EDITORIAL

Continue or withhold oral anticoagulation in high-risk patients undergoing pacemaker or ICD implantation

Jean-Claude Daubert* and Philippe Mabo

Service de Cardiologie et Maladies Vasculaires, Centre Hospitalier Universitaire, 35000 Rennes, France

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This editorial refers to ‘Preparation for pacemaker or implantable cardiac defibrillator implants in patients with high risk of thrombo-embolic events: oral anticoagulation or bridging to intravenous heparin? A prospective randomized trial†, by J.M. Tolosano et al., published in Volume 30 number 15, pp. 1880–1884.

Tolosana et al. have reported the results of a randomized study, which compared two procedures in preparation for implantation of pacemakers or cardioverter defibrillators (ICDs) in a small population of chronically anticoagulated patients at high risk of thrombo-embolic events. One group was randomly assigned to continued oral anticoagulation (OAC) reduced to a target international normalized ratio (INR) near 2.0 for the procedure, and the other to temporary replacement of OAC by heparin, as recommended by current guidelines for high-risk patients.

Consider the high proportion of chronically anticoagulated patients among the large population of cardiac device recipients, this is an important issue. In the recently published French PEOPLE registry, 11% of patients remained on OAC and nearly 20% received heparin at the time of procedure. This patient population is exposed to a dual risk during the critical period of re-arrangement of anticoagulation: (i) haemorrhage, particularly procedure-related pocket haematoma; and (ii) thrombo-embolism from under-anticoagulation during the peri-operative period. Furthermore, the choice of anticoagulation strategy directly influences the duration of hospitalization and overall cost of treatment.

The haemorrhagic risk

Except in special cases, OAC should not be withheld for minor procedures associated with a low risk of haemorrhage. In the presence of mechanical valve prostheses, it is currently recommended to continue OAC with an INR near 2.0. The implantation of cardiac devices is associated with an intermediate risk of local haemorrhage, which complicates procedures performed during full anticoagulation. The risk of pocket haematoma after pacemaker or ICD implantation under anticoagulation varies between 20 and 25% among past and recent studies including small numbers of patients, though it was lower in recently published, large, prospective single- or multicentre registries. Wiegand et al. found a 4.9% overall risk of pocket haematoma after 3164 pacemaker or ICD implantations, which required re-operation and prolongation of hospitalization in 44 and 38% of cases, respectively. In that study, 1069 procedures were performed in patients previously on OAC, discontinued 1–5 days earlier, and placed on i.v. unfractionated heparin (UFH) or on s.c. low-molecular-weight (LMWH) heparin. The overall rate of pocket haematoma was 12.2%, and tended to be higher in patients treated with full doses of LWMH (16.1%) than in patients treated with UFH (11.6%). No relationship was observed between development of pocket haematoma and pocket infection. In the PEOPLE registry, which enrolled 6319 consecutive patients at 44 French medical centres, the overall risk of pocket haematoma was 5.3%, nearly the same as that reported by Wiegand et al., though it was significantly higher [8.3%; relative risk (RR) = 1.57; P = 0.04] in the 715 patients who were on OAC. While the risk of pocket haematoma was also higher in the 1163 patients treated with heparin, the difference was not statistically significant (7.5%; RR = 1.42; P = 0.08). Finally, the development of pocket haematoma was not associated with an increased risk of infection (primary objective of the study).

These observations are consistent with the results reported by Tolosana et al., who observed (i) a 7.9% overall incidence of pocket haematoma; and (ii) no difference between patients on OAC (8.0%) and patients treated with heparin (7.8%). It is noteworthy that, in a small, similar, partially randomized study...
published in 2000, Michaud et al. found a 20% incidence of pocket haematoma after pacemaker or ICD implantation in patients treated with i.v. heparin, vs 4% in patients kept on OAC, vs 2% in patients who were not anticoagulated ($P < 0.001$).9

## Thrombo-embolic risk

The discontinuation and reintroduction of OAC raises the theoretical concern that it might cause a hypercoagulable state or a thrombotic rebound phenomenon.6 An increase in the markers of activation of thrombosis by abrupt discontinuation of OAC has been observed, although it is not clear that it increases the risk of thrombo-embolic events. There are also theoretical concerns that, when OAC is reintroduced, a hypercoagulable state might be induced by suppression of proteins C and S.

