Učinkovitost terapije kardiovaskularnim implantabilnim elektroničkim uređajima s defibrilatorskom komponentom ovisno o strategiji liječenja mehaničkom srčanom crpkom: podatci iz Registra PCHF-VAD

Effectiveness of cardiovascular implantable electronic devices with a defibrillator component therapy according to ventricular assist device implant strategy: data from the PCHF-VAD registry

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Uvod: Nosioci ljevostrane mehaničke srčane crpke (LVAD, engl. *left ventricular assist device*) uređaja tipično su predodređeni za jednu od tri strategije liječenja – premoštenje do transplantacije (BTT, engl. *bridge to transplantation*), premoštenje do odluke (BTD, engl. *bridge to decision*) ili trajna terapija (DT, engl. *destination therapy*). Strategija često odražava akutnu ili kroničnu narav zatajivanja srca, dob bolesnika, komorbiditete te opće stanje bolesnika.[1,2] Gotovo polovica nosioca LVAD uređaja istovremeno su liječeni i kardiovaskularnim implantabilnim elektroničkim uređajima s defibrilatorskom komponentom (CIED-D, engl. *cardiovascular implantable electronic devices with a defibrillator component*), pri čemu smo u ranijoj analizi dokazali povezanost CIED-D s boljim preživljenjem LVAD nosioca. Cilj istraživanja jest utvrditi mijenja li strategija liječenja LVAD uređajem učinkovitost CIED-D terapije.

Bolesnici i metode: Putem multicentričnog registra koji je obuhvaćao 12 europskih centara uključeno je 429 bolesnika s LVAD uređajima s kon-

Background: LVAD (left ventricular assist device) candidates are typically stratified according to three most typical treatment strategies – **BTT** (bridge to transplantation), **BTD** (bridge to decision) or **DT** (destination therapy), reflecting the acute vs. chronic state of disease, age, comorbidities and overall condition of the patient.[1,2] Approximately half of the European LVAD carriers are concomitantly treated with CIED-D (cardiovascular implantable electronic devices with a defibrillator component), in which we have shown substantial survival benefit from concomitant therapy. We aimed to investigate in more detail whether specific LVAD treatment strategies portended a difference in benefit from CIED-D therapy.

Methods: 429 patients with continuous flow LVADs have been included in a multicentre registry formed by 12 European centres (median age 56 (IQR 46-62), 82% male), 53% also had CIED-D. Patients were analyzed according to VAD intention (**Table 1**). Median follow-up time was 1.1 years (IQR 0.5-2.0) from the time of LVAD implant.

TABLE 1. Baseline characteristics of the studied left ventricular assist device population according to implant strategy.

	BTT (N=305)	BTD (N=68)	DT (N=56)	P value
Female gender, n (%)	53 (17.4%)	19 (27.9%)	4 (7.1%)	0.01
Age	50.28 ±12.68	51.54 ± 13.36	64.85 ± 7.30	<0.001
Etiology of disease				0.18
Dilated cardiomyopathy, n (%)	140 (45.9%)	23 (33.8%)	18 (32.1%)	
Ischemic cardiomyopathy, n (%)	132 (43.3%)	35 (51.5%)	31 (55.4%)	
Other cause of heart failure, n (%)	33 (10.8%)	10 (14.7%)	7 (12.5%)	
Arterial hypertension, n (%)	61 (20.0%)	15 (22.1%)	23 (41.1%)	0.003
Diabetes mellitus, n (%)	49 (16.1%)	13 (19.1%)	26 (46.4%)	<0.001
Chronic kidney disease, n (%)	63 (20.7%)	14 (20.6%)	24 (42.9%)	0.001
Coronary artery disease, n (%)	65 (21.3%)	17 (25.0%)	22 (39.3%)	0.015
Chronic obstructive pulmonary disease, n (%)	21 (6.9%)	6 (8.8%)	15 (26.8%)	<0.001
Atrial fibrillation/flutter, n (%)	86 (28.2%)	11 (16.2%)	29 (51.8%)	<0.001
Ventricular arrhythmias, n (%)	71 (23.3%)	15 (22.1%)	16 (28.6%)	0.65
Cerebrovascular accidents, n (%)	21 (6.9%)	8 (11.8%)	4 (7.1%)	0.39
No prior cardiac surgery, n (%)	265 (86.9%)	59 (86.8%)	52 (92.9%)	0.45
INTERMACS class, n (%)				<0.001
Class 1	49 (16.3%)	17 (26.2%)	3 (5.6%)	
Class 2	94 (31.3%)	18 (27.7%)	5 (9.3%)	
Class 3	89 (29.7%)	13 (20.0%)	28 (51.9%)	
Class 4-7	68 (22.7%)	17 (26.2%)	18 (33.3%)	
Device type, n (%)				<0.001
Heart Mate II	193 (63.3%)	26 (38.2%)	15 (26.8%)	
Heart Ware	56 (18.4%)	20 (29.4%)	16 (28.6%)	
Heart Mate 3	49 (16.1%)	22 (32.4%)	14 (25.0%)	
Other device	7 (2.3%)	0 (0.0%)	11 (19.6%)	
Prior life support, n (%)				<0.001
None	214 (73.0%)	42 (61.8%)	52 (92.9%)	
Extracorporeal membrane oxygenation	24 (8.2%)	8 (11.8%)	1 (1.8%)	
Temporary LVAD	2 (0.7%)	2 (2.9%)	0 (0.0%)	
Temporary BiVAD	0 (0.0%)	1 (1.5%)	0 (0.0%)	
Intraaortic balloon pump	42 (14.3%)	7 (10.3%)	3 (5.4%)	
Other life support	11 (3.8%)	8 (11.8%)	0 (0.0%)	
CIED-D therapy during VAD support, n (%)	137 (44.9%)	23 (33.8%)	42 (75.0%)	0.001

