Reversible De Novo Left Ventricular Trabeculations in Pregnant Women:
Implications for the Diagnosis of Left Ventricular Non-Compaction in
Low Risk Populations

Running title: Gati et al.; Reversible Left Ventricular Trabeculations in Pregnancy

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Abstract

Background—Patients with heart failure and chronic anemia frequently demonstrate left ventricular (LV) trabeculations which may be compatible with the diagnosis of left ventricular non-compaction (LVNC). We utilized the pregnancy model, which is characterized by reversible increase in cardiac preload and other changes in cardiac function, to assess the development of de novo LV trabeculations in women with morphologically normal hearts.

Methods and Results—102 primigravida pregnant women were evaluated longitudinally with a series of echocardiograms in the first trimester, third trimester and post-partum. Echocardiograms were analysed according to established guidelines. Increased LV trabeculations and the presence of LVNC were based on established criteria. Pregnancy was associated with an increased heart rate, stroke volume and cardiac output as well as increased LV volume and mass. During pregnancy 26 (25.4%) women developed increased trabeculations. 8 women showed sufficient trabeculations to fulfill both Chin and Jenni criteria for LVNC. During the post-partum follow-up period of 24±3 months, 19 (73%) women demonstrated complete resolution of trabeculations and 5 showed marked reduction in the trabeculated layer.

Conclusions—Pregnancy induces de novo LV trabeculations in a significant proportion of women. The results suggest that left ventricular trabeculations occur in response to increased LV loading conditions or other physiologic responses to pregnancy and are not specific for LVNC. These factors should be considered when assessing individuals with LV trabeculations outside the context of symptoms of heart failure or familial cardiomyopathy.

Key words: left ventricle, left ventricular noncompaction, pregnancy, echocardiography, longitudinal cohort study, left ventricular trabeculations
Introduction

Left ventricular non-compaction (LVNC) cardiomyopathy is an unclassified primary cardiomyopathy which is characterized by increased myocardial trabeculations and recesses. The precise stage of development and the natural history of the condition is not fully understood, however preliminary data are indicative of a morphologically and clinically heterogeneous disorder. Whereas some individuals present with overt heart failure, fatal arrhythmias, and thrombo-embolic events, others remain asymptomatic. Echocardiographic criteria to facilitate identification and assessment for LVNC rely on the presence of left ventricular (LV) myocardial trabeculations and a two-layer distinction between compacted and non-compacted myocardium (Figure 1).

The past two decades have witnessed significant advances in tissue harmonics, which have enabled detailed assessment of the ventricular myocardium. Such progress in image resolution has coincided with an increasing number of scientific reports relating to LVNC. The initial prevalence of LVNC was estimated to be less than 0.3% however, recent studies in patients with heart failure have reported a high proportion (almost 35%) of patients with myocardial trabeculations with nearly 25% fulfilling diagnostic criteria for LVNC, irrespective of the criterion used. A study of over 1000 athletes demonstrated that 18% exhibited increased LV trabeculations and 8% fulfilled echocardiographic criteria for LVNC. Sickle cell anaemia patients also reveal a high (28.3%) prevalence of increased LV trabeculations. A common theme among all three cohorts is the presence of an increased cardiac preload. Given the relatively low prevalence of the other primary cardiomyopathies in the general population, it is unlikely that all such individuals suffer from LVNC. Indeed, the most probable explanation for the increased trabeculations and recesses observed in these states is a physiologically determined
epiphenomenon in response to a chronic increase in cardiac preload.

Pregnancy is associated with doubling of maternal cardiac preload for at least 4 months. Based on the cardiovascular changes observed in pregnancy, a longitudinal pregnancy model was applied to evaluate whether increased LV trabeculations observed in the aforementioned situations are a cardiac response to increased preload, rather than LVNC. We hypothesized that women with a morphologically normal LV myocardium may develop LV trabeculations during pregnancy and such changes would resolve within a few weeks of delivery, following normalization of blood volume.

Methods

Subjects

We conducted a prospective longitudinal echocardiographic study of 102 primigravida pregnant women [66 Caucasian (white) and 36 African/Afro-Caribbean (black)] between 2010 and 2013. The women were recruited from two specialist antenatal units in South London (University Hospital Lewisham and St. George’s Hospital NHS Trust). All women were consented and evaluated by a self-reported health questionnaire, which required information relating to the presence of cardiac symptoms, drug history, previous miscarriages and a family history of premature cardiovascular disease or sudden cardiac death; physical examination; urine dipstick; 12-lead electrocardiogram; and 2-dimensional echocardiography. The women’s ethnicity was self-assigned. All women underwent repeat 12-lead ECG and 2-dimensional echocardiography between 28 to 36 weeks gestation and 3 to 12 months post-partum.

Selection criteria for the study included age 18-35 years old, primigravida status, singleton pregnancy, black or white ethnicity, absence of cardiac symptoms, a structurally
normal heart on echocardiography without any evidence of increased LV trabeculations and the ability to perform a full range of high quality images with clear definition of the endocardium in the standard planes in the third trimester of pregnancy.

