Published in final edited form as:

J Electrocardiol. 2018 ; 51(6 Suppl): S67–S71. doi:10.1016/j.jelectrocard.2018.07.010.

Atrial fibrillation observed on surface ECG can be atrial flutter or atrial tachycardia

Elyar Ghafoori, MS^{a,b,c,*}, Nathan Angel, PhD^e, Derek J. Dossall, PhD^{a,b,c,d}, Rob S. MacLeod, PhD^{a,b,c}, and Ravi Ranjan, MD, PhD^{a,b,c}

^aCardiovascular Medicine, University of Utah, Salt Lake City, UT, USA

^bDepartment of Bioengineering, University of Utah, Salt Lake City, UT, USA

^cNora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah, Salt Lake City, UT, USA

^dDepartment of Surgery, University of Utah, Salt Lake City, UT, USA

^eAcutus Medical, Carlsbad, CA, USA

Abstract

Background: Differentiating between atrial fibrillation (AF) and atrial tachycardia (AT) or atrial flutter (AFL) on surface ECG can be challenging. The same problem arises in animal models of AF, in which atrial arrhythmias are induced by pacing or pharmacological intervention with the goal of making mechanistic determinations. Some of these induced arrhythmias can be AFL or AT, even though it might appear as AF on the body-surface ECG based on irregular R-R intervals. We hypothesize that a dominant frequency (DF) analysis of the ECG can differentiate between the two distinct arrhythmias, even when it is not evident by the presence of flutter waves or beat-to-beat regularity when looking at brief recordings.

Methods: Canine model (n = 15, 10 controls and 5 Persistent AF animals with >6 months of AF) was used to test the hypothesis. Atrial arrhythmia was induced by rapid atrial pacing. Five blinded observers evaluated the 3 lead surface ECGs recorded during atrial arrhythmia and classified the rhythm as AFL/AT or AF. The 64-electrode Constellation (Boston Scientific) catheter was used to acquire left (entire group) and right (7 of 10 controls) atrial intracardiac electrograms. For the surface ECG and the intracardiac electrograms, Welch method with a hamming window and 50% overlap was used to calculate DF of two-minute segments. Mean of standard deviations of the DF values were calculated for both ECGs and intracardiac EGMs. Ground truth came from activations maps and DF analysis derived from the intracardiac electrograms recorded in the two chambers.

Results: Rapid pacing induced atrial arrhythmias in all the control animals. The ECG in 8 of the 10 control cases was read as AF by at least 80% percent of observers even though the EGMs from the Constellation showed organized activation and consistent DF (STD of DF < 0.001) in all the electrodes confirming the arrhythmia as AFL in 10/10 cases. In the persistent AF group, the DF from the three lead ECGs were significantly different (Mean of STDs = 2.65 ± 0.99) whereas the DF in the control animals with AFL was consistent across all ECG channels (Mean of STDs <

*Corresponding author at: 95 S 2000 E, Salt Lake City, UT 84112, USA. elyar.ghafoori@utah.edu (E. Ghafoori).

0.001), and the DF in the control animals ECGs was in agreement with the DF of the intracardiac electrograms.

Conclusion: Surface ECG recordings can mimic AF even when the underlying atrial arrhythmia is AFL in control canine models. DF variation of the signals from multiple surface ECG leads can help differentiate between the AF and AFL.

