Pulmonary thromboembolism in 102 consecutive patients with chronic atrial fibrillation. Diagnostic value of echocardiography

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Abstract

Background: Little is known about the incidence and diagnosis of pulmonary thromboembolism (PE) in patients with chronic permanent atrial fibrillation (CAF). Also it has not been established if echocardiography, a diagnostic tool useful in clinical evaluation of both diseases, is of value in diagnosis of PE in CAF patients.

Aim: To establish the prevalence of PE among patients suffering from CAF without or with poorly controlled anticoagulation as well as to evaluate the possibility to detect PE and to assess the diagnostic role of echocardiography.

Methods: Prevalence of PE in a population of 102 patients (52 males and 50 females at the mean age of 68 years, range 32-88 years) admitted to hospital between January and December 2004 with diagnosis of CAF was studied retrospectively. Echocardiography-based original algorithm of PE diagnosis in such patients was analysed.

Results: Among 102 patients with CAF, 20 (19%) cases of PE were diagnosed, including 12 with acute PE (APE) and 8 suffering from chronic thromboembolic pulmonary hypertension (CTEPH). Patients with CAF and APE as well as with CAF and CTEPH had increased right ventricular dimension (p=0.0002 and p=0.001, respectively), higher tricuspid pressure gradient (p=0.005 and p=0.001, respectively) and shorter pulmonary artery acceleration time (p=0.00006 and p=0.0004, respectively) estimated in echocardiography as compared to patients with CAF but without PE. Subjects with CAF and PE had also significantly decreased left ventricular dimension and better left ventricular performance.

Conclusions: A relatively high incidence of PE among patients with CAF not treated with anticoagulants or with poorly controlled anticoagulation therapy was noted. The important value of a diagnostic algorithm employing echocardiography in a diagnosis of clinically significant APE and CTEPH in this group of patients was also shown.

Key words: atrial fibrillation, pulmonary thromboembolism, echocardiography

Introduction

Atrial fibrillation (AF) is a common, easy to detect cardiac arrhythmia and its prevalence increases markedly after the age of 60 years. In a similar, age-adjusted population the incidence of pulmonary embolism (PE) is also higher, although establishment of its diagnosis is difficult. The coexistence of AF and peripheral artery embolisation has been extensively studied but little is known about the incidence and detection of PE in patients suffering from AF. Also, not much is known about whether echocardiography, an important tool in clinical evaluation of both individual diseases, can be useful in the diagnostics of PE in patients with AF.

The purpose of this retrospective study was to assess the prevalence of PE among patients with a diagnosis of
chronic permanent atrial fibrillation (CAF) not receiving or with poorly controlled anticoagulation, and to estimate the diagnostic value of our original algorithm based on clinical experience with echocardiography as a key examination.

**Methods**

One hundred and two consecutive patients (52 males and 50 females at the mean age of 68, range 32-88 years) admitted to hospital between January and December 2004 with a diagnosis of CAF were analysed retrospectively. Chronic AF was defined as AF that had lasted or recurred several times throughout a long period of time and was not intended to be cardioverted. Included patients did not receive oral anticoagulants (52 patients) or anticoagulation was poorly controlled (50 patients, 51% of INR measurements were found to be <2). Patients' medical history was analysed with the focus on current or previous comorbidities and all subjects were examined physically. Also performed were: ECG, chest X-ray, echocardiography, TSH level and T3 and T4 levels and whenever necessary, blood haematology and biochemistry.

Pulmonary embolism in patients with CAF was detected based on the experience-based diagnostic clinical algorithm. A preliminary diagnosis of acute pulmonary embolism (APE) was based on acute onset of clinical APE symptoms within the last 10 days and inability to exclude APE due to D-dimer concentrations <500 ug/ml, while that of chronic thromboembolic pulmonary hypertension (CTEPH) was based on the presence of chronic exertion dyspnoea and limited exercise tolerance. Further diagnostic work-up of PE was carried out only in patients with no documented concomitant disorders likely to explain the aforementioned complaints. Thus, the medical history of all patients was analysed, then they were evaluated clinically and their previous available medical records were evaluated, and eventually the echocardiographic examination was performed. Patients with well documented other causes of CAF and/or with both left ventricular and atrial function impairment or structural abnormalities were not diagnosed further to search for PE, similarly to patients without other recognised causes of CAF and no signs of right ventricular overload (RVO) in echocardiography. Eventually, pulmonary angiography was carried out only in patients without significant disorders that could cause CAF but with present RVO features in echocardiography.

