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Antithrombotic management in patients undergoing cardiac implantable electronic device implantation

Antitrombotično zdravljenje pri bolnikih pred vstavitvijo vsadne elektrostimulacijske naprave srca

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Abstract

Cardiac implantable electronic devices (CIEDs) are an established treatment option for arrhythmias, sudden cardiac death prevention, and heart failure. Approximately 1000 devices are implanted per million inhabitants in European countries each year. However, the main concern in patients with an indication for CIED implantation is frequently associated with comorbidities requiring antithrombotic medications. The invasive device implantation procedure represents a bleeding risk ranging from pocket hematoma to cardiac tamponade. On the other hand, temporary interruption of antithrombotic therapy increases the risk for thromboembolic events. Implanting CIEDs in patients on antithrombotic medications incites several clinical dilemmas of balancing thromboembolic risk against bleeding risk, as complications are associated with higher mortality rates in both aspects. The most common bleeding complication is pocket haematoma formation, which is associated with a prolonged hospital stay, higher cost, higher risk of pocket infection, and thus higher morbidity and mortality. Studies have shown that the heparin bridging strategy in patients on oral anticoagulants imposes a greater risk for pocket haematoma formation and no benefit in reducing thromboembolic events. Most procedures of CIED implantation can be performed safely with uninterrupted oral anticoagulants. Dual antiplatelet therapy increases the risk of pocket haematoma and should be avoided whenever possible.

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Izvleček

Vsadne elektrostimulacijske naprave so pomemben del zdravljenja malignih aritmij, srčnega popuščanja in preprečevanja nenadne srčne smrti. Letno se v evropskem prostoru vstavi približno 1.000 naprav na milijon prebivalcev. Glavna težava pri bolnikih, pri katerih je predvidena vstavitev elektrostimulacijske naprave, so pridružene bolezni, pri katerih je potrebno antitrombotično zdravljenje. Poseg pomeni povečano tveganje za krvavitev, ki se pri vsadnih elektrostimulacijskih napravah pokaže vse od hematoma v področju ležišča naprave do tamponade srca. Drugi del spektra tveganj pa je nevarnost, da nastopi trombembolični dogodek zaradi prehodne prekinitve antitrombotičnega zdravljenja. Antitrombotično zdravljenje v obdobju ob posegu pa pomeni pomembno klinično dilemo pri obravnavi tovrstnih bolnikov. Najpogostejši zaplet je hematom v ležišču naprave, ki terja daljšo hospitalizacijo, višje stroške in večje tveganje za okužbo ležišča, kar vodi do večje obolevnosti in smrtnosti. Prvotno so za preprečevanje morebitnih trombemboličnih dogodkov priporočali premostitev antitrombotične terapije s heparinom, vendar so kasneje raziskave pokazale, da ta strategija prinaša večje tveganje za hematom v ležišču naprave v primerjavi ali z neprekinjenim ali s kratkoročno prekinjenim peroralnim antitrombotičnim zdravljenjem. Hkrati niso opažali pomembne razlike v pojavnosti trombemboličnih dogodkov med obema skupinama bolnikov. Trenutno veljavna priporočila odsvetujejo premostitveno zdravljenje s heparini v obdobju ob posegu. Večino vstavitev vsadnih elektrostimulacijskih naprav lahko varno opravimo ob strategiji neprekinitve prejemanja peroralnega antikoagulacijskga zdravljenja. Dvojna antiagregacijska terapija pa je povezana s povečanim tveganjem za hematom ležišča naprave in se zato odsvetuje v obdobju ob posegu, če je to sploh mogoče.

1 Introduction

Cardiac implantable electronic devices (CIED) are an established treatment option for tachy- and bradyarrhythmia, sudden cardiac death prevention and heart failure. In the past decades, CIED technology and implantation techniques have improved immensely, and approximately 1000 devices are implanted per million inhabitants in European countries each year (1). Notably, patients eligible for the CIED frequently have comorbidities for which they need to take antithrombotic medications. For instance, 23-24% of patients with an indication for a permanent pacemaker (PPM) and 32-37% of those eligible for an implantable cardioverter defibrillator (ICD) require antithrombotic medications (2-4). The main indication for antithrombotic therapy is atrial fibrillation (AF), the most common type of arrhythmia and the major risk factor for thromboembolic complications and death (3,5). Antithrombotic therapy combined with an invasive device implantation procedure represents a bleeding risk ranging from pocket haematoma to cardiac tamponade (3). On the other hand, temporary interruption of antithrombotic therapy increases the risk for thromboembolic events.

