

Contents lists available at ScienceDirect

# IJC Heart & Vasculature



journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

# Impairments identified by comprehensive geriatric assessment in potential candidates for left ventricular assist device and heart transplantation

Lauren Dautzenberg<sup>a,\*,1</sup>, Linda W. van Laake<sup>b,1</sup>, Renee C.M.A. Raijman<sup>a,1</sup>, Geert J. Lefeber<sup>a,1</sup>, Wilma Knol<sup>a,1</sup>, Marish I.F. Oerlemans<sup>b,1</sup>, Faiz Z. Ramjankhan<sup>c,1</sup>, Susan A. Braithwaite<sup>d,1</sup>, Mieke D.J. Nagtegaal<sup>b,1</sup>, Marielle H. Emmelot-Vonk<sup>a,1</sup>, Huiberdina L Koek<sup>a,1</sup>

<sup>a</sup> Department of Geriatric Medicine, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

<sup>b</sup> Department of Cardiology, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

<sup>c</sup> Department of Cardiothoracic Surgery, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

<sup>d</sup> Department of Anesthesiology, University Medical Centre Utrecht, Utrecht University, Utrecht, the Netherlands

#### ARTICLE INFO

Keywords: Comprehensive geriatric assessment Impairments Screening Left ventricular assist device Heart transplantation

#### ABSTRACT

candidacy for LVAD and HTx.

*Background:* The aim of this study was to assess the prevalence of frailty and other impairments in potential left ventricular assist device (LVAD) and heart transplantation (HTx) candidates by performing a preoperative comprehensive geriatric assessment (CGA) and reviewing the treatment recommendations resulting from the CGA.

*Methods and results*: This cross-sectional study included 73 patients aged  $\geq$ 40 years who received a CGA as part of the patient selection procedure for LVAD and HTx. In every patient, a conclusion comprising frailty and other impairments was formulated based on the medical, mental, functional, and social domains and recommendations were made. The mean age was 58 years (range 40–71) and 70 % were male. In 97 % of patients, at least one impairment was identified by the CGA. The most common impairments were polypharmacy, high morbidity burden, reduced renal function, osteopenia, depression, poor quality of life, reduced functionality, (risk of) malnutrition, reduced grip strength and high caregiver burden. A small proportion of the potential LVAD and HTx candidates were frail (7 % according to Fried's frailty criteria, 6 % according to the Edmonton Frail Scale) and 39 % were pre-frail. The domains for which most impairments were found and the domains for which most treatment recommendations were given matched well, with the functional domain as the frontrunner. *Conclusion:* This study showed that most of the potential candidates for LVAD or HTx have impairments on at least one domain of the CGA. Impairments and associated risks can contribute to the decision making process for

1. Introduction

The lifetime risk of heart failure is high [1]. When chronic end-stage heart failure remains refractory in spite of individualized optimal medical and conventional device therapy, advanced therapies can be considered in selected patients, including heart transplantation (HTx) and left ventricular assist device (LVAD) [2].

Although LVAD implantation and HTx improve survival and quality of life [3,4], there is also a high risk of complications, leading to an intensive postoperative therapeutic regime and a thorough follow-up [5,6]. As recommended in the European Society of Cardiology heart failure guidelines, compliance with therapy and adequate social support are important elements of this therapeutic regime [2,7]. Furthermore, it is important that patients on LVAD support understand the technology, are able to undertake the burdensome self-care and to react appropriately to pump malfunction [2,8]. This requires substantial cognitive and functional skills [9]. Current literature refers to frailty [10] as an important predictor of outcomes after LVAD implantation [11–15]. Given the high risk of negative outcomes after LVAD or HTx, an adequate preoperative selection of potential candidates is necessary. Even when performed by a specialized, multidisciplinary team, patient selection is complex and unique to each patient [2]. The comprehensive

https://doi.org/10.1016/j.ijcha.2023.101318

 $<sup>^{\</sup>ast}$  Corresponding author at: Heidelberglaan 100, 3584 CX Utrecht, the Netherlands.

E-mail address: L.Dautzenberg@umcutrecht.nl (L. Dautzenberg).

<sup>&</sup>lt;sup>1</sup> This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Received 18 September 2023; Received in revised form 17 November 2023; Accepted 26 November 2023

<sup>2352-9067/© 2023</sup> The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

geriatric assessment (CGA) is a multidisciplinary assessment that systematically examines a patient according to the medical, mental, functional and social domains and can determine the degree of frailty [16,17]. Recent studies showed that a CGA is potentially of added value in the evaluation and treatment of patients with heart failure [18,19]. A recent study showed that having limitations in multiple domains of the CGA was significantly associated with adverse outcomes in patients with heart failure [20]. Awareness of the presence of capabilities and limitations in the individual patient may lead to improved patient selection for advanced therapies such as LVAD or HTx, and gives the potential to optimize and individualize treatment to improve the preoperative level of fitness. A few studies showed beneficial effects of a prehabilitation program on functionality and frailty in patients awaiting HTx, however, no studies have reported the impact on outcomes of LVAD or HTx yet [21]. In addition, care goals can be explored, social or mental support offered, the risk of complications such as delirium reduced and advice given on post-operative rehabilitation [22]. However, little is known about the yield of CGA in patients who are considered for advanced invasive therapy with LVAD or HTx in terms of found impairments and potential recommendations. Therefore, the aim of this study was to assess the prevalence of frailty and other impairments identified by a CGA in potential LVAD and HTx candidates. A secondary aim was to study which treatment recommendations resulted from the CGA.

#### 2. Methods

# 2.1. Study design and setting

This is a single center, cross-sectional study in a collaboration between the Department of Geriatrics, Cardiology and Cardiothoracic Surgery at the University Medical Centre Utrecht, a tertiary referral hospital for advanced heart failure in the Netherlands.

The study has been conducted in accordance with the Declaration of Helsinki and is approved by the local medical ethics committee (reference number MvdL/mb/20/500551).

#### 2.2. Study population

Cardiologists in second-line care can refer patients to tertiary-line care in the University Medical Centre Utrecht to consider therapies for advanced heart failure, when the patient progresses from stable heart failure to advanced heart failure. The criteria of the acronym "I need help" were often used for this purpose, which contains many of the core components for defining advanced heart failure, as recommended by the European heart failure guidelines [2,23,24]. Before a patient enters the screening program for LVAD or HTx, an experienced team of cardiologists makes an informal preselection of patients who appear unsuitable for LVAD or HTx based on clinical appearance. Reasons for rejecting a patient in advance include severe frailty determined by global clinical impression, evident lack of motivation or the presence of a contraindication such as an active malignancy. These patients were not included in this study. Patients that were not rejected in advance were subsequently included in the screening program. The screening program for LVAD and HTx included cardiopulmonary stress testing, prognostic stratification and invasive hemodynamic measurements. Careful selection for LVAD and HTx was conducted according to predefined criteria [24,25]. All patients over 40 years of age who were screened as potential candidate for LVAD implantation or HTx were included for additional screening at the geriatric outpatient clinic. As biological age is expected to exceed chronological age in chronic heart failure [26,27], the inclusion limit for screening at the geriatric outpatient clinic was set at 40 years. Patients intubated and/or sedated in the intensive care unit at the moment of screening were excluded from study participation, since it was not possible to perform a CGA under those conditions. Five patients who did not provide informed consent to participate in the study were also excluded.

