

The effect of anticoagulation therapy on perioperative bleeding risk in patients undergoing heart transplantation

 **Petra Mjehović***,
 **Mia Dubravčić**
Došen,
 **Marijan Pašalić,**
 **Maja Čikeš,**
 **Dora Fabijanović,**
 **Nina Jakuš,**
 **Hrvoje Jurin,**
 **Daniel Lovrić,**
 **Ivo Planinc,**
 **Jure Samardžić,**
 **Branka Golubić**
Čepulić,
 **Ines Bojanić,**
 **Sanja Mazić,**
 **Željko Čolak,**
 **Hrvoje Gašparović,**
 **Davor Miličić,**
 **Boško Skorić**

University of Zagreb School of
Medicine, University Hospital
Centre Zagreb, Zagreb, Croatia

KEYWORDS: heart transplantation, oral anticoagulation therapy, vitamin K antagonist, dabigatran, bleeding complications.

CITATION: *Cardiol Croat.* 2022;17(9-10):191-2. | <https://doi.org/10.15836/ccar2022.191>

***ADDRESS FOR CORRESPONDENCE:** Petra Mjehović, Klinički bolnički centar Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-91-8970-556 / E-mail: petra.mjehovic@gmail.com

ORCID: Petra Mjehović, <https://orcid.org/0000-0003-4908-4674> • Mia Dubravčić Došen, <https://orcid.org/0000-0003-0441-4772> • Marijan Pašalić, <https://orcid.org/0000-0002-3197-2190> • Maja Čikeš, <https://orcid.org/0000-0002-4772-5549> • Dora Fabijanović, <https://orcid.org/0000-0003-2633-3439> • Nina Jakuš, <https://orcid.org/0000-0001-7304-1127> • Hrvoje Jurin, <https://orcid.org/0000-0002-2599-553X> • Daniel Lovrić, <https://orcid.org/0000-0002-5052-6559> • Ivo Planinc, <https://orcid.org/0000-0003-0561-6704> • Jure Samardžić, <https://orcid.org/0000-0002-9346-6402> • Branka Golubić Čepulić, <https://orcid.org/0000-0002-3067-0414> • Ines Bojanić, <https://orcid.org/0000-0002-2985-7847> • Sanja Mazić, <https://orcid.org/0000-0003-4166-6768> • Željko Čolak, <https://orcid.org/0000-0003-0507-4714> • Hrvoje Gašparović, <https://orcid.org/0000-0002-2492-3702> • Davor Miličić, <https://orcid.org/0000-0001-9101-1570> • Boško Skorić, <https://orcid.org/0000-0001-5979-2346>

Background: Oral anticoagulation therapy for the prevention of thromboembolic complications of atrial fibrillation in patients awaiting heart transplantation (HTx) traditionally includes warfarin, and in the last few years it increasingly includes dabigatran. Anticoagulation must be reversed before the surgery. The possibility of rapid reversal of the anticoagulant effect of dabigatran with idarucizumab seems to represent an advantage¹. A comparison of bleeding complications between these two strategies has not been completely investigated.

Patients and Methods: We did a retrospective analysis of bleeding complications during and immediately after HTx performed in University Hospital Center Zagreb in 15 patients divided into 3 groups: patients who were on warfarin prior to HTx, patients who were on dabigatran prior to HTx, and control patients without indication for anticoagulation therapy. Patients were mutually paired to eliminate the influence of other risk factors including age, gender, etiology of heart failure, renal function, as well as whether surgery was primary or after previous sternotomy. For the comparison of bleeding complications we measured the utilization of blood products (red blood cells, platelets, fibrinogen, fresh frozen plasma (FFP), prothrombin complex (PC) and the amount of thoracic drainage within the first 24 hours after the HTx.

Results: There was no significant difference in the utilization of blood products as well as the amount of 24h thoracic drainage between these three groups (**Table 1**). Only 2/5 patients in the warfarin group were within the therapeutic INR range (2 pts below and 1 pts above the range). 24h thoracic drainage, FFP and PC consumption correlated with pretransplant INR (**Table 2**).

Conclusion: Although there was no difference in the consumption of blood products and 24h thoracic drainage between patients who were on warfarin or dabigatran anticoagulation before HTx, it should be noted that the majority of patients on warfarin were not within the therapeutic INR range, and it was precisely the elevated INR that significantly correlated with the consumption of blood products and 24h thoracic drainage. It is necessary to conduct a study on a larger number of patients in order to find out whether the pre-HTx use of warfarin is equally safe and effective as the use of dabigatran, in terms of the perioperative bleeding.

RECEIVED:
November 4, 2022

ACCEPTED:
November 10, 2022



TABLE 1. Comparison of different demographic and clinical characteristics, and crucial pretransplant/posttransplant laboratory findings between patient groups stratified according to anticoagulant use.

