# Outcomes of Pregnancies at Risk for Hypertensive Complications Managed Using Impedance Cardiography

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## ABSTRACT

We assessed the effect of antihypertensive therapy guided by impedance cardiography on maternal and fetal outcomes in pregnancies at risk for hypertensive complications. We performed a retrospective review of the outcomes of 318 singleton pregnancies with chronic hypertension or prior preterm delivery due to preeclampsia whose antihypertensive therapy was guided by impedance cardiography. Hemodynamic subsets were compared using analysis of variance. Impedance cardiography was used to evaluate cardiac output and total peripheral resistance starting at less than 24 weeks. All patients received atenolol; 24% required additional therapy with a vasodilator. The mean gestational age at delivery was $37 \pm 2$ weeks. Preeclampsia developed in 14%. The incidence of birth weight less than the 10th percentile was 10%. There were no perinatal deaths, and 75% of the infants spent $<3$ days in the hospital. Hyperdynamic patients had less preeclampsia, less severe preeclampsia, fewer deliveries $<34$ weeks, and fewer neonatal intensive care unit days compared with those requiring a vasodilator. Antihypertensive therapy guided by hemodynamic information results in pregnancies delivering at or near term, little preeclampsia, and no increase in growth restriction. Hyperdynamic patients have better outcomes than patients with increased total peripheral resistance.

**KEYWORDS:** Hypertension, preeclampsia, hemodynamics, impedance cardiography, atenolol

Hypertensive disorders in pregnancy are a significant cause of fetal and maternal morbidity in this country, with chronic hypertension affecting ~5% of gravidas and preeclampsia another 5%.[1,2] Twenty-five percent of chronically hypertensive gravidas will develop superimposed preeclampsia with its attendant risks of abruptio placentae, growth restriction, and maternal complications of severe disease.[3] In view of the risks and severe consequences due to superimposed preeclampsia, efforts to reduce its development are extremely important.

Eighteen years ago a hypothesis was advanced that a "hyperdynamic" state, characterized by elevated cardiac output, was involved in the pathogenesis of preeclampsia.[4] This was followed by a longitudinal study that demonstrated that, indeed, the cardiac output was elevated early in gestations that ultimately developed preeclampsia.[5] Following a study indicating that the hemodynamics could be appropriately pharmacologically modified,[6] a randomized trial of therapy (β blockers) aimed at decreasing the cardiac output in patients at risk

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demonstrated a statistically significant decrease in the incidence of preeclampsia.[7] A retrospective review of the effect of implementing a program of hemodynamic assessment and treatment in women at risk for preeclampsia demonstrated a remarkable decrease in the incidence of preeclampsia, severe disease, and premature delivery at the cost of a modest increase in the rate of growth restriction.[8] These previous findings indicate that a program of external, noninvasive maternal hemodynamic-guided normalization early in gestation possibly could be shown to reduce the later development of superimposed preeclampsia.

A Doppler ultrasound technique using a dedicated machine was used for hemodynamic assessment in earlier studies. Elevated cardiac output detected early in pregnancies via Doppler echocardiography in 1999 was shown to have a positive predictive value for the later development of preeclampsia.[9] More recently, a study using Doppler echocardiography to assess additional hemodynamic parameters demonstrated that first-trimester patients who would develop preeclampsia without fetal growth restriction had an elevated cardiac output, and those who developed preeclampsia with growth restriction had an elevated total peripheral resistance.[10] This difference in hemodynamics early in pregnancy between those patients who develop preeclampsia with and without growth restriction was confirmed in a recent study that used a completely different method (Modelflow method) of noninvasively determining cardiac output.[11]

Five years ago, we began a program of using impedance cardiography (BioZ, Cardiodynamics, San Diego, CA) for hemodynamic assessment to guide therapy of hypertensive pregnancies. The purpose of this report is to review the success of optimizing hypertensive management guided by hemodynamic assessment using impedance cardiography on maternal and fetal outcomes.