# 2.3. Comprehensive geriatric assessment

A CGA was performed in every patient as part of the patient selection procedure for LVAD and HTx, including patients screened for HTx with LVAD in situ. Depending on the clinical situation of the patient, the CGA was performed at the geriatric outpatient clinic or during admission on the cardiology ward. A CGA-trained physician or nurse practitioner performed the CGA, which included evaluation of the patient's medical, mental, functional, and social capabilities and problems. The CGA was based on the Dutch national guideline for CGA and adapted where appropriate for the specific population with advanced heart failure, using the Minnesota Living with Heart Failure Questionnaire to assess quality of life and Fried's frailty criteria to determine frailty. An overview of the components of the CGA, test instruments, corresponding references, ranges, and cut-off points is shown in online supplementary Table S1, [9,18,28]. In every patient, a conclusion comprising frailty and other impairments was formulated on the four mentioned domains and a plan of care was created around patient-centered goals. The treatment recommendations were grouped into the prespecified categories as mentioned in Table 2 of the manuscript and Supplementary Table S2.

The findings of the CGA were discussed in a multidisciplinary team including cardiologists, cardiothoracic surgeons, anesthesiologists, specialized heart failure nurses, intensivists and at least one geriatrician. During this deliberation, it was assessed whether a patient is a suitable candidate for LVAD or HTx. If the patient was deemed suitable for HTx, the patient was placed on the waiting list for Htx. If the patient was deemed suitable for LVAD implantation, the clinical situation determined the duration until LVAD implantation.

#### 2.4. Frailty assessment

In this study, Fried's frailty criteria (Supplementary Table S3) were used to determine frailty as recommended by the Frailty Heart Workgroup of the American Society of Transplantation [29,30].

In addition, we used the Edmonton Frail Scale (EFS) as a second and multi-domain instrument to assess frailty (Supplementary Table S4) [31]. Rolfson et al. demonstrated that the EFS is a valid tool for determining frailty when compared to the CGA and the EFS is used in several cardiac populations, including heart failure patients, in literature [32–35].

## 2.5. Demographic data

Demographic data included age, sex, etiology of the cardiomyopathy, previously implanted LVAD in potential HTx candidates and the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile [36]. INTERMACS (IM) uses a classification system of profiles (IM profile 1–7) to represent the severity of heart failure, which ranges from advanced New York Heart Association class 3 heart failure (IM 7) to critical cardiac shock (IM 1).

# 2.6. Statistical analysis

Continuous demographics are presented as mean and standard deviation (SD). Categorical demographics are expressed as number and corresponding percentage. Outcomes of the CGA, i.e. the impairments and treatment recommendations are also presented as means for continuous variables and numbers for categorical variables. The outcomes of the CGA were stratified by the presence of an LVAD (LVAD in situ vs. no LVAD in situ), age (40–59 years vs.  $\geq$ 60 years), and IM profile (IM 1–3 vs. IM 4–6). The 60-year limit was chosen because of a median age of 59, creating roughly two equally sized groups. Differences in impairments and treatment recommendations were determined with the Student's *t*-test or Mann-Whitney *U* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. For all

tests, a p-value  $\leq$  0.05 was considered statistically significant. Analyses were performed using the Statistical Package for the Social Sciences version 26 (SPSS Inc., Chicago III, United States).

# 3. Results

Data is presented for 73 potential LVAD and HTx candidates who consented to participate in this study between November 2020 and November 2021. Details on patient inclusion are presented in Fig. S1 of the Supplementary Material.

# 3.1. Demographics

Demographics of patients screened for LVAD or HTx are shown in Table 1. The mean age of the study population was 57.9 SD 7.4 years (range 40–71) and 51 patients (70 %) were male. Half of the patients (52 %) were screened for HTx, 45 % for LVAD, and in two patients both options were still open at the moment of the CGA.

# 4. Impairments resulting from the CGA

# 4.1. Frailty

According to Fried's frailty criteria, most patients were non-frail (54 %), 39 % of patients were pre-frail and 7 % were frail. According to the EFS, the majority of patients (86 %) were indicated non-frail. Six patients (9 %) were pre-frail and four (6 %) mildly frail (Table 1).

#### 4.2. Medical status

The mean Charlson Comorbidity index score was 2.1 SD 0.9. In one third of the patients the Charlson Comorbidity index was  $\geq$ 3, indicating a high morbidity burden. Half of the patients had a BMI > 25. Patients used an average of 7.3 chronic medications per day. Polypharmacy ( $\geq$ 5 medications) was present in 77 % of the patients and hyperpolypharmacy ( $\geq$ 10 medications) in 14 %. Bone mineral density was reduced in 63 % of the patients. Renal and liver function were impaired in respectively 29 % and 24 % of the patients.

# 4.3. Cognitive and psychological status

In 29 % of the patients depressive symptoms were present and in 14 % cognitive impairment. The majority of patients reported a reduced quality of life with almost half of the patients describing their quality of life as poor (44 %).

# 4.4. Functional status

Almost half of the patients (47 %) required assistance in the (instrumental) activities of daily living, mostly because of physical limitations due to heart failure. About one third (34 %) of patients were at risk of malnutrition and in 8 % of patients malnutrition was actually present. The Timed Up & Go test was abnormal in 6 % of the study population indicating impaired mobility. Muscle strength (handgrip strength corrected for age and sex) was impaired in more than half of the patients (58 %).

#### 4.5. Social status

A large proportion of patients needed care while living at home: 20 % of patients received caregiver assistance, 18 % household help and 4 % professional care. A quarter (27 %) of the caregivers experienced a high caregiving burden.

Fig. 1 shows the distribution of impairments resulting from the CGA across the different domains (medical, mental, functional and social). A total of 417 impairments were identified during this study. Most

#### Table 1

Results of the comprehensive geriatric assessment in patients screened for left ventricular assist device or heart transplantation.

