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Comparison of the course of SARS-CoV-2 infection in left ventricular assist device recipients implanted before and during COVID-19 pandemic

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Heart transplantation (HTX) or implantation of left ventricular assist devices (LVADs) are a proven and effective treatment for highly selected patients with end-stage heart failure (HF). Prior to the coronavirus disease 2019 (COVID-19) pandemic, there were approximately 3000 HTXs and 3000 LVADs performed annually in the United States (US) [1, 2]. However, the ongoing COVID-19 outbreak challenged all areas of medical service, including HTX and LVADs programs worldwide. COVID-19 turned out to be a very serious and unpredictable disease, frequently leading to respiratory failure and eventually multi-organ failure [3]. Patients suffering from comorbidities, including end-stage HF, are vulnerable to severe course of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [4]. Most likely, LVAD patients are particularly prone to various complications following COVID-19; however, except for dozens case reports being published, there is scarce of data on this subject. Therefore, the present study aimed to analyze rate of infection, clinical course, applied treatment, and outcome in all patients who were implanted with LAVD in the documented center. Uniquely, the course of COVID-19 infection was compared in patients who were operated on before and during the pandemic.

This is a single-center observational study that encompasses a period of 2 years during the pandemic between 1st January 2020 and 31st December 2021. All patient data were extracted from electronic medical records. Follow-up data was collected through June 2022. All SARS-CoV-2 tests were carried out with reverse transcriptase polymerase chain reaction assays. The study was approved by the relevant ethics committees (number 1072.6120.253.2021).

Comparisons of laboratory, clinical, echocardiographic, and hemodynamic parameters between the two groups were conducted with the U Mann-Whitney or Student t-test, depending on the normality of the distribution. All results were considered statistically significant with a p value < 0.05.

The study population consisted of all LVAD--recipients who survived (48 out of 73; 65.7%) until the beginning of the COVID-19 outbreak (being implanted between 20th October 2015 and

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Table 1. Characteristics of coronavirus disease 2019 (COVID-19) infection among left ventricular assist devices (LVAD) recipients implanted before and during pandemic era.

Parametr	Pre-COVID-19 period (n = 14)	COVID-19 period (n = 6)	P
Age [years]	60.8 (10.5)	62.7 (5.1)	**0.69**
Time since LVAD implantation till COVID-19 infection [months]	36 (24–38)	12 (11–14)	**0.001**
SpO_2 on admission [%]	86.5 (81–95)	95 (94–96)	**0.05**
Respiratory rate	25 (20–29)	20 (17–22)	0.23
Heart rate [bpm]	90 (85–97)	82.5 (70–95)	0.81
MAP [mmHg]	69 (56.5–85)	79 (72–86)	**0.01**
Temperature on admission [°]	37.6 (37.1–38.0)	37.2 (36.8–37.8)	0.38
WBC [10 ^ $10^3/\mu$L]	9.42 (8.95–15.7)	6.83 (2.86–8.,6)	**0.05**
Lymphocyte [%] [25–45%]	3.55 (1.8–5.5)	15.4 (14–16.4)	**0.05**
Neutrophil [%] [40–75%]	91.9 (90.5–94.9)	73.5 (55.6–80.0)	**0.05**
Prokalcytonina [ng/mL]	3.6 (0.65–11.1)	0.6 (0.1–0.9)	**0.02**
CRP [mg/L]	137.5 (101–193)	86.6 (68–101)	**0.03**
Troponin [< 0.1 ng/mL]	0.171 (0.076–0.254)	0.116 (0.035–0.56)	0.85
D-dimers [mg/dL]	3877 (2183–5310)	3250 (2800–6305)	0.86
NT-proBNP [pg/mL]	3255 (1372–8147)	2420 (1733–3760)	0.84
Interleukin 16 [pg/mL]	112.5 (95–134.6)	87 (25.3–94.0)	**0.05**
Fibrynogen [g/L]	5.75 (4.9–6.7)	6.25 (5–8)	0.59
Dexamethasone oral/i.v.	12 (85.7%)	5 (100%)	0.68
VKA	3 (21.4%)	1 (20%)	0.63
LMWH	11(78.6%)	4 (80%)	055
Antibiotics	12 (85.7%)	5 (100%)	0.86
Remdesivir	12 (85.7%)	4 (80%)	0.68
Length of hospitality [days]	26.5 (20.5–30)	20 (19–23)	0.71
Oxygen therapy [1/0]	14 (100%)	3 (60%)	0.08
High-flow nasal cannula	5 (41.6%)	0	–
Mechanical ventilation	2/14 (14.3%)	0	–
Inotropes	12/14 (85.71%)	2 (40%)	**0.04**
Inotropes [days]	19 (16–23)	16 (14–20)	0.56

