Longitudinal strain quantitates regional right ventricular contractile function

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Because of the complex anatomy and thin wall structure of the right ventricle (RV), the assessment of regional contractile function remains cumbersome, likely because of its complex anatomy and structure. We thought to investigate whether new Doppler-derived myocardial deformation indexes may quantify regional contractile function in varying loading conditions. In nine pigs, ultrasonic crystals were inserted longitudinally in the RV inflow and outflow tracts to assess regional contractile function. The same RV segments and the interventricular septum were imaged using apical echocardiographic views. Regional function was assessed using two parameters: 1) systolic strain (SS), representing the relative magnitude of segmental systolic shortening; and 2) its temporal derivative, peak systolic strain rate (SR), i.e., the maximal velocity of segmental shortening. Data were acquired at baseline and during partial pulmonary artery constriction (PAC) and inferior vena cava occlusion (IVCO). SS decreased significantly after PAC and IVCO in both the inflow and outflow tracts, but only during IVCO in the septum. SR was less sensitive to loading variations in all segments. A significant correlation was found between SS values derived from sonomicrometry and myocardial Doppler in RV segments (r = 0.84, P < 0.001). Thus regional strain and SR provide complementary information on the heterogeneous RV contractile function and can be accurately and noninvasively quantified using Doppler myocardial imaging.

The objective of the present study was to determine the accuracy of ultrasound-derived longitudinal systolic strain, the strain rate for assessing RV regional contractile function, in an experimental pig model of acute load variations using sonomicrometry as a reference technique.

MATERIALS AND METHODS

All animals were treated in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (NIH Pub. No. 85-23, Revised 1996).

Experimental Preparation

Nine male crossbred pigs (31 ± 2 kg) were premedicated with an intramuscular injection of ketamine (5 mg/kg) and anesthetized using a continuous infusion of pentobarbital sodium (0.25 mg·kg⁻¹·min⁻¹) and fentanyl (0.5 µg·kg⁻¹·min⁻¹). Animals were ventilated through a tracheotomy tube with a mixture of 50% air and 50% oxygen. Electrocardiogram acquired from limb leads was monitored continuously throughout the experiment. A cannula was inserted into the right jugular vein for administration of drugs and fluids. Two micromanometer-tipped catheter (Millar Instruments; Houston, TX) were positioned within the LV and RV cavities via the right carotid artery and jugular vein, respectively, to measure the LV pressure (LVP) and RV pressure (RVP) as well as the first derivatives of LVP and RVP (LV dP/dt and RV dP/dt, respectively). The heart was exposed using a median sternotomy and suspended in a pericardial cradle. Two pairs of ultrasonic crystals, used to assess contractile function, were inserted, via a small scalpel incision, in the RV myocardium.

RV volumes and ejection fraction can be estimated using either radionuclide angiography, magnetic resonance imaging, or three-dimensional echocardiography (20, 23, 26). However, a comprehensive approach to RV function would require the assessment of not only the global performance but mostly the regional heterogeneity of RV contraction (6).

RV regional myocardial function can be quantified using segmental strain (relative amount of deformation) and strain rate (velocity of deformation) in various pathophysiological situations including ischemia, stunning, myocardial hypertrophy, and pump failure (9, 17, 27, 32). Yet, the accuracy of strain rate imaging to quantify RV deformation remains to be evaluated.

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wall. The first pair of crystals was positioned longitudinally in the RV lateral free wall [inflow tract (IT)] ~10 mm below the tricuspid ring. The second pair was inserted in the RV outflow tract (OT), parallel to the pulmonary artery trunk axis, ~10 mm below the pulmonary valve plane. A snare was passed around the inferior vena cava for further occlusion to reduce RV preload. Another snare was passed around the pulmonary artery, 10 to 20 mm distal to the valve, for further tightening, aimed to increase RV afterload. The animals were allowed to stabilize for 30 min after these surgical procedures.

**Data Acquisition**

Echocardiography was performed using a Vivid 5 System (GE Ultrasound; Horten, Norway) and a 2.5-MHz transducer. Three myocardial regions were imaged from apical views: 1) the RV lateral free wall as part of the IT, 2) the RV anterior wall in the OT, and 3) the interventricular septum (IVS). High-frame rate (>120 frames/s) B-mode color myocardial velocity data were acquired during brief apnea and transferred to a personal computer workstation for off-line analysis. Pulse repetition frequency was adjusted to avoid aliasing.

Hemodynamic and sonomicrometry data were continuously digitized using commercially available software (IOX 1.567, Emka Technologies).