Demographics		N = 73	%	
Screening during hospitalization		28	38.4	
Screening for	HTx	38	52.1	
	LVAD	33	45.2	
D 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Both HTx/LVAD	2	2.7	
Previously implanted LVAD in		25	65.8	
Age	Years [Mean - SD]	57.9-7	4	
Sex	Male	51	69.9	
Etiology cardiomyopathy	Dilated	34	46.6	
	Ischemic	30	41.1	
	Congenital	2	2.7	
	Hypertrophic	4	5.5	
INTERMACS profile	Other	3	4.1	
INTERMACS prome	3	10	13.7	
	4	23	31.5	
	5	9	12.3	
	6	1	1.4	
	Not applicable due to	26	35.6	
The life	LVAD			
Franty Edmonton Frail scale	No frailty	59	85 5	
Editoritori Fran Scale	Pre-frail	6	87	
	Mild frail	4	5.8	
	Moderate frail	0		
	Severe frail	0		
	Missing	4	5.5	
Fried frailty criteria	No frailty	39	54.2	
	Pre-frail	28	38.9	
	Missing	1	14	
Medical domain	111351116	1	1.1	
BMI	kg/m <sup>2</sup> [Mean - SD]	25.7-3.	8	
	>25	32	50.8	
	Missing	10	13.7	
BSA	m <sup>2</sup> [Mean - SD]	1.98-0.	21	
Smolring status	Missing	10	13.7	
Shioking status	Current	1	1.4	
Alcohol use status	Current	33	46.5	
	Missing	2	2.7	
Comorbidity CCI [Mean - SD]		2.1-0.9		
High morbidity burden	$CCI \ge 3$	22	22 30.1	
Medication use	Number [Mean - SD]	7.3–2.4	7.3–2.4	
	Polypharmacy	54 10	1/2	
	Missing	3	4.1	
Reduced renal function	eGFR < 60	21	28.8	
Reduced liver function	$\text{MELD-score} \geq 14$	17	23.9	
	Missing	2	2.7	
Bone mineral density	Normal bone mineral	18	36.7	
	density	96	F0 1	
	Osteopenia	20 5	55.1 10.2	
	Missing	24	32.9	
Mental domain	0			
Mood	Depression	21	29.2	
	Missing	1	1.4	
MMSE	[Mean - SD]	28.9-0.	8	
MOCA Impaired cognition	[Mean - SD] MMSE $< 24 \text{ or } MOCA < 25$	27.2-2.	12.0	
Resilience Evaluation Scale	[Mean - SD]	26.8-5	2	
Accontence Distribution Deale	< 21	9	12.5	
	Missing	1	1.4	
Quality of life	Good	20	27.4	
	Moderate	21	28.8	
The sting of the state	Poor	32	43.8	
Functional domain		11	15 1	
Dependence in iADI		30	13.1 41 1	
Dependence in (i)ADL		34	46.6	
Nutritional status	At risk of malnutrition	25	34.2	
	(continued on next page)			

