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Relationships between blood pool and myocardial perfusion-gated SPECT global and regional left ventricular function measurements

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Abstract

Objective—Algorithms have been developed to quantify global and regional left ventricular (LV) function and asynchrony from myocardial perfusion (MP) and blood pool (BP)-gated single-photon emission computer-assisted tomography, but relationships between measurements from these two imaging modalities have not been documented. The objective of this investigation was to determine the degree to which automated BP and MP measurements agree with each other and are accurate, using cardiac magnetic resonance (CMR) as the reference standard. We also sought to determine the extent to which regions of abnormal phase correspond to segments exhibiting abnormal wall motion.

Materials and methods—We studied 20 patients with prior myocardial infarction (age 60 ± 11 years; 95% males) who had BP, MP, and ECG-gated CMR data acquisitions. MP and BP measured parameters included global ejection fraction (EF) and volumes, regional contraction phases, and standard deviations and bandwidths of phase versus R-R histograms. CMR algorithms used manually drawn endocardial and epicardial contours to measure global and regional wall motion and wall thickening. Regional measurements were resampled for all three imaging modalities into 17 conventional LV territories.

Results—BP LV counts significantly exceeded MP counts with a ratio of 5.2 : 1. There were no differences among the three methods for global EFs or volumes (analysis of variance $P = 0.86$ and 0.94). MP and BP correlated equally well ($P = 0.15$) versus CMR for global EFs (MP: $r = 0.87$ and BP: $r = 0.95$) and volumes ($r = 0.91$ for both). Phase histogram parameters correlated significantly for MP versus BP for phase standard deviation ($r = 0.79$) and phase bandwidth ($r = 0.93$). Detection of five patients with significantly extended phase bandwidth, indicative of asynchrony, showed ‘good agreement’ between MP and BP ($\kappa = 0.73$; McNemar's difference = 0%, $P = 0.48$). Abnormal regional BP EF predicted abnormal wall motion of specific LV segments (receiver-operating characteristic area = $85 \pm 2\%$), and abnormal regional MP wall thickening predicted abnormal CMR wall thickening (receiver-operating characteristic area = $87 \pm 3\%$). Abnormal MP phase was present in 25% of 67 dyssynergic segments and 64% of segments

adjacent to dyssynergic segments, indicating that locations of phase abnormalities were more widely distributed in the LV than sites of depressed wall motion.

Conclusion—MP and BP measures of LV global and regional function agreed well with each other and with independent CMR measurements. MP and BP phase measurements suggested that phase abnormalities were more widespread than localized wall motion abnormalities.

Keywords

cardiac-gated single-photon emission computer-assisted tomography; gated blood pool imaging; magnetic resonance imaging; myocardial perfusion imaging

Introduction

Left ventricular (LV) global function parameters derived from radionuclide imaging have long been recognized as an effective means of assessing prognosis in patients after myocardial infarction [1], and recent investigations have reported that regional wall motion provides valuable additional prognostic information [2]. Patients with LV dysfunction have both abnormal regional wall motion (dyssynergy) and abnormal synchronicity of contraction (asynchrony), but the relationship between these has not yet been established. Regional phase (time-to-peak segmental contraction) is one means of quantifying asynchrony, and algorithms have been written to obtain phase information from blood pool (BP)-gated single-photon emission computer-assisted tomography (SPECT) data [3,4], and from myocardial perfusion (MP)-gated SPECT data [5]. BP imaging may be preferred if information is required regarding function and asynchrony of both the LV and right ventricle [6], whereas MP imaging may be preferred if information is needed of both LV myocardial ischemia and asynchrony [7,8]. Both BP and MP-gated SPECT LV regional computations are relatively new, and the relationships between parameters computed by each of them have not previously been established.

The objective of this investigation was to determine accuracies of MP and BP-gated SPECT global and regional LV phase and function calculations and the degree to which they agree with one another, using cardiac magnetic resonance (CMR) as the reference standard. We also sought to determine the degree to which regions of abnormal phase correspond to regions of dyssynergy.

