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Physiological Determinants of Left Ventricular Mechanical Dispersion

A 2-Dimensional Speckle Tracking Echocardiographic Study in Healthy Volunteers

Two-dimensional speckle-tracking echocardiography enables the examiner to measure the timing of segmental myocardial shortening and its synchronicity by mechanical dispersion (MD). Prolonged MD reflects increased temporal heterogeneity of myocardial contraction and has been reported to be useful to stratify arrhythmic risk among patients with different cardiac conditions (1–3). Nonetheless, the physiological determinants of MD have not been comprehensively studied, and reference values for this parameter remain to be determined. Accordingly, a cross-sectional observational study was performed at the University of Padua (Padua, Italy) and Oslo University Hospital (Oslo, Norway). We included 334 white healthy volunteers without cardiovascular risk factors to establish reference values for this parameter and to determine how demographic, physiological, and hemodynamic parameters and echocardiographic image quality may affect MD values. All patients had normal physical examinations, electrocardiograms, and echocardiographic examinations. The study was approved by the University of Padua Ethics Committee (protocol #2380 P, approved on June 10, 2011) and the Regional Committee for Medical Research Ethics in Norway (#S-05376). MD was defined as the SD of the time from the peak of the R wave on the electrocardiogram to the peak negative strain using a 16-segment left ventricular model obtained from 3 optimized apical views for speckle-tracking echocardiography analysis with a frame rate between 50 and 80 frames/s. All calculations of MD and global longitudinal strain (GLS) were done using a commercially available software package (EchoPAC version BT113, GE Vingmed Ultrasound, Horten, Norway); post-systolic peaks were included, and the system pre-set spatial and temporal smoothing was not modified.

TABLE 1 Reference Values for Mechanical Dispersion Across Age Decades

		Age Groups (yrs)					
	Overall (N = 303)	18-30 (n = 63)	31-40 (n = 71)	41-50 (n = 67)	51-60 (n = 51)	>60 (n = 51)	p Value
MD, ms	34 ± 10	29 ± 8	30 ± 9	34 ± 10	37 ± 10	41 ±10	<0.001
ULN	56	49	50	55	64	64	<0.001

Values are mean ± SD. The p value refers to age group differences on analysis of variance.
MD = mechanical dispersion; ULN = upper limit of normal (97.5th percentile).

In our cohort, the median age was 42 years (range 18 to 79 years), 54% of the patients were female, body mass index was 23 ± 3 kg/m^2, left ventricular ejection fraction was 63 ± 7%, and GLS was −20.6 ± 2.2. MD was feasible in 96% of our subjects. Intraobserver and interobserver correlation coefficients were 0.95 (95% confidence interval: 0.89 to 0.98) and 0.94 (95% confidence interval: 0.88 to 0.98), respectively. MD did not differ between men and women or among the 4 image quality datasets (excellent, good, average, poor) ($p = 0.39$). However, MD values increased significantly with age (Table 1).

On bivariate analysis, MD showed correlation with image temporal resolution ($r = 0.16$; $p = 0.01$) and with GLS ($r = -0.39$; $p < 0.001$). Systolic blood pressure showed a tendency to correlate with MD ($r = 0.11$; $p = 0.06$). Age showed the strongest correlation with MD ($r = 0.43$; $p < 0.001$). Conversely, we did not find any correlation of MD with diastolic blood pressure ($p = 0.2$), sex ($p = 0.79$), end-diastolic volume index ($p = 0.94$), end-systolic volume index ($p = 0.95$), left ventricular ejection fraction ($p = 0.57$), heart rate (0.34), or image quality score ($p = 0.8$).

By using linear regression analysis, age, systolic blood pressure, body mass index ($p = 0.004$), early to late diastolic transmitral flow velocity (E/A ratio) ($p < 0.001$), E to early diastolic mitral annular tissue velocity (E/e′) ratio ($p = 0.007$), and GLS ($p < 0.001$) were found to be significant correlates of MD. Significant variables were entered in the multivariate regression analysis, after which only age ($p < 0.001$), GLS ($p < 0.001$), and E/e′ ratio ($p = 0.007$) were found to be independent correlates of MD, and together they accounted for 23% of its variability.

Given that aging leads to an increase in interstitial collagen deposition, and GLS and MD have been shown to correlate with myocardial fibrosis (1,4), it is plausible that increasing age leads to a progressive rise in MD. Accordingly, specific reference values for MD are provided, thus aiming to foster its application into clinical practice and expand its presence in the research arena. Further studies are needed to show whether age-specific reference values for MD may further improve arrhythmic risk stratification of patients and whether MD may be also a predictor of death or heart failure because it seems to reflect interstitial fibrosis.

