



HAL
open science

Outcomes of Left Ventricular Assist Device Implantation in Patients With Uncommon Etiology Cardiomyopathy

Vincent Galand, Erwan Flécher, Céline Chabanne, Bernard Lelong, Céline Goéminne, André Vincentelli, Clément Delmas, Camille Dambrin, François Picard, Frédéric Sacher, et al.

► To cite this version:

Vincent Galand, Erwan Flécher, Céline Chabanne, Bernard Lelong, Céline Goéminne, et al.. Outcomes of Left Ventricular Assist Device Implantation in Patients With Uncommon Etiology Cardiomyopathy. American Journal of Cardiology, 2020, 125 (9), pp.1421-1428. 10.1016/j.amjcard.2020.01.042 . hal-02502716

HAL Id: hal-02502716

<https://hal.science/hal-02502716v1>

Submitted on 22 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Outcomes of Left Ventricular Assist Device Implantation in Patients with Uncommon Etiology Cardiomyopathy

RUNNING TITLE: Uncommon cardiomyopathies in LVAD-recipients

AUTHORS: Vincent Galand, MD,^a Erwan Flécher, MD, PhD,^a Céline Chabanne, MD,^a Bernard Lelong, MD,^a Céline Goéminne, MD,^b André Vincentelli, MD, PhD,^b Clément Delmas MD,^c Camille Dambrin, MD PhD,^c François Picard, MD,^d Frédéric Sacher, MD, PhD,^d Michel Kindo, MD, PhD,^e Tam Hoang Minh, MD,^e Philippe Gaudard, MD,^f Philippe Rouvière, MD,^f Thomas Sénage, MD,^g Magali Michel, MD,^g Aude Boignard, MD,^h Olivier Chavanon, MD, PhD,^h Constance Verdonk, MD,ⁱ Walid Ghodhbane, MD,ⁱ Edeline Pelcé, MD,^j Vlad Gariboldi, MD, PhD,^j Matteo Pozzi, MD,^k Jean-François Obadia, MD, PhD,^k Pierre-Yves Litzler, MD, PhD,^l Frédéric Anselme, MD,^l Gerard Babatasi, MD, PhD,^m Katrien Blanchart, MD,^m Fabien Garnier, MD,ⁿ Marie Bielefeld, MD,ⁿ David Hamon, MD,^o Nicolas Lellouche, MD, PhD,^o Thierry Bourguignon, MD,^p Thibaud Genet, MD,^p Romain Eschalié, MD, PhD,^q Nicolas D'Ostrevy, MD,^q Emilie Varlet, MD,^r Jérôme Jouan, MD,^r Fabrice Vanhuyse, MD,^s Hugues Blangy, MD,^s Christophe Leclercq, MD, PhD,^a Raphaël P. Martins, MD, PhD,^a

AFFILIATIONS. ^aUniv Rennes, CHU Rennes, INSERM, LTSI - UMR 1099, F-35000 Rennes, France; ^bCHU Lille, Institut Coeur-Poumons, Cardiac Intensive Care Unit, Department of Cardiology, Department of Cardiac Surgery, Lille, France; ^cCentre Hospitalier Universitaire de Toulouse, Toulouse, France; ^dHôpital Cardiologique du Haut-Lévêque, LIRYC institute, Université Bordeaux, Bordeaux, France; ^eDépartement de chirurgie cardiovasculaire, hôpitaux universitaires de Strasbourg, Strasbourg, France; ^fDepartment of Cardiac Surgery, Anesthesiology and Critical Care Medicine, Arnaud de Villeneuve Hospital, CHRU Montpellier, Montpellier, France; ^gDepartment of Cardiology and Heart Transplantation Unit, CHU Nantes, France; ^hDepartment of Cardiology and Cardiovascular Surgery, CHU Michallon, Grenoble, France; ⁱDepartment of Cardiology and cardiac surgery, Bichat-Hospital, Paris, France; ^jDepartment of Cardiac Surgery, La Timone Hospital, Marseille, France ^kDepartment of Cardiac Surgery, "Louis Pradel" Cardiologic Hospital, Lyon, France; ^lDepartment of Cardiology and Cardiovascular Surgery, Hospital Charles Nicolle, Rouen, France; ^mDepartment of Cardiology and Cardiac Surgery, University of Caen and University Hospital of Caen, France; ⁿDepartment of Cardiology and cardiac surgery, University Hospital, Dijon, France; ^oDepartment of Cardiology and Cardiac Surgery, AP-HP CHU Henri Mondor, Créteil, France; ^pDepartment of Cardiology and Cardiac Surgery, Tours University Hospital, Tours, France; ^qCHU Clermont-Ferrand, Cardiology Department, Clermont-Ferrand, France; ^rEuropean Georges Pompidou Hospital, Cardiology Department, Paris, France; ^sDepartment of Cardiology and Cardiac Surgery, CHU de Nancy, Hopital de Brabois, Nancy, France.

