional labor, oxytocin requirements and cesarean deliveries.
- Consider pilot studies of hospitalized preterm labor patients, looking for dramatic positional variation in cardiac output

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Conflict of interest

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Appendix A. Supplementary data

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References

[1] Howard BK, Goodson JH, Mengert WF. Supine hypotensive syndrome in late pregnancy. Obstet Gynecol 1953 Apr;1(4):371–7. PMID: 13055188.
[2] Gyselaers W. Origins of abnormal placentation: why maternal veins must not be forgotten. Am J Obstet Gynecol 2023 Jun;228(6):613–21. https://doi.org/10.1016/j.ajog.2022.12.014. Epub 2022 Dec 17. PMID: 36539026.
[3] Gyselaers W, Lees C. Maternal low volume circulation relates to normotensive and preeclamptic fetal growth restriction. Front Med 2022 Jun 9;9:902634. https://doi.org/10.3389/fmed.2022.902634. PMID: 35755049; PMCID: PMC9218216.
[4] Gyselaers W, Thilaganathan B. Preeclampsia: a gestational cardiorenal syndrome. J Physiol. 2019 Sep;597(18):4695–714. https://doi.org/10.1113/JP274893. Epub 2019 Aug 14. PMID: 31343740.
[5] Archer TL, Suresh P, Ballas J. Don't forget aortocaval compression when imaging abdominal veins in pregnant patients. Ultrasound Obstet Gynecol 2011 Oct;38(4):479–80. https://doi.org/10.1002/uog.10065. Erratum in: Ultrasound Obstet Gynecol. 2021 Mar;57(3):516. PMID: 21837755.
[6] Archer TL, Suresh P, Shapiro AE. Cardiac output measurement, by means of electrical velocimetry, may be able to determine optimum maternal position during gestation, labour and caesarean delivery, by preventing vena caval compression and maximising cardiac output and placental perfusion pressure. Anaesth Intensive Care 2011 Mar;39(2):308–11. PMID: 21485686.
[7] Ballas J, Mantell K, Archer TL. Electrical cardiometry demonstrates the hemodynamics of aortocaval compression and autotransfusion during labor. Monterey, California: Poster and oral presentation at Society for Obstetric Anesthesia and Perinatology (SOAP) meeting; May .
[8] Feng SM, Liu J. Electrical velocimetry has limited accuracy and precision and moderate trending ability compared with transthoracic echocardiography for cardiac output measurement during cesarean delivery: a prospective observational study. Medicine (Baltim) 2020 Aug 21;99(34):e21914. https://doi.org/10.1097/MD.0000000000021914. PMID: 32846858; PMCID: PMC7447428.
[9] Valensise H, Farsetti D, Pometti F, Vasapollo B, Novelli GP, Lees C. The cardiac-fetal-placental unit: fetal umbilical vein flow rate is linked to the maternal cardiac profile in fetal growth restriction. Am J Obstet Gynecol 2023 Feb;228(2):222.e1–222.e12. https://doi.org/10.1016/j.ajog.2022.08.004. Epub 2022 Aug 6. PMID: 35944606.
[10] Foo FL, Mahendru AA, Masini G, Fraser A, Cacciatore S, MacIntyre DA, McEniery CM, Wilkinson IB, Bennett PR, Lees CC. Association between prepregnancy cardiovascular function and subsequent preeclampsia or fetal growth restriction. Hypertension 2018 Aug;72(2):442–50. https://doi.org/10.1161/HYPERTENSIONAHA.118.11092. Epub 2018 Jul 2. PMID: 29967040.
[11] Mulder EG, Ghossein-Doha C, Cauffman E, Lopes van Balen VA, Schiffer VMMM, Alers RJ, Oben J, Smits L, van Kuijk SMJ, Spaanderman MEA. Preventing recurrent preeclampsia by tailored treatment of nonphysiologic hemodynamic adjustments to pregnancy. Hypertension 2021 Jun;77(6):2045–53. https://doi.org/10.1161/HYPERTENSIONAHA.120.16502. Epub 2021 Apr 5. PMID: 33813842.
