Original articles

Left ventricular diastolic function in pregnancy-induced hypertension

Fabio De Conti, Rita Da Cortà, Daniele Del Monte*, Vincenzo Catena*, Giuseppe Berton**, Paolo Mormino§, Luciano Pecoraro§§, Piergiuseppe Piovesana

*Department of Cardiology, *Department of Anesthesia and Intensive Care, Camposampiero Hospital, Camposampiero (PD), **Department of Cardiology, Conegliano Hospital, Conegliano (TV), §Department of Internal Medicine, University of Padua, Padua, §§Department of Obstetrics and Gynecology, Camposampiero Hospital, Camposampiero (PD), Italy*

Key words:
Diastole; Echocardiography; Hypertension; Pregnancy.

Background. **Hypertension occurs in some 10% of pregnancies and its effects on the left ventricular (LV) morphology and systolic function have been well elucidated. Little is known, however, about the changes in LV diastolic function in such a condition. The aim of this study was to evaluate the LV diastolic function in women with pregnancy-induced hypertension (PIH) using new Doppler echocardiographic methods.**

Methods. **Twenty-two women with PIH (mean age 31.0 ± 4.1 years) were examined during the third trimester of pregnancy. Other 15 normotensive pregnant women (mean age 31.8 ± 5.7 years, p = NS) were used as controls. Doppler parameters of diastolic function included: mitral inflow variables, pulmonary venous flow (PVF) variables, M-mode color Doppler of LV inflow and pulsed tissue Doppler of the mitral annulus. Furthermore, patients underwent an echocardiographic evaluation immediately after delivery and 1 month later.**

Results. **PIH women showed an increased E/A ratio and an increase in the diastolic forward components of PVF. The ratio of systolic to diastolic time-velocity integral and the systolic fraction of time-velocity integrals subsequently decreased. Women with PIH also presented a significantly increased velocity of reversal PVF at atrial contraction, a decrease in the ratio between mitral and PVF duration at atrial contraction and a slower flow propagation velocity with M-mode color Doppler. LV wall thickness and mass were significantly higher in hypertensive pregnant women. In women with PIH the abnormal PVF parameters became similar to those of controls immediately after delivery, while the E/A ratio, M-mode flow propagation velocity and LV mass did so after 1 month.**

Conclusions. **Hypertension complicating pregnancy significantly affects ventricular diastolic filling. These alterations chiefly involve PVF, mitral inflow and intraventricular flow propagation velocities. The LV systolic function is preserved, in the presence of a transient LV remodeling.**

(Ital Heart J 2003; 4 (4): 246-251)

Received July 10, 2002; revision received March 3, 2003; accepted March 10, 2003.

Address:

Dr. Fabio De Conti

Divisione di Cardiologia
Ospedale Civile
Via P. Cosma, 1
35012 Camposampiero (PD)
E-mail: fabio.dc@tin.it

Hypertension complicates some 10% of all pregnancies and is a major cause of maternal and fetal morbidity and mortality[1]. Invasive and noninvasive techniques, such as echocardiography, allowed us to derive a large amount of data about the left ventricular (LV) systolic function and cardiac hemodynamics in normotensive and hypertensive women[2-7]. Little is known, however, about the LV diastolic function in patients with pregnancy-induced hypertension (PIH)[8,9]. Recently, new Doppler applications such as M-mode color Doppler and tissue Doppler imaging have been shown to be relatively load-independent and of interest in the assessment of the diastolic function[10,11]. On the other hand, PIH represents a spontaneous model for the evaluation of the effects of an acute and transient pressure overload in this para-physiological condition. The purpose of this study was to assess the morpho-functional adaptations of the left ventricle to transient hypertension during pregnancy, with special attention to the diastolic function, using the more recent Doppler applications.

