Heart Rate Asymmetry in Aortic Valve Stenosis Patients

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Abstract

Heart rate asymmetry is one of the measure of the autonomic nervous system activity. Here we use the Phase Rectified Signal Averaging method for heart rate asymmetry calculations and focus on Deceleration Capacity (DC) obtained for aortic valve stenosis patients just before surgical replacement of the aortic valve. In the study we used 6-h nighttime data from 107 patients aged 60-71 y.

We compare the results between male and female groups obtaining a larger diversity in males. Unfortunately, the decrease of the DC parameter, which is used as mortality risk marker in other several regulatory dysfunctions is not applicable for aortic stenosis in risk stratification. We did not observe distinction of patients who died earlier than one year after surgery.

In spite of this, we introduce the modified nDC and Acceleration Capacity (nAC) parameters for a better assessment of the ability to lengthen and shorten RR intervals.

1. Introduction

Since 2006, many papers on the application of the PRSA method for heart rate variability analysis were published. The main reasons are the amazing results for the new mortality risk predictor –deceleration capacity DC found for patients after myocardial infarction [1] and the simplicity of the numerical calculations of the method.

Later, Kantelhardt at al [2] showed a linear decrease of the DC with age and the problem of interpretation of the low values of DC for older patients, for whom the risk of mortality is generally increased. Moreover, among the patients after myocardial infarction and with diabetes mellitus (associated with autonomic dysfunction) the DC parameter was smaller than among similar patients but without diabetes.

The DC parameter was helpful for the assessment of the autonomic dysfunction for risk stratification in patients after myocardial infarction with preserved left ventricular function [3] and type 2 diabetes [4]. The subgroup of increased mortality risk is known as severe autonomic failure patients. Severe autonomic failure patients were defined [4] as those with a coincidence of an abnormal autonomic reflex function (measured by to descriptors of the heart rate turbulence: turbulence onset ≥0% and turbulence slope ≤2.5ms) and an abnormal tonic activity (measured by DC<4.5ms).

Aortic stenosis may be congenital, but more often is acquired. In adults, it usually occurs due to calcium deposits that narrow the valve and generally affects older people. This change in valve causes an obstruction of the blood flow.(Cardiology Journal 2007:14;510-517)

2. Medical data

We analyzed 6-h nighttime data of RR intervals from 107 patients (53 males and 54 females) of age 60-71y with aortic valve stenosis (AS) recorded just before surgical replacement of the aortic valve. The RR intervals were extracted from a 24 h Holter ECG recording using the Del Mar Reynolds system (Spacelabs) at the Institute of Cardiology (Warsaw, Poland). The data were checked manually by a cardiologist: normal beats were detected, artifacts were deleted. Each RR interval series contained less than 2.5% of arrhythmias. Diversity in the left ventricular ejection fraction and the mean aortic gradient of these patients is presented in the Fig. 1. The latter parameter is used to assess of the advancement of AS.

Table 1. Additional medical information about patients.

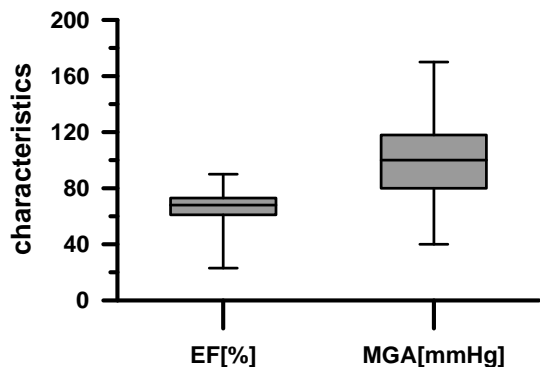| State	No. of patients
Hypertension	52
NYHA(I;II;III;IV)	14;26;45;22
Diabetes (type 1;2)	3;1

Fig. 1. Left ventricular ejection fraction and mean aortic gradient for group of analyzed patients with AS.