**Twelve-lead Electrocardiography**

A standard 12-lead ECG was performed using a Philips Pagewriter Trim III (Bothel, WA, USA) and analyzed as previously described.11,12

**Echocardiography**

Two-dimensional echocardiography was performed by a cardiologist with accreditation in echocardiography (S.G) using either the Philips Sonos 7500, or Philips iE33 (Bothel, WA, USA). Standard cardiac views were obtained and analyzed according to protocols specified by American Society of Echocardiography.13 All measurements were recorded as absolute values. Cardiac dimensions and volumes were assessed as previously described.8 LV mass was calculated with the formula of Devereux and indexed for body surface area.14 Assessment of diastolic function included pulsed wave Doppler across the mitral valve and tissue Doppler velocity imaging of the septal and lateral mitral valve annulus in the apical 4-chamber view. Stroke volume (SV) was calculated as the product of aortic Doppler flow velocity time integral (VTI) and cross-sectional area of the left ventricle outflow tract.15 Cardiac output (CO) was calculated by the product of stroke volume and heart rate (HR) derived from ECG monitoring.15 Mean arterial blood pressure (MAP) was calculated as diastolic blood pressure – systolic blood pressure/diastolic blood pressure. Total vascular resistance (TVR) was calculated in dynes·s·cm⁻⁵ using the standard formula: TVR = (MAP in mmHg/CO in L/min) ×80.16

All echocardiographic studies were saved to compact discs as numeric files to generate anonymity. Assessment for increased LV trabeculations and cardiac measurements were
repeated independently by an accredited cardiac physiologist (M.R.) blind to the identity, ethnicity and gestation stage of the women.

The original numerical files generated and labelled by SG were shuffled and renumbered before being presented back to SG to conduct the intra-observer variability assessment to ensure she was also blind to the identity, ethnicity and gestation stage of the women during the second analysis. Discrepancies between MP and SG relating to increased LV trabeculations or criteria for LVNC during inter-observer analysis were referred to RS (director of echocardiography at St George’s Hospital) and SS (director of inherited cardiac diseases). Both RS and SS were blind to the identity, ethnicity and gestation stage of the women.

**Determination and Definition of Increased Left Ventricular Trabeculation**

LV trabeculations were assessed in the short axis views at the level of the mitral valve, papillary muscle and apex as well as the four chamber and two chamber views. Care was taken to use only these standard views for every echocardiogram.

Myocardial trabeculations were defined as localized protrusions of the endocardial surface ≥3mm in diameter,8,17 associated with intertrabecular recesses on 2-D echocardiography (Figure 1). The definition of increased LV trabeculations was derived from a randomly selected asymptomatic and normotensive (BP<120/80mmHg) control population of 138 healthy non-pregnant females (91 white and 57 black), recruited from a population-screening program offered by the charity Cardiac Risk in the Young.18 Controls were of similar age and size as the pregnancy cohort (mean age: 30.0 ± 5.9 years v 30.7 ± 4.4 years; p=0.309 and BSA: 1.7 ± 0.6 m² v 1.8 ± 0.3 m²; p=0.122).

Increased LV trabeculation was defined as ≥ 95th centile of the distribution of
trabeculations in the population of women which corresponded to 3 trabeculations. This figure is identical to a previous description of increased LV trabeculations derived from a large cohort attending for echocardiography. Colour flow Doppler utilizing a Nyquist limit of 20-30 cm/s was applied when numerous small cavities within the endocardial surface were identified in a 2-layered structure.

The echocardiographic criteria by Chin and Jenni were used to define LVNC (Figure 1). The distribution of trabeculations was determined using the 16-segment model recommended by the American Society of Echocardiography.

**Ethical approval/consent**

The National Research Ethics Service, East London 2 Research Ethics Committee, granted ethical approval in the UK.

**Statistical analysis**

Statistical analyses were performed using SPSS version 18.0 (SPSS, Inc., Chicago IL). Variables were tested for normality using the Kolmogorov-Smirnov test. Values are expressed as either mean ± standard deviation (SD) or percentages, as appropriate. Differences within group means were compared with paired Student t-test or Wilcoxon’s test and differences between group means were compared using independent t-tests or Mann-Whitney U tests (for normally and non-normally distributed variables respectively). \( \chi^2 \) test or Fisher’s exact test was used as appropriate to test group differences of proportions. Repeated measures analysis of variance was performed to evaluate changes of the clinical and echocardiographic parameters during pregnancy and the postpartum period. Logistic regression was used to determine multiple-adjusted risk for the presence of increased (≥ 3) trabeculations during pregnancy in relation to ethnicity, age, body mass index, heart rate, blood pressure, LV stroke volume, LV cavity and volume size and LV
mass. Statistical significance was defined as a two-tailed $P$-value of $<0.05$ throughout.

Reproducibility of LV and RV measurements was assessed with intraclass correlation coefficient analysis and reported as intraclass correlation coefficient (95% confidence interval [CI]). Averaged measures were used as index for the reliability of two different rates. Intra-observer and inter-observer agreement for the presence of LV trabeculations was assessed by kappa statistics.