Methods

Patients. Between September 1999 and October 2000, we prospectively studied 22 women with singleton pregnancies and PIH aged 25 to 38 years (mean age 31.0 ± 4.1 years). Hypertension was diagnosed if, with the patient seated, the systolic and/or diastolic blood pressure measurements were ≥ 140/90 mmHg on at least two occasions after the 20th week of gestation[12]. Patients with gestational diabetes, a previous history of hypertension and systemic or cardiovascular disease were not included in

the study. Nine patients had proteinuria (defined as 24-hour urinary protein excretion ≥ 0.3 g). Each patient underwent three complete echocardiographic examinations: between the 28th and 38th week of gestation, within 72 hours after delivery and 30 ± 3 days after delivery. At the time of the first echocardiogram, all the patients were receiving antihypertensive drugs (10 patients nifedipine, 3 labetalol, 1 methyldopa, and 8 combination therapy). The control group consisted of 15 healthy pregnant women aged 19 to 39 years (mean age 31.8 ± 5.7 years, p = NS vs the study group) who were submitted to echocardiography between 28 and 38 weeks of gestation.

Echocardiographic examination. M-mode, two-dimensional and Doppler echocardiographic evaluation was carried out with an HP Sonos 5500 imaging system (Hewlett-Packard, Andover, MA, USA) equipped with a multifrequency (2-4 MHz) transducer. Patients were examined in the left lateral decubitus in a quiet environment and measurements were taken after a period of rest lasting at least 15 min. No measurements were taken in the presence of uterine contractions. The heart rate was determined using the R-R interval of a single lead electrocardiogram recorded simultaneously. All exams were performed by the same physician and recorded on videotape for subsequent off-line analysis.

Doppler examination. Doppler measurements were obtained during end-tidal-volume apnea and five cardiac cycles averaged. Mitral inflow velocities were recorded from a standard apical 4-chamber view by positioning a 1-2 mm sample volume between the tips of the mitral leaflets. From Doppler mitral inflow tracings, we measured peak early diastolic (E) and peak late diastolic (A) velocities, the velocity-time integrals (VTI) of early and late diastole, the deceleration time of the early diastolic flow and the duration of the late diastolic flow (A-dur). The isovolumetric relaxation time was measured from a modified 4-chamber view as the time between the end of forward systolic flow and the start of mitral inflow. Pulmonary venous flow (PVF) velocities were recorded in the apical 4-chamber view by positioning a 2-3 mm sample volume in the right upper pulmonary vein 5 to 10 mm proximal to its junction with the left atrium. The following measurements were obtained: the peak velocity of the systolic and diastolic flow, the systolic and diastolic VTI, the systolic to diastolic VTI ratio, the VTI systolic fraction (systolic VTI/systolic VTI + diastolic VTI), and the velocity and duration of the reversal wave corresponding to atrial contraction (a-vel and a-dur) (Fig. 1). A color M-mode recording of the LV inflow was obtained from an apical 4-chamber view by positioning the M-mode cursor through the