BTT = bridge to transplantation; BTD = bridge to decision; DT = destination therapy; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; BiVAD = biventricular assist device; CIED-D = cardiovascular implantable electronic devices with a defibrillator component; VAD = ventricular assist device.

tinuiranim protokom (medijan dobi 56 godina (IQR 46-62), 82% muškaraca), od kojih su 53% liječeni CIED-D terapijom. Bolesnici su stratificirani prema strategiji liječenja LVAD-om (**tablica 1**). Medijan praćenja bila je 1,1 godina (IQR 0.5-2.0) od implantacije LVAD uređaja.

Rezultati: Osnovni podatci o bolesnicima ovisno o strategiji liječenja prikazani su u **tablici 1.** Učestalosti događaja primarnog ishoda (ukupna smrtnost) bila je jednoliko raspoređena među skupinama (učestalost događaja na 100 osoba-godina): *BTT*: 22,4 [18.2-27.5], *BTD*: 23,5 [15.2-36.4], *DT*: 21,7 [13.7-34.5]), sa sličnim HR za ukupnu smrtnost u usporedbi s *BTT* skupinom: HR (95% CI) za *BTD* i *DT* iznosi 1.06 (0.65-1.73), p=0,809 i 1.00 (0.60-1.65), p=0,987. Kontinuirana CIED-D terapija za vrijeme LVAD potpore bila je povezana sa značajno boljim preživljenjem u skupinama *BTT* i *DT*: za skupinu *BTT* bolesnika CIED-D terapija bila je povezana sa 40% smanjenjem smrtnosti (p=0,017) te 65% za skupinu DT (p=0.032). Strategija LVAD liječenja nije mijenjala povezanost između liječenja primjenom CIED-D i smanjenja smrtnosti (interakcija p=0,055).

Zaključak: Ovom analizom nalazi se povezanost između liječenja CIED-D uređajem i smanjenja smrtnosti kod bolesnika predodređenih za liječenje *BTT* i *DT* strategijom. Međutim, niti *BTT* niti *BTD* strategija nije modificirala učinak CIED-D terapije na preživljenje. Ovaj nalaz potvrđuje važnost nastavka CIED-D terapije tijekom čitave LVAD potpore.

Results: Table 1 presents the baseline characteristics of patients according to LVAD treatment strategy. Crude event rates for the primary outcome (all-cause mortality) were equally distributed among the three groups (event rates per 100 person-years): *BTT*: 22.4 [18.2-27.5], *BTD*: 23.5 [15.2-36.4], *DT*: 21.7 [13.7-34.5]), with similar hazard ratios for all-cause death compared to *BTT* group in unadjusted analysis: HR (95% CI) for *BTD* and *DT* was 1.06 (0.65-1.73), p=0.809 and 1.00 (0.60-1.65), p=0.987, respectively. CIED-D use contiguously with an LVAD significantly altered survival in the *BTT* and *DT* groups: for *BTT* patients, CIED-D use carried a 40% mortality reduction (p=0.017) and 65% for *DT* group (p=0.032). However, LVAD treatment strategy at implantation did not modify the association between CIED-D therapy and mortality reduction (interaction p=0.055).

Conclusion: In this analysis, concomitant CIED-D therapy during LVAD support was associated with a reduction in mortality in patients receiving an LVAD as *BTT* and *DT*. However, neither *BTT* or *BTD* strategy modified the treatment effect of CIED-D on survival. This finding confirms the relevance of continuation of CIED-D therapy throughout the duration of LVAD support.

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