Discriminating atrial flutter from atrial fibrillation using a multilevel model of atrioventricular conduction

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BACKGROUND The discrimination between atrial flutter (AFlu) and atrial fibrillation (AFib) can be made difficult by an irregular ventricular response owing to complex conduction phenomena within the atrioventricular (AV) node, known as multilevel AV block. We tested the hypothesis that a mathematical algorithm might be suitable to discriminate both arrhythmias.

OBJECTIVES To discriminate AFlu with irregular ventricular response from AFib based on the sequence of R-R intervals.

METHODS Intracardiac recordings of 100 patients (50 patients with AFib and 50 patients with AFlu) were analyzed. On the basis of a numerical simulation of variable flutter frequencies followed by 2 levels of AV block in series, a given sequence of R-R intervals was analyzed.

RESULTS Although the ventricular response displays absolute irregularity in AFib, the sequences of R-R intervals follow certain rules in AFlu. We find that using a mathematical simulation of multilevel AV block, based on the R-R sequence of 16 ventricular beats, a stability of atrial activation could be predicted with a sensitivity of 84% and a specificity of 74%. When limiting the ventricular rate to 125 beats/min, discrimination could be performed with a sensitivity of even 89% and a specificity of 80%. In cases of AFlu, the atrial cycle length could be predicted with high accuracy.

CONCLUSION On the basis of the electrophysiological mechanism of multilevel AV block, we developed a computer algorithm to discriminate between AFlu and Afib. This algorithm is able to predict the stability and cycle length of atrial activation for short R-R sequences with high accuracy.

KEYWORDS Atrial flutter; Atrial fibrillation; Atrioventricular conduction; Multilevel AV block; AV node

ABBREVIATIONS **Δ** = increment in atriventricular block–type Wenckebach; **θ** = refractory period; **AFib** = atrial fibrillation; **AFlu** = atrial flutter; **AV** = atrioventricular; $\mathbf{AV_M}$ = atrioventricular conduction time in atrioventricular block–type Mobitz; $\mathbf{AV_{max}}$ = maximum atrioventricular conduction time; $\mathbf{AV_W}$ = atrioventricular conduction time in atrioventricular block–type Wenckebach; **CL** = cycle length; **ECG** = electrocardiogram/electrocardiographic; **LSQ** = least squares–type difference between simulation and measurements; **MAVB** = multilevel atrioventricular block; **ROC** = receiver-operating-characteristic; $\mathbf{R\text{-}R_{ECG}}$ = sequence of R-R intervals taken from the surface electrocardiogram; $\mathbf{R\text{-}R_{SIM}}$ = sequence of simulated R-R intervals

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Introduction

The correct discrimination between atrial fibrillation (AFib) and regular atrial arrhythmias including atrial flutter (AFlu) and focal atrial tachycardia poses a diagnostic challenge to both physicians and computerized algorithms.[1,2] As a result, misinterpretation rates of up to 80% have been reported in clinical practice.[1] AFib represents a high-frequency chaotic electrical activation of the atria exhibiting electrocardiographic (ECG) signs of fibrillation waves in combination with an absolutely irregular ventricular response. In contrast, electrical activation follows defined reentrant circuits in AFlu, resulting in regular flutter waves in the surface ECG. In the case of isthmus-dependent AFlu (typical AFlu), electrical activation produces a characteristic sawtooth pattern in the surface ECG. However, the discrimination between AFib and AFlu from the surface ECG can be made difficult by several factors. On one hand, AFib may present with coarse fibrillatory waves, which are reminiscent of AFlu.[3,4] On the other hand, AFlu may display atypical characteristics in the surface ECG, including hardly discernible low-voltage flutter waves as well as an irregular ventricular response, thereby mimicking AFib. However, the exact differentiation between AFib and AFlu is imperative with respect to treatment modalities as the effectiveness of antiarrhythmic agents is generally lower in AFlu and catheter ablation is

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often the superior option. Furthermore, atypical forms of AFlu are becoming increasingly important in clinical practice as a complication of left atrial ablation.