#### L. Dautzenberg et al.

#### Table 1 (continued)

Demographics $N = -90$ 73 Reduced 4-meter gait speed $-0$ Missing 8 11.0 Reduced TUGT $4$ 6.1 Missing 7 9.6 Reduced handgrip strength corrected for age and sex $-2$ Mobility $\geq 1$ fall in previous 6 7 9.7 months $-1$ Missing 1 1.1.4 Use of walking aid 5 6.8 Social domain Living situation At home without care 41 57.7 At home with household 13 18.3 help $-1$ At home with help from 14 19.7 caregiver At home with professional 3 4.2 care $-1$ Educational level $-2$ Educational level $-2$ Educational level $-2$ Educational level $-2$ Missing 1 1.4 Employed $-2$ Missing 1 1.4 Emp	Domographics		N	0/
Note that the set of the s	Demographics		N = 72	90
Malnutrition68.2Reduced 4-meter gait speed0Reduced TUGT4Reduced TUGT4Missing79.6Reduced handgrip strength corrected for age and sex21 fall in previous 679.7Mobility≥1 fall in previous 679.6Social domain1Living situationAt home without care4157.7At home with holsehold1318.3helpAt home with help from1419.7caregiver1At home with professional education34.19.7school2Educational levelSecondary vocational education101.4EmployedYes10Yes10Yes111.4EmployedYes1012.3111.4EmployedYes103101.23111.41219.0			73	
Reduced 4-meter gait speed0Reduced TUGT4Reduced TUGT4Missing79.6for age and gex2Mobility≥1 fall in previous 679.7months111.4Use of walking aid5565656565777.7		Malnutrition	6	8.2
Missing811.0Reduced TUGT46.1Meduced handgrip strength correctedMissing79.6for age and sex $21$ fall in previous 679.7Mobility $\geq 1$ fall in previous 679.7Mobility $\geq 1$ fall or previous 679.7Motility $\geq 1$ fall or previous 679.7Social domain $X$ $X$ $X$ Living situation $X$ thome without care419.7At home with household1318.3helpAt home with professional34.2 $X$ Care $X$ $X$ $X$ $X$ Educational levelPrimary and secondary27 $X$ Bachelor's/master's27 $X$ $X$ Gegree $X$ $X$ $X$ $X$ In a relationshipYes5879.5Garegiver burdenYes5879.5Garegiver burdenYes5879.5Garegiver burdenYes5	Reduced 4-meter gait speed		0	
Reduced TUGT46.1Missing79.6Reduced handgrip strength corrected for age and sex $\geq 1$ fall in previous 679.7Mobility $\geq 1$ fall in previous 679.7Social domain $= 1$ fall in previous 679.7Living situationAt home without care4157.7At home with household1318.3helpAt home with professional34.2care22.7Educational levelPrimary and secondary2737.5school22.737.5degreeMissing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5879.5Garegiver burdenYes5879.5Garegiver burdenYes5879.5 <td></td> <td>Missing</td> <td>8</td> <td>11.0</td>		Missing	8	11.0
Missing79.6Reduced handgrip strength corrected for age and sex $21$ fall in previous 6 months79.7Mobility $\geq 1$ fall in previous 679.7Mobility $\geq 1$ fall in previous 679.7Moths11.41.4Use of walking aid56.8Social domain4t home without care4157.7Living situationAt home with household1318.3help1419.7caregiverAt home with holp from1419.7caregiver4t home with professional34.2At home with professional22.7Educational levelPrimary and secondary2737.5school325.0educationeducation1825.025.0effreeMissing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5879.5Garegiver burdenYes5879.5Garegiver burdenYes5879.5Garegiver burdenYes5879.5Garegiver burden1727.0NoNo caregiver burden3454.0Higk caregiver burden1727.0No caregiver burden13.713.7	Reduced TUGT		4	6.1
Reduced handgrip strength corrected for age and sex       42       57.5         Mobility       ≥1 fall in previous 6       7       9.7         months       Missing       1       1.4         Use of walking aid       5       6.8         Social domain       41       57.7         Living situation       At home without care       41       57.7         At home with household       13       18.3         help		Missing	7	9.6
for age and sexMobility $≥1$ fall in previous 679.7monthsMissing11.4Use of walking aid56.8Social domain11.4Living situationAt home without care4157.7At home with household1318.3help119.7caregiver14.1At home with help from1419.7caregiver134.2care135.5Educational levelPrimary and secondary2737.5school125.025.0education11.4EmployedYes2635.6No3852.11.1.4In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.0NoNo caregiver burden1727.0No caregiver burden1727.0No caregiver burden1313.7	Reduced handgrip strength corrected		42	57.5
Mobility $\geq 1$ fall in previous 679.7monthsMissing11.4Missing11.4Use of walking aid56.8Social domainAt home without care4157.7Living situationAt home with household1318.3helpAt home with help from1419.7caregiverAt home with professional34.2careMissing22.7Educational levelPrimary and secondary2737.5schoolSecondary vocational1825.0educationBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.111.4In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden3454.0High caregiver burden1727.0No caregiver burden1219.013.713.7	for age and sex			
monthsMissing11.4Use of walking aid56.68Social domain157.7Living situationAt home without care4157.7At home with household1318.3help1419.7caregiver419.7caregiver4.2care22.7Educational levelPrimary and secondary2737.5school22.7Educational levelPrimary and secondary2737.5school1EmployedYes2635.6No3852.111.4EmployedYes5980.879.5Having childrenYes5879.5Caregiver burden3454.0116 caregiver burden34Having childrenYes5879.5Caregiver burden1727.0Nocaregiver burden1727.0No caregiver burden1219.013.713.7	Mobility	$\geq 1$ fall in previous 6	7	9.7
Missing Use of walking aid11.4Social domain156.8Social domainAt home without care4157.7At home with household1318.3help1419.7caregiverAt home with help from1419.7caregiver419.7care732.2Educational levelPrimary and secondary2737.5school22.737.5Bachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.18Having childrenYes5980.8Having childrenYes5879.5Caregiver burden1454.011.9Higk caregiver burden1727.0No caregiver burden1727.0No caregiver burden13.713.7		months		
Use of walking aid56.8Social domainAt home without care4157.7At home without care4157.7At home with household1318.3help1419.7At home with help from1419.7caregiverAt home with professional3At home with professional34.2care117.7Educational levelPrimary and secondary27Secondary vocational1825.0education1825.0education1825.0education1414.4EmployedYes2635.6No3852.1In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.0NoNo caregiver burden1727.0NoNo caregiver burden1219.0Missing1013.7		Missing	1	1.4
Social domain Living situation At home without care At home with household 13 18.3 help At home with help from 14 19.7 caregiver At home with professional 3 4.2 care Missing 2 2 2.7 Educational level Primary and secondary 27 37.5 school Secondary vocational 18 25.0 education Bachelor's/master's 27 37.5 degree Missing 1 1 4.4 Employed Yes 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 17 27.0 No caregiver burden 13		Use of walking aid	5	6.8
Living situationAt home without care4157.7At home with household1318.3help1318.3help1419.7caregiver34.2care4t home with professional3At home with professional level22.7Educational levelPrimary and secondary2737.5school325.0education825.0education825.0education11.4EmployedYes2635.6No3852.1In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.0No caregiver burden1727.0No caregiver burden1727.0No caregiver burden1313.7	Social domain			
At home with household1318.3helpAt home with help from1419.7At home with help from1419.7caregiverAt home with professional34.2CareMissing22.7Educational levelPrimary and secondary2737.5schoolSecondary vocational1825.0educationBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.11In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden3454.0High caregiver burden3454.0High caregiver burden1727.0Nocaregiver1013.7	Living situation	At home without care	41	57.7
helpAt home with help from1419.7caregiver-At home with professional34.2careMissing22.7Educational levelPrimary and secondary2737.5schoolBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.1-Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden3454.0-High caregiver burden1727.0No caregiver burden13.713.7	-	At home with household	13	18.3
At home with help from caregiver1419.7 raregiverAt home with professional care34.2 careAt home with professional care32.2Educational levelPrimary and secondary school2737.5 schoolEducational levelSecondary vocational education1825.0 educationBachelor's/master's degree2737.5 schoolEmployedYes2635.6 NoNo3852.1 Retired912.3In a relationship Having childrenYes5980.8 Having children79.5 StateLow caregiver burden3454.0 High caregiver burden1370.0 No caregiver13.7		help		
caregiver At home with professional 3 4.2 care Missing 2 2.7 Primary and secondary 27 37.5 school Secondary vocational 18 25.0 education Bachelor's/master's 27 37.5 degree Missing 1 1.4 Employed Yes 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver burden 17 27.0 No caregiver burden 17 27.0 Missing 10 13.7		At home with help from	14	19.7
At home with professional34.2careMissing22.7Educational levelPrimary and secondary2737.5schoolSecondary vocational1825.0educationBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.1Retired9In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.0No caregiver burden17Missing10113.7		caregiver		
care Missing 2 2.7 Feducational level 27 37.5 school 27 37.5 school 27 37.5 school 27 37.5 degree 27 37.5 degree 27 37.5 degree 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver burden 17 27.0 No caregiver burden 17 19.0 No caregiver burden 17 19.0 No caregiver burden 17 19.0 Missing 10 13.7		At home with professional	3	4.2
Missing22.7Educational levelPrimary and secondary school2737.5Secondary vocational1825.0educationBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden3454.0High caregiver burden1727.0No caregiver burden1727.0No caregiver1219.0Missing1013.713.713.7		care		
Educational levelPrimary and secondary school2737.5Secondary vocational education1825.0Bachelor's/master's degree2737.5Missing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.0NoNo caregiver burden1727.0No caregiver1013.7		Missing	2	2.7
school Secondary vocational 18 25.0 education Bachelor's/master's 27 37.5 degree Missing 1 1.4 Employed Yes 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver burden 17 27.0 No caregiver burden 17 19.0 Missing 10 13.7	Educational level	Primary and secondary	27	37.5
Secondary vocational1825.0educationBachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden3454.0High caregiver burden1727.0No caregiver1013.7		school		
education Bachelor's/master's 27 37.5 degree Missing 1 1.4 Employed Yes 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver burden 17 27.0 No caregiver 12 19.0 Missing 10 13.7		Secondary vocational	18	25.0
Bachelor's/master's2737.5degreeMissing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burden1727.019.0Missing1013.713.7		education		
degree Missing 1 1.4 Employed Yes 26 35.6 No 38 52.1 Retired 9 12.3 In a relationship Yes 59 80.8 Having children Yes 58 79.5 Caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver burden 17 27.0 Missing 10 13.7		Bachelor's/master's	27	37.5
Missing11.4EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burdenLow caregiver burden3454.0High caregiver burden1727.0No caregiver1013.7		degree		
EmployedYes2635.6No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burdenLow caregiver burden3454.0High caregiver burden1727.0No caregiver1013.7		Missing	1	1.4
No3852.1Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burdenLow caregiver burden3454.0High caregiver burden1727.0No caregiver1219.0Missing1013.7	Employed	Yes	26	35.6
Retired912.3In a relationshipYes5980.8Having childrenYes5879.5Caregiver burdenLow caregiver burden3454.0High caregiver burden1727.0No caregiver1219.0Missing1013.7	1 5	No	38	52.1
In a relationship     Yes     59     80.8       Having children     Yes     58     79.5       Caregiver burden     Ja     54.0       High caregiver burden     17     27.0       No caregiver     12     19.0       Missing     10     13.7		Retired	9	12.3
Having children     Yes     58     79.5       Caregiver burden     Low caregiver burden     34     54.0       High caregiver burden     17     27.0       No caregiver     12     19.0       Missing     10     13.7	In a relationship	Yes	59	80.8
Caregiver burden Low caregiver burden 34 54.0 High caregiver burden 17 27.0 No caregiver 12 19.0 Missing 10 13.7	Having children	Yes	58	79.5
High caregiver burden 17 27.0 No caregiver 12 19.0 Missing 10 13.7	Caregiver burden	Low caregiver burden	34	54.0
No caregiver 12 19.0 Missing 10 13.7	<u> </u>	High caregiver burden	17	27.0
Missing 10 137		No caregiver	12	19.0
11100115 10 10.7		Missing	10	13.7

Missing values are indicated for each variable in the table.

