Koncentracija kalcineurinskih imunosupresiva i pojavnost posttransplantacijskih komplikacija u mlađih bolesnika

Levels of calcineurin inhibitors and incidence of posttransplantational complications in younger heart transplantation recipients

Ivo Planinc*,
Dora Fabijanović,
Jana Ljubas Maček,
Boško Skorić,
Hrvoje Jurin,
Jure Samardžić,
Nina Jakuš,
Hrvoje Gašparović,
Maja Čikeš,
Davor Miličić

Medicinski fakultet
Sveučilišta u Zagrebu, Klinički
bolnički centar Zagreb,
Zagreb, Hrvatska
University of Zagreb School of
Medicine, University Hospital
Centre Zagreb, Zagreb,
Croatia

RECEIVED:
September 20, 2016

ACCEPTED:
October 10, 2016

KLJUČNE RIJEČI: kalcineurinski inhibitori, transplantacija srca, ishodi.

KEYWORDS: calcineurin inhibitors, heart transplantation, outcomes.

CITATION: Cardiol Croat. 2016;11(10-11):396-397. | DOI: <http://dx.doi.org/10.15836/ccar2016.396>

***ADDRESS FOR CORRESPONDENCE:** Ivo Planinc, Klinički bolnički centar Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-1-2367-467 / E-mail: ivo.planinc@gmail.com

ORCID: Ivo Planinc, <http://orcid.org/0000-0003-0561-6704> • Dora Fabijanović, <http://orcid.org/0000-0003-2633-3439>

Jana Ljubas Maček, <http://orcid.org/0000-0001-7171-2206> • Bosko Skorić, <http://orcid.org/0000-0001-5979-2346>

Hrvoje Jurin, <http://orcid.org/0000-0002-2599-553X> • Jure Samardžić, <http://orcid.org/0000-0002-9346-6402>

Nina Jakuš, <http://orcid.org/0000-0001-7304-1127> • Hrvoje Gašparović, <http://orcid.org/0000-0002-2492-3702>

Maja Čikeš, <http://orcid.org/0000-0002-4772-5549> • Davor Miličić, <http://orcid.org/0000-0001-9101-1570>

Uvod: Dob primatelja je poznati prognostički čimbenik u bolesnika liječenih transplantacijom srca. Iako je preživljenje lošije u starijih primatelja organa, pojavnost posttransplantacijskih komplikacija je veća u mlađih bolesnika, a u literaturi nije točno opisan patofiziološki mehanizam u podlozi navedenog. S druge strane, poznato je kako su mlađi bolesnici manje suradljivi u uzimanju terapije.^{1,2} U ovoj studiji istraživali smo postizemo li teže u mlađih bolesnika željene koncentracije imunosupresivnih lijekova (konc. im. lij.) kalcineurinske skupine i ima li to posljedica na ishode.

Pacijenti i metode: Retrospektivno su prikupljeni podatci 114 odrasla konsektivna bolesnika kojima je učinjena transplantacija srca u Kliničkom bolničkom centru Zagreb u razdoblju od 2010. do 2015. godine, a u daljnjju analizu je uključeno 94 bolesnika koji su bili praćeni najmanje 30 dana (medijan dobi 54 godina, 71 muškarac, medijan praćenja 28 mjeseci). Bolesnici su podijeljeni u dvije skupine na temelju medijana dobi. Promatrani ishodi su: ukupno preživljenje, pojava odbacivanja koje je zahtjevalo liječenje i pojava vaskulopatije srčanog presatka. Skupljeni su podatci o konc. im. lij. 30, 180 i 365 dana nakon transplantacije srca (tablica 1). Za usporedbu skupina korišteni su Pearsonov hi kvadrat test i Mann-Whitney test, a za ukupno preživljenje izračunate su Kaplan-Meier krivulje.

