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Septuagenarian population has similar survival and outcomes to younger patients after left ventricular assist device implantation

Les patients âgés de plus de 70 ans implantés d'une assistance cardiaque ventriculaire gauche à flux continue ont des résultats et une survie similaires que les patients de moins de 70 ans

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Abbreviations: HF, Heart Failure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, Left Ventricular Assist Device.

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KEYWORDS

Left ventricular assist device;
Elderly patients;
Septuagenarians;
Survival;
LVAD-related complications

Summary

Background. — Left ventricular assist device (LVAD) implantation may be an attractive alternative therapeutic option for elderly patients with heart failure who are ineligible for heart transplantation.

Aim. — We aimed to describe the characteristics and outcomes of elderly patients (i.e. aged ≥ 70 years) receiving an LVAD.

Methods. — This observational study was conducted in 19 centres between 2006 and 2016. Patients were divided into two groups—younger (aged < 70 years) and elderly (aged ≥ 70 years), based on age at time of LVAD implantation.

Results. — A total of 652 patients were included in the final analysis, and 74 patients (11.3%) were aged ≥ 70 years at the time of LVAD implantation (maximal age 77.6 years). The proportion of elderly patients receiving an LVAD each year was constant, with a median of 10.6% (interquartile range 8.0–15.4%) per year, and all were implanted as destination therapy. Elderly and younger patients had similar durations of hospitalization in intensive care units and total lengths of hospital stays. Both age groups experienced similar rates of LVAD-related complications (i.e. stroke, bleeding, driveline infection and LVAD exchange), and the occurrence of LVAD complications did not impact survival in the elderly group compared with the younger group. Lastly, when compared with younger patients implanted as destination therapy, the elderly group also exhibited similar mid-term survival.

Conclusion. — This work strongly suggests that selected elderly adults can be scheduled for LVAD implantation.

MOTS CLÉS

Assistance cardiaque ventriculaire gauche ; Patients âgés ; Septuagénaires ; Survie ; Complications de LVAD

Résumé

Contexte. — L'implantation d'une assistance cardiaque de longue durée (LVAD) peut être une séduisante alternative thérapeutique pour les patients insuffisants cardiaques âgés non éligible à une transplantation cardiaque.

Objectif. — Dans cette étude, nous décrivons les caractéristiques et résultats de l'implantation d'une assistance cardiaque mono-ventriculaire gauche chez des patients âgés de plus de 70 ans.

Méthodes. — Les patients implantés d'un LVAD dans 19 centres français entre 2006 et 2016 ont été inclus et divisés en deux groupes suivant l'âge à l'implantation (≥ 70 ou < 70 ans).

Résultats. — Un total de 652 patients ont été inclus et 74 (11,3 %) étaient âgés de plus de 70 ans à l'implantation du LVAD (maximal à 77,6 ans). La proportion de patients ayant ≥ 70 ans implanté d'un LVAD est constante chaque année avec une médiane de 10,6 % (8,0–15,4 %). Les 74 patients ont tous été implantés en thérapie définitive. Les deux groupes ont une durée d'hospitalisation (en réanimation et totale) similaire et développent un pourcentage identique de complications en lien avec le LVAD (accidents ischémiques, saignement, infection de câble, changement de LVAD). Le survenue d'une complication n'impact pas la survie chez les patients ≥ 70 ans par rapport au groupe < 70 ans. Enfin, parmi le sous-groupe de patients implantés en thérapie définitive, les deux populations (≥ 0 ou < 70 ans) ont une survie identique.

Conclusion. — Ce travail suggère que des patients insuffisants cardiaques âgés de plus de 70 ans et bien sélectionnés peuvent être de bons candidats à l'implantation d'un LVAD.