Cumulative mortality in the group analyzed is presented in Fig.2. It shows a radically increasing pattern in the 5 years (60 months), which is related to comorbidities and age of patients.
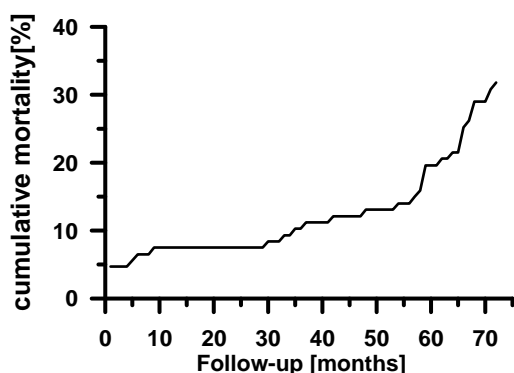

Fig. 2. Cumulative mortality in group of AS patients in 75 months follow-up after aortic valve replacement.

3. The phase rectified signal averaging method in heart rate variability analysis

The PRSA method was previously introduced for analysis of non-stationary and noisy data, which contains periodicities. Such oscillations (for example in the heart rate variability time series) are often difficult to observe in the frequency domain. Therefore, the analysis of (rather) long signals is reduced to small windows and an averaging is applied.

The first step of the method is defining the anchor points. The selection of such RR intervals, which increased relative to the previous one, must be used as anchor points to study the ability to lengthen the heart cycle. Another criterion for the anchor point is also possible – selecting shortening intervals, which are used for the analysis of the acceleration of the heart rhythm.

The second step of the PRSA method is the definition of the radius. The PRSA curve oscillates as a function of the distance from the anchor point at which it is calculated [1]. The radius parameter is strictly related to

the frequency scale of the periodicities obtained around the anchor points. Slow oscillations require a larger radius than fast ones. Usually, in HRV analysis, a radius of 40 to 60 points is applied. If the radius equals 60, then a segment of 120 points around anchor is selected. Segments for neighbouring anchors overlap. The anchor point is numbered as RR(0), the previous intervals as RR(-1), the following as RR(1).

Each anchor point and the radius parameter define a window. The selected windows are now aligned in such a way that the anchor points in the windows coincide. Finally, an averaging of each point in the windows of radius r is done and final PRSA curve is obtained. The averaged PRSA curve has increments and oscillations better visible than in the original signal.

3.1. Deceleration and acceleration capacity

The quantification of the PRSA curve was introduced by Schneider et al [2]. They suggested wavelet analysis and focused on the central part of the PRSA signal i.e. the closest to the anchor point. For the study of the lengthening and the shortening of RR intervals, the Haar wavelet should be used with scale 2 and time position 0 [5]. Therefore the DC(AC) parameter (depended on selection of the type of the anchor points) is given by formula:

$$DC\ (or\ AC) = \frac{X(0) + X(1) - X(-1) - X(2)}{4}$$

where $X(\cdot)$ are RR intervals adjacent to the anchor point.

This is then a procedure for averaging of four consecutive RR intervals and gives the mean increment in that range.

3.2. Modification of DC and AC

DC and AC factors are widely used as measures of the autonomic modulation [1-5]. It was shown [1] that a decreased values of DC (less than 2.5ms) are better mortality risk predictor in a group of patients after myocardial infarction than the left ventricular ejection fraction and the Standard Deviation of Normal to Normal Intervals. However, the definition for DC(or AC) presented above does not measure the beat by beat ability of lengthening (or shortening) RR intervals. This is because the X(1) and X(2) can represent just as well the increased and the decreased (averaged) RR intervals. The criterion for selection of anchor points gives information **only** about the relation between X(0) and X(-1). Therefore, we suggest using only X(0) and X(-1) in assessment of lengthening or shortening heart cycle and take the difference:

nDC(or nAC)= X(0)-X(-1)