Selective pulmonary angiography was performed through the ulnar or jugular vein and was preceded by a haemodynamic study of the pulmonary circulation. A proximal pulmonary embolism was defined when it involved the pulmonary trunk, main pulmonary arteries, lobar and segmental branches of the pulmonary vessels. A peripheral pulmonary embolism was detected if the embolic lesions within the pulmonary vasculature were confined to the pulmonary vessel distal to the segmental one. The culprit lesions were qualified as acute if they caused amputation of the pulmonary vessels and as chronic if they presented as either blurred filling defects in the vessels that led to flow restriction or obstruction or irregular lesions.

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**Statistical analysis**

Results are presented as mean ± standard deviation. Echocardiographic parameters of patients with CAF and PE were compared to subjects with CAF but without PE using Student’s t-test. A p value <0.05 was considered statistically significant.

**Results**

Among 102 patients with CAF, ischaemic myocardial damage was diagnosed in 46 cases, arterial hypertension in 11, dilated cardiomyopathy irrespectively of aetiology in 18, COPD in 3 and pneumonia in 4. More than one of the aforementioned risk factors of AF was noted in 8 patients. Forty-six subjects presented at least 1 clinical event of heart failure.

**Table I. Echocardiographic characteristics of 102 consecutive patients with CAF**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Means±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>68±14.1</td>
<td>32-88</td>
</tr>
<tr>
<td>LVED [mm]</td>
<td>54.1±7.8</td>
<td>32-68</td>
</tr>
<tr>
<td>EF [%]</td>
<td>54±12.1</td>
<td>28-78</td>
</tr>
<tr>
<td>LA [mm]</td>
<td>40.8±8.0</td>
<td>20-55</td>
</tr>
<tr>
<td>AcT [ms]</td>
<td>82±10.1</td>
<td>70-100</td>
</tr>
<tr>
<td>GT [mmHg]</td>
<td>31±24.7</td>
<td>22-70</td>
</tr>
<tr>
<td>RVED [mm]</td>
<td>20.1±7.1</td>
<td>10-35</td>
</tr>
</tbody>
</table>

*Abbreviations: LVED – left ventricular end-diastolic diameter, EF – ejection fraction, AcT – acceleration time, GT – maximum pressure gradient across tricuspid valve, RVED – right ventricular end-diastolic dimension*
Among 31 patients without any disorders that could cause CAF but with at least one feature of RVO in echocardiography, pulmonary angiography revealed PE in all 20 patients with preliminary clinical PE diagnosis. In 12 patients APE was detected, while chronic thromboembolic pulmonary hypertension with mean pulmonary pressure ranging from 20 to 40 mmHg was detected in another 8 cases. In patients with CAF and PE but without detection of any causal factor of CAF in the preliminary examination and with normal LV ventricular and atrial echocardiogram, the following concomitant abnormalities that would potentially provoke CAF were finally revealed: in the CAF+APE group one case of diabetes mellitus, two cases of chronic and mild renal failure, and in the CAF+CTEPH group stable, mild coronary artery disease in one patient. However, in the group of patients with CAF and concomitant disorders, 4 had GT >30 mmHg and 2 had AcT <90 ms. A comparison of the echocardiographic parameters of 82 patients with CAF but without PE with 8 patients presenting with CAF+APE is shown in Table II. Table III outlines a comparison of the echocardiographic parameters of 82 patients with CAF but without PE to 12 individuals with CAF+CTEPH.

**Table II. A comparison of echocardiographic parameters of 82 patients with CAF without PE and of 8 patients with CAF+APE**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CAF without PE</th>
<th>CAF+APE</th>
<th>p</th>
<th>&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>65.1±13.1</td>
<td>66.1±13.1</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>LVED [mm]</td>
<td>56.1±5.1</td>
<td>48.1±6.1</td>
<td>0.00025</td>
<td></td>
</tr>
<tr>
<td>LVEF [%]</td>
<td>53.1±12.1</td>
<td>58.1±8.1</td>
<td>0.0015</td>
<td></td>
</tr>
<tr>
<td>LA [mm]</td>
<td>42.2±5.6</td>
<td>41.8±7.7</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>AcT [ms]</td>
<td>92.1±10.1</td>
<td>79.4±12.3</td>
<td>0.00006</td>
<td></td>
</tr>
<tr>
<td>GT [mmHg]</td>
<td>21.1±14.1</td>
<td>38.8±9.1</td>
<td>0.0051</td>
<td></td>
</tr>
<tr>
<td>RVED [mm]</td>
<td>19.1±7.4</td>
<td>28.5±5.1</td>
<td>0.0002</td>
<td></td>
</tr>
</tbody>
</table>

