(LVHT), the recognition of NCVM is frequently delayed.\(^3\)\(^-\)\(^6\)

(ii) In 1990, Chin \textit{et al.}\(^2\) introduced diagnostic criteria for NCVM, including the X/Y ratio taken at the mentioned three ventricular levels.\(^2\) The subsequent introduction of both a competitive (N/C) ratio\(^6\) and a new non-specific term (LVHT) was confusing. Others and we realized that measurements taken in diastole enhance diagnostic specificity. In paediatrics, the mitral valve and papillary muscles are not usually areas with poor echocardiographic windows. False tendons or aberrant bands are easily discriminated against NCVM (numerous trabeculations, deep recesses, two-layered myocardium). There was no investigator disagreement on NCVM criteria.

(iii) Most previous studies exclusively addressed isolated NCVM (i-NCVM). But NCVM accompanies diverse forms of structural congenital heart disease (CHD).\(^4\)\(^,\)\(^5\) There is initial evidence that NCVM subgroups may be different in several regards.\(^5\) We attempted to characterize i-NCVM and non-isolated NCVM (ni-NCVM) in regard to cardiovascular complications. Surprisingly, the outcome was similarly poor. Structural CHD is well defined. ECG abnormalities or relative valve insufficiencies certainly do not qualify. Besides the defects stated, ni-NCVM comprised atrial and atrioventricular septal defects, anomalous pulmonary venous connections, atrial isomerism, Ebstein’s anomaly, tricuspid atresia, left ventricle (LV)-aortic tunnel, persistent ductus, and double aortic arch.

(iv) Not attempting a study on all aspects of NCVM, the investigation of genetic or neuro-muscular disorders was not included in our protocol. We introduced examples of the presumably heterogeneous genetic background, since some gene mutations were exclusively found in i-NCVM but not in ni-NCVM and vice versa.

(v) ECG abnormalities comprised bundle branch block, supraventricular and ventricular tachycardia, 5T-segment depression, and abnormal T waves. Patients presented for heart murmurs, failure to thrive, excessive sweating, exercise intolerance, palpitations, (pre-) syncope, and suspected or known CHD or a positive family history, among others. Reduced systolic function or ventricular dilation (56.3 and 50.0\% of patients at follow-up, respectively) was subsumed within the described CHF score. The anticoagulative therapy comprised digoxin, diuretics, ACE-inhibitors, and beta-blockers. Seven patients presented with a hypertrophied non-obstructive LV.

Coronary abnormalities commonly associated with right ventricular outflow obstruction were seen in four ni-NCVM patients. Coronary abnormalities affecting the LV function were not found. Follow-up data on six patients (9.1\%) were incomplete. Neither localization nor degree of non-compaction changed during follow-up in any patient. However, NCVM was missed in several patients on previous presentations.

References


between those with and without PAH is questionable, as the effect of therapy upon N-TproBNP levels is not known. Further, although the cutoff value of 395 pg/mL was derived from a prior study, this value was not adjusted for age and gender, which have been shown to influence absolute levels of measured natriuretic peptides. Additionally, recent evidence suggests that an inverse relationship between obesity and N-TproBNP exists. No adjustment for body mass index was performed.

Co-morbidities such as coronary artery disease may affect N-TproBNP levels. There appears to be differential assessment of the cases and controls as only the controls were required to undergo left heart catheterization to evaluate any possible coronary disease. Since elevation of BNP levels may occur in pre-clinical coronary heart disease not seen on echocardiography, the difference in N-TproBNP levels between cases and controls may be exaggerated by concomitant elevations due to undocumented coronary disease.

Finally, the analysis was not controlled for patients with interstitial lung disease associated with scleroderma (SSc-ILD). Although 'significant' ILD was an exclusion criterion for the study, a higher proportion of patients with evidence of SSc-ILD were included in the SSc-PAH group. It is unknown whether ILD may influence N-TproBNP levels independent of pulmonary hypertension. Further, the higher proportion of patients in the PAH group with ILD may bias the survival analysis. Our experience shows that patients with pulmonary hypertension related to SSc-ILD have much worse survival compared with those with PAH related to scleroderma.

References


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N-terminal brain natriuretic peptide in scleroderma-associated pulmonary arterial hypertension: reply

We read with interest the comments of Mathai and Hassoun, and agree that caution is required in using an NTproBNP level of 395 pg/mL to discriminate between those with scleroderma-associated pulmonary arterial hypertension (SScPAH) and those without this complication. The purpose of the study was to evaluate this level that had been determined in our previous study.

Given the consistency of our findings, we are now in the process of performing a much larger screening trial, to determine whether this threshold level is useful. The threshold level we identified (395 pg/mL) is substantially higher than that used in heart failure trials and is therefore less influenced by non-specific elevations seen with age and BMI, however, these issues will be addressed in the definitive study.

We have already evaluated the usefulness of clinical assessment in determining the prevalence of coronary disease in patients with scleroderma, and are therefore relatively confident that this is not a significant cause of non-specific elevations of NTproBNP in either population. We read with interest their experience in ILD-associated SscPAH. Our experience has been that although the response to therapy is less dramatic, the prognosis is not significantly different.  

We feel that the most important observation from this study is that 10-fold changes in NTproBNP during therapy are the strongest independent predictor of survival, and thus provides a potential rationale for goal-directed therapy.