



## Original Article

## Report of periprocedural oral anticoagulants in catheter ablation for atrial fibrillation: The Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF)

Yuji Murakawa, MD<sup>a,\*</sup>, Akihiko Nogami, MD<sup>b</sup>, Morio Shoda, MD<sup>c</sup>, Koichi Inoue, MD<sup>d</sup>, Shigeto Naito, MD<sup>e</sup>, Koichiro Kumagai, MD<sup>f</sup>, Yasushi Miyauchi, MD<sup>g</sup>, Teiichi Yamane, MD<sup>h</sup>, Norishige Morita, MD<sup>i</sup>, Hideo Mitamura, MD<sup>j</sup>, Ken Okumura, MD<sup>k</sup>, Kenzo Hirao, MD<sup>l</sup>, on behalf of the Japanese Heart Rhythm Society Members

<sup>a</sup> Fourth Department of Internal Medicine, Teikyo University, School of Medicine, 3-8-3 Mizonokuchi, Takatsu-ku, Kawasaki, Kanagawa 213-8507, Japan

<sup>b</sup> Cardiovascular Division, Faculty of Medicine, University of Tsukuba, Japan

<sup>c</sup> Department of Cardiology, Tokyo Women's Medical University, Japan

<sup>d</sup> Cardiovascular Center, Sakurabashi Watanabe Hospital, Japan

<sup>e</sup> Division of Cardiology, Gunma Prefectural Cardiovascular Center, Japan

<sup>f</sup> Heart Rhythm Center, Fukuoka Sanno Hospital, Japan

<sup>g</sup> Division of Cardiology, Nippon Medical School, Japan

<sup>h</sup> The Department of Cardiology, The Jikei University School of Medicine, Japan

<sup>i</sup> Division of Cardiology, Tokai University Hachioji Hospital, Japan

<sup>j</sup> Division of Cardiology, Tachikawa Hospital, Japan

<sup>k</sup> Division of Cardiology, Saiseikai Kumamoto Hospital, Japan

<sup>l</sup> Heart Rhythm Center, Tokyo Medical and Dental University, Japan

## ARTICLE INFO

## Article history:

Received 23 August 2016

Received in revised form

26 September 2016

Accepted 2 October 2016

Available online 27 October 2016

## Keywords:

Atrial fibrillation

Catheter ablation

Warfarin

Direct oral anticoagulant

## ABSTRACT

**Background:** To obtain a perspective of the current status of catheter ablation for the cure of atrial fibrillation, the Japanese Heart Rhythm Society conducted a nationwide survey: the Japanese Catheter Ablation Registry of Atrial Fibrillation. In this report, we aimed to evaluate the periprocedural use of direct oral anticoagulants with respect to thromboembolic or bleeding complications.

**Methods:** Using an online questionnaire, the Japanese Heart Rhythm Society requested electrophysiology centers in Japan to register the relevant data of patients who underwent atrial fibrillation ablation over selected five-months from 2011 to 2014. We compared the clinical profiles and the ablation data, including the incidence of pericardial effusion, major bleeding, and ischemic stroke among patients with periprocedural use of warfarin or a direct oral anticoagulant.

**Results:** A total of 204 institutions reported data on 6200 atrial fibrillation ablation sessions. We analyzed data obtained from 4698 subjects (Age  $63.2 \pm 10.6$  yr; 73.9% male, 26.1% female) who were administered warfarin or a direct oral anticoagulant, at least up to the day before atrial fibrillation ablation. Warfarin was administered to 54.7% of patients. Dabigatran, rivaroxaban, and apixaban were used in 21.9%, 12.9%, and 10.6% of patients, respectively. Clinical profiles of apixaban-treated patients were similar to those of warfarin-treated patients; they were different from the clinical profiles of patients treated with dabigatran or rivaroxaban. There were 104 complications in 103 subjects (2.2%). Complications were more frequent in older patients ( $65.3 \pm 8.6$  yr vs.  $63.1 \pm 10.7$  yr;  $P=0.012$ ), patients on chronic hemodialysis (4.9% vs. 1.1%;  $P=0.001$ ), or those treated with warfarin (66.0% vs. 54.4%;  $P=0.019$ ). Multiple logistic regression analysis revealed that age (OR, 1.02; 95% CI: 1.00–1.04;  $P=0.035$ ), chronic hemodialysis (OR, 4.40; CI: 1.68–11.50;  $P=0.003$ ), and assistance by 3-D mapping system (OR, 0.30; CI: 0.16–0.57;

\* Corresponding author.