ADDRESS FOR CORRESPONDENCE: Vincent Galand, MD. Service de Cardiologie et Maladies Vasculaires, CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France. Tel: + 33 299 282 507, Fax: +33 299 282 529, E-mail: vincent.galand35@gmail.com

ABSTRACT

The impact of uncommon etiology cardiomyopathies on Left-ventricular assist device (LVAD)-recipient outcomes is not very well known. This study aimed to characterize patients with uncommon cardiomyopathy etiologies and examine the outcomes between uncommon and ischemic/idiopathic dilated cardiomyopathy. This observational study was conducted in 19 centers between 2006 and 2016. Baseline characteristics and outcomes of patients with uncommon etiology were compared to patients with idiopathic dilated/ischemic cardiomyopathies. Among 652 LVAD-recipients included, a total of 590 (90.5%) patients were classified as ischemic/idiopathic and 62 (9.5%) patients were classified in the “uncommon etiologies” group. Main uncommon etiologies were: hypertrophic (n=12(19%)); cancer therapeutics-related cardiac dysfunction (CTRCD) (n=12(19%)); myocarditis (n=11(18%)); valvulopathy (n=9(15%)) and others (n=18(29%)). Patients with uncommon etiologies were significantly younger with more female and presented less co-morbidities. Additionally, patients with uncommon cardiomyopathies were less implanted as destination therapy compared to ischemic/idiopathic group (29% vs. 38.8%). During a follow-up period of 9.1 months, both groups experienced similar survival. However, subgroup of hypertrophic/valvular cardiomyopathies and CTRCD had significantly higher mortality compared to the ischemic/idiopathic or myocarditis/others cardiomyopathies. Conversely, patients with myocarditis/others etiologies experienced a better survival. Indeed, the 12-months survival in the myocarditis/others; ischemic/idiopathic and hypertrophic/CTRCD/valvulopathy group were 77%; 65% and 46% respectively. In conclusion, LVAD-recipients with hypertrophic cardiomyopathy, valvular heart disease and CTRCD experienced the higher mortality rate.

KEY WORDS: Left-ventricular assist device, uncommon cardiomyopathy etiology, survival.

INTRODUCTION

Left ventricular assist device (LVAD) implantation has been shown to improve survival in patients with refractory heart failure (HF) (1-3) and ischemic or idiopathic dilated cardiomyopathies represent more than 90% of the LVAD candidates (4). Previous studies demonstrated no difference in mortality between LVAD recipients with ischemic and non-ischemic (5; 6). Conversely, data regarding the impact of uncommon etiologies (i.e. non-ischemic and non-idiopathic dilated cardiomyopathies) in LVAD recipients are scarce. Indeed, only cases report or small studies focused on uncommon etiologies have been published thus far (7-9). In a recent analysis from the INTERMACS registry, restrictive and hypertrophic cardiomyopathies (HC) exhibited similar outcomes compared to patients with traditional dilated cardiomyopathy (10). However, others studies would be required to accurately investigate the outcomes of such candidates. In this study, we sought to characterize patients with an uncommon etiology and examine the outcomes between uncommon and ischemic/idiopathic dilated cardiomyopathy.