Hugo Rodríguez-Zanella, MD
Kristina Haugaa, MD, PhD
Francesca Boccalini, MD
Eleonora Secco, MD
Thor Edvardsen, MD, PhD
Luigi P. Badano, MD, PhD
Denisa Muraru, MD, PhD*

*Department of Cardiac, Thoracic, and Vascular Science
University of Padua
Via Giustiniani 2
35128 Padua
Italy
E-mail: denisa.muraru@gmail.com

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Clinical Significance of Right Ventricular Longitudinal Function Parameters After Aortic Valve Replacement

Changes in parameters of longitudinal systolic function after cardiac surgery (i.e., tricuspid annular plane systolic excursion [TAPSE] and peak systolic velocity [PSV] of tricuspid annulus obtained by M-mode or Doppler tissue imaging) have been described for many years, with almost no data on their clinical significance (1,2). We aimed at investigating, in a large prospective cohort, the natural course and long-term clinical significance of early alterations in right ventricular (RV) longitudinal function after aortic valve replacement (AVR) for aortic stenosis. We hypothesized that long-term prognosis after AVR would be the worst in patients with the lowest post-operative RV longitudinal function.

Between January 2009 and December 2015, we prospectively explored all consecutive patients referred to our heart valve clinic for AVR who presented with severe aortic stenosis, normal left ventricular ejection fraction (>50%), and TAPSE (>14 mm). Patients with another significant valvular disease, a medical history of previous cardiac surgery, or congenital heart diseases were excluded. TAPSE and PSV were assessed by transthoracic echocardiography 7 days after cardiac surgical procedures for all patients and 1 year after AVR in a subgroup of 100 patients. Patients were followed for major events (ME), defined as cardiovascular death, cardiac hospitalization, acute heart failure, and stroke. Events were adjudicated by 2 independent blinded investigators. The local ethics committee approved the protocol, and patients gave informed consent.

We hypothesized a rate of ME at 5 years of 15% in the quartile of patients with the highest post-operative TAPSE and a rate of 30% in the quartile of patients with the lowest post-operative TAPSE (3,4). This hypothesis implied that we had to analyze outcomes in at least 544 patients (i.e., 136 per quartile) to obtain a statistical power of 90% and a probability of a type I error of 0.05. Continuous variables were given as mean ± SD. One-way analysis of variance was used for repeated measure with the Bonferroni post hoc paired Student's *t* test. Time-related clinical events were plotted with Kaplan-Meier curves according to quartiles of RV function parameters and were compared with log-rank tests for trend. A value of $p < 0.05$ was considered statistically significant. Statistics were performed using MedCalc software version 16.4 (MedCalc, Ostend, Belgium).

Among 805 consecutive patients referred for first AVR, 617 patients were included and followed for prognosis. In these patients, the mean age was 71 ± 10 years. The population was 54% male, and one-third of the participants had diabetes. One-third underwent concomitant coronary artery bypass graft operation, and 80% received a biological prosthesis. As expected, TAPSE and PSV were both clearly decreased 7 days post-operatively (13.5 ± 3.8 mm vs. 22.1 ± 4.6 mm at baseline; $p < 0.0001$; and 8.4 ± 2.3 cm/s vs. 11.9 ± 3.0 cm/s at baseline; $p < 0.0001$, respectively), with an incomplete but significant recovery to pre-operative values 1 year after AVR in the subgroup with serial transthoracic echocardiography ($p < 0.0001$ for both). In these patients, who did not differ significantly from the entry population (data not shown), TAPSE was 23.5 ± 4.0, 13.0 ± 3.1, and 18.4 ± 3.5 mm, and PSV was 12.9 ± 3.0, 7.7 ± 2.0, and 9.5 ± 2.0 cm/s, respectively before, 7 days after, and 1 year after AVR.

The mean post-operative follow-up was 4.0 ± 2.3 years (median 4 years; range 1.9 to 6.1 years) for the 617 patients. ME occurred in 95 patients (15.5%), with 33 cardiovascular deaths, 71 cardiac hospitalizations, 36 cases of acute heart failure, and 38 strokes. No association was found between post-operative TAPSE values and ME occurrence as a whole (**Figure 1A**) or taken individually (data not shown).