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Every patient with atrial fibrillation has his (her) own optimal heart rate

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ABSTRACT

Heart rate control is an important part of atrial fibrillation (AF) treatment and the recommendation for the target rate has become lenient in the recent guideline. Since heart rhythm of AF patients is irregularly irregular with great rate variation, the number of effective ventricular contractions may be different within a given time period among patients with similar heart rates and it may further lead to different levels of cardiac output. Therefore, we propose that every AF patient has his (her) own optimal heart rate, or to say that, the target for rate control in each AF patient should be individualized. This optimal heart rate can be defined by pulse counting, echocardiography or cardiopulmonary exercise test. With this new target, patients will achieve higher cardiac output with better exercise tolerance and life quality, even an improved prognosis.

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice which affects about 1.5–2% of the general population [1]. Heart rate control is the first line therapy for patients with persistent and permanent AF [2,3]. Based on AFFIRM (atrial fibrillation follow-up investigation of rhythm management) [4] and RACE (rate control vs. electrical cardioversion for persistent atrial fibrillation) [5] study, the previous guideline of European Society of Cardiology (ESC) recommends 60–80 bpm at rest and 90–115 bpm during moderate exercise as a reasonable target [6]. However, the RACE II study published afterwards shows that the prognosis of patients taking less than 110 bpm as the target rate is not inferior to that of patients taking restrict criteria mentioned previously [7]. Thus, lenient rate control is considered appropriate by the recent guideline [2,3]. This update widens the range of rate control target.

As we know, the R–R intervals vary significantly among patients with AF and the severity of irregularity is different. When ventricular rate is given, the number of "effective heart beats", defined as ventricular contractions that can pump enough blood to the peripheral, differs from patient to patient, even though within the "less than 110 bpm" range recommended by the guideline. Consequently, an individualized target for each AF patient may be required.

The hypothesis

We hypothesize that each patient with AF has his (her) own "optimal" heart rate which should be determined based on his (her) own unique physical and psychological situations. This "optimal heart rate" can be set as the rate control target for the patient. It can be defined as the lowest heart rate or rate range that will produce the maximal effective ventricular contractions to maintain a higher cardiac output and to result in better life quality and exercise capacity simultaneously. This "optimal" rate can be defined by pulse counting, echocardiography, cardiopulmonary exercise test (CPX), etc. There should also be feasible monitoring methods to assist the patient to keep the target rate once it is set. The new individualized target rate will not only meet the needs for patients' daily activities, but also lead to a better prognosis.

Discussion

The characteristics of heart rate and rhythm of AF patients

The ventricular rate of patients with first detected episodes of AF may reach up to 108.6 ± 30.2 bpm, which suggests that uncontrolled ventricular rate of AF patients is often rapid [8]. Thus, rate-lowering therapy is required by most AF patients except for those with significant bradycardia.

The rhythm of AF is irregularly irregular and R–R intervals differ from beat to beat. The irregularity can be evaluated by heart rate variability (HRV) which can reflect both long-term and short-term variations of heart rate for patients with sinus or AF rhythm [9,10]. Though greater than sinus rhythm, the HRV of AF patients is also regulated by the vagal tone [9]. The circadian modulation is similar

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as the sinus rhythm and it reduces with ventricular rate increasing as well [10], or saying that, it is some kind of "regular" from a long-term perspective, but still unpredictable within a short period of time.

HRV parameters can be used not only to quantify the variation of heart rates, but also to predict patients' long-term prognosis. Among patients with stable coronary heart disease or advanced heart failure, SDANN [11,12] (standard deviation of average NN intervals in all 5-min segments of the entire recording) and the newly created index – heart rate variation fraction (HRVF) are associated with mortality and the latter one is more sensitive in identifying patients who are at high risk regardless of their heart rhythm [11].

The independent determinants of AF patients with lower HRV include advanced age, depressed left ventricular ejection function and diabetes mellitus [10], which should also be considered when setting the target rate for each AF patient.

The hemodynamic characteristics of patients with AF rhythm

The irregular rhythm of AF patients results in the variation of stroke volumes among different cardiac cycles (Fig. 1). Left ventricular stroke volumes of patients in AF rhythm correlate with the R–R intervals of the preceding or even the pre-preceding cardiac cycles, which should not only be interpreted by the Frank–Starling law, but also by the interval–force relation and the postextrasystolic potentiation [13,14].

Moreover, cardiac output is lower for patients with AF rhythm than sinus rhythm at similar ventricular rate levels due to the irregular rhythm. The cardiac output of AF canine models will further decrease 2–9% compared to that of dogs with regular ventricular rhythm [15,16] and a significant reduction is observed in those with pulse deficit [16]. Similar conclusion is drawn from the study when AF patients are transiently paced by different rhythm modulations after atrioventricular node ablation. Even paced at the same rate level, cardiac output is higher in the regular pacing group than in the patients pacing according to the playback of pre-ablation AF rhythm (5.2 ± 2.4 vs. 4.4 ± 1.6 L/min, $P < 0.01$) [17]. Though the irregularity may be ameliorated by some drugs that can also lower heart rate, such as digoxin and amiodarone [18], or by special pacing modulations for those who already had pacemakers implanted [19–22], the effectiveness of these methods is not satisfactory.

