Circulation: Heart Failure

Psychosocial Risk and Its Association With Outcomes in Continuous-Flow Left Ventricular Assist Device Patients

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BACKGROUND: Advanced heart failure therapies such as left ventricular assist device (LVAD) implantation require intricate follow-up and complex care. We sought to explore the burden of psychosocial risk factors among patients with LVAD and their impact on postimplant outcomes using the Interagency Registry for Mechanically Assisted Circulatory Support.

METHODS: Adult patients in the Interagency Registry for Mechanically Assisted Circulatory Support requiring durable LVAD between 2008 and 2017 were included. Individuals were determined to have psychosocial risk if they had one of the following: (1) limited social support; (2) limited cognition; (3) substance abuse (alcohol and drug); (4) severe psychiatric disease (including major depression and other major psychiatric diagnosis); and (5) repeated noncompliance. Univariate and multivariate Cox proportional hazard regression models were used to analyze predictors of survival and complications.

RESULTS: A total of 15 403 continuous-flow LVAD recipients were included. A total of 3163 (20.5%) had one or more psychosocial risk factors. The most prevalent psychosocial risk factor was substance abuse in 1941 (12.6%) recipients. Patients with psychosocial risk factors were significantly younger at LVAD implant, less likely to be White, and less likely to be female compared with those without psychosocial risk, P<0.001 for all. Patients with psychosocial risk were significantly more likely to receive an LVAD as destination therapy, P<0.001. In adjusted models, patients with psychosocial risk were at increased hazards for device-related infection, gastrointestinal bleeding, pump thrombosis, and readmission and reduced hazards for cardiac transplantation (P<0.05 for all). There was no statistically significant difference in survival on pump support or stroke.

CONCLUSIONS: Psychosocial risk is an important component of patient selection for advanced heart failure therapies. Addressing these specific components may help improve access to advanced therapies and post-LVAD outcomes.

Key Words: compliance ■ heart-assist devices ■ heart failure ■ risk factors ■ social support

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See Editorial by Eckman and Cogswell

Advanced heart failure therapies including continuous-flow left ventricular assist device (LVAD) implantation offer patients improved survival as well as quality of life.[1] Yet, these therapies are both medically complicated and require significant patient engagement with frequent follow-up appointments, intricate medication regimens, including therapeutic oral anticoagulation, and device management.[2,3] Therefore, candidate selection requires a comprehensive medical assessment as well as a multidisciplinary determination of psychosocial

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WHAT IS NEW?

- Nearly 1 in 5 left ventricular assist device recipients have psychosocial risk factors, such as limited social support, limited cognition, substance abuse, severe psychiatric disease, or noncompliance.
- Psychosocial risk is not associated with increased mortality on left ventricular assist device support. However, patients with psychosocial risk are at increased risk for device-related infection, gastrointestinal bleeding, pump thrombosis, and hospital readmission and are significantly less likely to receive cardiac transplantation.

WHAT ARE THE CLINICAL IMPLICATIONS?

- When evaluating advanced heart failure patients for left ventricular assist device therapy, special attention should be paid to psychosocial risk factors that may impact long-term complications on pump support.
- Psychosocial risk alone should not be an absolute contraindication to device therapy given lack of increased mortality in this population.
- Through developing systems of support, broader mental health resources, and access to addiction medicine specialists, we can help improve these outcomes as well as their candidacy for heart transplantation on device support.

Nonstandard Abbreviations and Acronyms

INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	left ventricular assist device
PACT	Psychosocial Assessment of Candidates for Transplantation

risk.[2,4–6] According to the 2018 International Society for Heart and Lung Transplantation Consensus recommendations for the psychosocial evaluation of adult cardiothoracic transplant candidates and candidates for long-term mechanical circulatory support, candidates should be evaluated for treatment adherence, mental health and substance use history, cognitive status, coping abilities, and social support as these may affect long-term outcomes.[7] Objective psychosocial assessment tools for transplant candidacy have been developed including the Stanford Integrated Psychosocial Assessment for Transplant,[8–10] Psychosocial Assessment of Candidates for Transplantation (PACT),[11] and the Transplant Evaluation Rating Scale[12,13] which have since been applied to LVAD recipients.[14–18] However, these retrospective studies have been limited by their small sample size and inadequate power to assess impact on outcomes.[19] The current study sought to explore the burden of psychosocial risk

factors among patients with LVAD and their impact on postimplant outcomes using the multicenter Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).

METHODS

Patient Population

The INTERMACS database was queried to identify adult patients (≥18 years old) who received durable continuous-flow mechanical circulatory support from 2008 through 2017. Patients who had received right ventricular mechanical circulatory support alone or total artificial heart were excluded. The data used in the study are available to other researchers for purposes of reproducing the results or replicating the procedure via data request from the National Heart, Lung, and Blood Institute Biological Specimen and Data Repository Information Coordination Center. The Columbia University Irving Medical Center Institutional Review Board approved this study.

Definition of Psychosocial Risk

We selected variables in 5 domains that have been previously described to be associated with psychosocial risk in patients with advanced heart failure: (1) cognitive function; (2) adherence; (3) psychopathology; (4) social support; and (5) substance abuse.[2] These domains are included in validated psychosocial assessment tools such as the Stanford Integrated Psychosocial Assessment for Transplant,[14,15,20] PACT,[16,17] and the Transplant Evaluation Rating Scale[18] which have been previously studied in LVAD recipients. Unfortunately, these objective psychosocial assessment tools require detailed survey data that is unavailable in the INTERMACS registry.

Relevant variables coded in the INTERMACS registry include limited social support, history of alcohol abuse, history of illicit drug use, limited cognitive understanding, repeated noncompliance, severe depression, and other major psychiatric illness. Individuals were determined to have psychosocial risk for the purposes of this analysis if they had one of the following: (1) limited social support; (2) limited cognitive understanding; (3) substance abuse (alcohol and drug); (4) psychiatric disease (including severe depression and other major psychiatric diagnosis); and (5) repeated noncompliance. Narcotic dependence was not included in history of substance abuse given the degree of missing data. Other relevant demographic and social variables were included, such as education, marital status, working for income, tobacco use, and others.