E-mail address: [murakawa@med.teikyo-u.ac.jp](mailto:murakawa@med.teikyo-u.ac.jp) (Y. Murakawa).

$P < 0.001$ ) were significantly related to the incidence of complications, while periprocedural direct oral anticoagulant was not a predictive factor for complication.

**Conclusions:** Compared with uninterrupted warfarin, the choice of a direct oral anticoagulant as a periprocedural oral anticoagulant did not significantly change the incidence of serious complications.

© 2016 Japanese Heart Rhythm Society. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Technological and technical innovations of catheter ablation for various arrhythmias are continuously being introduced into practice. Tenacious effort is required to ensure that in each country this treatment is performed in accordance with the international standards [1]. The Japanese Heart Rhythm Society (JHRS) conducted annual nationwide registries of patients who underwent catheter ablation for atrial fibrillation (AF): the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF) [2–4].

Currently, uninterrupted warfarin therapy is considered superior to interrupted anticoagulation strategy with respect to thromboembolic and bleeding complications [5–8]. Moreover, some studies, including our previous report [2], have evaluated the safety and efficacy of direct oral anticoagulants (DOAC) in the management of AF ablation [9–18]. However, the number of subjects analyzed in earlier studies is rather small. In this report, we compared the clinical features and incidence of bleeding complication and ischemic stroke during, and immediately after AF ablation among patients receiving periprocedural treatment with warfarin or a DOAC. The aim of this study was to elucidate the current status of the use of DOAC as a periprocedural anticoagulant during AF ablation in Japan, and to evaluate the periprocedural use of a DOAC with respect to thromboembolic or bleeding complications.

## 2. Material and methods

The method of this survey has previously been reported [3,4]. In short, the survey was performed retrospectively using an online questionnaire. The JHRS members were notified by e-mail. Data on patient backgrounds, methods of pulmonary vein isolation and related techniques, complications, as well as the periprocedural pharmacological treatments were collected for AF ablation sessions performed in September 2011, May 2012, September 2012, September 2013, and September 2014. Patient data included age, sex, previous AF ablation, AF type (paroxysmal, PAF; persistent, or long-standing, LS; persistent), thromboembolism risk factors, and echocardiographic parameters. When one of the oral anticoagulants (OACs) was intentionally continued at least up to the day before the AF ablation, they were considered to have been used periprocedural. The OAC administered on the day of AF ablation was not included in the data.

Although some patients had not received any periprocedural OAC, the reasons for this were beyond the scope of the survey, and the details of anticoagulant management might have widely varied in these patients. Moreover, the definition of periprocedural OAC was not precisely defined in the early stages of the survey; thus, some patients who were actually administered an OAC until the day before AF ablation, but not on the day of the procedure might have been inadvertently categorized as patients without periprocedural OAC. Therefore, in this report, only the data of subjects who were recorded as having received warfarin or a DOAC were analyzed.

Major bleeding complications included pericardial effusion (PE) that needed pericardiocentesis or surgery, hemothorax, retroperitoneal hematoma, and massive bleeding at the puncture site. Stroke was evaluated based on clinical parameters. Silent brain infarctions on magnetic resonance imaging, or transient ischemic attacks were not included. Centers with  $\geq 10$  procedures per month were defined as high-volume centers, and centers with  $\leq 9$  procedures per month were defined as low-volume centers.

The continuous variables with a normal distribution were expressed as the mean  $\pm$  SD. Comparison of continuous variables between two groups was done using unpaired Student's *t*-test. Comparisons of variables among the four study groups were performed using one-way analysis of variance with post-hoc Bonferroni test. Categorical variables were compared using Tukey's test. A multiple logistic regression analysis was performed for variables with univariate *P* value  $< 0.1$ , to detect the independent determinants for the occurrence of complications. A  $P < 0.05$  was considered statistically significant.