Ranges for instruments are available in Table S1 of the supplement.

ADL, activities of daily living; BMI, body mass index; BSA, body surface area; CCI, charlson comorbidity index; eGFR, estimated glomerular filtration rate; HTx, heart transplantation; iADL, instrumental activities of daily living; LVAD, left ventricular assist device; MELD, model for end-stage liver disease; MMSE, mini mental state examination; MoCA, montreal cognitive assessment; TUGT, timed up and go test.

impairments were related to the functional domain (37 %) and the medical domain (37 %).

#### 4.6. Treatment recommendations resulting from the CGA

The treatment recommendations, that are part of the integrated care plan that resulted from the CGA, are divided into 13 categories, see Table 2. The mean number of treatment recommendations per patient was 3.6 SD 1.6.

In one in eight patients (12 %), the suitability for HTx or LVAD implantation was determined negative or ambiguous. Of the five patients with an ambiguous advice, one patient was non-frail and the other four were pre-frail according to the Fried's frailty criteria. According to the EFS, four patients were non-frail and one pre-frail. Clinical factors of frailty status that led to an ambiguous advice were social or financial vulnerability, (a risk of) malnutrition, obesity (BMI 31.2), problems with cognition, decreased functional reserves, and the need of mental support to improve coping strategies. Of the three patients with a negative advice, one was indicated as non-frail by Fried's frailty criteria, one person as pre-frail and one person as frail. On the EFS, one person scored non-frail, the other two mildly frail. Findings that indicated this frailty status that led to a negative advice included a high morbidity burden, limited physical reserves, malnutrition, social vulnerability, cognitive impairment, mental problems, and decreased functionality and mobility.

Most recommendations were given for the following categories: recommendations regarding education (regarding the intervention and clinical course postoperatively), patient counselling, shared decision making and advance care planning (40 %), recommendations regarding delirium risk and prevention (36 %), recommendations regarding mobility and fall prevention (34 %), and recommendations regarding malnutrition or weight reduction (33 %).

Fig. 2 presents to which domains (medical, mental, functional and social) the treatment recommendations belong. A total of 163 treatment recommendations were provided. Most recommendations were related to the functional domain (36 %), followed by the mental domain (30 %) and medical domain (27 %).

# 4.7. Stratifications

Liver function was more often impaired in patients without LVAD in situ than in patients with LVAD (36 vs. 4 %). Quality of life was more often poor in the group without LVAD in situ (57 vs. 19 %). The group with LVAD in situ required more often assistance in activities of daily living (mainly requiring assistance with showering) than the group without LVAD in situ (27 vs 9 %). There was a trend of increased dependence in instrumental activities of daily living in patients without an LVAD in situ compared with patients with an LVAD in situ, with those without LVAD needing more help with household tasks, shopping and travelling, but this difference was not statistically significant (p = 0.07). There was also a trend of increased frailty in patients without an LVAD in situ when compared to patients with an LVAD in situ, however, again this difference was not statistically significant (p = 0.07) (Supplementary Table S5).

Patients older than 60 years used a significantly greater amount of chronic medications (8.1 vs. 6.5), and hyperpolypharmacy was more common (25 vs. 5 %), compared to patients younger than 60 years old. Renal function was more often impaired in patients over 60 years old (41 vs. 18 %) (Supplementary Table S6).

There was a trend of increased frailty, and decreased functionality and mobility in patients with IM profile 1–3 compared to patients with IM profile 4–6, however, the difference was not statistically significant (Supplementary Table S7).

In Supplementary Tables S8–S10 the differences in treatment recommendations for all the stratifications are presented.

# 5. Discussion

This study demonstrated that a small proportion of the potential LVAD and HTx candidates were frail, while over a third of patients were pre-frail (39%). In 97% of patients, at least 1 impairment was identified by the CGA. The most common impairments were polypharmacy, high morbidity burden, reduced renal function, osteopenia, depression, poor quality of life, reduced functionality, (risk of) malnutrition, reduced grip strength and high caregiver burden. Quality of life was worse in the group without LVAD in situ and the group with LVAD in situ required more often assistance in activities of daily living. Older patients more often had hyperpolypharmacy. The most common treatment recommendation that resulted from the CGA concerned recommendations regarding education, patient counselling, shared decision making and advance care planning. The domains for which most impairments were found and the domains for which most treatment recommendations were given matched well, with the functional domain as frontrunner.

In recent years, it has been recognized that heart failure is a multidomain condition [18]. Gorodeski et al. previously emphasized that the role of frailty, depression, cognitive impairment, nutrition, social environment, and care goals are each relevant to the implementation and success of medical therapy in this population [18]. The symptoms of heart failure and the physical domain of frailty (decreased exercise tolerance, symptoms of fatigue, and cachexia) correspond partly



**Fig. 1.** The distribution of impairments resulting from the comprehensive geriatric assessment across the different domains (medical, mental, functional and social). (i)ADL, (instrumental) activities of daily living; TUGT, timed up and go test. All impairments were classified according to the domain to which they relate (medical, mental, functional and social). Of the impairments, frailty was not subdivided into any of the domains because all domains together lead to frailty.

# Table 2

Treatment recommendations resulting from the comprehensive geriatric assessment.

Treatment recommendations categories:	$\mathbf{N} =$	%
	73	
Eligibility for LVAD/HTx intervention		91.8
Positive	59	88.1
Negative	3	4.5
Ambiguous	5	7.5
Missing	6	8.2
Recommendations regarding diagnosis and treatment of	13	17.8
osteoporosis and sarcopenia		
Recommendations regarding other somatic problems	15	20.5
Recommendations regarding medication modifications		20.5
Recommendations regarding (the analysis of) cognition		12.3
Recommendations regarding (the analysis of) mood and mental		19.2
support for both patients and relatives		
Recommendations regarding delirium risk and prevention		35.6
Recommendations regarding malnutrition and weight reduction	24	32.9
Recommendations regarding mobility and fall prevention		34.2
Recommendations regarding intoxications		1.4
Recommendations regarding (cardiac) rehabilitation		12.3
Recommendations regarding patient's care needs and		16.4
strengthening of social and financial support		
Recommendations regarding education, patient counselling, shared	29	39.7
decision making and advance care planning		
Other recommendations	1	1.4

HTx, heart transplantation; LVAD, left ventricular assist device.

because frailty and heart failure share common pathological pathways of low-grade inflammation and metabolic stress [9]. This may explain the difference in the number of pre-frail potential candidates according to the Fried's frailty criteria and the EFS: the Fried's frailty criteria partially overlap with symptoms of end-stage heart failure and this is less the case with the EFS. It is difficult to distinguish frailty and other impairments as symptoms of end-stage heart failure that may be reversible after LVAD or HTx from frailty and impairments that are (partially) independent of the heart failure. In case of reversibility, HTx or LVAD intervention will be considered to be more suitable than in case of irreversible impairments. Previous studies have already shown that frailty assessed by Fried's frailty criteria and handgrip strength improve significantly after LVAD and HTx [21]. There is also evidence that cognition, anxiety, and depression improve after LVAD implantation [29,37,38].