METHODS

The ASSIST-ICD is a retrospective, multicenter observational study (NCT02873169) of durable mechanical circulatory support devices implanted in 19 French tertiary centers. The methods of this study have been previously published (11). Briefly, patients aged ≥ 18 years implanted with axial HeartMate 2 (Abbott, Chicago, Illinois), Jarvik2000 (Jarvik Heart, Inc., New York, New York), or centrifugal HeartWare pumps (Medtronic, Columbia Heights, Minnesota) between February 2006 and December 2016 were included in the final analysis. The type of pump implanted depended on the local heart team's decision in each center. Exclusion criteria were: patients who underwent total artificial heart placement or pulsatile flow LVAD; history of heart transplant; and VentrAssist (Ventricor, Chatswood, NSW,

Australia) recipients. Patients deceased during LVAD surgery were excluded from the final analysis. This study was approved by the regional ethic 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 French authorities for retrospective studies.

Baseline data – including demographic characteristics, cardiac disease and heart failure history, echocardiography, and blood chemistry values – were collected from hospital files for all patients. Peri-operative data (such as the necessity of a combined surgery or a right extracorporeal life support) were collected. Follow-up was performed according to each institution's protocols. The LVAD controller monitor was checked during every clinical visit in each center, according to state-of-the-art standard of care for LVAD recipients. The last day of follow-up was December 31st 2016, the date of heart transplantation, or death, whichever occurred first.

Ischemic etiology was defined in patient with history of prior myocardial infarction or impaired left ventricular ejection fraction with coronary artery disease diagnosed using coronary angiogram. Other patients were classified as non-ischemic cardiomyopathy. Non-ischemic cardiomyopathy was secondly divided in two groups: 1) idiopathic dilated cardiomyopathy or 2) uncommon cardiomyopathy. An extensive work up was performed to precisely define the etiology of the non-ischemic patients. Cardiac magnetic resonance magnetic or nuclear imaging evaluation were performed on physicians' discretion. In case of young patients or for those with a familial history of dilated cardiomyopathy, genetic analyses were performed. If a specific etiology was found, the patient was classified as “uncommon cardiomyopathy” and in case of none specific etiology found, the cardiomyopathy was

classified as idiopathic. Notably, following the LVAD implantation, the removed apical portion of the LV was analyzed in all patients and they were re-classified in “uncommon cardiomyopathies” if a specific etiology was found. Lastly, in patients receiving heart transplantation, the native heart was also analyzed and patients were then re-classified in the “uncommon” group if a specific etiology was found.

The endpoints of the study included all-cause mortality and the rate of LVAD-related complications during the follow-up depending of uncommon or ischemic/idiopathic cardiomyopathy etiologies at baseline. Deaths were classified as cardiovascular death (cardiac or vascular cause), non-cardiac death, or unknown cause. Major LVAD-related complications collected were: driveline-infection, thrombosis, stroke, bleeding and LVAD exchange.

Qualitative variables are summarized with frequencies (percentage); continuous data as mean \pm standard deviation or median (interquartile range) depending on their distribution, which was assessed using the Kolmogorov-Smirnov test. Categorical variables were compared using the χ^2 tests 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).

RESULTS

Among 652 LVAD-recipients included in this study, a total of 590 (90%) patients were classified as ischemic/idiopathic etiologies (including 412 (63%) and 178 (27%) patients with ischemic or idiopathic dilated cardiomyopathy respectively) and 62 (9%) patients were classified in the “uncommon etiologies” group. Baseline characteristics were described in

Table 1. Briefly, patients with uncommon etiologies were significantly younger with a higher proportion of female and presented less co-morbidities. Additionally, uncommon etiologies group had significantly less dilated left ventricle compared to ischemic/idiopathic patients but exhibited similar left ventricular ejection fraction. Interestingly, patients with uncommon cardiomyopathies were less implanted as destination therapy compared to ischemic/idiopathic group while up to 8% of patients received a LVAD in bridge to recovery or bridge to decision (compared to 2% in the other group).

