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PREVENTION OF THROMBOEMBOLIC COMPLICATION BY TRANSESOPHAGEAL ECHOCARDIOGRAPHY GUIDED CONVERSION OF ATRIAL FIBRILLATION

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Summary. *Cardioversion in patients with atrial fibrillation is associated with an increased risk of embolic stroke. Screening for atrial thrombi with transesophageal echocardiography (TEE) before cardioversion should, in many patients, permit safe cardioversion to be done earlier than it would be possible with a prolonged conventional anticoagulation therapy.*
The aim of the study was to compare the feasibility and safety of transesophageal echocardiography-guided early cardioversion with those of conventional management of cardioversion in patients with atrial fibrilation. The study involved 95 patients with persistent atrial fibrillation lasting longer than two days and having cardioversion.
Forty patients underwent transesophageal echocardiography before cardioversion, with a short-term anticoagulation therapy. Cardioversion was conventionally guided in 55 patients (a long-term anticoagulation therapy and only transthoracal echocardiography). Atrial thrombi were detected in 20% of TEE group patients and led to the postponement of cardioversion. No embolization was recorded with this strategy. Embolization occurred in 6% of patients in the group receiving the conventional therapy. The cardioversion treatment was shorter in the TEE group ($p < 0.001$). Cardioversion was successful in 92% patients of the TEE group, and 78% patients of the conventional group. These results suggest that TEE-guided cardioversion is feasible and safe. The use of TEE may allow cardioversion to be done earlier, may decrease the risk of embolism associated with cardioversion.

Key words: *Fibrillation, transesophageal echocardiography, cardioversion, thromboembolism*

Introduction

It has been proved that patients with atrial fibrillation run a greater risk of developing congestive heart failure, thromboembolism complications and sudden cardiac death (1,2).

The mortality of patients with chronic atrial fibrillation is seven times higher compared to the patients with sinus rhythm, while the mortality of patients with atrial fibrillation is twice bigger than in the control group.

In the AF patients group the frequency of thromboembolic complications is five times larger.

The therapeutic goal is to achieve the caradioversion of the heart rhythm as early and as much safely for the patient as possible. Prolonged AF leads to the electric and mechanic remodeling of the left atrium, which results in a lower initial success of cardioversion and shorter retention of the sinus rhythm (2,3,4).

Cardioversion itself carries the risk of thromboembolism, where the most frequent source of the thromb is the left atrium and/or the left atrial apendage. In order to prevent thromboembolic complications it is necessary that the AF patients before and during the cardioversion are on the adequate anticoagulant therapy.

Compared to the prophylactic application of therapy, the conversion of atrial fibrillation into the sinus rhythm can be performed in two ways (5,6). An acute conversion (without delay) and the conventional approach to conversion. The acute conversion means that the patients with persistent AF lasting longer than 48 hours should be submitted to heparine infusion until the adequate activated partial thromboplastine time (aPTT) is achieved and cardioversion should be performed without delay, after transesofageal examination of the inside of LA or LAA has been made. The conventional approach to conversion means an oral anticoagulant therapy for three weeks before and four weeks after cardioversion.

By introducing transesofageal echocardiography (TEE) the existence of a thromb in the LA or the LAA can be ruled out with certainty before cardioversion.

The aim of our paper was to examine the signifi-

cance of transesophageal echocardiography (TEE) in AF cardioversion and the advantages of this method over the conventional approach to rhythm conversion. The main aim of this paper was to point to the advantages of TEE in safe cardioversion as well as in the possibilities for a faster and more successful performing of cardioversion.

Patients and Methods

The study included a group of 95 patients with persistent AF, lasting not less than 48 hours and not longer than a year. Persistent AF, by definition, does not spontaneously change into the sinus rhythm (7).

Inclusion criteria were: persistent AF and functional cardiac status of patients not greater than NYHA Class II, ejection fraction 57 % and more (evaluated by two-dimensional echocardiography, area length method). In this way we excluded the possible negative influence of the disfunction of the left ventricle on the success and duration of conversion. Exclusion criteria were: age >80 years, heart failure > NYHA Class II, acute myocardial infarction, unstable angina pectoris, electrocardiographic evidence of ventricular preexitation, sick sinus syndrome, hypokaliemia (potassium < 3.5 mEq/L). Patients receiving digoxin chronically or within 8 hours prior entry into the study were also excluded.

Forty patients were subjected to transesophageal examination while 55 patients were converted by the conventional approach.