CRP — C-reactive protein; IL-6 — interleukin 6; LMWH — low molecular weight heparin; MAP — mean arterial pressure; NT-proBNP — N-terminal pro-B-type natriuretic peptide; SpO_2 — oxygenation; VKA — vitamin K antagonist; WBC — white blood cells

31st December 2019 — i.e., the pre-COVID-19 period) and on all 31 patients implanted during the COVID-19 period. The rate of COVID-19 infection was similar among both groups (pre-COVID-19: 16 [33.3%] vs. COVID-19: 11 [35.5%]; p = 0.79]); however, LVAD recipients from the pre-COVID period more often required hospitalization due to COVID-19 (14/16 [87.5%] vs. 5/11 [45.5%]; p = 0.02). Three (18.8%) and 2 (18.2%) patients from the pre- and COVID-19 periods died due to COVID-19 (p = 0.97). The average vaccination rate was 63.3%. All of the hospitalized patients from the pre-COVID-19 period required oxygen therapy (nasal cannula/face mask) in comparison to two-thirds from the COVID-19 period. Five patients from the pre-COVID-19 period were subjected to high-flow nasal cannula or non-invasive ventilation, and 2 patients out of those required intubation and mechanical ventilation, whereas interventions of this kind were not applied to any of the COVID-19 period patients. None of the patients underwent extracorporeal membrane oxygenation therapy. Laboratory tests results showed higher levels of white blood cells, neutrophils and inflammatory markers in patients from the pre-COVID-19 period. There were no differences in the distribution

of COVID-19 specific therapies, including remdesivir and dexamethasone, between the groups (Table 1).

An extensive literature search revealed only two papers reporting the course of COVID-19 infection in a series of LVAD recipients, both from the US. The Trans-CoV-VAD registry performed in 9 centers in the US in 2020 reported on 40 LVAD patients with COVID-19; among those, 18% were oligo-symptomatic, and basically did not require any intervention. Twenty-six (60%) patients required hospitalization, out of whom 8 (20%) patients died [5]. The second paper on 28 LVAD patients with COVID-19 comes from Aurora, Colorado, and covers a period of 12 months (March 2020 – March 2021) [6]. Out of those, 17 (61%) were oligo-symptomatic; nonetheless, 24 (86%) of the patients were hospitalized. The authors report overall mortality as 9 (32%); however, only 5 (18%) patients died clearly as a result of COVID-19, whereas the remaining 4 (14%) patients died after prolonged and complicated hospitalizations.

Taking all of these results into account, it was noted that the COVID-19-related mortality rate of 18% found in the present group is highly comparable. This observed rate is at least 8–9 times higher than in the general population, which in Poland is reported to be 1.93%, and in the US, 1.8% [7]. Overall, with the group herein, the hospitalization rate due to COVID-19 was 70.4% (with a different rate being recorded between patients implanted before and during the COVID-19 pandemic), which is in line with hospitalization rates in the US, range from 60% to 86%. These observations potentially warrant a comment; although any hospital admissions during a pandemic should be kept to a minimum, nonetheless, physicians probably had a low threshold for admitting LVAD patients, particularly those infected with the highly unpredictable SARS-CoV-2. The length of hospital stay was also similar, with those reported by US researchers as being typical for a severe course of COVID-19.

Surprisingly, we noticed considerable differences in the management of COVID-19 between our patients and those in the US, e.g., while the clear majority of our group required some form of oxygen therapy, oxygen supplementation was provided to approximately half of patients from the Trans-CoV-VAD registry, and to 39% of those from the University of Colorado. In addition, while almost all of our hospitalized patients were treated with steroids, and 90% of them with remdesivir — this treatment was applied in 39% and 32% of patients respectively from the University of Colorado, and in 7 and only 1 patient respectively from the Trans-CoV-VAD registry. Remarkably, despite very conflicting or even a lack of evidence for its efficacy or recommendations for its use, hydroxychloroquine was used as a treatment drug in 6 patients from the Trans-CoV-VAD registry. Finally, it should be pointed out that despite numerous admonishments from our medical personnel, vaccination coverage remained quite low at approximately 62%; although this is slightly higher than in the general Polish population, it is grossly suboptimal for such a high-risk population.

One-third of LVAD patients contracted a COVID-19 infection. Although COVID-19 related mortality was several times higher than in the general population, it was similar in patients implanted in the pre- and COVID-19 periods.

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