Materials and methods

Patient population

We prospectively examined data of 20 patients evaluated after myocardial infarction (age 60 ± 11 years; 95% males). All patients had BP, MP, ECG-gated true fast imaging with steady-state precession (FISP) CMR data collections. All patients were selected from inpatients and outpatients at the St Francis Hospital, Roslyn, New York, USA. All signed a written informed consent form approved by the St Francis Hospital Institutional Review Board. All data were handled in compliance with the Health Insurance Portability and Accountability Act of 1996.

Cardiac magnetic resonance data acquisition

CMR data collection was performed on a 1.5 T scanner ('Sonata' Siemens Medical Solutions Inc., Malvern, Pennsylvania, USA). Breath-hold true-FISP cine CMR imaging was used to produce images of superior signal-to-noise ratio [9]. Multiplane localizers identified LV long and short axes. Contiguous end-expiration prospective ECG-gated breath-hold segmented k-space true-FISP LV short axis images were obtained over the

cardiac cycle for 11–13 planes with 128×256 matrices, using a field of view of 30–40 cmc. Partial k-space data were acquired for each of the frames per heartbeat, and then combined into a whole frame image over several heartbeats. Image slice thickness was 8 mm and temporal resolution was 40 ms or less, depending on heart rate. Breath-hold duration was 10–16 s per image sequence. Total data acquisition time was less than 30 min.

Cardiac magnetic resonance calculations

Endocardial and epicardial borders were drawn manually from apex to base by an experienced MR image analyst using commercially available software ('MASS,' Medis Inc., Leiden, The Netherlands) (Fig. 1). LV volumes were computed as the sum of slice thickness $\times$ cavity area.

CMR ejection fraction (EF) was computed from enddiastolic (ED) volume (EDV) and end-systolic (ES) volume (ESV). Using endocardial and epicardial drawings performed for 60° samples of short axis cines, regional CMR radial wall motion and wall thickening were computed by Medis 'MASS' algorithms as the difference between ED and ES. All 66–78 CMR regional values then were resampled into segments corresponding to conventional LV 17-segment model by weighted averaging. On the basis of previously reported CMR data for 10 normal volunteers, CMR regional wall motion was considered to be abnormal if less than 3.2 mm, and wall thickening abnormal if less than 17% [4].

Gated blood pool single-photon emission computer-assisted tomography image acquisition

Nine hundred and twenty-five megabecquerel ^{99m}Tc -pertechnetate was injected approximately 30 min after injection of 5 mg pyrophosphate. Data were acquired with LEHR collimators, using dual-detectors set at 90° relative to one another ('Forte' or 'Vertex' cameras; ADAC Inc., Milpitas, California, USA). BP tomograms were collected at 64 projections over a 180° circular arc as 64×64 matrices (pixel size 4.6 mm), for 20 s per projection for 15 min. Tomograms, with patients at rest, were acquired at 16 frames per R-R interval, using an R-wave window of $\pm 20\%$ [10].

Prereconstruction spatial smoothing was performed using Butterworth filtering (cutoff = 0.35 cycles/cm, power = 5.0) for gated tomograms, followed by ramp filtering in the transaxial plane. Filtered images were back projected to form transaxial slices, which were reoriented into short axis sections using manual choices of approximate LV symmetry axes.

Gated blood pool single-photon emission computer-assisted tomography image processing

Previously described BP algorithms, 'BP-SPECT' (Columbia University, New York, USA) [11], were modified to include new regional function subroutines written in IDL (RSI Inc., Boulder, Colorado, USA) [3], and executed on standard desktop PCs running Windows operating systems (Microsoft Corporation, Redmond, Washington, USA). All BP data were processed in a totally automated manner, with no operator interventions. Results of all numerical calculations were exported automatically by the algorithms to Excel spreadsheets for subsequent statistical analysis.

