Selective right ventricular impairment following coronary artery bypass graft surgery

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Abstract

Background: The right ventricle (RV) may be selectively impaired following coronary artery bypass graft (CABG) surgery. We tested this hypothesis in two study parts: a prospective cohort undergoing CABG, and a retrospective cross-sectional cohort of heart-failure patients with and without a history of CABG. Methods: In the prospective study, 20 patients undergoing CABG had echocardiography prior to surgery and 3 months postoperatively. In the retrospective study, 101 patients with established heart failure underwent echocardiography, 40 of whom had undergone previous CABG and 61 of whom had not. Myocardial tissue Doppler velocities were used as a measure of left and right ventricular function. To adjust for varying degrees of overall cardiac impairment, we calculated the ratio between the velocities of the RV and left ventricle (LV).

Results: In the prospective study, there was a significant fall in RV/LV ratio following CABG surgery. For S’, the ratio fell from 2.27 to 1.13 (50%, p < 0.0001), for E’ from 1.49 to 0.94 (37%, p < 0.0001) and for A’ from 1.66 to 1.05 (37%, p < 0.0001). In the retrospective study, the RV/LV ratio was lower in the CABG group compared with the non-CABG group for S’ (by 32%, p < 0.001), E’ (by 39%, p < 0.001) and A’ (by 37%, p < 0.001). In the retrospective study, even when the CABG patients were compared with the ischaemic aetiology heart-failure patients without CABG, a similar relative impairment was seen: 25% in S’ (p < 0.001), 34% in E’ (p < 0.001) and by 38% in A’ (p < 0.002).

Conclusions: Both prospectively and cross-sectionally, there is evidence of substantial, selective right ventricular impairment following CABG. These features cannot be explained simply by some general feature of ischaemia and, therefore, must be a consequence of surgery.

Keywords: Coronary artery bypass graft (CABG); Right ventricle; Tissue Doppler (TDI, DTI)

1. Introduction

Coronary artery bypass graft (CABG) surgery is a common treatment for coronary artery disease in left main-stem and multi-vessel disease. It has well-documented improvements in not only survival but also symptoms and exercise tolerance [1]. However, improvements in myocardial perfusion do not necessarily elicit improvements in ventricular function, as shown previously with both echocardiographic and radio-nucleotide studies [2].

Tissue Doppler imaging (TDI) is now in use as a quick, accessible, sensitive and robust method for assessing both left (LV) and right ventricular (RV) function prior to and following a CABG procedure [3—5]. Recent studies suggest that LV systolic function following a CABG procedure is maintained, whereas LV diastolic function initially shows a slight improvement [6], returning to preoperative levels over time [7]. This return to preoperative levels of function may be explained by a continued progression of coronary arterial disease. By contrast, in the right ventricle, short-term studies suggest that systolic and diastolic function may both be impaired immediately after surgery [8,9].

In this two-part study, we explore the effects of CABG surgery on relative LV and RV activity as assessed by TDI.

In the retrospective element of the study, we look for evidence of a specific RV impairment in a cross-sectional cohort of heart-failure patients who have had CABG, in comparison with other heart-failure patients who have not. We also divide the non-CABG cohort into those with ischaemic and non-ischaemic aetiology, thus allowing us to see if any changes in TDI velocities can be explained simply due to the presence of coronary arterial disease.

In the prospective element, we follow a cohort of patients from before CABG to 3 months following CABG surgery.

We analysed not only the absolute tissue Doppler velocities but also the ratio between RV and LV velocities. Use of this ratio attempts to correct for global cardiac...
impairment due to ongoing disease processes, to allow us to elucidate selective RV impairment following CABG.

2. Methods

2.1. Patient selection

For the retrospective, cross-sectional cohort of patients, we evaluated the clinical and echocardiographical records of outpatients who had undergone specialist heart-failure echocardiography at the St Mary’s Hospital. For each patient enrolled, we established from clinical records whether the aetiology was ischaemic and whether a CABG had been performed.