[12] Valensise H, Vasapollo B, Novelli GP, Giorgi G, Verallo P, Galante A, Arduini D. Maternal and fetal hemodynamic effects induced by nitric oxide donors and plasma volume expansion in pregnancies with gestational hypertension complicated by intrauterine growth restriction with absent end-diastolic flow in the umbilical artery. Ultrasound Obstet Gynecol 2008 Jan;31(1):55–64. https://doi.org/10.1002/uog.5234. PMID: 18098350.
[13] Tiralongo GM, Pisani I, Vasapollo B, Khalil A, Thilaganathan B, Valensise H. Effect of a nitric oxide donor on maternal hemodynamics in fetal growth restriction. Ultrasound Obstet Gynecol 2018 Apr;51(4):514–8. https://doi.org/10.1002/uog.17454. PMID: 28295749.
[14] Vasapollo B, Novelli GP, Farsetti D, Pometti F, Frantellizzi R, Maellaro F, Silvestrini M, Pais M, Valensise H. NO donors on top of anti-hypertensive therapy reduces complications in chronic hypertensive pregnancies with hypodynamic circulation. Eur J Obstet Gynecol Reprod Biol 2023 Oct 31;291:219–24. https://doi.org/10.1016/j.ejogrb.2023.10.033. Epub ahead of print. PMID: 37924629.
[15] Scott DB. Inferior vena caval occlusion in late pregnancy and its importance in anaesthesia. Br J Anaesth 1968;40(2):120–8. https://doi.org/10.1093/bja/40.2.120.
[16] Power GG, Longo LD. Sluice flow in placenta: maternal vascular pressure effects on fetal circulation. Am J Physiol 1973 Dec;225(6):1490–6. https://doi.org/10.1152/ajplegacy.1973.225.6.1490. PMID: 4202497.

[17] Fujita N, Higuchi H, Sakuma S, Takagi S, Latif MAHM, Ozaki M. Effect of right-lateral versus left-lateral tilt position on compression of the inferior vena cava in pregnant women determined by magnetic resonance imaging. Anesth Analg 2019 Jun;128(6):1217–22. https://doi.org/10.1213/ANE.0000000000004166. PMID: 31094791.
[18] Humphries A, Stone P, Mirjalili SA. The collateral venous system in late pregnancy: a systematic review of the literature. Clin Anat 2017;30(8):1087–95. https://doi.org/10.1002/ca.22959.
[19] Humphries A, Mirjalili SA, Tarr GP, Thompson JMD, Stone P. Hemodynamic changes in women with symptoms of supine hypotensive syndrome. Acta Obstet Gynecol Scand 2020 May;99(5):631–6. https://doi.org/10.1111/aogs.13789. Epub 2019 Dec 29. PMID: 31856296.
[20] Archer TL. Cardiac output-guided maternal position therapy for preterm labor-it's time for a trial. Acta Obstet Gynecol Scand 2022 Aug;101(8):931–2. https://doi.org/10.1111/aogs.14365. Epub 2022 May 6. PMID: 35514219; PMCID: PMC9564800.
[21] Archer TL. Position therapy in pregnancy: can trending maternal cardiac output put it on a more objective foundation? Acta Obstet Gynecol Scand 2021 Aug; 100(8):1539–40. https://doi.org/10.1111/aogs.14167. Epub 2021 Jun 13. PMID: 34121190.
[22] Archer TL. In: Archer TL, editor. Threats to fetal, placental and myometrial oxygenation: a unified hemodynamic approach. Switzerland: Springer; 2024 (In Press.
[23] Zwelling E. Overcoming the challenges: maternal movement and positioning to facilitate labor progress. MCN Am J Matern/Child Nurs 2010;35(2):72–80. https://doi.org/10.1097/NMC.0b013e3181caeab3.