**Results**

**Subjects**

Pregnant women had a mean age of $30.7 \pm 4.4$ years and a body surface area of $1.8 \pm 0.3 \text{m}^2$. The majority (64.7%) were white. None of the women had a family history of cardiomyopathy or premature (<40 years old) sudden cardiac death. All women were normotensive (blood pressure $\leq 120/80 \text{mmHg}$) and none revealed proteinuria.

**Haemodynamic and Structural Changes during Pregnancy**

Progression of pregnancy from the first trimester to the third trimester was accompanied by an increase in heart rate, stroke volume and cardiac output and a reduction in total vascular resistance. Advancing pregnancy was also associated with a modest (11-12%) increase in LV volume and LV mass (Table 1).

**Pregnant Women with Increased Left Ventricular Trabeculations**

Twenty-five percent of pregnant women developed increased LV trabeculations (Figure 2) which were more common in black women compared with white women (47.2% v 13.6%; $p=0.0003$), Of the total pregnancy cohort, 10 women (9.8%) fulfilled the Jenni criteria, 19 (18.6%) fulfilled the Chin criteria and 8 (7.8%) fulfilled both criteria for LVNC (Figure 3). Women fulfilling both
criteria did not show any significant ethnic predilection (black: n = 4; 11.1% v white: n = 4; 6.1%; p=0.459). During pregnancy, the Chin X to Y ratio at the site of maximal wall thickness averaged 0.43 ± 0.07 (range 0.35-0.5) and the Jenni non-compacted to compacted myocardial ratio at the site of maximal wall thickness averaged 2.2 ± 0.6 (range 2.1-3.4).

LV trabeculations were predominately distributed in the anterolateral territory (n=14), followed by infero-lateral (n=7), inferior (n=7), apical lateral (n=7) and apical inferior (n=6) regions.

**Differences in Electrocardiographic and Echocardiographic Parameters in Pregnant Women Exhibiting Increased Left Ventricular Trabeculations and Those with Normal Cardiac Morphology**

Pregnant women who developed LV trabeculations did not differ from those without LV trabeculations in terms of electrocardiographic abnormalities. One pregnant woman with LV trabeculations showed minor T-wave inversion in leads V1 and V2 on the baseline ECG as did one woman with normal myocardial morphology, which persisted during pregnancy and for 12 months post-partum. There were no significant differences in wall thickness, cavity size, indices of systolic and diastolic function or stroke volume between women in the two groups (Table 2). None of the women in the study exhibited abnormal systolic or diastolic function.

**Determinants of Increased Left Ventricular Trabeculations**

There was no significant association between increased LV trabeculations and age, body mass index, systolic BP, LV cavity dimension, stroke volume or LV mass.

Multiple-adjusted binary logistic regression demonstrated that ethnicity was the only independent predictor for the presence of increased (≥ 3) trabeculations during pregnancy. Black women were almost three times more likely to develop increased LV trabeculations than white
women during pregnancy following adjustment for age, body mass index, systolic BP, LV cavity dimension, LV stroke volume and LV mass. (OR: 2.7 95% CI 1.1, 6.7, p=0.034).

The Post-Partum Assessment in Pregnant Women

In the post-partum period, 18 (69.2%) women showed complete resolution of LV trabeculations over a mean duration time of 8.1 ± 4.2 months (Figure 2). 7 (27%) women continued to display LV trabeculations, which did not show any ethnicity predilection (black n=2, white n=5; p=0.202). The 7 women who continued to exhibit trabeculations did not reveal any differences in the number of trabeculated segments during or after pregnancy; LV trabeculations were primarily distributed in the apical inferior (n=5) and apical lateral (n=5) territory followed by mid-cavity region (n=3).

All 7 women were followed-up for an additional 24 ± 3 months and remained asymptomatic with blood pressures <120/80mmHg. One woman became pregnant again and was excluded from this analysis. At repeat echocardiographic assessment, 5 women continued to exhibit LV trabeculations and one woman showed complete regression of the myocardial anomaly. In the 5 women with persisting trabeculations, the non-compacted and compacted layers progressively decreased over time according to one or both criteria (Table 3). All 5 women continued to reveal normal LV systolic and diastolic function.

Reproducibility of Left Ventricular Measurements and Increased Left Ventricular Trabeculations

Interobserver Variability

LV measurements were highly reproducible at interobserver level (Table 4). There were no cases of disagreement with the independent reviewer with respect to increased LV trabeculations during the first trimester scans. There were 2 cases of disagreement with respect to increased LV
trabeculations during the third trimester translating to a kappa = 0.87 (p<0.001). The kappa value for the disparity in measurements relating to Chin criteria and Jenni criteria were 0.62, p=0.01 and 0.29; p=0.15 respectively. In the post-partum scans, there was 1 case where the independent reviewer disagreed with respect to increased LV trabeculations resulting in a kappa = 0.93 (p<0.001). The kappa value for disparity with respect to Chin criteria and Jenni criteria was 0.61; p=0.02 and 0.33; p=0.173 respectively.