For the prospective pre-/post-CABG cohort, we enrolled 20 patients who had CABG surgery at the St Mary’s Hospital Cardiothoracic Department. Patients underwent echocardiography 1 month prior to the procedure and at 3 months after the procedure. All patients had anterograde crystalloid cardioplegia through the aorta. As per the surgeon’s preference, eight of 20 patients had on-pump CABG and 12 of 20 patients had off-pump CABG.

2.2. Investigations

Each study participant underwent echocardiography using conventional two-dimensional (2D), pulsed-wave (PW) and TDI technique. The patients were placed in the left lateral decubitus position and scanned using a Sonos 7500 and IE33 Philips Medical Systems (Andover, MA, USA) echo-ultrasound imaging system. Both parasternal and apical imaging windows were achieved using a 5.5-1, 3.5 MHz transducer at a mean depth of 16 cm.

Tissue Doppler echocardiography was performed by experienced sonographers with standard apical four-chamber views obtained (Fig. 1). These were subsequently analysed by a single investigator (HY) who made the measurements blinded to the patient’s clinical data. Myocardial tissue Doppler peak systolic (S’), early diastolic (E’) and late diastolic (A’) velocities were measured (in cm s⁻¹) with reference to the lateral and septal aspects of the mitral annular ring and the lateral angle of the tricuspid valve (Fig. 1). RV:LV ratios were calculated for each patient. This is the ratio of the tricuspid annular velocity to the average of the septal and lateral mitral annular velocities.

As an independent measure of RV function, the myocardial performance (Tei) index was calculated for each patient. The isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT) and ejection time (ET) were derived from tissue Doppler tracings [10,11]. The Tei index was calculated as (IVRT + IVCT)/ET.

For the heart-failure cohort, the aetiology of the cardiomyopathy was determined with the aid of coronary angiography. Those with evidence of significant atherosclerotic disease (>50% reduction of the luminal diameter in a major coronary artery or a major branch) were classified as ischaemic. Those with evidence of minimally affected coronary vessels were classified as idiopathic. Where angiography had not been warranted on clinical grounds or patients declined, the case was termed unclassified (n = 3/101).

2.3. Statistics

Statistical analysis was performed using Excel (Microsoft, San Jose, CA, USA) and SPSS (SPSS Inc., Chicago, IL, USA). All continually variable data underwent tests for normality with the Shapiro–Wilk test and the Kolmogorov–Smirnov test with Lilliefors significance correction. Comparisons between the study groups were made using the unpaired Student’s t-test (for the retrospective study) and paired Student’s t-test (for the prospective study). All values where appropriate are expressed as mean ± standard deviation. A p-value of 0.05 was considered significant.

3. Results

3.1. Patient characteristics

In the retrospective cohort, 101 patients with RV tissue Doppler scans from the St Mary’s Hospital were recruited. There were 82 males and 19 females. The mean age was 66 ± 10.5 years. Of the 101 patients, 40 had a past history of CABG 2–24 years previously (median = 10 ± 4 years). A further 27 patients had ischaemic heart failure without CABG, of which 17 had a history of revascularisation with PCI. A total of 31 of 101 cases had non-ischaemic cardiomyopathy with minimal coronary disease on angiography. Three of 101 cases had no coronary angiograms and remain unclassified. Echocardiographic and tissue Doppler measurements are shown in Table 1.

For the prospective cohort, 20 patients undergoing CABG were recruited. There were 14 males and six females. The mean age was 67 ± 8 years. All patients underwent coronary angiography before procedure. Echocardiographic and tissue Doppler measurements are shown in Table 2.