**Experimental Protocol**

After baseline measurements, animals first underwent a partial pulmonary artery constriction (PAC) for a duration of 10 min (5 min for hemodynamic stabilization before the hemodynamics, sonomicrometry, and echocardiography data acquisition during the subsequent 5 min). PAC was adjusted to increase RV systolic pressure up to 40–50 mmHg. The pulmonary artery tightening was then released, and, after a 15-min recovery period, the inferior vena cava was occluded (IVCO) for 10 min (5 min for hemodynamic stabilization before data acquisition during the subsequent 5 min).

**Data Analysis**

**Echocardiography data.** Color myocardial velocity clips were analyzed using dedicated software (TVI, GE Ultrasound). Longitudinal strain rate was estimated by measuring the spatial velocity gradient over a computation area of 8 mm. Two operator-selected regions of interest were positioned, one within the basal segment of the RV free wall (IT) and the other 10 mm below the pulmonary valve (OT), to match the RV regions investigated by the two pairs of ultrasonic crystals. In addition, the midsegment of the IVS was investigated. Regional velocity and strain rate profiles were assessed for all three regions of interest. Strain rate profiles were averaged over three consecutive cardiac cycles using custom-made software (Speql 3.5, K. U. Leuven). The natural strain profile was obtained by integrating the mean strain rate values over time using end diastole as the reference point and converted to Lagrangian strain (Fig. 1) to allow the comparison with sonomicrometry data (4).

**Sonomicrometry.** Sonomicrometry data were digitized at a sampling frequency of 500 Hz. RV dp/dt was used to define the timing of the cardiac cycle for segment length measurements with ultrasonic crystals, end-diastolic length (EDL) was measured at the onset of the rapid increase in RV dp/dt, and end-systolic length (ESL) was measured at peak negative RV dp/dt. EDL and ESL values were averaged from three consecutive cardiac cycles in each sampling period and used to compute systolic segment shortening or systolic strain (scono), an index of regional systolic function defined as follows: $s_{cono} = \frac{(\text{mean EDL} - \text{mean ESL})}{\text{mean EDL}} \times 100\%$ (5). $s_{cono}$ was measured at baseline and during PAC and IVCO.

To allow comparison with echocardiography, sonomicrometry-derived strain and strain rate were computed. Indeed, $s_{cono}$ represents the end-systolic Lagrangian longitudinal strain. The sonomicrometry-derived strain rate was then calculated as the time derivative of strain to measure the peak systolic strain rate (SRcono) during the RV ejection period (Fig. 2).

**Statistical Methods**

Data are presented as means ± SE. Multiple comparisons were performed using ANOVA with a post hoc Duncan’s test. Least-squares regression analysis and Bland-Altman plots

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**Fig. 1.** Strain rate and strain computation from color Doppler myocardial imaging (DMI): DMI quantifies in-plane myocardial velocities. Strain rate was estimated using the velocity gradient over a defined area of computation (spatial velocity derivative, dv/dx). The strain rate profile was averaged over 3 consecutive heart cycles. Natural strain ($s_{N}$) was calculated as the time integral of strain rate (dv/dt) and converted to Lagrangian strain ($s_{L}$) to allow the comparison with sonomicrometry data. ES, end systole. Green dot and triangle indicate systolic strain and peak systolic strain rate, respectively.

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PAC and IVCO are shown in Fig. 3. At baseline, in both the IT and OT, longitudinal strain profiles first displayed a segment shortening over systole and then a segment lengthening back to near zero at the end of diastole (Fig. 3). The longitudinal strain rate profile was composed of five consecutive waves: two negative peaks during systole and three positive peaks during diastole. The first transient systolic peak (S1) indicates isovolumic contraction. The second dome-shaped peak (S2) corresponds to the RV ejection phase. During diastole, the three positive strain rate peaks match RV relaxation (D1), rapid early RV filling (D2), and atrial contraction (D3), respectively.

At baseline, $\varepsilon_{\text{echo}}$ was comparable in the IT and OT, averaging $18 \pm 2$ and $16 \pm 1\%$, respectively (Table 2). $\varepsilon_{\text{sono}}$ was similar in both regions, with a mean value of $1.08 \pm 0.07$ s$^{-1}$ in the IT and $1.22 \pm 0.15$ s$^{-1}$ in the OT.

For the IVS, the pattern of longitudinal deformation was comparable to RV segments. However, septal $\varepsilon_{\text{echo}}$ was significantly lower than within the IT and OT, averaging $10 \pm 3\%$ ($P < 0.01$).

