This editorial refers to ‘The young patient with asymptomatic atrial fibrillation: what is the evidence to leave the arrhythmia untreated?’\(^\dagger\), by K. Wasmer et al., on page 1439 and ‘Early management of atrial fibrillation to prevent cardiovascular complications’\(^\dagger\), by S. Natell et al., on page 1448

Since the publication of the AFFIRM trial,\(^1\) arrhythmology has been wrestling with the dilemma of ‘rate vs. rhythm control’ of atrial fibrillation (AF), with subtle variations on the theme. I suspect that some of our non-arrhythmologist colleagues may even experience some degree of ‘fatigue’ when the debate resurfaces. Two review papers now confront the dilemma from apparently different angles, but, in the end, they analyse similar facts and reach similar conclusions. Natell et al.\(^2\) devote their attention to early rhythm control of AF as a potential strategy to prevent progression and decrease cardiovascular complications. On the other hand, Wasner et al.\(^3\) discuss whether to fight for sinus rhythm in asymptomatic young patients. These reviews share the hypothesis that previous studies advocating rhythm control have failed to demonstrate any definitive benefit over rate control in the AF population, because their trials included patients at a late stage of the disease. They suggest that pursuing sinus rhythm at an early stage of the disease and with better therapeutic tools may improve AF control and decrease morbidity and mortality. The new hypothesis that early treatment would result in better results is plausible, but not yet demonstrated in large trials. Therefore, after reading both reviews, we may conclude that we are more or less where we were before. In actual clinical practice, however, it is clear that many physicians recommend antiarrhythmic drugs or ablation in middle-aged patients with few co-morbidities. Therefore, the present reviews provide good tools to rethink the question and generate hypotheses that may lead us to the new evidence required.

The authors try to define a patient profile that can be expected to maintain sinus rhythm based on ‘early rhythm management’ or the choice of ‘young’ patients. Due to our limited ability to determine the extent of disease in an individual patient’s atrium, the immediate question that arises is the specific definition of ‘early’ and ‘young’. In recent years, it has been shown that co-morbidities such as hypertension, structural heart disease, or obstructive sleep apnoea decrease the chances of maintaining sinus rhythm after ablation.\(^4–6\) The ECG pattern of AF has been proposed as a way to evaluate the extent of atrial disease.\(^7,8\) In addition, imaging techniques could help to stratify the probability of ablation success by defining left atrial size, spherical remodelling, or the proportion of fibrotic tissue.\(^4,9,10\) Therefore, it can be anticipated that new AF classifications would focus on differentiating the stages of atrial disease, which could result in better patient selection and a more favourable risk–benefit ratio for therapeutic interventions such as antiarrhythmic drugs or ablation (Figure 1).

A second important consideration that is only vaguely mentioned in these papers is aetiology. If we want to prevent and effectively treat AF, it is important to detect patients at risk and to treat predisposing conditions more effectively in order to avoid irreversible damage to the atrium. With the probable exception of its monogenic forms, AF results from the additive effects of conditions such as ageing, pressure–volume overload, or inflammatory–infiltrative diseases. Therefore, we may be able to decrease AF prevalence in middle-aged individuals and avoid an AF epidemic at the population level if we achieve better control of established risk factors such as hypertension, obesity, diabetes, sleep apnoea, and excessive endurance sports practice. At the individual level, the aetiological factors and modulators that create AF should be identified early and treated aggressively to avoid progression. For example, treatment of obesity and sleep apnoea has improved outcomes in patients at risk of AF.\(^11,12\) On the other hand, patients with so-called ‘lone AF’ often have a long-term pattern of excessive endurance training;\(^13\) if this is not identified and considered as a risk factor, which is usually the case, exercise habits remain unmodified. Therefore, the aetiological conditions must be explored in every patient with AF.

A third consideration in the review by Nattel et al.\(^2\) is the hypothesis that a mechanism-based therapy will allow personalized AF therapies in the near future. In recent years, many cellular and tissue-related contributing mechanisms have been described, such as altered calcium handling, ion channel abnormalities, autonomic dysfunction, atrial fibrosis, and fatty infiltration. If one of these mechanisms is the predominant factor in an individual patient case,
this opens up the possibility of patient-specific therapy. Defining the role of ganglion ablation, renal denervation, calcium blockers, angiotensin-converting enzyme (ACE) inhibitors, statins, micro-RNA modulation, and antioxidants opens up a new field of research on therapeutic targets that goes beyond antiarrhythmic medications. Whether more specific treatment of these mechanisms could result in satisfactory control of the disease remains to be established.

It is now quite clear that the old ‘rate vs. rhythm control’ debate is becoming obsolete as more doctors look to rhythm control as a first option, mainly due to the advent of AF ablation. This therapy is highly effective when applied in appropriate patients, with high probability of successful outcome. Even if complete control is not achieved, significant improvement is observed in many patients. Recent technological improvements such as contact measurements, single-shot techniques, better 3D reconstructions, and even robotic approaches may lead to much safer and more reliable procedures, with better results. Therefore, early management with AF ablation is already the approach preferred by many patients over other therapeutic options. The challenge will be to avoid unnecessary procedures in patients with very low chances of successful outcomes. Therefore, careful evaluation is necessary, including not only clinical categorization such as paroxysmal vs. persistent AF but also the evaluation of other potentially predictive parameters (atrial size, degree of fibrosis, co-morbidities, etc.). Nevertheless, AF ablation remains hampered by several limitations that will have to be overcome. First of all, ablation continues to require high technology and sophisticated tools. It also requires a large number of well-trained electrophysiologists, a resource that may not be available to many patients around the world. Finally, in an environment that requires cost containment, the payers demand a highly cost-effective technique, and it may be difficult to generate these data. Ongoing studies such as CABANA (NCT00911508 at ClinicalTrials.gov) and EAST may clarify the cost–benefit of early ablation. However, patients who participate in these studies often have major co-morbidities; this is likely to limit the effectiveness of ablation and underestimate the efficacy of ablation in selected candidates.

In summary, despite the lack of strong evidence in favour of early detection and rhythm control in AF, there is a trend toward more aggressive pursuit of sinus rhythm in young patients and in recently diagnosed AF. While waiting for results from ongoing studies, clinical decisions should probably be based on symptom relief and the probability of long-term maintenance of sinus rhythm based on clinical and ECG characteristics and imaging techniques.

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References


