Antithrombotic regimens in patients awaiting heart transplant: a single-center experience

Tomasz Urbanowicz¹, Anna Olasińska-Wiśniewska¹, Veronica Cassadei¹, Ewa Straburzyńska-Migaj², Piotr Buczkowski¹, Marek Jemielity¹

¹ Department of Cardiac Surgery and Transplantology, Poznan University of Medical Sciences, Poznań, Poland
² 1st Department of Cardiology, Poznan University of Medical Sciences, Poznań, Poland

Introduction  Patients with congestive heart failure are at high risk of death and 1.4% to 2.4% annual risk of stroke. The latter substantially increases with atrial fibrillation and other risk factors included in the CHA₂DS₂-VASc score.¹ ³ Nowadays, non–vitamin K antagonist oral anticoagulants (NOACs) are the recommended drug class in this population.⁴ Their major disadvantage is the immediate reversal of the antithrombotic effect in urgent surgery.

We present a single-center approach to antithrombotic and antiplatelet therapy in patients awaiting and undergoing heart transplant (HTx).

Methods  Between the years 2017 and 2019, 84 patients were put on a waiting list for HTx in our Department of Cardiac Surgery and Transplantology. Twenty of them (17 men and 3 women; mean [SD] age, 44 [13] years) underwent HTx. They were referred for this procedure because of dilated (10 [50%]), ischemic (9 [45%]), and hypertrophic (1 [5%]) cardiomyopathy. Three patients (15%) were treated with dabigatran for chronic atrial fibrillation; the mean CHA₂DS₂-VASc score was 2.3, and the mean HAS-BLED score was 1.3. In the study group, there was no history of major bleeding, end-stage kidney disease (mean [SD] serum creatinine level, 156 [43] µmol/l), or liver dysfunction (mean [SD] aspartate aminotransferase level, 56 [13] IU/l).

Statistical analysis  Data were entered and analysed using the Statview 5.0 software (SAS Institute, Inc., Cary, North Carolina, United States).

Ethics  The study was approved by an ethics committee and all patients provided written informed consent.

Results and discussion  All the study patients had HTx performed using the Lower-Shumway technique after a mean (SD) number of 256 (140) days of being put on the waiting list for transplant. The mean (SD) cold ischemia time was 218 (38) minutes, and the mean (SD) cross-clamping time was 181 (30) minutes. There was no perioperative death in the study group.

Non–vitamin K oral anticoagulants  Two men with chronic atrial fibrillation, the first (36 years) diagnosed with ischemic cardiomyopathy and the second (48 years) with dilated cardiomyopathy, were transferred into the operation room 22 and 18 hours after receiving the last dose of dabigatran, respectively. Owing to a relatively short half-life of dabigatran elimination in the plasma (7 to 9 hours), we decided not to administer a reversal agent. A 43-year-old patient with dilated cardiomyopathy and atrial fibrillation received 5 g of idarucizumab (Praxbind, Boehringer Ingelheim Pharma, Ingelheim, Germany). The mean postoperative drainage volume in those men was 634 ml and 579 ml, respectively. Neither pericardial nor pleural fluids were detected during the postoperative hospital stay.

Oral anticoagulants (warfarin)  There were 5 patients (25%) treated with warfarin: 3 (15%) with a mechanical valve prosthesis and 2 (10%) receiving mechanical paracorporeal circulatory support.
Patients with a mechanical valve prosthesi s treated with warfarin within the therapeutic range of the international normalized ratio (INR) on admission were transferred into the operation room without INR correction. The mean (SD) cold ischemia time was 238 (14) minutes. After protamine administration, the standard protocol of fresh frozen plasma and platelet concent rante infusion was augmented by prothrombin complex concentrate administration if needed. The mean (SD) postoperative drainage volume in this patient subgroup was 712 (53) ml (Table 1).

One patient developed heparin-induced thrombocytopenia after 2 weeks of unfractionated heparin infusion during intra-aortic balloon pump treatment before HTx, which was diagnosed based on a platelet count decrease from 361 to 64 × 10³/mm³. The patient had no thrombotic complications and was subsequently treated with bivalirudin infusion before and during surgery. After 1 week, the patient’s platelet count increased to 153 × 10³/mm³. The bivalirudin infusion was adjusted following the activated clotting time.

