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CLINICAL RESEARCH

Atrial fibrillation

Short-term dabigatran interruption before cardiac rhythm device implantation: multi-centre experience from the RE-LY trial

Vidal Essebag^{1,2*}, Riccardo Proietti^{3,4}, David H. Birnie⁵, Jia Wang⁶, James Douketis⁷, Benoit Coutu⁸, Ratika Parkash⁹, Gregory Y. H. Lip¹⁰, Stefan H. Hohnloser¹¹, Andrew Moriarty¹², Jonas Oldgren¹³, Stuart J. Connolly⁶, Michael Ezekowitz¹⁴, and Jeff S. Healey⁶

¹McGill University Health Center, 1650 Cedar Ave, Room E5-200, Montreal, QC, Canada H3G 1A4; ²Hôpital Sacré-Coeur de Montréal, Montreal, QC, Canada; ³Cardiology Department, Morriston Hospital, Swansea University, Heol Maes Eglwys, Morriston, Swansea SA6 6NL, UK; ⁴Cardiology Department, Luigi Sacco Hospital, Milan, Italy; ⁵University of Ottawa Heart Institute, Ottawa, ON, Canada; ⁶Population Health Research Institute, McMaster University, Hamilton, ON, Canada; ⁷St. Joseph's Healthcare, Department of Medicine, McMaster University, Hamilton, ON, Canada; ⁸Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; ⁹Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; ¹⁰University of Birmingham Institute of Cardiovascular Sciences, City Hospital, Birmingham, UK; ¹¹Klinikum der Johann-Wolfgang-Goethe Universität, Frankfurt, Germany; ¹²Craigavon Area Hospital, Portadown, ARM, Northern Ireland; ¹³Uppsala Clinical Research Center and Department of Medical Sciences, Cardiology, Uppsala University, Uppsala, Sweden; and ¹⁴Thomas Jefferson Medical College and the Heart Center, Wynnewood, PA, USA

Short-term dabigatran interruption before cardiac rhythm device implantation: multi-centre experience from the RE-LY trial

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Aims

Cardiac implantable electronic device (CIED) surgery is commonly performed in patients with atrial fibrillation (AF). The current analysis was undertaken to compare peri-operative anticoagulation management, bleeding, and thrombotic events in AF patients treated with dabigatran vs. warfarin.

Methods and results

This study included 611 patients treated with dabigatran vs. warfarin who underwent CIED surgery during the RE-LY trial. Among 201 warfarin-treated patients, warfarin was interrupted a median of 144 (inter-quartile range, IQR: 120–216) h, and 37 (18.4%) patients underwent heparin bridging. In dabigatran-treated patients (216 on 110 mg bid and 194 on 150 mg bid), the duration of dabigatran interruption was a median of 96 (IQR: 61–158) h. Pocket hematomas occurred in 9 (2.20%) patients on dabigatran and 8 (3.98%) patients on warfarin ($P=0.218$). The occurrence of pocket hematomas was lower with dabigatran compared with warfarin with heparin bridging (RD: -8.62%, 95% CI: -24.15 to -0.51%, $P=0.034$) but not when compared with warfarin with no bridging ($P=0.880$). Ischemic stroke occurred in 2 (0.3%) patients; one in the warfarin group (without bridging) and one in the dabigatran 150 mg bid group ($P=0.735$).

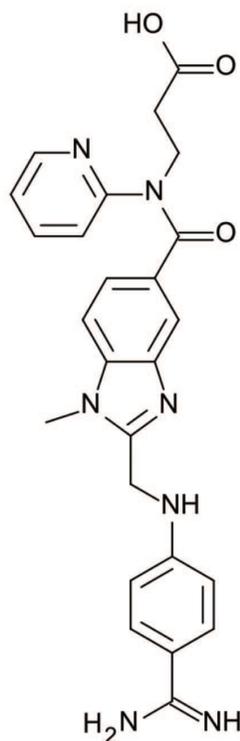
Conclusion

In patients treated with dabigatran undergoing CIED surgery, interruption of dabigatran is associated with similar or lower incidence of pocket hematoma, when compared with warfarin interruption without or with heparin bridging, respectively. Whether uninterrupted dabigatran can reduce pocket hematoma or ischemic stroke remains to be evaluated.



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What's new?

