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Correlation of heart rate and radionuclide index of left ventricular contraction and relaxation

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Since the cardiac function indices derived from radionuclide ventriculography (RNV) are considered to depend on the heart rate, we studied the relationship between systolic or diastolic indices and heart rates in patients with normal RNV and devised a method of correcting these indices according to the heart rate.

For the systolic indices, the heart rate showed significant correlation with ET (r=−0.640), PER (r=0.791) and TPE (r=−0.401) but not with EF, 1/3 EF, MNSER or 1/3 MNSER. For the diastolic indices, the heart rate correlated well with FT (r=−0.938), RFT (r=−0.736), SFT (r=−0.803), 1/3 FF (r=−0.758), PFR (r=0.759), 1/3 PFR (r=0.742) and TPF (r=−0.389) but not with AFT, 1/3 MNDFR or AFF.

These results indicate that many systolic and diastolic indices derived from RNV are affected by the heart rate, So when cardiac function is evaluated with the use of radionuclide indices, those which are independent of the heart rate should be used, or they should be corrected for the heart rate.

As a method of correction, we proposed a rotating method obtained by manipulation of the regression equation of heart rates and indices. This new method is certain and easier to use when the correcting equations are set into a computer program.

Key words: radionuclide index, left ventricular contraction, diastolic function, relation of heart rate

INTRODUCTION

The indices of cardiac function derived from radionuclide ventriculography (RNV) are expressed as changes of ventricular volume or of time intervals, or a combination of the two. Therefore, the heart rate, which determines the time interval, may be an important factor influencing the indices of cardiac function derived from RNV.

Diastolic cardiac function is now often evaluated from RNV. Diastolic time intervals are affected more by heart rate than are systolic time intervals. We selected 27 normal RNV records at various heart rates and correlated the heart rate with the systolic and diastolic indices derived from RNV, and then produced an equation to correct the indices for the heart rate.

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MATERIAL AND METHODS

Subjects

Normal RNV records were picked retrospectively from 937 studies performed in our hospital during the past 3 years. The following criteria were used for the selection: no evident cardiovascular disease, age range 20 to 60 years, heart rate 50 to 90 beats per minute, and ejection fraction obtained by RNV above 50%. If there was any abnormality in the chest radiograph, electrocardiogram or echocardiogram, the RNV was not selected. The records of 27 patients met these criteria, 17 males and 10 females. The age range was 39±13 years (mean±1 SD), the heart rate 67±10 beats/min and the ejection fraction 60±5%.

Radionuclide ventriculography (RNV) and computer processing
Following the intravenous administration of 20 mCi Technetium-99m-labeled human serum albumin, gated equillibrium cardiac images were obtained at rest in the left anterior oblique (LAO) projection with slight caudal tilt, with a gamma scintillation camera (Shimadzu LFOV) equipped with a low-energy, all purpose, parallel-hole collimator. The angle of LAO was adjusted to allow the clearest separation between the ventricles.

Thirty consecutive frames, gated by the R wave of the ECG, were acquired in a 64×64 byte mode and stored in the computer memory for 5 minutes. As the cycle time (R-R time interval) was different beat by beat even in sinus rhythm, the frames far from the R wave may have less accumulation of count rates. Therefore, we corrected the count rates in the later frames by the frequency of the accumulation.

Curve analysis
The left ventricular (LV) time-activity curve was generated from a region of interest (ROI) assigned on the LV in the end-diastolic image. The edge of the LV blood pool was determined on the isocount border of 60% of the maximum activity in the LV. The background region was assisgned on the inside of the ROI of the end-diastolic LV image and outside the ROI of the end-systolic LV image. From these two ROIs, a background corrected LV activity curve was obtained. Multiple harmonics of Fourier series were retained for the analysis of the LV time-activity curve. The selection of the term was set on the curve to allow the best fit by visual judgement (usually four to six harmonics were selected). From this fitted curve and its first derivative curve, we derived systolic and diastolic variables for the indexing of cardiac function (Fig. 1).

