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Bayesian network analyses in atrial fibrillation – A path to better therapies?☆

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ABSTRACT

Despite several major innovations in atrial fibrillation (AF) management, including the improved detection of AF and advances in catheter-ablation-based rhythm control, AF remains a major health-care burden. Recent advances have enabled curation of increasingly large data sets, which, together with improvements in AF detection through screening and continuous rhythm monitoring, enable novel 'big data' approaches to better predict and classify AF. In this issue of the *International Journal of Cardiology Heart & Vasculature*, Drs. Ebana and Furakawa describe an approach to shed light on potential causal links between several risk factors and atrial arrhythmias from the superior vena cava using a Bayesian network analysis. This approach may be a relevant step from statistical association towards identification of causative mechanisms and together with experimental work and mechanistic computer models may help to establish tailored mechanism-based therapies for AF.

The management of atrial fibrillation (AF) requires an integrative approach involving treatment of concomitant cardiovascular diseases, prevention of AF-associated stroke and heart failure through anticoagulation and rate control, as well as restoration/maintenance of normal sinus rhythm ('rhythm control') for symptomatic treatment [1,2]. Despite several major innovations in AF management, including the improved detection of AF and advances in catheter-ablation-based rhythm control, AF remains a major health-care burden, negatively affecting morbidity and mortality in millions of patients [1]. Available rhythm-control therapies have suboptimal efficacy and current antiarrhythmic drugs are associated with an increased risk of malignant ventricular arrhythmias [3]. The limitations of current AF therapies have at least in part been attributed to a one-size-fits-most approach that ignores the diversity of underlying mechanisms that may predispose to AF [3,4]. Accumulating evidence suggest that AF should be considered a symptom of an atrial cardiomyopathy resulting from a wide range of risk factors, including genetic predisposition, advancing age, as well as systemic and cardiovascular diseases [5], which are modulated by modifiable lifestyle factors including exercise and alcohol intake [6]. Nonetheless, AF is usually only classified as paroxysmal or persistent based on the duration of AF episodes. This classification does not inform about underlying mechanisms. For example, although ectopic (triggered) activity-promoting atrial calcium-handling abnormalities are a common finding in patients with paroxysmal AF, long-standing persistent AF, and patients with heart failure who are at an increased risk of developing AF, the underlying molecular mechanisms are distinct [4,7], strongly suggesting a need for tailored mechanism-based therapy for optimal AF management [4].

Recent advances have enabled curation of increasingly large data sets, which, together with improvements in AF detection through screening and continuous rhythm monitoring, enable novel 'big data' approaches to better predict and classify AF. For example, recent studies have employed logistic regression and machine-learning approaches to show that ECG characteristics of atrial premature complexes [8] and a combination of clinical risk factors (age, sex, and BMI) and biomarkers (elevated BNP and FGF-23) [9] help to identify patients developing AF. In this issue of *International Journal of Cardiology Heart & Vasculature*, Drs. Ebana and Furakawa describe another approach to shed light on potential causal links between several risk factors and atrial arrhythmias from the superior vena cava (SVC) [10]. The authors employed a Bayesian network analysis, which produces a directed graph representing probabilistic causal relationships between clinical characteristics on a combined data set of 2170 patients undergoing AF ablation to provide information on the type of AF (factors potentially contributing to SVC-dependent arrhythmogenesis) and on the consequences of treatment (recurrence of AF after catheter ablation). In particular, the study

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implicates gender, body-mass index and a previously identified genetic risk score as contributing factors to SVC arrhythmogenesis [10]. Although this work can never fully establish causality and has several additional limitations, including limited clinical input variables, lack of mechanistic parameters, and heterogeneity between cohorts demanding careful validation in additional data sets, it may nonetheless represent an interesting first step from statistical association towards identification of causative mechanisms. Indeed, together with experimental work and mechanistic computer models, which are highly suitable for cause-and-effect studies [11], such data-driven approaches may then help to establish tailored mechanism-based therapies for AF.

Taken together, it appears likely that we will be seeing increasingly sophisticated approaches to analyze large clinical data sets, providing new strategies to classify AF patients and potentially identify tailored therapies for individual subgroups of AF patients. The final 'proof of the pudding' will have to come from future randomized clinical trials evaluating whether these tailored approaches can indeed improve outcomes in AF patients compared to the current one-size-fits-most strategy.

Conflict of interest

None (both authors).

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References

[1] P. Kirchhof, S. Benussi, D. Kotecha, A. Ahlsson, D. Atar, B. Casadei, et al., ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS, Eur. Heart J. 37 (2016) (2016) 2893–2962.
[2] T.Y. Chang, J.N. Liao, T.F. Chao, J.J. Vicera, C.Y. Lin, T.C. Tuan, et al., Oral anticoagulant use for stroke prevention in atrial fibrillation patients with difficult scenarios, Int. J. Cardiol. Heart Vasc. 20 (2018) 56–62.
[3] G.A. Dan, D. Dobrev, Antiarrhythmic drugs for atrial fibrillation: imminent impulses are emerging, Int. J. Cardiol. Heart Vasc. 21 (2018) 11–15.
[4] J. Heijman, J.B. Guichard, D. Dobrev, S. Nattel, Translational challenges in atrial fibrillation, Circ. Res. 122 (2018) 752–773.
[5] A. Goette, J.M. Kalman, L. Aguinaga, J. Akar, J.A. Cabrera, S.A. Chen, et al., EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication, Heart Rhythm. 14 (2017) e3–e40.
[6] H. Ayinde, M.L. Schweizer, V. Crabb, A. Ayinde, A. Abugroun, J. Hopson, Age modifies the risk of atrial fibrillation among athletes: a systematic literature review and meta-analysis, Int. J. Cardiol. Heart Vasc. 18 (2018) 25–29.
[7] C.E. Molina, I.H. Abu-Taha, Q. Wang, E. Rosello-Diez, M. Kamler, S. Nattel, et al., Profibrotic, electrical, and calcium-handling remodeling of the atria in heart failure patients with and without atrial fibrillation, Front. Physiol. 9 (2018) 1383.
[8] S.I. Im, D.H. Park, B.J. Kim, K.I. Cho, H.S. Kim, J.H. Heo, Clinical and electrocardiographic characteristics for prediction of new-onset atrial fibrillation in asymptomatic patients with atrial premature complexes, Int. J. Cardiol. Heart Vasc. 19 (2018) 70–74.
[9] W. Chua, Y. Purmah, V.R. Cardoso, G.V. Gkoutos, S.P. Tull, G. Neculau, et al., Data-driven discovery and validation of circulating blood-based biomarkers associated with prevalent atrial fibrillation, Eur. Heart J. (2019)https://doi.org/10.1093/eurheartj/ehy815 in press.
[10] Y. Ebana, T. Furukawa, Networking analysis on superior vena cava arrhythmogenicity in atrial fibrillation, Int. J. Cardiol. Heart Vasc. 22 (2019) 150–153.
[11] E. Grandi, D. Dobrev, J. Heijman, Computational modeling: what does it tell us about atrial fibrillation therapy? Int. J. Cardiol. (2019)https://doi.org/10.1016/j.ijcard.2019.01.077 (In press).