Background

Heart failure (HF) is a rapidly growing global epidemic affecting almost 40 million people worldwide [1]. Secondary to shifts in the global age distribution, as well as general population growth, the absolute number of patients with HF has increased drastically in the last decade, especially among elderly patients [2]. Indeed, recent data demonstrated that each 10-year age increase from 65 to 85 years doubled the incidence rate of HF in men, whereas in women the incidence rate was tripled from 65 to 74 years and from 75 to 84 years [3]. Treating elderly patients with advanced HF remains challenging, as heart transplantation is not considered for patients aged > 70 years at most centres in the USA and Europe [4]. Additionally, in France, patients with severe HF aged > 65 years are usually ineligible for heart transplantation, limiting the therapeutic options in these most severe patients.

Left ventricular assist device (LVAD) implantation has been shown to improve survival in patients with refractory HF [5], and may represent an attractive alternative therapeutic option for elderly patients who are ineligible for heart transplantation.

In this study, we aimed to describe the characteristics and outcomes of elderly patients (i.e. aged ≥ 70 years) receiving an LVAD in a large multicentre observational cohort.

Methods

Study design

ASSIST-ICD (ClinicalTrials.gov identifier: NCT02873169) was a retrospective multicentre observational study of durable mechanical circulatory support devices implanted in

patients treated in 19 tertiary care centres in France. The study methods have been reported previously [6]. Briefly, patients aged ≥ 18 years implanted with axial HeartMate II™ (Abbott, Chicago, IL, USA), Jarvik 2000® (Jarvik Heart, Inc., New York, NY, USA) or centrifugal HeartWare™ (Medtronic, Minneapolis, MN, USA) pumps between February 2006 and December 2016 were included. Exclusion criteria were total artificial heart placement or pulsatile flow LVAD, history of heart transplantation or receipt of a VentrAssist™ device (Ventracor, Chatswood, NSW, Australia).

This study was approved by the regional ethics committees, the French Advisory Committee on the Treatment of Research Information in the Field of Health (CCTIRS) and the French National Commission of Informatics and Civil Liberties (CNIL). A non-opposition letter was sent to the patients, as requested by the French authorities for retrospective studies.

Data collection and study population

Baseline data – including demographic characteristics, cardiac disease and HF history, history of arrhythmia before LVAD implantation, HF medical therapy, echocardiography and blood chemistry values – were collected from hospital files for all enrolled patients. The echocardiographic and blood sample data used for the analysis were the last performed before LVAD implantation. Follow-up was performed according to each institution's protocols. The last day of follow-up was 31 December 2016, the date of heart transplantation or the date of death, whichever occurred first.

For the purpose of this study, patients were divided in two groups, younger and elderly, based on age at time of LVAD implantation. The younger group included patients aged < 70 years, and the elderly group included patients aged ≥ 70 years.

Endpoints

The primary endpoint of the study was all-cause mortality. Deaths were classified as cardiovascular death (cardiac or vascular cause), non-cardiovascular death or unknown cause. Secondary endpoints included the occurrence of LVAD related complications (i.e. thrombosis, stroke, infection, bleeding and LVAD replacement).

Statistical analysis

Qualitative variables are expressed as numbers (percentages), and continuous data are expressed as means \pm standard deviations or medians (interquartile ranges) depending on their distribution, which was assessed using the Kolmogorov–Smirnov test. Categorical variables were compared using the χ^2 test or Fisher's exact test. Continuous variables were compared using Student's *t* test or the Mann–Whitney U test for two-group comparisons. Survival rates were summarized using Kaplan–Meier estimates, and log-rank tests were used to compare groups. A *P*-value < 0.05 was considered statistically significant. The analyses were performed with the SPSS statistical package, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics

From 2006 to 2016, 659 patients were implanted with a continuous-flow LVAD, and were included in the study. Among these, seven were excluded (three patients received a VentrAssist™ and four patients died during the LVAD surgery). A total of 652 patients were included in the final analysis, and were followed for 9.1 (2.5–22.1) months. Among this population, 74 patients (11.3%) were aged ≥ 70 years at the time of LVAD implantation (maximal age 77.6 years) (Fig. 1A). As illustrated in Fig. 1B, the proportion of elderly patients receiving an LVAD each year was constant, with a median of 10.6% (8.0–15.4%) of patients aged ≥ 70 years implanted per year.