This article aims to present the available data and summarise the European Society of Cardiology recommendations on perioperative antithrombotic therapy management in patients undergoing CIED implantation (6).

2 Bleeding and thromboembolic risks in patients undergoing device implantation

Implantation of CIEDs in patients on antithrombotic medications incites several clinical dilemmas of balancing thromboembolic risk on the one hand and bleeding risk on the other, as complications are associated with greater mortality rates in both aspects (3,5,7).

The CIED implantation procedure is considered a low-bleeding-risk procedure. Pocket haematoma is the most common bleeding complication, with an average incidence rate of approximately 4% (8). Clinically relevant pocket haematoma is defined as one being associated with patient discomfort, prolonged hospitalisation time, need for repeated follow-up visits, and surgical revision (Figure 1) (9). Bleeding risk tends to be higher in more complex devices and upgrades than in *de novo* implantations. The incidence of pocket haematoma is approximately 2.5% in patients undergoing ICD implantation, > 3% in case of cardiac resynchronisation therapy-pacemaker (CRT-P) or defibrillator (CRT-D), and 4.2% when upgrading a device to CRT-P or CRT-D (9). Pocket haematoma significantly affects morbidity and mortality, prolongs hospitalisation, and increases costs (8). In the BRUISE CONTROL INFECTION study, clinically significant pocket haematoma was associated with a seven-fold increased risk of device infection within one year after its implantation (10). Other potential bleeding complications in CIEDs implantation procedures are rare. Haemothorax resulting

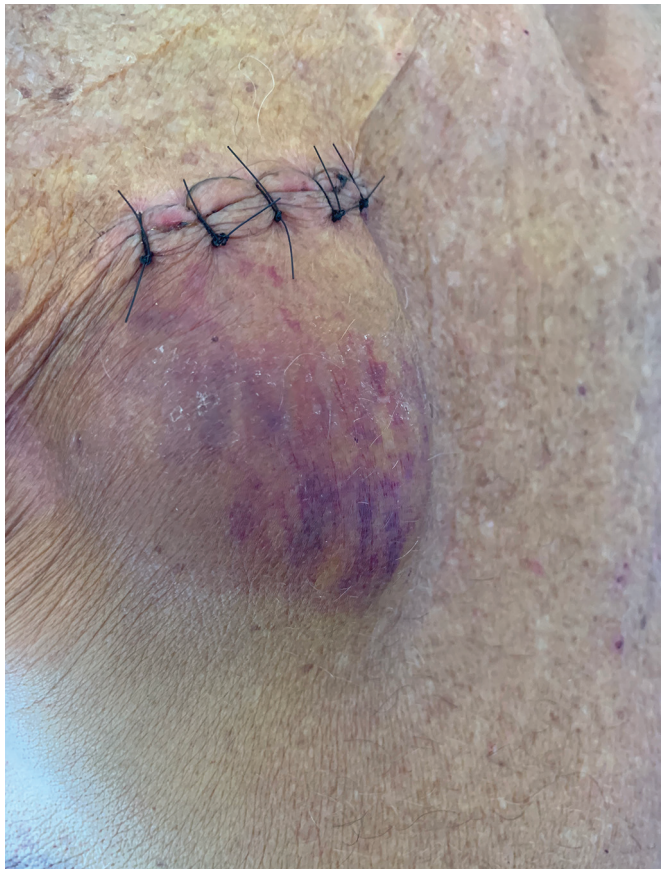

Figure 1: Clinically relevant pocket haematoma is defined as one being associated with patient discomfort, prolonged hospitalisation time, need for repeated follow-up visits, and surgical revision.
Source: personal archive.

from the injury of the vascular access site is anecdotal. Pericardial effusion and cardiac tamponade resulting from lead perforation are reported in 0.3% of cases (8).

