Prediction of the Supraventricular Arrhythmias in Hypertensive Patients with Different Forms of the Left Ventricular Geometry

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Abstract

Left ventricular hypertrophy (LVH) in course of hypertension has been linked to the development of atrial fibrillation (AF) and other supraventricular arrhythmias (SVA). The aim was to discover the predictors of electrical instability which could identify hypertensives with the risk of SVA and to investigate the role of different types of left ventricle (LV) geometry on the risk of arrhythmias. The second aim was to evaluate two types of filtering of signal-averaging ECG in the prediction of cardiac arrhythmias in hypertensive patients.

Statistical analysis including generalized additive models (GAM) were performed. Maximum heart rate (HRmax), duration of P-wave in Butterworth filtered atrial SAECG (hfP_S), envelope of the last 10ms P-wave vector magnitude (obw10_S) and left atrial internal area (LAar) were identified as the model of SVA predictors.

1. Introduction

The most important risk factors for atrial fibrillation (AF) are age, male gender, hypertension, thyrotoxicosis, smoking, diabetes, left ventricular (LVH) hypertrophy, left atrial enlargement, valvular and coronary heart disease, congestive heart failure, and stroke [1,5]. LVH in course of hypertension has been linked to the development of AF and other supraventricular arrhythmias (SVA). However, the relationship between different forms of LV geometry and SVA has not been fully elucidated. Few studies have shown the utility of P-wave signal averaged electrocardiogram (P-SAECG) [7,8]. Using P-wave signal averaging electrocardiogram (P-SAECG) in patients after coronary bypass grafting (CABG) it has shown that patients with longer filtered duration have a risk of AF [9].

The aim of our study was to discover the predictors of electrical instability which could identify hypertensives with the risk of SVA and to investigate the role of different types of LV geometry on the risk of these arrhythmias. The second aim was to evaluate two types of filtering of signal-averaging ECG in the prediction of SVA in hypertensive patients.

2. Methods

2.1. Study protocol

145 uncomplicated patients with mild to moderate hypertension were enrolled in our study. Patients underwent a clinical examination (at the begin of the study): BP measurement, ABPM, ECG, 24-hour Holter monitoring ECG, echocardiographic tracings and atrial SAECG. The study protocol was approved by the local medical Ethics Committee. All patients gave written, informed consent before entering the study.

Table 1. Patients characteristic

Characteristics	males	females
Numbers	100	45
Age (years)	47,7 ± 9,7	52,5 ± 8,9
Mean body mass index (kg/m^2)	28,8 ± 3,4	27,3 ± 3,9
LVM	247,5 ± 52,6	197 ± 46,0
LVMI	120,3 ± 22,6	109,5±23,6

2.2. BP – measurement and ABPM

We recorded BP at rest with mercury sphygmomanometer and with an ABPM device. The patients rested for at least 10 min in a room with comfortable temperature, before the recording of BP. The mean of the three measurements was considered the mean BP and used to statistical calculation.

With the ABPM device (Spacelabs 90202) we recorded each patient's BP every 15 min in the daytime (6 AM – 11PM) and every 30 min in the nighttime (11 PM - 6 AM). For the statistical calculation the mean BP in 24h, during daytime and during nighttime. All ABPM measurements were done during normal activity of each patient. The WHO classification was used as a reference values.

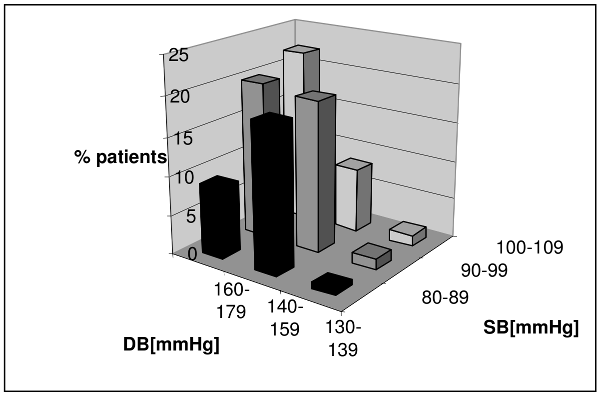

Figure 1. Mean value of recorded BP (DB and SB) for all patients.