Baseline characteristics are described in Table 1. The elderly group had significantly more men, with a lower body mass index and a longer duration of HF at the time of LVAD implantation. The patients in this group also had significantly more history of supraventricular tachycardia before LVAD, and were more often implanted with cardiac resynchronization therapy devices. Lastly, elderly patients presented more altered renal function, and all received an LVAD as destination therapy. Interestingly, the younger group were more likely to be implanted with temporary mechanical support (especially extracorporeal life support) compared with elderly patients (24.0% vs 6.8%, respectively). Notably, among the group aged < 70 years, a total of 95 patients (16.4%) failed to be placed on the high-emergency heart transplantation list, and were consequently implanted with an LVAD as bridge to transplantation. No difference was found between groups regarding cardiovascular risk factors, echocardiography and perioperative variables.

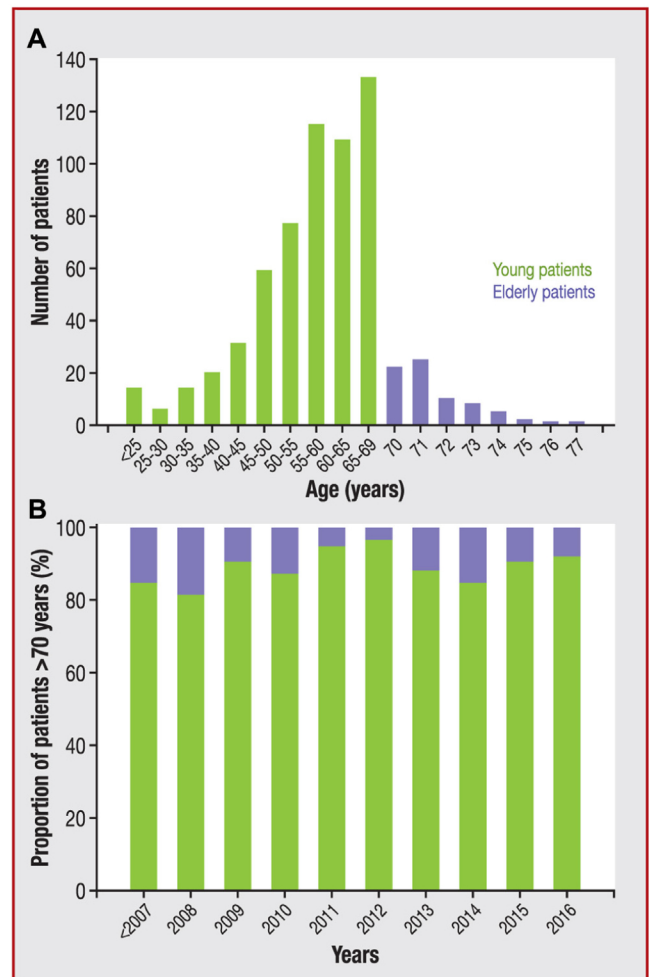


Figure 1. A. Number of patients implanted with a left ventricular assist device (LVAD), depending on age category. B. Proportion of patients aged ≥ 70 years implanted with an LVAD per year.

Outcomes

Elderly and younger patients had similar durations of hospitalization in intensive care units and total lengths of hospital stays: 14.0 (7.0–21.5) vs 14.0 (7.0–27.0) days and 37.0 (30.0–61.0) vs 41.0 (30.0–58.7) days, respectively (Table 1). After a median follow-up of 9.1 (2.5–22.1) months, both age groups experienced a similar rate of LVAD-related complications (i.e. stroke, bleeding, driveline infection and LVAD exchange) (Table 2). Notably, the type of bleeding was also similar in the two groups. Importantly, the occurrence of LVAD-related complications did not impact survival in the elderly group compared with the younger group (Fig. 2).