To allow a comparison of the results obtained by the original formula for parameter DC and our new factor nDC, we additionally introduce the simple averaging:
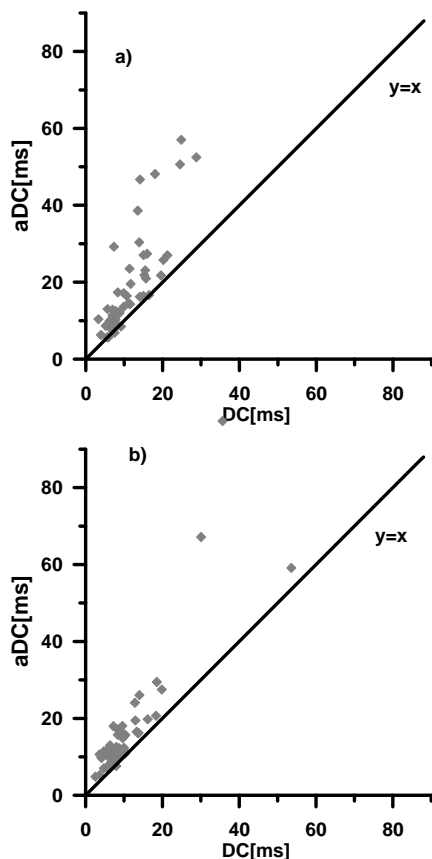
aDC(or aAC)= [X(0)-X(-1)]/2.

Fig. 3. DC parameter vs. aDC in AS patients: a)male b)female. aDC is limited only to two points, while DC take into account four central points of PRSA curve. aDC values are in general much larger than classic values of DC.

In Fig. 3, we present the results of this comparison for a group of male (a) and female (b) patients with AS. This result indicates that the original definition underrates the actual ability of the system to change the RR interval. For aDC values larger than 20 ms, the males exhibit a larger spread than the females. Moreover, it can be seen that for most AS patients aDC concentrates below 30ms.

3.3. Comparison of the DC and AC

We divided the patients analyzed into three subgroups: the patients who died during the first year after surgery, the patients who died between one and five years after operation and those patients who lived longer. The means and medians of the DC, AC, nDC and nAC parameters compared among the subgroups are presented in Table 2 and Table 3. Note, however, that number of patients in subgroups is unequal (compare with Fig. 2). The group of

patients that died during first year consisted of 8 pts, between 1 and 5 yrs – 14pts and the last group – 85 patients.

Table 2. Comparison of DC and nDC parameters among subgroups of AS patients.

Subgroup	Mean DC[ms]	Median DC[ms]	Mean nDC[ms]	Median nDC[ms]
T*<1y	11,3	9,4	35,9	26,5
1y<T*<5y	14,5	11,6	48,1	34,7
T*>5y	10,6	8,6	34,3	24,6

Table 3. Comparison of AC and nAC parameters among subgroups of AS patients.

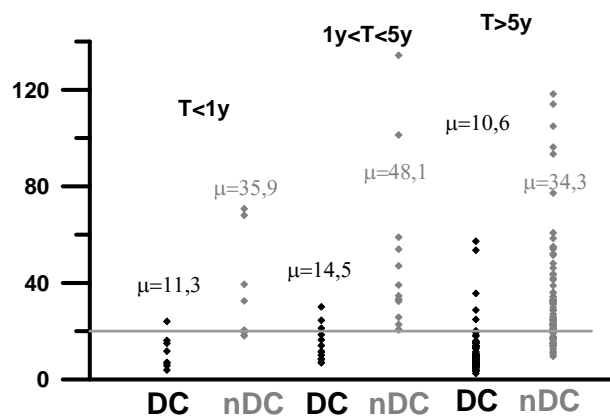| Subgroup	Mean AC[ms]	Median AC[ms]	Mean nAC[ms]	Median nAC[ms]
T*<1y	-10,3	-8,7	-33,0	-24,8
1y<T*<5y	-12,7	-10,1	-42,5	-34,7
T*>5y	-9,4	-8,1	-30,8	-24,0

*time of living after surgery

Fig. 4. DC parameter and nDC in AS patients with division into subgroups.