## 3. Results

### 3.1. General observations

Two-hundred-and-four institutions reported the data of 6200 AF ablation sessions. Among them, 1502 patients were registered as not having received periprocedural OAC treatment. We analyzed the data of the remaining 4698 subjects (age  $63.2 \pm 10.6$  yr; 73.9% male, 26.1% female) who were administered warfarin or a DOAC up to the day before AF ablation.

In the population, there were 77.9% first AF ablation sessions, 64.2% ( $n = 3017$ ) patients with PAF, 22.2% ( $n = 1043$ ) patients with persistent AF, and 13.6% ( $n = 638$ ) patients with LS-persistent AF.

### 3.2. Periprocedural anticoagulant strategies

As a periprocedural OAC, warfarin was administered to 54.7% of patients (2568). Dabigatran and rivaroxaban were used in 21.9% of patients (1027) and 12.9% of patients (606), respectively. The remaining 10.6% patients (497) were treated with apixaban. A total of 45.3% of patients (2130) were taking a DOAC at least up to the day before AF ablation.

### 3.3. Comparison of patient profiles

As shown in Table 1, the percentage of PAF in patients treated with warfarin (60.7%) is significantly smaller than those treated with dabigatran (66.8%;  $P < 0.01$ ) or rivaroxaban (72.6%;  $P < 0.01$ ). Lone AF was less frequent in patients with uninterrupted warfarin (20.0%) or apixaban (17.9%), than in those treated with dabigatran (25.7%) or rivaroxaban (25.6%). The CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were relatively high in patients treated with warfarin and apixaban. Thus, the clinical profiles of apixaban-treated patients were similar to those of warfarin-treated patients, but were not to those of patients treated with either of dabigatran or rivaroxaban.

**Table 1**  
Comparison of clinical and procedural profiles among four patient groups.

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	P value					
					W vs. D	W vs. R	W vs. A	D vs. R	D vs. A	R vs. A
Number of patients:	2568 (54.7%)	1027 (21.9%)	606 (12.9%)	497 (10.6%)						
Age (yrs)	61.2 ± 10.6	63.8 ± 10.3	62.7 ± 11.2	64.6 ± 10.9	**			*	**	*
Male	75.2%	76.0%	71.5%	66.4%			**		**	
First session	75.5%	78.9%	81.6%	84.1%		**	**			
PAF	60.7%	66.8%	72.6%	66.6%	**	**		*		
Lone AF	20.0%	25.7%	25.6%	17.9%	**	*			**	**
CHADS <sub>2</sub> score	1.16 ± 1.07	0.92 ± 0.98	0.86 ± 0.92	1.05 ± 1.07	**	**				*
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	1.95 ± 1.48	1.59 ± 1.35	1.64 ± 1.32	1.98 ± 1.49	**	**			**	**
LVEF (%)	62.6 ± 10.4	64.4 ± 8.8	64.6 ± 9.2	63.5 ± 9.4	**	**	*			
LAD (mm)	40.9 ± 6.6	40.3 ± 6.5	39.2 ± 7.0	39.8 ± 7.1	**	**	**			
Procedure time (hrs)	3.5 ± 1.2	3.3 ± 1.2	3.5 ± 1.2	3.5 ± 1.2						
Hemodialysis	2.2%	0.0%	0.0%	0.0%	**	**	**			
Deep sedation	50.4%	42.3%	55.6%	47.5%	**			**		**

LVEF: left ventricular ejection fraction, LAD: left atrial diameter, LAD: left atrial diameter, W: warfarin, D: dabigatran, R: rivaroxaban, A: apixaban.

\*  $P < 0.05$ ,

\*\*  $P < 0.01$ .