Systolic function indices
(1) Ejection time (ET), (2) Ejection fraction (EF)=stroke counts (SC)/end-diastolic counts (EDC), (3) 1/3 EF=SC at the first one third (1/3 SC)/EDC, (4) Mean normalized systolic ejection rate (MNSER)=SC/ET/EDC, (5) 1/3 MNSER=1/3 SC / 1/3 ET/EDC, (6) Peak ejection rate (PER) and (7) Time to peak ejection (TPE).

Diastolic function indices
(1) Filling time (FT), (2) Rapid filling time (RFT), (3) Slow filling time (SFT), (4) Atrial filling time (AFT), (5) 1/3 Filling fraction (1/3 FF)=filling counts in the first third of diastole (1/3 FC)/SC, (6) 1/3 Mean normalized diastolic filling rate (1/3 MNDFR)=1/3 FF / 1/3 FT, (7) Peak filling rate (PFR), (8) 1/3 PFR=filling rate in the first one third of diastole, (9) Time to peak filling (TPF), (10) Rapid filling fraction (RFF)=rapid filling counts (RFC)/SC, (11) Slow filling fraction (SFF)=slow filling counts (SFC)/SC, and Atrial filling fraction (AFF)=atrial filling counts (AFC)/SC.

RESULTS

Relationship between systolic indices and heart rate (Fig. 2 and Table)
Significant correlations were obtained between heart rate and ET ($r=-0.640$, $p<0.01$), PER ($r=0.791$, $p<0.01$) and TPE ($r=-0.401$, $p<0.05$), but not between heart rate and EF ($r=-0.271$), 1/3 EF ($r=-0.291$), MNSER ($r=0.251$) or 1/3 MNSER ($r=-0.147$).

Relationship between diastolic indices and heart rate (Fig. 3 and Table)
Significant correlations were observed between heart rate and FT ($r=-0.938$, $p<0.01$), RFT ($r=-0.736$, ($p<0.01$), SFT ($r=-0.803$, $p<0.01$), 1/3 FF ($r=-0.758$, $p<0.01$), PFR ($r=0.759$, $p<0.01$), 1/3 PFR ($r=0.742$, $p<0.01$) and TPF (r=%0.389, $p<0.05$), but not between heart rate and AFT ($r=-0.350$), 1/3 MNDFR ($r=0.353$), RFF ($r=0.138$), SFF ($r=-0.027$) or AFF ($r=-0.070$).

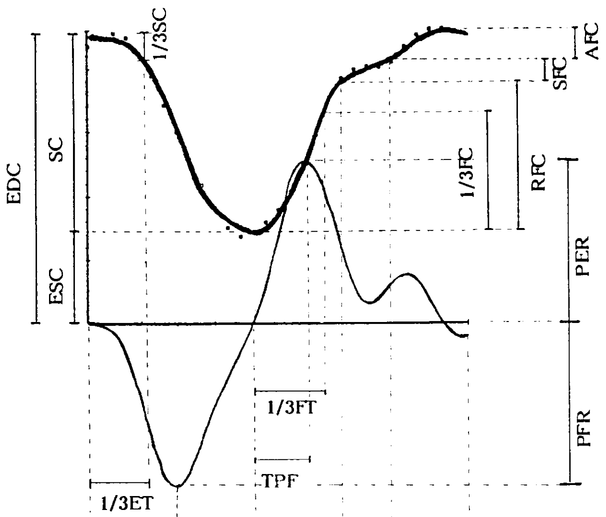

Fig. 1 Systolic and diastolic indices of cardiac function derived from radionuclide left ventricular curve and its derivative curve. Abbreviations are shown in Table and in method section.