Patients were examined by two-dimensional echocardiography device (Toshiba SSH144). The first group of 40 patients had transesophageal echocardiography (TEE) with the transesophageal multiplan transducer which gave insight into the morphology, function, contents of the left atrium (LA) and the left atrial apendage (LAA). The cross-sections were used: the horizontal cross-section at the aorta level, and the vertical one of the two cavities. If by TEE a thromb was detected in the LA and/or LAA, cardioversion was postponed for three weeks, during which the patient was treated with oral anticoagulant drugs. The desired INR (International normalized ratio INR = PT p/PTko was 2.5–3. (PTp is a marker of the prothrombine time of the patient, PTk is the control prothrombine time in sec.).TEE was repeated in three weeks and the persistance of the thromb would mean that the conversion would not be performed, while the absence of or a melted thromb was the indication to carry out the conversion. The findings of stagnated echos in LAA and/or LA have not been a counterindication to carry out the conversion. These patients have been treated by the anticoagulant therapy to reach aPTT between 80–90 (or INR 3–3.5 during the conversion).

In patients with a newly-discovered AF a continuous heparine infusion was included (1000 iu/h) and when the adequate activated partial thromboplastine time (aPTT 60–80s) was achieved, TEE was performed. Heparine infusion was applied during TEE, during and after cardioversion. On the second day of heparine infusion, oral anticoagulant theraphy was also included until the INR 2–3 was achieved. Oral anticoagulant therapy was retained for four weeks after the rhythm conversion. Apart from the newly-discovered AF, TEE was performed also in the group of patients who were treated in pre-hospital conditions with the oral anticoagulant therapy at least for three weeks, until the adequate INR was achieved.

The second group consisted of patients with the conventional approach to conversion. All the patients were at the oral anticoagulant therapy for at least three weeks, with INR 2–3, after which rhythm conversion was performed, without TEE examination. A dosage of 160 mg Aspirin daily has been administrated to all the patients. The approach to conversion was the following: propafenon bolus injections 2 mg per kg or up to 3mg per kg in short infusions (15 min). If the sinus rhythm has not been established a β blocker (metoprotol) was included in the dose of 25–50 mg together with the oral application of propafenon (dose 600–900mg per day). If after 72 hours of therapy the sinus rhythm failed to be established, electroconversion was performed, with the patient's consent. Electrocardioversion was performed with the force of 100 J, and in case it was not successful, the force of electrocardioversion was increased. The initial success of cardioversion was achieved by the establishing of the stable sinus rhythm in the first attempted electrocardioversion. Conversion was defined as the stable sinus rhythm that persisted for at least 1 hour. During the conversion period electrocardiogram was monitored, blood pressure was measured every 2 hours and 12–lead electrocardiogram was recorded every 12 hours, and immediately upon conversion to the sinus rhythm.

Results

Indication for cardiversion was established in 95 patients with AF. The group of patients with TEE (40) was considerably younger (53.7 ± 4.2) compared to the group of conventionally treated patients (62.14 ± 6.8) ($p < 0.05$). Female patients prevailed in both groups (60% and 65%), without statistically significant difference.

Compared to the primary disease, the frequency of rheumatic valvular disease did not statistically significantly differ in the groups. The average duration of atrial fibrillation (in months) was shorter in the group of patients who were submitted to transesophageal echocardiography (6.8 ± 4.1), compared to the conventionally treated group (9.2 ± 5.1), without a statistically significant difference.

The frequency of a thromb in the group of patients with the TEE was 20%. Three weeks after the application of the oral anticoagulant therapy the thromb persisted in 50% of the patients.

Table 1. Patient population characteristics

	TEE Group (n=40)	Conventional Group (n=55)
Age (years)	53.7 ± 4.2	62.14 ± 6.8*
Gender (male/female)	16/24	20/35
Atrial fibrillation duration (months)	6.8 ± 4.2	9.2 ± 5.1
Ejection fraction(%) (area lenght)	57.0±2..5	61.0±3.9

* p<0.05

The basic disease in the group of patients with the present thromb in the LA or LAA in 83% was the disease of the native mitral valve. One female patient had hypertrophyc obstructive cardiomyopathy.

The rhythm conversion was attempted in 36 patients, in which the preceding TEE ruled out the existence of a thromb. In that group of patients there were no thromboembolic complications. Before cardioversion, stagnated echos in LAA have been found in four patients. By repeated TEE after cardioversion, the thrombs in LAA of these patients have not been found. In the group of patients with the conventional approach to conversion (55 patients), 6% of the patients had thromboembolic complications. In the group of patients with thromboembolic complications 75% of the patients had the valvular disease, 20% the coronar disease.

The size of the LA (49.5 ± 8.37) (measured by transthoracic echocardiography), in the group of patients in whom the thromb was verified by TEE and in the group of patients who suffered the cerebrovascular stroke (CVI), was considerably larger compared to the LA of the group of patients without the verified thromb and without the CVI (45.2 ± 6.09) ($p < 0.05$).