**Intraobserver Variability**

There were only 2 cases of disparity with respect to increased LV trabeculations for third trimester scans during re-analysis by first author (S.G.) translating to a kappa = 0.93 (p<0.001). There was no disparity for first trimester or post-partum scans.

**Discussion**

The clinical entity LVNC is established in the paediatric population and is usually associated with other congenital cardiac abnormalities that increase cardiac preload. The issue of adult LVNC, which was first described by Engberding\(^1\) in 1984 is less clear, particularly since current diagnostic echocardiographic and MRI derived criteria for LVNC are based on small cohorts and have not been validated prospectively in large populations.\(^2\) This study revealed that *de novo* LV trabeculations occurred in 25% of pregnant women. The majority of women (69.2%) with trabeculations demonstrated complete resolution and a further 12% showed gradual regression towards normal morphology over a 2 year follow up period.

The absence of symptoms or echocardiographic features of LV dysfunction suggests that it is highly unlikely that such a large proportion of the women with trabeculations suffered from an incomplete phenotypic manifestation of LVNC particularly as the left ventricle was
morphologically normal at time of recruitment into the study. We have previously reported increased LV trabeculations amongst a large cohort of athletes and sickle cell anaemia patients; 8% of both cohorts fulfilled criteria for LVNC.\(^7\) A study by Kohli et al\(^7\) reported that 24% of heart failure patients exhibited features consistent with LVNC.\(^7\) We believe that the common factor in all three situations is an increased cardiac preload. All of the aforementioned studies have been cross-sectional, therefore, it has been impossible to ascertain whether increased LV trabeculations is a \textit{de novo} response to an increased cardiac preload, an exaggeration of anomalies that were already present due to incomplete manifestation of LVNC, or whether they form part of a normal morphologic spectrum in some healthy individuals.

We postulated that LV trabeculations represented a normal response to an increased cardiac preload in some individuals. Pregnancy is an attractive natural physiological model for testing the hypothesis in human subjects as it is associated with a 50% increase in plasma volume, stroke volume and cardiac output. The demonstration that pregnancy induces \textit{de novo} LV trabeculations in women with normal myocardial morphology indicates that LV trabeculae are an epiphenomenon to increased preload in several disease states including heart failure\(^7\) and chronic anemia\(^9\) but also physiological states such as high level athletic training.\(^8\)

The study revealed that progression of pregnancy from the first to the third trimester was associated with a reversible increase in stroke volume, cardiac output, LV volumes and LV mass. Although it is possible that LV trabeculations may have simply been more visible in those women with the greatest increases in LV volume, we did not identify any differences in LV volumes or stroke volume in women who developed trabeculations compared with those women with normal morphology. Therefore, it is possible that in some individuals, a preliminary adaptive response to wall tension consists of a modest increase in LV volume and mass as well
as the development of trabeculations. We suspect that these changes are likely to be more
obvious in individuals who have been subject to a longer preload stress such as athletic training,
chronic anaemia and heart failure.

The overall number of women fulfilling criteria for LVNC was small (n=8) therefore we
were unable to discern any statistical differences between the two ethnic groups. However, our
analysis revealed that black ethnicity was an important determinant of increased LV
trabeculations in this study. These observations concur with previous studies reporting an
increased prevalence of both LV trabeculations and criteria for LVNC in black patients with
heart failure\(^7\) and black athletes compared with Caucasians.\(^8\) The higher prevalence of LV
trabeculations during pregnancy in black women is probably synonymous with the greater
magnitude of left ventricular hypertrophy due to the increased LV afterload in hypertensive
black patients\(^21\) and suggests that some confounding ethnicity specific genetic factors could be
involved in the exaggeration of this phenomenon.

It is important to emphasize that the temporal pattern of \textit{de novo} development of LV
trabeculations as pregnancy progressed and subsequent resolution in the postpartum period was
observed in both ethnic groups. These findings indicate that LV trabeculations are part of a
physiological spectrum of cardiac adaptation in both Afro-Caribbean and Caucasian patients.
Therefore, such morphology should not be considered specific for the diagnosis of LVNC in
either of these ethnic groups in the absence of cardiac symptoms, familial disease, LV
dysfunction, or ventricular tachycardia.

This study does not necessarily support the notion that most patients with heart failure
and increased LV trabeculations probably do not have genuine LVNC. However, it provides an
alternative and adequate explanation for the high prevalence of LV trabeculations observed in
low-risk populations such as athletes\textsuperscript{8} and those attending for echocardiograms in the absence of any suspicious features of heart failure.\textsuperscript{22} Such cases are an increasingly frequent source of diagnostic dilemmas and may occasionally lead to an erroneous life-long diagnosis. Our observations have important implications for the diagnosis and management of LVNC in asymptomatic individuals harbouring LV trabeculations outside the context of familial heart failure or sudden cardiac death. The findings suggest that a more thorough assessment of current diagnostic criteria and entities relating to adult LVNC is crucial for a better understanding of this currently unclassified cardiomyopathy. The low inter-observer kappa values (0.29) for the Jenni criteria, which are measured in end systole, versus the Chin criteria (0.62) which are measured in end diastole, suggest that future echocardiographic LVNC criteria will be more reproducible if LV measurements are made in diastole.