The thromboembolic risk depends on the anticoagulation indication and comorbidities (Table 1). Low-risk patients are those with less than a 5% annual risk of a thromboembolic event without anticoagulation, and high-risk patients are those with more than a 10% risk of thromboembolism per year (11,12). Considering this risk estimate, we can calculate a thromboembolic risk of temporary periprocedural discontinuation of an anticoagulant. For example, in a patient with an annual risk of 5% (0.01% daily risk), a five-day withdrawal of anticoagulants before the procedure would translate into a 0,05% periprocedural risk of thromboembolism. However, a study of patients that interrupted warfarin therapy for any reason showed that the risk of thromboembolism is highest in the first 90 days after interruption and subsides thereafter (5). Another observational trial of short interruption of warfarin (<5 days) found a 0.7% risk of TE, which is ten times higher than the calculated risk (7). Data from the Ljubljana registry show a similar increase in TE risk even in the temporary discontinuation of dabigatran and rivaroxaban (13). Thus, it seems likely that the prothrombotic milieu of the postoperative state somewhat increases the thrombotic risk.

The traditional approach to periprocedural anticoagulant management during the vitamin K antagonists (VKA) era was the discontinuation of oral anticoagulants and bridging with standard or low molecular weight heparin (LMWH). Before a patient underwent CIED implantation, VKA was discontinued five days before the planned procedure and bridged with LMWH or continuous intravenous (i.v.) heparin three days before the procedure. The procedure was usually performed when the INR level was less than 1.5 and i.v. heparin was stopped four hours before the procedure or in case LMWH was prescribed 24 hours before the procedure. The rationale was to minimise the risk of thromboembolic events and facilitate optimal haemostasis during the procedure (11,14). Despite several trials that showed increased bleeding risk with this approach, it is still widely adopted in clinical practice. The European snapshot survey on procedural routines for electronic device implantations from 2016 showed that bridging was still used in 20% of patients on VKA and 23% on non-vitamin K antagonist oral anticoagulants (NOAC), while antiplatelet drugs were mainly continued (15).

3 Available data on uninterrupted antithrombotic therapy in patients undergoing device implantation

3.1 Vitamin K antagonists

The BRUISE CONTROL trial randomised 681 device recipients with at least moderate thromboembolic risk into the warfarin continuation group or interruption with the full heparin bridging group. In the heparin bridging group, warfarin was stopped five days before the procedure and three days before the procedure heparin was started. Heparin was held 24 h before the procedure and resumed 24 h afterwards. Warfarin was started 12-24 h after the procedure, and heparin was continued until the INR was in the therapeutic range. The median INR in the warfarin continuation group was 2.3. The safety monitoring board terminated the study prematurely due to a significant difference in the primary outcome (clinically significant pocket

Table 1: Perioperative thromboembolic risk. Adapted from Douketis JD, et al., 2012 and Doherty JU, et al. 2017 (11,12).

Indication for anticoagulant therapy	High thromboembolic risk (> 10% annual risk)	Moderate thromboembolic risk (5-10% annual risk)	Low thromboembolic risk (< 5 % annual risk)
AF	• $CHADS_2$ score 5-6 • CHA_2DS_2-VASc score 7-9 • Recent (within 3 months) stroke or TIA • Rheumatic valvular heart disease	• $CHADS_2$ score 3-4 • CHA_2DS_2-VASc score 5-6	• $CHADS_2$ score 0-2 • CHA_2DS_2-VASc score ≤ 4
Mechanical heart valve	• Any mitral valve prosthesis • Caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 months) stroke or TIA	• Bi-leaflet aortic valve prosthesis and 1 or more of the following risk factors: AF, prior stroke or TIA, hypertension, diabetes, congestive heart failure, age > 75 years	• Bi-leaflet aortic valve prosthesis without AF and no other risk factors for stroke
VTE	• Recent (within 3 months) VTE • Severe thrombophilia (e.g. deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies)	• VTE within the past 3 to 12 months • Non-severe thrombophilia (e.g. heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 months or palliative	• VTE > 12 months previous and no other risk factors

Legend: AF – atrial fibrillation; VTE – venous thromboembolism; TIA – transient ischaemic attack; CHA_2DS_2-VASc – Congestive heart failure, Hypertension, Age >75 years, Diabetes mellitus, Stroke or transient ischemic attack, Vascular disease, Age 65 to 74 years, Sex category.

haematoma) between the study groups. Pocket haematoma occurred in 3.5% of the patients in the continued oral anticoagulation group and 16% of those bridged with heparin (Figure 2). There were no differences in the occurrence of stroke or other adverse events between the groups (16). Furthermore, a meta-analysis