The objective of this study was to develop a computer algorithm for an automated discrimination between AFib and regular atrial arrhythmias (AFlu and atrial tachycardia). Our algorithm is based on the observation that the irregularity of ventricular activation in AFib and AFlu follows two distinct electrophysiological mechanisms. Although irregularity is caused by chaotic atrial activation in AFib, a serial arrangement of atrioventricular (AV) block levels (multilevel AV block [MAVB]) is causative in AFlu.[5] The description of this type of AV block dates back to the 1960s when Watanabe and Dreifus[6] identified multiple block levels in series within AV nodes of rabbit hearts. Similar results could be obtained later in humans using intracardiac recordings.[7] Ventricular activation patterns resulting from MAVB are often complex for visual recognition (Online Supplemental Figure 1). However, a computer algorithm should be able to identify the underlying levels of AV block. On the basis of the electrophysiological mechanism of MAVB, we developed a computer algorithm for the automated discrimination between AFib and AFlu. We show that our algorithm is able to predict the stability and cycle length (CL) of atrial activation even for short sequences of R-R intervals with high accuracy.

Methods

Recording and processing of electrophysiological data

Electrophysiological data were obtained retrospectively from patients exhibiting AFib or AFlu with irregular ventricular response during invasive electrophysiological testing or catheter ablation. All procedures were performed without continuous sedation. Diagnostic catheters were inserted through the right or left femoral vein. Depending on the type of the procedure, atrial electrograms were recorded either using a duodecapolar or quadripolar catheter placed in the right atrium or using a decapolar or quadripolar catheter placed in the coronary sinus. Electrophysiological signals were processed and stored using a commercially available electrophysiological recording system (BARD Clearsign, C. R. Bard Inc, Lowell, MA). Segments of 40 seconds were selected manually from the data files for further analysis. Segments containing premature ventricular beats were excluded. The discrimination between AFib and AFlu was performed using electrical signals measured at the atrial electrodes by an expert in the field of cardiac electrophysiology. For AFib, we found that all examples exhibit highly irregular intervals of atrial activation (qualitative assessment) in combination with a short mean atrial CL (182 ms). These data correspond well with the threshold of 200 ms that is referred to in the European guideline for the management of AFib.[8] In contrast, intracardiac recordings taken from patients with AFlu exhibited highly regular intervals in combination with a mean atrial CL of 240 ms. In many cases, the correct rhythm diagnosis could be proved further by evaluating the reaction of the arrhythmia to catheter ablation. Among the group of AFlu cases, further quantitative assessment revealed an AA variation below 5 ms. The exact timing of the R-R intervals was determined carefully from the surface ECG ($R\text{-}R_{ECG}$) using built-in calipers and transferred to a data sheet. Forty-second segments of 50 patients presenting with AFlu and 50 patients presenting with AFib were extracted. The study design was approved by the ethics committee of the University of Heidelberg and conforms to the standards defined in the Helsinki Declaration.

Mathematical model of MAVB

MAVB was simulated by a combination of 2 levels of second-degree AV block in series (Figure 1A). Combinations that were allowed included AV block–type Mobitz followed by AV block–type Wenckebach or vice versa. All signals leaving the first block level served as input for the second block level. Figure 1B displays a typical example of MAVB exhibiting AV block–type Mobitz on the first level and AV block–type Wenckebach on the second level. For the simulation of AV block–type Mobitz, a first incoming signal was conducted through the block level with a conduction time (AV_M). As soon as this signal traversed the block level, a refractory period (θ) was initiated. All following signals entering the block level during this period were dropped (Figure 1C). As soon as the refractory period timed out, the next signal was again conducted with the conduction time AV_M. For the simulation of AV block–type Wenckebach, a first incoming signal was subjected to a fixed conduction time (AV_W). The conduction time of the next incoming signal was determined by adding an increment (Δ) to the conduction time AV_W (Figure 1D). This increment was added from beat to beat until the total conduction time exceeded a predefined margin (AV_{max}). As soon as the total conduction time exceeded this threshold, the beat was dropped and the next signal was again conducted with the conduction time AV_W. For a given CL, conduction time AV_M and refractory period θ (Mobitz) or threshold AV_{max}, and conduction time AV_W and an increment Δ (Wenckebach), a forward simulation can be performed as described above. This yields a series of time points of signals exiting the second block level. We used it to define the sequence of simulated R-R intervals ($R\text{-}R_{SIM}$) that can be compared with $R\text{-}R_{ECG}$.

Discrimination between regular and irregular atrial activation

For each data instance, we used mathematical optimization to determine the values of the patient-specific parameters AV_M, AV_W, CL, θ, AV_{max}, Δ with simulation results that had the smallest difference between $R\text{-}R_{SIM}$ and $R\text{-}R_{ECG}$. The latter was analyzed blinded to all clinical data and served as the input of our discrimination algorithm. We used a least