- Data available on patients on Dabigatran therapy undergoing cardiac implantable electronic device (CIED) are scarce and fragmented. In this study, the peri-operative management of Dabigatran is compared with warfarin in a sub-analysis of a large randomized trial (RE-LY).
- In this paper, a strategy of short-term interruption of Dabigatran is compared vs. warfarin with and without interruption. Moreover, data on both formulations (110 and 150 mg) are reported. The outcomes are thoroughly assessed with respect to major and minor bleeding, pocket hematomas, ischemic, and haemorrhagic stroke.
- Since its introduction in the market, Dabigatran has had a widespread use in the clinical practice. As with warfarin, a large proportion of patients on Dabigatran undergo CIED surgery. Determining the optimal strategy for the peri-operative management of Dabigatran has an urgent clinical relevance.

Table 1 Baseline characteristics for patients who had CIED surgery

Characteristics	All patients N = 611	Dabigatran 110 N = 216	Dabigatran 150 N = 194	Warfarin N = 201	P-value
Age(year), mean(SD)	72.6 (8.3)	72.2 (8.4)	72.5 (8.5)	73.1 (7.8)	0.533
BMI(kg/m ²), mean(SD)	29.6 (6.1)	30.1 (7.2)	29.5 (5.3)	29.3 (5.7)	0.372
CrCl(mL/min), median(IQR)	66.0 (51.2–84.9)	67.5 (51.8–85.4)	68.8 (53.1–83.2)	64.4 (49.2–86.4)	0.431
CHADS ₂ , mean(SD)	2.2 (1.0)	2.1 (1.0)	2.3 (1.1)	2.2 (1.1)	0.309
Male, n(%)	419 (68.6)	154 (71.3)	131 (67.5)	134 (66.7)	0.554
Prior VKA, n(%)	349 (57.1)	132 (61.1)	101 (52.1)	116 (57.7)	0.177
CAD, n(%)	244 (39.9)	90 (41.7)	81 (41.8)	73 (36.3)	0.442
PVD, n(%)	39 (6.4)	11 (5.1)	17 (8.8)	11 (5.5)	0.257
Prior stroke, n(%)	54 (8.8)	17 (7.9)	17 (8.8)	20 (10.0)	0.755
Prior history of bleeding on OAC, n(%)	59 (9.7)	21 (9.7)	20 (10.3)	18 (9.0)	0.901
Aspirin, n(%)	270 (44.2)	92 (42.6)	97 (50.0)	81 (40.3)	0.128
Clopidogrel, n(%)	49 (8.0)	11 (5.1)	22 (11.3)	16 (8.0)	0.067

BMI, body mass index; CrCl, creatinine clearance; CAD, coronary artery disease; OAC, oral anticoagulation; PVD, peripheral vascular disease; VKA, vitamin K antagonists.

Table 2 Outcomes within 30 days of CIED surgery in dabigatran vs. warfarin groups

Event	Dabigatran 110 mg		Dabigatran 150 mg		Dabigatran (both doses)		Warfarin		Dabigatran vs. warfarin ^a			
	N	%	N	%	N	%	N	%	RD (%)	95% CI	P	
Bleeding events												
Minor bleeding	7	3.24	7	3.61	14	3.41	10	4.98	-1.56	-5.83 to 1.70	0.408	
Major bleeding	2	0.93	2	1.03	4	0.98	2	1.00	-0.02	-2.77 to 1.73	>0.999	
Fatal bleeding	0	0.00	0	0.00	0	0.00	0	0.00	–	–	–	
Pocket hematoma	5	2.31	4	2.06	9	2.20	8	3.98	-1.78	-5.69 to 1.08	0.218	
Requiring red blood cell transfusion	1	0.46	1	0.52	2	0.49	4	1.99	-1.50	-4.63 to 0.33	0.085	
Thrombotic events												
Cardiovascular death ^b	1	0.46	1	0.52	2	0.49	0	0.00	0.49	-1.50 to 1.82	0.408	
Stroke	0	0.00	1	0.52	1	0.24	1	0.50	-0.25	-2.63 to 1.04	0.735	
Systemic embolism	0	0.00	0	0.00	0	0.00	0	0.00	–	–	–	
Ischemic stroke or systemic embolism	0	0.00	1	0.52	1	0.24	1	0.50	-0.25	-2.63 to 1.04	0.735	
Myocardial infarction	0	0.00	1	0.52	1	0.24	0	0.00	0.24	-1.73 to 1.43	0.599	
Pulmonary embolism	0	0.00	0	0.00	0	0.00	0	0.00	–	–	–	
Cardiovascular death, ischemic stroke, systemic or pulmonary embolism	1	0.46	2	1.03	3	0.73	1	0.50	0.23	-2.15 to 1.77	0.829	

^aRD comparing dabigatran (both doses) vs. warfarin. Separate analyses comparing each group of dabigatran dose (110mg and 150mg) according to treatment allocation vs. warfarin yielded all *P*-values non-significant.