**Table 2**  
Periprocedural oral anticoagulation, complications, and clinical and procedural profiles.

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Total
Number of patients	2568 (54.7%)	1027 (21.9%)	606 (12.9%)	497 (10.6%)	4698
PE+bleeding+stroke (pts.)	68 (2.6%)	15 (1.5%)	14 (2.3%)	6 (1.2%)	103 (2.2%)
Pericardial effusion (PE)	39 (1.5%)	5 (0.5%)*	5 (0.8%)	2 (0.4%)	51 (1.1%)
Bleeding	29 (1.1%)	9 (0.9%)	8 (1.3%)	4 (0.8%)	40 (0.8%)
Stroke	1 (0.0%)	1 (0.1%)	1 (0.2%)	0	3 (0.1%)

Both PE and bleeding event occurred in one patient treated with warfarin.

\*  $P < 0.05$  vs. warfarin.

**Table 3**  
Clinical profiles, procedures of AF ablation, and periprocedural OAC.

	PE + bleeding + stroke		P value
	+	(-)	
n	103	4595	
Age (yr)	65.3 ± 8.6	63.1 ± 10.7	0.012
Gender (male)	71.8%	74.0%	0.616
First session	83.5%	77.8%	0.616
PAF	63.1%	64.2%	0.812
Lone AF	21.4%	21.8%	0.922
Low-volume center	39.8%	35.8%	0.404
CHADS <sub>2</sub> score	1.11 ± 1.08	1.06 ± 1.04	0.637
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	1.99 ± 1.49	1.83 ± 1.44	0.271
LVEF (%)	63.9 ± 9.3	63.3 ± 9.8	0.500
LAD (mm)	40.7 ± 6.4	40.4 ± 6.7	0.683
Chronic hemodialysis	4.9%	1.1%	0.001
Deep anesthesia	57.3%	48.8%	0.089
3-D mapping	81.6%	93.6%	< 0.001
Irrigation catheter	75.7%	82.7%	0.064
Cryoballoon	1.0%	2.5%	0.327
CFAE ablation	12.6%	10.5%	0.491
LA linear ablation	21.4%	24.6%	0.448
Warfarin	66.0%	54.4%	0.019
Dabigatran	14.6%	22.0%	0.070
Rivaroxaban	13.6%	12.9%	0.832
Apixaban	5.8%	10.7%	0.113

PE: pericardial effusion, AF: atrial fibrillation, PAF: paroxysmal atrial fibrillation, LVEF: left ventricular ejection fraction, LAD: left atrial diameter, LA: left atrium, CFAE: complex fractionated atrial electrogram

### 3.4. Complications

A total of 104 complications occurred in 2.2% of patients (103). The incidences of PE, major bleeding, and stroke are shown in

**Table 2.** In one patient treated with periprocedural apixaban, PE required surgical repair, while pericardiocentesis was performed in 50 patients. Hemothorax, retroperitoneal hematoma, and massive bleeding at the puncture site were seen in one, three, and 46 patients, respectively. Ischemic stroke was diagnosed in three patients. Both PE and hemothorax occurred in one patient treated with warfarin. The clinical profiles, procedures of AF ablation, and the choices of periprocedural OACs were compared among patients, with or without complications (**Table 3**). Complications were more frequent in older patients (65.3 ± 8.6 yr vs. 63.1 ± 10.7 yr;  $P = 0.012$ ), patients on chronic hemodialysis (4.9% vs. 1.1%;  $P = 0.001$ ), or those treated with warfarin (66.0% vs. 54.4%;  $P = 0.019$ ). Furthermore, 3-D mapping systems were used more frequently in patients without complications (81.6% vs. 93.6%;  $P < 0.001$ ). In the high-volume and low-volume centers, complications occurred in 1.7% and 2.6% of procedures, respectively ( $P = 0.434$ ).

**Table 4** shows the results of the multiple logistic regression analysis. Age, chronic hemodialysis, and lack of assistance of the 3-D mapping system were significantly related to complications, while the choice of periprocedural OAC was not significantly associated with the incidence of complications.