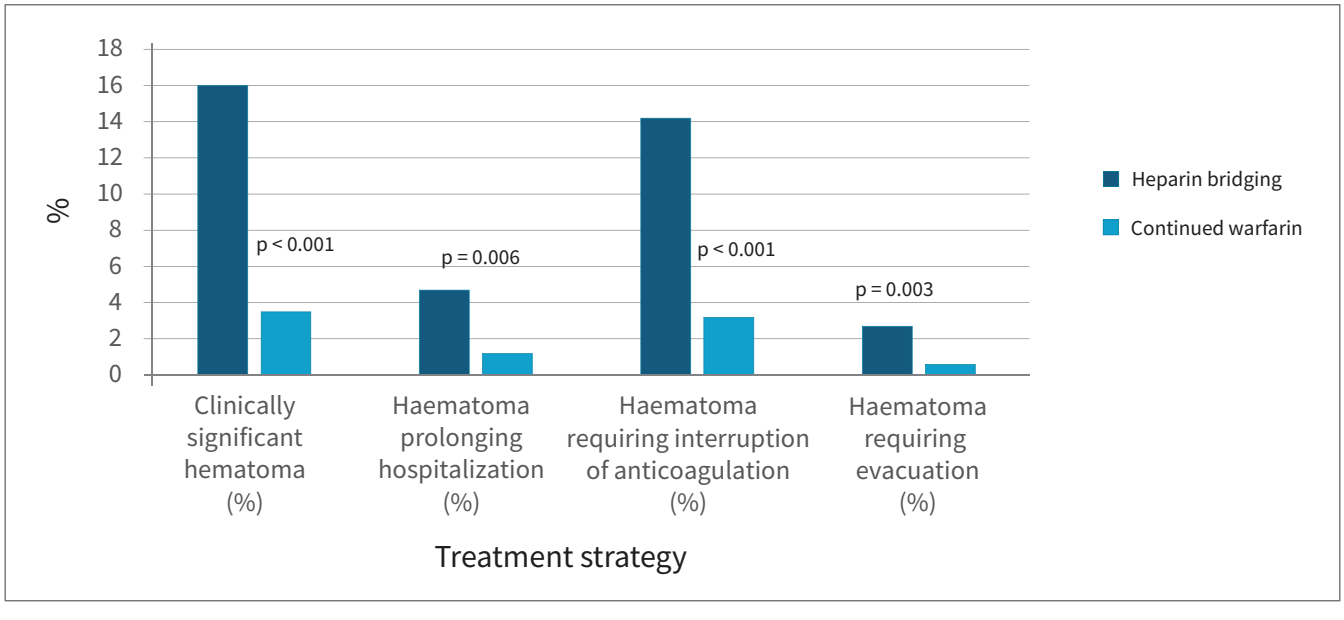

Figure 2: BRUISE CONTROL trial- outcomes. Adapted from Birnie DH N et al., 2013 (16).

of seven randomised controlled trials that included 2191 patients demonstrated a significantly lower risk of postoperative bleeding in patients on continued VKA compared to heparin bridging with no difference in the risk of thromboembolic events between the two strategies (17).

BRIDGE trial was conducted in a population of patients planned for any elective surgical procedure, but it addressed the question of forgoing anticoagulation altogether in the perioperative period. It is important to stress that high thromboembolic risk was an exclusion criterion, and the mean $CHADS_2$ score was 2.3. There was no significant difference in the occurrence of stroke or other thrombotic events between the arms (VKA discontinuation without vs. with heparin bridging) (18).

While the BRIDGE trial suggested relative safety with anticoagulant cessation in a low-risk patient population, a meta-analysis of 15 studies that included almost 6000 patients demonstrated an increased thromboembolic risk associated with oral anticoagulant cessation without bridging compared with heparin bridging (1.07% vs. 0.50%). However, there was no difference in thromboembolic events when warfarin was continued. Consistent with the results of previous studies, there was a significantly increased risk of pocket haematoma with heparin bridging and prolonged hospital stay. In addition, warfarin continuation was not associated with increased pocket haematoma compared to warfarin discontinuation (19).

Evidence shows that bridging VKAs with heparins is associated with significantly increased bleeding risk. In most patients, uninterrupted VKA therapy is safe, while short interruption of oral anticoagulation might be considered in patients whose bleeding risks outweigh the thromboembolic risk.

