Differences in early outcomes for left ventricular assist device recipients implanted before and during the COVID-19 pandemic

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INTRODUCTION

Advanced heart failure (HF) affects between 1% and 10% of all HF patients, and its prevalence is increasing. Prognosis is particularly poor, with mortality ranging from 25% to 75% of patients after one year [1]. As advanced HF is severe and progressive, it is of paramount importance that the appropriate timing is found for successful but, otherwise, highly-sophisticated therapies. These interventions are not without risk and entail high costs; they include heart transplantation (HTX) or implantation of left ventricular assist devices (LVADs). Over the years, LVADs have become a mature and effective option in selected patients with advanced HF [1]. Ever since the first cases of the coronavirus disease (COVID-19) were reported at the end of 2019, the pandemic has continued to spread globally, profoundly impacting healthcare systems worldwide. Presently, it is unknown to what extent LVAD programs and the qualification process for patients have been affected during the COVID-19 outbreak. Since the introduction of an LVAD program at our center, more than 100 patients have undergone LVAD implantation. As in other centers, our experience has substantially accumulated over the years, clearly indicating a "learning curve" [2]. Thus, for the first time, we present an analysis of the impact of COVID-19 on the LVAD program.

METHODS

This is a single-center observational study. The study population involved all of the 104 patients who were implanted with an LVAD in Krakow, Poland, including 73 patients implanted between 20th October 2015 (first LVAD implantation) and 31st December 2019 (i.e., the pre-COVID-19 period), and 31 patients implanted from 1st January 2020 to 31st December 2021 (i.e. during the COVID-19 period). Patient demographics, clinical characteristics, laboratory, echocardiographic, management, and outcomes were extracted from the electronic medical records. Follow-up data were collected through June 2022. The main outcomes of our study were survival rate, number, and reasons for urgent hospital admissions, including right heart failure, drive line infections, stroke, LVAD thrombosis, gastrointestinal bleeding, and serious ventricular arrhythmia (ventricular tachycardia/fibrillation). The study was approved by the relevant ethics committee (number 1072.6120.253.2021).

Statistical analysis

Continuous data were presented as means (standard deviations) or medians with interquartile ranges. The normality of distribution of variables was assessed with the Shapiro-Wilk test. Comparisons of laboratory, clinical, echocardiographic, and hemodynamic pa-

Table 1. Six-month outcomes for LVAD recipients

Parameter	Pre-COVID-19 group (n = 73)	COVID-19 group (n = 31)	*P*-value
Survival rate, n (%)	60 (82.2)	23 (74.2)	0.23
Death during hospitalization for implantation, n (%)	10/13 (76.9)	6/8 (75)	0.32
Number of patients hospitalized for LVAD-related causes, n (%:)	21 (35)	15 (65.2)	**0.03**
RHF	**6 (28.6)**	**13 (86.7)**	**0.007**
Drive-line infection	9 (42.9)	1 (6.7)	0.15
Stroke	1 (4.8)	0	0.72
LVAD thrombosis	0	1 (6.7)	0.28
Gastrointestinal bleeding	3 (14.3)	0	0.37
VF/VT	2 (9.5)	0	0.52
NYHA, median (IQR)	1.5 (1–2)	2.5 (1.5–3.0)	0.007
NYHA, n (%)	I — 22 (36.7)	I — 3 (13.0)	<0.001
	II — 27 (45.0)	II — 2 (8.7)	
	III — 8 (13.3)	III — 13 (56.5)	
	IV — 3 (5.0)	IV — 5 (21.7)	
NYHA III–IV, n (%)	11 (18.3)	18 (78.3)	<0.001
NT-proBNP, pg/ml median (IQR)	1386 (745–2315)	**2721.5 (1274–37 975**)	0.05
Hb, g/dl, median (IQR)	12.6 (11.5–14.2)	12.8 (10.8–13.7)	0.35
PLT, × 10^3/µl, median (IQR)	221.5 (190–265)	256 (197–323)	0.16
INR, median (IQR)	2.3 (2.02–2.74)	1.91 (1.7–2.9)	0.23
LDH, U/L, median (IQR)	399 (318–472)	216 (212–228)	<0.001
eGFR, ml/min/m^2, median (IQR)	71.5 (57–87)	65 (45–105)	0.9
Creatinine, µmol/l, median (IQR)	99 (85–122)	121.5 (99–141)	0.09
Sodium, mmol/l, median (IQR)	140 (138–142)	138 (133–141)	0.06
Potassium, mmol/l, median (IQR)	4.4 (4.1–4.6)	4.9 (4.5–5.9)	<0.001
Aspat, U/l, median (IQR)	25 (20–30)	22.5 (19–28)	0.49
Alat, U/L, median (IQR)	21 (16–30)	17.5 (12–30)	0.36
Bilirubin, µmol/l, median (IQR)	10.9 (7.4–14.9)	8.4 (6.6–13.5)	0.24

