Assessment of regional timing of left ventricular systolic longitudinal movement by Doppler tissue synchronization imaging in structurally normal hearts

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Abstract  Aims: To study the feasibility of a new semiautomatic echocardiographic modality called Tissue Synchronization Imaging (TSI) for measurement of the longitudinal left ventricular (LV) movement.

Methods and results: TSI was used in 20 subjects with structurally normal hearts to measure the time aspect of the regional longitudinal LV systolic movement in the apical four chamber view. Inter- and intraobserver agreement and the beat to beat variation were tested and compared to previously manually measured peak systolic delay (PSD) between the interventricular septum (IS) and the lateral free wall (LFW) at basal and mid LV, respectively (n=19). TSI showed acceptable reproducibility and close correlation to manually measured PSD. The TSI method did not show false synchronous regional LV movement when synchrony was defined as a PSD $\leq 25$ ms. After minor adjustment of the TSI interval, 76.9% of the synchronous LV patterns in basal LV were correctly classified as compared to manual measurements.

Conclusions: The TSI method is accurate for clinical screening to reveal synchrony. At the present development the TSI method is not accurate enough to quantify regional systolic LV asynchrony, and still manual measurement of PSD is mandatory.

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Introduction

In several studies the new myocardial tissue Doppler modalities including tissue velocity imaging (TVI), Strain Imaging and Strain Rate Imaging have been used in different settings to study myocardial contractility.\(^1\)–\(^3\) Especially in ischemic heart disease the methods are accurate for quantification of regional myocardial function\(^4\) and for assessment of myocardial viability.\(^5\),\(^6\) Recent development of the tissue Doppler modalities providing high time resolution of \(<10\) ms and the increasing interest concerning the hemodynamic importance of the time aspects of LV myocardial contraction in patients with severe heart failure (HF),\(^7\) have increased the importance of these methods both in research and clinical practice.

The inter- and intraventricular systolic asynchronous contraction may deteriorate the impaired systolic LV function in HF patients. Cardiac resynchronization therapy (CRT) effected by biventricular cardiac pacing of both right ventricle and LV is a new electrical therapy which can provide a significant clinical improvement in approximately 70\% of patient population with severe HF accompanied by bundle branch block.\(^8\) One of the suggested mechanisms for explaining the hemodynamic effects of CRT is resynchronization of the intraventricular LV contraction during isovolumic contraction (IVC) and during ejection. Both the baseline asynchronous LV contraction and the resynchronization by CRT can be disclosed by using color-TVI (c-TVI)\(^9\),\(^10\) or Strain Rate Imaging.\(^11\) So far the assessment of the timing of regional LV movement by using c-TVI has been performed by manual analysis incorporating, either the measurement c-TVI velocity peaks in correlation to the onset of QRS complex in the simultaneously recorded ECG,\(^9\) or by measuring the absolute time difference of regional LV peak velocities.\(^10\) In human subjects with structurally normal hearts and normal ECGs synchronous regional LV contraction has been documented by using c-TVI\(^12\) and a significant asynchronous LV contraction in HF patients with bundle branch block as compared to subjects with structurally normal hearts.\(^13\) Occurrence of left bundle branch block in the ECG has hitherto been used as an electrical surrogate for mechanical LV asynchronous contraction in patients with severe HF. The demonstration of LV asynchronous contraction even in HF patients with normal QRS width\(^14\) call for another method than ECG to show mechanical asynchronous LV contraction in patients with severe HF and bundle branch block who are potential candidates for CRT.

