Predictor Value Markers of SIRS for Recurrence of Arrhythmia in Patients with Coronary Heart Disease Combined Hypertension and Persistent Atrial Fibrillation

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Abstract

Aim of the study was to determine the predictor value, relative to the recurrence of arrhythmia SIRS markers (IL-1β, TNF-α) and endothelin-1 in the absence of dilatation of the left atrium in patients with CHD combined with hypertension stage II and persistent AF.

Methods: The results of the study based on data from a comprehensive survey and dynamic monitoring of 62 CHD combined with II stage HT and persistent AF, in total 62 persons of the average age was 58.7 ± 0.5 years. Patients setting was conducted in the period from 2012 to 2013 year.

Results: We found that linear size of the left atrium found credible predictor value, the area under the curve (AUC = 0.61) and at the optimum point distribution 3.7 cm the sensitivity was 76.0 % and specificity of 48.7 % (95 % CI AUC 0.5000-0.7042). Significantly (AUC = 0.72) the levels of IL-1β was at the cut-off point of 1.5 PG/ml (the sensitivity of 44.0 % and specificity of 94.6 % (95 % CI AUC 0.5740-0.8380)) to recurrence of AF in patients with CHD combined with HT and persistent AF (tab. 1). The cut-off point for the level of FNO-α significantly (AUC = 0.93), according to ROC analysis was 1.7 PG/ml (the sensitivity of 91.9 per cent and the specificity was 76.0 per cent (95 % CI AUC
The results of the analysis of the ROC-analysis showed a significantly (AUC = 0.93) high predictor value of endothelin-1, under the optimal cut-off point threshold distribution of 2.2 fmol/l, sensitivity amounted to 96.0 % and specificity of 89.2 % (95 % CI AUC 0.8634-1.000).

Keywords: arrhythmia, atrial fibrillation, cytokines, endothelial dysfunction, inflammation, SIRS

Introduction

Atrial fibrillation (AF) is one of the most common cardiac arrhythmia in clinical practice, which leads to disability. Increasing of left atrium (LA) [4] size is deemed a recognized AF recurrence predictor usually accompanied with structural and electrophysiological remodeling of atrial myocardium: the larger the left atrium size is, the higher the probability of AF recurrence is. The likelihood of arrhythmias affected by inflammatory mediators served as the basis for a number of studies on the inflammatory theory of arrhythmogenesis [2, 5]. The assumption about the correlation between inflammation and alteration of atria was made based on histological examination of the atrial myocardium in 12 patients with isolated AF, refractory to antiarrhythmic therapy [1]. Hence the cardiologists worldwide are searching for independent predictors of the risk of recurrence of arrhythmia in patients with persistent form of AF which could predict such risk prior to dilatation of the left atrium. In view of the foregoing, the prediction of the risk of arrhythmia recurrence in patients with elevated levels of markers of Systemic Inflammatory Response Syndrome (SIRS) [3] is an urgent issue.

The aim of the study is to determine the predictive value relative to the recurrence of arrhythmia SIRS markers (IL-1β, TNF-α) and endothelin-1 in the absence of dilatation of the left atrium in patients with CHD combined with hypertension (HT) stage II and persistent AF.

Material and methods

The results of the study are based on findings of a comprehensive survey and dynamic monitoring of patients with CHD combined with II stage HT and persistent AF, in total 62 persons aged 45 to 65 years (average age 58.7 ± 0.5 years). Patients setting was conducted in the period 2012 – 2013.

Criteria for inclusion in the study: Male and female patients at the age from 45 to 65 years old; patients with persistent atrial fibrillation (PAF), II stage HT with mild-to-moderate BP, ischemic heart disease, angina of effort FC I-II or coronary arterial involvement (stenosis 50-70 %). Known duration of such disease makes more than 6 months.

Criteria for exclusion from the study: Acute myocardial infarction; heart failure of the class higher than II according to NYHA Classification; diabetes mellitus, impaired glucose tolerance; bronchial asthma; cardiomyopathy, myocar-
ditis; acute inflammatory diseases.

Echocardiography. The assessment of intracardiac hemodynamics parameters was performed using echocardiography with Ultima PRO 30 device ("Radmir", Ukraine). Echocardiography was performed using the standard method according to the standard Research Protocol for patients with CHD in M- and B echolocation modes in the parasternal and the apical transducer positions using 2.5 MHz transducer.

The level of Interleukin-1β, tumor necrosis factor-α and Endothelin-1 in blood plasma was determined by ELISA method using standard sets IL-1β-ELISA-best", "IL-4-ELISA-best", "TNF-alpha ELISA-best" (Vector-best, Russia) and ENDOFELIN reagents made by Biomedica (Germany) according to the method described in the application instruction for the test systems. The analysis was performed using "SUNRISE TS" (Austria) immunoassay analyzer.