## MATERIALS AND METHODS

A retrospective review of the database maintained by the Maternal Hypertension Center was conducted following approval by the Investigational Review Board of Cabell-Huntington Hospital/Joan C. Edwards School of Medicine. Informed consent was waived by the Institutional Review Board as standard treatment was provided, and results were tracked by record review. Patients had been referred for a history of chronic hypertension, or a past history of premature severe preeclampsia. Three hundred twenty patients with singleton pregnancies and initial evaluation at less than 24 weeks' gestational age were identified over a 5-year period. One hundred sixty-eight patients (53%) had chronic hypertension only (hypertension prior to pregnancy or at less than 20 weeks); 72 (23%) had a prior preterm delivery (<34 weeks) due to preeclampsia; the remainder had both. Two pregnancies were excluded from analysis due to delivery at a nonviable gestational age due to incompetent cervix or preterm labor. Previous antihypertensive medications had been stopped approximately 1 week prior to testing on all patients who records were reviewed, with no adverse effects noted.

Hemodynamic assessment was performed using impedance cardiography,[12] a noninvasive diagnostic tool that detects and measures changes in electrical impedance in the thorax proportional to blood flow from the aorta. Impedance cardiography was conducted with the patient seated with two pairs of electrodes placed on each side of the neck and trunk (Fig. 1). Blood pressure was assessed in the right arm by the integrated automated cuff. Mean arterial pressure and cardiac output were measured and total peripheral resistance calculated. Measurements were obtained on all patients in the seated position per clinic protocol. Hemodynamics were characterized as hyperdynamic if the cardiac output was greater than 7.4 L/min and mixed if the mean arterial pressure was greater than 100 mm Hg and the cardiac output was less than 7.4 L/min, or normal. Hyperdynamic patients were treated with atenolol at dose ranges of 25 to 200 mg per day, with doses guided by serial monthly reassessments of cardiac hemodynamics. Patients with mixed hemodynamics were treated with atenolol and the vasodilator nifedipine XL[Q1] at dose ranges of 30 to 120 mg per day. Dosages were again guided by serial assessments. Diuretics were utilized in patients with elevated thoracic fluid content and those with elevated cardiac output on maximal doses of β blockers. Goals of therapy included an

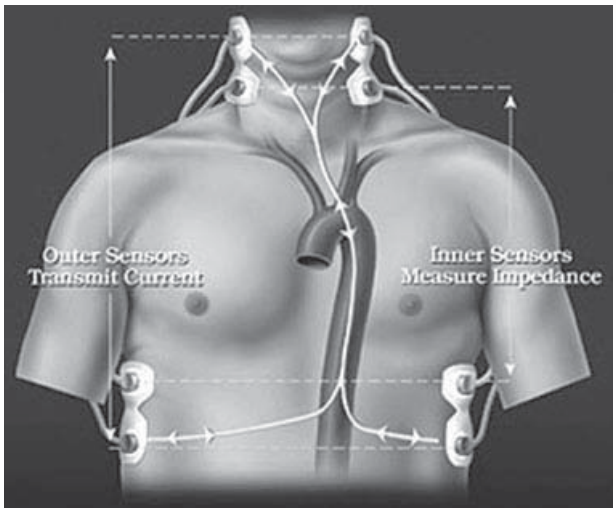


**Figure 1** Hemodynamic monitoring with impedance cardiography. A low-level alternating current is then used to detect and measure changes in electrical impedance of the thorax, which are proportional to blood flow. (Used with permission from Cardiodynamics, San Diego, CA[Q2].)

optimal mean arterial pressure and optimal cardiac output. All patients were otherwise managed by their referring physicians. Monthly sonograms for fetal growth were obtained with twice-weekly fetal assessment with nonstress tests and biophysical profiles begun at 32 weeks. Decisions for delivery were made by the referring physicians. Compliance with medications and follow-up visits appeared to be improved anecdotally as patients were able to view their hemodynamic data in real time.