Keywords

Electrocardiography; Atrial fibrillation; Atrial flutter

Introduction

Atrial Fibrillation (AF) is the most common cardiac arrhythmia and a major cause of stroke [1]. Sometimes other atrial arrhythmias like atrial flutter (AFL) or atrial tachycardia (AT) can mimic AF on surface ECG. Accurate ECG interpretation of the atrial tachyarrhythmia facilitates optimal management. Atrial fibrillation is characterized by a more disorganized electrical activity in the atrium as compared to atrial flutter (AFL) or atrial tachycardia (AT). Multiple micro-reentrant and focal activation can be simultaneously present in AF. This chaotic activation presents itself on electrocardiogram (ECG) with absence of regular P wave, irregular RR intervals and fibrillatory waves. Unlike AF, in AT and AF there is organized activity with a single focal or re-entrant driver, respectively. As a result, in both AFL and AT ventricular activation can be regular and in AFL saw-tooth flutter waves is commonly seen on the surface ECG. At times, despite the regular atrial activity in AFL and AT due to block in the AV node, specially, at high rates the ventricular activity is not regular and the surface ECG can mimic AF. As a result the differentiation between AF and AFL/AT can be a persistent challenge in ECG based diagnosis of atrial arrhythmias, especially when looking at brief periods of surface ECG [2]. Atrial flutter can represent itself with variable RR intervals [3]. Coarse fibrillation waves during AF can be mistaken for AFL or rapid focal AT [4].

The same problem arises in animal models of AF, which are routinely used to study arrhythmia mechanisms or test drugs [5–7]. Most of these animals are healthy and undergo arrhythmia induction by rapid pacing with or without pharmacological intervention. While there is no structural or electrical remodeling in healthy animals, lone-AF induction that is sustained can be questionable [8,9] leading to mischaracterization of the underlying mechanism of these arrhythmias. We hypothesized that some of these induced atrial arrhythmias in control animals can be atrial flutter (AFL), even though it might appear as AF on the body-surface ECG. We provide a spectral analysis where dominant frequency (DF) of the ECG leads can differentiate between the two distinct arrhythmias, even when it is not evident by the presence of flutter \fibrillation waves or beat-to-beat regularity.

Method

Study design

We used a canine model for the study. Ten healthy controls and five chronic paced AF animals with persistent AF were used (AF > 6 month). In the AF animals, rapid long term

atrial pacing was used to induce persistent AF. These animals were in persistent AF at the time of the signal acquisition. The study protocol was approved by Institutional Animal Care and Use Committee (IACUC).

Electrophysiological study

All animals underwent an electrophysiology (EP) study to record atrial electrograms along with surface ECG signals. Animals were sedated using Propofol and then intubated for general anesthesia using Isoflurane (1–3%). Percutaneous femoral venous access was obtained bilaterally. A 5 Fr sheath was placed in the femoral artery for continuous arterial pressure monitoring. Left sided access was obtained by crossing the intra-atrial septum under intra cardiac echocardiogram (ICE) and fluoroscopic guidance using a SL0 sheath and a BRK-1 (St Jude Medical) needle. A 64 pole basket catheter (Constellation, Boston Scientific™) was used to record atrial electrograms (EGMs). Atrial EGMs were acquired in the left atrium (LA) for the entire study group. In seven of the control animals, we also had simultaneous recording in the right atrium (RA). Simultaneous three lead surface ECG was placed on canine torso (2 lead on one side and one lead on the other side of the torso) and collected during these recording. In the control animals, atrial arrhythmia was induced by rapid burst pacing in atrium. The entire recording was acquired at 4 kHz sampling rate.

Analysis

In the control animals, we recorded ECG and EGMs after induction until it terminated. In the persistent AF animals, we recorded for a maximum of 30 min.

EGM Analysis: Unipolar signals were used in the analysis. We analyzed a two-minute segment of each unipolar signal. Custom written computer software developed under MATLAB (MathWorks, Inc., Natick, MA) was used. A band-pass (low frequency cut off: 0.1 Hz – high frequency cut off: 200 Hz) filter was used for preprocessing of the signals. Welch's method was used to estimate power spectrum density (PSD) function on two-minute segments of EGMs for each animal. A hamming window with 50% of data overlap was employed in PSD estimation. The dominant frequency (DF) was calculated for each electrode, as the frequency that has the highest power in the PSD of each segment. We subtracted global far-field QRSs from the local atrial electrograms, using template matching, where QRSs were detected on surface ECG. Subsequently, we detected atrial activations as maximum downward slope on the electrograms, to make activation maps. Activation maps were used to investigate underlying mechanism of the arrhythmia. We report the percentage of beat-to-beat covered cycle length by the activation map.