LV volumes were divided into 17 subvolumes for each segment of the R-R interval. Counts of each subvolume were fit to third order Fourier harmonics, using a moving frame of reference [12]. Each of the 17 LV segments corresponded to the conventional LV mapping [13]. BP regional EFs were calculated from count changes from ED to ES for each of the 17 subvolumes (Fig. 2), as were regional phases (Fig. 3). Phase was expressed as percent of the R-R interval, and equivalently in units of degrees ranging from 0° to 360°. Phase histograms

were formed by tabulating the number of pixels undergoing peak systolic contraction at each phase of the 16 segments of the R-R interval (Fig. 4). BP phase histogram bandwidths, standard deviations, and peak phases were computed, with bandwidth defined as the percent of the R-R interval for which 95% of contraction phases were observed [5].

Gated myocardial perfusion single-photon emission computer-assisted tomography image acquisition

Scans were acquired after an intravenous injection of 111 MBq ^{201}Tl , followed by nongated resting SPECT MP imaging. Exercise or pharmacologic stress then was performed with 1.11 GBq of $^{99\text{m}}\text{Tc}$ -sestamibi injected at peak stress. Poststress MP imaging was performed 30–60 min later, using one of two commercially available dual-detector γ cameras ('Forte' and 'Vertex,' ADAC Laboratories). Data were acquired with patients at rest using low-energy high-resolution collimators in 64×64 matrices of pixel size 4.6 mm, at 16 frames per R-R interval, using an R-wave window of $\pm 20\%$ of mean preacquisition heart rate. Heart rate data were recorded automatically in image files. Data were acquired for 25 s/projection for 32 projections per detector over a total arc of 180° , from the right anterior oblique- 45° projection to the left posterior oblique- 45° projection. Total acquisition time was 15–16 min.

Gated myocardial perfusion single-photon emission computer-assisted tomography image processing

Reconstructed tomographic slices were produced by filtered back-projection, using a preprocessing Butterworth filter (power = 5.0, cutoff = 0.50 cycles/cm). No scatter or attenuation corrections were applied to gated data. Standard Emory Cardiac Toolbox (Emory University, Atlanta, Georgia, USA) algorithms were used to calculate LV EDV, ESV, and EF, whereas MP was assessed quantitatively and compared with normal databases to produce summed stress scores, summed rest scores, and the percentage of the total myocardial surface that was hypoperfused [14].

Polar perfusion maps were generated for each gated segment of the R-R interval. Counts versus time curves were constructed at each pixel location in common across polar maps for all gates. From the 16 polar maps of myocardial counts versus time were constructed a single polar map of wall thickening. Time-activity curves were fit to the principal component of a Fourier series of count versus time curves at each pixel. The peak of the fitted curve corresponded to the time of ES because of the partial volume effect [15]. MP phase histograms were formed by tabulating the number of pixels undergoing peak systolic count increases for every time bin (Fig. 5) [5].

All pixels were assigned to a specific LV segment, corresponding to one of the 17 LV segments in the conventional model used for regional perfusion analysis [13]. The mean phase value for all pixels belonging to a segment was then computed. Polar maps of mean phase for the 17 segments then were constructed for each patient.

Visual assessment

Independent visual assessment of LV wall motion was performed by one experienced nuclear cardiologist, without knowledge of any calculations or any other clinical test results. MP visual assessment was performed with cines displayed simultaneously in orthogonal views without superimposed computed outlines. LV wall motion for each of the 17 segments was graded on a 5-point scale (0 = normal, 1 = mildly hypokinetic, 2 = moderately hypokinetic, 3 = akinetic, and 4 = dyskinetic). MP regional readings also were dichotomized, on the basis of a segment judged to be at least moderately hypokinetic.

On a separate occasion, the same observer performed visual assessments of BP tomographic slices, blinded to previous MP wall motion assessments and to all other measurements and clinical data. Reading sessions were separated by at least 1 month to avoid recall bias.