Statistical Analysis

Descriptive analyses were conducted for all baseline variables and are presented as means and standard deviations for continuous variables and numbers and percentages for categorical variables. Differences between groups were quantified using the independent t test and χ^2 test when appropriate. Kaplan-Meier survival estimates were used to assess post-LVAD implant outcomes, with log-rank testing used to compare groups. Univariate and multivariate Cox proportional hazard regression models were used to analyze predictors of LVAD outcomes, including survival on pump support, cardiac transplantation, device-related infection

Table 1. Baseline Clinical Characteristics by Psychosocial Risk Status

Variable	Overall (n=15 403, 100%)	Psychosocial Risk (n=3163, 20.5%)	No Psychosocial Risk (n=12 240, 79.5%)	P Value
Demographics				
Age at implant	56.9±13.0	52.3±12.9	58.1±12.7	<0.001
Female gender, n (%)	3322 (21.6)	577 (18.2)	2745 (22.4)	<0.001
Race, n (%)				<0.001
White	10 151 (65.9)	1838 (58.1)	8313 (67.9)	
Black	3787 (24.6)	1005 (31.8)	2782 (22.7)	
Asian	254 (1.6)	36 (1.1)	218 (1.8)	
American Indian	116 (0.8)	34 (1.1)	82 (0.7)	
Pacific Islander	53 (0.3)	19 (0.6)	34 (0.3)	
Other	688 (4.5)	163 (5.2)	525 (4.3)	
Unknown	417 (2.7)	86 (2.7)	331 (2.7)	
Ethnicity				
Hispanic	1019 (6.6)	233 (7.4)	786 (6.4)	0.137
Blood type O, n (%)	7177 (46.6)	1458 (46.1)	5719 (46.7)	0.384
BMI, kg/m^2	28.5±6.8	28.4±7.0	28.6±6.8	0.406
BSA, m^2	2.05±0.30	2.05±0.30	2.05±0.30	0.261
Ischemic cause of HF	6873 (44.6)	1202 (38.0)	5671 (46.3)	<0.001
Social factors				
Marital status				<0.001
Single	2986 (19.4)	970 (30.7)	2016 (16.5)	
Married	9513 (61.8)	1405 (44.4)	8108 (66.2)	
Domestic partner	1825 (11.8)	560 (17.7)	1265 (10.3)	
Divorced/separated	514 (3.3)	108 (3.4)	406 (3.3)	
Widowed	252 (1.6)	66 (2.1)	186 (1.5)	
Unknown	313 (2.0)	54 (1.7)	259 (2.1)	
Education level				<0.001
None	29 (0.2)	9 (0.3)	20 (0.2)	
Grade school	382 (2.5)	121 (3.8)	261 (2.1)	
High school	5062 (32.9)	1276 (40.3)	3786 (30.9)	
College/tech school	2872 (18.6)	627 (19.8)	2245 (18.3)	
Associate/bachelor	1920 (12.5)	278 (8.8)	1642 (13.4)	
Postgraduate	802 (5.2)	98 (3.1)	704 (5.8)	
Not applicable	12 (0.1)	1 (0.0)	11 (0.1)	
Unknown	4324 (28.1)	753 (23.8)	3571 (29.2)	
Working for income	2502 (16.2)	410 (13.0)	2092 (17.1)	<0.001
HIV	48 (0.3)	16 (0.5)	32 (0.3)	0.028
Narcotic dependence	100 (0.6)	72 (2.3)	28 (0.2)	<0.001
Device-related factors				
Device type				0.483
LVAD	14 800 (96.1)	3046 (96.3)	11 754 (96.0)	
LVAD+RVAD	603 (3.9)	117 (3.7)	486 (4.0)	
LVAD type				<0.001
Centrifugal	4396 (28.5)	731 (23.1)	3665 (29.9)	
Axial	11 007 (71.5)	2432 (76.9)	8575 (70.1)	
Device strategy				<0.001
Transplant listed	3866 (25.1)	520 (16.4)	3346 (27.3)	
Transplant eligible	4204 (27.3)	961 (30.4)	3243 (26.5)	

(Continued)

Table 1. Continued

Variable	Overall (n=15 403, 100%)	Psychosocial Risk (n=3163, 20.5%)	No Psychosocial Risk (n=12 240, 79.5%)	P Value
Destination therapy	7232 (47.0)	1661 (52.5)	5571 (45.5)	
Bridge to recovery	49 (0.3)	12 (0.4)	37 (0.3)	
Other	52 (0.3)	9 (0.3)	43 (0.4)	
INTERMACS profile				<0.001
Profile 1	2655 (17.3)	567 (21.4)	2088 (17.2)	
Profile 2	5288 (34.5)	1146 (36.4)	4142 (34.0)	
Profile 3	5117 (33.4)	1072 (34.1)	4045 (33.2)	
Profile 4−7	2260 (14.8)	361 (11.5)	1899 (15.6)	
NYHA class IV	12 025 (78.1)	2613 (82.6)	9412 (76.9)	<0.001
6MWT>300 m	1101 (32.9)	223(31.9)	878 (33.2)	0.541
IV inotropes	5421 (35.2)	1179 (37.3)	4242 (34.7)	0.001
IABP	4234 (27.5%)	923 (29.2)	3311 (27.1)	0.017
ECMO	865 (5.6%)	180 (5.7)	685 (5.6)	0.837
Mechanical ventilation	1120 (7.3%)	249 (7.9)	871 (7.1)	0.144
Dialysis	412 (2.7)	88 (2.8)	324 (2.6)	0.675
Comorbid conditions				
Severe diabetes mellitus, n (%)	1503 (9.8)	366 (11.6)	1137 (9.3)	<0.001
Active smoking, n(%)	715 (4.6)	297 (9.4)	418 (3.4)	<0.001
Pulmonary HTN	3390 (22.0)	914 (28.9)	2476 (20.2)	<0.001
PVD, n (%)	712 (4.6)	163 (5.2)	549 (4.5)	0.111
CHF therapy				
β-blocker	7376 (47.9)	1392 (44.0)	5984 (48.9)	<0.001
ACE inhibitor	3501 (22.7)	728 (23.0)	2773 (22.7)	<0.001
Angiotensin receptor blocker	1328 (8.6)	200 (6.3)	1128 (9.2)	0.031
Aldosterone antagonist	5937 (38.5)	1276 (40.3)	4661 (38.1)	<0.001
Loop diuretic	12 866 (83.5)	2680 (84.7)	10 186 (83.2)	0.047
AICD	12 089 (78.5)	2420 (76.5)	9669 (79.0)	<0.001

