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Rate control in atrial fibrillation

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REPLY

We thank Dr. Alfonso for his comments about our study (1). His observations provide an opportunity: 1) to analyze the implications of the procedural finding of balloon slippage in patients with in-stent restenosis (ISR) treated by conventional balloon angioplasty; 2) to report whether a specific subgroup of patients benefited from cutting balloon angioplasty; and 3) to discuss the possible benefit of lesion pre-dilatation using the cutting balloon in patients with ISR treated with drug-eluting stenting.

First, analysis of the Restenosis Cutting Balloon Evaluation Trial (RESCUT) database shows that in the group treated with conventional balloon angioplasty, balloon slippage was associated with a higher percentage, although not statistically significant, of residual dissections (11.1% vs. 6.9%; $p = 0.35$), and a higher percentage of additional stent implantation (9.5% vs. 3.5%; $p = 0.21$) mainly due to type D, E, and F dissections. However, recurrent restenosis rate at six months was not higher when balloon slippage was observed.

Second, the analysis performed with the multivariate technique to determine whether any specific subset of ISR patients/lesions benefited from the cutting balloon treatment (i.e., short vs. long lesions, small vs. large vessel, diabetics vs. nondiabetics, short time vs. long time by previous implanted stent, first vs. >1 prior ISR on the same vessel) did not uncover any significant effect.

Third, although a recent study failed to demonstrate long-term benefits after the use of cutting balloon in ISR patients undergoing adjunctive gamma brachytherapy (2), in the Registry Novoste (RENO) (3) where brachytherapy was performed using beta-radiation, pretreatment with cutting balloon significantly reduced six-month target-vessel revascularization compared with conventional angioplasty (10.2% vs. 16.6%; $p = 0.04$).

However, we do not believe that the use of cutting balloon will translate into clinical or angiographic benefit for patients with ISR treated with drug-eluting stents (DES), as a result of the procedural differences in the treatment of ISR using adjunctive brachytherapy compared with restenting with a DES. In the first case, before adjunctive brachytherapy, it is recommended to optimally treat ISR by conventional/cutting balloon angioplasty or atherectomy, avoiding additional stenting to reduce the risk of late stent thrombosis, whereas in the case of restenting with a DES, an optimal balloon pretreatment of ISR is not necessary, nor is the use of cutting balloon to avoid balloon slippage, because the operator can reduce the risk of vessel injury at the stent edges, even in the event of balloon slippage, by simply predilatating the ISR lesion using an undersized noncompliant conventional balloon.

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Rate Control in Atrial Fibrillation

We read with great interest the substudy of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) investigators on the approaches to control rate in atrial fibrillation (AF) (1). Recent studies show that rate control may be adopted as first-choice therapy in a variety of patients with AF (2,3). The optimal level of heart rate during AF is, however, still unknown.

In the AFFIRM study, in accordance with the guidelines (4), a strict rate-control approach was applied that includes a resting heart rate ≤ 80 beats/min and either a 6-min walk test heart rate ≤ 110 beats/min or a mean heart rate on a 24-h Holter recording ≤ 100 beats/min, in combination with a maximum heart rate $\leq 110\%$ of predicted maximum heart rate. The present study shows that this (strict) rate-control approach can be successfully achieved in two-thirds of the patients and that, in line with previous data, beta-blockers are most effective to accomplish this goal (5). Serious adverse effects were uncommon. However, to obtain adequate rate control, atrioventricular node ablation and pacemaker implantation was performed in 108 of the 2,027 patients (5.3%), and an additional 147 patients (7.3%) had a pacemaker implanted for symptomatic bradycardia. In comparison, in the RAte Control versus Electrical cardioversion (RACE) study, a more lenient rate-control approach was followed (resting heart rate < 100 beats/min) (3). In that study, 46% of the patients were treated with a beta-blocker. Severe drug adverse effects were also rare (0.8%). In contrast to the AFFIRM study, however, a pacemaker was implanted in only 3 of the 256 patients (1.2%, all after atrioventricular node ablation).

Unfortunately, the AFFIRM investigators give no data on the influence of the level of rate control on mortality and morbidity. Therefore, it still remains unknown whether strict rate control is associated with an improved prognosis. To answer the question of which approach to rate control is most effective we will start the RAte Control Efficacy in permanent atrial fibrillation study (RACE II).

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The AFFIRM Study: Approaches to Control Rate in Atrial Fibrillation

The optimal heart rate for patients with atrial fibrillation (AF) remains unclear; current guidelines are primarily based on clinical experience (1). Recent randomized studies suggest combining beta-blockers or calcium channel blockers with digoxin to achieve better rate control at rest and during exercise (2-4). However, I believe clarification of the "approach to control rate in AF" by the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) investigators (4) is justified.

A total of 2,027 patients were randomized to the rate control arm of the AFFIRM trial between 1995 and 1999. Of these, 248 crossed over to the rhythm-control group due to "uncontrolled symptoms" and 108 underwent AV nodal ablation due to failure of pharmacologic therapy. Rate-control data at rest are available in only 740 (36.5%) patients, which deteriorates further to 361 (17.8%) if data regarding heart-rate control during exercise are desired.

This relative lack of data may be explained by the fact that 1,055 (52%) patients were in sinus rhythm at the time of randomization. The proportion of those in the rate-control group who maintained sinus rhythm during follow-up is unclear. Published data for the entire trial population suggest a similar number (49%) remaining in sinus rhythm at study end.

Therefore, the majority of data on rate control of AF comes from a minority of patients randomized to a rate-control strategy. Because of the nature of data collection (only patients with AF at the time of assessment were selected for analysis), care should be taken in interpreting these results. The data predominantly represent patients with persistent and permanent AF and significantly underrepresent those with paroxysmal AF.

It is difficult to make conclusions on the control of ventricular rate during paroxysms of AF from this study, the occurrence of which greatly depends on variations of the autonomic tone (5).

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REPLY

We thank Dr. Van Gelder and colleagues and Dr. Shelton for their interest in our study (1). We agree with Dr. Van Gelder and colleagues that the optimal heart rate in atrial fibrillation (AF) during rest and exercise is unknown. Perhaps minimal effort to achieve rate control during AF is sufficient. However, absence of adequate rate control can lead to adverse consequences such as tachycardia-induced cardiomyopathy. Our Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) substudy was not designed to evaluate the mortality and morbidity of inadequate rate control; thus, we cannot comment on these end points.

Both ablation of the atrioventricular junction and pacemaker insertion were allowed "innovative" therapies in the AFFIRM study, and they may have contributed to the relatively frequent use of this approach. Furthermore, attempting to achieve more "stringent" rate control may have led to more symptomatic drug-induced bradycardia and subsequent pacemaker insertion in the AFFIRM study, compared to the more "lenient" criteria used in the RAte Control versus Electrical cardioversion (RACE) study. However, the patient population in the AFFIRM study was not directly comparable to that in RACE, and pacemaker implantation per capita in the U.S. is higher than in Europe. These factors may have influenced the differences between these two studies.

We agree that a long-term, prospective, randomized trial would be useful. We applaud Dr. Van Gelder and colleagues for pursuing answers to some of these difficult issues in the RAte Control Efficacy in permanent atrial fibrillation (RACE II) study.

Dr. Shelton concurs that the optimal approach to rate control remains primarily based on clinical experience. He notes that 248 patients in the AFFIRM study crossed over to the rhythm-control group, and 108 patients underwent ablation of the atrioventricular junction (1). Many patients (approximately one-half) in the