Quantification of Contraction Synchronicity and Contraction Work in Coronary Artery Disease

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Abstract

Purpose This study quantified the contraction synchronicity (CS; with 100% representing full synchrony and −100% dyssynchrony) and contraction work (CW, millijoules per centimeter squared; representing myocardial area) in patients with reduced left ventricular ejection fraction (LVEF) associated with coronary artery disease (CAD).

Methods CS, CW and LVEF in 104 subjects (54 CAD patients and 50 control subjects without CAD) were measured using rest electrocardiography-gated single-photon emission computed tomography (ECG SPECT). Contraction amplitude (CA), synchronous contraction index (SCI), and CW were evaluated using the program Quantification of Segmental Function by Solving the Poisson Equation (QSFP) developed in-house.

Results The mean CA, SCI and CW of 17 segments in the control subjects were $33.8 \pm 4.1\%$ ($\pm$ SD), $96.6 \pm 1.4\%$, and 6.9 ± 1.0 mJ/cm², respectively. In the patients with CAD, the respective values were $26.1 \pm 7.3\%$, $82.1 \pm 16.8\%$, and 5.4 ± 1.6 mJ/cm². In the CAD patients with LVEF <40% ($n = 14$), the mean CA, SCI, and CW were $17.9 \pm 4.0\%$, $63.0 \pm 18.4\%$, and 3.5 ± 1.1 mJ/cm², respectively. These values were significantly lower than in the control subjects

($p < 0.005$). Using receiver operating characteristic analysis, values for the area under the curve showing the performance of CA, CS, CW and LVEF in the diagnosis of CAD were 0.81, 0.86, 0.78, and 0.84, respectively.

Conclusion Asynchrony shown using the QSFP is useful for CAD detection.

Keywords Contraction amplitude · Contraction synchronicity · Contraction work · Left ventricular ejection fraction · Coronary artery disease

Introduction

Uniform contraction synchronicity (CS) and uniform contraction amplitude (CA) are believed to promote maximal cardiac output with minimal energy expenditure. This may provide useful information for the management of patients with coronary artery disease (CAD) and heart failure [1]. Ischemic injury of the myocardium is believed to manifest as abnormal left ventricular (LV) contraction because of the inability of the myocardium to achieve simultaneous full shortening and full relaxation leading to asynchronous contraction. LV functional assessment is usually based on LV ejection fraction (LVEF), calculated using automatic quantitative gated single-photon emission computed tomography (SPECT) software (QGS software) [2]. LVEF is closely related to the synchronous contraction of the myocardium [3, 4] and to reductions in CA. Few studies have investigated the use of nuclear cardiology for evaluation of the relationships between LVEF and CS or contraction work (CW) in CAD patients [5–7]. Therefore, we sought to determine whether CS and CW could be used as alternative indices for the detection of CAD, independent of myocardial perfusion imaging. We quantified CS and CW in patients with reduced LVEF associated with CAD using

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electrocardiographically-gated myocardial perfusion SPECT (ECG SPECT) and the program Quantification of Segmental Function by Solving the Poisson Equation (QSFP) [8–10].

Materials and Methods

Patient Selection

Included in the study were 104 subjects comprising 54 patients with CAD (48 men, mean age 68.9 ± 10.6 years) and 50 control subjects without CAD (27 men, mean age 62.8 ± 15.4 years) matched for age and sex. The control subjects were chosen from among 262 patients who were documented as having a low risk of CAD, a normal electrocardiogram, and normal perfusion imaging based on the Japanese Assessment of Cardiac Events and Survival Study by Quantitative Gated SPECT (J-ACCESS) database [11]. Other exclusion criteria for the control subjects included a history of diabetes mellitus, hemodialysis, imaging artifacts that would have affected ECG SPECT results, and structural cardiac diseases such as cardiomyopathies. The 54 patients who underwent coronary angiography had coronary stenosis of 50% or more, and 22 had one-vessel disease, 26 had two-vessel disease and 6 had three-vessel disease. The left anterior descending (LAD) coronary artery, the left circumflex (LCX) coronary artery, and the right coronary artery (RCA) were involved in 42, 27 and 25 patients, respectively. The CAD patients were divided into two groups according to LVEF ($\text{LVEF} \geq 40\%$ and $<40\%$) to confirm the detection precision of QSFP. This retrospective study was approved by the institutional review board of the hospital on 22 March 2011.