3.2 Non-vitamin K antagonist Oral Anticoagulants

In patients with non-valvular AF, NOACs are preferred over VKAs for stroke prevention (20,21). The analysis of the RE-LY trial that included patients who underwent CIED implantation during the study's duration showed that interruption of dabigatran was associated with a similar or lower incidence of pocket haematoma compared with warfarin interruption without or with heparin bridging, respectively (22). The same observations were noted in the ROCKET-AF study with rivaroxaban and ARISTOTLE with apixaban, respectively (23,24).

In the BRUISE CONTROL-2 trial, 662 device recipients with AF (CHA_2DS_2-VASC score of ≥ 2) were randomised to either continued or interrupted NOAC. In the continued NOAC group, anticoagulants were not interrupted; patients received the morning dose on the day of surgery and the next dose as scheduled. For apixaban and dabigatran, 12h passed between the pre- and post-op doses and 24h for rivaroxaban. In the interrupted arm, NOACs were stopped two days before the surgery and started 24h after, with 72 hours passing between the pre-and post-operative doses. It was shown that both strategies were associated with similarly low rates of pocket haematoma and that uninterrupted NOACs were not associated with any major perioperative bleeding events. In addition, there was no difference in the occurrence of thromboembolic events (Figure 3) (25).

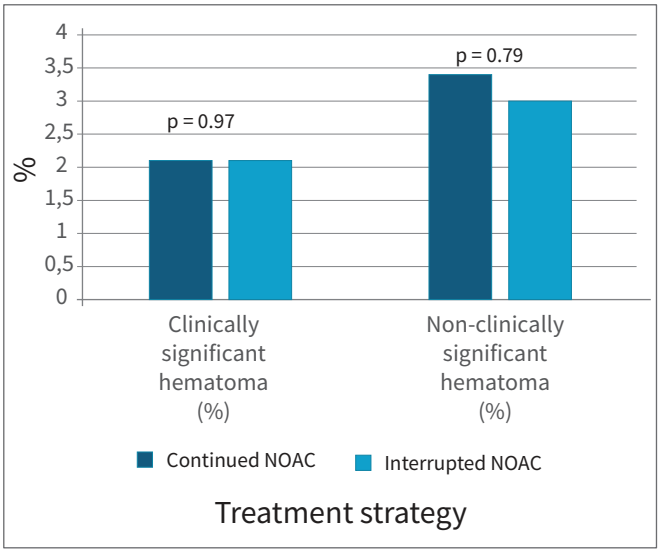

Figure 3: BRUISE CONTROL-2 trial- outcomes. Adapted from Birnie DH et al., 2018 (25).
Legend: NOAC – non-vitamin K oral anticoagulants.

Thus, an uninterrupted NOAC strategy seems safe in CIED procedures. Still, patient characteristics, such as age, body weight, kidney function, and concomitant medication, should be considered to determine the optimal strategy.

3.3 Antiplatelet drugs

To the best of our knowledge, there are no prospective randomised trials on the use of antiplatelet drugs in patients undergoing CIED implantation. However, several observational and retrospective studies suggest an increased risk of clinically significant pocket hematoma in patients receiving dual antiplatelet therapy

with or without concomitant oral anticoagulants (26-28). Since antiplatelet effects typically last about 5-7 days, there is often insufficient time to avoid antiplatelet action during device implantation. In elective patients who are not at increased thrombotic risk, i.e., more than one month after elective percutaneous coronary intervention (PCI) or more than six months after acute coronary syndrome (ACS), it should be considered that dual antiplatelet therapy is avoided. In such cases, the $P2Y_{12}$ inhibitor should be discontinued 3-7 days before the procedure (6,29).

4 Antithrombotic therapy management in patients undergoing device implantation

Device implantation is considered to be a low-bleeding-risk procedure. The recent 2021 European guidelines for cardiac pacing include recommendations on perioperative antithrombotic therapy management in patients undergoing standard transvenous CIED implant procedures. Epicardial lead placement and lead extractions are procedures with higher bleeding risk, and periprocedural antithrombotic management in these patients is beyond the scope of this paper (6).