The underlying cause of the 62 patients with uncommon cardiomyopathy, is described in **Figure 1**. Major etiologies were: hypertrophic cardiomyopathy (HC) (n=12 (19%)); cancer therapeutics-related cardiac dysfunction (CTRCD) (n=12 (19%)); myocarditis (n=11 (18%)); valvulopathy (n=9 (15%)) and others etiologies (n=18 (29%)). Of note, among patients with HC, 4 had advanced dilated hypertrophic cardiomyopathy and 8 had a pure hypertrophic phenotype. Additionally, valvulopathy etiology included aortic disease (n=3), mitral disease (n=5), or both aortic and mitral diseases (n=1). Among those patients, 6 had history of cardiac surgery prior to LVAD implantation.

During a follow-up period of 9.1 (2.5-22.1) months, a total of 293 (45%) patients died (**Table 2**) and both groups experienced similar survival (**Figure 2, panel A**). However, patients with uncommon cardiomyopathy had diverse survival depending of the underlying etiology. Indeed, those with HC, CTRCD or valvulopathy cardiomyopathy experienced lower survival probability than patients with myocarditis or other etiologies (**Figure 2, panel B**). Consequently, 2 subgroups of “uncommon” patients could were defined depending of this survival rate differences: 1) HC / CTRCD / valvulopathy group and 2) myocarditis / others group (**Table 3**). As illustrated in the **Figure 2, panel C**, LVAD-recipients with HC/valvular etiologies and CTRCD had significantly higher mortality compared to the ischemic/idiopathic or myocarditis / others cardiomyopathies. Conversely, patients with myocarditis/others

etiologies experienced a better survival. Indeed, the 12-months survival in the myocarditis/others; ischemic/idiopathic and HC/CTRCD/valvulopathy group were 77%; 65% and 46% respectively. Interestingly, the underlying etiology did not influence the immediate post-operative mortality (<30 days) but only impacted long-term survival. Of note, non-cardiac death was the main cause of death among patients with uncommon etiology (65%) (**Table 2**).

During follow-up, 199 (30%) patients underwent heart transplantation. As shown in **Table 2** there was no difference in heart transplant rate between uncommon and ischemic/idiopathic cardiomyopathies. However, as described in the **Table 3**, myocarditis/others group exhibited significantly higher rate of heart transplantation compared to HC/CTRCD/valvulopathy group. Lastly, no difference was noted regarding the occurrence of LVAD-related complication between uncommon and ischemic/idiopathic groups (**Table 2**). Similarly, **Table 3** shows no difference between the 2 sub-groups of uncommon etiologies. However, despite being non-significant, first major LVAD-related complication tended to occur earlier among patients in the HC/CTRCD/valvulopathy subgroup than myocarditis/others sub-group (2.8 (1.3-9.6) vs. 7.6 (1.9-14.2) months respectively; $p=0.382$). Additionally, **Figure 3** illustrates that after 6-months follow-up, 45% of patients included in the HC/CTRCD/valvulopathy subgroups experienced at least 1 major LVAD-associated complication compared to 31% patients in the myocarditis/others subgroups.

In the light of the impact of the underlying etiology on survival, baseline characteristics were compared between HC/CTRCD/valvular diseases and myocarditis/others etiologies in **Table 4**. Briefly, myocarditis/others group had higher bilirubin level prior to LVAD implantation and lower rate of diabetes mellitus. Despite non-significant results, this group trends to be younger with more male gender and had numerically larger left ventricle size.