Statistical analyses

Statistical analyses were performed using commercially available software (Medcalc, version 7.5.0.0., Medcalc Software Inc., Mariakerke, Belgium). Values are reported as means $\pm$ 1 standard deviation. Frequencies and percentages were used to characterize categorical variables. One-way analysis of variance (ANOVA) was used to determine whether differences were significant among multiple methods using a Bonferroni's correction for probability values. Correlation between continuous variables was determined using linear regression, generating Pearson's correlation coefficients. Post-hoc power analysis was performed to determine the number of cases needed to produce statistically meaningful Pearson's correlation coefficients. Bland–Altman analyses of measurement differences versus means were used to assess biases, trends, and limits of agreement. Agreement between methods for discriminating normal from abnormal values was determined using the κ -statistic [16], and McNemar's test was used to determine whether measurement differences were statistically significant. Receiver-operating characteristic (ROC) analyses were performed to quantify the ability of BP regional EF to discriminate normal from abnormal dichotomous CMR wall motion, and the ability of MP regional wall thickening to discriminate normal from abnormal dichotomous CMR wall thickening. Except for ANOVA, probability values (P) less than 0.05 were considered statistically significant.

Results

Data characterization

Examination of the MP-gated SPECT and BP-gated SPECT data sets showed that none of the patients had arrhythmias during data acquisition that could have potentially complicated visual or quantitative analyses [17]. There also was no evidence of patient motion during either BP or MP data acquisition for any of the patients.

There were 6.1 ± 2.3 million LV BP total counts in BP SPECT data, significantly more ($P < 0.0001$) than the 1.7 ± 2.3 million LV myocardial total counts in MP SPECT data. In each case, BP LV counts exceeded MP counts, with a mean ratio of 5.2 : 1 (range = 1.3–14.9).

CMR LV EF was $52 \pm 15\%$ (range = 18–67%) and CMR EDV was 166 ± 69 ml (range = 88–360 ml). MP summed stress score was 15 ± 8 (range = 3–27) and percentage of MP defects was $13 \pm 11\%$ (range = 0–32%).

Global parameters

There were no differences among the three methods for global EFs or volumes (ANOVA $P = 0.86$ and 0.94 , respectively). MP and BP correlated equally well ($P = 0.15$) versus CMR for global EFs for MP and BP ($r = 0.87$ and 0.95 , respectively), and correlated equally well versus CMR for volumes for MP and BP ($r = 0.91$ for both) (Table 1). Power analysis confirmed that only seven to nine cases would have been needed in order for these Pearson's correlation coefficients to be statistically meaningful, whereas 20 data sets were sampled in deriving these parameters. Bland–Altman analyses indicated a tendency for both MP and BP to overestimate the highest EFs ($P = 0.02$). Detection of cases of abnormal global EF less than 50% showed 'good agreement' [16] for MP versus CMR ($\kappa = 0.68$; 5% McNemar's difference, $P = 1.00$) and 'very good agreement' for BP versus CMR ($\kappa = 0.89$; 5% McNemar's difference, $P = 1.00$). Previous analyses involving control groups at low

likelihood for cardiac disease have found that the lower limit for normal LV EF is 54% for 'Emory Cardiac Toolbox' MP calculations [18], and 52% for 'BP-SPECT' BP calculations [3].

Regional left ventricular parameters

Although the peak phase did not correlate significantly between MP and BP ($r = 0.008$, $P = 0.97$), there were significant correlations for phase standard deviation ($r = 0.79$, $P < 0.001$) and bandwidth ($r = 0.93$, $P < 0.0001$) (Fig. 6). Power analysis confirmed that more than the minimum necessary number of data sets was analyzed in order for these Pearson's correlation coefficients to be statistically meaningful. Bland–Altman analysis showed significant trend (slope = -0.35 ± 0.09 , $P = 0.0007$) and bias (intercept = $24^\circ \pm 10^\circ$, $P = 0.03$) of BP versus MP phase histogram bandwidth values; nonetheless, discrimination of the five patients with phase bandwidths above the previously established asynchrony normal limit of 125° [18] showed 'good agreement' between BP and MP ($\kappa = 0.73$; McNemar's difference = 0%, $P = 0.48$). Discrimination of abnormal phase standard deviation above the previously established asynchrony normal limit of 22° [18] demonstrated 'fair agreement' between MP and BP ($\kappa = 0.38$; McNemar's difference = 35%, $P = 0.02$).