Given the safety concerns surrounding cardiac MRI in the first trimester, the conclusions from this study were based solely on echocardiographic assessment although cardiac MRI may be considered the ‘gold-standard’ assessment for myocardial trabeculations.\textsuperscript{23} We suspect that the prevalence of \textit{de novo} trabeculations would have been even higher with cardiac MRI and helped to strengthen our message. We have previously published a study revealing a high prevalence of left ventricular trabeculations in athletes\textsuperscript{8} in which athletes fulfilling echocardiographic criteria for LVNC\textsuperscript{2,3} also revealed cardiac MRI features of the disorder.\textsuperscript{24}

During the assessment for trabeculations, we attempted to be as meticulous as possible to make measurements in the same standard images each time. It is possible that our short axis measurements when transcending from the level of the papillary muscles towards the left ventricular apex may have varied by a millimeter or two between serial echocardiograms in any given pregnant woman. Therefore, we may have failed to detect trabeculations in some women
as a result of these inherent practical limitations of echocardiography. Nevertheless this limitation does not deter from the fact that 1 in 4 women with completely normal LV morphology went on to develop a significant number of trabeculations as pregnancy progressed.

The potential impact of high concentrations of oestrogen on the development of trabeculations cannot be excluded with certainty, however, a high proportion of LV trabeculations and non-compaction criteria are also observed in males with heart failure and sickle cell anemia and male athletes, suggesting that an increased cardiac preload is the most plausible explanation for this epiphenomenon. Evaluation of first-degree relatives of women in whom increased LV trabeculations persisted was not conducted but may have provided valuable information for establishing whether increased LV trabeculations has a genetic predisposition.

Conclusions

Pregnancy induces de novo LV trabeculations in a significant proportion of women. Our observation provides an explanation for the high prevalence of increased trabeculations identified in low risk individuals subject to increased cardiac loading conditions. These factors should be taken into consideration in asymptomatic individuals with LV trabeculations and those fulfilling echocardiographic criteria for LVNC outside the context of symptoms of heart failure or familial cardiomyopathy.

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Papamichael. Study design, data collection, statistical analysis and preparation of manuscript. Dr Abbas Zaidi. Study design, data collection, and preparation of manuscript. Dr Nabeel Sheikh. Study design, data collection, and preparation of manuscript. Mr Matt Reed. Study design, data analysis, and preparation of manuscript. Dr Rajan Sharma. Quality control of the data. Revision of manuscript for intellectual content. Professor Baskaran Thilaganathan. Interpretation of data. Revision of manuscript for intellectual content. Professor Sanjay Sharma. Lead for study. Study design, data collection, and quality control of data, preparation and revision of manuscript, responsible guarantor of overall content.

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**Conflict of Interest Disclosures:** None.

**References:**


Table 1. Longitudinal comparison of echocardiographic parameters in women during and post-pregnancy‡

<table>
<thead>
<tr>
<th>Parameters</th>
<th>First Trimester n=102</th>
<th>Third Trimester n=102</th>
<th>Post-partum n=102</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>13.7 ± 2.7</td>
<td>35.1 ± 5.0</td>
<td>33.6 ± 17.2</td>
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<td>BMI (kg/m²)</td>
<td>24 ± 4.0</td>
<td>28.2 ± 3.9</td>
<td>25.9 ± 4.2</td>
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<tr>
<td>HR (bpm)</td>
<td>79.1 ± 13.3</td>
<td>89.1 ± 11.5</td>
<td>73.3 ± 6.0</td>
<td>&lt;0.001</td>
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<td>SBP (mmHg)</td>
<td>110 ± 12.3</td>
<td>113 ± 10.3</td>
<td>110 ± 8.5</td>
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<td>MAP (mmHg)</td>
<td>80.8 ± 10.8</td>
<td>82.4 ± 6.9</td>
<td>79.3 ± 6.0</td>
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<tr>
<td>TVR (dyne/s/cm⁵)</td>
<td>1290 ± 374</td>
<td>950 ± 212</td>
<td>1404 ± 301</td>
<td>&lt;0.001</td>
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<td>LVM (g)</td>
<td>132 ± 42.0</td>
<td>150 ± 33.9</td>
<td>125 ± 30.5</td>
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<tr>
<td>Simpson EF (%)</td>
<td>61.8 ± 8.6</td>
<td>61.6 ± 8.1</td>
<td>62.6 ± 7.5</td>
<td>0.484</td>
</tr>
<tr>
<td>CO (L)</td>
<td>5.1 ± 1.7</td>
<td>7.2 ± 1.4</td>
<td>4.7 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>94.6 ± 20.4</td>
<td>107.5 ± 21.0</td>
<td>87.8 ± 13.1</td>
<td>&lt;0.001</td>
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<td>LVED (mm)</td>
<td>44 ± 9</td>
<td>45 ± 5</td>
<td>43 ± 5</td>
<td>0.327</td>
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<tr>
<td>SV (mls)</td>
<td>37.3 ± 12.7</td>
<td>39.8 ± 10.8</td>
<td>33.7 ± 10.6</td>
<td>0.015</td>
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<td>Max-LVWT (mm)</td>
<td>9.0 ± 2.0</td>
<td>9.0 ± 2.0</td>
<td>9.0 ± 1.0</td>
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<td>33.7 ± 10.6</td>
<td>0.015</td>
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<td>Decel Time (ms)</td>
<td>202 ± 53</td>
<td>192 ± 55.7</td>
<td>209 ± 50.1</td>
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<td>S’ septal</td>
<td>9.0 ± 1.4</td>
<td>9.3 ± 1.8</td>
<td>8.6 ± 1.3</td>
<td>&lt;0.001</td>
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<td>E/E’ (septal)</td>
<td>7.5 ± 2.7</td>
<td>7.8 ± 2.8</td>
<td>7.4 ± 2.1</td>
<td>0.227</td>
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<tr>
<td>S’ lateral</td>
<td>11.3 ± 2.2</td>
<td>11.1 ± 2.5</td>
<td>10.9 ± 2.2</td>
<td>&lt;0.001</td>
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<tr>
<td>E/E1 (lateral)</td>
<td>5.4 ± 2.0</td>
<td>5.7 ± 1.9</td>
<td>5.2 ± 1.4</td>
<td>0.241</td>
</tr>
</tbody>
</table>