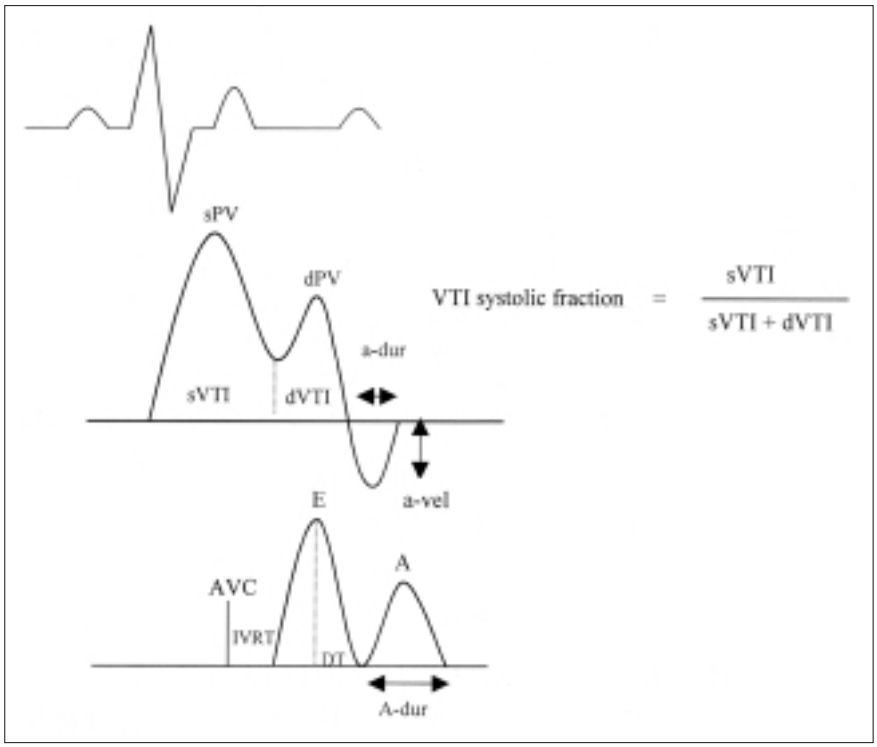

Figure 1. *Schematic diagram of the pulmonary venous flow* (top) *and of the mitral inflow* (bottom). *The pulmonary venous flow variables include: duration of the reverse a wave (a-dur); velocity of the reverse a wave (a-vel); peak velocity of the pulmonary diastolic wave (dPV); peak velocity of the pulmonary systolic wave (sPV); diastolic velocity-time integral (dVTI); and systolic velocity-time integral (sVTI). The sVTI to dVTI ratio and VTI systolic fraction were also calculated. The mitral inflow variables include: peak late diastolic velocity (A); deceleration time of the mitral E wave (DT); peak early diastolic velocity (E); and isovolumetric relaxation time (IVRT). AVC = aortic valve closure.*

center of the mitral inflow region with the M-mode scan line parallel to the direction of flow observed at two-dimensional color Doppler. The flow propagation velocity was measured in accordance with the recommendations of Garcia et al.[10] as the slope of the first aliasing velocity from the mitral tips to a position 4 cm distally into the left ventricle. If needed, the color velocity scale was adjusted and/or the baseline shifted to produce color aliasing. Pulsed tissue Doppler of the mitral annulus was recorded from the apical 4-chamber view by placing the sample volume at the level of the mitral annulus on the lateral aspect. The peak early diastolic velocity, peak atrial contraction velocity and their ratio were measured.

M-mode and two-dimensional examination. M-mode measurements of the LV septum, posterior wall and LV cavity were made using a long-axis parasternal view in accordance with the criteria of the American Society of Echocardiography[13]. The LV fractional shortening was calculated as the difference between LV end-diastolic diameter and LV end-systolic diameter divided by LV end-diastolic diameter. The LV mass was calculated during end-diastole using the Penn convention[14] and indexed to the body surface area. The relative wall thickness was calculated during end-diastole as the ratio between the double of the posterior wall thickness to LV end-diastolic diameter. Two-dimensional images in the apical 4-chamber view were obtained to calculate LV end-diastolic volume, LV end-systolic volume and ejection fraction using the modified Simpson's rule[15].

Statistical analysis. Continuous variables were expressed as mean ± SD. Differences between mean values were analyzed using the two-tailed unpaired Student's t-test. When serial changes in the variables were compared, repeated measures ANOVA was used. If intergroup differences were found, Tukey's *post hoc* test was used. A p value of < 0.05 was considered statistically significant.

In order to determine the interobserver and intraobserver variability, variables for 10 randomly selected patients were analyzed by two observers in a blinded fashion (interobserver variability) and by the same observer a week apart (intraobserver variability).

Results

The characteristics of the patients with PIH and controls are reported in table I. At the time of the study 10 patients presented with mild dyspnea and 1 patient developed pulmonary edema requiring aggressive medical therapy immediately after delivery. The remaining subjects had uneventful pregnancies. All the newborns were healthy and presented normal birth weights.

Doppler echocardiographic data. The Doppler echocardiographic measurements obtained in the patients with PIH and controls are reported in table II. Compared with controls, PIH patients presented with a higher E/A ratio. Most parameters of PVF also showed significant differences between the two groups: in the PIH patients, an increase in both the peak diastolic velocity and diastolic VTI was found without any change in the systolic indexes. Consequently a reduction in the systolic to diastolic VTI ratio and systolic fraction of VTI was obtained. The peak A wave velocity (a-vel) was higher in subjects with PIH (44 ± 11 vs 35 ± 9.5 cm/s, $p = 0.01$) while no significant differences in the duration of mitral and PVF at atrial contraction (A-dur and a-dur) were found. However, their ratio was significantly lower in hypertensive women than in controls ($p < 0.001$). M-mode color Doppler of the mitral inflow showed a steep reduction in the flow propagation velocity in hypertensive women compared to controls while no significant differences between the two groups regarding pulsed tissue Doppler parameters were found.