ECG Analysis: Five observers were assigned to diagnose the rhythm on the ECG strips of the control animals and the five chronic AF animals (AF > 6 month). These observers were blinded to the animal group and the EGM analysis. We similarly estimated the PSD of ECG signals for both control and chronic AF animal models and calculated the DF for each lead for every animal. Subsequently, we calculated the standard deviation of DFs in all lead to assess the DF difference. A *t*-test was employed to compare standard deviations of DFs in ECG leads between AF and control group.

Results

We successfully recorded surface ECGs and atrial EGMs in 10 control animals and 5 persistent AF animals. Eight of 10 ECGs in the control animals were diagnosed as AF by majority of observers (>80%). All 5 of 5 ECGs in the AF animals were diagnosed as AF.

Fig. 1A shows an activation map for one beat based on the local left atrial EGMs recorded at the 64 electrodes in the Constellation in one of the control animals. The activation map was identical for each beat and covered $99.7 \pm 0.4\%$ of the cycle length of the AFL and $52.4 \pm 4.9\%$ for AT inductions. Fig. 1B shows the PSD of all the 64 electrograms in the LA, for the same atrial arrhythmia. The DF for all the 64 electrodes for each of the atrial arrhythmia recorded in the control animal is shown in Table 1. The DF for all the 64 EGMs for each control animal was the same (the standard deviation at each of the 64 electrode was less 0.001 Hz). On the other hand, DF was significantly different among the 64 EGMs recorded for each chronic AF animal model (the mean of standard deviations for all the 64 electrodes was 2.85 ± 0.98 Hz). Table 2 describes our findings on chronic AF animals. Fig. 2A shows the surface ECG from a control animal. There is no regularity of the R-R interval and the presence of flutter waves is not clear. This was read as AF by all the ECG readers. Fig. 2B shows the consistent atrial dominant frequencies among ECG leads for the same episode. Although the ECG appears to have characteristics of AF, PSD of ECG leads reveals organized activation in atria. Fig. 2C is the surface ECG from a persistent AF animal. Once again, the R-R intervals are irregular. Fig. 2D shows the power density of the surface ECG and it shows the lack of any consistent peak. In Fig. 2E, the ECF for atrial tach is shown, where RR intervals are regular and PSD shows consistent atrial dominant frequencies among ECG leads (Fig. 2F).

In the 10 control animals, we found both reentrant ($n = 6$) and focal ($n = 4$) activation mechanisms based on activation maps. We were able to cover >99% of the atrial cycle length in the reentrant induced AFLs. Table 1 describes our findings for the entire control group. PSD of the ECG signals were consistent between all leads and had the same DF that was observed on all the 64 channel EGMs. Unlike control animals we observed significantly different DFs in the ECG in chronic AF animals (mean STD = 2.65 ± 0.98 Hz), which is significantly different from control group (p -value = 0.008). The DFs for each of the three surface ECG lead for all the chronic AF animals is described in Table 2.

Discussion

There were two major findings in this study. First, atrial tachyarrhythmia, AT or AFL in control animals can present with ECG findings of AF. Secondly, spectral analysis on multiple ECG leads (minimum of 3 leads) can reliably differentiate between AF and AT/AFL. This study was unique in that the diagnosis was determined by invasive EP study in a large group of animal models by doing a detailed recording.