Heparin bridging in patients receiving VKAs should be entirely avoided. In most patients, the procedure can be safely performed on continued oral anticoagulation with prothrombin times in the therapeutic range (INR < 3). However, brief discontinuation of VKA without heparin bridging might be considered in patients with high bleeding and low thromboembolic risk. In patients receiving NOACs, device implantation can be safely performed with continuous anticoagulation. However, the patient's characteristics (age, history of bleeding complications, concomitant medication, kidney function) and surgical factors should be considered in managing anticoagulation therapy perioperatively. In case of NOAC interruption, the timings should be decided according to kidney function and the type of NOAC. In patients with normal kidney function, the last dose of NOAC should be taken 24 h before the elective procedure. For those patients who are on dabigatran with creatinine clearance (CrCl) of 50-79 ml/min, the last dose should be taken > 36 h before the procedure; in CrCl of 30-49 ml/min, the last dose should be taken > 48 h before the procedure. For activated factor Xa inhibitors and CrCl above 30 ml/min, the last dose should be taken > 24h before the procedure, and in those with CrCl of 15-29 ml/min, the last dose should be taken 36 h or more before surgery. NOACs can be resumed 6-8 h after the procedure; generally, it is recommended to resume therapy 24 h post-procedure (21,30).

Dual antiplatelet therapy should be avoided where

Table 2: The algorithm for perioperative antithrombotic management. Adapted from Glikson M et al., 2021 and Burri H et al., 2021 (6,29).

VKA	NOAC	Dual antiplatelet therapy		OAC + antiplatelet
		Thrombotic risk after PCI		
		Intermediate or low > 1 month PCI > 6 months ACS	High < 1 month PCI < 6 months ACS	
Continue (or consider interrupting without heparin bridging if CHA_2DS_2-VASc ≤ 4)	Continue or interrupt as per operator preference and patient thromboembolic risk†	Continue Aspirin and discontinue P2Y12 inhibitor: - ticagrelor 3 days* - clopidogrel 5 days* - prasugrel 7 days*	Continue DAPT	Continue OAC (VKA or NOAC) Discontinue antiplatelet per patient-specific risk/benefit analysis

Legend: VKA – vitamin K antagonists; NOAC – non-vitamin K oral anticoagulants; OAC – oral anticoagulant; PCI – percutaneous coronary intervention; ACS – acute coronary syndrome; DAPT – dual antiplatelet therapy.
* – before the procedure
† – in case of interruption:
normal kidney function: last dose 24 h before the procedure and resume 24 h afterwards;
apixaban/rivaroxaban: CrCl 15-29 ml/min last dose ≥ 36 h before the procedure;
dabigatran: CrCl 50-79 ml/min last dose ≥ 36 h before the procedure, CrCl 30-49 ml/min last dose ≥ 48 h before the procedure.

possible due to the higher risk of clinically significant pocket hematoma. However, patients in the first month after PCI or in the first six months after ACS should continue with dual antiplatelet therapy. In others, $P2Y_{12}$ inhibitors should be discontinued several days before the planned procedure, depending on the specific medication used (3 days for ticagrelor, 5 days for clopidogrel, and 7 days for prasugrel).

A good surgical technique with meticulous attention paid to haemostasis, as described in the recent EHRA practical guide on optimal implantation technique for conventional pacemakers, should be the norm in all patients. A compressive bandage applied above the device pocket on the day of surgery may be considered to reduce the possibility of pocket haematoma (29).

An algorithm of perioperative anticoagulation management in patients undergoing CIED implantation adapted after the ESC guidelines and the EHRA practical guide on optimal implantation technique is shown in Table 2 (6,29).

5 Conclusions

Most CIED implantation procedures can be safely performed with uninterrupted VKAs or NOACs. Discontinuing oral anticoagulants with heparin bridging should be avoided as it imposes a greater risk for clinically significant pocket haematoma without significantly reducing thromboembolic events.

Conflict of interest

None declared.