[24] Souter V, Nethery E, Kopas ML, Wurz H, Sitcov K, Caughey AB. Comparison of midwifery and obstetric care in low-risk hospital births. Obstet Gynecol 2019 Nov;134(5):1056–65. https://doi.org/10.1097/AOG.0000000000003521. PMID: 31599830.
[25] Thuillier C, Roy S, Peyronnet V, Quibel T, Nlandu A, Rozenberg P. Impact of recommended changes in labor management for prevention of the primary cesarean delivery. Am J Obstet Gynecol 2018 Mar;218(3):341.e1–9. https://doi.org/10.1016/j.ajog.2017.12.228. Epub 2017 Dec 29. PMID: 29291413.
[26] Karimu AL, Burton GJ. The effects of maternal vascular pressure on the dimensions of the placental capillaries. Br J Obstet Gynaecol 1994 Jan;101(1):57–63. https://doi.org/10.1111/j.1471-0528.1994.tb13011.x. PMID: 8297870.
[27] West JB. A lifetime of pulmonary gas exchange. Phys Rep 2018 Oct;6(20):e13903. https://doi.org/10.14814/phy2.13903. PMID: 30350350; PMCID: PMC6198137.
[28] Ramasubramanian R, Johnson RF, Downing JW, Minzter BH, Paschall RL. Hypoxemic fetoplacental vasoconstriction: a graduated response to reduced oxygen conditions in the human placenta. Anesth Analg 2006 Aug;103(2):439–42. https://doi.org/10.1213/01.ane.0000222468.76942.d8. PMID: 16861430.
[29] Hampl V, Jakoubek V. Regulation of fetoplacental vascular bed by hypoxia. Physiol Res 2009;58(Suppl 2):S87–94. https://doi.org/10.33549/physiolres.931922. PMID: 20131940.
[30] Howard RB, Hosokawa T, Maguire MH. Hypoxia-induced fetoplacental vasoconstriction in perfused human placental cotyledons. Am J Obstet Gynecol 1987 Nov;157(5):1261–6. https://doi.org/10.1016/s0002-9378(87)80307-1. PMID: 3688085.
[31] Howard RB. Control of human placental blood flow. Med Hypotheses 1987 May;23(1):51–8. https://doi.org/10.1016/0306-9877(87)90180-0. PMID: 3614003.
[32] Archer TL. Neuraxial anesthesia and the supine position cause non-reassuring fetal status. In: Obstetric anesthesia: a case- based and visual approach. first ed. Switzerland: Springer; 2020. https://doi.org/10.1007/978-3-030-26478-9_2. Ch 2, Figure 2.4, p.25. Ed TL Archer.
[33] Byrne BM, Howard RB, Morrow RJ, Whiteley KJ, Adamson SL. Role of the L-arginine nitric oxide pathway in hypoxic fetoplacental vasoconstriction. Placenta 1997 Nov;18(8):627–34. https://doi.org/10.1016/s0143-4004(97)90003-5. PMID: 9364597.
[34] Bednov A, Espinoza J, Betancourt A, Vedernikov Y, Belfort M, Yallampalli C. L-arginine prevents hypoxia-induced vasoconstriction in dual-perfused human placental cotyledons. Placenta 2015 Nov;36(11):1254–9. https://doi.org/10.1016/j.placenta.2015.08.012. Epub 2015 Aug 31. PMID: 26342955.
[35] King RG, Gude NM, Di Iulio JL, Brennecke SP. Regulation of human placental fetal vessel tone: role of nitric oxide. Reprod Fertil Dev 1995;7(6):1407–11. https://doi.org/10.1071/rd9951407. PMID: 8743139.
[36] D'Oliveira M, Sykes MK, Chakrabarti MK, Orchard C, Keslin J. Depression of hypoxic pulmonary vasoconstriction by sodium nitroprusside and nitroglycerine. Br J Anaesth 1981 Jan;53(1):11–8. https://doi.org/10.1093/bja/53.1.11. PMID: 6779843.