To the best of our knowledge, no other studies have been published in which a CGA was performed in potential candidates for LVAD or HTx. There are also no studies with treatment recommendations resulting from (individual components of the) CGA in this population. One study found a modest beneficial effect of a shared decision-support intervention on the quality of decision-making among patients and caregivers considering LVAD therapy [39]. In recipients of HTx, a positive effect of cardiac rehabilitation and nutritional supplementation was found on major adverse cardiac events and in-hospital mortality and sepsis, respectively [40,41]. Studies have been conducted in which a CGA was performed in the heart failure population [42,43], however, extrapolation of these findings to our study is hampered due to differences in heart



**Fig. 2.** The distribution of the treatment recommendations resulting from the comprehensive geriatric assessment across the different domains (medical, mental, functional and social). All treatment recommendations were classified according to the domain to which they relate (medical, mental, functional and social). The treatment recommendations related to the eligibility for LVAD/HTx and recommendations regarding education, patient counselling, shared decision making and advance care planning, were not assigned to one specific domain as all domains taken together result in whether a person is appropriate for the intervention and are input for an advance care planning (ACP) conversation. In ACP conversations, the healthcare professional discusses with the patient what goals of care fit with the patient's values, beliefs and health status. This way, appropriate care and treatment is determined for the short term and direction is given for appropriate care and treatment in future scenarios.

failure severity and mean age of the study population. Studies in which some individual components of the CGA have been assessed showed that depression, anxiety, non-compliance, malnutrition, multimorbidity, psychiatric problems, reduced functionality, social support, cognition and quality of life are frequent in patients (screened for) LVAD or HTx [44–48]. Again, comparison with the results of the current study is complicated by the differences in percentage of patients with an LVAD in situ and timing of the trajectory of LVAD and HTx (current study) to actual implantation or transplantation and many years of follow-up.

The past 10 years, an increasing amount of research has been conducted on the prevalence of frailty in patients undergoing LVAD or HTx. In the most recent systematic review frailty was found in 21 % of LVAD patients [49]. A recent study (2022) in patients who underwent LVAD implantation found that one week prior to surgery, 54 % of the patients were frail according to Fried's frailty criteria [50]. This rate is higher than the 9 % frailty according to Fried's criteria in patients without LVAD in situ in the current study. In the current study, informal prescreening has already taken place, with the cardiologist already deciding not to screen for LVAD and HTx for obviously very vulnerable patients. In two recent studies of 60 and 99 patients on the HTx waiting list, 11 and 31 % of the patients appeared to be frail according to the Fried's frailty criteria [46,51]. A direct comparison between the current study and other studies is limited by the fact that frailty is dynamic and heterogeneity exists with respect to heart failure severity, presence of an LVAD, INTERMACS profile, age etc.

# 6. Strengths and limitations

This study was the first to perform a CGA in this specific group of patients with end-stage heart failure. A large amount of information was collected on this inception cohort of patients at the time of screening for LVAD and HTx, in different domains, through interviews, the use of multiple testing instruments and additional (laboratory/radiological) examination. The CGA was performed by well-trained healthcare professionals in geriatrics, ensuring the quality of the data of this study.

This study also has a few limitations. For eight patients it was not possible to perform the 4-meter walk test because they were immobile. These values were considered missing in the analyses, leading to a potential overestimation of walking speed and mobility in the study population. Second, delirium risk was often estimated during the CGA based on clinical features, but not in a systematic, quantifying way using a diagnostic instrument. For this reason, we were unable to assess an increased delirium risk as an impairment. The distribution of impairments and treatment recommendations resulting from the CGA across the four domains would be more congruent if delirium risk was included as an impairment. Third, the study population was relatively heterogeneous including patients screened for both LVAD and HTx, both with and without LVAD in situ, screened at the geriatric outpatient clinic or during admission on the cardiology ward. Stratifications were performed to gain more insight into the effect of different patient characteristics on identified impairments and treatment recommendations. However, the stratification by IM profile included only 47 patients,

which may have created a power problem.

# 7. Clinical implications and future research

This study has demonstrated that, despite the relatively young population already informal pre-selected by cardiologists, impairments are common in all four domains of the CGA. Decision making regarding patient selection for LVAD and HTx is complex and unique for each patient. The comprehensive information obtained through a CGA can be incorporated into this (complex) decision making. Discussion of goals of care with patients and near-ones ensures that the intervention matches the patient's values. Social and mental support can be provided. Impairments are also potential targets for improving physical fitness before surgery, with exercise, physical rehabilitation and nutritional supplementation potentially effective in improving preoperative frailty in patients with heart failure; however, no studies have reported the impact of prehabilitation on the outcomes after LVAD or HTx yet [21]. Also, based on these impairments, recommendations can be made for postoperative rehabilitation or prevention of complications like delirium. A geriatrician is trained to translate findings from the CGA into the above mentioned multidisciplinary interventions. It is recommended that future research investigate the effect of these multidisciplinary interventions on the patient-selection process and outcomes of LVAD and HT<sub>x</sub>.

Previous studies have shown that components of the CGA (frailty, cognition and depression) are of prognostic value for mortality after LVAD and HTx [52,53]. Future research should examine the prognostic value of impairments identified by the CGA in order to further optimize the decision making process. Also, the reversibility of impairments after LVAD implantation or HTx should be investigated.

#### 8. Conclusion

This study showed that in 97 % of the potential candidates for LVAD and HTx at least 1 impairment was identified by the CGA. A small proportion of potential candidates were indicated as frail, yet over a third of patients appeared pre-frail. The domains for which most impairments were found and the domains for which most treatment recommendations were made matched well, with the functional domain as frontrunner. Impairments and associated risks can contribute to the decision making process concerning candidacy for LVAD and HTx, and are potential targets for improving pre-operative fitness. The prognostic value of these impairments needs further investigation.

# 9. Sponsor's Role

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

# CRediT authorship contribution statement

Lauren Dautzenberg: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft. Linda W. van Laake: Conceptualization, Methodology, Writing – review & editing. Renee C.M.A. Raijman: Methodology, Writing – review & editing. Geert J. Lefeber: Data curation, Investigation, Software, Validation, Writing – review & editing. Wilma Knol: Conceptualization, Methodology, Supervision, Writing – review & editing. Marish I.F. Oerlemans: Methodology, Writing – review & editing. Faiz Z. Ramjankhan: Conceptualization, Methodology, Writing – review & editing. Susan A. Braithwaite: Methodology, Writing – review & editing. Mieke D.J. Nagtegaal: Investigation, Writing – review & editing. Marielle H. Emmelot-Vonk: Conceptualization, Methodology, Supervision, Writing – review & editing. Huiberdina L Koek: Conceptualization, Methodology, Supervision, Writing – review & editing.