**Low-molecular-weight heparin** Seven patients were treated with low-molecular-weight heparin. The therapy was not withdrawn prior to surgery due to its urgency. The mean (SD) postoperative drainage volume was 710 (145) ml.

**Aspirin** Five patients were receiving acetylsaliclyc acid before HTx, as they were diagnosed with ischemic heart disease. The mean (SD) postoperative drainage volume in these patients was 690 (123) ml.

All study patients were treated with low-molecular-weight heparin during hospitalization and acetylsalicylic acid at a dose of 75 mg daily, which was initiated within 5 days after surgery. None of the patients required anticoagulation therapy. No bleeding complications were observed. We did not observe any differences between patient groups in terms of procedural complications.

Within the first postoperative year, patients were treated with standard triple immunosuppressive therapy including calcineurin inhibitor, mycophenolate mofetil, and oral steroids. Our study was a single-center analysis of antithrombotic regimens used in patients awaiting HTx. Patients qualified for HTx most often require oral anticoagulation or antiplatelet treatment. Generally, both kinds of therapy should be interrupted in a planned manner before most of surgical procedures. However, HTx is performed on an urgent basis. Therefore, an optimal strategy of anticoagulation reversal should be implemented in the operating center in advance. The interruption of pharmacotherapy may increase the risk of either bleeding or thromboembolic events. These complications may be, however, related not only to drugs but also to preoperative factors, including kidney function or the EuroSCORE.

Low-molecular-weight heparin Seven patients were treated with low-molecular-weight heparin. The therapy was not withdrawn prior to surgery due to its urgency. The mean (SD) postoperative drainage volume was 710 (145) ml.

**Aspirin** Five patients were receiving acetylsalicylic acid before HTx, as they were diagnosed with ischemic heart disease. The mean (SD) postoperative drainage volume in these patients was 690 (123) ml.

All study patients were treated with low-molecular-weight heparin during hospitalization and acetylsalicylic acid at a dose of 75 mg daily, which was initiated within 5 days after surgery. None of the patients required anticoagulation therapy. No bleeding complications were observed. We did not observe any differences between patient groups in terms of procedural complications.

Within the first postoperative year, patients were treated with standard triple immunosuppressive therapy including calcineurin inhibitor, mycophenolate mofetil, and oral steroids. Our study was a single-center analysis of antithrombotic regimens used in patients awaiting HTx. Patients qualified for HTx most often require oral anticoagulation or antiplatelet treatment. Generally, both kinds of therapy should be interrupted in a planned manner before most of surgical procedures. However, HTx is performed on an urgent basis. Therefore, an optimal strategy of anticoagulation reversal should be implemented in the operating center in advance. The interruption of pharmacotherapy may increase the risk of either bleeding or thromboembolic events. These complications may be, however, related not only to drugs but also to preoperative factors, including kidney function or the EuroSCORE.

Low-molecular-weight heparin Seven patients were treated with low-molecular-weight heparin. The therapy was not withdrawn prior to surgery due to its urgency. The mean (SD) postoperative drainage volume was 710 (145) ml.

**Aspirin** Five patients were receiving acetylsalicylic acid before HTx, as they were diagnosed with ischemic heart disease. The mean (SD) postoperative drainage volume in these patients was 690 (123) ml.

All study patients were treated with low-molecular-weight heparin during hospitalization and acetylsalicylic acid at a dose of 75 mg daily, which was initiated within 5 days after surgery. None of the patients required anticoagulation therapy. No bleeding complications were observed. We did not observe any differences between patient groups in terms of procedural complications.

Within the first postoperative year, patients were treated with standard triple immunosuppressive therapy including calcineurin inhibitor, mycophenolate mofetil, and oral steroids. Our study was a single-center analysis of antithrombotic regimens used in patients awaiting HTx. Patients qualified for HTx most often require oral anticoagulation or antiplatelet treatment. Generally, both kinds of therapy should be interrupted in a planned manner before most of surgical procedures. However, HTx is performed on an urgent basis. Therefore, an optimal strategy of anticoagulation reversal should be implemented in the operating center in advance. The interruption of pharmacotherapy may increase the risk of either bleeding or thromboembolic events. These complications may be, however, related not only to drugs but also to preoperative factors, including kidney function or the EuroSCORE.