Maternal and fetal outcomes were documented at the time of the postpartum hemodynamic evaluation, including preeclampsia (systolic blood pressure [SBP] >140, diastolic blood pressure [DBP] >90 and greater than 300 mg of protein in a 24-hour urine collection or 2+ or greater on a urine dipstick[13]), severe preeclampsia (SBP >160; DBP >110; fetal compromise; hemolytic anemia, elevated liver enzymes, and low platelet count [HELLP syndrome]; neurological symptoms; pulmonary edema; proteinuria; and/or oliguria), birth weight, Apgar scores, and number of days in the neonatal intensive care unit. Birth weight percentiles were calculated by linear interpolation from the results published by Doubilet et al.[14]

Comparisons between the hyperdynamic and mixed hemodynamic subgroups were made using one-way analysis of variance for continuous variables and chi-square for categorical variables.

## RESULTS

The maternal characteristics at the time of initial evaluation are shown in Table 1. For any given mean arterial pressure, there were dramatic differences in cardiac output and total peripheral resistance. The hyperdynamic subset of patients had significantly higher body surface areas and higher cardiac outputs and lower total peripheral resistances ($p < 0.0001$) than the mixed hemodynamic subgroup. Of the 22 patients with severe hypertension (SBP >160 or DBP >110), 14 (63%) were hyperdynamic and the cardiac output ranged from 4.7 to 12.2 L/min. Outcome data are presented in Table 2. Overall, only 8% of patients delivered at less than 34 weeks. The median number of days an infant spent in the nursery was the same as the mother's hospitalization (3 days). Figure 2 shows the distribution of birth weight percentiles. Ten percent were less than the 10th percentile. Twelve patients developed severe preeclampsia (4%), delivering at a mean gestational age of $31.7 \pm 3.9$ weeks. Of these 12, 1 (8%) developed HELLP syndrome, two fetuses (17%) showed sonographic evidence of compromise, and 10 (83%) had accelerated hypertension. There were no perinatal deaths.

**Table 1 Maternal Characteristics on Initial Evaluation**

| Characteristic | Hyperdynamic ($n = 242$) | Mixed Hemodynamics ($n = 76$) |
|---|---|---|
| Gravidity | $2.3 \pm 1.4$ | $2.3 \pm 1.2$ |
| Weight (kg) | $108 \pm 24$ | $83 \pm 21$ |
| Initial gestational age (wk) | $16 \pm 4$ | $15 \pm 4$ |
| Mean arterial pressure (mm Hg) | $98 \pm 11$ | $108 \pm 10$ |
| Cardiac output (L/min) | $8.1 \pm 1.3$ | $6.1 \pm 1.1$ |
| Total peripheral resistance (dyne · s · $cm^{-5}$) | $935 \pm 183$ | $1378 \pm 344$ |

The average gestational age at delivery was slightly lower in the mixed hemodynamic group, and the frequency of delivery at less than 34 weeks was higher. This is possibly due to the increased risk of preeclampsia (10% versus 27%) and contributed to the lower average birth weight percentile and more days in the hospital. In the hyperdynamic group, the average (and median) gestational age at delivery was 37 weeks, with only 10% developing preeclampsia.