Modifications of RV load. PAC as well as IVCO induced clear modifications in both the timing and amplitude of systolic and diastolic events, as depicted by the echocardiographic longitudinal strain and strain rate, in both the IT and OT of the RV.

PULMONARY ARTERY CONSTRICTION. Within the IT, the major change in the strain rate profile was a delay of the peak of the ejection phase (S2) toward early diastole, with a consecutive delay of the D1 wave (RV relaxation) and fusion with the D2 wave (early RV filling) (Fig. 3).
Within the IVS, IVCO induced a decrease in $\varepsilon_{\text{echo}}$ from 10 ± 3 to 3 ± 2% ($P < 0.05$), whereas $S_{\text{echo}}$ remained unaffected (Table 2).

**Comparison Between Strain Rate Imaging and Sonomicrometry**

Baseline strain rate profiles, derived from raw sonomicrometric data (i.e., direct recording of segment length), closely resemble strain rate profiles recorded by echocardiography, be it within the IT or OT. However, $S_{\text{echo}}$ did not parallel sonomicrometry measurements after the changes in loading conditions (Table 2).

Systolic strain values obtained by echo, in both the IT and OT, were comparable to those obtained using sonomicrometry, whatever the RV loading conditions (Table 2), and showed a linear correlation for the whole range of values obtained during afterload and preload alterations ($\varepsilon_{\text{echo}} = 0.98\varepsilon_{\text{sono}} + 0.44$, $r = 0.84$, $P < 0.0001$; Fig. 4).

**DISCUSSION**

In the present study, we demonstrated that longitudinal deformation measurements derived from ultrasonic strain rate imaging allows accurate analysis and noninvasive quantification of regional RV contractile function under varying loading conditions.

**Quantification of Regional Contractile Function**

The RV and LV differ markedly in their anatomy, mechanics, and loading conditions. The thick-walled, bullet-shaped LV behaves as a pressure pump ejecting in a high resistance arterial system, whereas the crescent-shaped, thin-walled RV is a volume pump ejecting in a low-resistance pulmonary arterial circulation.

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**Table 2. Sonomicrometry and echocardiographic data during preload and afterload alterations**

<table>
<thead>
<tr>
<th></th>
<th>Pulmonary Artery Constriction</th>
<th>Inferior Vena Cava Occlusion</th>
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<tr>
<td><strong>Inflow tract</strong></td>
<td></td>
<td></td>
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<tr>
<td>$\varepsilon_{\text{sono}}$, %</td>
<td>17 ± 2</td>
<td>14 ± 1*</td>
</tr>
<tr>
<td>$\varepsilon_{\text{echo}}$, %</td>
<td>18 ± 2</td>
<td>13 ± 2*</td>
</tr>
<tr>
<td>$S_{\text{echo}}$, s⁻¹</td>
<td>1.00 ± 0.06</td>
<td>1.23 ± 0.19*</td>
</tr>
<tr>
<td>$S_{\text{sono}}$, s⁻¹</td>
<td>1.08 ± 0.07</td>
<td>1.12 ± 0.20</td>
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<tr>
<td><strong>Outflow tract</strong></td>
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<tr>
<td>$\varepsilon_{\text{sono}}$, %</td>
<td>17 ± 2</td>
<td>11 ± 2*</td>
</tr>
<tr>
<td>$\varepsilon_{\text{echo}}$, %</td>
<td>18 ± 1</td>
<td>11 ± 2*</td>
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<tr>
<td>$S_{\text{echo}}$, s⁻¹</td>
<td>1.15 ± 0.13</td>
<td>1.34 ± 0.27*</td>
</tr>
<tr>
<td>$S_{\text{sono}}$, s⁻¹</td>
<td>1.22 ± 0.15</td>
<td>1.23 ± 0.25</td>
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<tr>
<td><strong>Interventricular septum</strong></td>
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<tr>
<td>$\varepsilon_{\text{echo}}$, %</td>
<td>10 ± 3</td>
<td>9 ± 3</td>
</tr>
<tr>
<td>$S_{\text{echo}}$, s⁻¹</td>
<td>1.65 ± 0.21</td>
<td>2.00 ± 0.34</td>
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</tbody>
</table>

Values are means ± SE. $\varepsilon_{\text{sono}}$ and $\varepsilon_{\text{echo}}$, systolic strain using sonomicrometric and echocardiographic, respectively; $S_{\text{sono}}$ and $S_{\text{echo}}$, peak systolic strain rate using sonomicrometry and echocardiography, respectively. *$P < 0.05$ vs. baseline.
Normal RV ejection is generated by a peristaltic contraction from the IT and apex to the RV OT, resulting in RV free wall shortening toward the IVS. The septum is a component of the RV and contributes to its performance.