Gated SPECT

ECG SPECT was performed at rest with $^{99\text{m}}\text{Tc}$ -tetrofosmin. After injection of 600 MBq of the tracer, the patients lay supine for approximately 60 min before the start of the ECG SPECT examination. The images were acquired with a dual-head rotating gamma camera (Millennium; GE-Yokogawa Medical, Tokyo, Japan) fitted with a low-energy parallel-hole general purpose collimator. A set of 36 projection images were obtained (step-and-shoot method, 25 s per projection, 64×64 matrices) over a 90° arc at 16 frames per cardiac cycle. The data acquisition was completed in approximately 14 min. The collected data were reformatted into a set of short-axis images (matrix size 64×64 ; voxel size $8.85 \times 8.85 \times 8.85$ mm) by reconstruction with filtered back-projection and reorientation without attenuation correction. A Butterworth filter with a cut-off frequency of 0.35 cycles/cm was used to filter the gated images. The projection images were obtained in the Digital Imaging and Communications in Medicine (DICOM) file format.

Quantitative Analysis

The QSFP program was written using X-code v. 2.0, which is designed to operate on Macintosh personal computers and to transfer data online from a SPECT system. The final contraction maps were obtained in approximately 10 s. The cardiac wall was divided into 17 segments according to the American Heart Association criteria [12]. The segmental accumulation of the perfusion agents, CA, the synchronous contraction index (SCI; quantitative index of CS; 100% represents full synchrony and -100% dyssynchrony), and CW (millijoules per centimeter squared; myocardial area) were calculated and expressed as the sums or the sums weighted with each corresponding area on the cardiac surface, and were drawn on polar maps. Similarly, LVEF was measured using ECG SPECT and the QSFP program. Details of the QSFP methods employed have been described previously [8–10].

Statistical Analysis

Statistical analysis was performed with StatView 5.0 (SAS Institute Inc., Cary, NC, USA). Continuous variables are expressed as means $\pm$ one standard deviation. A two-tailed Student's *t* test was performed for unpaired samples. Pearson correlation analysis was used to evaluate the relationships between LVEF and CA, SCI and CW. A *p* value of <0.05 (two-tailed) was considered statistically significant. To determine the performance of CA, CS, CW and LVEF in the diagnosis of CAD, receiver operating characteristic (ROC) curves were constructed, and the sensitivities, specificities, optimal cut-off points, and areas under the curve (AUC) were calculated.

Results

Table 1 shows the results for control subjects and patients with CAD, and Fig. 1 shows the mean values of the myocardial function parameters comparing control subjects and CAD patients and comparing patients with $\text{LVEF} \geq 40\%$ and $<40\%$. In control subjects, the mean CA, SCI and CW for the 17 segments were $33.8 \pm 4.1\%$, $96.6 \pm 1.4\%$ and 6.9 ± 1.0 mJ/cm², respectively. No significant difference in CA, SCI and CW was observed between men and women in the control group. However, LVEF was significantly different between men and women ($p < 0.005$). In the patients with CAD, the corresponding values were $26.1 \pm 7.3\%$, $82.1 \pm 16.8\%$ and 5.4 ± 1.6 mJ/cm², respectively. Mean LVEF was $71.3 \pm 8.0\%$ in control subjects and $51.3 \pm 16.5\%$ in patients with CAD. In CAD patients with an $\text{LVEF} < 40\%$ ($n = 14$), the mean CA, SCI and CW in the 17 segments were $17.9 \pm 4.0\%$, $63.0 \pm 18.4\%$, and

Table 1 Myocardial function parameters in control subjects ($n = 50$) and patients with CAD ($n = 54$)