Abbreviations: Alat, alanine aminotransferase; Aspat, aminotransferase aspartate; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; IQR, interquartile range; INR, international normalized ratio; LDH, lactate dehydrogenase; LVAD, left ventricular assist device; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; PTL, platelet; RHF, right heart failure; VE, ventricular extrasystole; VT/VF, ventricular tachycardia/fibrillation

rameters between the two groups were conducted with the Mann–Whitney U test or Student's t-test, depending on the normality of the distribution. Categorical data were presented as numbers (percentages), and χ^2 or Fisher's exact tests were used to compare them. Results were considered statistically significant when the *P*-value was <0.05. Statistical analyses were conducted with Statistica 13.1.

RESULTS AND DISCUSSION

The annual number of procedures was similar in both periods. The LVAD recipients during the COVID-19 period were older: mean (standard deviation) 60.6 (8.5) vs. 56.1 (10.2); *P* = 0.02. The etiology of HF differed between the groups: before the COVID-19 pandemic, the majority of patients had HF due to coronary artery disease (CAD; n = 60; 82.2%), with the remaining patients suffering from dilated cardiomyopathy (DCM). However, during the COVID-19 period, there were 18 (58.1%) patients with CAD, and 13 (41.9%) with DCM (*P* = 0.009). Another difference was that more than two-thirds (69.9%) of the patients from the pre-COVID-19 period were in New York Heart Association (NYHA) class IV in comparison to one-third (32.3%) from the COVID-19 period (*P* = 0.02) (Supplementary material, *Table S1*).

There were no differences in terms of the 6-month survival rate: 60 (82.2%) vs. 23 (74.2%) (*P* = 0.23) between patients operated on before and during the COVID-19 pandemic. In both groups, the substantial majority of deaths occurred during hospitalization for implantation (76.9% of all deaths in the pre-COVID-19 and 75% in the COVID-19 periods; *P* = 0.32). Nonetheless, it turned out that more patients from the COVID-19 period required hospitalization in the first 6 months. There were also significant differences among the causes of admissions between the groups, with right heart failure (RHF) as the main cause of hospitalization during the COVID-19 outbreak (13/15 [86.7%] vs. 6/21 [28.6%]; *P* = 0.007) (Table 1). Still, at the 6-month follow-up, patients from the COVID-19 period displayed inferior functional status compared to the pre-COVID-19 group (NYHA class: median [interquartile range] 1.5 [1–2] vs. 2.5 [1.5–3.0]; *P* = 0.007); in terms of the number of patients in NYHA class III–IV (18 [78.3%] vs. 11 [18.3%]; *P* <0.001).