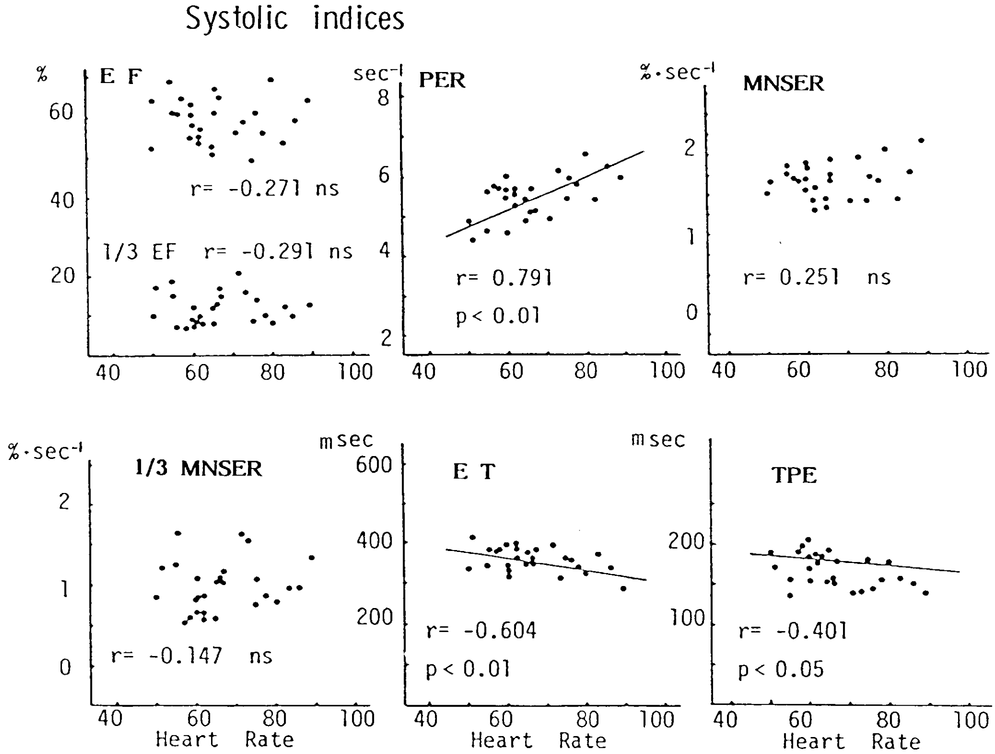

Fig. 2 Relationship between systolic indices (ordinate) and heart rate (abscissa).

Table 1 Correlation between redionuclide indices and heart rate, and correction

Indices	Regression equation	r	p	Correcting equation
systolic				
ET	y=−1.49x+458	−0.604	0.01	ETᶜ=ET+1.49 HR−100
EF	y=−0.117x+67.0	−0.271	ns	
1/3 EF	y=−0.00961x+18.1	−0.291	ns	
MNSER	y=0.0041x+1.39	0.251	ns	
1/3 MNSER	y=−0.00396x+1.25	−0.147	ns	
PER	y=0.0412x+2.72	0.791	0.01	PERᶜ=PER−0.0412 HR+2.79
TPE	y=−0.635x+209	−0.401	0.05	TPEᶜ=TPE+0.635 HR−42
diastolic				
FT	y=−10.7x+1,272	−0.938	0.01	FTᶜ=FT+10.7 HR−715
RFT	y=−2.86x+409	−0.736	0.01	RFTᶜ=RFT+2.86 HR−194
SFT	y=−8.69x+759	−0.803	0.01	SFTᶜ=SFT+8.69 HR−588
AFT	y=−1.82x+270	−0.350	ns	
1/3 FF	y=−0.906x+119	−0.758	0.01	1/3 FFᶜ=1/3 FF+0.906 HR−61
1/3 MNDFR	y=0.0246x+1.62	0.353	ns	
PFR	y=0.0519x+1.77	0.759	0.01	PFRᶜ=PFR−0.052 HR+3.51
1/3 PFR	y=0.0782x−1.11	0.742	0.01	1/3 PFRᶜ=1/3 PFR−0.078 HR+5.22
TPF	y=−0.780x+196	−0.389	0.05	TPF=ᶜTPF+0.78 HR−53
RFF	y=0.0709x+70.8	0.138	ns	
SFF	y=−0.0167+12.0	−0.027	ns	
AFF	y=−0.0487x+17.8	−0.070	ns	