During the study period, a total of 291 patients died: 41 (55.4%) in the elderly group, and 250 (43.2%) in the younger group ($P = 0.06$). The cause of death was similar in both groups. Of note, among the older patients, the median time to death was 1.9 (0.4–16.0) months after LVAD implantation, and 18 (24.3%) of these patients died within the 30-day postoperative period. Nevertheless, there was no difference regarding the baseline characteristics of patients who died or survived during the postoperative period (Table 3). As

Table 1 Baseline characteristics for younger and elderly recipients of a left ventricular assist device.

	Patients aged \geq 70 years (n = 74)	Patients aged < 70 years (n = 578)	P
Age (years)	71.7 (70.7–72.8)	58.2 (50.0–64.7)	< 0.001
Male sex	70 (94.6)	491 (84.9)	0.038
Body mass index (kg/m ²)	24.2 (21.9–26.8)	25.4 (22.8–28.1)	0.010
Hypertension	31 (41.9)	202 (34.9)	0.30
Diabetes mellitus	22 (29.7)	132 (22.8)	0.24
Dyslipidaemia	44 (59.5)	239 (41.3)	0.005
Heart failure aetiology			0.32
Ischaemic	46 (62.2)	366 (63.3)	
Idiopathic	24 (32.4)	154 (26.6)	
Other	4 (5.4)	58 (10.0)	
Heart failure duration (months)	138.7 (13.0–234.7)	55.7 (1.9–154.6)	< 0.001
LVEDD before LVAD (mm)	71.0 (64.0–75.0)	69.0 (63.0–75.0)	0.16
LVEF before LVAD (%)	20.0 (15.0–25.0)	20.0 (15.0–25.0)	0.60
History of ventricular arrhythmia	24 (32.4)	199 (34.4)	0.83
History of supraventricular arrhythmia	49 (66.2)	253 (43.8)	< 0.001
ICD before LVAD	46 (62.2)	357 (61.8)	0.83
CRT before LVAD	31 (41.9)	167 (28.9)	0.031
Drugs before LVAD			
Beta-blocker	53 (71.6)	370 (64.0)	0.25
ACE inhibitor	49 (66.2)	312 (54.0)	0.06
ARB	6 (8.1)	62 (19.5)	0.031
MRA	44 (59.5)	312 (54.0)	0.44
Cardiogenic shock before LVAD	34 (50.1)	315 (54.5)	0.21
Temporary mechanical support			
CIABP	8 (10.8)	73 (12.6)	0.28
Impella ^{®a}	3 (4.1)	60 (10.4)	0.13
ECLS	5 (6.8)	139 (24.0)	0.001
Serum biology			
Creatinine (μ mol/L)	128.0 (101.0–164.0)	112.0 (86.0–145.0)	0.007
Serum sodium (μ mol/L)	135.0 (130.0–138.5)	136.0 (132.0–139.0)	0.10
Total bilirubin (μ mol/L)	17.0 (11.2–28.0)	16.0 (10.0–27.0)	0.36
Type of LVAD			0.30
HeartMate II [™]	52 (70.3)	423 (73.2)	
HeartWare [™]	13 (17.6)	114 (19.7)	
Jarvik 2000 [®]	9 (12.2)	41 (7.1)	
LVAD indication			< 0.001
Bridge to transplantation	0 (0)	387 (67.0)	
Destination therapy	74 (100)	173 (29.9)	
Bridge to decision/recovery	0 (0)	18 (3.1)	
Surgery combined with LVAD	12 (16.2)	83 (14.4)	0.80
Temporary right ECLS during surgery	8 (10.8)	73 (12.6)	0.33
Total days in ICU	14.0 (7.0–21.5)	14.0 (7.0–27.0)	0.30
Total days in hospital	37.0 (30.0–61.0)	41.0 (30.0–58.7)	0.90

Data are expressed as median (interquartile range) or number (%). ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; CIABP: counterpulsation intra-aortic balloon pump; CRT: cardiac resynchronization therapy; ECLS: extracorporeal life support; ICD: implantable cardioverter-defibrillator; ICU: intensive care unit; LVAD: left ventricular assist device; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MRA: mineralocorticoid receptor antagonist.