6MWT indicates 6 minute walk test; ACE, angiotensin-converting enzyme; AICD, automated implantable cardioverter-defibrillator; BMI, body mass index; BSA, body surface area; ECMO, extracorporeal membrane oxygenation; HF, heart failure; HTN, hypertension; IABP, intraaortic balloon pump; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; IV, intravenous; LVAD, left ventricular assist device; NYHA, New York Heart Association; PVD, peripheral vascular disease; and RVAD, right ventricular assist device.

gastrointestinal bleeding, device thrombosis (suspected or confirmed), stroke (ischemic or hemorrhagic), and rehospitalization for any cause. Patients were censored if they were transplanted or explanted without new device implant. The last date of follow-up for all patients was October 2017. The multivariate model was adjusted for age, gender, race, heart failure cause, body surface area, year of implant, history of right ventricular assist device use, pump type (axial versus centrifugal), INTERMACS profile, device strategy (destination therapy versus bridge to transplant or recovery), creatinine, bilirubin, and albumin levels, all factors which have been known to be associated with post-transplant or post-LVAD outcomes. All P values were reported as 2-sided tests with $P<0.05$ considered statistically significant. SPSS Statistics, Version 25.0 (Armonk, NY: IBM) was used to perform statistical analysis.

RESULTS

Baseline Characteristics

Among eligible participants in the INTERMACS registry, 15 403 individuals received a continuous-flow LVAD from 2008 to 2017 (Table 1). Within this population, 3163 (20.5%) had one or more psychosocial risk factor. The most prevalent psychosocial risk factor was substance abuse in 1941 (12.6%) of LVAD recipients (alcohol abuse in 1211 [7.9%] and drug abuse in 1167 [7.6%]) with limited social support being the second most prevalent in 759 (4.9%) of the study population (Figure 1A). The majority of patients with psychosocial risk had only one of the 5 risk factors (Figure 1B).

Patients with psychosocial risk factors were significantly younger at LVAD implant (52.3±12.9 versus 58.1±12.7 years), less likely to be White (1838 [58.1%] versus 8313 [67.9%]), and less likely to be female (577
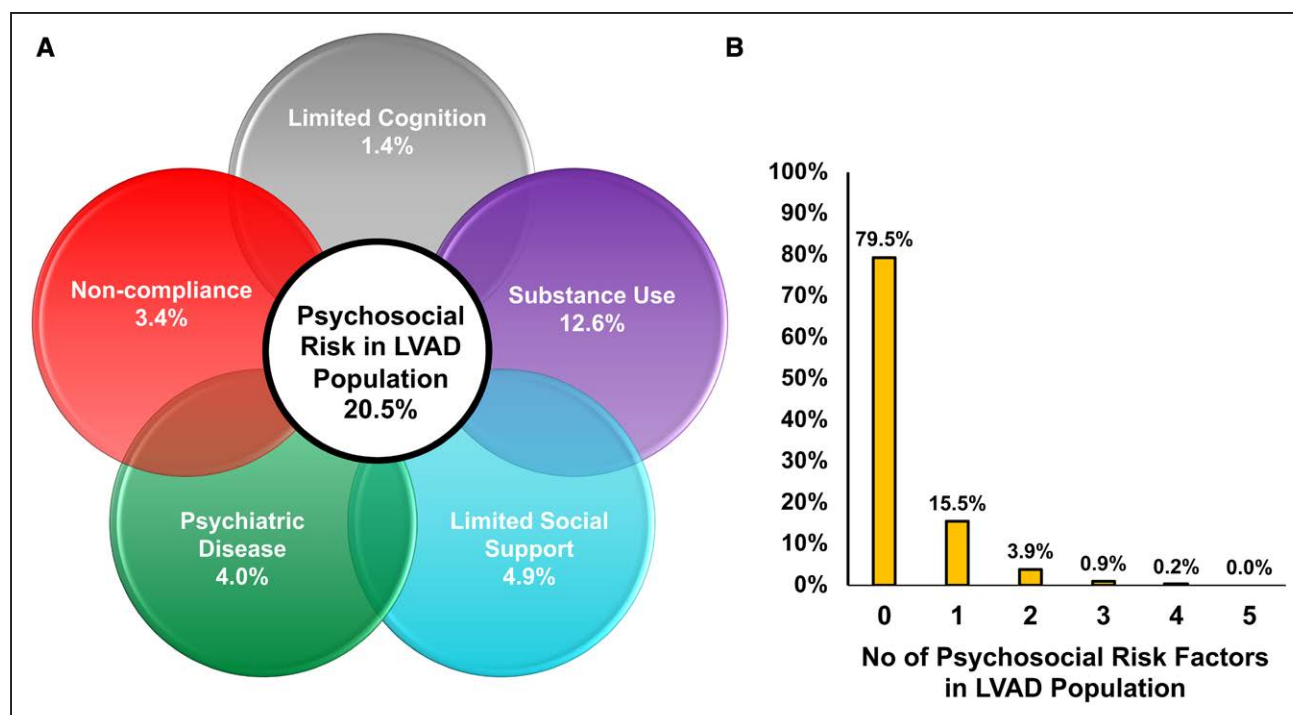
Figure 1. The burden of psychosocial risk factors in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).
A, This schematic highlights the 5 domains used to characterize psychosocial risk: social support, cognition, substance use, psychopathology, and noncompliance. The respective frequency of various psychosocial risk factors in the INTERMACS database is also shown. In **B**, a bar graph highlights that the majority of patients with psychosocial risk had only one of the 5 risk factors. LVAD indicates left ventricular assist device.