**Table III. A comparison of echocardiographic parameters of 82 patients with CAF without PE and of 8 patients with CAF+CTEPH**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CAF without PE</th>
<th>CAF+CTEPH</th>
<th>p</th>
<th>&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>65.1±13.5</td>
<td>68.5±10.3</td>
<td>NS</td>
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<tr>
<td>LVED [mm]</td>
<td>56.1±5.1</td>
<td>47.1±6.1</td>
<td>0.0002</td>
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<tr>
<td>LVEF [%]</td>
<td>53.1±12.2</td>
<td>61.2±10.1</td>
<td>0.0018</td>
<td></td>
</tr>
<tr>
<td>LA [mm]</td>
<td>42.2±5.6</td>
<td>42.0±5.4</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>AcT [ms]</td>
<td>92.1±10.1</td>
<td>72.6±9.6</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>GT [mmHg]</td>
<td>21.1±14.2</td>
<td>43.8±7.5</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>RVED [mm]</td>
<td>19.1±7.4</td>
<td>31±5.2</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: see Table I

**Discussion**

Atrial fibrillation is the most common cardiac arrhythmia and its prevalence increases with age. It is estimated that after the age of 60 years, the prevalence of AF is 50 to 90 cases per 1000 subjects in the general population, and arterial hypertension as well as myocardial damage are considered the predominant underlying disorders of this arrhythmia [2]. Although the age-range of our 102 patients with CAF was wide, the mean age was 68 years, and in 57 patients at least one of the two previously mentioned disorders increasing the risk of AF was noted. However, it is estimated that incidence of PE is approximately 0.5 cases per 1000 individuals a year in the general population, although this seems to underestimate the real frequency of PE because the majority of PE events are not detected in alive patients [3]. Incidence of PE as well as AF increases rapidly above the age of 60 years [4], suggesting not uncommon coexistence of these disorders, and is consistent with our unpublished findings regarding high prevalence of PE in AF patients, particularly among those without anticoagulation or with inadequate control of such therapy, but free from any well known risk factors of AF. It is also consistent with the results of long-term follow-up of spontaneous AF in 55 patients over the age of 60 years. During this follow-up period an APE event was observed in 5 patients, and one of them died [5]. This raises the suspicion that there may be undetected cases of PE among patients with AF in whom a clear reason for this arrhythmia is not found (their percentage may be as high as 32%) [6]. Moreover, coexistence of PE with AF is usually a subject of published case reports [7, 8].

Our clinical analysis of 102 consecutive patients with CAF seems to support these suggestions, because PE was diagnosed in 19% of CAF patients without or with poorly controlled anticoagulation. Interestingly, no case of peripheral embolism was noted in this group of patients. Despite the fact that such a high percentage of PE diagnosis may be associated with department profile, another study revealed that as many as 31% of such patients had PE [9]. In the selected group of patients with AF the potential for PE development may be much higher. Pulmonary embolism was detected in 90% of hospitalised patients aged over 80 years [10]. In another study, only AF was found to be an independent risk factor of venous thromboembolisation in a population of 539 consecutive patients with stroke [11].

The results of the studies on PE would support the concept of an association between these two diseases. However, in the reports on the value of echocardiography...
in diagnosis and prognosis prediction of APE, AF was observed rarely, in only 0-4% of cases [12, 13]. This may be a result of excluding AF electrocardiograms during analysis of components of their records. However it is also possible that in the aforementioned studies the only real reason for such a low rate of PE diagnosis was poor sensitivity of PE diagnosis in patients with AF.

Our study is of a retrospective design and it evaluated the effectiveness of a diagnostic algorithm developed on the basis of the extensive clinical experience of our centre. Analysing the relatively high 8% rate of CTEPH detection in our patients with CAF, it seems that the retrospective nature of this study had no impact on result overestimation, because all cases of PE were detected by pulmonary angiography. The same incidence rate of CTEPH in patients after APE episode was reported by Remy-Jardin et al. [14]. However, basing a preliminary diagnosis only on the absence of another documented cause of CAF (including the absence of significant impairment of LV function or its structural abnormalities in echocardiography), on clinical presentation suggesting PE and on a lack of echocardiographic features of RVO (see Tables II and III) may underestimate the number of patients with PE. Undetected cases of PE in our study may include patients with CAF accompanied by myocardial ischaemic damage, dilated cardiomyopathy, arterial hypertension or COPD. These disorders not only frequently coexist with CAF but are also associated with underestimated risk factors of PE such as myocardial infarction and heart or respiratory failure [15]. They have similar clinical presentation that may limit proper PE diagnosis in the case of their coexistence [16].

Assessing the presented herein method of PE diagnosis in patients with CAF it seems that except for higher awareness of increased rate of PE in the case of CAF, echocardiographic examination as a key tool in our diagnostic algorithm is of particular importance. The presence of RVO echocardiographic signs could serve as a confirmation of PE suspected after pulmonary angiography in patients without detected disorders typically related to CAF or significant LV structural and functional abnormalities. The PE diagnosis in this particular group of patients was even more valuable as no cases of acute venous thrombosis on physical examination as well as no venous thromboembolic disease or malignancy in the history were noted. Although the index proposed by Wells et al. was not calculated, our patients would probably be found in the low clinical risk group with respect to PE [17].

