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RESEARCH LETTER

Oral Anticoagulation and Factor VIII Replacement Therapy in Patients With Hemophilia Undergoing Pulsed-Field or Radiofrequency Catheter Ablation for Atrial Fibrillation

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Hemophilia is characterized by reduced or unmeasurable levels of coagulation factor VIII (hemophilia A) or factor IX (hemophilia B).[1] Since the introduction of clotting factor concentrates, the life expectancy of patients with hemophilia has increased to over 70 years making them more likely to be confronted with age-related comorbidities like atrial fibrillation (AF). Anticoagulation is one of the main components of AF management to reduce the risk of AF-related strokes. However, hemophiliacs have a high bleeding tendency making it challenging to find a balance between coagulation and anticoagulation in patients with coexistent hemophilia and AF.[1] According to guidelines and expert opinions, coagulation factor concentrate is given prophylactically to maintain trough factor levels >80% during the periprocedural period and ≥30% during the next 4 to 6 weeks in patients undergoing AF ablation.[1]

Pulsed-field ablation (PFA) has demonstrated tissue selectivity via application of ultra-rapid electrical pulses causing irreversible electroporation and subsequent cellular death. Notably, cardiomyocytes exhibit a lower threshold for irreversible electroporation than other cell types including the endothelial cells that remain unaffected during the procedure.[2] Thus, given the fact that endothelial injury promotes thrombus formation, it is prudent to speculate that in its absence anticoagulation management would be less challenging in patients with AF with hemophilia undergoing PFA.

In this case series, we report our experiences with patients with hemophilia undergoing radiofrequency ablation (RFA) or PFA.

This multicenter study included consecutive patients with hemophilia undergoing AF ablation.

Patients' data were collected from IRB-approved institutional databases and retrospective medical record review. The data that support the findings of this study are available from the corresponding author upon reasonable request.

ABLATION PROCEDURE

All patients received pulmonary vein isolation plus isolation of left atrial posterior wall using either RFA or PFA. The ablation procedures have been described in detail in earlier publications.[3]

COAGULATION MANAGEMENT

Patients received clotting factor replacement to bring the preprocedure level to 60% to 150%. During the

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Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
IQR	interquartile range
PFA	pulsed-field ablation
RFA	radiofrequency ablation

ablation procedure, heparin boluses of 6000 to 12 000 units were given to maintain an ACT of 300 to 500 seconds.

Anticoagulation was continued for at least 45 days following the RFA and 1 week in the PFA group. In addition, patients received factor VIII replacement therapy for 1 week in the PFA group to up to 5 weeks in the RFA group. All patients were monitored for thromboembolic events for 1-year.

This series included 8 patients (no. 6: hemophilia B, others: hemophilia A; age: 61.8±6.978 (median, 62.5; interquartile range [IQR], 68–57) years of which 3 (37.5%) received PFA and 5 subjects underwent RFA for drug-refractory AF. Mean CHA_2DS_2-VASc score were 2.67±1.15 (median, 2; IQR, 4–2) and 2.80±1.48 (median, 3; IQR, 4–1.5) and the HAS-BLED score were 3.33±1.53 (median, 3; IQR, 5–2) and 2.80±1.10 (median, 2; IQR, 4–2) in the PFA and the RFA cohorts, respectively.

Details of pre- and postprocedural factor VIII replacement therapy and anticoagulation are provided in the Table. Preprocedural clotting factor level (PFA, 93.43±47.99% [median, 61; IQR, 161.3–58] versus RFA, 66.44±4.61% [median, 59; IQR, 68.6–56.5]) and the amount of clotting factor administered (PFA, 3323.33±365.56 IU [median, 3250; IQR, 3720–3000] versus RFA, 2096.00±839.48 [median, 1670; IQR, 3000–1405]) were similar in the patients receiving PFA or RFA. Following the procedure, patients with PFA received less clotting factor replacement therapy compared with the RFA group (PFA, 78 866.67±1761.63; median, 79 100; IQR, 80 500–77 000) versus RFA (152 260.00±29 704.51 IU; median, 140 000; IQR, 182950–127700). The duration of the replacement therapy was also lower in the PFA group (6.65±0.229; median, 6; IQR, 7–5) versus (31±3.316; median, 30; IQR, 32–30) days.

No bleeding or thromboembolic events were reported at 1-year follow-up.