DISCUSSION

Our study is among the first to evaluate the impact of uncommon cardiomyopathy etiologies in a large cohort of LVAD-recipients. The main results of this study are: 1) Uncommon etiologies may represent up to 10% of LVAD candidates. 2) Underlying etiology impacts long-term survival but does not influence immediate post-operative mortality (<30 days). HC, CTRCD or valvular cardiomyopathies impact patient's survival compared to ischemic/idiopathic and myocarditis/others etiologies. 3) Myocarditis and others cardiomyopathies were associated with the best survival after LVAD implantation.

Non-ischemic dilated cardiomyopathies may be the consequence of various etiologies such as advanced HC, chronic valvulopathy, myocardial non compaction, infectious, toxins, infiltrative or neuromuscular diseases (12). Despite advances in heart failure drugs therapy, the prognosis of patients with dilated cardiomyopathy and specific underlying uncommon etiology remains poor. Indeed, a previous study demonstrated that among a population of more than 1200 dilated cardiomyopathies, those with cardiomyopathy due to infiltrative myocardial diseases, HIV infection, or doxorubicin therapy had an especially poor prognosis (13). Furthermore, patients with severe uncommon cardiomyopathies have generally been excluded from clinical trials and management of such patients with advanced HF remains unclear without standardized strategy. Similarly, patients with uncommon etiologies were not included in LVAD trials and heart transplantation remains often the preferred strategy for those who progress to advanced HF.

Our study highlighted that almost 10% of patients scheduled for LVAD implantation had an uncommon cardiomyopathy. This result is relatively consistent with previous publish data and strongly suggests that this situation is not uncommon in our clinical practice. Indeed,

Topilski et al. study was focused on restrictive or HC, these patients representing 9.6% (8/83) of the population included (7).

A limited number of studies have specifically evaluated the impact of uncommon etiologies on post-LVAD outcomes. Pastel et al. focused on patients with restrictive or hypertrophic etiologies and did not show any mortality difference after a 4-years follow-up compared to dilated cardiomyopathy (10). However, in a subgroup of patients with very small pre-implant left ventricle size (i.e. < 5cm), survival was far inferior with a 6-months mortality >50%, suggesting that LVAD devices may not be suitable for pure restrictive/hypertrophic phenotype. Additionally, patients with HC etiology exhibited significantly higher rate of bleeding events during follow-up and LVAD-related infections beyond the third post-operative month. Additional study did not demonstrate a difference in terms of survival between restrictive/hypertrophic and dilated/ischemic cardiomyopathies among a population of 83 LVAD-recipients (7). Similarly, the use and outcomes of LVAD in chemotherapy-induced cardiomyopathy has been investigated among the INTERMACS registry patients, suggesting an equivalent survival compared to idiopathic/ischemic etiologies. However, authors demonstrated that CTRCD etiology was more associated with right ventricular failure and more frequently required temporary right ventricular assist device implantation at the time of LVAD surgery (14).

In our study, patient's survival did not differ between all pooled uncommon etiologies and ischemic/idiopathic cardiomyopathies. However, subgroups of uncommon etiologies potentially influenced survival. Indeed, patients with HC, CTRCD or valvular cardiomyopathies experienced the higher mortality rate among LVAD-recipients. Conversely, myocarditis or others cardiomyopathies exhibited the lower post-LVAD mortality with a 12-months survival of 77%. To the best of our knowledge, this study is the first to demonstrate the probably impact of the underlying etiology on LVAD-recipients survival. Despite few

significant differences, baseline characteristics comparison could possibly highlight some explanation of the impact of etiology on long-term survival. Indeed, HC/CTRCD/valvulopathy group had smaller left ventricle diameter at baseline and could hypothetically compromise LVAD function. Additionally, this group underwent significantly lower rate of heart transplantation (15.2% vs. 51.2%) which deeply influence long-term survival. Indeed, 6 (50%) patients with valvular disease had cardiac surgery prior to LVAD implantation and history of cancer among the patients with CTRCD strongly limited the access to heart transplant after LVAD implantation. Lastly, previous studies assessed that HC and CTRCD increase the risk of bleeding in LVAD recipients (4; 14).