The value and accuracy of myocardial Doppler motion and deformation indexes have been widely demonstrated for the assessment of normal and abnormal LV function (1, 5, 8, 14–17, 24, 27, 32). With respect to the RV, prior studies have shown the feasibility and value of myocardial velocity acquisitions and processing of derived parameters like velocity acceleration and strain (18, 19, 28–31). Yet, although some of these studies have pointed out the spatial heterogeneity of RV contraction (18, 30), none have attempted to validate the accuracy of Doppler-derived regional RV function parameters.

Using sonomicrometry as a reference method, we demonstrated that strain can address regional contractile function of the RV under various loading conditions. Variations in global and regional RV contractile function parameters (i.e., RVP, RV dP/dt, and sonomicrometric segment shortening) at baseline or after IVCO or PAC were very similar to those previously described in the literature (3, 10, 25). Mostly, we found a good correlation between Doppler-derived longitudinal strain and sonomicrometry segment length measurements, both in the IT and OT. The accuracy of ultrasonic strain remained the same under very different loading conditions (Fig. 4), from low preload (during IVCO) to high afterload (during PAC), both conditions being known to trigger different adaptative heart rate or inotropic responses. In other words, our study supports that strain rate imaging appears to be a reliable and robust technique for the evaluation of RV function. However, compared with sonomicrometry, the amplitude of systolic strain rate was less sensitive for regional RV function variations during loading modulations. Yet, the strain rate profile remained of valuable help for the analysis of the temporal pattern of regional RV function.

Regional and Temporal Analysis of RV Function

In the present study, we investigated three anatomic components of RV contraction, i.e., the IT, OT, and IVS. We found a differing contractile response of these regions, especially during acute pressure overload, in which IT and OT function was altered, whereas septal performance was unaffected. After the acute afterload increase, the unaltered septal systolic strain rate and strain might be related to the absence of pericardium and diminished coupling among the two ventricles. These findings support the need for a comprehensive assessment of the regional heterogeneity of contraction in the experimental and clinical evaluation of RV dysfunction.

Longitudinal strain and strain rate imaging appears well suited for functional assessment of the heterogeneous and complex anatomy of the RV. Echocardiography and sonomicrometry strain data were well matched both in the IT and OT. This may be of major interest for diseases with alterations of the contractile function initially limited to a specific region of the RV, e.g., ischemic cardiomyopathies or Uhl’s disease, and also to pathologies with important changes in RV shape and potentially overemphasized regional contraction heterogeneity like in pulmonary hypertension (13).

In addition to the quantification of regional systolic and diastolic deformation amplitude, strain rate and strain profiles allowed the assessment of the timing of regional events and their variations with loading conditions. Increased afterload after PAC resulted in a shift of myocardial shortening from early-mid to end systole or even early diastole (postsystolic shortening), whereas a reduction in preload caused by IVCO induced earlier systolic shortening. Thus the analysis of the strain temporal profile may give insight into the mechanism of the observed alteration in RV function. From a more pragmatic clinical standpoint, these longitudinal deformation indexes may help in evaluation of loading conditions of the RV.

Study Limitations

Only longitudinal deformation was investigated in this work. This partial approach to myocardial deformation does not allow the description of the complex three-dimensional pattern of RV contraction (22). Furthermore, the results of our investigation regarding the variations and heterogeneity of regional RV function should be extrapolated with caution to the clinical setting mainly because of the impact of the pericardial constraint (12).

Another limitation is the nonsimultaneous acquisition of echocardiography and sonomicrometry data during the experiment (because the two ultrasonic techniques strongly interfere). This might explain the observed discrepancy between sonomicrometry and myocardial Doppler technique for peak systolic strain rate values (Table 2). Another explanation for this is a potential error in strain rate estimation with echocardiography due to spatial derivation of myocardial velocities resulting in noisy estimation (4).

In conclusion, the present study demonstrates that Doppler-derived longitudinal strain allows an accurate and comprehensive analysis of RV function. The combined qualitative analysis of regional deformation pattern and the quantification of regional systolic strain values appear as a very promising approach for the investigation of RV heterogeneous contraction and dysfunction with potential clinical applications in the setting of heart failure, pulmonary hypertension, congenital heart disease, or ischemic cardiomyopathy.

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REFERENCES