Table 2. Patient population characteristic according to detected thromb (by TEE)

	With thromb	Withouth thromb
Age (years)	53.1±3.12	53.1±3.12
Gender (male/female)	2/6	14/18
Underlying heart disease		
Valvular HD*	83%	6.2%**
Coronary HD*	25%	61%
Systemic hypertension	8.7%	63%**
Left atrial diametar (mm)	49.5 ± 8.37	45.2 ± 6.09***
Atrial fibrillation duration (months)	7.2 ± 3.1	5.8 ± 4.1

* HD-heart disease, ** p<0.001, *** p<0.05

The average time of conversion in the group of patients with TEE was considerably shorter (3.4 ± 2.01, in days) compared to the duration of the conversion procedure in the conventionally treated group (23.6 ± 3.21) ($p < 0,001$) (Fig. 1). In patients with a detected thromb the average time of conversion was not calculated because the conversion was postponed. Conversion also includes the period of the application of anticoagulant therapy in the preparation of the procedure. In the group with TEE only two patients were submitted to a long-lasting oral anticoagulant therapy.

The side effects of propafenon were an alergic reaction in one patient and a hypotension reaction in another one.

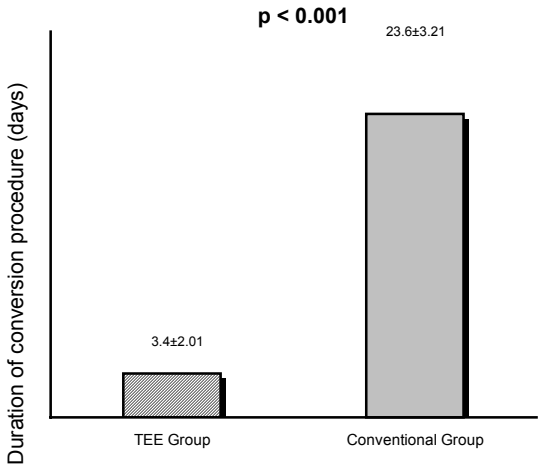

Fig. 1. Duration of conversion procedure

The initial success of conversion was higher in the group with TEE (92%), compared to the conventionally treated group (78%) (Fig. 2).

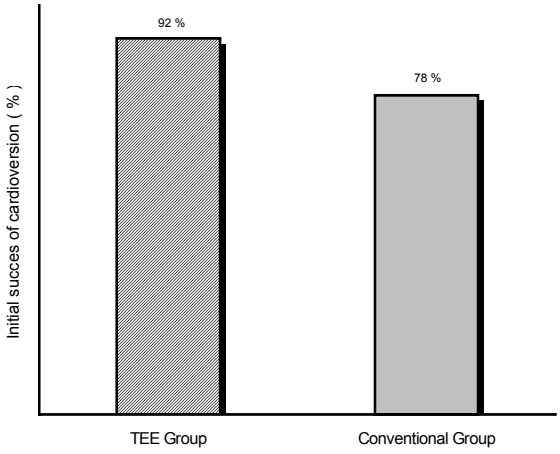

Fig. 2. Initial succes of cardioversion

In the group of patients with TEE two patients were converted by intravenous application of propafenon (6%), whereby these were the patients with the shortest duration of atrial_fibrillation in the group (up to 2 months). Twenty five patients (75%) of the group with TEE were converted by adding of oral medicament therapy (intravenous propafenon+ oral propafenon + oral metoprolol /atenolol). In 6 patients (18%) after the unsuccessful medicament therapy the sinus rhythm was established by electroconversion with the force of l00 J. In three patients the sinus rhythm was not initially established, so it was necessary to repeat electroconversion with a greater force.

In the group of patients with the conventional approach to conversion there were no patients in whom the successful conversion was performed by the intravenous application of propafenon, while after 72 hours of oral therapy the sinus rhythm was established in 69% of patients. Initial electrocardioversion was successful

in 30,2% of patients with the conventional approach to conversion.