## DISCUSSION

The efficacy of managing hypertension by using noninvasive hemodynamic assessment in nonpregnant patients has previously been reported.[15] Measurement of hemodynamic parameters by impedance cardiography

**Table 2 Maternal and Fetal Outcomes**

| Characteristic | Hyperdynamic ($n = 242$) | Mixed Hemodynamics ($n = 76$) | $p$ Value |
|---|---|---|---|
| Gestational age (wk) | $36.8 \pm 2.1$ | $35.6 \pm 2.6$ | 0.001 |
| Birth weight percentile | $51.8 \pm 27$ | $43.6 \pm 26$ | 0.02 |
| Preeclampsia (all) | 24 (10%) | 20 (27%) | 0.0002 |
| Severe preeclampsia | 6 (2.5%) | 7 (9.2%) | 0.002 |
| Delivery <34 wk | 14 (5.7%) | 11 (14.5%) | 0.02 |
| Apgar at 1 min | $7.9 \pm 1.4$ | $7.5 \pm 1.8$ | NS |
| Apgar at 5 min | $8.7 \pm 1.2$ | $8.6 \pm 1.2$ | NS |
| NICU days | $2.9 \pm 0.5$ | $6.6 \pm 0.9$ | 0.002 |

NICU, neonatal intensive care unit; NS, not significant.

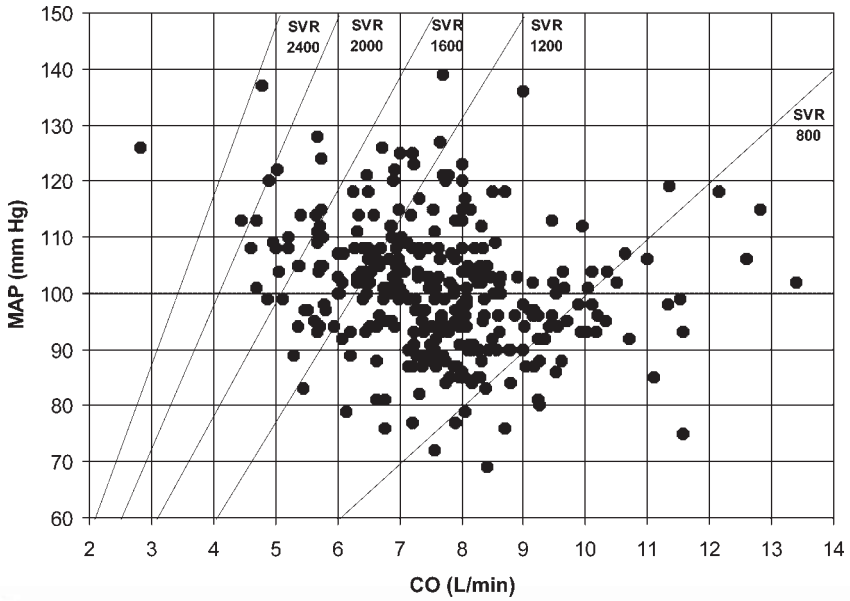


**Figure 2** Heterogeneity of hemodynamics in 318 hypertensive gravidas less than 24 weeks' gestation.

confirms the heterogeneous nature of hypertension in the first half of pregnancy as previously published.[6,8–11] As shown in Fig. 2, a mean arterial pressure of 100 mm Hg was associated with a wide range in cardiac output, from 4.5 to 11.5 L/min. This heterogeneity may be responsible for the variable and generally disappointing results of previously published randomized trials of antihypertensive monotherapy in pregnancy.[16] A vasodilator would be an inappropriate medication for a patient with a cardiac output greater than 10 L/min, as would a β blocker for a patient with a cardiac output of 4 L/min. It is precisely this variability that may account for the incidence of growth restriction associated with the use of atenolol. A quarter of the patients in this study were vasoconstricted enough to require an additional medication. This is the group that very well may end up