2.3. ECG

On the base of the standard 12-lead ECG (CardioPerfect 3,4: 50mm/s, 10mm/mV) were measured:
-duration P (Pd) – was defined as the time interval (in msec) between the earliest onset of the P wave and latest offset in in II lead,
-dispersion P (ΔP) – was defined as difference between the longest and the shortest P wave (msec),
-PQ interval (PQ) – PQ was measured from the beginning P wave to the beginning the Q wave (msec.).

2.4. 24-hour Holter monitoring ECG

Ambulatory electrocardiography was carried out using the Oxford Medilog MR45 recorder. Patients were encouraged and advised to undertake their usual daily activities except bathing and swimming. They were also advised to note the time and details of any symptoms perceived. The timings of falling asleep and
waking-up were noted as accurately as possible. Analysis included the occurrence of important SVA (ISVA). ISVA was defined as an occurrence of Paroxysmal Atrial Fibrillation (PAF), an episode of supraventricular tachycardia or supraventricular premature beats>100/24hour.

2.5. Echocardiography

Examinations were performed using a Hewlett-Packard Sonos 2500 recorder with 3,5 MHz transducer. In each patient 2-dimmentional and M-mode tracing were obtained.

The left ventricular end-systolic diameter (LVESD), the left ventricular end-diastolic diameter (LVEDD), the posterior wall thickness at end-diastole (PWT) and the intraventricular septal thickness at end-diastole were obtained according to the recommendations American Society of Echocardiography [2].
Left ventricular mass (LVM) was calculated using the Penn formula [3]:
$LVM= 1,04 *[(IVS+LVEDD+PWT)^3 – LVEDD^3] – 13,6$

Left ventricular mass index (LVMI) was defined as relation LVM and the body surface area (SA) in m^2 and was calculated using the Du Bois formula as follows:
$SA = 0,007184 * H^{0,725} * W^{0,425}$
where H is height in cm and W is weight in kg. LVH was confirmed when LVMI ≥ 111 g/m^2 in men and LVMI ≥ 106 g/m^2 in women [4].

All patients had also measured internal diameters of left atrium in short and long axis and areas of left and right atrium (LAsax, LAlax, LAar, RAar).
According to LV geometry at the echocardiogram, patients were divided into four groups:

- with normal LV geometry (n=30);
- with concentric remodeling (n=29);
- with eccentric LVH (n=40)
- with concentric LVH (n=46).

The patients did not differ significantly between the groups in terms of age and sex.

2.6. Acquisition and analysis of the P-SAECG

The P-SAECG was recorded from an X,Y,Z leads home- system. The P-wave was retained as a triggered of the averaging process, and the signals were digitized as at frequency of 1kHz with 12-bit accuracy. A sinus template was selected manually by the operator. P-waves were recorded until a noise endpoint of 0,7 µV was achieved in the PQ interval. Approximately 150 beats were used to complete the signal averaging. The P-wave complex of filtered X,Y and Z leads were combined to a vector magnitude $(X^2+Y^2+Z^2)^{0,5}$.

In our analysis we included innovatory parameters (figure 2) and two different types of filtration procedures

1. 45-150Hz Kaiser filter (index K)
2. 40-250Hz Butterworth filter (index S).

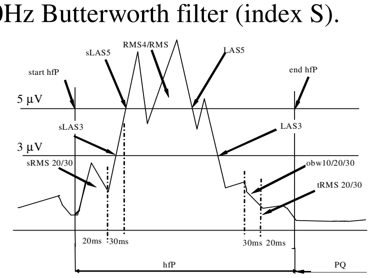

Figure 2. Parameters of P-wave complex.

3. Statistics

Full data set analysis for all outcomes without imputation of missing values were performed. Linear regression were performed for comparisons of variables between groups. Significance was set at a p value < 0.05. After preliminary analyses we determined independent predictors of atrial fibrillation by using stepwise logistic regression analysis, with results confirmed by forward selection and backward elimination. Then generalized additive models (GAM) were performed. These models assume that the mean of the dependent variable depends on an additive predictor through a nonlinear link function. Generalized additive models permit the response probability distribution to be any member of the exponential family of distributions.