Abbreviations: r=correlation coefficient, p=probability, HR=heart rate, ET=ejection time, EF=ejection fraction, MNSER=mean normalized systolic ejection rate, PER=peak ejection rate, TPE=time to peak ejection, FT=filling time, RFT=rapid filling time, SFT=slow filling time, AFT=atrial filling time, FF=filling fraction, MNDFR=mean normalized diastolic filling rate, PFR=peak filling rate, TPF=time to peak filling, RFF=rapid filling fraction, SFF=slow filling fraction, AFF=atrial filling fraction.

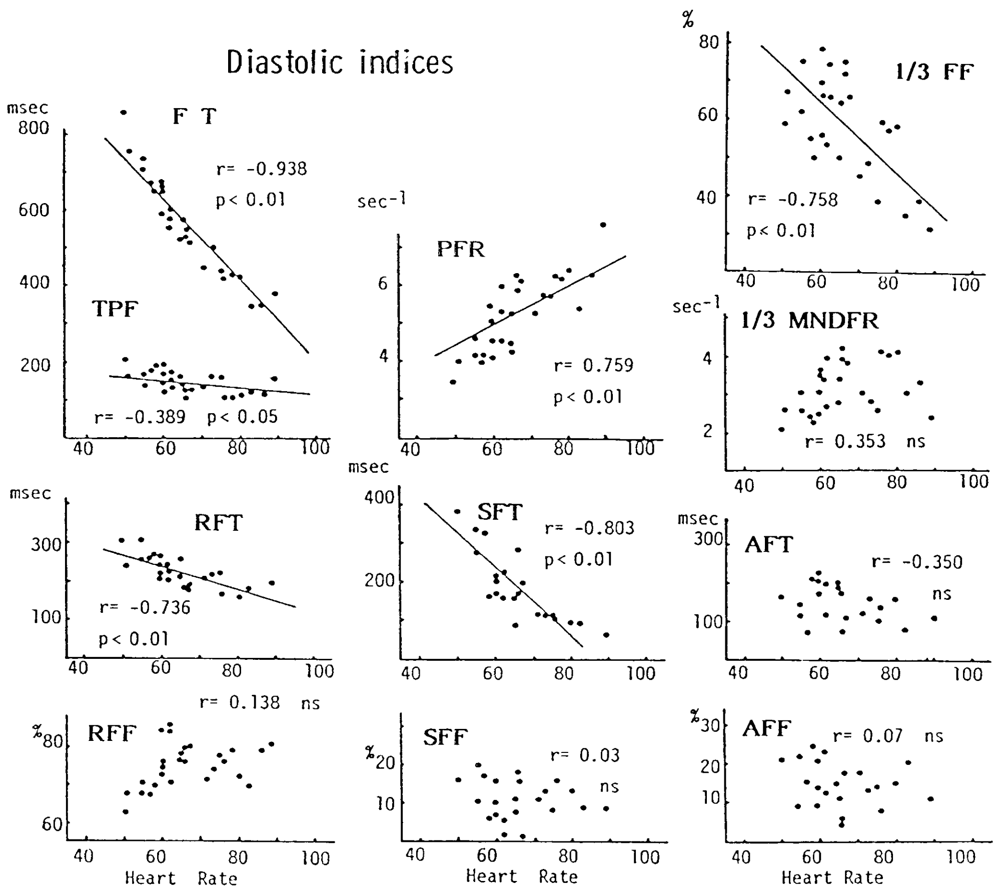

Fig. 3 Relationship between diastolic indices (ordinate) and heart rate (abscissa).