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Table 2 Outcomes in younger and elderly recipients of a left ventricular assist device.

	Patients aged ≥ 70 years (<i>n</i> = 74)	Patients aged < 70 years (<i>n</i> = 578)	<i>P</i>
Total death	41 (55.4)	250 (43.2)	0.06
Cause of death			0.30
Cardiovascular	14 (34.1)	111 (44.4)	
Non-cardiovascular	27 (65.9)	135 (54.0)	
Unknown	0 (0)	4 (1.6)	
LVAD thrombosis	6 (8.1)	78 (13.5)	0.28
Stroke	9 (12.2)	79 (13.7)	0.86
Bleeding	16 (21.6)	93 (16.1)	0.30
Cerebral bleeding	3 (18.7)	31 (33.3)	0.38
Digestive bleeding	9 (56.2)	37 (39.8)	0.34
Subcutaneous	1 (6.2)	10 (10.7)	0.92
Other	3 (18.7)	15 (10.7)	0.92
Percutaneous driveline infection	16 (21.6)	155 (26.8)	0.41
LVAD replacement	3 (4.1)	30 (5.2)	0.89

Data are expressed as number (%). LVAD: left ventricular assist device.

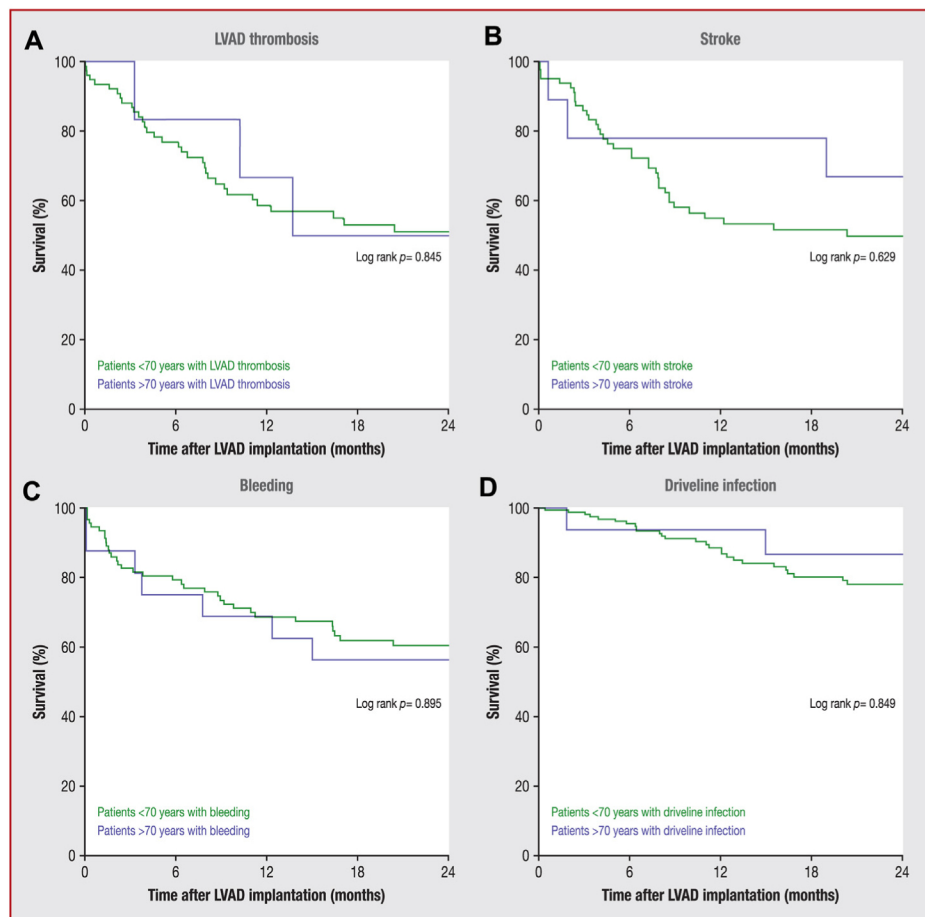


Figure 2. Survival curves depending on the occurrence of each left ventricular assist device (LVAD)-related complication in elderly and younger patients. A. Survival depending on the occurrence of pump thrombosis. B. Survival depending on the occurrence of stroke. C. Survival depending on the occurrence of bleeding. D. Survival depending on the occurrence of driveline infection.

Table 3 Baseline characteristics of elderly patients, according to death or survival during the 30-day postoperative period.

	30-day postoperative mortality (n = 18)	No 30-day postoperative mortality (n = 56)	P
Age (years)	71.4 (70.7–72.0)	71.8 (70.8–72.9)	0.45
Male sex	18 (100)	52 (92.9)	0.57
Body mass index (kg/m ²)	23.9 ± 3.8	24.6 ± 3.6	0.52
Hypertension	8 (44.4)	23 (41.1)	0.98
Diabetes mellitus	4 (22.2)	18 (32.1)	0.32
Dyslipidaemia	9 (50.0)	35 (62.5)	0.51
Previous sternotomy	1 (5.6)	2 (2.7)	0.75
Heart failure aetiology			0.45
Ischaemic	11 (61.1)	35 (62.5)	
Idiopathic	7 (38.9)	17 (30.4)	
Other	0 (0)	4 (7.1)	