[18.2%] versus 2745 [22.4%]) compared with those without psychosocial risk, *P*<0.001 for all. They were significantly more likely to be active smokers (297 [9.4%] versus 418 [3.4%], *P*<0.001) and less likely to be working for income (410 [13.0%] versus 2092 [17.1%], *P*<0.001). Patients in the psychosocial risk group were also significantly more likely to be seropositive for HIV (16 [0.5%] versus 32 [0.3%], *P*=0.028) as well as be dependent on narcotics (72 [2.3%] versus 28 [0.2%], *P*<0.001). Individuals with psychosocial risk were significantly less likely to be married (1405 [44.4%] versus 8108 [66.2%], *P*<0.001) and less likely to have a college degree (278 [8.8%] versus 1642 [13.4%], *P*<0.001) with associate/bachelor degrees.

In addition, those with psychosocial risk factors were overall sicker patients: they were significantly more likely to be New York Heart Association Class IV (2613 [82.6%] versus 9412 [76.9%], *P*<0.001) and INTERMACS profile 1 at the time of implant (567 [21.4%] versus 2088 [17.2%], *P*<0.001). Similarly, they were significantly more likely to be on intravenous inotropes (1179 [37.3%] versus 4242 [34.7%], *P*=0.001) and intraaortic balloon pump therapy (923 [29.2%] versus 3311 [27.1%], *P*=0.017) before LVAD implant than those patients without psychosocial risk. This was also reflected by statistically significantly higher central venous pressures, pulmonary artery diastolic pressure, and pulmonary capillary wedge pressure, although

these differences are likely not clinically significant (Table I in the Data Supplement). There were no statistically significant differences in the use of extracorporeal membrane oxygenation, mechanical ventilation, and dialysis between groups.

With regard to device strategy, patients with psychosocial risk were significantly more likely to receive an LVAD as destination therapy (1661 [52.5%] versus 5571 [45.5%]) and significantly less likely to be listed for transplant (520 [16.4%] versus 3346 [27.3%]), *P*<0.001 for both.

Postimplant Outcomes

At the end of the follow-up period, 11 740 individuals (76.2%) remained alive on pump support. Patients with high psychosocial risk paradoxically had improved survival on LVAD support in unadjusted univariate analysis. However, when adjusted for clinical risk factors, psychosocial risk was not significantly associated with survival on pump support (hazard ratio [HR], 0.99 [95% CI, 0.91–1.09], *P*=0.90; Table 2). Other major psychiatric disease was significantly associated with worsened survival (HR, 1.38 [95% CI, 1.07–1.77], *P*=0.012).

Device-related infections occurred in 2363 (15.3%) individuals. Any psychosocial risk was significantly associated with increased hazards for device-related infection in the unadjusted and adjusted regression model

Table 2. Hazard Ratio Estimates for LVAD Outcomes by Psychosocial Risk

LVAD Outcomes	Unadjusted Cox Regression		Adjusted Cox Regression*	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Survival on pump support (n=11 740)				
Any psychosocial risk	0.84 (0.77–0.92)	<0.001	0.99 (0.91–1.09)	0.902
Limited social support	0.90 (0.77–1.05)	0.182	0.96 (0.81–1.13)	0.608
Limited cognition	0.81 (0.63–1.05)	0.107	0.84 (0.64–1.11)	0.213
Substance abuse				
ETOH abuse	0.82 (0.72–0.93)	0.002	0.96 (0.84–1.10)	0.533
Drug use	0.68 (0.59–0.79)	<0.001	0.97 (0.83–1.14)	0.703
Psychiatric disease				
Severe depression	0.89 (0.72–1.10)	0.272	0.95 (0.76–1.19)	0.653
Other major psychiatric Dx	1.08 (0.85–1.37)	0.529	1.38 (1.07–1.77)	0.012
Noncompliance	0.94 (0.78–1.13)	0.515	1.16 (0.95–1.40)	0.137
Cardiac transplantation (n=3738)				
Any psychosocial risk	0.82 (0.76–0.90)	<0.001	0.85 (0.80–0.91)	<0.001
Limited social support	0.68 (0.57–0.81)	<0.001	0.82 (0.68–0.99)	0.038
Limited cognition	0.67 (0.51–0.89)	0.005	0.66 (0.49–0.89)	0.006
Substance abuse				
ETOH abuse	0.93 (0.83–1.05)	0.249	0.88 (0.77–0.99)	0.041
Drug use	0.95 (0.84–1.07)	0.392	0.84 (0.74–0.96)	0.011
Psychiatric disease				
Severe depression	0.82 (0.66–1.01)	0.066	0.81 (0.64–1.02)	0.068
Other major psychiatric Dx	1.12 (0.88–1.41)	0.357	1.10 (0.86–1.41)	0.444
Noncompliance	0.62 (0.50–0.78)	<0.001	0.68 (0.54–0.86)	0.001
Device-related infection (n=2363)				
Any psychosocial risk	1.40 (1.28–1.54)	<0.001	1.29 (1.17–1.43)	<0.001
Limited social support	1.57 (1.35–1.84)	<0.001	1.44 (1.22–1.69)	<0.001
Limited cognition	1.22 (0.94–1.59)	0.132	1.22 (0.92–1.61)	0.161
Substance abuse				
ETOH abuse	1.30 (1.14–1.49)	<0.001	1.26 (1.09–1.45)	0.002
Drug use	1.43 (1.25–1.63)	<0.001	1.24 (1.07–1.44)	0.004
Psychiatric disease				
Severe depression	1.22 (0.97–1.53)	0.083	1.12 (0.88–1.42)	0.345
Other major psychiatric Dx	1.62 (1.26–2.08)	<0.001	1.46 (1.12–1.90)	0.006
Noncompliance	1.58 (1.31–1.90)	<0.001	1.37 (1.13–1.67)	0.002
Gastrointestinal bleeding (n=3775)				
Any psychosocial risk	0.98 (0.90–1.06)	0.532	1.20 (1.11–1.31)	<0.001
Limited social support	0.96 (0.82–1.11)	0.555	1.06 (0.91–1.24)	0.467
Limited cognition	1.13 (0.91–1.05)	0.267	1.24 (0.99–1.56)	0.058
Substance abuse				
ETOH abuse	1.02 (0.90–1.14)	0.794	1.22 (1.08–1.38)	0.002
Drug use	0.74 (0.65–0.85)	<0.001	1.08 (0.93–1.24)	0.325
Psychiatric disease				
Severe depression	1.08 (0.89–1.30)	0.432	1.26 (1.03–1.53)	0.023
Other major psychiatric Dx	0.88 (0.68–1.13)	0.319	1.17 (0.90–1.53)	0.223
Noncompliance	1.10 (0.93–1.31)	0.250	1.40 (1.17–1.67)	<0.001
Device thrombosis (suspected or confirmed; n=1870)				
Any psychosocial risk	1.27 (1.14–1.41)	<0.001	1.19 (1.06–1.33)	0.002
Limited social support	1.27 (1.05–1.53)	0.013	1.19 (0.98–1.45)	0.087