Statistical Analysis

The adequacy of the mathematical models were estimated according to the method of selected points and analysis of receiver operating characteristics (ROC – Receiver Operating Characteristic curve analysis). At that, the area under the ROC curve (AUC – Area under the ROC curve) and its 95% CI was calculated. The model was considered adequate, when a statistically significant difference in AUC values was larger than 0.5 [6]. The cut-off point was found using the J-Youden index. For statistical data processing the statistical software package PSPP (version 0.7.9, license GNU GPL) was used.

Results and Discussion

We used two datasets: the first one included the patients who had recurrence of atrial fibrillation (n = 25), and the second one – the patients (n = 37) who had no recurrence of AF during 18 weeks of follow-up (Table. 1).

Table 1. Predictors value of the markers of recurrence of arrhythmia in patients with CHD combined with HT and persistent AF (n = 62)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cut-off point</th>
<th>Se, %</th>
<th>Sp, %</th>
<th>+ LR</th>
<th>- LR</th>
<th>AUC</th>
<th>CI 95 % AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA, cm</td>
<td>3,7</td>
<td>76,0 %</td>
<td>48,7 %</td>
<td>1,5</td>
<td>0,5</td>
<td>0,61</td>
<td>0,5000-0,7042</td>
</tr>
<tr>
<td>IL-1β, PG/ml</td>
<td>1,5</td>
<td>44,0 %</td>
<td>94,6 %</td>
<td>8,1</td>
<td>0,6</td>
<td>0,72</td>
<td>0,5740-0,8380</td>
</tr>
<tr>
<td>FNO-α, PG/ml</td>
<td>1,7</td>
<td>91,9 %</td>
<td>76,0 %</td>
<td>5,7</td>
<td>0,1</td>
<td>0,93</td>
<td>0,8244-0,9936</td>
</tr>
<tr>
<td>ET-1, fmol/l</td>
<td>2,2</td>
<td>96,0 %</td>
<td>89,2 %</td>
<td>8,9</td>
<td>0,1</td>
<td>0,93</td>
<td>0,8634-1,000</td>
</tr>
</tbody>
</table>
The marker like the left atrium linear size showed a significant predictive value, the area under the curve (AUC = 0.61), and with the optimal distribution point of 3.7 cm the sensitivity made 76.0% and the specificity made 48.7% (95% CI AUC 0.5000-0.7042). The levels of IL-1β with the optimal distribution point of 1.5 PG/ml significantly (AUC = 0.72) featured the sensitivity of 44.0% and the specificity of 94.6% (95% CI AUC 0.5740-0.8380) prior to recurrence of AF in patients with CHD combined with HT and persistent AF (Tab. 1). According to ROC analysis, the optimal distribution point for the FNO-α level significantly (AUC = 0.93) made 1.7 PG/ml (with the sensitivity of 91.9% and the specificity of 76.0% (95% CI AUC 0.8244-0.9936). The results of the performed ROC-analysis showed a significantly (AUC = 0.93) high predictor value of endothelin-1, and with the optimal distribution threshold of 2.2 fmol/l, the sensitivity amounted to 96.0% and the specificity amounted to 89.2% (95% CI AUC 0.8634-1.000).

The performed scientific studies ascertained that the SIRS mediators are involved in formation and progression processes and also pertain to complications of atherosclerosis. The inflammatory process constitutes a complex and essential component of the body, and associated changes are in process in many organs and systems located far away from the focus of inflammation. The idea that the inflammatory processes are involved in the pathogenesis of cardiac arrhythmias is not a new one, but the markers of an inflammatory condition as a component of persistent AF progression in predicting the recurrence of arrhythmia are still poorly studied. Assessment of the severity of SIRS according based on the endothelin-1 concentration and determining the level of FNO-α may have a predictive value, regarding the recurrence of arrhythmia in patients with CHD combined with HT and persistent AF without dilatation of the left atrium.

Perhaps it is too soon to include nonspecific indicators of inflammatory condition and endothelial dysfunction as the common SIRS markers in stratification risk of recurrence of arrhythmia in patients with persistent AF [7], but they can be useful in evaluating the efficiency of treatment programs that require further study and analysis.

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**Ethical Declaration.** The study was approved by the local ethics committee of State Institute «Zaporizhzhia Medical Academy of Postgraduate Education of Ministry of Health of Ukraine». The study was carried out in conformity with the Declaration of Helsinki.
References


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