Animal models play an important role in investigating mechanisms of cardiac arrhythmias. AF animal models have been used since late 1800s, to understand AF, the underlying mechanisms and test treatment strategies [9]. The result from AF animal models are being

incorporated into clinical studies and therapeutic methods [10,11]. Thus, the accuracy and reliability of the results can have a significant impact in AF treatment strategies and outcomes. Numerous AF animal studies done with the goal of identifying the underlying mechanism have involved control animals [8,12]. Here we show that these inductions could have been AT or AFL and not necessarily AF even though the surface ECG might appear to be AF. Hence, the conclusions drawn from these studies might show a more simplistic mechanism underlying AF. We recognize the small sample size of our study with 10 animals in the control group and the 5 in the AF group. Despite the small size the DF variation was statistically significant indicating the robustness of our findings.

Observing atrial activity on surface ECG is dependent on the lead axis and given the lack of standard leads for animals identifying atrial activity on one or two leads might be challenging. The diagnosis between AF and AT/AFL is also dependent on RR interval variability, which partly relies on AV node conduction. Since, AV node is innervated, the activation rate of AV node can be influenced by sympathetic/vagal balance, which can create RR variability and create a variable RR interval giving a false impression of AF.

Spectral analysis is much more reliable compared to temporal analysis. DF is well known method in analyzing the electrograms in AF [13]. We showed that DF can extract information related to atrial activation from surface ECG signals, where DF, found on surface ECG was in agreement with DF that was calculated in intracardiac electrograms and can be very useful in correctly identifying the underlying atrial arrhythmia. The surface ECG power spectrum analysis in AF showed a much broader frequency spectrum (Fig. 2D) than that associated with AFL (Fig. 2A and F). When doing such analysis one has to be aware of harmonics associated with ventricular activity as it can result in peaks at higher frequency. When looking at ECG in AF there was a much broader power spectrum and no one distinct peak arguing against it being just ventricular harmonics. When analyzing the ECG in AFL or AT the peak was much narrower but given that the ventricular activity is tightly coupled to atrial activity this is to be expected. Despite this tight coupling just looking at the surface ECG might not be enough in making the correct rhythm determination as shown in Fig. 1A where there is significant ventricular beat to beat variability and the DF analysis can be very useful.

In some of the AF animal ECG analysis the DFs were the same in two of the three ECG leads in our study. This was likely because those leads were placed quite close to each other. Hence, it is important to compare the DF seen in all the ECG leads, specially, those that are not placed very close to each other.

Conclusion

AFL or AT can appear with characteristics of AF on surface ECG. The intra-cardiac mapping can accurately identify the underlying mechanism albeit at the expense of being invasive. However, we show that spectral analysis on multiple ECG leads can differentiate between AF and AFL. We show that dominant frequency was consistent on all ECG leads in AFL and AT while it varied in AF.

Acknowledgments

Funding sources

This work was supported by 1R56HL128674 (RR).

References

- [1]. Psaty BM, et al. Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997;96(7):2455–61. [PubMed: 9337224]
- [2]. Krummen DE, et al. Accurate ECG diagnosis of atrial tachyarrhythmias using quantitative analysis: a prospective diagnostic and cost-effectiveness study. *J Cardiovasc Electrophysiol* 2010;21(11):1251–9. [PubMed: 20522152]
- [3]. Krummen DE, Feld GK, Narayan SM. Diagnostic accuracy of irregularly irregular RR intervals in separating atrial fibrillation from atrial flutter. *Am J Cardiol* 2006;98 (2):209–14. [PubMed: 16828594]
- [4]. Knight BP, et al. Electrocardiographic differentiation of atrial flutter from atrial fibrillation by physicians. *J Electrocardiol* 1999;32(4):315–9. [PubMed: 10549907]
- [5]. Andrade J, et al. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. *Circ Res* 2014; 114(9):1453–68. [PubMed: 24763464]
- [6]. Nakashima H, et al. Angiotensin II antagonist prevents electrical remodeling in atrial fibrillation. *Circulation* 2000;101(22):2612–7. [PubMed: 10840013]
- [7]. Morillo CA, et al. Chronic rapid atrial pacing. Structural, functional, and electrophysiological characteristics of a new model of sustained atrial fibrillation. 1995;91(5):1588–95.
- [8]. Wijffels MCEF, et al. Atrial fibrillation begets atrial fibrillation. *Circulation* 1995;92: 1954–68. [PubMed: 7671380]
- [9]. Nattel S, et al. Mechanisms of atrial fibrillation: lessons from animal models. *Prog Cardiovasc Dis* 2005;48(1):9–28. [PubMed: 16194689]
- [10]. Zaman AB, M.A.B.M.B.J et al. Focal impulse and rotor mapping (FIRM): conceptualizing and treating atrial fibrillation. *Journal of Atrial Fibrillation* 2014;7(2):1103. [PubMed: 27957100]
- [11]. Jalife J, Berenfeld O, Mansour M. Mother rotors and fibrillatory conduction: a mechanism of atrial fibrillation. *Cardiovasc Res* 2002;54(2):204–16. [PubMed: 12062327]
- [12]. Mazgalev T, et al. Atrioventricular nodal conduction during atrial fibrillation in rabbit heart. *Am J Physiol Heart Circ Physiol* 1982;243(5) (H754-H760).
- [13]. Sanders P, et al. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. *Circulation* 2005;112(6):789–97. [PubMed: 16061740]