[37] Annest SJ, Gottlieb ME, Rhodes GR, Paloski WH, Barie P, Newell JC, Shah DM. Nitroprusside and nitroglycerine in patients with posttraumatic pulmonary failure. J Trauma 1981 Dec;21(12):1029–31. https://doi.org/10.1097/00005373-198112000-00004. PMID: 6798221.
[38] Weygandt GR, Kopman EA, Ludbrook PA. Mechanism of nitroglycerin-induced hypoxemia. Catheter Cardiovasc Diagn 1980;6(4):387–95. https://doi.org/10.1002/ccd.1810060407. PMID: 6781754.
[39] Benoit A, Ducas J, Girling L, Schick U, Prewitt RM. Acute cardiopulmonary effects of nitroglycerin in canine oleic acid pulmonary edema. Anesthesiology 1985 Jun;62(6):754–8. https://doi.org/10.1097/00000542-198506000-00009. PMID: 3923869.
[40] Zhang J, Bricker L, Wray S, Quenby S. Poor uterine contractility in obese women. BJOG 2007 Mar;114(3):343–8. https://doi.org/10.1111/j.1471-0528.2006.01233.x. Epub 2007 Jan 22. PMID: 17261121.
[41] Vince K, Brkić M, Poljičanin T, Matijević R. Prevalence and impact of pre-pregnancy body mass index on pregnancy outcome: a cross-sectional study in Croatia. J Obstet Gynaecol 2021 Jan;41(1):55–9. https://doi.org/10.1080/01443615.2019.1706157. Epub 2020 Feb 6. PMID: 32027189.
[42] DeBolt CA, Sarker M, Trejo FE, Feldman K, Kaplowitz E, Rattner P, Paul K, Jagannatham S, Ferrara L, Doulaveris G, Bernstein PS, Brustman L, Glazer KB, Stone J, Bianco A. Association between obesity and fetal acidosis at scheduled cesarean delivery. Obstet Gynecol 2022 Dec 1;140(6):950–7. https://doi.org/10.1097/AOG.0000000000004968. Epub 2022 Nov 2. PMID: 36357997.
[43] Kominiarek MA, Vanveldhuisen P, Hibbard J, Landy H, Haberman S, Learman L, Wilkins I, Bailit J, Branch W, Burkman R, Gonzalez-Quintero VH, Gregory K, Hatjis C, Hoffman M, Ramirez M, Reddy UM, Troendle J, Zhang J, Consortium on Safe Labor. The maternal body mass index: a strong association with delivery route. Am J Obstet Gynecol 2010 Sep;203(3):264.e1–7. https://doi.org/10.1016/j.ajog.2010.06.024. Epub 2010 Jul 31. PMID: 20673867; PMCID: PMC2933947.
[44] Barau G, Robillard PY, Hulsey TC, Dedecker F, Laffite A, Gérardin P, Kauffmann E. Linear association between maternal pre-pregnancy body mass index and risk of caesarean section in term deliveries. BJOG 2006 Oct;113(10):1173–7. https://doi.org/10.1111/j.1471-0528.2006.01038.x. PMID: 16972860.
[45] Ehrenberg HM, Durnwald CP, Catalano P, Mercer BM. The influence of obesity and diabetes on the risk of cesarean delivery. Am J Obstet Gynecol 2004 Sep;191 (3):969–74. https://doi.org/10.1016/j.ajog.2004.06.057. PMID: 15467574.
[46] Sarkar RK, Cooley SM, Donnelly JC, Walsh T, Collins C, Geary MP. The incidence and impact of increased body mass index on maternal and fetal morbidity in the low-risk primigravid population. J Matern Fetal Neonatal Med 2007 Dec;20(12):879–83. https://doi.org/10.1080/14767050701713090. PMID: 17963180.