In practice, the thrombo-embolic risk of discontinuing OAC depends on individual indications and on the duration of OAC interruption. At highest risk are (i) patients with (a) mechanical mitral or tricuspid valve prostheses, (b) mechanical aortic valve prostheses with any risk factor, including atrial fibrillation (AF), previous thrombo-embolism, left ventricular ejection fraction $<0.30\%$, or disorders associated with hypercoagulation, (c) older-generation thrombogenic artificial valves, or (d) mechanical valve,10,11 and (ii) patients in AF with mitral valve stenosis or histories of stroke, transient ischaemic attack, or systemic embolism.9 The individual thrombo-embolic risk in AF specifically can be assessed, using the CHADS2 score.10

There is general consensus with respect to the increase in thrombo-embolic risk incurred by the highest risk patients when OAC is discontinued without supplemental heparinization. Therefore, the latest American College of Cardiology/American Heart Association (ACC/AHA) professional guidelines have formulated the Class IIa, level of evidence B, recommendation ‘...to start therapeutic doses of intravenous UFH when the INR falls below 2, to be stopped 4 to 6 hrs before the procedure, and restarted as early after surgery as bleeding stability allows, and continued until INR is again therapeutic with warfarin therapy’.3 LMWH could be used instead of i.v. UFH11 after discontinuation of warfarin, as suggested by a recent study of 650 patients, including 215 recipients of mechanical valves, in which the risk of thrombo-embolism was 0.62%, and major haemorrhages 0.95%.12

Less strict recommendations have been formulated for lower risk patients, which allow a temporary interruption of OAC without heparin substitution. For example, the ACC/AHA guidelines for management of patients with heart valve disease have formulated the following Class IIa, level of evidence B indication: ‘In patients with low risk of thrombosis, defined as those with bileaflet mechanical aortic valve with no risk factors, it is recommended that warfarin be stopped 48 to 72 hrs before the procedure and restarted within 24 hrs after the procedure. Heparin is usually unnecessary’.4 Similarly, the ACC/AHA/European Society of Cardiology guidelines for the management of patients with AF have issued a Class IIa, level of evidence C recommendation ‘In patients with AF who do not have mechanical prosthetic heart valves, it is reasonable to interrupt anticoagulation for up to 1 week without substituting heparin for surgical or diagnostic procedures that carry a risk of bleeding; and a Class IIb, level of evidence C recommendation ‘When surgical procedures require interruption of oral anticoagulant therapy for longer than 1 week in high-risk patients, unfractionated heparin may be administered or LMWH by subcutaneous injection, although the efficacy of these alternatives in uncertain’.9 It is, however, noteworthy that these recommendations are based on expert consensus, and that the amount of clinical evidence remains small.

In summary, the current recommendations offer two choices: (i) in high-risk patients, discontinuation of OAC and temporary anticoagulation with warfarin, UFH, or LMWH; or (ii) in low-risk patients, discontinuation of OAC for $\leq 72$ h in the presence of valve disease,2 or $\leq 1$ week in patients in AF without heparinization.

Tolosona et al.1 studied a third, little explored option, which consists of continuing OAC while lowering the target INR to 2.0, without supplemental heparin. The study was limited by (i) a relatively small sample size; (ii) a mix of high and lower risk, including 12 patients in AF and three moderate risk factors, corresponding to a CHADS2 score of 3; and (iii) an imperfect monitoring of thrombo-embolic events. Ideally a large, confirmatory multicentre trial would need to be planned, in order to record a much larger adverse clinical events rate. Despite these limitations, this study contributes important information. Compared with the usual interruption of OAC and temporary heparin substitution, this new strategy of continuing OAC to reach a 2.0 target INR at the time of procedure increased neither the haemorrhagic (7.8% vs 8%) nor the thrombo-embolic (0% in both groups) risk. However, the strategy of continuing OAC significantly decreased the mean duration of hospitalization from $5.5 \pm 2$ to $3.2 \pm 3$ days ($P < 0.0001$). While these observations are of high interest, they cannot be universally applied, and must be interpreted with particular consideration of the short half-life of the vitamin K antagonist used in this trial (acenocoumarol), which differs markedly from that of warfarin, generally used in other countries. Whether similar results would have been observed with warfarin is uncertain. Furthermore, the data pertaining to duration of hospitalization and putative health care cost savings must be interpreted as a function of each country’s health care system, and might not be directly applicable to regions other than Catalonia or Spain. The 4.3-day mean duration of hospitalization seems relatively long for the type of procedure studied. Finally, the application of these results is limited to the implantation of pacemakers and ICDs, associated with an intermediate risk of haemorrhage, and does not extend to cardiac or non-cardiac operations associated with a higher haemorrhagic risk.

Since the haemorrhagic risk associated with pacemaker or ICD implantation procedures performed during anticoagulation is relatively low, it appears logical to favour the simplest and least expensive strategy. The study by Tolosona et al. suggests that, in a majority of high-risk patients, continuing OAC in lower doses is safe and cost-effective. We believe that this management strategy could be included in upcoming practice guidelines.

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References