(*Continued*)

Table 2. Continued

LVAD Outcomes	Unadjusted Cox Regression		Adjusted Cox Regression*	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Limited cognition	1.10 (0.81–1.50)	0.544	1.06 (0.77–1.47)	0.723
Substance abuse				
ETOH abuse	1.05 (0.89–1.24)	0.539	1.08 (0.91–1.29)	0.363
Drug use	1.37 (1.18–1.60)	<0.001	1.19 (1.01–1.41)	0.038
Psychiatric disease				
Severe depression	1.40 (1.10–1.77)	0.006	1.27 (0.99–1.63)	0.061
Other major psychiatric Dx	1.57 (1.19–2.07)	0.002	1.37 (1.01–1.85)	0.042
Noncompliance	1.43 (1.16–1.77)	<0.001	1.29 (1.03–1.62)	0.024
Stroke (ischemic or hemorrhagic; n=2279)				
Any psychosocial risk	1.02 (0.92–1.12)	0.765	1.11 (0.99–1.24)	0.067
Limited social support	0.97 (0.80–1.17)	0.726	0.98 (0.80–1.20)	0.846
Limited cognition	1.00 (0.75–1.35)	0.959	0.96 (0.70–1.32)	0.788
Substance abuse				
ETOH abuse	1.01 (0.87–1.18)	0.853	1.15 (0.98–1.35)	0.084
Drug use	0.89 (0.76–1.05)	0.169	1.00 (0.84–1.19)	0.976
Psychiatric disease				
Severe depression	0.88 (0.67–1.15)	0.349	0.89 (0.67–1.18)	0.420
Other major psychiatric Dx	1.12 (0.83–1.51)	0.467	1.15 (0.84–1.59)	0.380
Noncompliance	1.28 (1.04–1.56)	0.018	1.38 (1.11–1.71)	0.004
Hospital readmission (n=11 323)				
Any psychosocial risk	1.08 (1.03–1.13)	0.002	1.14 (1.08–1.19)	<0.001
Limited social support	1.06 (0.98–1.15)	0.169	1.13 (1.04–1.24)	0.005
Limited cognition	1.00 (0.87–1.14)	0.948	1.09 (0.94–1.26)	0.263
Substance abuse				
ETOH abuse	1.06 (0.99–1.14)	0.071	1.11 (1.03–1.19)	0.005
Drug use	1.03 (0.96–1.11)	0.373	1.09 (1.01–1.17)	0.022
Psychiatric disease				
Severe depression	1.20 (1.07–1.33)	0.001	1.18 (1.06–1.33)	0.004
Other major psychiatric Dx	1.42 (1.25–1.62)	<0.001	1.40 (1.22–1.60)	<0.001
Noncompliance	1.04 (0.94–1.15)	0.439	1.10 (0.99–1.22)	0.085

BSA indicates body surface area; ETOH, alcohol; Dx, diagnosis; HF, heart failure; HR, hazard ratio; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; and RVAD, right ventricular assist device.

*Adjusted for age, gender, race, BSA, implant year, HF cause, RVAD use, pump type (axial vs centrifugal), INTERMACS class, device strategy (destination vs bridge), creatinine, bilirubin, and albumin levels.

(HR, 1.29 [95% CI, 1.17–1.43], P<0.001). When each individual risk factor was examined, the subpopulations with limited social support, substance abuse, other major psychiatric diagnosis, and history of noncompliance independently were each significantly associated with increased hazards for device-related infections (P<0.05 for all; Table 2, Figure 2).

During the study period, gastrointestinal bleeding occurred in 3775 (24.5%) individuals while pump thrombosis occurred in 1870 (12.1%). Psychosocial risk was significantly associated with increased hazards for gastrointestinal bleeding (adjusted HR, 1.20 [95% CI, 1.11–1.31], P<0.001). This was driven by increased hazards of gastrointestinal bleeding among patients with alcohol abuse, severe depression and a history of noncompliance

(P<0.05 for all). Patients with psychosocial risk factors were also at significantly increased hazards for device thrombosis (suspected or confirmed; adjusted HR, 1.19 [95% CI, 1.06–1.33], P=0.002). This was driven by increased hazards among those with drug use, other major psychiatric disease, and a history of noncompliance (P<0.05 for all).