Left ventricular segmental analysis

CMR apical wall motion correlated significantly with BP apical EF ($r = 0.74$, $P = 0.0002$). There was 'good agreement' between abnormal CMR wall motion values for BP regional EF ($\kappa = 0.79$; 10% difference, $P = 0.48$), MP visual analysis ($\kappa = 0.75$; 13% difference, $P = 0.48$), and BP visual analysis ($\kappa = 0.80$; 10% difference, $P = 0.48$).

On the basis of previously reported CMR normal limits [4], 67 segments had abnormally depressed regional wall motion and the remaining 213 segments had normal motion by CMR. On a segment-by-segment basis, dyssynergic segments were significantly predicted by regional BP EF values below 50% (ROC area = $85 \pm 2\%$, $P < 0.0001$), and were similarly well predicted ($P = 0.51$) by the presence of abnormal wall motion as seen on visual examination of MP cines (ROC area = $87 \pm 3\%$) and visual examination of BP cines (ROC area = $84 \pm 3\%$). MP wall thickening correlated significantly with CMR wall thickening ($r = 0.73$, $P = 0.0003$), and on a segment-by-segment basis abnormal regional MP wall thickening predicted abnormal CMR wall thickening (ROC area = $87 \pm 2\%$).

Abnormal MP phase was present in 25% of 67 dyssynergic segments, 64% of segments adjacent to dyssynergic segments, and 24% of segments remote from abnormal wall motion segments. Abnormal BP phase was present in 36% of dyssynergic segments, 78% of segments adjacent to dyssynergic segments, and 17% of segments remote from abnormal wall motion segments. Thus, presence of a wall motion abnormality was most closely associated with phase abnormalities in adjacent LV segments.

Discussion

The BP methodology of this investigation has been previously shown to have realistic normal limits [3,19], with global EF values correlating well with CMR measurements [4]. The MP algorithms used here also have previously been shown to yield global EFs that correlate well with CMR [14]. Therefore, although it is not surprising that both BP and MP LV global measurements of this study agreed well with CMR, it is encouraging that they agreed so well with each other, considering that the BP and MP algorithms used completely different LV modeling assumptions; whereas MP EF is computed from separately, independently computed EDV and ESV values [14], BP EF is computed from changes in tomographic counts within loosely defined three-dimensional volumes large enough to

encompass all of the likely LV counts [11]. Although there were no significant differences among the three methods for determining EFs and volumes, the tendency of radionuclide imaging to overestimate the highest EFs is not surprising, given the well-known partial volume effects of these tests when attempting to image objects below an imaging system's spatial resolution [20].

Regarding relationships between BP and MP asynchrony measurements, it is understandable that a more global phase histogram parameter, such as bandwidth, would be more consistent between modalities than a parameter more localized in time, such as phase of peak ES contraction. The former is a more cumulative measure of asynchrony that should not be affected by data acquisitions performed with different heart monitors, whereas the latter would be more prone to differences among heart monitors. In addition, the measurement of peak phase derived from data such as that depicted in Fig. 5 would be expected to be more susceptible to noise, as asynchrony was severe in this case, effectively distributing the location of phases among R-R interval locations in a rather chaotic manner. In contrast, computing the length of time encompassing 95% of phases about the peak phase in Fig. 5 should be less influenced by noise. As phase histogram bandwidth, specifically, is one of the main asynchrony parameters that so far has been found likely to be of use in assessing patients before and after cardiac resynchronization therapy [7], and is a highly reproducible MP parameter [8], it is fortuitous that BP and MP methods produce essentially the same bandwidth measurements.

The finding that BP and MP locations of abnormal phase were most closely associated with locations contiguous to locations of abnormal wall motion was an unexpected finding. Myocardial regions with abnormal wall motion frequently demonstrate asynchrony, which is also common in segments with visually normal wall motion adjacent to and remote from dyssynergic segments. This finding suggests that patients with LV dysfunction may have distorted LV synchronicity, extending beyond the area of visually recognized hypokinesis, and impairing LV function to a greater extent than that which could be expected from simple analysis of regional wall motion.