The objective of the present study was to test the feasibility of a new semiautomatic TSI algorithm to disclose synchronous longitudinal LV contraction in subjects with structurally normal hearts. The study subjects had a synchronous regional LV contraction pattern defined as a PSD between the interventricular septum and lateral free wall movement in basal and mid LV segments \(<\pm 10\) ms measured by a manual method for post processing c-TVI images. This manual method has been described in detail from our laboratory.\(^12\)

Material and methods

Patients

Post processing of routinely recorded echocardiographic images was performed after approval and informed consent in 11 females and nine males (mean age 44 ± 17 years) with no structural heart disease. All subjects had normal sinus rhythm and normal QRS morphology with a QRS duration of average 86 ± 12 ms measured from the surface ECG. The echocardiographic measurements of ejection fraction and LV diameters were normal.\(^12\)

Echocardiographic methods (Figs. 1 and 2)

A digital ultrasound machine with combined phased array transducer, providing tissue, spectral and color Doppler images was used (System FiVe, GE Vingmed Ultrasound, Horten, Norway). At frame rates close to 100 frames per second (fps) c-TVI data were recorded in the apical four-chamber view with the subjects in the left lateral recumbent position. The post processing procedure was performed by using a dedicated computer (EchoPAC-PC, version 3.0.x, GE Vingmed Ultrasound). C-TVI profiles were examined using a 6 × 18 mm LV midwall region of interest. The heart rate during the examination was measured from the simultaneously recorded electrocardiogram.

For manually assessment of the regional time aspect of the longitudinal LV movement pattern, the first occurring systolic c-TVI peak was used to measure the PSD (TVI-PSD) between the interventricular septum and the lateral free wall, at basal and mid-LV levels, respectively. The occurrence of regional time difference of systolic c-TVI peaks within \(±25\) ms, i.e. TVI-PSD less than \(±25\) ms between interventricular septum and lateral free wall was defined as true synchronous regional LV
Figure 1  Example of basal peak systolic delay (TSI-PSD) calculation. TSI recording, automatic TSI-PSD measurement at two basal and two mid left ventricular (LV) segments (upper left box).

Figure 2  Example of basal peak systolic delay (TVI-PSD) calculation. Left panel: Tissue velocity cineloop and grey scale picture in apical four chamber view. Right panel: Tissue velocity profiles: yellow and red line = interventricular septum; green and blue line = lateral free wall. TVI-PSD: difference between yellow and blue systolic peak appearance (red asterisk). Green asterisk: biphasic systolic peak in the red TVI profile, second peak higher than first.
contraction in this study. 25 ms as a cut off value is based on the manual findings of less than $\pm$ 10 ms mean difference in the structurally normal heart, adding the inaccuracy of the method 10 ms (because of the frame rate of 100 fps) and an additional 5 ms margin.

The semiautomatic measured TSI interval started after a delay of 60 ms from the peak R of the detected QRS. This delay was automatically set by the ultrasound machine and the end of TSI measurement was set to 200 ms after end-systole. The time interval to end-systole from the onset of QRS was calculated automatically in ms according to the formula $400 \pm 1.25 \times$ heart rate (beats/min).

For the semiautomatic TSI measurement of PSD (TSI-PSD), the exclusion of c-TVI peaks during IVC is mandatory. The accuracy of the automatic TSI to exclude the IVC peak velocities was tested by manually measurement of the time delay from IVC velocity peaks (mean of basal IS and LFW IVC peak) to the start of TSI measurement in the basal LV segments.

In the first automatic approach the measurement of TSI-PSD was performed using the default start delay of TSI of 60 ms from the onset of QRS. In each LV midwall site, the time to peak tissue velocity was measured using the default circular sampling region of interest with 5 mm radius, placed midwall. The measurement tool reported the median value within this measurement region. In the second semiautomatic approach, the occurrence of a second systolic TVI peak (biphasic systolic peaks) in the c-TVI velocity profile resulted in a TSI interval adjustment. The end of the TSI interval was set to the first minimum of the TVI profile after the first systolic c-TVI peak.

For assessment of interobserver and intraobserver agreement the mean values of the TSI-PSD for two cardiac cycles were used. The post-processing procedure was performed twice at an interval of at least ten days by observer 1 and the TSI measurements were also performed once by observer 2 in 10 random patients.

The previously described manually measured synchrony of the LV movement pattern during systole was compared to the TSI-PSD, comparing the mean of two consecutive beats, after examining the beat to beat variability of TSI-PSD. A TSI-PSD $< \pm 25$ ms was considered a synchronous contraction pattern.