There were 2279 (14.8%) individuals with ischemic or hemorrhage stroke during the study period. There was no statistically significant association with risk of stroke (ischemic or hemorrhagic) among patients with any psychosocial risk in an adjusted Cox regression model (HR, 1.11 [95% CI, 0.99–1.24], P=0.07). However, noncompliance was associated with a significantly increased risk of stroke (HR, 1.38 [95% CI, 1.11–1.71], P=0.004).
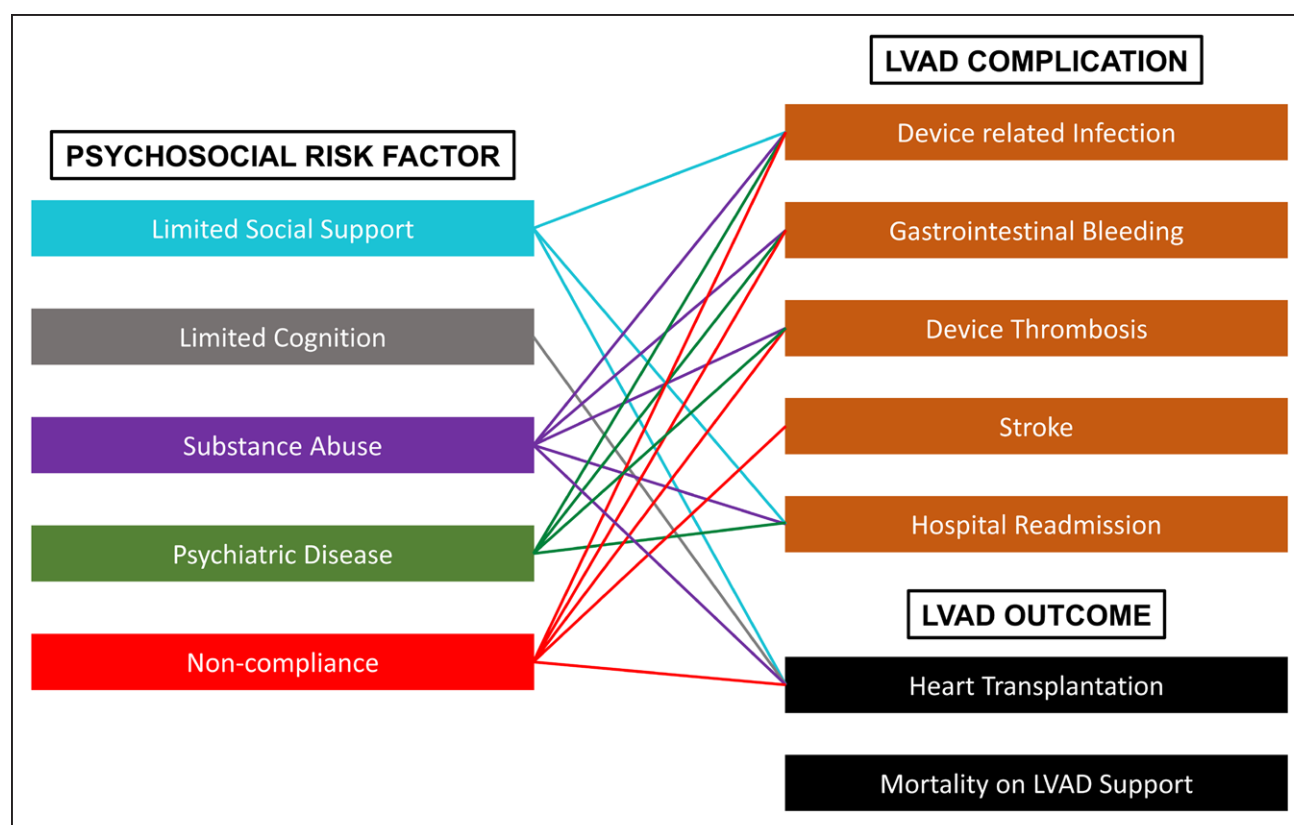
Figure 2. Psychosocial risk domains and associated outcomes.
Network diagram is shown displaying associations between each domain of psychosocial risk to left ventricular assist device (LVAD) complications and outcomes. Connections were made between risk factors and outcomes if the adjusted hazard ratios were statistically significant. The multivariate model used was adjusted for age, gender, race, heart failure cause, body surface area (BSA), year of implant, history of right ventricular assist device (RVAD) use, pump type (axial vs centrifugal), Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile, device strategy (destination therapy vs bridge to transplant or recovery), creatinine, bilirubin, and albumin levels.

Hospital readmissions were common, occurring in 11 323 (73.5%) patients throughout the study period. In addition, patients with psychosocial risk factors had significantly increased hazards for all-cause hospital readmission (adjusted HR, 1.14 [95% CI, 1.08−1.19], $P<0.001$). Nearly all subpopulations were at significantly increased hazards for hospital readmissions with the exception of limited cognition and history of non-compliance where no statistically significant associations were seen.

Approximately one in 4 patients received cardiac transplantation (n=3738 [24.2%]). Patients with psychosocial risk factors were significantly less likely to undergo cardiac transplantation (adjusted HR, 0.85 [95% CI, 0.80−0.91], $P<0.001$). At 3-year follow-up, the incidence of transplant was 41.0% in the no psychosocial risk group, compared with 35.9% in the group with at least one psychosocial risk factor (log-rank $P<0.001$).

Additive Impact of Multiple Psychosocial Risk Factors

An additional analysis was performed to assess the impact of the number of psychosocial risk factors on outcomes. In patients with 2 or more psychosocial risk factors, the hazards of cardiac transplantation were significantly lower (adjusted HR, 0.72 [95% CI, 0.61−0.87], $P<0.001$) compared with those without psychosocial risk (Table 3). The hazards of device-related infection, gastrointestinal bleeding, device thrombosis, and hospital readmission were all significantly higher in the group with 2 or more psychosocial risk factors. Survival on pump support was still not significantly different, even among the subgroup with 2 or more psychosocial risk factors (adjusted HR, 0.94 [95% CI, 0.79−1.12], $P=0.49$). Patients with 2 or more psychosocial risk factors had significantly higher risk of driveline infection compared with patients with only one psychosocial risk factor (adjusted HR, 1.22 [95% CI, 0.80−0.91], $P=0.034$, Table II in the Data Supplement).

