Do we always need anticoagulation before cardioversion of atrial fibrillation in ladies?

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Risk stratification for thromboembolism and stroke, as well as estimation of bleeding risk are cornerstones of management of patients with atrial fibrillation (AF) (1-3). Current ACC and ESC practice guidelines recommend prevention of thromboembolism (TE) and stroke in patients using oral anticoagulation (OAC) or novel OAC (NOAC) in patients at high risk of these events (1-3), including patients with AF of short duration (<48 hours) undergoing electrical cardoversion (EC).

ESC 2010 guideline (2) recommends peri-EC heparin or low molecular weight heparin (LMWH) followed by OAC with vitamin K antagonist (INR 2.0-3.0) as class 1B recommendation for patients at high risk of stroke. Further for patients with clear AF duration <48 hours and without TE risk factors - per-iEC heparin or LMWH may be considered with no need for further post-EC OAC therapy as class 2B recommendation (2, 3).

ACC 2014 guideline on management of patients with AF (1) endorses as class 1c recommendation for patients with AF or atrial flutter <48-hour duration and with high risk of stroke, intravenous heparin or LMWH, or administration of a factor Xa or direct thrombin inhibitor, as soon as possible before or immediately after EC, followed by long- term anticoagulation therapy; and as class 2b recommendation - anticoagulation (heparin, LMWH, or new OAC) or no antithrombotic therapy with no OAC therapy post-EC may be considered for patients with AF <48 hours and low TE risk undergoing EC.

However, there are patient's categories that perfectly fit neither in category of low nor high risk.

These challenging cases usually require individual carefully weighed approach and management of such case was the topic of recent debate at ACC 2015 meeting in San Diego, CA on March 16:

Cardioversion of AF With and Without Anticoagulation? A 67 – Year Old Woman Presents to the ER in AF That Began 24 Hours Ago. She Has No Past Medical History. Can She Be Cardioverted Without Anticoagulation on Board? (4).

To proceed with decision whether to use anticoagulation for prevention of TE and stroke in this female patient the first step in decision-making is to estimate the risk according to currently recommended CHA_2DS_2-Vasc score (1, 3), that includes major risk factors for stroke - age>75 years (2) and previous stroke/ transient ischemic attack/ TE (2); and clinically relevant non-major risk factors: chronic heart failure (1), hypertension (1), diabetes (1), vascular disease (1), age 65-74 years (1) and female gender (1).

Our patient did not have major risk factors for stroke and thromboembolism, however her age of 67 years and female gender account for CHA_2DS_2-Vasc score of 2, thus putting her in category of high risk patient that needs anticoagulation. However, if she were 2 years younger she would have score 1, attributed to her female gender.

It must be emphasized that TE risk was correlated with incremental increase in age, but clear cut-off values were validated for population <65 years and ≥75 years while risk for 65-74 years the risk is less established (4).

It is also worth mentioning that she did not have structural heart disease or other condition that was the cause of AF, allowing to consider she had a lone AF of <24 hours of duration.

Do we always need to use anticoagulation in this otherwise presumably active female patient with lone AF of short duration?

ESC 2012 update of AF guideline recommends antithrombotic therapy to prevent TE in all patients with AF, except in those patients (both male and female) who are at low risk (age <65 years and lone AF). This update further endorses as class 2a recommendation that female patients <65 years with lone AF (but still have a CHA_2DS_2-VASc score of 1 by virtue of their gender) are at low risk and no antithrombotic therapy should be considered (3).

Canadian guidelines 2014 update recommendation for EC in emergency room specifies that patients <65 years with lone AF

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absence of other risk factors (CHADS2 score -0) irrespective of gender can be considered truly low risk and do not require antithrombotic therapy (5).

Thus, assuming our patient has lone AF clearly of <48 hours duration without other major and clinically relevant risk factors for stroke and thromboembolism, except her age of 67 years, female gender can be discounted as a risk factor for stroke and TE.

Several latest registry/cohort studies and systematic analysis addressed question on overall risk of stroke and TE in patients with AF <48 hours undergoing EC, and analyzed risk according to time from AF onset, gender and CHA_2DS_2-Vasc score risk categories (6-10).

Recent analysis of 6 studies on EC of acute AF without peri-OAC reported that the overall TE/ stroke event rate was low and varied between 0-0.9%, the highest rate was seen in elderly women ≥75 years (6).