[47] Walsh J, Foley M, O'Herlihy C. Dystocia correlates with body mass index in both spontaneous and induced nulliparous labors. J Matern Fetal Neonatal Med 2011 Jun;24(6):817–21. https://doi.org/10.3109/14767058.2010.531313. Epub 2010 Dec 15. PMID: 21158492.
[48] Lynch CM, Sexton DJ, Hession M, Morrison JJ. Obesity and mode of delivery in primigravid and multigravid women. Am J Perinatol 2008 Mar;25(3):163–7. https://doi.org/10.1055/s-2008-1061496. Epub 2008 Feb 25. PMID: 18300188.
[49] Karlsson S, Patavoukas E, Sterpu I, Wallstrom T, Wiberg-Itzel E. Body mass index and labor outcome associated with the level of amniotic fluid lactate. *A cross-sectional study of women with labor dystocia.* J Matern Fetal Neonatal Med 2022 Dec;35(25):8521–9. https://doi.org/10.1080/14767058.2021.1986811. Epub 2021 Oct 25. PMID: 34696678.
[50] Mehraban SS, Pessolano JC, Ponterio JM, et al. The vertical dimension of obesity: adverse pregnancy outcomes in the short obese versus tall obese parturient. J Obstet Gynaecol 2022;42(1):43–8. https://doi.org/10.1080/01443615.2021.1871887.
[51] Leybovitz-Haleluya N, Sheiner E, Wainstock T. Obstetric and perinatal outcome in short-stature patients. Int J Gynaecol Obstet 2023 Jun 2. https://doi.org/10.1002/ijgo.14907. Epub ahead of print. PMID: 37269046.
[52] Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. Am J Obstet Gynecol 2018 Feb;218(2S):S745–61. https://doi.org/10.1016/j.ajog.2017.11.577. PMID: 29422210.
[53] Erez O, Romero R, Jung E, Chaemsaithong P, Bosco M, Suksai M, Gallo DM, Gotsch F. Preeclampsia and eclampsia: the conceptual evolution of a syndrome. Am J Obstet Gynecol 2022 Feb;226(2S):S786–803. https://doi.org/10.1016/j.ajog.2021.12.001. PMID: 35177220; PMCID: PMC8941666.

[54] Redman CWG, Staff AC, Roberts JM. Syncytiotrophoblast stress in preeclampsia: the convergence point for multiple pathways. Am J Obstet Gynecol 2022 Feb; 226(2S):S907–27. https://doi.org/10.1016/j.ajog.2020.09.047. Epub 2021 Feb 2. PMID: 33546842.
[55] Hung TH, Skepper JN, Burton GJ. In vitro ischemia-reperfusion injury in term human placenta as a model for oxidative stress in pathological pregnancies. Am J Pathol 2001 Sep;159(3):1031–43. https://doi.org/10.1016/S0002-9440(10)61778-6. PMID: 11549595; PMCID: PMC1850466.
[56] Cindrova-Davies T, Yung HW, Johns J, Spasic-Boskovic O, Korolchuk S, Jauniaux E, Burton GJ, Charnock-Jones DS. Oxidative stress, gene expression, and protein changes induced in the human placenta during labor. Am J Pathol 2007 Oct;171(4):1168–79. https://doi.org/10.2353/ajpath.2007.070528. Epub 2007 Sep 6. PMID: 17823277; PMCID: PMC1988867.
[57] Burton GJ, Cindrova-Davies T, Yung HW, Jauniaux E. Hypoxia and reproductive health: oxygen and development of the human placenta. Reproduction 2021 Jan;161(1):F53–65. https://doi.org/10.1530/REP-20-0153. PMID: 32438347.
[58] Hung TH, Skepper JN, Charnock-Jones DS, Burton GJ. Hypoxia-reoxygenation: a potent inducer of apoptotic changes in the human placenta and possible etiological factor in preeclampsia. Circ Res 2002 Jun 28;90(12):1274–81. https://doi.org/10.1161/01.res.0000024411.22110.aa. PMID: 12089065.