For evaluating the TSI method concerning the sensitivity and specificity of the TSI-PSD for disclosure of synchrony was compared to the previously published TVI-PSD method, which is the best available method to compare to so far.

Statistics

The data are expressed as mean values and standard deviations. If not mentioned otherwise the data from the corrected TSI interval measurements are described. The statistical methods used were Bland-Altman agreement statistics, the Student’s $t$-test for parametric, the Wilcoxon signed ranks or Sign test for non-parametric data, and the Pearson linear correlation, as appropriate. A $P<0.05$ was considered statistically significant.

Results

All subjects had acceptable echocardiographic recordings for analysis. During the echocardiographic study the heart rate was $71\pm14$ beats/minute and the c-TVI frame rate was $102\pm11$ fps. One subject had an insufficient ECG recording and therefore had to be excluded from TSI measurements. One subject had a poorly defined c-TVI profile in mid LV which was not included in the analysis.

TSI interval

The TSI interval start excluded IVC tissue velocity peaks in all cases without manual adjustment with a mean margin of $69\pm48$ ms (range 11–201 ms). The mean delay from onset of QRS to start TSI interval was $96.5\pm33.2$ ms. In 14 of the 19 included measurements, the end of TSI interval had to be adjusted manually because of the occurrence of biphasic systolic TVI peaks (example see asterisk of Fig. 2). The corrected TSI interval length was $218\pm171.2$ ms (range 60–485 ms)

TSI-PSD variability (Fig. 3)

The beat to beat variability in all measurements of TSI-PSD was $15\pm30$ ms (correlation coefficient 0.68, $P=0.002$) at basal and $-3\pm24$ ms (correlation coefficient 0.79, $P=0.00$) at mid LV. The beat to beat variability in all measurements between TVI-PSD and TSI-PSD was not significantly different (basal $1\pm11$ ms versus $15\pm30$ ms and mid LV $-3\pm24$ versus $-5\pm18$ ms). In the 13 subjects with correctly detected synchronous LV contraction, the beat to beat TVI-PSD was $-5\pm9$ ms and the TSI-PSD was $10\pm17$ ms (ns).

The intraobserver variability at basal part was $2\pm10$ ms (11±21 ms versus $10\pm20$ ms, ns), and at mid LV parts 0±20 ms (18±24 ms versus 20±37 ms, ns).
The interobserver variability at basal LV was $4 \pm 14$ ms ($11 \pm 20$ ms versus $16 \pm 24$ ms, ns) and at mid LV parts $2 \pm 19$ ms ($18 \pm 24$ ms versus $19 \pm 34$ ms, ns). Compared to TVI-PSD at basal LV no subject demonstrated false synchronous LV contraction. Six patients were classified correctly to synchronous LV contraction, two correctly to asynchronous LV contraction, and two with previously synchronous LV contraction to asynchronous LV contraction. In mid LV two subjects had false synchronous LV contraction.

**Agreement with manually measured TVI-PSD (Fig. 4, Table 1)**

The agreement between TSI-PSD and TVI-PSD was $-8 \pm 45$ ms (correlation coefficient $0.93$, $P=0.043$) at basal and $20 \pm 54$ ms (correlation coefficient $0.28$, $P=0.058$) in mid LV part. In the subjects correctly defined as having synchronous LV contraction ($n=13$) by using manually adjusted TSI interval, the PSD agreement between the TSI-PSD and TVI-PSD was $6 \pm 11$ ms at basal and $32 \pm 48$ ms at mid LV segments, but did not reach significant correlation. In the 6 subjects, showing synchronous LV contraction by using the default TSI interval, the agreement between TVI-PSD and TSI-PSD was $11 \pm 12$ ms at basal and $31 \pm 43$ ms at mid LV, but did not reach statistical significant correlation.