On the other hand, registry study from Denmark (7) assessed risk of 30-day TE and stroke in patients undergoing EC with and without peri-OAC therapy in 16274 pts. Overall 2.2% of patients developed TE and 1.8% stroke/transient ischemic attack. The study showed that patients not receiving prior or post EC OAC had 2.47 (95%CI 1.49-4.77) fold increased risk of TE, while in patients receiving OAC therapy either prior or after EC the risk of TE was nonsignificant. In univariate analysis the risk for CHA_2DS_2-Vasc score 0-1, age 65-74 and female gender did not reach statistical significance. This emphasizes the need for careful risk assessment of patients undergoing EC.

In Finnish cardioversion (FinCV) study (9), TE and stroke risk was assessed in 2481 patients with AF <48 hours of duration undergoing EC without peri -OAC therapy. The overall rate of TE was low -0.7%. Interaction analysis demonstrated that risk of TE development was increased up to 9.8% in patients older than 60 years with diabetes and heart failure, while in younger patients without these risk factors the risk was equal to 0.2% (8).

In another analysis of FinCV study on risk of TE according to the time of AF onset, authors established relationship between time from symptom onset and risk of TE. Risk was lowest for AF <12 hours of duration, and highest and significant for AF duration of 24-48 hours, while in patients admitted within 12-24 risk for TE was not significant falling between low and high risk categories (9).

In another study (10), evaluating the risk of stroke and TE according to CHA_2DS_2-Vasc score excluding age, it was shown that the risk associated with hypertension and sex was not significant in patients aged <65 years. In the multivariate analysis, only heart failure, previous stroke or thromboembolism, and vascular disease remained significant independent predictors of stroke and thromboembolism.

Swedish cohort study (11) addressed the question whether females had a higher risk for stroke as compared to men. It was demonstrated that women with AF have a moderately increased risk of stroke compared with men, however women younger than 65 years and without other risk factors have a low risk for stroke, and do not need anticoagulant treatment. In this study, female had higher TE event rate 0.7% vs 0.5% than men but for CHA_2DS_2Vasc score <2, age <65 and <65-74 years no difference was found in risk between female and male. The unadjusted stroke incidence was higher in the women of age group of ≥75 years (HR-1.24, 95%CI 1.18-1.30, p<0.0001) compared to men, while no difference in risk was reported for age groups <65 and 65-74 years (women vs men: age <65 years, HR 1.09 95%CI 0.86-1.39, p=0.48 and age 65-74 years -HR 1.04 95%CI 0.91-1.20, p=0.53) (9).

Thus, the current evidence, based on cohort studies and real time practice data on risk of TE in patients with AF demonstrates no increase in risk for TE/stroke in female patients younger than 65 years without other comorbidities and risk factors. The risk for active female patients with lone AF without risk factors of 67 years (category of 65-74 years) fells in somewhat gray zone needs further validation. It seems that shorter duration of AF is associated with lower risk of TE/stroke events and current practice data based on guidelines recommendations for EC of patients with clear AF<48 hours overall is associated with low risk of events.

Hence, our 67-year old female patient with lone AF without major and clinically relevant risk factors and duration of arrhythmia of 24 hours can be considered at low risk for TE stroke events with no need for pre- or post-EC oral anticoagulation therapy.

How can we reduce the potential risk of stroke in this particular patient? Additional tests can employed before EC to minimize risks of TE events. Several studies have suggested that patients with AF can be acutely anticoagulated with heparin/oral anticoagulant and proceed directly to EC without prolonged anticoagulation if no atrial thrombus or spontaneous is seen on pre-cardioversion TEE (12, 13).

Should we use heparin or LMWH pre-EC, though no definite benefit has been shown, it is commonly used for EC and is recommended as class 2b recommendation (1-3, 14).

In summary, in this particular case of 67-year old female with lone AF of 24-hour duration the decision how to proceed with anticoagulation pre- EC should be based on the individual approach with careful assessment of risk for stroke and TE. The OAC pre-cardioversion would not be necessary as we defined she is at low risk of stroke. To reduce risk, TEE seems to be useful to exclude the spontaneous echocontrast and left atrial thrombi. The EC can be performed under cover of heparin or LMWH and no post-EC OAC is required. For cases with AF <48 hours who are at high risk of stroke peri-cardioversion anticoagulation is advised (15).

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Bilmece

Ne her şeyim, ne hiçim
Söyle dünyam ne biçim
Bir kör düğüm ki içim
Çözdükçe dolaşıyor

Şevket Rado

Cevap: Diastolic heart failure
(Baş Editör)

Puzzle

I am Neither everything nor nothing,
Tell what kind of my world it is,
My heart is so tangled that
It kinks up as I untangle

Şevket Rado

Answer: Diastolic heart failure
(Editor-in-Chief)