## 4. Discussion

### 4.1. Major findings

The major findings of the present study are as follows: (1) DOACs are used in 50% of patients who underwent AF ablation with a periprocedural OAC; (2) clinical profiles of apixaban-treated patients are similar to those of warfarin-treated patients, but not

**Table 4**  
Results of multiple logistic regression analysis.

	Odds ratio	95% CI	P value
Age (yr)	1.02	1.00–1.04	0.035
Chronic hemodialysis	4.40	1.68–11.50	0.003
Deep anesthesia	1.29	0.86–1.92	0.220
3-D mapping	0.30	0.16–0.57	< 0.001
Irrigation catheter	1.07	0.61–1.89	0.808
Warfarin	1.34	0.80–2.23	0.263
Dabigatran	0.90	0.45–1.77	0.751

95% CI: 95% confidence interval

to those treated with either of the other two DOACs; and (3) periprocedural use of a DOAC did not significantly affect the incidence of major complications.

#### 4.2. Earlier studies

The meta-analysis suggests that patients treated with rivaroxaban have a similar incidence of thromboembolic events and major bleeding compared with warfarin [17]. The rate of serious complications in patients on apixaban undergoing AF ablation is low, and similar to that seen in patients treated with uninterrupted warfarin [18]. One study has reported that dabigatran increases the risk of bleeding and ischemic stroke [14]. However, several other studies have concluded that dabigatran may safely be substituted for warfarin [2,9–11,13,15]. Although there are several articles that report an increase or decrease in adverse events with periprocedural DOACs, most studies find no remarkable differences in bleeding and thrombotic events between warfarin and DOACs [19].

#### 4.3. Interpretation of the present results

In the present study, the overall incidence of PE, major bleeding, and stroke does not show significant difference among the DOAC or warfarin treated patients. Pericardial effusion occurs infrequently among patients treated with dabigatran, than in patients treated with warfarin. Some differences in the clinical profiles among patients treated with warfarin and those treated with three DOACs suggest that warfarin and apixaban have been used in patients with frailer or clinically complicated profiles. Considering the diverse clinical features among DOAC treated patients, the choice of specific DOACs seems to have been made individually, on the basis of presumed merits and demerits of each anticoagulant to a certain extent. Moreover, none of the DOACs drastically increased or decreased the number of serious complications assessed in our present study.

#### 4.4. Limitations

In this study, the data of patients were collected from a large number of centers. Thus, we assume that our observations may offer a perspective of periprocedural anticoagulant management during AF ablation. The risk of early complications is related to many factors, such as underlying heart diseases, and the procedures used for ablation [3]. Because of significant variations in clinical features among different DOACs, it may be possible that the present results fail to elucidate the advantages or disadvantages of each DOAC. Diagnosis of the complications was entirely entrusted to individual physicians. Special care must be taken to interpret the present results that might have been biased by the limitations inherent to observational studies. Finally, because details of the dosage regimen of OACs, and of heparin usage in individual patients were not included in this survey, it is

not possible to identify the most suitable anticoagulant management of AF ablation from the results.

## 5. Conclusions

DOACs are widely used in Japan as safe substitutes for warfarin, without significant increase in ischemic stroke and bleeding complications. Warfarin and apixaban are used in patients with frail or complicated profiles. Choice of any DOAC as a periprocedural OAC does not significantly affect the incidence of serious complications.

## Conflict of interest

All authors declare no conflict of interest related to this study.

## Acknowledgement

This survey was conducted with the voluntary support of the JHRS members.

