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CLINICAL ARTICLE

Invasive diagnostic procedures and risk of hypertensive disorders in pregnancy

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ABSTRACT

Objective: To determine whether the risk of hypertensive complications differs among low-risk women who undergo prenatal diagnosis via chorionic villus sampling (CVS) and amniocentesis. *Methods:* In a retrospective study, data were analyzed from women who underwent prenatal diagnosis by CVS or amniocentesis at Alexandra Maternity Hospital, Athens, Greece, between 1998 and 2011. All women had either transabdominal CVS at 10–13 weeks of pregnancy with a 20-gauge needle, or amniocentesis at 17–21 weeks with a 22-gauge needle, both under direct ultrasound guidance. Only women who had cytogenetically normal pregnancies and delivered at the study hospital were included. The main outcome measure was the development of hypertensive complications. *Results:* Overall, 3243 women who underwent CVS and 6875 woman who underwent amniocentesis met the inclusion criteria, and their outcomes were analyzed. In total, 237 women (2.3%) developed hypertensive disorders during their pregnancy. The incidence of pre-eclampsia (2.4% vs 0.8%) and total hypertensive disorders (3.8% vs 1.7%) was significantly higher ($P < 0.001$) in the CVS group than in the amniocentesis group. *Conclusion:* Women who underwent CVS had a significantly higher risk of developing hypertensive disorders in comparison to those who underwent amniocentesis. This finding warrants further investigation via a well-designed prospective randomized trial.

1. Introduction

Most pregnant women have a screening test for chromosomal defects in the first trimester via the measurement of nuchal translucency and biochemical markers. For most women who have abnormal results, the diagnostic procedure of choice is chorionic villus sampling (CVS). With the widespread use of first-trimester aneuploidy screening, the demand for CVS is increasing in everyday practice. The diagnostic accuracy of the method is approximately 99%, which is similar to that of amniocentesis. However, CVS provides the opportunity for a safer termination of pregnancy and, at the same time, it values the patient's privacy because the results are available in the first trimester. Although there is extensive literature on the risk of pregnancy loss after an invasive diagnostic test [1,2], data on other complications arising from these procedures are scarce. Such information is extremely important for patients who seek prenatal diagnosis.

A few studies have shown a relationship between CVS and increased risk of hypertensive disorders in pregnancy [3–5]. The underlying pathophysiology of pre-eclampsia is not completely understood. Among the plausible theories, a dysfunction of the placenta is thought to be responsible for the occurrence of the complication. Impaired placental formation at the beginning of pregnancy is thought to lead to hypertensive disorders later in the third trimester. Studies supporting the relationship of CVS to hypertensive complications are based on the assumption that focal placental disruption during the procedure increases the risk of pre-eclampsia.

In 2005, Silver et al. [3] reported that CVS performed in the late first trimester was associated with a higher rate of hypertensive disorders of pregnancy compared with early amniocentesis. The same association was also observed among nulliparous women who underwent CVS [4]. Moreover, it was reported that women who went on to develop pre-eclampsia after CVS had higher levels of maternal serum α-feto protein (MSAFP) and pregnancy-associated placental protein-A (PAPP-A) after the procedure compared with those who did not develop this complication [5]. However, subsequent studies failed to find any association between CVS and increased risk of hypertensive disorders of pregnancy [6–9].

The various methodologies used in the studies—mainly the different control groups and the failure to adjust for several maternal characteristics—is likely to have led to the conflicting results. Until a prospective well-designed trial aimed at investigating the potential relationship between CVS and hypertensive disorders gives a definitive answer to this question, it remains useful to report single-center experience. Therefore, the aim of the present study was to examine whether

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CVS entails a different risk of hypertensive complications compared with second-trimester genetic amniocentesis among low-risk women attending a tertiary care center for prenatal diagnosis.

2. Materials and methods

In a retrospective study, data were reviewed from pregnant women who underwent CVS or amniocentesis at the Division of Feto-Maternal Medicine at Alexandra Hospital, Athens University, in Athens, Greece, between January 1, 1998, and December 31, 2011. Approval for the study was obtained from the ethics committee of the hospital, and all women gave signed consent before undergoing the procedure.

All study women had either transabdominal CVS at 10–13 weeks of gestation with a 20-gauge needle, or an amniocentesis at 17–21 weeks with a 22-gauge needle. Each procedure was performed under ultrasonographic visualization.

Maternal demographics, past obstetric history, past medical history, indication for the procedure, ultrasonographic findings, placenta site, number of attempts, needle insertion, and pregnancy outcome were recorded in the hospital's computerized database. Only cytogenetically normal pregnancies of women who delivered in the study hospital were included in the analysis. Exclusion criteria were the presence of a multiple pregnancy, known congenital abnormalities, suspected confined placental mosaicism, chronic hypertension, pregestational diabetes mellitus, chronic renal disease, autoimmune disorders, inherited thrombophilia, and antiphospholipid antibody syndrome. Moreover, women who underwent amniocentesis and had a transplacental needle insertion, and those who underwent a repeated procedure (CVS, amniocentesis, or both) were also excluded from the study.

