Utjecaj poslijetransplantacijske ishemijsko-reperfuzijske ozljede i staničnog odbacivanja na razvoj vaskulopatije presatka

Influence of post-transplant ischemia-reperfusion injury and cellular rejection on the development of cardiac allograft vasculopathy

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Uvod: Vaskulopatija presatka (CAV) je kronična komplikacija transplantacije srca (HTx) koja predstavlja izazov u liječenju zbog difuznog uzorka zahvaćanja koronarnih arterija. Teži stupnjevi bolesti nisu prikladni za revaskularizaciju, zbog čega retransplantacija često ostaje jedina mogućnost liječenja.[1-3]

Bolesnici i metode: Od ukupno 176 bolesnika u praćenju nakon HTx, učinjene u razdoblju između 2001. i 2015. godine, 129 bolesnika je podvrgnuto barem jednoj koronarografiji kojom je u 45 bolesnika dokazan CAV (te dodatno u dva bolesnika na temelju kliničkog i obdukcijskog nalaza). Prosječna dob iznosila je 51,6 ± 12,6 godina, 78 % bolesnika su bili muškog spola, a prosječno vrijeme praćenja 3 godine (IQR 2-6 godina). Pojavnost CAV-a evaluirana je koronarografijom i analizirana s obzirom na trajanje vremena ishemije (VI), rane koncentracije visokoosjetljivog troponina T (hsTnT) te stupnja staničnog odbacivanja (SO).

Rezultati: Rane vrijednosti hsTnT (unutar 3 mjeseca poslije HTx) značajno su više kod produljenog VI (p = 0,040), no nemaju prediktivni značaj za pojavnost CAV-a (p = 0,529) niti učestalije SO. VI presatka ne korelira s učestalošću značajnog SO. Bolesnici s težim stupnjem CAV-a imali su značajno kraće preživljavanje od onih bez CAV-a ili s blažim/umjerenim oblicima bolesti (p = 0,016) (**slika 1**). SO,

Introduction: Cardiac allograft vasculopathy (CAV) is a chronic heart transplant complication (HTx) that presents a treatment challenge owing to the diffuse pattern of coronary artery involvement. Severe forms of the disease are not suitable for revascularization, which is why retransplantation often remains the only treatment option.[1-3]

Patients and Methods: Out of a total of 176 patients following HTx, between 2001 and 2015, 129 patients were subjected to at least one coronary artery angiography by which 45 patients were CAV positive (and additionally in two patients based on clinical and autopsy findings). The mean age was 51.6±12.6 years, 78% of patients were male and the average follow-up was 3 years (IQR 2-6 years). The presence of CAV was evaluated by coronary artery angiography and analyzed with respect to the duration of ischemic time (IT), the early concentration of high-sensitive troponin T (hsTnT) and the degree of cellular graft rejection (CR).

Results: Early hsTnT values (within 3 months after HTx) are significantly higher with prolonged IT (p=0.040) but have no predictive significance for CAV (p=0.529) or more frequent CR. IT does not correlate with the frequency of significant CR. Patients with severe CAV had significantly shorter survival than those without CAV or with mild/moderate forms of disease (p=0.016) (**Figure 1**). CR, ex-

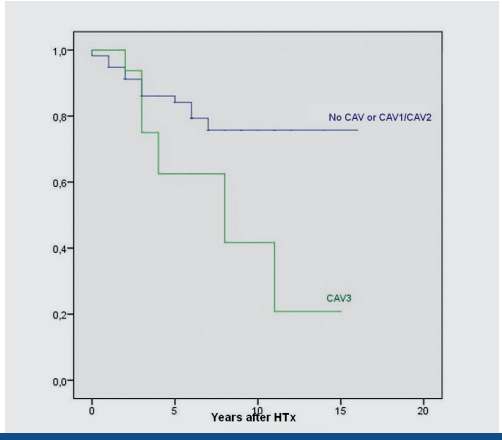

FIGURE 1. Patient survival curves depending on the degree of vasculopathy: CAV-free patients or those with mild-to-moderate CAV (CAV1/CAV2) had significantly longer survival in comparison to patients with severe CAV (CAV3).

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izraženo prosječnim indeksom odbacivanja bolesnika, izrazito povisuje rizika nastanka CAV-a (p <0,001, OR 16.0), uključujući i epizode blagog SO tijekom 1. godine nakon HTx. CAV je dokazan u 36 % bolesnika CAV (N = 47/131), a bio je uzrok direktne kasnije smrtnosti u 10,2 % bolesnika. Udio bolesnika bez incidencije CAV-a krajem 1. godine iznosio je 86 %, 2. godine 75 %, 5. godine 57 % i krajem 10. godine 25 %.

Zaključak: Izraženija ishemijsko-reperfuzijska ozljeda presatka, određena duljim VI-je, praćena je višim koncentracijama hsTnT-a rano poslije HTx. Produljeno VI ne stvara sklonost češćem SO, kasnijem razvoju CAV-a ili kraćem preživljavanju. Bolesnici s CAV-om imaju značajno kraće preživljavanje samo kod težih oblika bolesti, dok se blaži i umjereni oblici uspješnije liječe i ne utječu na preživljavanje. Stanično odbacivanje je povezano s višim rizikom razvoja CAV-a, što može imati bitne implikacije u kliničkom praćenju i liječenju.

pressed as an average patient rejection index, significantly increases the risk of CAV (p<0.001, OR 16.0), including episodes of mild CR during the first year after HTx. CAV was proven in 36% of CAV patients (N=47/131) and was the cause of direct later mortality in 10.2% of patients. Freedom from CAV at the end of the 1st year was 86%, 2nd 75%, 5th 57% and 10th 25%.

Conclusion: More pronounced reperfusion-ischemic injury, determined by longer IT, correlated with higher concentrations of hsTnT early after HTx. The prolonged IT does not present predisposition for a stronger CR, later development of CAV or shorter survival. CAV patients have significantly shorter survival only in more severe forms of the disease, while milder and moderate forms are more effectively treated and therefore do not affect survival. Cellular rejection is associated with higher risk of CAV development, which may have important implications in clinical monitoring and treatment.

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