Table. Pre- and Postprocedure Oral anticoagulation and Clotting Factor Replacement Therapy

Pre-procedure					Post-procedure					
Patient (type of procedure)	Clotting factor administered (IU)	Administration strategy (dosage)	Clotting factor level (%)	Pre-procedure OAC	Post-procedure OAC	Clotting factor administered (IU)	Administration strategy (dosage)	Clotting factor level (%)		
								24 h	72 h	1 wk
1 (PFA-PVI)	3720	2 doses of 1860 IU–12 h apart	161.30	Apixaban, 5 mg BID	Apixaban, 5 mg BID for 7 d	79 100	5 doses of 1130 units 12 hourly over a week	84	78.9	137
2 (PFA-PVI)	3000	2 doses of 1500 IU–12 h apart	58.00	Apixaban, 5 mg BID	Apixaban, 5 mg BID for 7 d	77 000	5 doses of 1100 units 12 hourly over a week	67	81	128.9
3 (PFA-PVI)	3250	2 doses of 1575 IU–12 h apart	61.00	Apixaban, 5 mg BID	Apixaban, 5 mg BID for 7 d	80 500	5 doses of 1150 units 12 hourly over a week	72	79	130
4 (RFA-PVI)	1250	1 dose of 1250 IU–24 h before the procedure	66.00	Initially warfarin then Apixaban, 5 mg BID	Apixaban, 5 mg BID for 45 d	120 400	2150 units, 12 hourly for 28 d	54.3	156	131.6
5 (RFA-PVI)	1560	1 dose of 1560 IU–24 h before the procedure	71.20	Warfarin, 5 mg daily	Apixaban, 5 mg BID for 45 d	192 500	2750 units, 12 hourly for 35 d	56.9	82.7	100.8
6 (RFA-PVI)	3000	1 dose of 3000 IU–24 h before the procedure	59.00	Enoxaparin, 90 mg BID	No OAC	140 000	One dose of 5000 units followed by 2500 units 12 hourly for 28 d	38.7	54	62.9
7 (RFA-PVI)	1670	1 dose of 1670 IU–24 h before the procedure	56.00	Apixaban, 5 mg BID	Apixaban, 5 mg BID for 45 d	135 000	2250 units, 12 hourly for 30 d	58.5	67	89
8 (RFA-PVI)	3000	1 dose of 3000 IU–24 h before the procedure	57.00	Apixaban, 5 mg BID	Apixaban, 5 mg BID for 45 d	173 400	2550 units, 12 hourly for 34 d	59.1	69	88

BID indicates twice a day; OAC, oral anticoagulation; PFA, pulsed-field ablation; PVI, pulmonary vein isolation; and RFA, radiofrequency ablation.

To the best of our knowledge, this is the first series to report the difference in anticoagulation and clotting factor replacement therapy in patients with AF with hemophilia undergoing PFA or RFA. The current gold-standard treatment for hemophilia is prophylactic factor VIII replacement therapy that requires intravenous (IV) infusion. With a half-life of 10 hours, the IV infusion is essential twice daily to maintain the concentrations of the clotting factor high enough to provide adequate support for coagulation to prevent spontaneous bleeding.[4] The inconvenience of such frequent IV infusions and maintenance of a central venous line for an extended period cannot be overemphasized. Moreover, the burden of frequent IV infusions compromises the quality of life by making active lifestyles challenging.[4] In patients with AF with hemophilia, the type, intensity, and duration of antithrombotic therapy are determined, by the risk of AF-associated ischemic stroke, the bleeding risk, and the need for replacement therapy ensuring a level of coagulation factor that allows for safe antithrombotic treatment.[5] Endothelial injury induced by the thermal effect of RF ablation is known to enhance the risk of thromboembolism whereas PFA is documented to not cause any injury to the vascular endothelium. In this series, following the PFA procedure, the factor VIII replacement therapy and oral anticoagulation could be safely discontinued after 1 week without any bleeding or thromboembolic events during the 1-year follow-up period.

The findings from this case series suggest that in hemophilia patients undergoing AF ablation, it might be possible to safely discontinue factor VIII replacement therapy and oral anticoagulation after a relatively shorter period following PFA compared with radiofrequency ablation. However, larger studies are required to replicate these findings before any major conclusions can be reached.

ARTICLE INFORMATION

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Dr Natale is a consultant for Abbott, Biosense Webster, Biotronik, Boston Scientific and iRhythm. Dr Dello Russo is a consultant for Abbott Medical. Dr Burkhardt is a consultant for Biosense Webster and Stereotaxis. Dr Di Biase is a consultant for Biosense Webster, Boston Scientific, Stereotaxis, and St. Jude Medical and has received speaker honoraria from Medtronic, Atricure, EPiEP, and Biotronik. The other authors report no conflicts.

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