References

1. Raatikainen MJ, Arnar DO, Merkely B, Nielsen JC, Hindricks G, Heidbuchel H, et al. A Decade of Information on the Use of Cardiac Implantable Electronic Devices and InterventionalElectrophysiological Procedures in the European Society of Cardiology Countries: 2017Report from the European Heart Rhythm Association. Europace. 2017;19:ii1-90. DOI: 10.1093/europace/eux258 PMID: 28903470
2. DeSimone CV, DeSimone DC, Cha YM. Contemporary Management of Antiplatelet and Anticoagulation for Cardiac ImplantableDevice Procedures. Circ Arrhythm Electrophysiol. 2019;12(10):e007863. DOI: 10.1161/CIRCEP.119.007863 PMID: 31610719
3. Stewart MH, Morin DP. Management of Perioperative Anticoagulation for Device Implantation. Card Electrophysiol Clin. 2018;10(1):99-109. DOI: 10.1016/j.ccep.2017.11.008 PMID: 29428146
4. Zacà V, Marcucci R, Parodi G, Limbruno U, Notarstefano P, Pieragnoli P, et al. Management of antithrombotic therapy in patients undergoing electrophysiological devicesurgery. Europace. 2015;17(6):840-54. DOI: 10.1093/europace/euu357 PMID: 25712980
5. 5Raunsø J, Selmer C, Olesen JB, Charlot MG, Olsen AM, Bretler DM, et al. Increased short-term risk of thrombo-embolism or death after interruption of warfarintreatment in patients with atrial fibrillation. Eur Heart J. 2012;33(15):1886-92. DOI: 10.1093/eurheartj/ehr454 PMID: 22199117
6. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, et al.; ESC Scientific Document Group. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021;42(35):3427-520. DOI: 10.1093/eurheartj/ehab364 PMID: 34455430
7. Garcia DA, Regan S, Henault LE, Upadhyay A, Baker J, Othman M, et al. Risk of thromboembolism with short-term interruption of warfarin therapy. Arch Intern Med. 2008;168(1):63-9. DOI: 10.1001/archinternmed.2007.23 PMID: 18195197
8. Reynolds MR, Cohen DJ, Kugelmass AD, Brown PP, Becker ER, Culler SD, et al. The frequency and incremental cost of major complications among medicare beneficiariesreceiving implantable cardioverter-defibrillators. J Am Coll Cardiol. 2006;47(12):2493-7. DOI: 10.1016/j.jacc.2006.02.049 PMID: 16781379
9. Zacà V, Marcucci R, Parodi G, Limbruno U, Notarstefano P, Pieragnoli P, et al. Management of antithrombotic therapy in patients undergoing electrophysiological devicesurgery. Europace. 2015;17(6):840-54. DOI: 10.1093/europace/euu357 PMID: 25712980
10. Essebag V, Verma A, Healey JS, Krahn AD, Kalfon E, Coutu B, et al.; BRUISE CONTROL Investigators. Clinically significant pocket hematoma increases long-term risk of device infection:BRUISE CONTROL INFECTION study. J Am Coll Cardiol. 2016;67(11):1300-8. DOI: 10.1016/j.jacc.2016.01.009 PMID: 26988951
11. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Preventionof Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based ClinicalPractice Guidelines. Chest. 2012;141(2):e326S-50S. DOI: 10.1378/chest.11-2298 PMID: 22315266
12. Doherty JU, Gluckman TJ, Hucker WJ, Januzzi JL, Ortel TL, Saxonhouse SJ, et al. 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulationin Patients With Nonvalvular Atrial Fibrillation: A Report of the American Collegeof Cardiology Clinical Expert Consensus Document Task Force. J Am Coll Cardiol. 2017;69(7):871-98. DOI: 10.1016/j.jacc.2016.11.024 PMID: 28081965
13. Vene N, Mavri A, Gubenšek M, Tratar G, Vižintin Cuderman T, Pohar Perme M, et al. PLoS One. 2016;11(6):e0156943. DOI: 10.1371/journal.pone.01569434 PMID: 27280704
14. Mavri A, Blinc A, Peternel P. Antikoagulacijsko zdravljenje. 1. izd. Ljubljana: Slovensko zdravniško društvo, Sekcija za antikoagulacijsko zdravljenje in preprečevanjetrombemboličnih bolezni pri Združenju za žilne bolezni; 2017.
15. Deharo JC, Sciaraffia E, Leclercq C, Amara W, Doering M, Bongiorni MG, et al.; Coordinated by the Scientific Initiatives Committee of the European Heart Rhythm Association. Perioperative management of antithrombotic treatment during implantation or revisionof cardiac implantable electronic devices: the European Snapshot Survey on ProceduralRoutines for Electronic Device Implantation (ESS-PREDI). Europace. 2016;18(5):778-84. DOI: 10.1093/europace/euw127 PMID: 27226497

16. Birnie DH, Healey JS, Wells GA, Verma A, Tang AS, Krahn AD, et al.; BRUISE CONTROL Investigators. Pacemaker or defibrillator surgery without interruption of anticoagulation. N Engl J Med. 2013;368(22):2084-93. DOI: 10.1056/NEJMoa1302946 PMID: 23659733