M-mode and two-dimensional data. Hypertensive patients presented a significantly increased LV wall thickness and mass, with a higher, even though not significantly, relative wall thickness. The LV end-diastolic and end-systolic dimensions, LV fractional shortening and LV ejection fraction were similar in both groups (Table III).

Sixteen out of the 22 PIH patients underwent an echocardiographic control within 3 days of delivery and 20 about 1 month later (30 ± 3 days after delivery). Two patients were lost to follow-up because they moved abroad. PVF measurements became similar to those of the control group within 72 hours of delivery

Table I. Baseline subject characteristics.

	Hypertensives (n=22)	Controls (n=15)	p
Age (years)	31.0 ± 4.1	31.8 ± 5.7	NS
Body surface area (m^2)	1.86 ± 0.2	1.82 ± 0.1	NS
Weeks of gestation	34.7 ± 4	34.8 ± 4	NS
Heart rate at first echocardiogram (b/min)	84.5 ± 9.0	81.5 ± 12	NS
Systolic blood pressure (mmHg)	155.7 ± 18	120.3 ± 8.2	< 0.001
Diastolic blood pressure (mmHg)	99.7 ± 8.9	76.3 ± 6.3	< 0.001

Table II. Doppler echocardiographic data.

Variable	Hypertensives (n=22)	Controls (n=15)	p
Mitral inflow			
E (cm/s)	93.5 ± 21	82 ± 19	NS
A (cm/s)	63.5 ± 11	66.5 ± 8.5	NS
E/A ratio	1.53 ± 0.5	1.24 ± 0.3	0.047
A-dur (ms)	125 ± 24	141 ± 24	NS
E (VTI) (cm)	12.5 ± 4.6	11.5 ± 3.0	NS
A (VTI) (cm)	6.0 ± 1.7	6.3 ± 1.2	NS
DT (ms)	158 ± 32	168 ± 42	NS
IVRT (ms)	89 ± 14	84 ± 6	NS
Pulmonary venous flow			
sPV (cm/s)	60.0 ± 19.5	58.5 ± 12.4	NS
dPV (cm/s)	68.0 ± 13	55.5 ± 10	0.003
sVTI (cm)	13.4 ± 3.6	13.7 ± 2.9	NS
dVTI (cm)	12.2 ± 2.8	9.3 ± 2.6	0.003
sVTI/dVTI ratio	1.15 ± 0.41	1.53 ± 0.34	0.005
sVTI/(sVTI+dVTI) ratio	0.52 ± 0.08	0.60 ± 0.01	0.001
a-vel (cm/s)	44 ± 11	35 ± 9.5	0.01
a-dur (ms)	132 ± 22	119 ± 24	NS
A-dur/a-dur ratio	0.94 ± 0.17	1.19 ± 0.14	< 0.001
Pulsed tissue Doppler			
eTDI (cm/s)	20.0 ± 3.5	20.8 ± 4.1	NS
aTDI (cm/s)	15.7 ± 5.2	14.0 ± 2.4	NS
eTDI/aTDI ratio	1.39 ± 0.5	1.5 ± 0.4	NS
M-mode color Doppler			
FPV (cm/s)	42.3 ± 8.2	54.8 ± 4.6	< 0.001

A = peak velocity of the mitral A wave; aTDI = peak late diastolic velocity; A-dur = duration of the mitral A wave; a-dur = duration of the reverse a wave; a-vel = velocity of the reverse a wave; dPV = peak velocity of the pulmonary diastolic wave; DT = deceleration time of the mitral E wave; dVTI = diastolic velocity-time integral; E = peak velocity of the mitral E wave; eTDI = peak early diastolic velocity; FPV = flow propagation velocity; IVRT = isovolumetric relaxation time; sPV = peak velocity of the pulmonary systolic wave; sVTI = systolic velocity-time integral; VTI = velocity-time integral.

Table III. M-mode and two-dimensional echocardiographic data.