Rezultati: Iako je značajno veći broj bolesnika u mlađoj skupini imao subterapijske konc. im. lij. 30 dana nakon transplantacije srca, u kasnijim vremenskim točkama nije bilo razlike, a unutar skupine nije bilo razlike u ishodima u odnosu na subterapijske konc. im. lij. Također, gledajući sve bolesnike, nije utvrđeno razlike u ishodima u odnosu na subterapijske konc. im. lij. Uspoređujući skupine, ukupno preživljenje i pojavnost vaskulopatije se nisu značajno razlikovali, dok je jedina statistički značajna razlika veća pojavnost odbacivanja koje je zahtjevalo liječenje u mlađoj skupini.

Zaključak: U mlađih bolesnika promatrane populacije našega centra teže postizemo ciljne vrijednosti kalcineurin-

Introduction: Recipient age is a well-established risk factor in heart transplantation. Although older recipients have worse survival, incidence of posttransplantational complications is higher in younger recipients, and so far there is no clear evidence of exact pathophysiological mechanism driving the latter. However, it is well known that younger patients have worse therapy compliance.^{1,2} In this study, we investigated if there is difference in achieving target immunosuppressive drugs levels according to age, and if it is associated with worse outcomes.

Patients and Methods: This is a single center, retrospective study that included 114 adult consecutive patients who underwent heart transplantation from 2010-2015., and of those 94 with at least 30-day follow up were selected for further analysis (median age 54, 71 male, median follow-up 28 months). Study population was divided into 2 groups according to age. We observed outcomes of overall survival, graft rejection episodes that were treated, and occurrence of vasculopathy. Immunosuppressive drug levels at days 30, 180, and 365 after heart transplantation were collected (Table 1). Pearson chi-squared, and Mann-Whitney tests were used for group comparisons, while Kaplan-Meier curves were used for survival analysis.

Results: Although significantly higher number of younger patients had subtherapeutic immunosuppressive drug levels at day 30, at other time points there was no difference; as well as there was no difference in outcomes among younger patients according to drug levels. Furthermore, taking into account all the patients, there was no difference in outcomes based solely on subtherapeutic drug levels. Study groups differed significantly only in incidence of graft rejection requiring treatment, that was more frequently observed in younger group of patients.

Conclusions: In our study population we achieved target immunosuppressive drug levels harder in younger patient at

skih imunosupresiva 30 dana nakon transplantacije srca, no navedeno nema značajnog utjecaja na ishod bolesnika. Također, mlađi bolesnici imaju slično preživljenje i pojavnost vaskulopatije kao stariji bolesnici, no veću pojavnost odbacivanja koje zahtjeva liječenje.

30-days after heart transplantation, however without influence on survival. Furthermore, younger patients had similar survival and occurrence of vasculopathy as older patients, and higher occurrence of graft rejection requiring treatment.

TABLE 1. Patients achieving subtherapeutic immunosuppressive drug levels at 30, 180, and 365 days after heart transplantation according to age groups. Comparison of outcomes (graft rejection requiring treatment and vasculopathy) between study groups.

	Younger patients (<54 years)	Older patients (>54 years)	
N	47	47	
Subtherapeutic immunosuppressive drug levels (calcineurin inhibitors)			
- 30 days after heart transplantation	25/47 (53%)	13/47 (28%)	p=0.012
- 180 days after heart transplantation	10/44 (23%)	12/39 (31%)	P=0.407
- 365 days after heart transplantation	3/38 (8%)	2/29 (7%)	P=0.878
Graft rejection requiring treatment	13/47 (28%)	2/47 (4%)	p=0.002
Vasculopathy	13/44 (30%)	6/46 (13%)	p=0.055

LITERATURE

1. Grady KL, Jalowiec A, White-Williams C. Patient compliance at one year and two years after heart transplantation. J Heart Lung Transplant. 1998;17:383-394.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9588583>
2. Tjang YS, van der Heijden GJ, Tenderich G, Körfer R, Grobbee DE. Impact of recipient's age on heart transplantation outcome. Ann Thorac Surg. 2008;85(6):2051-5.
DOI: <http://dx.doi.org/10.1016/j.athoracsur.2008.02.015>