	Control subjects ($n = 50$)		CAD patients ($n = 54$)					
			All patients ($n = 54$)		LVEF <40% ($n = 14$)		LVEF $\geq$ 40% ($n = 40$)	
	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)
Contraction amplitude (%)	25.4–42.1	33.8 (4.1)	10.4–40.5	26.4 (7.6)	10.4–23.6	17.9 (4.0)	18.0–40.5	29.0 (5.8)
Synchronous contraction index (%)	92.7–98.7	96.6 (1.4)	15.3–98.2	82.1 (16.8)	15.3–84.6	63.0 (18.4)	51.8–98.2	88.8 (9.7)
Contraction work (mJ/cm ²)	4.7–9.3	6.9 (1.0)	2.5–8.4	5.4 (1.6)	2.5–5.9	3.5 (1.1)	4.0–8.4	6.1 (1.1)
Left ventricular ejection fraction (%)	51.1–87.9	71.3 (8.0)	19.3–79.1	51.3 (16.5)	19.3–37.1	30.4 (5.9)	40.7–78.2	58.6 (12.2)

3.5 ± 1.1 mJ/cm², respectively. These values were significantly lower in patients with CAD than in control subjects ($p < 0.005$), and were also significantly lower ($p < 0.05$) in CAD patients with an LVEF $\geq$ 40% ($n = 40$).

Figure 2 shows the relationships between LVEF and CA, SCI and CW in patients with CAD. Both CA and CW were strongly correlated ($r = 0.91$ and 0.88) with LVEF. The correlation between LVEF and SCI was slightly weaker ($r = 0.78$). The ROC analysis of the performance of CA, CS, CW and LVEF in the diagnosis of CAD is shown in Table 2. The AUC values for CA, CS, CW and LVEF in this analysis were 0.81, 0.86, 0.78 and 0.84, respectively. Polar maps of tracer

uptake, CA, SCI and CW in a control subject and a CAD patient are shown in Fig. 3. In contrast to control subjects, regional CA, regional SCI and regional CW in patients with CAD were significantly lower with smaller areas than in the normal region (LCX artery area) due to low accumulation of ^{99m}Tc-tetrofosmin. Polar maps of tracer uptake, CA, SCI and CW in a CAD patient are shown in Fig. 4. Although LVEF was in the normal range, the regional CA, regional SCI and regional CW were confined to areas of decreased uptake on the polar maps. Coronary angiography after SPECT examination revealed stenosis of the LAD and LCX arteries, and there was a correlation

Fig. 1 Myocardial function parameters in control subjects and CAD patients: **a** contraction amplitude, **b** synchronous contraction index, **c** contraction work, and **d** left ventricular ejection fraction

Fig. 2 Relationships between LVEF and contraction amplitude (CA **a**), synchronous contraction index (SCI **b**) and contraction work (CW **c**) in patients with CAD

between these areas and the areas of decreased uptake (regional CA, regional SCI, and regional CW).

Discussion

The increase in blood volume in the LV stretches the cardiac wall in a tangential direction, causing the cardiac muscles to contract with greater force [13]. Herman et al. [14] found that local ischemic myocardial injury manifests first as abnormal contractions rather than alterations in wall motion, corresponding to the centrifugal or centripetal wall motion relative to the center of the LV cavity. Delhaas et al. [15] identified myocardial CW as a helpful index for both normal and diseased hearts. Therefore, we hypothesized that the assessment of CA, SCI and CW could serve as alternative indices for the detection of CAD. To our knowledge, the present study is the first to demonstrate the clinical value of CS and CW as measured by SPECT for the diagnosis of CAD. CW was calculated by applying Laplace's law under the assumption of a rectangular area of 100 mm Hg pressure using a thin-wall model in QSFP [9]. Based on echocardiographic findings, Nakano et al. [16] measured a posterior CW of 7.0 ± 1.8 mJ/cm³ in a normal heart with an approximate LV pressure of 120 mm Hg. Although LV pressure was not measured accurately in the present study, we obtained a mean CW value of 6.9 ± 1.0 mJ/cm² in control subjects. This value was sufficiently

in line with that reported by Nakano et al. [16]. These measurements are affected not only by the patient's blood pressure, but also by the heart rate and physical stature, height, and weight. Therefore, these factors need to be included in the analyses for identification of factors that influence CW.