4. Results

Logistic regressions were used to determine risk and protective factors that could significantly predict ISVA. For all parameters odds ratio (OR) with 95% confidence interval (CI) were calculated. Table 2 presents the odds ratios obtained when the log odds of each parameters was predicted using a single predictor.

Table 2. Predictors of SVA

Logistic regressions					
parameters		OR	95% CI		p
LAlax	[cm]	2,40	1,25	4,59	0,008
LAar	[cm^2]	1,18	1,05	1,32	0,004
HRmax	[/min]	1,03	1,01	1,05	0,007
RMS40/RMS_K		7,00	1,11	44,2	0,038
obw20_K	[μV/ms]	1,10	1,04	1,17	0,049
hfP_S	[ms]	1,13	1,08	1,18	0,0001
RMS40/RMS_S		10,9	1,19	99,5	0,035
LAS3_S	[ms]	1,10	1,02	1,19	0,012
sLAS3_S	[ms]	1,17	1,11	1,25	0,0001
sLAS5_S	[ms]	1,13	1,08	1,19	0,0001
obw10_S	[μV/ms]	1,49	1,30	1,70	0,0001
obw20_S	[μV/ms]	1,10	1,04	1,17	0,002
obw30_S	[μV/ms]	1,08	1,03	1,13	0,0005

Graphical presentation of estimated risk of ISVA by instantaneous change in several important predictor was presented on figure 3.

After this analysis, applying forward selection and backward elimination, the most important predictors was selected for GAM model calculation. Maximum heart rate (HRmax), duration of P-wave in Butterworth filtered atrial SAECG (hfP_S), envelope of the last 10ms P-wave vector magnitude (obw10_S) and left atrial internal area (LAar) were identified as the model of SVA predictors.

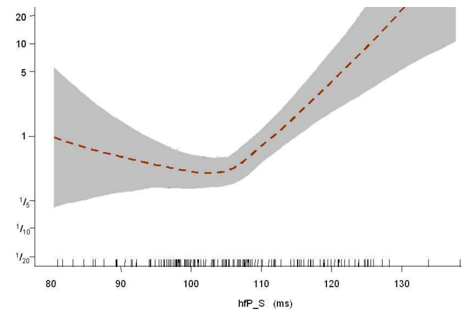

Figure 3. Estimated risk of SVA by instantaneous change duration of P-wave in Butterworth filtered atrial SAECG - hfP_S. Dotted lines estimated risk under logistic model; Solid line shows indicate 95% confidence intervals (CI).

ISVA was observed most common in pts with concentric LVH (9 pts). Receiver operator characteristic (ROC) curves plotted for each of the ISVA predictors were showed on fig.4. Area under the curve (AUC) was calculated and presented in table 3.

Table 3. Area under the ROC curve for four predictors.

	AUC		AUC
obw10_S	0,84	LAar	0,69
hfP_S	0,80	HRmax	0,64

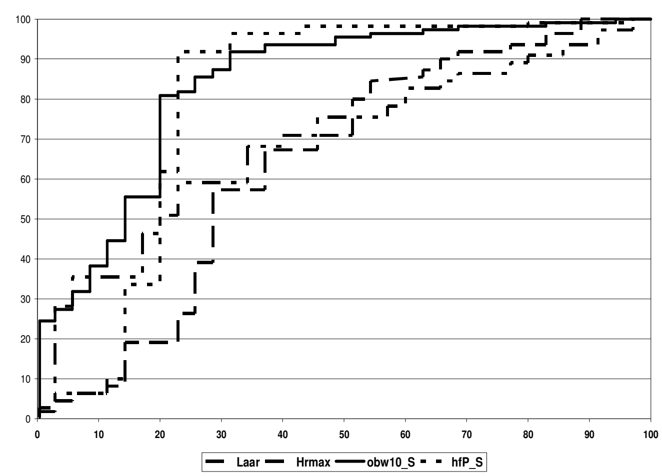

Figure 4. Receiver operator characteristic (ROC) for each of predictors.

