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Non-invasive assessment of atrial electrophysiology: A vital part of the medical work-up in the setting of atrial arrhythmia

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Atrial fibrillation (AF) is the most common form of arrhythmia encountered in clinical practice, accounting for approximately one third of hospital admissions for cardiac rhythm disturbances [1]. The number of hospital admissions due to AF increased over recent decades, probably as a result of an aging population and a rising prevalence of predisposing risk factors [2]. The major drawback of the routine cardioversion strategy is the high rate of relapse to AF. The instigation of prophylactic pharmacological antiarrhythmic therapy increases the proportion maintaining sinus rhythm (SR), but the rhythm maintenance strategy still fails in approximately half of the patients [3]. Studies such as AFFIRM [4] and RACE [5], have demonstrated that accepting permanent AF, with appropriate rate control and thromboembolic prophylaxis, results in comparable clinical outcome. However, further analyses of AFFIRM have shown that although the rate- and rhythm-control strategies had comparable outcome, the presence of SR was indeed associated with a lower risk of death, i.e., the risk of death was lower in patients in whom a rhythm-control strategy was chosen and successful, than when a rate-control strategy was chosen [6]. On the other hand, the use of antiarrhythmic drugs was associated with a higher mortality when adjusted for the presence of SR, i.e., the risk of death was higher in patients in whom a rhythm-control strategy was chosen but failed, than when a rate-control strategy was chosen [6]. These findings highlight the need for analyses of the characteristics of atrial electrophysiology in each patient with or at risk for AF, in order to increase the chance of success, whichever treatment strategy is chosen. Given the large number of patients with AF, characterization must be based on results from an easily administered and interpreted methods, i.e., a non-invasive approach is preferred.

Non-invasive methods for evaluating the atrial electrophysiology during AF have been developed [7, 8]. Although the techniques differ to some extent the main parameter of these analyses is an index of the atrial refractory period (expressed as atrial fibrillatory rate). Atrial fibrillatory rate has been shown to correlate well with invasive measures of atrial refractoriness [7, 9] and to carry valuable information regarding anti-arrhythmic drug response [10] and maintenance of SR following cardioversion [11, 12]. For analysis during SR, the P wave signal averaged ECG (SA-ECG) was introduced already in the early 1980's [13]. The bandpass filtering was designed to eliminate unwanted signals that would obscure the low-amplitude late-potentials of tissue depolarization. The assumption was that the ability to analyze these low level cardiac signals enables one to identify patients with delayed myocardial conduction, a pre-requisite factor for any arrhythmia, ventricular as well as atrial. Several studies have shown an association between filtered P wave duration and AF [14, 15]. The predictive properties of the method have foremost been studied in the setting of postoperative AF, where it in several studies has been shown to predict AF development with high sensitivity and specificity [16–18]. Moreover, analyses of P wave morphology derived from P wave SA-ECG without the commonly applied bandpass filtering, was in a recent publication shown to enable identification of the

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interatrial conduction route used with high accuracy [19]. The clinical implications of these findings remain to be explored in future studies. Despite the fact that the overall results of P wave SAECG analysis are very promising and are likely to add value in the clinical evaluation of patients at risk of developing AF, the method is still hampered by lack of standardization and harmonization of the different methods used as well as of a basic electrophysiological knowledge of what is the invasive correlate to the non-invasive measures [20–22].

The ambitious research program conducted by Kutarski et al. published in the current and previous issues of "Cardiology Journal" addresses a number of important issues associated with method validation and an increased electrophysiological understanding [23–27]. Via an innovative study design and a patient material thoroughly covered in five separate publications, they are able to investigate the relationship between P wave SAECG analyses performed on externally and internally recorded ECG signals and the response of these parameters to different pacing sites. In the initial study P wave SA-ECG, performed on internally (i.e., via the pacemaker electrodes) and externally recorded signals, are compared [23]. The authors notice differences in the measurements, which they state may be of methodological importance. This may well be, but a note of caution is warranted, the concept of SA-ECG was developed and studied using three orthogonal leads. The intracardiac bipolar leads used by the authors are unlikely to be strictly orthogonal, which complicates the interpretation of the vector signal and hence most of its derived parameters. In the following studies, the authors focus on the electrophysiological consequences of right atrial appendage pacing [24], coronary sinus pacing [25] and biatrial acing [26]. The authors conclude, based on their P wave SA-ECG findings that biatrial pacing seems favorable, coronary sinus pacing may also be favorable while right atrial appendage pacing seems to be unfavorable in terms of atrial electrophysiology. Data on this topic in the literature are scant [28, 29], but the few studies that exist are largely in keeping with the findings of Kutarski et al. [23–27]. However, the possible differences in clinical beneficial or non-beneficial effects of the different atrial pacing sites are yet to be proven in large, randomized clinical trials [30]. In that regard, studies like the ones from Kutarski et al. may well prove valuable in identifying suitable methods to estimate surrogate end-points indicating positive or negative electrophysiological changes at an early stage.

The study presented in the current issue of "Cardiology Journal" by Kutarski et al. [27], which summarizes their previous findings, represent an important continuation of the task of increasing our knowledge about basic electrophysiological properties obtained via non-invasive analyses. In the long run, these kinds of methods are likely to lead to optimization of the resources used and even more importantly to improved patient care. However, to do so improved method validation and standardization, like the one in the presented articles, is mandatory.

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