This study questions the selection of LVAD-candidates and the potential need for a tailored management based on the underlying etiology. Indeed, specific etiologies (i.e. HC, CTRCD and valvular diseases) are associated with worst outcomes and a 6-months mortality up to 40%. The heart failure team should probably carefully manage these patients and propose, if possible, an early heart transplantation in those implanted in bridge to transplantation. Additionally, this group rapidly exhibited major LVAD-related complication with up to 50% of patients within the first 6 months.

Our observational study has some limitations, including its retrospective design, which may have affected the results. Additionally, this registry illustrated French medical practice and results could potentially not be extrapolate to other population. The limited number of included patients with uncommon etiology could also limit the interpretation of the results.

In conclusion, uncommon cardiomyopathies represent up to 10% of LVAD candidates. Specific etiologies (i.e. HC, CTRCD and valvular diseases) are associated with worst outcomes. Further studies will be needed to analyze the optimal delay for heart transplantation and propose a tailored management based on the cardiomyopathy etiology.

ACKNOWLEDGEMENTS: This research was supported by the French Federation of Cardiology and Rennes University Hospital.

FUNDING: This research was funded by the French Federation of Cardiology.

Journal Pre-proof

REFERENCES

- 1- Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, Conte JV, Bogaev RC, MacGillivray TE, Naka Y, Mancini D, Massey HT, Chen L, Klodell CT, Aranda JM, Moazami N, Ewald GA, Farrar DJ, Frazier OH; HeartMate II Investigators. HeartMate II Investigators. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. *J Am Coll Cardiol* 2009; 54:312-321.
- 2- Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD, Conte JV, Naka Y, Mancini D, Delgado RM, MacGillivray TE, Farrar DJ, Frazier OH; HeartMate II Clinical Investigators. HeartMate II Clinical Investigators. Use of a continuous-flow device in patients awaiting heart transplantation. *N Engl J Med* 2007; 357 :885-896.
- 3- Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatooles AJ, Delgado RM 3rd, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH; HeartMate II Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009; 361(23):2241-2251.
- 4- Patel SR, Saeed O, Naftel D, Myers S, Kirklin J, Jorde UP, Goldstein DJ. Outcomes of Restrictive and Hypertrophic Cardiomyopathies After LVAD: An INTERMACS Analysis. *J Card Fail* 2017; 23(12):859-867.
- 5- Abubakar H, Subahi A, Adegbala O, Yassin AS, Akintoye E, Abdulrahman A, Ahmed A, Alade A, Pahuja M, Afonso L. Comparison of In-Hospital Outcomes of Patients With-Versus-Without Ischemic Cardiomyopathy Undergoing Left Ventricular Assist Device Placement. *Am J Cardiol* 2019; 123(3):414-418.

- 6- Tsiouris A, Borgi J, Karam J, Nemeh HW, Paone G, Brewer RJ, Morgan JA. Ischemic versus nonischemic dilated cardiomyopathy: the implications of heart failure etiology on left ventricular assist device outcomes. *ASAIO J* 2013; 59(2):130-135.
- 7- Topilsky Y, Pereira NL, Shah DK, Boilson B, Schirger JA, Kushwaha SS, Joyce LD, Park SJ. Left ventricular assist device therapy in patients with restrictive and hypertrophic cardiomyopathy. *Circ Heart Fail* 2011; 4(3):266-275.
- 8- Kornberger A, Stock UA, Risteski P, Beiras Fernandez A. Left ventricular non-compaction cardiomyopathy and left ventricular assist device: a word of caution. *J Cardiothorac Surg* 2016; 11(1):108.
- 9- Sayin OA, Ozpeker C, Schoenbrodt M, Oz F, Borgermann J, Gummert J, Morshuis M. Ventricular assist devices in patients with chemotherapy-induced cardiomyopathy: new modalities. *Acta Cardiol* 2015; 70(4):430-4.
- 10- Patel SR, Saeed O, Naftel D, Myers S, Kirklin J, Jorde UP, Goldstein DJ. Outcomes of Restrictive and Hypertrophic Cardiomyopathies After LVAD: An INTERMACS Analysis. *J Card Fail* 2017; 23(12):859-867.
- 11- Galand V, Flécher E, Auffret V, Boulé S, Vincentelli A, Dambrin C, Mondoly P, Sacher F, Nubret K, Kindo M, Cardi T, Gaudard P, Rouvière P, Michel M, Gourraud JB, Defaye P, Chavanon O, Verdonk C, Ghodbane W, Pelcé E, Gariboldi V, Pozzi M, Obadia JF, Litzler PY, Anselme F, Babatasi G, Belin A, Garnier F, Bielefeld M, Hamon D, Radu C, Pierre B, Bourguignon T, Eschalier R, D'Ostrevy N, Bories MC, Marijon E, Vanhuyse F, Blangy H, Verhoye JP, Leclercq C, Martins RP; ASSIST-ICD Investigators.. Predictors and Clinical Impact of Late Ventricular Arrhythmias in Patients with Continuous-Flow Left Ventricular Assist Devices. *JACC Clin Electrophysiol* 2018;4(9):1166-1175

