Hypertensive disorders of pregnancy (HDP) are a major cause of maternal and fetal morbidity and death. To date, the prediction of these disorders and their complications has been based on many clinical characteristics, hemodynamics, and placental indicators (either with Doppler evaluation of uterine artery and/or levels of circulating angiogenic proteins). Early identification of asymptomatic women more likely to develop HDP and other complications would help clinicians in planning appropriate monitoring during pregnancy, potentially treating the condition with preventive strategies before the blood pressure actually increases, and with a possible delay or mitigation of its consequences.

Pregnancy is usually associated with a reduction of uterine artery resistance attributable to a correct trophoblast invasion, inducing a reduction of total vascular resistance (TVR). This process reaches its nadir in the second trimester. When these mechanisms fail, uterine artery resistance and TVR do not fall and HDP and/or other complications of pregnancy, such as fetal growth restriction, may develop.

Many methods have been used in the past for the prediction of HDP. The first one has been the uterine artery Doppler interrogation in the second trimester, and has been introduced since the past 2 decades of the past century. Lately, biochemical and central hemodynamic parameters have been used to refine and improve the classification and the prediction of HDP.

In this issue of the Journal of the American Heart Association, McLaughlin et al propose an interesting approach to the HDP. The authors use different methods, such as clinical characteristics of the mothers, local (uterine artery resistance) and central (TVR) hemodynamics, and placental biochemical indicators, to identify the best predictive approach to the HDP.

The study included 46 normotensive women, of whom 20 were at low risk and 26 were at high risk of developing HDP. The high-risk group was selected through abnormal placental biochemistry, abnormal placental shape or texture, abnormal uterine artery Doppler, and abnormal clinical risk factor score. The authors added to the evaluation a noninvasive hemodynamic assessment performed between 22 and 26 weeks’ gestation through transthoracic bioactance. The statistical approach was interesting for identifying clusters of parameters predicting the different class of risk for HDP.

Interestingly, although no woman was hypertensive at the time of the hemodynamic evaluation in the second trimester, the high-risk group showed low stroke volume (SV) and a high peripheral resistance hemodynamic profile with lower placental growth factor levels.

Strikingly, the higher the risk of developing HDP, the higher is the hemodynamic compromise: in women in the cluster of high and moderate risk of developing HDP, TVR was 45% and 24% higher, respectively, than in the low-risk cluster. One of the strengths of the study was the normotensive profile of women at the time of the hemodynamic evaluation, so that blood pressure was at best in the high normal level. Nevertheless, if we look at mean arterial pressure in the 3 clusters of risk, we can notice that is higher as the risk increases, although the absolute levels of blood pressure suggest that blood pressure measurements are unlikely to predict satisfactorily the hypertensive disorders that have yet to appear. Instead, the markedly elevated TVR was reflected in significantly reduced cardiac output (CO), mainly because of a low SV. These data thus indicate a vascular dysfunction in the preclinical phase of HDP during the second trimester of pregnancy.

The inclusion of maternal hemodynamics in combination with well-established clinical and biochemical parameters...
The question that arises, and that McLaughlin et al. try to discuss, is related to the usefulness of the hemodynamic monitoring of pregnancy for directing a preventive treatment. In normotensive high-risk patients and gestational hypertensive women, elevated TVR early in pregnancy strongly correlates with subsequent severe complications (i.e., preeclampsia, severe hypertension, fetal growth restriction, abruption placentae, and Hemolysis, Elevated Liver enzymes, and Low platelet count [HELLP] syndrome). Some interesting studies have noted that, in established gestational hypertension with high TVR, the intervention based on a hemodynamic approach may be useful for the reduction of severe complications during pregnancy. In particular, a reduction of TVR by >20% in hypertensive patients appears to reduce severe complications; however, other reports have also demonstrated that a hemodynamic approach to the antihypertensive therapy versus standard care may significantly reduce the rate of severe maternal hypertension. On the other hand, some authors pose some caution on the basis of a well-done meta-analysis that evidenced how an excessive reduction of mean blood pressure could be harmful for the baby because of a reduction of placental perfusion. In this meta-analysis, however, no data on CO were taken into account. The standard care and the international guidelines, in fact, only look at the blood pressure levels, without any definitive evidence on the superiority of this approach for maternal and fetal outcomes in pregnancy hypertension. Actually, the way we achieve TVR reduction during gestational hypertension, when this is high, should be the focus of our pharmacological intervention. The reduction of TVR may be achieved in different ways: (1) a reduction of blood pressure alone; (2) an increase in CO (increasing heart rate, SV, or both); or (3) a combination of blood pressure reduction and CO increase. The reduction of blood pressure alone might be ineffective in reducing TVR significantly, in particular when the circulation is underfilled and the high blood pressure becomes essential in maintaining placental perfusion. That is why when reducing blood pressure in a patient with high TVR—low CO gestational hypertensive status, we need to induce an increase of SV-CO to avoid placental underperfusion. In this view, the datum of maternal hemodynamic profile (derived from echocardiography; transthoracic bioimpedance; Doppler noninvasive techniques, such as UltraSonic Cardiac Output Monitor or Non-Invasive Cardiac Output Monitor; or any other technique) appears to be crucial. This information differentiates patients with high blood pressure and high TVR—low SV-CO, who need a reduction of blood pressure associated with an increase in CO-SV, from those with high blood pressure and low or normal TVR (mainly characterized by high SV-CO), for whom our target of treatment might be represented almost exclusively by the blood pressure levels. Therefore, heart rate, SV, and blood pressure (the 3 parameters accounting for the maternal hemodynamic profile included in TVR) should be taken into account together when choosing a pharmacological treatment for pregnant hypertensive patients.
previous early preeclampsia, high TVR in the nonpregnant state precedes the recurrence of preeclampsia during a second pregnancy,"20 this preventive approach might be extended also to this group of women.

In summary, McLaughlin et al13 provide a stratification of patients in whom maternal hemodynamic characteristics gain a double role:

1. A role in the identification of patients who will subsequently develop HDP, next to placental growth factor and endoglin.

2. A role in a possible “preventive approach” of the HDP in which the pathological condition is not represented by the high blood pressure, but by the altered hemodynamic variable that precedes the elevation of blood pressure and its potentially dramatic consequences.

Hemodynamics can easily be detected with noninvasive methods. This tool may become, in the future, essential for the stratification and, possibly, the preventive treatment of HDP. Is this dream coming true? Much work clearly remains to be done.

Disclosures
None.

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