[59] Thuring A, Laurini R, Marsál K. Uterine venous blood flow in normal and complicated pregnancies: a methodological study. Ultrasound Obstet Gynecol 2010 Apr;35(4):462–7. https://doi.org/10.1002/uog.7572. PMID: 20127752.
[60] Salafia CM, López-Zeno JA, Sherer DM, Whittington SS, Minior VK, Vintzileos AM. Histologic evidence of old intrauterine bleeding is more frequent in prematurity. Am J Obstet Gynecol 1995 Oct;173(4):1065–70. https://doi.org/10.1016/0002-9378(95)91327-0. PMID: 7485294.
[61] Phung J, Wang CA, Reeders J, Chan EC, Riveros C, Zakar T, Paul JW, Pennell CE, Smith R. Preterm labor is a distinct process from term labor following computational analysis of human myometrium. Am J Obstet Gynecol 2022 Jan;226(1):106.e1–106.e16. https://doi.org/10.1016/j.ajog.2021.07.002. Epub 2021 Jul 7. PMID: 34245680.
[62] Phung J, Wang C, Reeders J, Zakar T, Paul JW, Tyagi S, Pennell CE, Smith R. Preterm labor with and without chorioamnionitis is associated with activation of myometrial inflammatory networks: a comprehensive transcriptomic analysis. Am J Obstet Gynecol 2023 Mar;228(3):330.e1–330.e18. https://doi.org/10.1016/j.ajog.2022.08.036. Epub 2022 Aug 21. PMID: 36002050.
[63] Integrative HMP, iHMP) Research Network Consortium. The integrative human microbiome project. Nature 2019 May;569(7758):641–8. https://doi.org/10.1038/s41586-019-1238-8. Epub 2019 May 29. PMID: 31142853; PMCID: PMC6784865.
[64] Quenby S, Pierce SJ, Brigham S, Wray S. Dysfunctional labor and myometrial lactic acidosis. Obstet Gynecol 2004 Apr;103(4):718–23. https://doi.org/10.1097/01.AOG.0000118306.82556.43. Erratum in: Obstet Gynecol. 2004 Jun;103(6):1344. PMID: 15051564.
[65] Wray S, Alruwaili M, Prendergast C. Hypoxia and reproductive health: hypoxia and labour. Reproduction 2021 Jan;161(1):F67–80. https://doi.org/10.1530/REP-20-0327. PMID: 33112773.
[66] Wiberg-Itzel E. Amniotic fluid lactate (AFL): a new predictor of labor outcome in dystocic deliveries. J Matern Fetal Neonatal Med 2022 Dec;35(25):7306–11. https://doi.org/10.1080/14767058.2021.1946790. Epub 2021 Nov 10. PMID: 34758684.
[67] Wiberg-Itzel E, Wray S, Åkerud H. A randomized controlled trial of a new treatment for labor dystocia. J Matern Fetal Neonatal Med 2018 Sep;31(17):2237–44. https://doi.org/10.1080/14767058.2017.1339268. Epub 2017 Jun 22. PMID: 28587493.
[68] Archer TL. Obstructed uterine venous return: a preventable cause of dysfunctional labor? Reproduction 2021 Apr;161(4):V15–7. https://doi.org/10.1530/REP-21-0002. PMID: 33617462.
[69] Archer TL. Transthoracic echocardiography and electrical cardiometry elucidate the hemodynamics of autotransfusion during labor under epidural analgesia. Int J Obstet Anesth 2017 May;31:113–5. https://doi.org/10.1016/j.ijoa.2017.03.010. Epub 2017 Mar 24. PMID: 28676402.
[70] Archer TL. Normal pregnancy, labor and delivery—without epidural analgesia. In: Obstetric anesthesia: a case- based and visual approach. first ed. Switzerland: Springer; 2020. p. 10–3. https://doi.org/10.1007/978-3-030-26478-9_2)(7A. Ch 1, Figures 1.3-1.8.