Heart failure duration (months)	118.8 (33.2–262.0)	140.0 (10.1–226.1)	0.93
LVEDD before LVAD (mm)	69.5 (63.0–74.5)	72.0 (65.5–75.2)	0.41
LVEF before LVAD (%)	20.0 (15.0–26.0)	20.0 (17.2–24.7)	1.00
History of ventricular arrhythmia	5 (27.8)	19 (33.9)	0.85
History of supraventricular arrhythmia	10 (55.6)	39 (69.6)	0.42
ICD before LVAD	11 (61.1)	35 (62.5)	0.86
CRT before LVAD	9 (50.0)	22 (39.3)	0.60
Serum biology			
Creatinine (μmol/L)	111.5 (85.0–152.0)	129.0 (102.0–189.0)	0.23
Serum sodium (μmol/L)	134.1 ± 5.2	135.5 ± 7.3	0.36
Total bilirubin (μmol/L)	17.0 (12.5–28.3)	16.8 (11.0–27.1)	0.68
Cardiogenic shock before LVAD	6 (33.3)	24 (42.9)	0.66
Type of LVAD			0.61
HeartMate II™	13 (72.2)	39 (69.6)	
HeartWare™	2 (11.1)	11 (19.6)	
Jarvik 2000®	3 (16.7)	6 (10.7)	
Surgery combined with LVAD	5 (27.8)	7 (12.5)	0.15
Temporary right ECLS during surgery	3 (16.7)	5 (8.9)	0.39
Early ventricular arrhythmias in ICU	2 (11.1)	10 (17.9)	0.72

Data are expressed as median (interquartile range), mean ± standard deviation or number (%). CRT: cardiac resynchronization therapy; ECLS: extracorporeal life support; ICD: implantable cardioverter-defibrillator; ICU: intensive care unit; LVAD: left ventricular assist device; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction.

illustrated in Fig. 3A, elderly patients had a similar 2-year survival compared with younger patients. Importantly, when compared with younger patients implanted as destination therapy, the elderly group also exhibited similar mid-term survival (Fig. 3B).

Discussion

The major findings of this multicentre study are that:

- septuagenarian candidates for LVAD are not uncommon, and represent up to 10% of French patients receiving an LVAD;
- elderly and younger patients have similar mid-term survival and;
- both groups experience a similar rate of LVAD-related complications, and the occurrence of a complication does not impact survival in elderly patients.