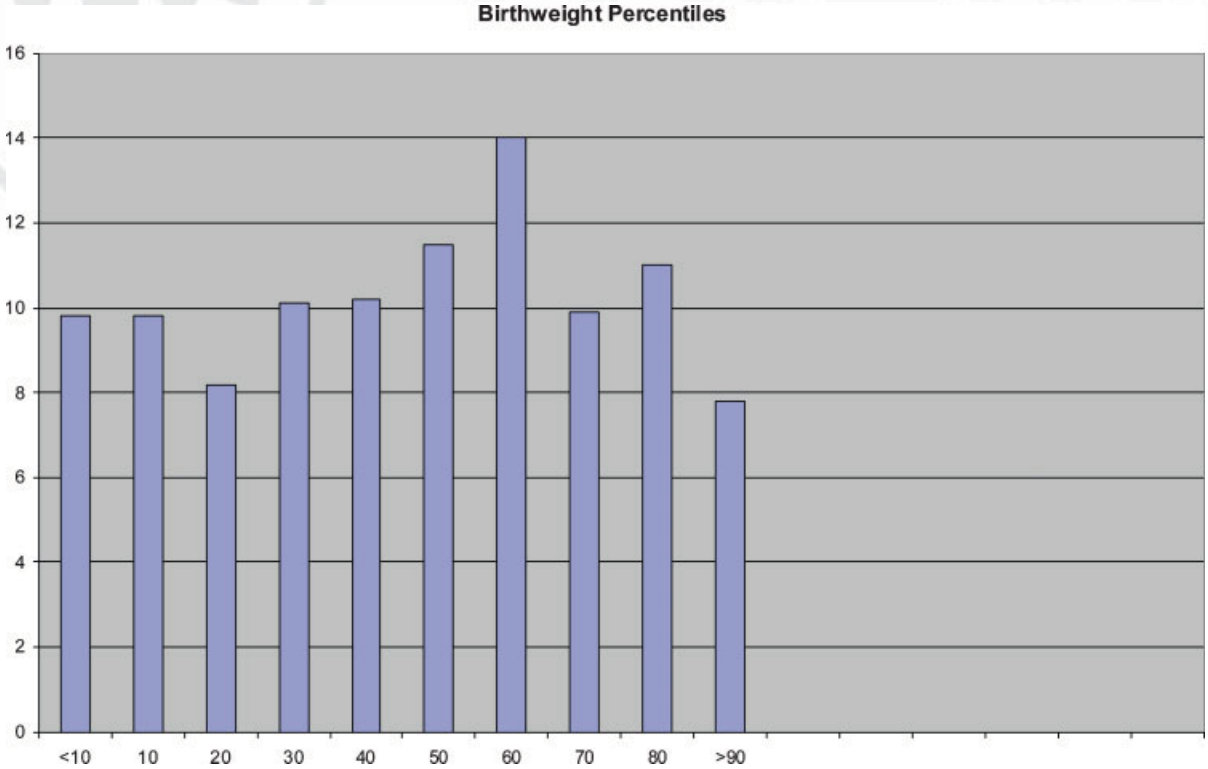


**Figure 3** Distribution of birth weight percentiles[Q3].

Q3

growth restricted if treatment for blood pressure is limited to increasing doses of atenolol, as previously described.[17] Findings of this study indicate that guiding pharmacological therapy by measurement of the cardiac output results in no increase in growth restriction. The average gestational age at delivery was slightly lower in the mixed hemodynamic group, and the frequency of delivery at less than 34 weeks was higher. This is possibly due to the increased risk of preeclampsia (10% versus 27%), which contributes to the lower average birth weight percentile and more days in the hospital.

The published recurrence risk for preeclampsia ranges from 20 to 40% in patients with previous severe preeclampsia, chronic hypertension, or both.[3,16] Early, targeted antihypertensive therapy appears to have substantially reduced this risk to 14%. Most infants (92%) were delivered after 34 weeks with a median gestational age of 37 weeks and minimal neonatal intensive care unit stays. In addition, perinatal mortality seems to have been substantially reduced from published reports.[3,16] In summary, impedance cardiography is a safe, rapid, noninvasive method of providing hemodynamic data in the outpatient setting.

## DISCLOSURES

Dr. Chaffin has a 9.7% indirect equity interest in a company Medical Information Systems Technology, LLC. MIST was formed to market the database program that stores and reports the information from the BioZ impedance cardiography machine.

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