Variable	Hypertensives (n=22)	Controls (n=15)	p
IVSD (cm)	1.0 ± 0.1	0.87 ± 0.3	< 0.001
LVPWD (cm)	0.97 ± 0.1	0.85 ± 0.1	< 0.001
LVEDD (cm)	5.0 ± 0.4	4.8 ± 0.3	NS
LVESD (cm)	3.0 ± 0.3	3.0 ± 0.3	NS
FS (%)	38 ± 0.03	36 ± 0.04	NS
LVEDV (ml/m^2)	85 ± 13	87 ± 14	NS
LVESV (ml/m^2)	29 ± 8.1	32 ± 6.0	NS
EF (%)	65 ± 4	64 ± 4	NS
LV mass index (g/m^2)	96.7 ± 18	77.0 ± 7	< 0.001
RWT	0.40 ± 0.04	0.36 ± 0.04	0.05

EF = ejection fraction; FS = fractional shortening; IVSD = interventricular septal thickness in diastole; LVEDD = left ventricular end-diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVESD = left ventricular end-systolic diameter; LVESV = left ventricular end-systolic volume; LVPWD = left ventricular posterior wall thickness in diastole; RWT = relative wall thickness.

(peak velocity of diastolic flow 58.4 ± 10.6 cm/s; diastolic VTI 10.2 ± 3.1 cm; systolic VTI/diastolic VTI 1.75 ± 0.8; systolic fraction 0.61 ± 0.08; a-vel 35.3 ± 5.9 cm/s; A-dur/a-dur 1.16 ± 0.13). At 1 month of follow-up, echocardiography revealed that M-mode flow propagation velocity (49.4 ± 9.3 cm/s), E/A ratio (1.43 ± 0.28), interventricular septal thickness (0.94 ± 0.13 cm), LV posterior wall thickness (0.9 ± 0.1 cm), and LV mass index (91.5 ± 16.8) were comparable to those of controls (p = NS vs control subjects for all measurements).

Reproducibility of measurements. Interobserver and intraobserver variabilities of PVF velocities, eTDI/aTDI ratio, and flow propagation velocity are shown in table IV.

Table IV. Reproducibility of measurements.

	Variability (%)	
	Interobserver	Intraobserver
PVF velocities		
sPV	1.4 ± 3.9	0.8 ± 4.0
dPV	1.0 ± 4.5	0.6 ± 3.6
sVTI	1.8 ± 3.0	1.2 ± 3.1
dVTI	1.7 ± 3.5	1.1 ± 4.1
a-vel	2.1 ± 3.2	1.2 ± 2.8
a-dur	2.5 ± 3.4	2.0 ± 3.1
eTDI/aTDI ratio	2.5 ± 3.8	0.8 ± 3.6
FPV	3.0 ± 3.5	1.2 ± 2.8

aTDI = peak late diastolic velocity; a-dur = duration of the reverse a wave; a-vel = velocity of the reverse a wave; dPV = peak velocity of the pulmonary diastolic wave; dVTI = diastolic velocity-time integral; eTDI = peak early diastolic velocity; FPV = flow propagation velocity; PVF = pulmonary venous flow; sPV = peak velocity of the pulmonary systolic wave; sVTI = systolic velocity-time integral.

Discussion

PIH represents a spontaneous model for the study of the effects on LV function of a transient and acute pressure overload superimposed on a chronic volume overload status. While LV systolic function and LV morphological adaptation to the volume and pressure overload in pregnancy have been extensively studied, little is known about diastolic function. Recently, diastolic dysfunction has emerged as an important contributor to the symptoms of cardiac disease even in the presence of a normal or almost normal systolic function and it often represents the first alteration in coronary artery disease, cardiomyopathies and systemic hypertension[16]. On the other hand, Doppler echocardiography, due to technological improvement, has become a well accepted and reproducible method for the study of diastole[17,18].