The value and the limitations of echocardiography in PE diagnosis are known. It is also accepted that a normal result of echocardiography does not exclude PE, because only in half of haemodynamically stable patients with PE is it abnormal [18]. Detection of RVO features in the echocardiographic study of the haemodynamically stable patients with APE diagnosis classified them to a patient group of submassive APE with unfavourable prognosis in comparison with non-massive (mild) APE patients [19]. Thus, potential cases of non-massive APE of less clinical importance could go undiagnosed among 102 patients with CAF. However, in the group of patients with CAF but without any other disorders associated with the risk of cardiac arrhythmia, echocardiography documented diagnosis of 12 cases of clinically significant APE and 8 of CTEPH. An analysis of the echocardiographic results also revealed that undetected cases of clinically significant PE might exist among patients suffering from CAF accompanied by COPD, ischaemic heart disease and dilated cardiomyopathy. In 6 of them, parameters of RVO were present that could be a result of left heart disease or COPD-related cor pulmonale, but they might also be subjects with undiagnosed PE.

Previous considerations lead to the conclusion that the presented herein clinical experience-based diagnostic algorithm of PE in the population of patients with CAF without or with poorly controlled anticoagulation may be of very high specificity and relatively low sensitivity. However, its practical diagnostic value should be analysed with regard to disorders that also require anticoagulation. In this context, a question about the rationale of any diagnostic work-up of PE in patients with CAF should be asked. However, it seems to be justified in our opinion. Diagnosis of APE in these patients requires addition of heparin to oral anticoagulants, particularly in the early period of treatment. This is important because anticoagulants present initially prothrombotic action, especially when started at higher doses [20]. It may also determine the need for anticoagulation in patients with CAF aged <60 years and without any clinical cardiac disease, diabetes mellitus or hypertension who according to ACCP guidelines require only long-term aspirin treatment [21]. In contrast, CTEPH diagnosis in patients with CAF requires not only life-long anticoagulation but also surgical endarterectomy in cases with high pulmonary pressure and proximal embolic obstructive lesions.

Conclusions

A retrospective analysis of 102 consecutive patients suffering from CAF without or with inadequate anticoagulation showed relatively high incidence of APE and CTEPH.

The echocardiographic features of right ventricular overload were helpful in the detection of clinically
significant APE and CTEPH in a group of patients with CAF but without concomitant risk factors of its development.

References
Zatorowość płucna w materiale 102 kolejnych chorych z utrwalonym migotaniem przedsionków. Wartość rozpoznawcza echokardiografii

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Streszczenie

Wstęp: Niewiele wiadomo o występowaniu i rozpoznawaniu u chorych z przewlekłym migotaniem przedsionków (CAF) zatorowości płucnej (PE). Nie ustalono także, czy echokardiografia, badanie użyteczne w ocenie obu schorzeń, może być wykorzystana w diagnostyce PE w CAF.

Cel: Ustalenie występowania PE wśród chorych z nieantykoagulowanym lub niedostatecznie antykoagulowanym CAF, możliwości jej rozpoznania i roli diagnostycznej echokardiografii.

Metodyka: Retrospektywnie zbadano występowania PE w populacji 102 chorych (52 mężczyzn, 50 kobiet, średni wiek 66,9 lat, zakres 32–90 lat) przyjętych na oddział od stycznia do grudnia 2004 r. z rozpoznaniem CAF. Analizowano własny algorytm diagnozowania PE w CAF opierający się na badaniu echokardiograficznym.

 Wyniki: Wśród 102 chorych z CAF rozpoznano 20 przypadków (19%) PE, wśród nich 12 przypadków ostrej PE (APE) i 8 przypadków zakrzepowo-zatorowego nadciśnienia płucnego (CTEPH). Echokardiograficznie chorzy z CAF+APE i CAF+CTEPH, w porównaniu z chorymi z CAF i bez PE mieli większy wymiar prawej komory (odpowiednio, p=0,0002 i p=0,001), wyższy gradient ciśnienia przez zastawkę trójdzielną (p=0,005 i p=0,001) i krótszy czas akceleracji (p=0,00006 i p=0,0004). Chorzy z CAF i PE mieli też istotnie mniejszy wymiar i lepszą funkcję lewej komory.

Wnioski: Stwierdzono stosunkowo częste występowanie PE u nieantykoagulowanych lub niedostatecznie antykoagulowanych chorych z CAF i wykazano dużą wartość algorytmu diagnostycznego z zastosowaniem echokardiografii w rozpoznawaniu istotnej klinicznie APE i CTEPH w tej grupie chorych.

Słowa kluczowe: migotanie przedsionków, zatorowość płucna, echokardiografia

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