Pre-eclampsia was defined as a blood pressure of 140/90 mm Hg or higher, as confirmed in 2 readings in 4–6 hours, and proteinuria of 300 mg or more in a 24-hour urine specimen after 20 weeks of gestation. Gestational hypertension was defined as a blood pressure of 140/90 mm Hg or higher, as confirmed in 2 readings in 4–6 hours, without any other systemic features of pre-eclampsia after 20 weeks of gestation. Women who were diagnosed with hypertension before 20 weeks were classified as having chronic hypertension and were excluded from the study.

Over the study period, there were no changes in clinical obstetric practice at the study hospital that might confound the relationship between exposure and outcome. Moreover, the same operator team, using the same technique, performed all of the invasive diagnostic procedures.

Statistical analyses were carried out with SPSS version 17.0 (IBM, Armonk, NY, USA). Continuous variables are described as the mean ± SD or median (interquartile range). Quantitative variables are expressed by the absolute frequency (percentage). Percentages were compared via the χ^2 test. Parametric Student *t* test was used to compare 2 means if the distribution was approximately normal; the non-parametric Mann–Whitney test was used if the normality assumption was not satisfied.

Multiple logistic regression analysis was used to assess the association of the procedure (CVS vs amniocentesis) with pre-eclampsia, gestational hypertension, or pre-eclampsia with gestational hypertension together after adjusting for maternal age, primigravidity, smoking, and body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters). The adjusted odds ratio (95% confidence interval) is presented from the results of the regression analysis. All *P* values presented from the analyses are 2-tailed and significance was set at a level of 0.05.

3. Results

During the study period, 3243 women who underwent CVS and 6875 who underwent amniocentesis met the inclusion criteria and were included in the analysis. The demographics of the 2 study groups are presented in Table 1. All women were white, but women in the amniocentesis group were significantly older.

Table 1
Characteristics of the study population by procedure.[a]

	CVS (n = 3243)	Amniocentesis (n = 6875)	*P* value
Age, y	30.0 ± 5.9	35.5 ± 4.5	<0.001[b]
Gestational age at procedure, wk	11.3 (1.1)	17.6 (1.4)	<0.001[b]
Primigravida	1461 (45.1)	2819 (41.0)	<0.001[c]
Smoker	196 (6)	446 (6.5)	0.393[c]
BMI	28.3 ± 4.8	28.4 ± 5.1	0.348[c]
Preterm delivery (<37 wk)	417 (12.9)	928 (13.5)	0.376[c]
Birth weight, g	3280 (3000–3560)	3300 (3000–3600)	0.240[d]

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CVS, chorionic villus sampling.
[a] Values are given as mean ± SD, number (percentage), or mean (interquartile range).
[b] By Student *t* test.
[c] By χ^2 test.
[d] By Mann–Whitney test.

Of the women who underwent CVS, 2694 (83.1%) had the procedure because both parents had the β-thalassemia trait; the remaining 549 women had it for fetal karyotyping. Regarding amniocentesis, most women (6378; 92.8%) had the procedure for fetal karyotyping mainly owing to advanced maternal age (>35 years), 401 (5.8%) had it for DNA analysis, and 96 (1.4%) had it for PCR studies.

Table 2 shows the pregnancy outcome of both groups. In total, 237 (2.3%) developed hypertensive disorders during their pregnancy. The rate of pre-eclampsia and that of total hypertensive complications were significantly higher in the CVS group than in the amniocentesis group.

Multiple logistic regression analysis showed that women in the CVS group had a 2.89-fold greater likelihood of having pre-eclampsia compared with women in the amniocentesis group (Table 3). Similarly, the same group of women had 1.50-fold greater likelihood of having gestational hypertension and 2.21-fold greater likelihood of having pre-eclampsia or gestational hypertension compared with women in the amniocentesis group.

4. Discussion

The present found that women who underwent CVS had a significantly higher risk of developing hypertensive disorders during their pregnancy compared with those who underwent amniocentesis. The risk was approximately 2.2 times higher for any hypertensive disorder and approximately 2.9 times higher for pre-eclampsia. Some studies have reported similar results in the past [3–5], although others not only failed to find any relationship between CVS and pre-eclampsia, but also observed a protective effect [6–9]. In the absence of a prospective randomized trial with a primary outcome to measure the risk of

Table 2
Comparison of study variables between chorionic villus sampling and amniocentesis groups.[a]

Variable	CVS (n = 3243)	Amniocentesis (n = 6875)	*P* value[b]
Pre-eclampsia			
No	3165 (97.6)	6822 (99.2)	<0.001
Yes	78 (2.4)	53 (0.8)	
Gestational hypertension			
No	3199 (98.64)	6813 (99.1)	0.036
Yes	44 (1.36)	62 (0.9)	
Pre-eclampsia or gestational hypertension			
No	3121 (96.2)	6760 (98.3)	<0.001
Yes	122 (3.8)	115 (1.7)	

Abbreviation: CVS, chronic villus sampling.
[a] Values are given as number (percentage).
[b] By χ^2 test.