DISCUSSION

The current study examines the burden of psychosocial risk factors among patients who have received LVADs and its association with postimplant outcomes. The important findings include (1) one or more psychosocial risk factors was present in ≈20% of LVAD recipients; (2) patients with psychosocial risk were more likely

Table 3. Additive Impact of Psychosocial Risk Factors on LVAD Outcomes

LVAD Outcomes	Unadjusted Cox Regression		Adjusted Cox Regression*	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Survival on pump support				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	0.87 (0.79–0.96)	0.004	1.01 (0.91–1.12)	0.842
2+ Psychosocial risk factors	0.76 (0.64–0.89)	0.001	0.94 (0.79–1.12)	0.495
Cardiac transplantation				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	0.87 (0.79–0.95)	0.002	0.86 (0.78–0.95)	0.003
2+ Psychosocial risk factors	0.70 (0.59–0.82)	<0.001	0.72 (0.60–0.86)	<0.001
Device-related infection				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	1.31 (1.18–1.46)	<0.001	1.23 (1.10–1.37)	<0.001
2+ Psychosocial risk factors	1.40 (1.28–1.54)	<0.001	1.49 (1.27–1.76)	<0.001
Gastrointestinal bleeding				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	0.97 (0.89–1.06)	0.546	1.18 (1.07–1.29)	0.001
2+ Psychosocial risk factors	0.98 (0.85–1.14)	0.803	1.29 (1.11–1.51)	0.001
Device thrombosis (suspected or confirmed)				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	1.21 (1.07–1.36)	0.002	1.15 (1.01–1.31)	0.031
2+ Psychosocial risk factors	1.47 (1.23–1.76)	<0.001	1.32 (1.09–1.59)	0.005
Stroke (ischemic or hemorrhagic)				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	1.03 (0.92–1.15)	0.656	1.12 (1.00–1.27)	0.059
2+ Psychosocial risk factors	0.98 (0.81–1.19)	0.864	1.06 (0.86–1.30)	0.585
Hospital readmission				
0 Psychosocial risk factor	…	…	…	…
1 Psychosocial risk factor	1.06 (1.00–1.12)	0.022	1.12 (1.06–1.18)	<0.001
2+ Psychosocial risk factors	1.12 (1.03–1.22)	0.006	1.21 (1.11–1.32)	<0.001

HR indicates hazard ratio; and LVAD, left ventricular assist device.

to be young, non-White, men with more severe cardiac disease; and (3) patients with psychosocial risk were at increased hazards for device-related infection, gastrointestinal bleeding, pump thrombosis, and hospital readmission compared with those without psychosocial risk, with particular risk factors contributing to different outcomes. However, overall psychosocial risks were not significantly associated with survival or stroke. Taken together, these findings highlight the adverse outcomes associated with psychosocial risk and the need for programs to address these factors to improve both LVAD outcomes and access to heart transplantation.

In our study, 1 in 5 LVAD recipients had at least one marker of elevated psychosocial risk. Our definition of psychosocial risk incorporated 5 distinct domains, all of which are mentioned in the 2018 International Society for Heart and Lung Transplantation consensus statement[7] and are captured in previously validated objective psychosocial assessments such as the Stanford Integrated Psychosocial Assessment for Transplant,[14,15,20] PACT,[16,17] and the Transplant Evaluation Rating Scale (Figure 3).[18] The most common risk factor was substance abuse, followed by limited social support, severe psychiatric disease, noncompliance, and limited cognition. Notably, the majority of patients with psychosocial risk had only one psychosocial risk factor with a small minority having 2 or 3 of the 5 risk factors. This likely reflects that patients would not have been deemed appropriate candidates if they had multiple co-existing risk factors.

Patients with psychosocial risk were significantly more likely to be young, non-White, men with more severe cardiac disease. They were more likely to require inotrope therapy as well as intraaortic balloon pump therapy before LVAD implant. Yet, patients with psychosocial risk were significantly more likely to receive an LVAD as destination therapy and significantly less likely to be listed for transplant. One can suspect that many of these patients would medically be candidates for transplant
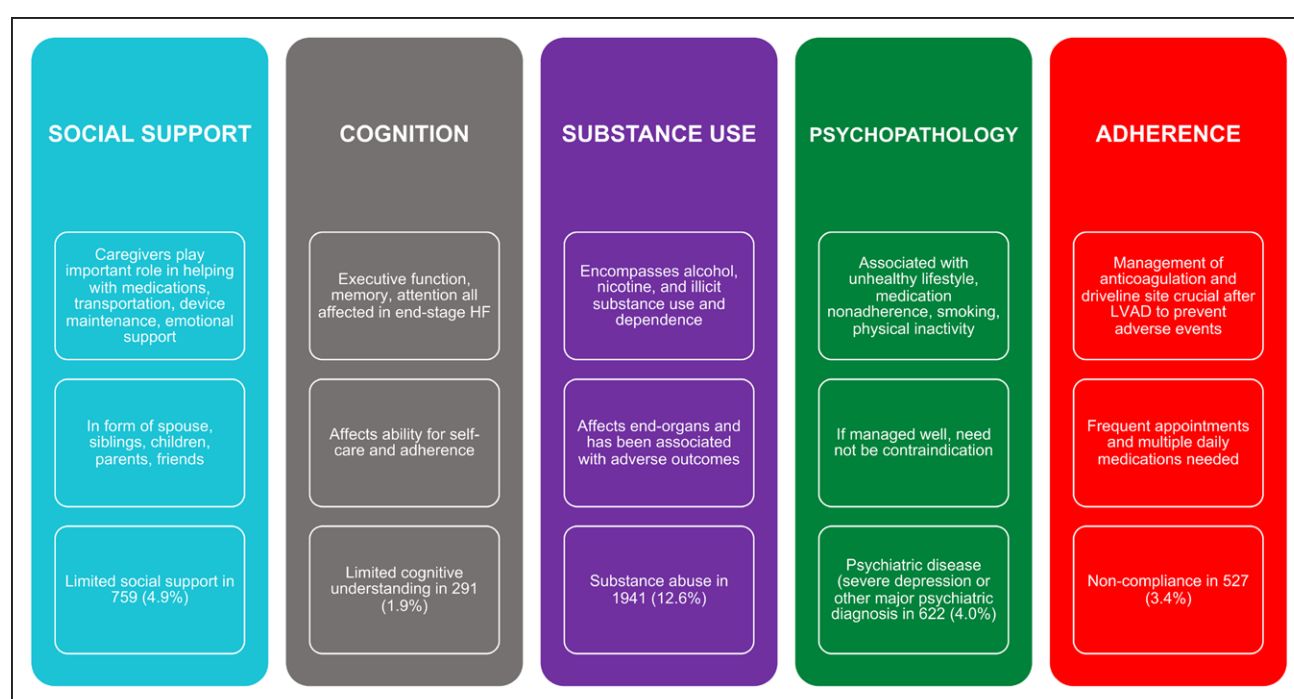
Figure 3. The 5 domains of psychosocial risk.
Descriptions of each of the 5 psychosocial risk domains are shown.