‡Data expressed as mean ± SD

Ao, aortic annulus diameter; BMI, body mass index; CO, cardiac output; DBP, diastolic blood pressure; Decel Time, deceleration time; E, early diastolic mitral inflow velocity; A, late diastolic inflow velocity; E’, peak early diastolic mitral annular velocity of lateral and septal wall; E/E’, ratio of peak early diastolic mitral inflow velocity to peak early diastolic mitral annular velocity; EF, LV ejection fraction; HR, heart rate; LA, left atrial volume; LVED, LV end-diastolic diameter; LVM, left ventricular mass; MAP, mean arterial pressure; Max-LVWT, maximal left ventricular wall thickness; RA, right atrial volume; RVID, basal right ventricular dimension; S’, systolic annular peak velocity; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.
Table 2. Comparison of echocardiographic parameters in pregnant women in the third trimester with and without left ventricular trabeculations.‡

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pregnant women with increased LV trabeculations</th>
<th>Pregnant women without increased LV trabeculations</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>36.8 ± 0.9</td>
<td>35.8 ± 4.8</td>
<td>0.242</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.7 ± 0.3</td>
<td>1.8 ± 0.3</td>
<td>0.371</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.1 ± 4.1</td>
<td>28.2 ± 4.3</td>
<td>0.918</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>88.9 ± 11.2</td>
<td>90.0 ± 11.5</td>
<td>0.733</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>113 ± 7.5</td>
<td>114 ± 10.8</td>
<td>0.562</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>66.0 ± 6.3</td>
<td>66.4 ± 6.4</td>
<td>0.672</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>81.6 ± 5.6</td>
<td>82.5 ± 6.4</td>
<td>0.573</td>
</tr>
<tr>
<td>TVR (dyne/s/cm⁵)</td>
<td>926 ± 213</td>
<td>947 ± 198</td>
<td>0.546</td>
</tr>
<tr>
<td>Ao (mm)</td>
<td>26.6 ± 3.1</td>
<td>27.0 ± 4.1</td>
<td>0.714</td>
</tr>
<tr>
<td>LA volume (mls)</td>
<td>38.6 ± 7.1</td>
<td>39.1 ± 9.7</td>
<td>0.740</td>
</tr>
<tr>
<td>Max-LVWT (mm)</td>
<td>10 ± 0.5</td>
<td>9.0 ± 2.0</td>
<td>0.392</td>
</tr>
<tr>
<td>LVED (mm)</td>
<td>46.0 ± 4.0</td>
<td>44 ± 5.0</td>
<td>0.264</td>
</tr>
<tr>
<td>LVES (mm)</td>
<td>28.0 ± 3.8</td>
<td>30.0 ± 4.4</td>
<td>0.357</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>106.4±17.5</td>
<td>106.7±22.3</td>
<td>0.949</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>38.5±11.0</td>
<td>41.1±10.8</td>
<td>0.305</td>
</tr>
<tr>
<td>Simpson EF (%)</td>
<td>62.4 ± 7.9</td>
<td>61.2 ± 7.9</td>
<td>0.534</td>
</tr>
<tr>
<td>SV (mls)</td>
<td>82.4 ± 12.9</td>
<td>80.2 ± 12.9</td>
<td>0.501</td>
</tr>
<tr>
<td>CO (L)</td>
<td>7.3 ± 1.6</td>
<td>7.2 ± 1.3</td>
<td>0.620</td>
</tr>
<tr>
<td>LVM (g/BSA)</td>
<td>89.5 ± 19.4</td>
<td>83.8 ± 20.8</td>
<td>0.229</td>
</tr>
<tr>
<td>RVID (mm)</td>
<td>33.0 ± 4.9</td>
<td>32.0 ± 5.5</td>
<td>0.720</td>
</tr>
<tr>
<td>RA volume (mls)</td>
<td>35.9 ± 9.6</td>
<td>35.9 ± 9.7</td>
<td>0.975</td>
</tr>
<tr>
<td>E (m/s)</td>
<td>0.88 ± 0.3</td>
<td>0.91 ± 0.2</td>
<td>0.602</td>
</tr>
<tr>
<td>A (m/s)</td>
<td>0.61 ± 0.5</td>
<td>0.54 ± 0.5</td>
<td>0.581</td>
</tr>
<tr>
<td>Decel Time (ms)</td>
<td>207 ± 74.0</td>
<td>186 ± 51.0</td>
<td>0.150</td>
</tr>
<tr>
<td>S’ septal</td>
<td>9.4 ± 1.3</td>
<td>9.4 ± 1.9</td>
<td>0.969</td>
</tr>
<tr>
<td>E’ septal (cm/s)</td>
<td>10.6 ± 2.9</td>
<td>10.0 ± 2.4</td>
<td>0.097</td>
</tr>
<tr>
<td>E/E’ (septal)</td>
<td>7.9 ± 2.8</td>
<td>7.6 ± 2.9</td>
<td>0.784</td>
</tr>
<tr>
<td>S’ lateral</td>
<td>11.6 ± 2.7</td>
<td>11.0 ± 2.5</td>
<td>0.317</td>
</tr>
<tr>
<td>E’ lateral (cm/s)</td>
<td>13.7 ± 3.8</td>
<td>14.0 ± 3.1</td>
<td>0.666</td>
</tr>
<tr>
<td>E/E’ (lateral)</td>
<td>6.2 ± 2.1</td>
<td>5.4 ± 1.8</td>
<td>0.084</td>
</tr>
</tbody>
</table>