Proportion of elderly LVAD candidates

Elderly symptomatic patients with end-stage HF and optimal medical therapy remain challenging to manage. Indeed, heart transplantation is rarely performed in such patients, and only 2% of heart transplantations are performed in adults aged > 70 years [7]. Additionally, older age has also been described as a strong predictor of deaths and complications (including rejection and malignancy) after transplantation [8]. Consequently, current guidelines from the USA recommend that only carefully selected patients aged ≥ 70 years may be considered for cardiac transplantation, suggesting that this therapeutic option is not optimal in this population [4]. Conversely, LVAD implantation as a destination therapy may represent an attractive alternative for these patients.

In our cohort, we observed that elderly patients were not uncommon, representing up to 10% of the overall LVAD population. Similar results have been reported in LVAD registries from the USA, with proportions of 11.7% and 14% of patients

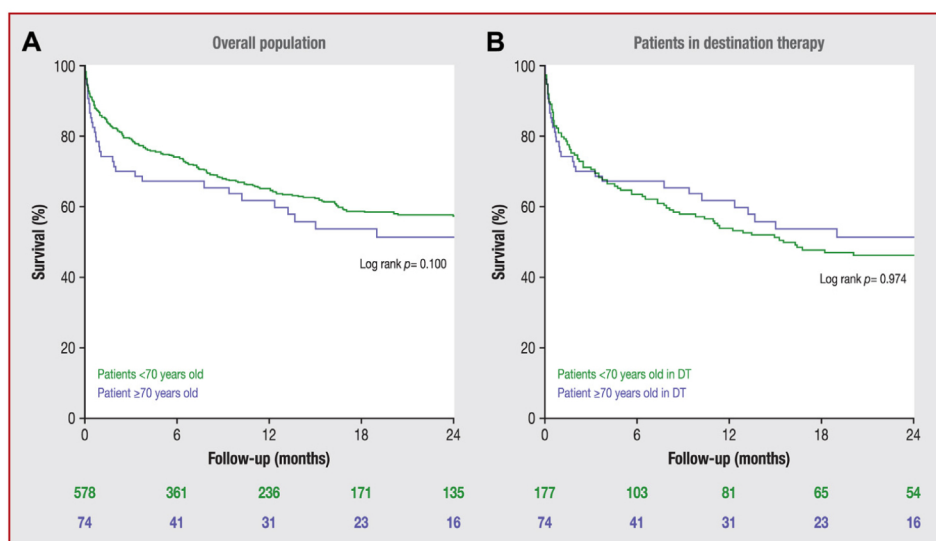


Figure 3. A. Two-year survival curves for elderly and younger patients implanted with a left ventricular assist device (LVAD). B. Two-year survival curves for elderly and younger patients implanted with an LVAD as destination therapy.

aged ≥ 70 years [9,10]. These data suggest that, despite a higher incidence, elderly patients with advanced HF are probably not referred for LVAD discussion and implantation. Indeed, elderly patients are more likely to be associated with frailty, neurocognitive dysfunction, low nutritional status and chronic associated diseases, possibly explaining the low proportion of elderly LVAD recipients.

Outcomes in elderly LVAD recipients

We observed that, despite being older with a lower body mass index, a longer duration of HF and worse renal function, elderly patients experienced similar mid-term survival compared with younger patients. Interestingly, in the subset of LVAD recipients implanted as destination therapy, both groups had similar survival. These data are supported by previous works reporting no difference in overall mortality between younger and older patients. Indeed, in a cohort of 55 patients, those aged ≥ 70 years had similar survival to patients aged < 70 years [11]. Similarly, in a larger registry with up to 1100 LVAD recipients, an age ≥ 70 years was not associated with increased mortality in multivariable analysis [10]. Conversely, in a recent Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) analysis enrolling up to 20,000 patients in the USA, the authors showed increased mortality depending on age at baseline, with better survival in the younger population [12]. This difference between results in the USA and Europe can probably be explained by French patients being more ill at baseline. Indeed, we showed that 16.4% of the younger group did not benefit from a high-emergency heart transplantation, and were consequently implanted with an LVAD. This result suggests that a subset of the younger patients were particularly ill at baseline, with advanced cardiogenic shock, requiring temporary mechanical support as a bridge to LVAD implantation. These data support young French LVAD candidates being potentially more ill at baseline than elderly patients, impacting the long-term survival of this population. Conversely, in the INTERMACS analysis, $< 5\%$ of the