Low-molecular-weight heparin Seven patients were treated with low-molecular-weight heparin. The therapy was not withdrawn prior to surgery due to its urgency. The mean (SD) postoperative drainage volume was 710 (145) ml.

**Aspirin** Five patients were receiving acetylsalicylic acid before HTx, as they were diagnosed with ischemic heart disease. The mean (SD) postoperative drainage volume in these patients was 690 (123) ml.

All study patients were treated with low-molecular-weight heparin during hospitalization and acetylsalicylic acid at a dose of 75 mg daily, which was initiated within 5 days after surgery. None of the patients required anticoagulation therapy. No bleeding complications were observed. We did not observe any differences between patient groups in terms of procedural complications.

Within the first postoperative year, patients were treated with standard triple immunosuppressive therapy including calcineurin inhibitor, mycophenolate mofetil, and oral steroids. Our study was a single-center analysis of antithrombotic regimens used in patients awaiting HTx. Patients qualified for HTx most often require oral anticoagulation or antiplatelet treatment. Generally, both kinds of therapy should be interrupted in a planned manner before most of surgical procedures. However, HTx is performed on an urgent basis. Therefore, an optimal strategy of anticoagulation reversal should be implemented in the operating center in advance. The interruption of pharmacotherapy may increase the risk of either bleeding or thromboembolic events. These complications may be, however, related not only to drugs but also to preoperative factors, including kidney function or the EuroSCORE.

Low-molecular-weight heparin Seven patients were treated with low-molecular-weight heparin. The therapy was not withdrawn prior to surgery due to its urgency. The mean (SD) postoperative drainage volume was 710 (145) ml.

**Aspirin** Five patients were receiving acetylsalicylic acid before HTx, as they were diagnosed with ischemic heart disease. The mean (SD) postoperative drainage volume in these patients was 690 (123) ml.

All study patients were treated with low-molecular-weight heparin during hospitalization and acetylsalicylic acid at a dose of 75 mg daily, which was initiated within 5 days after surgery. None of the patients required anticoagulation therapy. No bleeding complications were observed. We did not observe any differences between patient groups in terms of procedural complications.

Within the first postoperative year, patients were treated with standard triple immunosuppressive therapy including calcineurin inhibitor, mycophenolate mofetil, and oral steroids. Our study was a single-center analysis of antithrombotic regimens used in patients awaiting HTx. Patients qualified for HTx most often require oral anticoagulation or antiplatelet treatment. Generally, both kinds of therapy should be interrupted in a planned manner before most of surgical procedures. However, HTx is performed on an urgent basis. Therefore, an optimal strategy of anticoagulation reversal should be implemented in the operating center in advance. The interruption of pharmacotherapy may increase the risk of either bleeding or thromboembolic events. These complications may be, however, related not only to drugs but also to preoperative factors, including kidney function or the EuroSCORE.
safe for approximately 2 half-lives of the drug prior to a surgical intervention. Postponing surgery seems to be reasonable in most cases, but it is impossible in solid organ transplant. Therefore, a reversal agent, currently available for dabigatran, enables prompt patient preparation before HTx.

Considering the availability of idarucizumab, the recommendations in our institution were altered for patients awaiting HTx, indicating the need for dabigatran use. There is still lack of clear guidelines in the field of the antithrombotic regimen before HTx. Therefore, we believe that they should be implemented to increase patient safety. We compared complication rates in our study subgroups and did not find any significant differences in the postoperative drainage volumes and bleeding events. However, our observations are limited by the small number of patients included in the study. Nevertheless, the availability of a reversal agent is crucial when performing urgent surgery including HTx and, therefore, we encourage the use of dabigatran in the pre-HTx period.

Conclusions The antithrombotic regimens are particularly problematic in urgent cardiac surgery. The reversibility of NOAC activity using its specific antidote should be considered a possible and safe option in HTx procedures.

ARTICLE INFORMATION

CONFLICT OF INTEREST  None declared.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND 4.0), allowing third parties to download articles and share them with others, provided the original work is properly cited, not changed in any way, distributed under the same license, and used for non-commercial purposes only. For commercial use, please contact the journal office at kardiologiapolska@ptkardio.pl.


REFERENCES