3.2. Cross-sectional retrospective cohort: effect of CABG on relative RV:LV velocity ratio

In the retrospective group, patients with a history of CABG had a significantly lower RV:LV velocity ratio than those who
did not (Fig. 2). For peak systolic velocity (S'), the RV:L V ratio was 32% lower in CABG patients compared with the non-CABG group (1.45 vs 2.11, p < 0.001). For early diastolic velocity (E'), the RV:L V ratio was 39% lower in the CABG group compared with the non-CABG group (1.11 vs 1.83, p < 0.001). For late diastolic velocity (A), the RV:L V ratio was 37% lower in the CABG group compared with the non-CABG group (1.20 vs 1.92, p < 0.001).

When CABG patients were compared with the non-CABG patients with ischaemic aetiology, a similar relative impairment was seen: by 25% in S' (1.45 vs 1.92, p < 0.001), by 34% in E' (1.11 vs 1.69, p < 0.001) and by 38% in A' (1.20 vs 1.92, p < 0.002). Of note, there were significant differences in the 2D of the ischaemic CABG and ischaemic non-CABG groups: both left atrial size (4.9 cm vs 4.5 cm, p = 0.02) and LV systolic dimensions (5. cm vs 4.3 cm, p = 0.02) were larger in the CABG group.

No significant differences were seen between the RV:L V ratio between the ischaemic non-CABG group and the non-ischaemic group. For S' RV:L V ratio = 1.92 (95% confidence interval (CI): 1.68–2.16) versus 2.29 (95% CI: 1.98–2.60), p = 0.14. For E' RV:L V ratio = 1.69 (95% CI: 1.36–2.02) versus 1.99 (95% CI: 1.55–2.42), p = 0.39. For A' RV:L V ratio = 1.92 (95% CI: 1.46–2.38) versus 1.95 (95% CI: 1.59–2.30), p = 0.89.

When the duration from CABG was considered relative to the RV:L V ratio, no significant differences were seen over different time periods, with similar levels of relative RV:L V impairment being seen between the 2- and 24-year period considered in this study.

### 3.3. Prospective cohort: effect of CABG on relative RV:L V velocity ratio

In a separate part of the study, 20 patients undergoing CABG underwent TDI 1 month before and 3 months after surgery. There was a significant fall in RV:L V ratio following CABG surgery in all tissue Doppler parameters (Figs. 3 and 4). The RV:L V ratio for S' fell from 2.27 to 1.73 (50%, p < 0.0001), for E' from 1.49 to 0.94 (37%, p < 0.0001) and for A' from 1.66 to 1.05 (37%, p < 0.0001). There was no significant difference in RV:L V ratios between those who had on-pump CABG compared with those who had off-pump CABG.

Significant deterioration was seen in right ventricular TDI velocities (S' by 54%, p < 0.0001; E' by 41%, p < 0.0001; A' by 49%, p < 0.0001) following CABG. This was accompanied by a significant rise in RV Tei index (0.49—0.61, p < 0.0001) following CABG. This was accompanied by a significant rise in RV Tei index (0.49—0.61, p < 0.0001).

In contrast to long-axis RV activity, LV function was well preserved, with no significant differences between tissue Doppler S' velocities at the septal (6 cm s\(^{-1}\)–5.3 cm s\(^{-1}\)), p = 0.97) or lateral (6.3 cm s\(^{-1}\)–6.1 cm s\(^{-1}\), p = 0.17) angle of the mitral annulus following CABG. There were no significant differences in LVEF or fractional shortening. There was a significant decrease in LV end-diastolic dimension (4.64–4.35, p = 0.01), postoperatively.

### 4. Discussion

In this study, we found a significant and selective impairment of the right ventricle following CABG surgery.
RV:L V ratios for heart-failure patients who have not had CABG. There was no significant difference shown as mean ± standard error. Patients who have had CABG have significant systolic (S) impairment. Ratio between right ventricular and left ventricular peak systolic (S), early diastolic (E) and late diastolic (A') velocities. Data is shown as mean ± standard deviation. Starred values are statistically significant.

Table 2
Echocardiographic characteristics of prospective cohort (n = 20).