It is also noteworthy that BP and MP global and regional LV function findings were so similar, considering that there were on average over five times more BP counts than MP counts to which the algorithms were applied. A concern regarding MP data could be the reliability of regional phase and function assessment in cases of severe hypoperfusion. Yet, despite the fact that some of the patients in this investigation had severe, extensive MP defects, the results of BP and MP calculations essentially were the same. A possible explanation for this is that, even when applied to count-poor input data, Fourier analysis does an adequate job of data sampling when data are time-cyclic, as BP and MP-gated SPECT data are.

Study limitations

The particular pulse sequence CMR methodology used for this investigation is optimal for depicting the LV endocardial and epicardial boundaries [9], generating highly reproducible and accurate measurements of LV EFs and volumes. The regional CMR measurements of this investigation are optimal for identifying LV segments with abnormally depressed wall motion, but are not necessarily optimal at identifying locations of abnormal contraction phases. 'Tagged' myocardial sequences are more appropriate for optimally analyzing regional phases [21]. Future CMR data acquisitions using different pulse sequences will be needed to test directly the ability of BP and MP-gated SPECT to pinpoint LV segments of abnormal phase, using CMR information.

The number of patients of this investigation ($N = 20$) is small. This is reflective of the practical difficulties inherent in collecting all three types of data – BP, MP, and CMR – for patients after myocardial infarction. Although power analysis indicated that conclusions drawn from our data are statistically justified, nonetheless, larger sample sizes would certainly have been preferable. Thus, further investigations in larger sample sizes and among patient groups of other cardiac conditions are warranted.

Conclusion

BP and MP LV global and regional function and phase measurements agreed well with each other and correlated strongly with CMR measurements. On a segment-by-segment basis, abnormal regional BP EF accurately predicted abnormal wall motion on CMR, and abnormal regional MP wall thickening accurately predicted abnormal wall thickening on CMR. Although segments with abnormal wall motion frequently also had abnormal phase, abnormal phases extended beyond localized areas of dyskinesia, suggesting a wider area involving asynchrony.

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Fig. 1. End-diastolic short axis cardiac magnetic resonance left ventricular sections are shown from apex to base, with superimposed manually drawn endocardial and epicardial boundaries for a patient with congestive heart failure.

Fig. 2.

The polar plot of left ventricular regional ejection fractions (EFs) for the same patient as in Fig. 1, for whom blood pool apical EF = abnormally low value of 50%.

Fig. 3.

The polar plot of left ventricular regional phases for the same patient as in Figs 1 and 2, for whom blood pool phase was significantly delayed at 50% of the R-R interval versus 25% of R-R at the lateral wall.

Fig. 4.

The blood pool phase histogram for the same patient as Figs 1–3, showing an unusually broad, bimodal, histogram of standard deviation = 36° and bandwidth = 112° .

Fig. 5.

The myocardial perfusion (MP) phase histogram for the same patient as Figs 1–4, showing a similarly wide bimodal MP histogram of standard deviation = 36° and bandwidth = 105° .

Table 1

Gated SPECT MP and BP correlations versus CMR for global EFs and end-diastolic volumes

	Pearson's <i>r</i>	Intercept	Slope	<i>P</i>
MP vs. CMR EF	0.87	$-8 \pm 8\%$	1.13 ± 0.15	< 0.0001
BP vs. CMR EF	0.94	$-7 \pm 5\%$	1.17 ± 0.09	< 0.0001
MP vs. CMR volume	0.91	-16 ± 12 ml	1.12 ± 0.09	< 0.0001
BP vs. CMR volume	0.91	-8 ± 19 ml	1.06 ± 0.11	< 0.0001

BP, blood pool; CMR, cardiac magnetic resonance; EF, ejection fraction; MP, myocardial perfusion; SPECT, single-photon emission computer-assisted tomography.