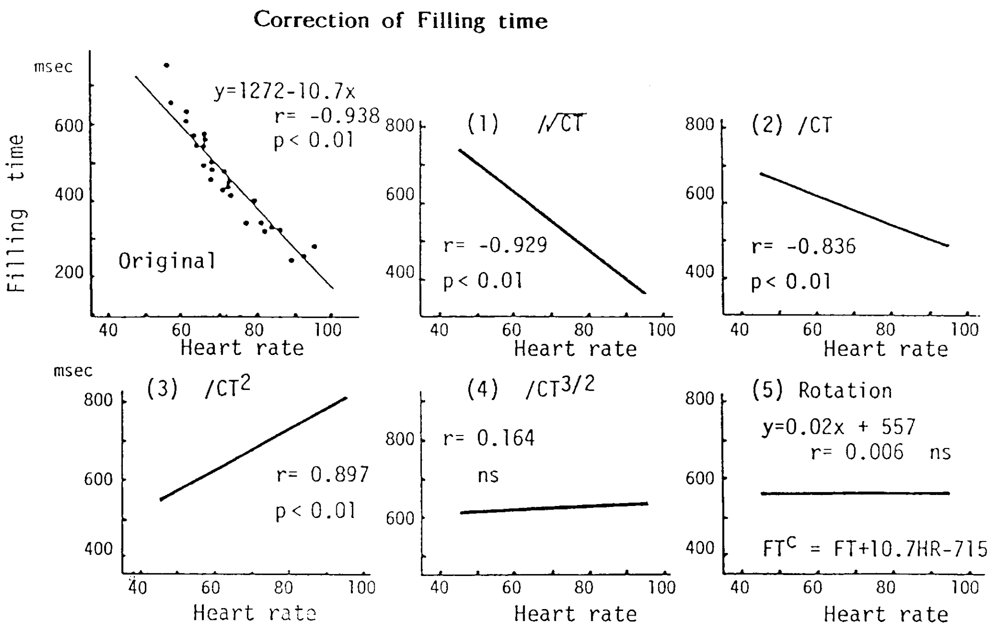

Fig. 4 Correction by heart rate in example of filling time. CT=cycle time (sec)

Correlation of indices by heart rate (Fig. 4)

Figure 4 illustrates the various methods of correction by heart rate in an example of filling time (FT). Between ET and heart rate an inverse correlation was found ($r=-0.938$, $p<0.01$). After correction by division by the square root of the cycle time (CT) or by the CT itself, the correlation was reduced ($r=-0.929$ or -0.836, respectively) but the significance ($p<0.01$) remained. With division by the square of CT, the correlation was reversed ($r=0.897$) but still significant ($p<0.01$). The correlation was abolished by division by $CT^{3/2}$ ($r=0.164$). Another way of complete correction by heart rate is obtained by rotation of the regression line ($FT=1272-10.7\times HR$); that is, if the regression line is rotated in the axis of the mean values of these parameters (ET and HR) to become parallel to the abscissa (HR), the correlation can be completely aborted ($r=0.006$). So the equation of the correction is obtained by the manipulation of the regression line (corrected FT= original $FT+10.7\times HR-715$). This correction is not difficult if the equations are set in a computer program.

Table shows the correcting equations of other systolic and diastolic indices obtained by this rotating method.

DISCUSSION

Various cardiac function indices used often in the clinical field are placed in the following three categories: (1) time (2) length, area and volume (3) pressure. The cardiac indices derived from radionuclide ventriculography are expressed by a combination of time and volume (counts). Therefore, it seems that the indices derived from radionuclide ventriculography would necessarily be affected by the heart rate, which decides the cardiac cycle time.