The CA, SCI and CW values were significantly lower in patients with CAD than in control subjects ($n = 54$, $p < 0.005$), and were also significantly lower in CAD patients with an LVEF $< 40\%$ ($n = 14$) than in CAD patients in general ($p < 0.05$). According to the ROC analysis, the performance (AUC) in the diagnosis of CAD was in the order CS (highest), LVEF, CA and CW (lowest). However, LVEF showed the lowest detection sensitivity (64.8%), compared with CS (72.2%), CA (70.4%), and CW (77.8%). These results show that the indices calculated using the QSFP are highly sensitive for the detection of CAD. Figure 3 indicates that in patients with CAD, the areas with a low CA, low SCI or low CW were small with low ^{99m}Tc-tetrofosmin accumulation. This made it difficult to determine the areas in patients with poor LV function, as the latter can easily be recognized through visual inspection under non-uniform uptake distribution conditions. These indices reflect the severity of coronary artery stenosis. In patients with CAD, LVEF was correlated with CA ($r = 0.91$), CW ($r = 0.88$), and SCI ($r = 0.78$). LVEF has previously been identified as one of the predictors of myocardial viability [17–20]. However, the information provided by LVEF alone might not be sufficient for it to serve as a

Table 2 ROC analysis of the performance of contraction amplitude, contraction synchronicity, contraction work and LVEF in the diagnosis of CAD

	AUC (%)	Sensitivity (%)	Specificity (%)	Cut-off point	<i>p</i> value
Contraction amplitude	0.81	70.4	84.0	$\leq 29.7\%$	< 0.0001
Contraction synchronicity	0.86	72.2	92.0	$\leq 94.7\%$	< 0.0001
Contraction work	0.78	77.8	68.0	≤ 6.4 mJ/cm ²	< 0.0001
LVEF	0.84	64.8	98.0	$\leq 58.3\%$	< 0.0001

Fig. 3 Polar maps of tracer uptake, contraction amplitude, synchronous contraction index (SCI), and contraction work in a control subject (82-year-old male) and a patient with CAD (78-year-old male with two-vessel

disease). In the CAD patient, the LAD artery (segments 5 and 7) showed 75–90% stenosis and the RCA (segment 3) showed 90% stenosis

predictive index [21, 22]. Figure 4 indicates that CA, SCI and CW could be auxiliary to the LVEF for assessment of cardiac function. There was a correlation between the areas of stenosis in the LAD and LCX arteries and areas of decreased CA, SCI and CW. With regard to regional CA, SCI and CW, the areas of decrease were quantified as 27.3%, 86.3% and 5.1 mJ/cm², respectively, and all indices were lower than the cut-off point. Asynchrony shown by the QSFP is useful for CAD detection, and may provide additional information, independent of myocardial perfusion imaging.

Fig. 4 Polar maps of tracer uptake, contraction amplitude, synchronous contraction index (SCI), and contraction work in a CAD patient (76-year-old female) with normal LVEF (67%). The LAD artery (segment 9) and the LCX artery (segment 11) showed 90% stenosis. The areas of decreased LV function could be quantified and visually inspected despite the non-uniform distribution on the polar maps

Conclusions

CA and SCI may be used to detect LV asynchrony associated with CAD, and CW during asynchronous contraction might elucidate the mechanisms of reduced LVEF. Asynchrony shown by the QSFP is useful for CAD detection, and may provide additional information, independent of myocardial perfusion imaging.

Compliance with Ethical Standards

Conflict of Interest Takanaga Niimi, Mamoru Nanasato and Hisatoshi Maeda declare that they have no conflict of interest associated with this study.

Ethical Approval The study was approved by an institutional review board and was performed in accordance with the ethical standards laid down in the Helsinki Declaration of 1964 and later revisions. All subjects in the study gave written informed consent or the institutional review board waived the need to obtain informed consent.

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