Although the rhythm irregularity can impair ventricular function, the reduction of rate variability is related to an ominous prognosis, which suggests that patients with more "regular rhythm" may have higher mortality [23,24]. As a contradiction, a tradeoff may be called to balance the impact of irregularity and the prognosis for each patient.

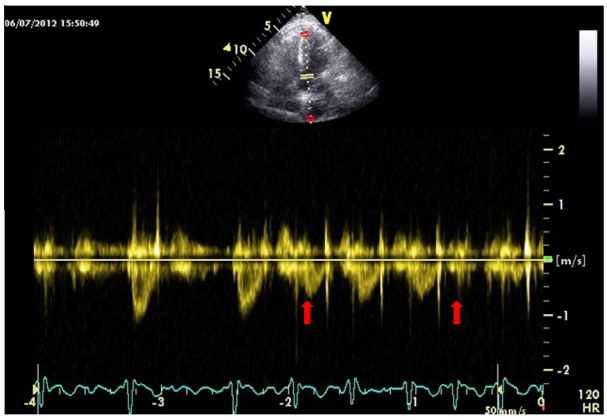

Fig. 1. A pulse wave Doppler imaging of a patient with atrial fibrillation. The ventricular rhythm of the patient is irregularly irregular and the morphology of the aortic blood flow spectrum differs from beat to beat as the length of the R-R intervals vary, which indicates that the output of each contraction is different. Some of the flow spectrum appears to be rather low during short R-R intervals and suggests insufficient blood ejection (red arrows).

The upper and lower limit for heart rate control target

As the ventricular rate of AF patients is often fast, the upper limit of rate control is important. It has been raised to 110 bpm in the new guideline, which would be considered as tachycardia for sinus rhythm. Some researchers also believe that the ventricular rate for AF patients should be 20–50% more than sinus rhythm to maintain similar ventricular performances for the loss of atrial function [25]. However, Cieslinski et al. [26] discovers that the total filling time of the left ventricle for AF patients is positively correlated to the corresponding cardiac cycle length. According to the linear equation, the mitral valve will fail to open when the R–R interval is under 264 ms and thus the ventricular contraction causes no ejection. So a minimum R–R interval is required to assure the effectiveness of each ventricular contraction. Rapid ventricular rate may as well lead to tachycardiomyopathy while rate control therapy in those patients results in significant improvement in cardiac function [27].

Furthermore, rapid rate can worsen patients' prognosis. However, results from a recent research shows no difference in prognosis among AF patients in spite of their rate control levels, even far exceed the RACE II standard [28]. But the consensus has been reached by most large-scale studies that both long-term all-cause and cardiovascular mortality increases significantly in populations with higher heart rate levels whatever they are initially healthy, with coronary heart disease or heart failure and it is probably due to the higher sympathetic tone [29–32]. Contrary conclusions should not be made among AF patients as their HRV is also regulated by autonomic nerves [9,10]. Whether a lenient upper limit of rate control target for AF patients is appropriate still needs further investigation.

As for the lower limit, it is set in the previous guideline and removed from the recent one. Since cardiac output will not keep increasing when the heart rate is too slow or the R–R interval is out of a reasoned range, a lower limit may be necessary for AF patients. The majority of the ventricle filling is accomplished within 100 ms after mitral valve opening and further prolonging of cardiac cycle cannot lead to parallel increasing of the left ventricular preload volume [33]. It has been depicted by a prior study that left ventricular ejection time is correlated with the filling time of the preceding cardiac cycle in a curvilinear fashion with the transition point at about 400 ms, which may be the upper limit for the parallel increasing of ventricular filling [26].

Moreover, a relatively higher heart rate is required for AF patients to compensate for the reduction of ventricular function caused by rhythm irregularity. Thus, a lower limit is necessary as well. Because the degree of irregularity and the daily needs differ from patient to patient, the lower limit should also be individualized. For example, to reach a similar cardiac output level as a sinus rhythm one with the average heart rate at 60 bpm, an AF patient with a more irregular rhythm may need a target rate at 85 bpm while for the one with a relatively regular rhythm, 80 bpm might already be optimal.

Life quality and exercise tolerance

A previous study shows no obvious difference in patients' life quality among different heart rate control levels, but some AF patients, especially those with the most severe symptoms are excluded from the study [34]. Palpitation is a major symptom in AF patients [2,3] and the heart rate varies when symptoms appear. Therefore, rate control therapy based on the patient's own