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<thead>
<tr>
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<th>Preoperative</th>
<th>Postoperative</th>
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<tr>
<td><strong>Routine echo</strong></td>
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<tr>
<td>Left ventricular end diastolic dimension (cm)</td>
<td>4.64 ± 0.7</td>
<td>4.35 ± 0.6</td>
<td>0.01*</td>
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<td>Left ventricular end systolic dimension (cm)</td>
<td>3.44 ± 0.7</td>
<td>3.34 ± 0.7</td>
<td>0.21</td>
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<tr>
<td>LV fractional shortening (%)</td>
<td>26 ± 7</td>
<td>24 ± 9</td>
<td>0.42</td>
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<tr>
<td>LV ejection fraction (%)</td>
<td>58 ± 13</td>
<td>54 ± 16</td>
<td>0.38</td>
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<tr>
<td>Intraventricular septum in diastole (cm)</td>
<td>1.23 ± 0.2</td>
<td>1.27 ± 0.2</td>
<td>0.37</td>
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<tr>
<td>Intraventricular septum in systole (cm)</td>
<td>1.51 ± 0.3</td>
<td>1.53 ± 0.3</td>
<td>0.40</td>
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<tr>
<td>Left atrial area (cm²)</td>
<td>20.4 ± 4</td>
<td>21.3 ± 5</td>
<td>0.71</td>
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<tr>
<td>Mitral A wave (cm s⁻¹)</td>
<td>73 ± 25</td>
<td>74 ± 21</td>
<td>0.87</td>
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<tr>
<td>Mitral A wave (cm s⁻¹)</td>
<td>85 ± 28</td>
<td>75 ± 20</td>
<td>0.11</td>
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<tr>
<td>E/A ratio</td>
<td>0.97 ± 0.65</td>
<td>1.03 ± 0.33</td>
<td>0.67</td>
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<tr>
<td>Tei Index</td>
<td>0.49 ± 0.1</td>
<td>0.61 ± 0.1</td>
<td>0.0002</td>
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<tr>
<td>Estimated pulmonary arterial pressure (mmHg)</td>
<td>21.9 ± 5</td>
<td>19.8 ± 5</td>
<td>0.50</td>
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**TDI**

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<tr>
<td>Right ventricle (cm s⁻¹)</td>
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<tr>
<td>S'</td>
<td>13.7 ± 2.3</td>
<td>6.3 ± 1.4</td>
<td>&lt;0.0001*</td>
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<tr>
<td>E'</td>
<td>9.2 ± 2.5</td>
<td>5.4 ± 1.8</td>
<td>&lt;0.0001*</td>
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<tr>
<td>A'</td>
<td>14.2 ± 4.4</td>
<td>7.3 ± 1.9</td>
<td>&lt;0.0001*</td>
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<tr>
<td>Septal LV (cm s⁻¹)</td>
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<tr>
<td>S'</td>
<td>6 ± 1.4</td>
<td>5.3 ± 1.4</td>
<td>0.17</td>
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<tr>
<td>E'</td>
<td>6.2 ± 1.8</td>
<td>5.2 ± 1.1</td>
<td>0.06</td>
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<tr>
<td>A'</td>
<td>8.9 ± 2</td>
<td>7.2 ± 2</td>
<td>0.001</td>
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<tr>
<td>Lateral LV (cm s⁻¹)</td>
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<tr>
<td>S'</td>
<td>6.3 ± 2</td>
<td>6.1 ± 1.3</td>
<td>0.97</td>
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<tr>
<td>E'</td>
<td>6.3 ± 1.8</td>
<td>7.3 ± 2.6</td>
<td>0.15</td>
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<tr>
<td>A'</td>
<td>7.9 ± 2</td>
<td>6.9 ± 2.1</td>
<td>0.36</td>
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<tr>
<td>RV:L V ratio</td>
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<tr>
<td>S'</td>
<td>2.27 ± 0.5</td>
<td>1.13 ± 0.2</td>
<td>&lt;0.0001*</td>
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<tr>
<td>E'</td>
<td>1.49 ± 0.5</td>
<td>0.94 ± 0.4</td>
<td>&lt;0.0001*</td>
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<tr>
<td>A'</td>
<td>1.66 ± 0.4</td>
<td>1.05 ± 0.3</td>
<td>&lt;0.0001*</td>
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Echocardiographic measurements of pre/post-CABG group. Results expressed as value ± standard deviation. Starred values are statistically significant.

