Normal Ranges of Left Ventricular Strain: A Meta-Analysis

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Background: The definition of normal values of left ventricular global longitudinal strain (GLS), global circumferential strain, and global radial strain is of critical importance to the clinical application of this modality. The investigators performed a meta-analysis of normal ranges and sought to identify factors that contribute to reported variations.

Methods: MEDLINE, Embase, and the Cochrane Library database were searched through August 2011 using the key terms "strain," "speckle tracking," "left ventricle," and "echocardiography" and related phrases. Studies were included if the articles reported left ventricular strain using two-dimensional speckle-tracking echocardiography in healthy normal subjects, either in the control group or as a primary objective of the study. Data were combined using a random-effects model, and effects of demographic, hemodynamic, and equipment variables were sought in a meta-regression.

Results: The search identified 2,597 subjects from 24 studies. Reported normal values of GLS varied from −15.9% to −22.1% (mean, −19.7%; 95% CI, −20.4% to −18.9%). Normal global circumferential strain varied from −20.9% to −27.8% (mean, −23.3%; 95% CI, −24.6% to −22.1%). Global radial strain ranged from 35.1% to 59.0% (mean, 47.3%; 95% CI, 43.6% to 51.0%). There was significant between-study heterogeneity and inconsistency. The source of variation was sought between studies using meta-regression. Blood pressure, but not age, gender, frame rate, or equipment, was associated with variation in normal GLS values.

Conclusions: The narrowest confidence intervals from this meta-analysis were for GLS and global circumferential strain, but individual studies have shown a broad range of strain in apparently normal subjects. Variations between different normal ranges seem to be associated with differences in systolic blood pressure, emphasizing that this should be considered in the interpretation of strain. (J Am Soc Echocardiogr 2013;26:185-91.)

Keywords: Strain, Meta-analysis, Normal range, Echocardiography

Recent developments in speckle-tracking echocardiography have enabled the quantitative assessment of myocardial function via image-based analysis of myocardial dynamics.[1] Important applications of this technique include global assessment of left ventricular (LV) function using global longitudinal strain (GLS), global radial strain (GRS), and global circumferential strain (GCS)[2,3] and regional assessment including measurement of the transmural distribution of strain,[4] assessment of radial synchrony,[5] and tissue characterization.[6] Speckle-tracking echocardiographic measurement of these parameters has been validated against sonomicrometry[7] and magnetic resonance imaging.[8]

The routine application of myocardial strain in clinical practice requires the definition of a normal range and an understanding of its reliability; each aspect is specific to the application as a marker of global or regional function, in each image plane (longitudinal, circumferential, and radial). A variety of parameters might potentially influence the measurement of strain, including features specific to patients (age, gender, race, ethnicity, anthropometric variables), hemodynamic factors (heart rate, blood pressure), and cardiac factors (LV size, wall thickness).[9] One cause for concern is the variation in recorded measurements among different vendors due to proprietary differences in the software used to calculate deformation.[10] Because GLS is the simplest deformation parameter, and probably the closest to routine clinical application, we sought to define its normal range by providing a synthesis of all studies that reported normal or control patients. We also sought to evaluate the role of the vendor as a contributor to variation among reported normal ranges, particularly in relation to other sources of variation.

METHODS

Search Strategy

We searched MEDLINE, Embase, and the Cochrane Library database using the key terms "strain," "speckle tracking," "echocardiography," and "left ventricle," completing this search on August 8, 2011. To ensure the identification of all relevant trials, the reference lists of

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Abbreviations

GCS = Global circumferential strain

GLS = Global longitudinal strain

GRS = Global radial strain

LV = Left ventricular

ROI = Region of interest

these articles were scrutinized to further identify studies pertinent to the topic. The search was limited to adult human studies published in English; abstracts without full text, review articles, editorial comments, and letters to the editor were excluded. The search strategy, study selection, and analysis adhered to Quality of Reporting of Meta-Analyses guidelines.[11]

Study Selection

From these lists, studies were included if the articles reported LV strain using two-dimensional speckle-tracking echocardiography in healthy normal subjects. This review incorporates both observational studies that used control groups with normal results on echocardiography (which may have been obtained for patients referred to the echocardiography laboratory who therefore could have had subclinical dysfunction), as well as studies explicitly describing the recruitment of normal subjects from the community.

Data Collation

Clinical, echocardiographic, and strain data were extracted from individual studies by one author (T.Y.), verified by a second (T.H.M.), and entered into an electronic database. Where available, these data included group numbers and demographic, clinical, and echocardiographic data. Mean GLS, GRS, and GCS were extracted from the text, tables, or graphs. In situations in which we believed that multiple articles were published from a single data set, the largest study was assessed.

