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Atrial fibrillation and heart failure

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The prevalence of atrial fibrillation is increasing with aging population and with continuously improving survival of patients with underlying cardiovascular disorders [1]. Proper identification and treatment of patients with atrial fibrillation is of major importance to diminish cardiac and cardiovascular consequences of atrial fibrillation. Patients with congestive heart failure and left ventricular dysfunction are particularly predisposed to atrial fibrillation since the underlying disease process frequently contributes to pathology in atrial myocardium and enlargement of atrial size [2–5]. Presence of chronic atrial fibrillation in patients without evidence of heart failure might successively lead to development of signs of left ventricular dysfunction and symptoms of heart failure. Mechanistic links between heart failure and atrial fibrillation may include: volume-related atrial dilatation, increased dispersion of refractoriness in atria, catecholamine-induced atrial fibrosis, and atrial channel remodeling [5–9].

Atrial fibrillation seems to influence the prognosis in heart failure patients although data are controversial. In the SOLVD cohort [10] of 6517 patients with mean ejection fraction of 27%, atrial fibrillation was found in 419 patients (6%). Atrial fibrillation in this study was found to be significantly associated with an increased risk of mortality, congestive heart failure hospitalization, and also arrhythmic death. In the data from the V-HeFT and PRIME studies as well as in the PRIME II study, atrial fibrillation was not an independent predictor of mortality [11, 12]. In particular, the PRIME II study [12], analyzed 409 patients with class III and IV NYHA class heart failure and mean ejection fraction of 23%, among which 84 patients (20%) had atrial fibrillation. Atrial fibrillation was not found to be an independent predictor of mortality after adjustment for clinical covariates in this cohort. The MADIT II trial [13], which enrolled postinfarction patients with low ejection fraction (≤ 30%), showed that atrial fibrillation was found in 8% of patients, much lower percentage than in the PRIME II study, however, the MADIT II had two-thirds of patients in NYHA class I and II.

There is more consistency in findings from various prior studies regarding the association of atrial fibrillation with risk of hospitalization for heart failure. Atrial fibrillation is an independent and significant predictor of hospitalization for congestive heart failure, which was documented in all the above quoted studies. For example, in the MADIT II, atrial fibrillation at baseline was associated with twice higher risk of hospitalization for heart failure in comparison to patients in sinus rhythm.

In this issue of the journal, Grzybczak and coworkers [14] presented interesting data regarding the prognostic significance of atrial fibrillation in a cohort of 152 patients with heart failure (EF < 40%). Atrial fibrillation was identified in relatively large proportion of 53 patients (35%), although, it is worth emphasizing that paroxysmal atrial fibrillation was present in 32 of these patients. Therefore remaining 21 patients with persistent atrial fibrillation reflect about 14% of the overall studied population with predominantly NYHA class III and mean EF in the range of 35%. As expected, patients with AF had signs and symptoms of more advanced heart failure. In this retrospective study, the follow-up ranged from about 1 to 6 years, with mean follow-up of about 3 years. Crude mortality rates were higher in atrial fibrillation patients (28%) *vs.* sinus rhythm patients (17%). Similarly to the mentioned above studies, Grzybczak et al. [14] could not

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confirm predictive value of atrial fibrillation for mortality in the multivariate analysis. Importantly, the authors evaluated separately cohorts of patients with paroxysmal and persistent atrial fibrillation and the crude mortality rates in the group with persistent atrial fibrillation was 43% whereas group with paroxysmal atrial fibrillation had rates similar (19%) to those of sinus rhythm patients.

For comparison, a 2-year mortality rates in MADIT II (EF ≤ 30%) patients (mostly persistent atrial fibrillation patients) were found to reach 39% whereas sinus rhythm patients had 20% 2-year mortality rates [13]; therefore corresponding to those found by Grzybczak et al. [14]. In both studies, multivariate analyses were dominated by age, which no doubt is a strong predictor of mortality, especially in patients with severe left ventricular dysfunction. But age is not as clinically useful predictor as multivariate models suggest. Clinical meaning of atrial fibrillation and its consequences are very relevant for clinical course of a given patient much more than age *per se*. Twice higher mortality rates in atrial fibrillation patients than in sinus rhythm patients call for more aggressive approaches in prevention and treatment of this difficult arrhythmia. MADIT II data indicate that over 60% of patients with atrial fibrillation reach endpoint of hospitalization for heart failure or death. This very high rate requires comprehensive treatment which might require cardiac resynchronization therapy and in increasing number of cases also ablation of atrial fibrillation. Cardiac resynchronization therapy in heart failure patients with atrial fibrillation might require or probably should require atrio-ventricular node ablation to obtain proper benefit of the resynchronization of left ventricle.

Proper management of patients with chronic atrial fibrillation requires maintaining acceptable heart rate control. Satisfactory heart rate control usually is defined when mean heart rate remains below 80 bpm. Continuous tendency to tachycardia in atrial fibrillation patients leads to deterioration of hemodynamic parameters and development or aggravation of heart failure. Several studies including the AFFIRM trial [15] demonstrated that rate control results in a similar outcome to rhythm control in atrial fibrillation patients. However, the question could be asked what parameters are sufficient to determine proper rate control in atrial fibrillation when rate of heart rate is very variable.