Considering a regional time difference of $< \pm 25$ ms in basal LV as synchronous, manually measured time difference showed synchronous LV contraction in 17 of the 19 subjects. The default TSI interval delay measurement classified correct synchronous LV contraction in 6 subjects. By using the manually adjusted TSI interval added additional 7 subjects as correctly synchronous, improving the sensitivity from $28.6\%$ to $76.9\%$, and the positive predictive value of the TSI method was calculated to $100\%$.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Number of patients with synchronous and asynchronous left ventricular contraction measured by tissue synchronicity imaging (TSI) as compared to manually measurements</th>
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<td></td>
<td>Manual PSD</td>
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<td>Mid LV ($n=18$)</td>
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PSD: peak systolic delay; synchronous: PSD $\leq \pm 25$ ms; asynchronous: PSD $> \pm 25$ ms; LV: left ventricle; results after manual adjustment of the TSI interval.

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negative predictive value from 23.1% to 57.1%. In three subjects the LV contraction was correctly classified as asynchronous both in default TSI and corrected TSI interval measurement. In four subjects the measurements suggested asynchronous as LV contraction both in default and corrected TSI measurement, but were defined as synchronous by manually measuring systolic TVI peaks. No false synchronous TSI measurements were detected in default TSI interval measurement, and the specificity and positive predictive value was calculated to be 100% respectively. One false synchronous TSI measurement was found among the corrected TSI interval measurements, and thus the calculated specificity was 80% and positive predictive value was 91%.

Discussion

In the medical literature there is an increasing interest in the regional time aspect of LV contraction after the introduction of CRT as a promising treatment of severe HF patients refractory even to optimal medical therapy. The diagnosis of mechanical LV asynchronous contraction based on occurrence of bundle branch block in surface ECG is not a sensitive and specific marker of asynchronous LV contraction, and supplementary methods to disclose time delay of regional LV contraction are needed. Methods such as gated blood pool scintigraphy and 3D tagged magnetic resonance imaging have been used to disclose asynchronous LV contraction pattern. The latter methods have a relatively low time resolution of about 30 ms while the c-TVI method may be superior since this method has a time resolution of about 10 ms and more.

So far new echocardiographic methods like c-TVI have been used to demonstrate LV synchronous contraction in structural normal hearts, to document asynchronous LV contraction in HF patients with and without conduction disturbance, and even demonstrate a resynchronization of the LV contraction pattern by CRT. A time consuming manual methods for measuring the regional LV contraction pattern by using c-TVI profiles has so far been the only available method to disclose PSD. In the present study a new semiautomatic method for disclosing LV regional contraction pattern based on c-TVI was tested for the first time in a clinical study.

The new semiautomatic TSI algorithm is a feasible and reproducible method to disclose synchronous LV contraction pattern in subjects with structurally normal hearts. However, in many study subjects a manual minor adjustment of the TSI interval was necessary with the current algorithm. Based on our experience, the IVC velocity peak might not be as clearly defined in patients with HF as in subjects with structurally normal hearts. HF patients also suffer from asynchronous LV contraction during the IVC and the new studied semiautomatic method was not designed for assessment of asynchrony during IVC. Therefore, manually assessment of LV contraction patterns to disclose asynchronous contraction during IVC by using c-TVI is still necessary.

The findings of two asynchronous systolic TVI patterns in basal and four in mid LV might be unexpected, but even the distribution of the standard deviation of the time to peak main systole has shown asynchrony even in control subjects. The presence of biphasic systolic LV tissue velocity profiles in a large proportion of normal subjects make the analysis of c-TVI profiles prior to the application of the studied TSI method necessary. Their appearance might even be of more importance for the evaluation in HF patients. By adjusting the TSI interval and excluding the second systolic TVI peak, the time aspect of systolic events could be measured sufficiently even in cases with biphasic tissue velocity peaks.

The results suggest an acceptable inter- and intraobserver agreement of TSI-PSD measurement, especially in basal LV parts. The beat to beat TSI-PSD variability as compared to the manually measurement, was not significant different, but showed a slightly increased variability. Application of the semiautomatic method to screen HF patients might be sensitive and specific enough to exclude those patients with synchronous LV contraction pattern who are most probably not candidates for CRT.