patients were under extracorporeal membrane oxygenation support before LVAD implantation [12].

We also showed that the total duration of stays in intensive care units/hospitals was similar in the two groups. This result is consistent with data published previously [9,13], and possibly suggests that elderly patients did not experience more postoperative issues during the 30 days after LVAD implantation. This hypothesis is supported by a study of 128 enrolled LVAD recipients that demonstrated that older patients (defined as > 65 years of age) exhibited a similar 30-day rate of adverse events to younger patients [14].

Lastly, our results highlighted that both age groups had similar LVAD complication rates during a median follow-up of 9.1 (2.5–22.1) months. Importantly, the occurrence of LVAD complications did not impact survival in the elderly group compared with younger patients. Similarly, Adamson et al. showed that the incidence of adverse events was similar in patients aged ≥ 70 years and < 70 years [11]. However, discrepant results have been published previously from the INTERMACS registry, showing that patients aged > 70 years exhibited a higher incidence of stroke and gastrointestinal bleedings compared with younger patients, but experienced a lower incidence of driveline infection.

Clinical implications

This study provides important information about LVAD candidate selection. Indeed, advanced age should not be a contraindication when selecting a patient for LVAD therapy, but this has to be interpreted in the light of co-morbidities, frailty, nutritional status and social support [15]. This work strongly suggests that selected elderly adults can be scheduled for LVAD implantation. Consequently, this study is a plea to include a geriatrician in the multidisciplinary HF team, in order to provide an extensive evaluation of septuagenarian LVAD candidates (including familial support, autonomy, car driving, depression risk, etc.). Additionally, a careful neurocognitive assessment is specifically crucial, as cognitive decline can occur in up to 29.2% of older LVAD recipients at

1 year postimplantation [16]. Elderly LVAD candidates should also benefit from long-term psychological support, as destination therapy implantation may increase the risk of suicide attempts [17].

The increase in elderly patients with end-stage HF will probably lead to an increase in elderly LVAD recipients in the next decade, highlighting the critical need for palliative care in this population. Indeed, a relationship with the palliative care team, the patient and the family should probably be established early, and directives could possibly be written in advance.

Study limitations

Our observational study has some limitations, including its retrospective design, which may have affected the results. Additionally, we cannot provide an extensive description of the elderly group, including nutritional, neurocognitive and social assessments. Indeed, these considerations are crucial for the LVAD indication in this population. Furthermore, we only described survival and the occurrence of LVAD complications, and we did not report hospitalization rate, quality of life and functional status, which are essential in elderly patients. However, as published previously, patients aged ≥ 70 years have shown significant improvement in the 6-minute walk distance and quality of life score at 6 months after LVAD implantation [11]. Finally, we acknowledge that these findings may reflect clinical practice in France, but may not necessarily be extended to other populations. Our survival results in particular have to be considered in the light of the highly severe population that we included. Indeed, more than half of the population was estimated to be in cardiogenic shock at time of LVAD implantation. Earlier referral is now gaining more acceptance in our country.

Conclusions

Elderly patients (aged ≥ 70 years) are common among LVAD recipients, representing up to 10% of LVAD candidates. These patients have similar 2-year survival compared with younger LVAD recipients, and experience similar rates of LVAD complications without impacting survival.

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Disclosure of interest

The authors declare that they have no competing interest.

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