In this issue of the journal, Chudzik et al. [16] describe experience with novel approach to rate control by evaluating the coefficient of irregularity of atrial fibrillation. Coefficient of irregularity is defined as standard deviation of heart rate over mean heart rate. Significant heart rate irregularity is found when the coefficient of irregularity exceeds 0.20 [17]. Chudzik et al. [16] demonstrated that in three quarters of studied patients who met criteria for satisfactory rhythm control based on mean heart rate < 80 bpm coefficient of irregularity had abnormal values indicating insufficient rate control. The verification of the findings by pacemaker memory data in studied patients provides even further evidence for the importance of monitoring heart rate irregularity in addition to mean heart rate. As pointed out by the authors, substantial number of so called well-controlled atrial fibrillation patients remains at increased risk of heart failure development or progression.

Holter monitoring could be used to compute coefficient of irregularity and since heart rate variability calculation is included in all Holter systems, physicians could start using heart rate variability algorithms in atrial fibrillation patients. Currently, SDNN, computed as part of heart rate variability programs, is neglected by clinicians since it does provide limited insight into the autonomic control of the heart. The pioneering work by Chudzik and coworkers [16] opens the door for practical usage of SDNN and maybe RMSSD, assuming proper annotation of recordings. It needs to be further explored whether coefficient of irregularity outperforms SDNN or RMSSD in evaluating irregularities of atrial fibrillation, i.e., whether the adjustment for heart rate in the equation contributes to better illustration of heart rate behavior in atrial fibrillation. Nonlinear methods could also provide some insight to the same phenomenon. Other questions which need to be raised include the effect of pharmacological agents on measured variation as well as the prognostic significance of the coefficient regarding the risk of progression of heart failure and risk of cardiac events.

As always research begets research and both studies, by Grzybczak et al. [14] and by Chudzik et al. [16], open the list of questions which are to be answered by new studies conducted by researchers eager to get closer to the truth and to the optimal patient management.

References

1. Cha YM, Redfeld MM, Shen WK, Gersh BJ. Atrial fibrillation and ventricular dysfunction. A vicious electromechanical cycle. Circulation, 2004; 109: 2839–2843.
2. Steinberg JS. Atrial fibrillation: an emerging epidemic? Heart, 2004; 90: 239–240.

3. Meisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. Am J Cardiol, 2003; 91 (Suppl): 2D–8D.
4. Benjamin EJ, Levy D, Vazirir SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population based cohort: A Framingham Heart Study. JAMA, 1994; 271: 840––844.
5. Ehrlich JR, Narrel S, Hohnloser SH. Atrial fibrillation and congestive heart failure: specific considerations at intersection at two common and important cardiac disease sets. J Cardiovascular Electrophysiol, 2002; 13: 399–405.
6. Solti F, Vecsey T, Kekesi V et al. The effect of atrial dilatation on the genesis of atrial arrhythmias. Cardiovasc Res, 1989; 23: 882–886.
7. Danshi Li, Fareh S, Ki Leung T, Nattel S. Promotion of atrial fibrillation by heart failure in dogs: atrial remodeling of a different sort. Circulation, 1999; 100: 87–95.
8. Yue L, Feng J, Gaspo R et al. Ionic remodeling underlying action potential changes in a canine model of atrial fibrillation. Circ Res, 1997; 81: 512–525.
9. Wang Framingham Wang TJ, Larson MG, Levy D et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation, 2003; 107: 2920–2925.
10. Dries DL, Exner DV, Gersh BJ, Domanski MJ, Waclawiw MA, Stevenson LW. Atrial fibrillation is associated with an increased risk for mortality and heart failure progression in patients with asymptomatic and symptomatic left ventricular systolic dysfunction: a retrospective analysis of the SOLVD trials. J Am Coll Cardiol, 1998; 32: 695–703.
11. Carson PE, Johnson GR, Dunkman WB, Fletcher RD, Farrell L, Cohn JN. The influence of atrial fibrillation on prognosis in mild to moderate heart failure: the V-HeFT Studies. Circulation, 1993; 87 (Suppl VI): VI102–VI110.
12. Crijns HJ, Tjeerdsma G, de Kam PJ et al. Prognostic value of the presence and development of atrial fibrillation in patients with advanced chronic heart failure. Eur Heart J, 2000; 21: 1238–1245.
13. Zareba W, Steinberg JS, McNitt S, Daubert JP, Piotrowicz K, Moss AJ; MADIT II Investigators. Implantable cardioverter-defibrillator therapy and risk of congestive heart failure or death in MADIT II patients with atrial fibrillation. Heart Rhythm, 2006; 3: 631–637.
14. Grzybczak R, Nessler J, Piwowarska W. Atrial fibrilaltion as a prognostic factor in patients with systolic heart failure. Folia Cardiol, 2006; 13: 503–510.
15. The Atrial Fibrillation Follow up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med, 2002; 347: 1825–1833.
16. Chudzik M, Wranicz JK, Cygankiewicz I, Klimczak A, Goch JH. Is mean heart rate a reliable predictor in the pharmacotherapy of patients with atrial fibrillation. Folia Cardiol, 2006; 13: 473–479.
17. Greenhut SE, Fraser J, Steinhaus B, Feld G, Hughes W. Optimized standby rate reduces the ventricualr rate variability in pacemkaer patients with atrial fibrillation. Pacing Clin Electrophysiol, 1996; 19: 1780–1785.