Discussion

Atrial fibrillation results in the loss of electric and mechanical activity of the atrium, which leads to the absence of the atrial contribution to the contraction of the ventricles. The following consequences have been noted:

- the increase of the pulmonary arterial pressure, pulmonary capillary pressure and the decrease of the stroke volume for about 30%, in patients with paroxysmal and chronic atrial fibrillation (2).
- the creation of the conditions for the creation of a thromb in the atrii (A) and/or left atrial appendages (LAA)
- blood stagnation in A or AA, the damage of the atrium endocard, hypercoaguability condition (1)

It has been proved that as soon as 12 hours after the onset of AF there appears blood hypercoaguability that is retained for seven days after the establishing of the sinus rhythm (1). The distension of LA, inadequate or irregular contractility, suppress vasopresin secretion and increase the ANP secretion. This results in the increase of blood viscosity, the damage of the LA endocard endotelium, the activation of the coagulation system and the formation of the conditions for the creation of a thromb. As a result, there is increase in risk for stroke in patients with atrial fibrillation (8). According to the Framingham study (9), there is a 5.6 – fold embolic risk in non-rheumatic atrial fibrillation as compared to the control group and 17.6 fold risk in atrial fibrillation of rheumatic origin (4,8). The attributable risk of stroke in AF patients rose from 1.5% in the age group 50 to 59 to 23.5% in the age group 80 to 89 (9).

Atrial fibrillation itself causes persistent left atrial dysfunction. A degree of dysfunction as well as the size of left auricle correlate with the duration of atrial fibrillation. Prolonged AF has as a consequence a more difficult set up and maintenance of the sinus rhythm. Atrial fibrillation duration before cardioversion defines the recovery time after the procedure. In patients with paroxysmal AF (PAF) the frequency of thrombembolism is 6,4% while in those with chronic AF(HAF) it is 32% (10). Patients with a history of embolic stroke are at a higher risk of recurrence (4,11,12).

The significance of TEE lies in a possibility to have an insight into the content and function of LA and LAA immediately before cardioversion in order to avoid with certainty the rhythm conversion in the patients with the thromb in LA and/or LAA. It is also possible in patients without a verified thromb to make cardioversion without delay and shorten the duration of AF. However, the cardioversion process itself, especially electroconversion (and low energy) has got a risk of forming the thromb. Black et al. (13) multicentric study indicated a possibility to form a thromb in LAA during or immediately after conversion.The papers of Giovani (14) indicated a case of a patient forming thromb in LAA after internal defibrillation, but there was a record of inadequate anticoagulant therapy with the patient.

Grim et al. (15) have demonstrated that the cardioversion itself (especially electrocardioversion) depresses a function of LA and LAA in the following seven days. Predisposed factors for the thromb formation during conversion were a degree of malfunctions and size of LA and LAA, the presence as well as a degree of stagnated echos in LA and LAA (13–17). However, it has been demonstrated that in the group of the patients, where in the area of decreased contractility of LA and LAA the thromb has been formed during and/or after cardioversion, there has not been recorded embolic complications since the thromb dislocation has not occurred. In the case when the thromb has already been formed, the preserved contractility of the LAA enables the dislocation of the thromb (6).

The results of extensive studies examining primary prevention of embolism in patients with atrial fibrillation, have shown the risk reduction of 44-81% in the patients treated by warfarin (18–20). Guided by the experiences of other studies in the prevention of the thromb occurrence, we insisted not only on optimal anticoagulant doses but on higher target values of aPTT and INR, in the group of the patients with stagnated echos in LAA. In this group of patients there have not been thrombembolic complications. Target INR has not exceeded 4, as it has been indicated that in such a case the risk of bleeding increases. In this way, transesophageal echocardiography enabled a separation of the risk group of the patients for the thromb occurrence during or immediately after cardioversion and a possible special anticoagulant regime.

We consider it necessary to evaluate the size, content and function of LA and LAA by transesophageal echocardiography as an objective to prevent thrombembolic complications before cardioversion. The conclusion suggests itself that conversion of AF into the sinus rhythm should be done as early and as safely for the patient as possible. ACUTE study (3,5) has shown that patients with AF that lasts longer than 48 hours should subjected to conversion without delay. Before conversion it is necessary to make the insight into the contents of the LA and LAA, by means of transesophageal echocardiography. TEE should be performed immediately after the adequate anticoagulant effect of the heparine has been achieved. Rhythm conversion should start at latest 6 hours after TEE because thromb formation is possible at that period. Anticoagulant therapy is applied before, during and four weeks after the conversion. By TEE echocardiography we avoid the rhythm conversion in patients with a thromb, but not the possibility of thromb formation during and immediately after the conversion. A shorter duration of AF and of the cardioversion procedure itself provide the conditions for a greater