The current algorithm in the semiautomatic method is not designed for accurate measurement of the LV peak tissue velocity values. Regional contraction may not be correctly measured because of premature/delayed movement of the different myocardial regions (tethering). However, timing parameters of LV regional contraction are less dependent of the Doppler beam angle to the LV tissue, and even reduced or averaged tissue velocity peaks show the same time aspect of the tissue velocity profiles.

The method works sufficiently well for detection of regional LV synchronous contraction during the LV ejection period in structurally normal hearts in cases with well-defined TVI profiles recorded from basal LV. The problem of defining the mechanical systole in HF patients by using the surface
ECG or a mathematically defined systolic period used in this method is obvious and additional recordings are recommended, i.e. phonocardiogram. A definition of the LV ejection period as the time from aortic valve opening to aortic valve closure based on a Doppler measurement of the aortic flow was considered, but had to be abandoned because no simultaneous recording was possible.

The occurrence of postsystolic contraction/shortening (delayed longitudinal contraction) in HF patients might also be a shortcoming of the examined semiautomatic method. One approach excluding the delayed postsystolic longitudinal contraction by only measuring during LV ejection phase, and a second approach including the postsystolic contraction by measuring during a long TSI interval. In the latter approach the LV regional pure systolic asynchronous contraction may be overestimated. Thus, a close look at the TVI profiles before using TSI and the adjustment of the TSI interval might be necessary for distinction of the two described scenarios in HF patients with postsystolic LV contraction/shortening. Reduction of the default TSI interval was considered, but the possible occurrence of late synchronous LV systolic TVI peaks might suggest the use of the default TSI interval for screening to be better.

The new semiautomatic TSI algorithm might be an easier method for screening of regional LV contraction pattern as compared to the previously used manual c-TVI method. Based on the results in this study TSI can sufficiently disclose but not quantify synchronous LV contraction in subjects with structurally normal hearts at least in basal LV segments.

Limitations

Only the apical four-chamber view was examined in this methodological study because this view provided the best images for precise analysis of c-TVI data, whereas the other apical LV views showed less acceptable recordings and were less reproducible. Published data suggesting the greatest amount of asynchrony between basal IS and LFW support our decision to evaluate the TSI method in the chosen view, as well as the fact that best quality of echocardiography images is achieved in the 4 chamber view (especially in heart failure patients). Apical parts of the LV were omitted from the analysis because of the low TVI amplitudes, which do not show the clearly defined c-TVI profiles for measuring PSD. Only structural normal hearts with assumed synchronous LV contraction were examined, and both structurally normal hearts with conduction disturbance and HF patients have to be examined in further studies. For detecting regional systolic changes strain and strain rate imaging which reflect deformation and thereby demonstrates local myocardial contractile function might be superior, but the latter more angle dependent method is in our experience not as robust for evaluating temporal aspects of LV contraction pattern. The TSI method might be able to demonstrate possible synchrony in the failing heart and thereby assume minor effect of CRT in those patients. This issue has to be examined in future studies in CRT patients. The method is not able to quantify asynchrony or resynchronization effected by CRT in the actual version, but further improvements might include those possibilities and are subject to further investigation.

Conclusions

By finding no false synchronous results concerning assessment of LV contraction in subjects with structurally normal hearts, the semiautomatic TSI method demonstrated to be a promising screening method to assess the regional LV contraction pattern in basal LV, when using a three step approach. As a first step when using the default TSI interval 37.5% of the subjects could be classified correctly as having synchronous LV contraction in basal LV and 28.6% in mid LV. As a second step by adjusting the end of TSI interval to exclude inappropriate systolic TVI peaks, the subjects were correctly classified as having synchronous LV contraction in 76.5% when sampling from basal LV and in 76.9% when sampling from mid LV. Thus, manual measurement of LV regional systolic contraction pattern is still necessary to obtain a 100% correctly classification of the LV contraction pattern. The findings in the present study might be applicable to screen HF patients regarding LV contraction synchrony, but no studies are hitherto done in this cohort of patients. However, for measuring and even quantifying regional LV contraction asynchrony, TVI-PSD measurement is still necessary.

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References