The difference between the first and last subgroup could be taken to be relatively small, if we do not observe the patients for whom nDC<20 ms. Only one patient in the first subgroup has nDC smaller than 20ms, while in the last 26 patients. In middle subgroup no patient had smaller than 20ms. But these patients, who died between one and five years after surgery had increased DC, nDC and a much smaller AC, nAC. Note however, that patients who lived longer than five years after operation have the smallest DC, nDC but the largest AC and nAC. We stress that the smallest values of DC for AS patients are still much larger than cutoffs for risk stratification presented in papers [1,3,4]. The problem of the increased values of the DC (or a decreased AC) was not discussed before. Our results suggest that the increased values of the DC may indicate a negative prognosis in risk stratification as in patients with AS.

3.4. Uncertainty of DC parameters

We suggest simple way of estimating the uncertainty of the DC parameter. Here, we do not take into consideration the accuracy of the R peak determination from ECG signal, which of course have an impact on the final value of the uncertainty of DC.

For the four points at the center of the PRSA curve (X(-1), X(0), X(1), X(2)), the standard errors of the each mean are calculated. Next, we estimated the uncertainty by the propagation of errors method [6] and obtained the formula:

$$\Delta DC = \left\{ \left[\frac{\partial DC}{\partial X(0)} \right]^2 [\Delta X(0)]^2 + \left[\frac{\partial DC}{\partial X(-1)} \right]^2 [\Delta X(-1)]^2 \right. $$
$$+ \left[\frac{\partial DC}{\partial X(1)} \right]^2 [\Delta X(1)]^2 $$
$$\left. + \left[\frac{\partial DC}{\partial X(2)} \right]^2 [\Delta X(2)]^2 \right\}^{1/2} $$

Where the $\Delta X(i)$ is the standard error of the mean.

We obtained the uncertainty for DC parameter and expressed it in percent of the DC values. Uncertainty of DC varied from 1,7% to 14,9%, while for nDC from 0,34% to maximum 7,4%. The latter is this much smaller.

4. Conclusions and final remarks

We study the DC parameters in a group of 107 patients of aortic valve stenosis patients recorded just before aortic valve replacement. We also introduced a modified formula for DC and AC computations, which measures directly the ability to lengthen and shorten heart cycle from beat to beat changes. The classical forms of DC and AC parameters do not represent these abilities because they seem to average the RR intervals too many points away from the anchor points. We limited the calculations to only those RR intervals which increased (for nDC) or decreased (for nAC) in the heart cycle adjacent to the anchor point. Note, however, that the formula for DC and AC has its origin in wavelet analysis (see sec. 3.1). On the other hand our modified nDC and nAC better reflect the physiological abilities of the modulation of hearth cycle length.

Our parameter nDC as well as classical the DC parameter do not discriminate patients with an increased mortality risk. What is more the smallest DC values were obtained for those ST patients who lived longer than five y. after surgery (see sec. 3.3).

We suggested a simple way for the computation of the uncertainty of DC and nDC. The level of uncertainty of DC in comparison (measured in percentages) to values of DC is much larger than for our modified nDC (see sec. 3.4). In this estimation, we do not take into account accuracy of the R peak determination and other factors acting on the final values of the parameters DC and nDC.

Finally, note that our analysis was done on shorter time series than in references [1-4]. We used 6-h nighttime data. This could result in increased values of both DC and nDC, because the distribution of RR intervals has usually a larger standard deviation than that for 24-h signals. Moreover, our analysis is limited to older patients, which probably enhances the difficulties in assessing mortality risk. On the other hand, this limitation was related to fact that the AS patients are often older but the age group chosen here seems to be the most representative. We should also ask the question if in this age group prediction of survival longer than 5 yrs can really be based on a single measurement.

Acknowledgements

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