Therapy groups:	No anticoagulation (n=5)	Warfarin (n=5)	Dabigatran (n=5)	p-value
Male gender, N (%)	4 (80)	4 (80)	4 (80)	1.000
Age at the time of HTx [y] (IQR)	53 (53-57)	59 (46-60)	62 (46-63)	0.756
Ischemic CMP, N (%)	1 (20)	1 (20)	1 (20)	1.000
Resternotomy, N (%)	1 (20)	1 (20)	1 (20)	1.000
eGFR [mL/min/1,73m ²] (IQR)	71 (66-84)	65 (53-71)	65 (50-76)	0.423
Erythrocyte concentrate [mL] (IQR)	260 (0-1510)	250 (250-1020)	550 (470-730)	0.755
FFP [mL] (IQR)	1020 (910-1060)	1310 (1240-1380)	1060 (1030-1150)	0.385
Platelet concentrate [doses] (IQR)	8 (6-8)	8 (8-8)	5 (0-10)	0.919
Fibrinogen [g] (IQR)	2 (2-3)	2 (2-2)	2 (2-4)	0.698
Prothrombin complex [IU] (IQR)	0 (0-0)	0 (0-2500)	0 (0-0)	0.117
Thymoglobulin (IQR)	24 (22-24)	26 (24-29)	28 (24-30)	0.363
Thoracic drainage within the first 24h [mL] (IQR)	400 (300-700)	450 (400-550)	600 (450-650)	0.643
Hemoglobin before HTx [g/L] (IQR)	139 (137-146)	125 (121-160)	142 (138-149)	0.756
Platelets before HTx [10E9/L] (IQR)	205 (200-260)	282 (270-292)	188 (174-202)	0.102
PT-INR before HTx (IQR)	0.96 (0.92-1.15)	2.40 (1.18-2.41)	1.09 (1.06-1.13)	0.230
APTT before HTx [s] (IQR)	24.60 (23.25-26.40)	36.9 (27.7-37.5)	31.3 (28.9-47.3)	0.079
Fibrinogen before HTx [g/L] (IQR)	3.75 (3.35-4.15)	4.20 (3.40-5.70)	3.85 (3.70-4.95)	0.693
Hemoglobin 1st day after HTx [g/L] (IQR)	101 (93-111)	107 (95-112)	96 (95-100)	0.485
Platelets 1st day after HTx [10E9/L] (IQR)	113 (94-163)	135 (129-171)	98 (92-131)	0.330
PT-INR 1st day after HTx (IQR)	1.02 (0.99-1.09)	1.22 (1.03-1.43)	1.18 (1.10-1.23)	0.259
APTT 1st day after HTx [s] (IQR)	25.7 (24.6-27.4)	27.7 (23.9-28.4)	25.4 (24.6-25.9)	0.635
Fibrinogen 1st day after HTx [g/L] (IQR)	4.50 (3.80-6.70)	3.50 (3.40-3.70)	3.4 (3.0-3.4)	0.068
Hemoglobin 7th day after HTx [g/L] (IQR)	102 (96-111)	100 (92-101)	88 (88-92)	0.150
Platelets 7th day after HTx [10E9/L] (IQR)	117 (97-193)	112 (104-154)	93 (73-108)	0.228
PT-INR 7th day after HTx (IQR)	1.00 (0.98-1.02)	1.01 (0.95-1.12)	1.08 (1.06-1.11)	0.203
APTT 7th day after HTx [s] (IQR)	20.5 (19.1-21.0)	22.8 (21.3-23.3)	21.7 (21.1-22.2)	0.172
Fibrinogen 7th day after HTx [g/L] (IQR)	2.3 (2.2-3.3)	3.4 (2.9-5.2)	3.5 (2.3-3.5)	0.438

HTx – Heart Transplant; CMP – cardiomyopathy; eGFR – estimated Glomerular filtration rate; FFP – Fresh Frozen Plasma; PT-INR – Prothrombin Time – International Normalized Ratio; APTT – Activated Partial Thromboplastin Time.

TABLE 2. Potential predictors of periprocedural bleeding in the observed heart transplant patient population.

Correlation Pair	Spearman ρ	Correlation Significance
Total Chest Output in 24h & Pretransplant PT-INR	0.645	0.009*
Packed Red Blood Cell Transfusion Volume & Ischemic Etiology of Heart Failure	0.543	0.036*
Fresh Frozen Plasma Transfusion Volume & Pretransplant PT-INR	0.661	0.007*
Platelet Transfusion Volume & Ischemic Etiology of Heart Failure	0.583	0.022*
Prothrombin Complex Concentrate Transfusion & Pretransplant PT-INR	0.592	0.020*

PT-INR – Prothrombin Time – International Normalized Ratio

* P < 0.05

LITERATURE

- Crespo-Leiro MG, López-Vilella R, López Granados A, Mirabet-Pérez S, Díez-López C, Barge-Caballero E, et al. Use of Idarucizumab to reverse the anticoagulant effect of dabigatran in cardiac transplant surgery. A multicentric experience in Spain. Clin Transplant. 2019 Dec;33(12):e13748. <https://doi.org/10.1111/ctr.13748>