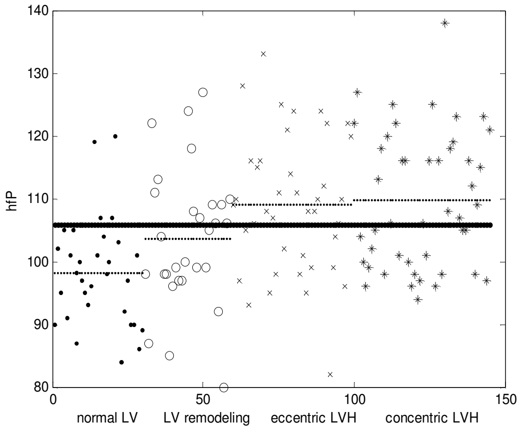

Figure 5. hfP_S duration for four groups (at the baseline).(Solid line – mean value for all patients, dotted line – mean value for each group)

5. Discussion

It has been postulated that the P-wave signal averaged might show atrial areas of delayed electrical conduction. Electrical atrial potential can be modified by several factors: myocardial changes with intra-atrial conduction abnormalities, left atrial hypertension, left atrial distension and chronicity of disease [11]. The hfP wave duration can be also affected by changes in autonomic tone [12].

Slow atrial conduction may cause increase of signal averaged P-wave duration which is found as a risk factor of an occurrence of atrial fibrillation and other atrial arrhythmias, especially hfP. The importance of this parameter was confirmed also in our study. In hypertensives signal averaged ECG P-wave duration can be used as a good marker of risk of PAF. (fig. 5)

P wave signal-averaging could be useful also to identify patients at risk for the transition from paroxysmal to chronic form of AF. It is clinically important to predict the transition because it has been reported that mortality and risk of thromboembolism are higher in patients with chronic AF than in those with the paroxysmal form. Even the presence of sinus node dysfunction in patients with paroxysmal AF can be evidenced. The main recent applications of P wave signal-averaging for AF management have been done in two important clinical settings: prediction of relapse after electrical cardioversion and control of antiarrhythmic drug efficacy.[10]

Our study shows that none of parameters of standard 12 leads ECG is useful for prediction important atrial arrhythmias and only HRmax from Holter monitoring has predictive values for estimation of SVA occurrence probability.

6. Conclusion

1) Noninvasive tests, especially Butterworth filter filtered atrial SAECG and echocardiography, can be useful tools to identify hypertensive patients with risk of ISVA.
2) Concentric LVH is a risk factor of significant ISVA in hypertensives.

References

[1] Verdecchia P. et al : Atrial Fibrillation in Hypertension. Hypertension. 2003;41:218-223.
[2] Sahn DJ, DeMaria AN, Kislo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography measurements. Circulation 1978;58:1072-83
[3] Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation 1977;7:409-415
[4] Ganau A, Devereux RB, et al. Patterns of left ventricular hypertrophy and geometric remodelling in essential hypertension. J Am Coll Cardiol 1992;19:1550-1558
[5] Healey JS, et al: Atrial Fibrillation: Hypertension as a Causative Agent, Risk Factor for Complications, and Potential Therapeutic Target. Am J Cardiol 2003;91(suppl): 9G–14G
[6] Platonov PG.: Detection of inter-atrial conduction defects with unfiltered signal-averaged P-wave ECG in patients with lone atrial fibrillation. Europace 2000;2: 32–41
[7] Ishimoto N, et al.: Signal-averaged P-wave abnormalities and atrial size in patients with and without idiopathic paroxysmal atrial fibrillation. Am Heart J 2000;139:684-89
[8] Aytemira K, et al.: The signal-averaged P-wave duration is longer in hypertensive patients with history of paroxysmal atrial fibrillation as compared to those without. International Journal of Cardiology 2005;103:37– 40
[9] Budeus M, et al.: Amiodarone prophylaxis for atrial fibrillation of high-risk patients after coronary bypass grafting: a prospective, double-blinded, placebo-controlled, randomized study. European Heart Journal 2006;27:1584–1591
[10] Michelucci A, et al.: P Wave Assessment: State of the Art Update. Cardiac Electrophysiology Review 2002;6:215–220
[11] Kasser I, Kennedy JW.: The relationship of increased left atrial volume and pressure to abnormal P waves on the electrocardiogram. Circulation 1969 39:339-334
[12] Cheema AN, et al.: Effects of autonomic stimulation and blockade on signal-averaged P wave duration. J Am Col Cardiol 1995;26:497-502

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