At the beginning of the COVID-19 pandemic, all HTX programs were jeopardized. Bearing in mind the numerous advantages of HTX over LVAD, the fact remains that LVAD pumps are readily available and can be scheduled for implantation whenever needed, a set of circumstances that

will never be the case for HTX. Overall, according to the 12th INTERMACS report, there were 26 688 continuous-flow LVAD procedures in the years 2011–2020, with a precipitous decrease in 2020 due to the pandemic [1]. However, there are also centers, including our own (reporting 16 implants in 2020 and 15 in 2021, which closely parallels the 14–20 annual procedures in 2016–2019) which recorded similar rates of LVAD implantation during the pandemic years [1].

For at least the last 10 years, it has been a common trend worldwide that older patients burdened with more comorbidities have been implanted with LVADs [1]. At the same time, clinical status at the index procedure has gradually become less severe; approximately 10 years ago, the vast majority of patients were in NYHA class IV or INTERMACS 1–2 profile, whereas at present, the majority are in 3–4 INTERMACS [1, 2]. Although we did not observe significant differences in INTERMACS scores between patients from the pre-COVID-19 and COVID-19 periods, before COVID-19, 6 of 73 (8.2%) patients were in INTERMACS 1 while no such patient was implanted during the COVID-19 period. We report that patients implanted during the COVID-19 pandemic were at least four years older than before the pandemic, which reflects a global trend. Importantly, we also observed a significant shift in the HF etiology, which was predominantly CAD before the pandemic; however, during the COVID-19 outbreak itself, the ratio of CAD and DCM etiology was found to be similar.

In the first randomized REMATCH trial (LVAD vs. medical therapy), 1-year survival after LVAD implantation was 52% and only 25% in medically treated patients. In the most recent (pre-COVID-19 years), 1 and 2-year survival soared to 82.8% and 74.1%, respectively; still, this is somewhat inferior to the 1-year survival rate of more than 90% of patients after HTX [1]. Additional data have been provided by Gyoten et al. [3], who recently published 1-, 3-, and 5-year survival rates following LVAD implantation (2009–2020) of 66%, 49.4%, and 37.4%, respectively. To the best of our knowledge, no separate data on survival following LVAD implantation in patients during the COVID-19 pandemic has been published yet. Here, we report a 6-month survival rate of 82.2% and 74.2% in LVAD recipients from the pre-COVID-19 and COVID-19 periods, respectively. Although numerically the 6-month survival rate in patients implanted during the COVID-19 pandemic appears a little worse, it is statistically insignificant and seems to be within an acceptable range.

It is worth noting that the majority of deaths occurred during hospitalization for implantation, which is typical and was also reported previously [2–4]. Unfortunately, complications still occur following LVAD implantation, e.g. in one report from the UK, 5 years after the LVAD procedure, 26.1% of patients suffered a stroke, 23.6% acquired an LVAD-related infection, and 13.4% underwent LVAD re-implantation. Patients implanted during the COVID-19 outbreak were more often hospitalized for LVAD-related complications than those operated on previously. Interestingly, we noticed distinct causes for hospitalization during those two periods. In the pre-COVID-19 period, it was mainly drive-line infections, gastrointestinal bleeding, and strokes with RHF which were found to occur in approximately one-fourth of cases. This was different during the COVID-19 period when it was predominantly RHF which was encountered in more than half of the hospitalized patients. Perhaps, it is too early to draw any firm conclusions, but it may be that right ventricle in older patients is more susceptible to the increased flow created by the LVAD. We also saw that patients from the COVID-19 period more often had atrial fibrillation, a confirmed cause of progressive RHF. It is not surprising that both end-stage HF candidates for LVADs and LVAD recipients are particularly vulnerable to severe and complicated course of SARS-CoV-2 infection as this association has been already demonstrated. Lastly, latent SARS-CoV-2 infections, primarily affecting the lungs, may impose an additional burden on the right ventricle.

In conclusion, we found that LVAD recipients implanted during the COVID-19 pandemic differ significantly from those operated on earlier in terms of numerous variables, including age, HF etiology, and LV diameter. Although 6-month mortality was similar in both groups, patients implanted during the COVID-19 pandemic were more frequently re-admitted for RHF.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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