# **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2023.101318.

#### References

- [1] V.L. Roger, Epidemiology of heart failure, Circ. Res. 113 (2013) 646-659.
- [2] T.A. McDonagh, M. Metra, M. Adamo, R.S. Gardner, A. Baumbach, M. Böhm, et al., 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 42 (2021) 3599–3726.
- [3] E.A. Rose, A.C. Gelijns, A.J. Moskowitz, D.F. Heitjan, L.W. Stevenson, W. Dembitsky, et al., Long-term use of a left ventricular assist device for end-stage heart failure, N. Engl. J. Med. 345 (2001) 1435–1443.
- [4] K.K. Khush, W.S. Cherikh, D.C. Chambers, M.O. Harhay, D. Hayes, E. Hsich, et al., The international thoracic organ transplant registry of the international society for heart and lung transplantation: thirty-sixth adult heart transplantation report — 2019; focus theme: donor and recipient size match, J. Heart Lung Transplant. 38 (2019) 1056–1066.
- [5] E.J. Molina, P. Shah, M.S. Kiernan, W.K. Cornwell, H. Copeland, K. Takeda, et al., The society of thoracic surgeons intermacs 2020 annual report, Ann. Thorac. Surg. 111 (2021) 778–792.
- [6] S.L. McCartney, C. Patel, J.M. Del Rio, Long-term outcomes and management of the heart transplant recipient, Best Pract. Res. Clin. Anaesthesiol. 31 (2017) 237–248.
- [7] E.M. Defilippis, K. Breathett, E.M. Donald, S. Nakagawa, K. Takeda, H. Takayama, et al., Psychosocial risk and its association with outcomes in continuous-flow left ventricular assist device patients, Circ. Heart Fail. 13 (2020) E006910.
- [8] T. Jaarsma, L. Hill, A. Bayes-Genis, H.P.B. La Rocca, T. Castiello, J. Čelutkienė, et al., Self-care of heart failure patients: practical management recommendations from the heart failure association of the european society of cardiology, Eur. J. Heart Fail. 23 (2021) 157–174.
- [9] E.M. DeFilippis, S. Nakagawa, M.S. Maurer, V.K. Topkara, Left ventricular assist device therapy in older adults: addressing common clinical questions, J. Am. Geriatr. Soc. 67 (2019) 2410–2419.
- [10] A. Clegg, Frailty in older people, Lancet 381 (2013) 752–762.
- [11] S.R. Aili, R. De Silva, K. Wilhelm, S.R. Jha, R. Fritis-Lamora, E. Montgomery, et al., Validation of cognitive impairment in combination with physical frailty as a predictor of mortality in patients with advanced heart failure referred for heart transplantation, Transplantation 106 (2022) 200–209.
- [12] S.M. Joseph, J.L. Manghelli, J.M. Vader, T. Keeney, E.L. Novak, J. Felius, et al., Prospective assessment of frailty using the fried criteria in patients undergoing left ventricular assist device therapy, Am. J. Cardiol. 120 (2017) 1349–1354.
- [13] G. Yost, G. Bhat, Relationship between handgrip strength and length of stay for left ventricular assist device implantation, Nutr. Clin. Pract. 32 (2017) 98–102.
- [14] Y. Moayedi, J.G. Duero Posada, F. Foroutan, L.A. Goldraich, A.C. Alba, J. MacIver, et al., The prognostic significance of frailty compared to peak oxygen consumption and B-type natriuretic peptide in patients with advanced heart failure, Clin. Transplant. 32 (2018) e13158.
- [15] P. Macdonald, Frailty of the Heart Recipient, Transplantation, vol. 105, Lippincott Williams and Wilkins, 2021, pp. 2352–2361.
- [16] D. Wieland, V. Hirth, Comprehensive geriatric assessment, Cancer Control. 10 (2003) 454–462.
- [17] D.M. Jones, X. Song, K. Rockwood, Operationalizing a frailty index from a standardized comprehensive geriatric assessment, J. Am. Geriatr. Soc. 52 (2004) 1929–1933.
- [18] E.Z. Gorodeski, P. Goyal, S.L. Hummel, A. Krishnaswami, S.J. Goodlin, L.L. Hart, et al., Domain management approach to heart failure in the geriatric patient: present and future, J. Am. Coll. Cardiol. 71 (2018) 1921–1936.
- [19] C. Vitale, I. Spoletini, G.M. Rosano, Frailty in heart failure: implications for management, Card. Fail. Rev. 4 (2018) 104–106.
- [20] J.H.I. Wiersinga, H.F.M. Rhodius-Meester, E.E.F. Kleipool, L. Handoko, A.C. van Rossum, S.S. Liem, et al., Managing older patients with heart failure calls for a holistic approach, ESC Heart Fail. 8 (2021) 2111–2119.
- [21] S.R. Aili, J.E. Villanueva, Y. Joshi, S. Emmanuel, P. Macdonald, Prevention and reversal of frailty in heart failure, Circ. J. 86 (2022) 14–22.
- [22] R.W. Squires, A.R. Bonikowske, Cardiac rehabilitation for heart transplant patients: considerations for exercise training, Prog. Cardiovasc. Dis. 70 (2022) 40–48.
- [23] J. Baumwol, "I Need Help"-a mnemonic to aid timely referral in advanced heart failure, J. Heart Lung Transplant. 36 (2017) 593–594.
- [24] N. de Jonge, K. Damman, F.Z. Ramjankhan, N.P. van der Kaaij, S.A.J. van den Broek, M.E. Erasmus, et al., Listing criteria for heart transplantation in the Netherlands, Netherlands Heart J. 29 (2021) 611–622.
- [25] E.V. Potapov, C. Antonides, M.G. Crespo-Leiro, A. Combes, G. Färber, M. M. Hannan, et al., 2019 EACTS expert consensus on long-term mechanical circulatory support, Eur. J. Cardio.-Thorac. Surg. 56 (2019) 230–270.