given their age, acuity of illness, and preserved end-organ function. As the most common psychosocial risk factor in our analysis was substance use, we hypothesize that this likely precluded their candidacy in addition to active smoking which was significantly higher in the psychosocial risk group. We have previously demonstrated that LVAD recipients of lower socioeconomic status have similar demographics (young and non-White), less likely to be married, more likely to have public insurance, and less likely to be employed.[21] Notably, in this analysis, socioeconomic status did not significantly impact post-LVAD outcomes. Furthermore, substance use disorders nationally are most commonly seen in young men.[22,23] This highlights the need for screening and implementation of effective psychological and medical treatments for substance use disorders in this population.[24] With effective treatment and close follow-up, these patients may become candidates for heart transplantation in the future.

Following LVAD implant, patients with psychosocial risk were at increased hazards for multiple device-related complications. After adjusting for many patient-specific and device-specific factors, patients with psychosocial risk remained at significantly increased hazards for device-related infection, gastrointestinal bleeding, pump thrombosis, and hospital readmission compared with those without psychosocial risk. Prior studies that have evaluated retrospectively psychosocial risk in LVAD recipients have found mixed results but have been limited by small sample sizes. For example, Halkar et al[17] used the PACT to retrospectively examine 230 patients

with LVAD and found no associations between psychosocial risk and readmissions, pump thrombosis, driveline infections, gastrointestinal bleeding, or survival.[17] Of note, 97% of the study population had PACT scores in the range of acceptable to excellent candidate. However, Maltby et al[16] found a significant association between lower psychosocial risk and readmissions after LVAD implant with no differences in survival, a finding also replicated in other studies.[25,26] However, given the increased risk of other complications, these patients likely have worse quality of life. One strength of our analysis was the significantly larger sample size which gave us adequate power to explore these associations.

Notably, the HRs for most outcomes were similar, indicating an ≈20% increased risk of complications in patients with only one psychosocial risk factor. Yet, this may be an acceptable risk when compared with withholding of LVAD therapy altogether in these higher-risk patients who are typically young with severe heart failure syndromes, particularly when we found no difference in survival on pump support. The risk of these complications nearly doubled in patients with 2 or more risk factors. In addition, we may be able to mitigate these risks by developing systems of support, providing access to addiction medicine, and broader mental health resources for our patients. These may also help to improve their candidacy for organ transplantation.

We also found that different psychosocial variables may be more associated with specific outcomes in the LVAD population. These variables may differ from heart transplant recipients. For example, increased

gastrointestinal bleeding was primarily observed in subpopulations of patients with alcohol abuse, severe depression, and a history of noncompliance, whereas pump thrombosis was driven primarily by those with major psychiatric disease other than depression, drug use, and history of noncompliance. This is not surprising given that alcohol abuse can lead to the development of coagulopathy as well as mucosal injury leading to increased bleeding.[27] Typically, there is an inverse relationship between bleeding and clotting. However, we found an increased hazards for both gastrointestinal bleeding and pump thrombosis among those with a history of noncompliance, reflecting an inability to maintain therapeutic oral anticoagulation perhaps developing both subtherapeutic and supratherapeutic internationalized normalized ratio values.[28]

Our study has limitations that should be acknowledged. Perhaps, the most significant limitation is the fact that INTERMACS only includes patients who have received an LVAD implant; therefore, it does not include psychosocial risk for those who were not deemed eligible for the therapy. This study was a retrospective analysis using registry data. Furthermore, there may be center-specific differences regarding how patients were coded as having limited social support, limited cognitive understanding, or repeated noncompliance. These can be challenging to define and, therefore, may be subject to biases. For example, perhaps, non-White individuals are more likely to be coded for specific risk factors when compared with White individuals due to unconscious biases. In addition, for substance abuse, it is unclear when this occurred in relation to the timing of VAD implant. Information regarding rehabilitation treatments were not available nor was information regarding neurocognitive assessments. This highlights the importance of using formal psychosocial assessment tools in future multicenter studies.

In conclusion, patients with psychosocial risk factors are at risk for adverse outcomes and complications after LVAD implantation. Five broad categories, including social support, cognition, substance use, psychopathology, and noncompliance, may each predict their own set of post-LVAD complications. However, these factors exist within a broader societal, cultural, and economic context. Therefore, to ensure equitable access to advanced heart failure therapies, we must also address these factors through developing interventions in future studies.

ARTICLE INFORMATION

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Disclosures

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