initial success and maintenance of the sinus rhythm. Since one of the aims of this study was to demonstrate the significance of the shorter duration of the process of cardioversion (at, consequently, of the shorter duration of AF) as one of the possible reasons of a greater initial success of cardioversion, the choice of the mode of conversion has been made accordingly. The first line of medicaments for fast conversion of persistent AF (according to Health Maintenance organization management of atrial fibrillation (7)), with minimal structural heart diseases (≤ NYHA II), include flecainidin, propafenol, quinidil and sotalol. Ibutilid has recently come to use as well. In order to emphasize the advantages of the method of TEE guided conversion, which offers us the possibility of performing the conversion safely and quickly, we chose the model of fast conversion of patients with persistent AF and the maintained function of the LV. In everyday clinic practice we have propafenon for intravenous and oral application at our disposal. The application of β blockers was aimed at fast achievement of the control of the ventricle rate and also of the prevention of the possible 1:1 AV conduction effect of propafenon. The data in literature show that the application of propafenon before the electrocardioversion procedure enables the use of a lesser DC and a greater initial success of cardioversion (21).

As with other antiarrhythmic drugs, the duration of atrial fibrillation seems to be an important factor influencing the efficacy of intravenous application of propafenone for achieving successful cardioversion. In studies recruiting patients with recent onset atrial fibrillation (< 7 days), success rates have ranged from 57 to 91% (22,23). In patients with longer duration atrial fibrillation (mean of 8 months), the reported success rate was only 9%. In our study, for patients with persistent atrial fibrillation (up to 2 months) in TEE group, the success rate was 6%. In conventional conversion group, intravenous application of propafenon was unsuccessful.

Conclusions

By performing TEE in patients with AF, cardioversion in patients with the existent thromb in LA or LAA is avoided with certainty. In our group of patients with TEE there were no thromboembolic complications, as was the case with the group of patients with the conventional way of cardioversion. Also, TEE enabled us to identify the groups of patients prone to thromb formation, in whom a special regime of anticoagulant therapy was applied.

TEE enabled performing cardioversion in a shorter period of time (without delay) and our opinion is that it explains a greater initial success of cardioversion in the group of patients with TEE. Electrocardioversion is a safe and fast method of AF conversion if the adequate anticoagulation prevention of thromboembolism has been previously achieved and if by TEE the existence of a thromb in the LA and LAA has been ruled out.

The number of days in hospital was considerably shorter in the group of patients with TEE, with a greater economic use because of the decrease of embolic stroke incidence.

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TRANSEZOFAGEALNOM EHOKARDIOGRAFIJOM VOĐENA KONVERZIJA ATRIJALNE FIBRILACIJE U PREVENCIJI TROMBOEMBOLIJSKIH KOMPIKACIJA

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Kratak sadržaj: *Kardioverzija u bolesnika sa pretkomorskim treperenjem (fibrillatio atriorum) udružena je sa povećanim rizikom za embolijski inzult. Otkrivanje pretkomorskih tromba transezofagealnom ehokardiografijom (TEE) pre kardioverzije, obezbedjuje da se bezbedna kardioverzija uradi ranije nego što bi to bilo izvedeno sa prolongiranom konvencionalnom antikoagulantnom terapijom. Cilj rada je bio kompariranje pogodnosti izvođenja i sigurnosti rane kardioverzije-vođene transezofagealnom ehokardiografijom sa konvencionalno vođenom kardioverzijom u bolesnika sa pretkomorskom fibrilacijom. Ispitivanje je ukljucilo 95 bolesnika sa perzistentnom pretkomorskom fibrilacijom koja traje duže od dva dana i postavljena je indikacija za kardioverziju. Pre kardioverzije, 40 bolesnika je podvrgnuto pregledu transezofagealnom ehokardiografijom, sa kratkotrajnom antikoagulantnom terapijom. Kardioverzija je konvencionalno vodjena u 55 bolesnika (dugotrajna antikoagulantna terapija i samo transtorakalna ehokardiografija). Pretkomorski tromb je nadjen u 20% bolesnika TEE grupe pri čemu je kardiovezija odložena. Embolijske komplikacije nisu zabeležene sa pomenutom strategijom vodjenja kardioverzije. U grupi bolesnika sa konvencionalnim načinom vodjenja kardioverzije embolijske komplikacije su zabeležene u 6% slučajeva. Trajanje procedure kardioverzije je bilo kraće u TEE grupi ($p<0,001$). Uspešnost kardioverzije je bila 92% u TEE grupi, i 78% u konvencionalno tretiranoj grupi. Rezultati ovog rada ukazuju da je kardioverzija pretkomorske fibrilacije vođena transezofagelanom ehokardiografijom, pogodna za izvođenje i sigurna. Transezofagelna ehokardiografija omogućuje izvodjenje kardioverzije ranije i smanjuje rizik embolizma udruženog sa kardioverzijom.*

Ključe reči: *Pretkomorska fibrilacija, transezofagealna ehokardiografija, kardioverzija, tromboembolizam*

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