Fig. 2. Selective impairment of the right ventricle in heart-failure patients who have had CABG. Ratio between right ventricular and left ventricular peak systolic (S'), early diastolic (E') and late diastolic (A') velocities. Data are shown as mean ± standard error. Patients who have had CABG have significant relative impairment of right ventricular velocities, compared to other heart-failure patients who have not had CABG. There was no significant difference between the ischemic non-CABG patients and the non-ischaemic patients in RV:L V ratios for S', E' or A'.

Fig. 3. Selective impairment of the right ventricle following CABG surgery. Ratio between right ventricular and left ventricular peak systolic (S'), early diastolic (E') and late diastolic (A') velocities. Data is shown as mean ± standard error. In these 20 subjects, who are distinct from the heart-failure subjects in Fig. 2, there is significant relative impairment of the right ventricle following CABG.

Not only is there an absolute reduction in RV tissue Doppler velocity, but also a reduction in the RV:L V tissue Doppler ratio, indicating that this is not a manifestation of global myocardial injury. The retrospective study, in which the median date from CABG is 10 years, taken together with the prospective surgery study, suggests that the effects of such surgery on the right ventricle may be permanent.

The selective RV impairment cannot plausibly be attributed to simple progression of global heart disease, ischaemic or otherwise. Within the non-CABG heart-failure group, the non-ischaemics and ischaemics have the same RV:L V ratio. However, within the ischaemic aetiology heart-failure group, the CABG patients have a lower RV:L V ratio than the non-CABG patients.

4.1. Tissue Doppler and ventricular function

Assessment of RV function by conventional 2D echocardiography can be both subjective and challenging. This is in part due to the anatomy of the RV: its shape and volume dependence, and its complex motion during the cardiac cycle where rotation around the long axis is accompanied by contractions along the long and short axes. By adjusting the pulsed-wave sample so that it is in line with the RV longitudinal excursion plane, tissue Doppler can estimate RV long-axis function by assessing the low-frequency, high-amplitude motions of the tricuspid annulus against the stationary apex [12]. This has been demonstrated to be an accurate correlate of radionucleotide-determined RV ejection fraction (RVEF) [13]. Tissue Doppler is also highly reproducible (~5% inter-observer variation [14]) and easily integrated into existing echocardiography protocols. In the context of ischaemic heart disease, where longitudinal LV function declines before circumferential function on conventional 2D echocardiography, tissue Doppler may be particularly useful in revealing myocardial hibernation before such dysfunction is evident on 2D echocardiography [15].
4.2. Selective RV impairment after CABG

A selective impairment of the RV after CABG was first suggested over 20 years ago [16]. Subjective analyses showed an impairment of RV filling, contraction and overall function during surgery itself, and which persisted immediately following surgery. This impairment was seen irrespective of whether cardiopulmonary bypass was used and despite use of newer techniques of myocardial protection [17].

More objective quantification has been obtained through the use of tissue Doppler. RV impairment occurs immediately after CABG and has not been shown to recover to preoperative levels over the 18 months studied thus far [7]. In a single study, there was a small improvement in tricuspid systolic velocities 1 year post-CABG (9.7 cm s\(^{-1}\)) compared with 1 month (8.7 cm s\(^{-1}\)) and 3 months (8.7 cm s\(^{-1}\)) post-CABG (preoperative = 11.8 cm s\(^{-1}\)) [8]. It was hypothesised that this might be due to recovery of stunned myocardium implying RV impairment may be a relatively short-lived phenomenon. These findings have not been reproduced elsewhere. Our retrospective study suggests any effects on CABG on the RV are likely to be permanent, since they are readily detectable in patients an average of 10 years in the past.