17. Sant'anna RT, Leiria TL, Nascimento T, Sant'anna JR, Kalil RA, Lima GG, et al. Meta-analysis of continuous oral anticoagulants versus heparin bridging in patientsundergoing CIED surgery: reappraisal after the BRUISE study. Pacing Clin Electrophysiol. 2015;38(4):417-23. DOI: 10.1111/pace.12557 PMID: 25546244

18. Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, et al.; BRIDGE Investigators. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. N Engl J Med. 2015;373(9):823-33. DOI: 10.1056/NEJMoa1501035 PMID: 26095867

19. Proietti R, Porto I, Levi M, Leo A, Russo V, Kalfon E, et al. Risk of pocket hematoma in patients on chronic anticoagulation with warfarin undergoingelectrophysiological device implantation: a comparison of different peri-operativemanagement strategies. Eur Rev Med Pharmacol Sci. 2015;19(8):1461-79. PMID: 25967723

20. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developedin collaboration with the European Association for Cardio-Thoracic Surgery (EACTS):The Task Force for the diagnosis and management of atrial fibrillation of the EuropeanSociety of Cardiology (ESC) Developed with the special contribution of the EuropeanHeart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373-498. DOI: 10.1093/eurheartj/ehaa612 PMID: 32860505

21. Steffel J, Collins R, Antz M, Cornu P, Desteghe L, Haeusler KG, et al.; External reviewers. 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin KAntagonist Oral Anticoagulants in Patients with Atrial Fibrillation. Europace. 2021;23(10):1612-76. DOI: 10.1093/europace/euab065 PMID: 33895845

22. Essebag V, Proietti R, Birnie DH, Wang J, Douketis J, Coutu B, et al. Short-term dabigatran interruption before cardiac rhythm device implantation: multi-centreexperience from the RE-LY trial. Europace. 2017;19(10):1630-6. DOI: 10.1093/europace/euw409 PMID: 28339794

23. Leef GC, Hellkamp AS, Patel MR, Becker RC, Berkowitz SD, Breithardt G, et al. Safety and Efficacy of Rivaroxaban in Patients With Cardiac Implantable ElectronicDevices: Observations From the ROCKET AF Trial. J Am Heart Assoc. 2017;6(6):e004663. DOI: 10.1161/JAHA.116.004663 PMID: 28615214

24. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al.; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981-92. DOI: 10.1056/NEJMoa1107039 PMID: 21870978

25. Birnie DH, Healey JS, Wells GA, Ayala-Paredes F, Coutu B, Sumner GL, et al. Continued vs. interrupted direct oral anticoagulants at the time of device surgery,in patients with moderate to high risk of arterial thrombo-embolic events (BRUISECONTROL-2). Eur Heart J. 2018;39(44):3973-9. DOI: 10.1093/eurheartj/ehy413 PMID: 30462279

26. Kutinsky IB, Jarandilla R, Jewett M, Haines DE. Risk of hematoma complications after device implant in the clopidogrel era. Circ Arrhythm Electrophysiol. 2010;3(4):312-8. DOI: 10.1161/CIRCEP.109.917625 PMID: 20558847

27. Tompkins C, Cheng A, Dalal D, Brinker JA, Leng CT, Marine JE, et al. Dual antiplatelet therapy and heparin "bridging" significantly increase the risk ofbleeding complications after pacemaker or implantable cardioverter-defibrillator deviceimplantation. J Am Coll Cardiol. 2010;55(21):2376-82. DOI: 10.1016/j.jacc.2009.12.056 PMID: 20488310

28. Essebag V, Healey JS, Joza J, Nery PB, Kalfon E, Leiria TL, et al. Effect of Direct Oral Anticoagulants, Warfarin, and Antiplatelet Agents on Risk ofDevice Pocket Hematoma: combined Analysis of BRUISE CONTROL 1 and 2. Circ Arrhythm Electrophysiol. 2019;12(10):e007545. DOI: 10.1161/CIRCEP.119.007545 PMID: 31610718

29. Burri H, Starck C, Auricchio A, Biffi M, Burri M, D'Avila A, et al. EHRA expert consensus statement and practical guide on optimal implantation techniquefor conventional pacemakers and implantable cardioverter-defibrillators: endorsedby the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS),and t. EP Eur. 2021;23(7):983-1008. PMID: 33878762

30. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al.; ESC Scientific Document Group. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitaminK antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018;39(16):1330-93. DOI: 10.1093/eurheartj/ehy136 PMID: 29562325