## References

- [1] Da Costa A. Catheter ablation procedures: role of nation-wide registries. *Europace* 2009;11:133–4. <http://dx.doi.org/10.1093/europace/eun354>.
- [2] Murakawa Y, Nogami A, Shoda M, et al. Nationwide survey of catheter ablation for atrial fibrillation: the Japanese catheter ablation registry of atrial fibrillation (J-CARAF)—A report on periprocedural oral anticoagulants. *J Arrhythm* 2015;31:29–32. <http://dx.doi.org/10.1016/j.joa.2014.05.003>.
- [3] Inoue K, Murakawa Y, Nogami A, et al. Clinical and procedural predictors of early complications of ablation for atrial fibrillation: analysis of the national registry data. *Heart Rhythm* 2014;11:2247–53. <http://dx.doi.org/10.1016/j.hrthm.2014.08.021>.
- [4] Murakawa Y, Nogami A, Shoda M, et al. Nationwide survey of catheter ablation for atrial fibrillation: the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF)—report of 1-year follow-up. *Circ J* 2014;78:1091–6 [PMID: 24662400].
- [5] Di Biase L, Burkhardt JD, Mohanty P, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. *Circulation* 2010;121:2550–6. <http://dx.doi.org/10.1161/CIRCULATIONAHA.109.921320>.
- [6] Santangeli P, Di Biase L, Horton R, Burkhardt JD, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications: evidence from a meta-analysis. *Circ Arrhythm Electrophysiol* 2012;5:302–11. <http://dx.doi.org/10.1161/CIRCEP.111.964916>.
- [7] Hakalahti A, Uusimaa P, Ylitalo K, et al. Catheter ablation of atrial fibrillation in patients with therapeutic oral anticoagulation treatment. *Europace* 2011;13:640–5. <http://dx.doi.org/10.1093/europace/eur038>.
- [8] Wazni OM, Beheiry S, Fahmy T, Barrett C, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratio: comparison of strategies of anticoagulation management in the periprocedural period. *Circulation* 2007;116:2531–4. <http://dx.doi.org/10.1161/CIRCULATIONAHA.107.727784>.
- [9] Shurrab M, Morillo CA, Schulman S. Safety and efficacy of dabigatran compared with warfarin for patients undergoing radiofrequency catheter ablation of atrial fibrillation: a meta-analysis. *Can J Cardiol* 2013;29:1203–10. <http://dx.doi.org/10.1016/j.cjca.2013.07.005>.
- [10] Kim JS, She F, Jongnarangsin K, et al. Dabigatran vs. warfarin for radiofrequency catheter ablation of atrial fibrillation. *Heart Rhythm* 2013;10:483–9. <http://dx.doi.org/10.1016/j.hrthm.2012.12.011>.
- [11] Providência R, Albenque JP, Combes S, et al. Safety and efficacy of dabigatran versus warfarin in patients undergoing catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *Heart* 2014;100:324–35. <http://dx.doi.org/10.1136/heartjnl-2013-304386>.
- [12] Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility & safety of uninterrupted rivaroxaban for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. *J Am Coll Cardiol* 2014;63(9):82–8. <http://dx.doi.org/10.1016/j.jacc.2013.11.039>.
- [13] Kaseno K, Naito S, Nakamura K, et al. Efficacy and safety of periprocedural dabigatran in patients undergoing catheter ablation of atrial fibrillation. *Circ J* 2012;76:2337–42 [PMID: 22785434].

- [14] Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility and safety of dabigatran versus warfarin for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. *J Am Coll Cardiol* 2012;59:1168–74. <http://dx.doi.org/10.1016/j.jacc.2011.12.014>.
- [15] Rillig A, Lin T, Plesman J, et al. Apixaban, rivaroxaban, and dabigatran in patients undergoing atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2016;27:147–53. <http://dx.doi.org/10.1111/jce.12856>.
- [16] Potpara TS, Larsen TB, Deharo JC, et al. Oral anticoagulant therapy for stroke prevention in patients with atrial fibrillation undergoing ablation: results from the First European Snapshot Survey on Procedural Routines for Atrial Fibrillation Ablation (ESS-PRAFA). *Europace* 2015;17:986–93. <http://dx.doi.org/10.1093/europace/euv132>.
- [17] Li W, Gao C, Li M, et al. Safety and efficacy of rivaroxaban versus warfarin in patients undergoing catheter ablation of atrial fibrillation: a meta-analysis of observational studies. *Discov Med* 2015;19:193–201 [PMID: 25828523].
- [18] Blandino A, Bianchi F, Biondi-Zoccai G, et al. Apixaban for periprocedural anticoagulation during catheter ablation of atrial fibrillation: a systematic review and meta-analysis of 1691 patients. *J Interv Card Electrophysiol* 2016;46:225–36. <http://dx.doi.org/10.1007/s10840-016-0141-6>.
- [19] Abed HS, Chen V, Kilborn MJ, et al. Periprocedural management of novel oral anticoagulants during atrial fibrillation ablation: controversies and review of the current evidence. *Heart Lung Circ* 2016. <http://dx.doi.org/10.1016/j.hlc.2016.04.027> [Epub ahead of print].