In women with PIH we observed several changes in Doppler indexes of diastolic function, chiefly in the assessment of PVF and LV filling by means of M-mode color Doppler. The PVF pattern was characterized by an increase in the diastolic component of forward flow with a reduction in the systolic filling fraction. Previous studies using both transesophageal and transthoracic echocardiography[19-21] have shown a close inverse relationship between the systolic fraction of PVF and the mean pulmonary capillary pressure. More recently, Rossvoll and Hatle[22] demonstrated that the systolic filling fraction of PVF was the velocity index that best correlated with the pre-A pressure (LV pressure before atrial systole). In addition, we found an increase in the a-wave velocity and a reduction in the A-dur/a-dur ratio; the difference between PVF reversal and forward mitral flow duration during atrial systole was found to be the best indicator of LV end-diastolic pressure[23-25]. Rossvoll and Hatle[22] showed that a PVF reversal exceeding the duration of the mitral A wave predicted a LV end-diastolic pressure > 15 mmHg with a sensitivity of 0.85 and a specificity of 0.79. Moreover, Cecconi et al.[26] showed that an A-dur/a-dur ratio < 0.90 predicted a LV end-diastolic pressure > 20 mmHg. Since mitral flow velocity curves reflect PVF curves, the increase in the E/A ratio we observed in hypertensive pregnant women might be due to an increased left atrial pressure. The Doppler parameters of PVF and mitral inflow in our control group are in keeping with those reported by Mesa et al.[8] about LV diastolic function in normal human pregnancy. They observed a progressive decrease in the E/A ratio and in the diastolic component of PVF throughout pregnancy, which is the opposite of what occurs in patients with PIH.

Hypertensive women showed also a lower flow propagation velocity at M-mode color Doppler, a new application for the study of diastolic function that proved to be relatively load-independent and to provide an accurate estimate of LV relaxation both in experimental and in clinical studies[10,27]. It is based on the principle that the velocity at which the flow propagates within the ventricle is related to the intraventricular gradients produced by a suction force during early filling; a reduction in these gradients, due to abnormal relaxation, produces a delayed apical filling so reducing the flow propagation velocity. The absence, in our study, of significant changes in pulsed tissue Doppler parameters between women with PIH and normal pregnant subjects could be explained by a lower sensitivity of these indexes, chiefly in the presence of volume overload. In agreement with Vasquez Blanco et al.[7], in hypertensive women we found an increase in the interventricular septal thickness, LV posterior wall thickness and LV mass index, without any changes in LV diastolic diameter and volume. LV wall thickening is likely to be due to an increase in the myocardial interstitial volume; the redistribution of body fluids in pre-eclamptic states, with an increase in the interstitial and a fall in the intravascular volume, is a well known phenomenon[28]. Furthermore, this geometric pattern differs from the one that Robson et al.[29] and Katz et al.[30] observed in normal pregnancy characterized by progressive LV enlargement related to the increased ratio between the LV end-diastolic radius and posterior wall thickness. On the other hand, systolic function parameters were similar in both groups of patients. The rapid modification of abnormal PVF parameters immediately after delivery suggests that they are more dependent on hemodynamic conditions than on mitral inflow measurements. The return of the morphological parameters to normal values in the early *post-partum* has also been reported by other authors[8].

Study limitations. PIH patients were taking antihypertensive drugs at the time of the first echocardiogram. This factor may have influenced the Doppler measure-

ments. Besides, the persistence of systemic hypertension in some patients might have also interfered with the echo-Doppler parameters.

In conclusion, the present study shows that hypertension complicating pregnancy significantly affects PVF, mitral inflow and intraventicular flow propagation velocities. This is likely to be due to alterations in the diastolic filling dynamics.

LV systolic function is preserved, in the presence of a transient LV remodeling. Additional studies including larger numbers of patients should be undertaken to better understand the pathophysiology of diastole and its role in the complications of PIH.