4.3. Clinical impact of impaired RV function

This is not a survival study: it simply reports the effect of CABG on RV velocities. Other workers have identified the relationship between poor RV function and adverse clinical outcomes, particularly in heart-failure patients. Low tricuspid annulus acceleration, low RV systolic velocities and low RV diastolic velocities are all positively correlated with an increased risk of cardiac death or hospitalisation [18]. The presence of all three features results in a six-fold increase in the relative risk of hospitalisation or cardiac death [18].

Clinical impact of RV dysfunction may be difficult to elucidate in post-CABG patients where the beneficial effects of a global revascularisation procedure on LV function may mask any adverse effects of RV impairment. Three months post-CABG, exercise capacity improves in spite of a fall in RV systolic and diastolic velocities [9]. This does not mean that this decline in RV longitudinal function is harmless. Nor should we assume that it is unavoidable.

4.4. Potential mechanisms

Although a well-known phenomenon, no clear cause for RV dysfunction post-CABG is widely accepted. Initial theories suggested RV hypoperfusion during cardioplegia [19—21], particularly in situations where there was severe right coronary artery disease and poor retrograde filling of RV territories [22], may be contributing to RV impairment. However, the findings from these studies were conflicting and no consensus was reached. Recent data suggest RV impairment exists even when off-pump CABG is used and, therefore, independent of cardioplegia techniques [7]. Another theory considered was the development of pericardial adhesions impairing ventricular filling. However, this is not very plausible because the decrease in RV function seen after CABG is very rapid [23] and intervention to prevent adhesion formation fails to preserve RV function [24]. It is possible that the thin-walled RV may be more susceptible to dysfunction secondary to inflammation or effusions post-surgery. These may result from local tissue damage or from a systemic inflammatory response, both known to occur during CABG [25]. Other theories, such as perioperative temperature variations and the deleterious effects of pericardial disruption on RV filling and function are plausible, but require further investigation.

4.5. Limitations

Our study supports the hypothesis of a selective and permanent impairment of RV function following CABG. However, observational studies, even if prospective, always carry risks. Where there is a significant background variation with time, it can be difficult to be certain that an intervention is the cause of any changes seen, and therefore a randomised controlled trial is the gold standard. However, in this case, the fall in relative RV velocities between preoperative and postoperative echocardiography is so large (S’: by 50%, E’: by 37% and A’: by 37%) and so consistent that it
seems implausible it is not caused by CABG. Moreover, there a similar effect is visible in the cross-sectional cohort of patients in whom CABG patients had their surgery an average of a decade ago. This strongly suggests that the relationship with CABG surgery is not an accidental one, but causative and long lasting.

While tissue Doppler analysis has high reproducibility and correlates very well with other assessments of RV function, measuring this at a single point, and LV function with two sample points, represents a limited assessment of ventricular function. This can be particularly true in ischaemic cardiomyopathy, where areas of infarction have greatly reduced velocities, not necessarily representative of global LV function. Future studies using tissue Doppler should sample and average a greater number of points for a more accurate estimate of ventricular function.

We also cannot be certain that RV longitudinal function by TDI fully represents RV function. Further work, using 3D imaging to fully visualise the RV's complex shape, would be needed to allow definitive assessment of change in RV function. Our data may be grounds for the design of such a study.

Further elucidation of the mechanisms of this phenomenon may best be examined intra-operatively. This will allow specific assessment of when during a CABG procedure right ventricular function becomes impaired.

5. Conclusions

There is a marked and seemingly permanent impairment selectively impacting the right ventricle after CABG surgery. This is not plausibly a manifestation of ischaemic heart disease, because patients with ischaemic heart disease, who do not undergo CABG, do not manifest this selective impairment. This effect is present in patients whose surgery was a decade ago, and is also readily demonstrable in patients undergoing surgery now. Its mechanism is not yet elucidated.

References