‡Data expressed as mean ± SD

Abbreviations: Ao, aortic annulus diameter; BMI, body mass index; BSA, body surface area; CO, cardiac output; DBP, diastolic blood pressure; Decel Time, deceleration time; E, early diastolic mitral inflow velocity; A, later diastolic inflow velocity; E’, peak early diastolic mitral annular velocity of lateral and septal wall; E/E’, ratio of peak early diastolic mitral inflow velocity to peak early diastolic mitral annular velocity; EF, LV ejection fraction; HR, heart rate; LA, left atrial volume; LVED, LV end-diastolic diameter; LVEDV, LV end-diastolic volume; LVES, LV end-systolic diameter; LVESV, LV end-systolic volume; LVM, left ventricular mass; MAP, mean arterial pressure; Max-LVWT, maximal left ventricular wall thickness; RA, right atrial volume; RVID, basal right ventricular dimension; S’, systolic annular peak velocity; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.
**Table 3.** Demographic and serial echocardiographic data on the 6 subjects with persistent LV trabeculations in the post-partum period.\(^a\)

| Subject | Age (Yrs) | Ethnicity | Symptoms | Blood Pressure (mmHg) | ECG change | Max-LVWT (mm) | LVED (mm) | Simpson EF (%) | E/A | LV Trabeculations present | Chin ratio x/y during pregnancy | Chin ratio x/y post-partum (months) | Jenni NC/C ratio during pregnancy | Jenni NC/C ratio post-partum (months) | Jenni NC/C ratio 24 months post-partum | Distribution of LV Trabeculations at 24 months post-partum |
|---------|-----------|-----------|----------|-----------------------|------------|---------------|-------------|----------------|-----|-----------------------------|--------------------------------------|---------------------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------------|--------------------------------------------------|
| 1       | 34        | White     | No       | 120/70                | None       | 7             | 46          | 60             | 1.2 | Yes                         | 0.3                                   | 0.3                             | 0.5                             | 3.4                             | 3.1                             | 2.3                             | Apical Inferolateral                  |
| 2       | 38        | White     | No       | 110/62                | None       | 7             | 45          | 66             | 1.2 | Yes                         | 0.3                                   | 0.3                             | 0.4                             | 2.1                             | 1.6                             | 1.5                             | Apical Inferolateral                  |
| 3       | 36        | White     | No       | 100/64                | None       | 9             | 45          | 64             | 1.4 | Yes                         | 0.4                                   | 0.5                             | 0.6                             | 2.3                             | 2.0                             | 1.3                             | -                              |
| 4       | 38        | White     | No       | 116/68                | None       | 10            | 50          | 66             | 2.1 | Yes                         | 0.4                                   | 0.5                             | 0.5                             | 2.5                             | 2.3                             | 2.3                             | Mid-lateral & Apical lateral          |
| 5       | 21        | Black     | No       | 124/68                | None       | 10            | 50          | 70             | 1.7 | Yes                         | 0.5                                   | 0.5                             | 0.5                             | 2.2                             | 2.2                             | 2.0                             | Apical Inferolateral                  |
| 6       | 38        | Black     | No       | 130/72                | None       | 9             | 42          | 60             | 1.2 | Yes                         | 0.3                                   | 0.3                             | 0.3                             | 2.4                             | 2.3                             | 2.3                             | Mid-lateral & Apical lateral          |