References

1. Lindheimer MD. Hypertension in pregnancy. Hypertension 1993; 22: 127-34.
2. Bader RA, Bader ME, Rose DJ, Braunwald E. Hemodynamics at rest and during exercise in normal pregnancy as studied by cardiac catheterization. Eur J Clin Invest 1955; 34: 1524-36.
3. Poppas A, Shroff SG, Korcarz CE, et al. Serial assessment of the cardiovascular system in normal pregnancy. Role of arterial compliance and pulsatile arterial load. Circulation 1997; 95: 2407-15.
4. Clapp JF III, Capeless E. Cardiovascular function before, during, and after the first and subsequent pregnancies. Am J Cardiol 1997; 80: 1469-73.
5. Geva T, Mauer MB, Striker L, Kirshon B, Pivarnik JM. Effects of physiologic load of pregnancy on left ventricular contractility and remodeling. Am Heart J 1997; 133: 53-9.
6. Bosio PM, McKenna PJ, Conroy R, O'Herlihy C. Maternal central hemodynamics in hypertensive disorders of pregnancy. Obstet Gynecol 1999; 94: 978-84.
7. Vasquez Blanco MV, Grosso O, Bellido CA, et al. Left ventricular geometry in pregnancy-induced hypertension. Am J Hypertens 2000; 13: 226-30.
8. Mesa A, Jessurun C, Hernandez A, et al. Left ventricular diastolic function in normal human pregnancy. Circulation 1999; 99: 511-7.
9. Degli Espositi D, Borghi C, Cassani A, et al. Abnormal left ventricular structure and function in pregnancy complicated by pre-eclampsia. (abstr) J Am Coll Cardiol 1998; 31 (Suppl A): 889.
10. Garcia MJ, Thomas JD, Klein AL. New Doppler echocardiographic applications for the study of diastolic function. J Am Coll Cardiol 1998; 32: 865-75.
11. Oki T, Tabata T, Yamada H, et al. Clinical application of pulsed Doppler tissue imaging for assessing abnormal left ventricular relaxation. Am J Cardiol 1997; 79: 921-8.
12. National High Blood Pressure Education Program. National high blood pressure education program working group report on high blood pressure in pregnancy. Am J Obstet Gynecol 1990; 163 (Part 1): 1691-712.
13. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072-83.
14. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation 1997; 55: 613-8.
15. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989; 2: 358-67.
16. Yamamoto K, Redfield MM, Nishimura RA. Analysis of left ventricular diastolic function. Heart 1996; 73 (Suppl 2): 27-35.
17. Appleton CP, Hatle LK. The natural history of left ventricular filling abnormalities: assessment of two-dimensional and Doppler echocardiography. Echocardiography 1992; 9: 437-57.
18. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. J Am Coll Cardiol 1997; 30: 8-18.
19. Nishimura RA, Abel MD, Hatle LK, Tajik AJ. Relation of pulmonary vein to mitral flow velocities by transesophageal Doppler echocardiography: effect of different loading conditions. Circulation 1990; 81: 1448-97.
20. Kuecherer HF, Muhiudeen IA, Kusumoto FM, et al. Estimation of mean left atrial pressure from transesophageal pulsed-Doppler echocardiography of pulmonary venous flow. Circulation 1990; 82: 1127-39.
21. Brunazzi MC, Chirillo F, Pasqualini M, et al. Estimation of left ventricular diastolic pressure from precordial pulsed Doppler analysis of pulmonary venous and mitral flow. Am Heart J 1994; 128: 293-300.
22. Rossvoll O, Hatle LK. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. J Am Coll Cardiol 1993; 21: 1687-96.
23. Appleton CP. Hemodynamic determinants of Doppler pulmonary venous flow velocity components: new insights from studies in lightly sedated normal dogs. J Am Coll Cardiol 1997; 30: 1562-74.
24. Appleton CP, Galloway JM, Gonzales M, Gaballa M, Bansight MA. Estimation of left ventricular filling pressures using two-dimensional and Doppler echocardiography in adult patients with cardiac disease. Additional value of analyzing left atrial size, left atrial ejection fraction and the difference in duration of pulmonary venous and mitral flow velocity at atrial contraction. J Am Coll Cardiol 1993; 22: 1972-82.
25. Meijburg HW, Visser CA. Pulmonary venous flow as assessed by Doppler echocardiography: potential clinical applications. Echocardiography 1995; 12: 425-40.
26. Cecconi M, Manfrin M, Zanoli R, et al. Doppler echocardiographic evaluation of left ventricular end-diastolic pressure in patients with coronary artery disease. J Am Soc Echocardiogr 1996; 9: 241-50.
27. Takatsuji H, Mikami T, Urasawa K, et al. A new approach for the evaluation of left ventricular diastolic function: spatial and temporal analysis of left ventricular filling flow propagation by color M-mode Doppler echocardiography. J Am Coll Cardiol 1996; 27: 365-71.
28. Brown MA, Gallery ED. Volume homeostasis in normal pregnancy and pre-eclampsia: physiology and clinical implications. Baillieres Clin Obstet Gynaecol 1994; 8: 287-310.
29. Robson SC, Hunter S, Boys RJ, Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol 1989; 256 (Part 2): H1060-H1065.
30. Katz R, Karliner JS, Resnik R. Effects of a natural volume overload state (pregnancy) on left ventricular performance in normal human subjects. Circulation 1978; 58: 434-41.