^bCardiovascular deaths included one death due to heart failure and another death post-myocardial infarction.

Table 3 Clinical characteristics of patients with pocket hematoma within 30 days after the first CIED surgery

Patient number	Randomized group	Sex	Age (years)	Creatinine clearance (mL/min)	Last dose prior to procedure (h)	Pre-procedure bridging	Post-procedure bridging	First dose after procedure (h)	Use ASA	Use clopidogrel
1	Dabi 110	Female	72	92	19	Yes: unfractionated heparin	No	4	Yes	No
2	Dabi 110	Male	68	124	61	No	No	71	No	No
3	Dabi 110	Male	70	103	39	No	No	32	No	No
4	Dabi 110	Male	77	65	49	No	No	54	No	No
5	Dabi 110	Male	81	47	–	No	No	45	Yes	No
6	Dabi 150	Female	76	63	43	No	No	24	No	No
7	Dabi 150	Male	67	47	396	No	No	106	No	No
8	Dabi 150	Male	78	56	40	No	No	57	No	No
9	Dabi 150	Male	85	71	40	No	No	7	Yes	No
10	Warfarin	Female	59	50	63	No	Yes: unfractionated heparin	7	No	No
11	Warfarin	Male	54	89	142	No	No	30	Yes	Yes
12	Warfarin	Male	64	110	134	No	No	32	Yes	No
13	Warfarin	Male	70	50	59	Yes: LMWH	Yes: unfractionated heparin	293	No	No
14	Warfarin	Male	73	48	302	Yes: LMWH	Yes: LMWH	170	No	No
15	Warfarin	Male	74	58	158	Yes: LMWH	Yes: LMWH	80	Yes	No
16	Warfarin	Male	78	69	179	No	No	84	No	No
17	Warfarin	Male	79	51	89	No	No	151	Yes	No

LMWH, low molecular weight heparin.

Table 4 Outcomes within 30 days of CIED surgery in dabigatran vs. warfarin groups according to use of heparin bridging

Event	Dabigatran (both doses)		Warfarin with bridging		Warfarin without bridging		Dabigatran vs. Warfarin with bridging			Dabigatran vs. Warfarin w/o bridging		
	N	%	N	%	N	%	RD (%)	95% CI	P	RD (%)	95% CI	P
Bleeding events												
Minor bleeding	14	3.41	4	10.81	6	3.66	-7.40	-22.89 to 0.78	0.040	-0.24	-4.69 to 2.87	0.961
Major bleeding	4	0.98	1	2.70	1	0.61	-1.73	-14.68 to 1.40	0.417	0.37	-2.61 to 2.06	0.756
Fatal bleeding	0	0.00	0	0.00	0	0.00	–	–	–	–	–	–
Pocket hematoma	9	2.20	4	10.81	4	2.44	-8.62	-24.15 to -0.51	0.034	-0.24	-4.20 to 2.33	0.880
Requiring RBC transfusion	2	0.49	2	5.41	2	1.22	-4.92	-18.86 to 0.08	0.034	-0.73	-4.02 to 0.90	0.385
Thrombotic events												
Cardiovascular death	2	0.49	0	0.00	0	0.00	0.49	-10.79 to 2.11	0.938	0.49	-1.96 to 1.85	0.462
Stroke	1	0.24	0	0.00	1	0.61	0.24	-11.06 to 1.80	0.983	-0.37	-3.30 to 0.96	0.562
Systemic embolism	0	0.00	0	0.00	0	0.00	–	–	–	–	–	–
Ischemic stroke or systemic embolism	1	0.24	0	0.00	1	0.61	0.24	-11.06 to 1.80	0.983	-0.37	-3.30 to 0.96	0.562
Myocardial infarction	1	0.24	0	0.00	0	0.00	0.24	-11.06 to 1.80	0.983	0.24	-2.19 to 1.43	0.719
Pulmonary embolism	0	0.00	0	0.00	0	0.00	–	–	–	–	–	–
Cardiovascular death, ischemic stroke, systemic or pulmonary embolism	3	0.73	0	0.00	1	0.61	0.73	-10.53 to 2.56	0.854	0.12	-2.84 to 1.73	0.961



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Conclusion

In patients treated with dabigatran 110 or 150 mg bid undergoing CIED surgery, peri-operative interruption of dabigatran for a median of 4 days is associated with similar or lower incidence of pocket hematoma, when compared with warfarin interruption without or with heparin bridging, respectively. Whether uninterrupted dabigatran can reduce pocket hematoma or ischemic stroke remains to be evaluated.