\(^a\)Abbreviations: C, compacted; E/A, ratio of early to late diastolic mitral inflow velocity; EF, LV ejection fraction; HR, heart rate; LVED, LV end-diastolic diameter; Max-LVWT, maximal left ventricular wall thickness; NC, non-compacted
Table 4. Interobserver Intraclass Correlation Coefficients for First, Third Trimester and Post-partum echocardiograms.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>First Trimester (n=102)</th>
<th>Third Trimester (n=102)</th>
<th>Post-Partum (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ao (mm)</td>
<td>0.95 (0.92-0.98)</td>
<td>0.95 (0.90-0.97)</td>
<td>0.97 (0.94-0.98)</td>
</tr>
<tr>
<td>LA volume (mls)</td>
<td>0.95 (0.91-0.98)</td>
<td>0.96 (0.92-0.98)</td>
<td>0.97 (0.94-0.98)</td>
</tr>
<tr>
<td>Max-LVWT (mm)</td>
<td>0.79 (0.61-0.88)</td>
<td>0.87 (0.78-0.93)</td>
<td>0.87 (0.76-0.92)</td>
</tr>
<tr>
<td>LVED (mm)</td>
<td>0.81 (0.67-0.89)</td>
<td>0.74 (0.56-0.85);</td>
<td>0.89 (0.82-0.94)</td>
</tr>
<tr>
<td>Simpson EF (%)</td>
<td>0.60 (0.34-0.77)</td>
<td>0.86 (0.74-0.92)</td>
<td>0.70 (0.51-0.83)</td>
</tr>
<tr>
<td>CO (L)</td>
<td>0.81 (0.66-0.98)</td>
<td>0.87 (0.77-0.93)</td>
<td>0.70 (0.49-0.83)</td>
</tr>
<tr>
<td>RVID (mm)</td>
<td>0.97 (0.94-0.98)</td>
<td>0.94 (0.90-0.97)</td>
<td>0.95 (0.90-0.97)</td>
</tr>
<tr>
<td>RA volume (mls)</td>
<td>0.88 (0.78-0.94)</td>
<td>0.94 (0.89-0.97)</td>
<td>0.79 (0.65-0.88)</td>
</tr>
</tbody>
</table>

*Coefficients expressed with 95% confidence intervals

Abbreviations: Ao, aortic annulus diameter; CO, cardiac output; LA, left atrial volume; LVED, LV end-diastolic diameter; Max-LVWT, maximal left ventricular wall thickness; RA, right atrial volume; RVID, basal right ventricular dimension

Figure Legends:

Figure 1. Graphic representation of increased LV trabeculations and intertrabecular recesses on short axis echocardiographic views and interpretation criteria of Chin and Jenni criterion for LV non-compaction. Abbreviations: LV, left ventricle; X, distance from the epicardial surface to the trough of the intertrabecular recess; Y, distance from the epicardial surface to the peak of trabeculation.

Figure 2. 2-D echocardiographic example of a woman who developed de novo LV trabeculations during progression of pregnancy, which regressed in the postpartum period. Abbreviations: LV, Left ventricle.

Figure 3. 2-D echocardiographic example of one of 8 women who fulfilled both the Chin and Jenni criteria for non-compaction during the third trimester of pregnancy. Abbreviations: C,
compacted layer; NC, non-compacted layer; X, distance from the epicardial surface to the trough of the intertrabecular recess; Y, distance from the epicardial surface to the peak of trabeculations.
Figure 1

Definition of Increased LV Trabeculation
> 3 trabeculations measuring >3mm in diameters

Diagnostic criteria for LVNC
(A) Jenni Criteria
1) 2-layered structure with a compacted epicardial (C) and non-compacted endocardial layer (NC)
2) NC/C ratio > 2 at end-systole
3) Colour Doppler evidence of Intertrabecular Recesses supplied by intraventricular blood
4) Absence of co-existing cardiac structural abnormalities

(B) Chin
1) 2-layered structure with an epicardial compacted and endocardial non-compacted layer
2) X/Y ratio ≤ 0.5 at end-diastole
8% Pregnant Women in the Third Trimester Fulfilled Both Chin and Jenni Criteria For LVNC

Systole NC/C > 2

Diastole XY < 0.5
Reversible De Novo Left Ventricular Trabeculations in Pregnant Women: Implications for the Diagnosis of Left Ventricular Non-Compaction in Low Risk Populations
Sabiha Gati, Michael Papadakis, Nikolaos D. Papamichael, Abbas Zaidi, Nabeel Sheikh, Matthew Reed, Rajan Sharma, Baskaran Thilaganathan and Sanjay Sharma

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