#### L. Dautzenberg et al.

- [26] M.R. Hamczyk, R.M. Nevado, A. Barettino, V. Fuster, V. Andrés, Biological versus chronological aging: JACC focus seminar, J. Am. Coll. Cardiol. 75 (2020) 919–930.
- [27] P. Moons, A. Marelli, Born to age: when adult congenital heart disease converges with geroscience, JACC Adv. 1 (2022), 100012.
- [28] Guideline Comprehensive geriatric assessment. Utrecht: Federatie Medisch Specialisten; 2021. Available at: https://richtlijnendatabase.nl/richtlijn/comprehe nsive\_geriatric\_assessment\_cga/startpagina\_-comprehensive\_geriatric\_assessment\_ cga.html Accessed December 12, 2022.
- [29] J. Kobashigawa, P. Shah, S. Joseph, M. Olymbios, G. Bhat, K. Dhital, et al., Frailty in heart transplantation: report from the heart workgroup of a consensus conference on frailty, Am. J. Transplant. 21 (2021) 636–644.
- [30] L.P. Fried, C.M. Tangen, J. Walston, A.B. Newman, C. Hirsch, J. Gottdiener, et al., Frailty in older adults: evidence for a phenotype, J. Gerontol. – Ser. A Biol. Sci. Med. Sci. 56A (2001) 146–157.
- [31] D.B. Rolfson, S.R. Majumdar, R.T. Tsuyuki, A. Tahir, K. Rockwood, Validity and reliability of the edmonton frail scale, Age Ageing 35 (2006) 526–529.
- [32] K. Studzińska, P. Wąż, A. Frankiewicz, I. Stopczyńska, R. Studnicki, R. Hansdorfer-Korzon, Employing the multivariate edmonton scale in the assessment of frailty syndrome in heart failure, J. Clin. Med. 11 (2022) 4022.
- [33] S. Sze, P. Pellicori, J. Zhang, J. Weston, A.L. Clark, Identification of frailty in chronic heart failure, JACC Heart Fail. 7 (2019) 291–302.
- [34] S. Blanco, J. Ferrières, V. Bongard, O. Toulza, F. Sebai, S. Billet, et al., Prognosis impact of frailty assessed by the Edmonton frail scale in the setting of acute coronary syndrome in the elderly, Can. J. Cardiol. 33 (2017) 933–939.
- [35] L. Koizia, S. Khan, A. Frame, G.W. Mikhail, S. Sen, N. Ruparelia, et al., Use of the Reported Edmonton Frail Scale in the assessment of patients for transcatheter aortic valve replacement. A possible selection tool in very high-risk patients? J. Geriatr. Cardiol. 15 (2018) 463–466.
- [36] L.W. Stevenson, F.D. Pagani, J.B. Young, M. Jessup, L. Miller, R.L. Kormos, et al., INTERMACS profiles of advanced heart failure: the current picture, J. Heart Lung Transplant. 28 (2009) 535–541.
- [37] G. Yost, G. Bhat, E. Mahoney, A. Tatooles, Reduced anxiety and depression in patients with advanced heart failure after left ventricular assist device implantation, Psychosomatics 58 (2017) 406–414.
- [38] J.J. Choi, M.A. Oldham, T. Pancharovski, A. Rubano, P. Walsh, J.D. Alexis, et al., Cognitive change after left ventricular assist device implantation: a case series and systematic review, J. Acad. Consult. Psych. 63 (2022) 599–606.
- [39] L.A. Allen, C.K. McIlvennan, J.S. Thompson, S.M. Dunlay, S.J. LaRue, E.F. Lewis, et al., Effectiveness of an intervention supporting shared decision making for destination therapy left ventricular assist device: the DECIDE-LVAD randomized clinical trial, JAMA Intern. Med. 178 (2018) 520–529.
- [40] K.E. Uithoven, J.R. Smith, J.R. Medina-Inojosa, R.W. Squires, T.P. Olson, The role of cardiac rehabilitation in reducing major adverse cardiac events in heart transplant patients, J. Card. Fail. 26 (2020) 645–651.

- [41] A.M. Karim, M. Aljammal, M.S. Panhwar, A. Kalra, Impact of malnutrition and interventions on patients receiving heart transplant, J. Heart Lung Transplant. 39 (2020) S256–S257.
- [42] E.E.F. Kleipool, J.H.I. Wiersinga, M.C. Trappenburg, A.C. van Rossum, C.S. van Dam, S.S. Liem, et al., The relevance of a multidomain geriatric assessment in older patients with heart failure, ESC Heart Fail. 7 (2020) 1264–1272.
- [43] C. Rodriguez-Pascual, E. Paredes-Galan, A. Vilches-Moraga, A.I. Ferrero-Martinez, M. Torrente-Carballido, F. Rodriguez-Artalejo, Comprehensive geriatric assessment and 2-year mortality in elderly patients hospitalized for heart failure, Circ. Cardiovasc. Qual. Outcomes 7 (2014) 251–258.
- [44] S. Lundgren, C.Y.M. Poon, A. Selim, B.D. Lowes, R. Zolty, A. Burdorf, et al., Depression and anxiety in patients undergoing left ventricular assist device implantation, Int. J. Artif. Organs. 41 (2018) 76–83.
- [45] R.N. Sladen, M.A. Shulman, A. Javaid, C. Hodgson, P.S. Myles, D. Mcgiffin, et al., Postdischarge functional capacity, health-related quality of life, depression, anxiety, and post-traumatic stress disorder in patients receiving a long-term left ventricular assist device, J. Card. Fail. 28 (2022) 83–92.
- [46] A. Ayesta, M.J. Valero Masa, M.T. Vidán, R. Luna-López, J. Segovia-Cubero, M. D. García-Cosío, et al., Prevalence and characterization of frailty, depression, and cognitive impairment in patients listed for heart transplantation: Results of the FELICITAR prospective registry, Clin. Transplant, 35 (2021) e14391.
- [47] V. Jain, A. Karim, A. Bansal, K. Bhatia, A. Gage, M.S. Panhwar, et al., Relation of malnutrition to outcome following orthotopic heart transplantation, Am. J. Cardiol. 142 (2021) 156–157.
- [48] M. Gomis-Pastor, E. Roig Mingell, S. Mirabet Perez, V. Brossa Loidi, L. Lopez Lopez, A. Diaz Bassons, et al., Multimorbidity and medication complexity: new challenges in heart transplantation, Clin. Transplant. 33 (2019) e13682.
- [49] G. Tse, M. Gong, S.H. Wong, W.K.K. Wu, G. Bazoukis, K. Lampropoulos, et al., Frailty and clinical outcomes in advanced heart failure patients undergoing left ventricular assist device implantation: a systematic review and meta-analysis, J. Am. Med. Dir. Assoc. 19 (2018) 255–261.
- [50] H.G. Uzun, E. Simsek, C. Engin, T. Yagdi, H. Karapolat, M. Ozbaran, et al., Relation between frailty and 1-year outcomes after implantation of a left ventricular assist device, Am. J. Cardiol. 173 (2022) 88–93.
- [51] U. Ali, L. Giudicatti, F. Lee, C. Fazackerley, K. Slimani, C. Merry, et al., Outcomes of cardiac transplantation in Western Australia – a contemporary single centre experience, Heart Lung Circ. 31 (2022) 1685–1691.
- [52] M.A. Pavol, A.K. Boehme, J.Z. Willey, J.R. Festa, R.M. Lazar, S. Nakagawa, et al., Predicting post-LVAD outcome: is there a role for cognition? Int. J. Artif. Organs. 44 (2021) 237–242.
- [53] B.S. Bürker, L. Gullestad, E. Gude, O.E. Havik, A. Relbo Authen, I. Grov, et al., The predictive value of depression in the years after heart transplantation for mortality during long-term follow-up, Psychosom. Med. 81 (2019) 513–520.