Statistical Analysis

The means and 95% CIs of GLS, GCS, and GRS were computed using random-effects models weighted by inverse variance.[12] Between-study heterogeneity was assessed using Cochran's Q test (on the basis of the pooled RR by Mantel-Haenszel), as well as by measuring inconsistency (I^2, the percentage of total variance across studies attributable to heterogeneity rather than chance).[13] Because a number of important variables that influence strain differed among studies, we performed a regression using a general linear model to assess their influence on the variation in normal strain measurements. Statistical analysis was performed using standard software packages (Stata version 10.0, StataCorp LP, College Station, TX; and Comprehensive Meta-Analysis, Biostat, Englewood, NJ), with two-tailed P values $< .05$ considered significant.

RESULTS

Study Selection

In total, 201 titles were screened for relevance, of which there were 28 valid studies of GLS in a total of 2,597 subjects, from which 24 articles were considered eligible (Figure 1). From 24 articles, 13 articles (14 studies) with a total of 599 patients were eligible for the meta-analysis of GCS and 12 articles with 568 patients for GRS. The patient characteristics of the included studies are listed in Table 1.[14-36]

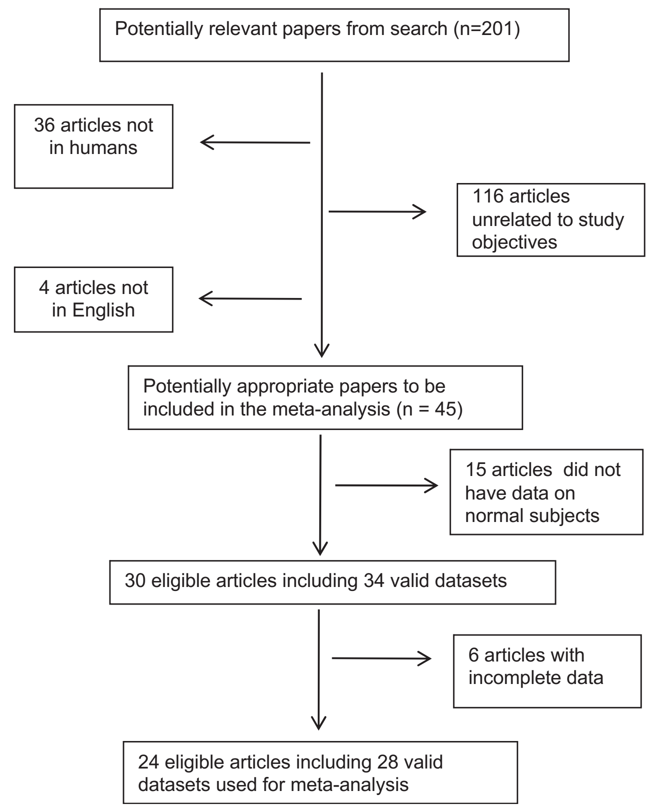

Figure 1 Study design. This flow chart illustrates the selection process for published reports.

Normal Ranges

Reported normal values of GLS (Figure 2) varied from −15.9% to −22.1% (mean, −19.7%; 95% CI, −20.4% to −18.9%). Between-study heterogeneity was evidenced by a Cochran's Q statistic of 1,935 ($P < .0001$) and inconsistency by an I^2 value of 99. Normal GCS (Figure 3) varied from −20.9% to −27.8% (mean, −23.3%; 95% CI, −24.6% to −22.1%). GRS (Figure 4) ranged from 35.1% to 59.0% (mean, 47.3%; 95% CI, 43.6% to 51.0%). Both GCS and GRS showed between-study heterogeneity and inconsistency, similar to that of GLS. The funnel plot of all selected 25 articles showed no publication bias (Figure 5).

Causes of Variability

Age (47 ± 11 years), male gender (51 ± 24% men), body mass index (24.3 ± 1.6 kg/m^2), systolic blood pressure (124 ± 5 mm Hg), frame rate (66 ± 13 frames/sec), and equipment vendor were considered the variables most likely to influence GLS (Table 2). In a general linear model, only mean blood pressure was independently associated with higher values of strain. Vendor was not significantly associated with mean absolute GLS, and GLS in normal patients, assessed in 23 data sets using EchoPAC software (GE Healthcare, Milwaukee, WI), was no different from the measurement in five data sets using non-EchoPAC software (−19.65 ± 1.78% vs −19.67 ± 1.80%, $P = .98$).

DISCUSSION

This is the first synthesis of the literature on the normal range of global strain. Although it emphasizes the association of strain with systolic blood pressure, differences in vendor and other variables shown to