Fig. 1.

A) Reentrant atrial flutter is observed on left atrial activation time map that was calculated from constellation electrograms in the left atrium. B) Calculated PSD over the all the electrograms indicates consistent DF assuring the arrhythmia to be atrial flutter.

Fig. 2.

A) The surface ECG in a controlled animal during AFL that more closely resembles AF based on beat-to-beat variability and absence of P or flutter waves. B) Computed PSD of the three lead ECGs of same AFL as in (A) and it shows that the DFs are consistent in all three leads. C) The surface ECG of a chronic AF animal during sustained AF. D) Computed PSD of the three lead ECGs of AF as in (B) and it shows that the DFs are not consistent among the three leads. E) The surface ECG in control animal during AFL that appears to be AFL based on traditional ECG markers like consistent beat to beat interval. F) Computed PSDs of

the three lead ECGs of the same AFL as in (E) and it shows that DFs are consistent in all three leads.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Summary of findings in the control animal group.

Animal number	ECG diagnosis	Mechanism	Total coverage (%)	DF
1	AFL	Reentry	100	7.65
2	AF	Reentry	100	6.38
3	AF	Reentry	NA	7.86
4	AF	AT/Focal	48	8.20
5	AF	Reentry	99	7.41
6	AF	AT/Focal	NA	8.05
7	AFL	Reentry	99	7.02
8	AF	Focal	57	7.04
9	AF	Focal	NA	9.50
10	AF	Reentry	100	8.01

ECG Diagnosis: The diagnosis of the rhythm by >80% of the blinded observers. Mechanism: Identified mechanism based on activation/propagation map computed over the 64 channel Constellation EGM recording.

Total Coverage: The percent of the total arrhythmia cycle length that was covered by all the activations seen in the recordings.

DF: Frequency that has the highest power on PSD function. This was the same for all the surface ECG and all the basket/baskets EGMs in the Control animals (STD at each electrode was <0.001).

The coverage was not available (NA) for the animal models, where we recorded only in one chamber.

Table 2

Summary of findings in the chronic AF animal group.

Animal number	EGM mean DF (Hz)	Lead 1 DF (Hz)	Lead 2 DF (Hz)	Lead 3 DF (Hz)
1	8.41±	3.61	8.43	6.33
2	6.81±	1.46	5.69	13.75
3	7.43±	1.83	8.6	4.02
4	10.42±	3.68	10.89	5.64
5	9.41±	3.61	10.34	10.35

EGM Mean DF: Average of DFs for all basket/baskets EGMs.

Lead 1 DF (Hz): DF calculated for lead 1 ECG.

Lead 2 DF (Hz): DF calculated for lead 2 ECG.

Lead 3 DF (Hz): DF calculated for lead 3 ECG.