It has been appreciated that the heart rate is an important factor influencing the parameters of cardiac function obtained from the ECG,[1] systolic time intervals (STI)[2-4] and echocardiography.[5,6] The duration of the Q-T interval in the ECG varies with cycle time, and numerous formulae have been suggested to correct for heart rate. Bazett proposed a formula for estimating the Q-T interval corrected for heart rate.[1] In applying STI measurements, a correction must be made for differences in heart rate. The regression equation best describing the relationship of STI to heart rate derived by Weissler et al has been generally adopted for this purpose.[7] In echocardiography the measurements of ejection phase indices, such as mean rate of circumferential fiber shortening (Vcf) and posterior wall velocity, have been corrected by normalization of the heart rate.[8-10] Similarly, in the evaluation of left ventricular relaxation by echocardiography, it is known that the cardiac cycle time is an important variable affecting the indices.[5,6]

Although it is assumed that the radionuclide index of cardiac function is influenced by heart rate because it has a factor of time, there have been few reports to date of detailed investigations of this relationship. Recently, abnormal cardiac relaxation has been demonstrated by radionuclide ventriculography in a variety of disease states. Since the diastolic phase is more dependent on cardiac cycle time than the systolic phase, it seems that diastolic phase indices must be corrected for the heart rate. The present study was undertaken to elucidate the relationship between heart rate and all the indices in the systolic and diastolic phases measured by radionuclide ventriculography.

In this investigation, from a large number of RNV studies, only 27 records were selected because absence of heart disease and normal cardiac function were among the criteria for selection. We did this selection as carefully as possible, especially excluding diseases such as ischemic and hypertensive heart diseases which may appear to have normal function because the systolic phase function is normal at times. But these diseases are known to have frequent impairment of diastolic relaxation which may be more difficult to demonstrate. To exclude these diseases, we used various noninvasive examinations; consequently, it is very probable that in all 27 cases there was no significant disease and cardiac function was normal. The above 80 or below 60 inclusion of heart rate may be a point of discussion, but in these cases it was proved that there was no heart disease. Age is a factor influencing diastolic function. The extension of the criteria to 60 years of age was partly due to the fear that there would be too few cases.

In this study, we examined as many cardiac indices as possible in both systole and diastole. Of these indices, ET, TPE, FT, RFT or SFT involve time intervals and are therefore dependent on the heart rate.

So it is understable that the correlation of these indices with the heart rate is greater than that of other indices.

EF, the most utilized index of cardiac function, correlated poorly with the heart rate in our study, but Ricci et al reported in inverse relationship EF and heart rate.[11] This difference may be due to the range of heart rates studied. Their results were obtained during atrial pacing at increments of heart rate from 83 to 154 beats per minute, while ours were obtained from patients with heart rates of 50 to 90 beats per minute.

Although the correlation between diastolic function indices and heart rate has not been studied enough, there have been some reports on the relation of PFR to heart rate.[6,12–17] In echocardiograms, Fifer et al[14] reported that dD/dt analogous to PFR showed a weak correlation with the heart rate ($r = 0.28$, $p < 0.05$), and that this correlation vanished when dD/dt was multiplied by 1/R-R. In RNV studies, some investigators have not observed any correlation between PFR and HR,[15,17] while others have noted a positive correlation.[13,16] Polak et al[16] reported a slight correlation in normal subjects and in patients with coronary artery disease (CAD). Interestingly, this correlation differed in these two groups. In normal subjects PFR values increased more for a given increment in heart rate than in CAD patients, and they suggested that the discriminative ability of PFR might be enhanced at higher heart rates. Our study of normal subjects showed a good correlation between PFR and HR ($r = 0.759$, $p < 0.01$). Since an increase in HR shortens the diastolic filling interval, the enhancement of PFR at higher HR seems to be a sort of compensation for reduced diastolic filling due to a shortened diastolic interval.

For the correction of cardiac indices by cardiac cycle time, the formula presented by Bazett[1] has been the most popular. Bazett's formula is very simple (corrected value=measured value divided by the square root of the cardiac cycle time), but there is a problem in its application uniformly to all cardiac indices. As shown in Figure 4, FT could not be completely corrected by this formula. Instead of Bazett's formula, we present a new method of correction, the rotating method. Although correction by our method is complete and applicable to all cardiac indices, it is somewhat complicated. Therefore, it may be easier to use if the correcting equation is set in a computer program.

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