VOL. 11, NO. 7, 2018
ISSN 1936-878X/$36.00

iMAIL

LETTERS TO THE EDITOR

Müller Maneuver as a Tool for Stress Echocardiography

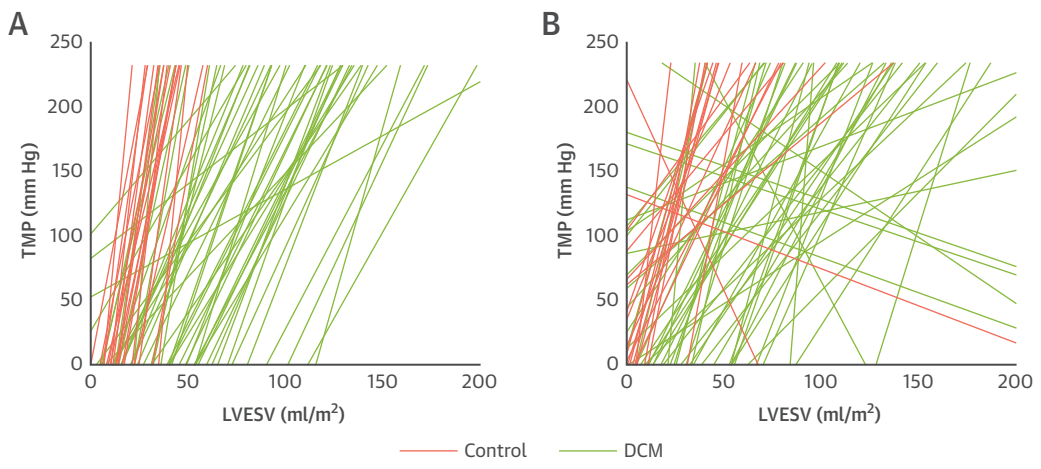
Evaluation of Exercise Capacity in Patients With Dilated Cardiomyopathy

The Müller maneuver (MM) has been incorporated as one of the physiologic, low-intensity stresses tests. Increasing negative intrathoracic pressure during MM causes an increase in left ventricular (LV) transmural pressure (TMP) (1), which theoretically acts as an elevated LV afterload. This study aimed to evaluate the utility of MM for stress echocardiography in patients with dilated cardiomyopathy (DCM) by analyzing the changes in LV end-systolic volume (ESV) during MM in relation to estimated LV end-systolic elastance (Ees) and exercise capacity.

Fifty consecutive patients (n = 36 men; mean age 57 ± 14 years) with DCM and 20 healthy subjects (n = 20 men; mean age 31 ± 5 years) underwent echocardiography and cardiopulmonary exercise testing. This study was approved by the ethics committee and informed consent was obtained from all subjects. The MM was repeated 5 times with mouth pressure of −20 to −40 mm Hg for 10 s. Instantaneous blood pressure was monitored by finger plethysmography to calculate instantaneous TMP as the sum of absolute values of intraoral pressure and systolic blood pressure × 0.9. Echocardiographic images were acquired at 3 different time points for each MM: 1) pre-MM; 2) the early phase of MM, that is, the first or second beat after the onset of MM; and 3) the middle phase of MM, that is the fifth beat after the onset of MM. Simultaneous biplane echocardiography was used to acquire apical 4-chamber and 2-chamber views. All subjects performed a standard symptom-limited, cycle ergometer-based, maximal exercise test to obtain peak oxygen uptake (VO_2). Ees was estimated noninvasively (2). Continuous variables were compared using the Mann-Whitney *U* test. LVESV against TMP was plotted for each patient to obtain the r value by Spearman's correlation coefficient and slope by univariate linear regression. Correlations of the slope with estimated Ees and peak VO_2 were also assessed using Spearman's correlation coefficient. A multivariate linear regression model was used to evaluate the determinant of peak VO_2. A value of $p < 0.05$ was considered statistically significant.

In the early phase of MM, the slope between LVESV and TMP showed a similar trend in each group (Figure 1A) and was significantly lower in patients with DCM than in healthy subjects (3.9 ± 2.0 mm Hg/ml/m^2

FIGURE 1 Plots of LVESV and TMP During MM



Plots of LVESV and TMP in healthy subjects **(pink lines)** and patients with DCM **(green lines)** in the **(A)** early and **(B)** middle phases of MM. DCM = dilated cardiomyopathy; LVESV = left ventricular end-systolic volume; MM = Müller maneuver; TMP = transmural pressure.

vs. 9.5 ± 2.8 mm Hg/ml/m^2; $p < 0.001$). This slope between LVESV and TMP significantly correlated with estimated Ees ($r = 0.81$) and peak VO_2 ($r = 0.82$; both $p < 0.001$). Multivariate analysis revealed that the slope in the early phase of MM was the determinant of peak VO_2 (standardized $\beta = 0.73$; $p < 0.001$). In contrast, the results were scattered in the middle phase of MM (**Figure 1B**). There was no significant difference in the slope between the 2 groups (3.2 ± 3.8 mm Hg/ml/m^2 vs. 4.3 ± 3.8 mm Hg/ml/m^2; $p = 0.3$). The slope in the middle phase of MM was not associated with estimated Ees ($r = 0.24$; $p = 0.05$) or peak VO_2 ($r = 0.13$; $p = 0.3$). R values in the individual slope were 0.84 ± 0.12 at early phase and 0.51 ± 0.36 at middle phase, respectively.

In 25 patients and 10 healthy subjects who had both simultaneous biplane echocardiography and 1-beat real-time 3-dimensional echocardiography (RT3DE), the results of MM stress echocardiography with RT3DE (the slope) significantly correlated with estimated Ees ($r = 0.75$; $p < 0.001$) and peak VO_2 ($r = 0.76$; $p < 0.001$).

Previous studies using MM as a simulation of obstructive apnea strongly suggest the presence of sequential changes in LV pre-load (3), and sympathetic nerve activity during MM (4). Earlier timing of measurements during MM may be preferable for assessing Ees and exercise capacity, while minimizing the interference from confounding factors. Reproducibility of MM varies depending on the patient. Volume measurement allowed us to calculate the slope between LVESV and TMP during MM, which can minimize the possible effect of the low reproducibility of MM on the results. However, it was not investigated whether the MM stress echocardiography can apply to other cardiac diseases or predict long-term outcomes, which may be clarified by future improvement of the feasibility of RT3DE. This is the first study to show the utility of MM as a tool for stress echocardiography in the evaluation of Ees and exercise capacity in patients with DCM. This method provides quantitative measurement which may be helpful for serial assessment of disease progression and guidance of therapy.

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https://doi.org/10.1016/j.jcmg.2017.10.005

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Topographic Pattern of Valve Calcification

A New Determinant of Disease Severity in Aortic Valve Stenosis

The pathophysiology of degenerative aortic valve stenosis (AS) is intimately related to the development of calcific deposits in the valve structure. Multidetector computed tomography (MDCT), a reliable method to delineate the tridimensional heart geometry, has been shown to accurately quantify the global aortic valve calcium content (1). Currently, the relationship between calcium location and hemodynamic disease severity is poorly understood (2). The present prospective study was conducted to test the hypothesis of whether the location of valve calcification influences the functional severity of AS.