- 12- Japp AG, Gulati A, Cook SA, Cowie MR, Prasad SK. The Diagnosis and Evaluation of Dilated Cardiomyopathy. *J Am Coll Cardiol* 2016;67(25):2996-3010.
- 13- Felker GM, Thompson RE, Hare JM, Hruban RH, Clemetson DE, Howard DL, Baughman KL, Kasper EK. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. *N Engl J Med* 2000; 342(15):1077-1084.
- 14- Oliveira GH, Dupont M, Naftel D, Myers SL, Yuan Y, Tang WH, Gonzalez-Stawinski G, Young JB, Taylor DO, Starling RC. Increased need for right ventricular support in patients with chemotherapy-induced cardiomyopathy undergoing mechanical circulatory support: outcomes from the INTERMACS Registry (Interagency Registry for Mechanically Assisted Circulatory Support). *J Am Coll Cardiol* 2014; 63(3):240-248.

FIGURES LEGEND

FIGURE 1: Major etiologies of uncommon cardiomyopathies.

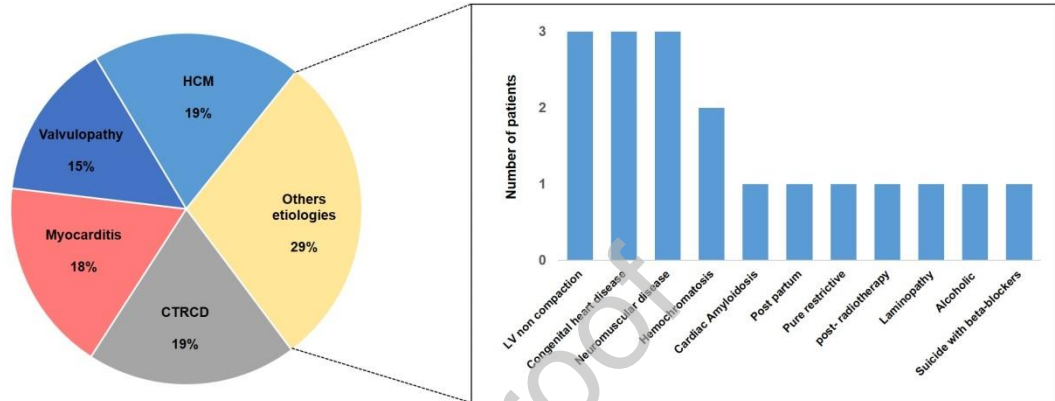


FIGURE 2: Survival curves. Panel A: Survival curve between uncommon and ischemic/idiopathic dilated cardiomyopathies. Panel B: Survival curve among the main uncommon etiologies. Panel C: Survival curve between two subgroups of uncommon etiologies and ischemic/idiopathic dilated cardiomyopathies.

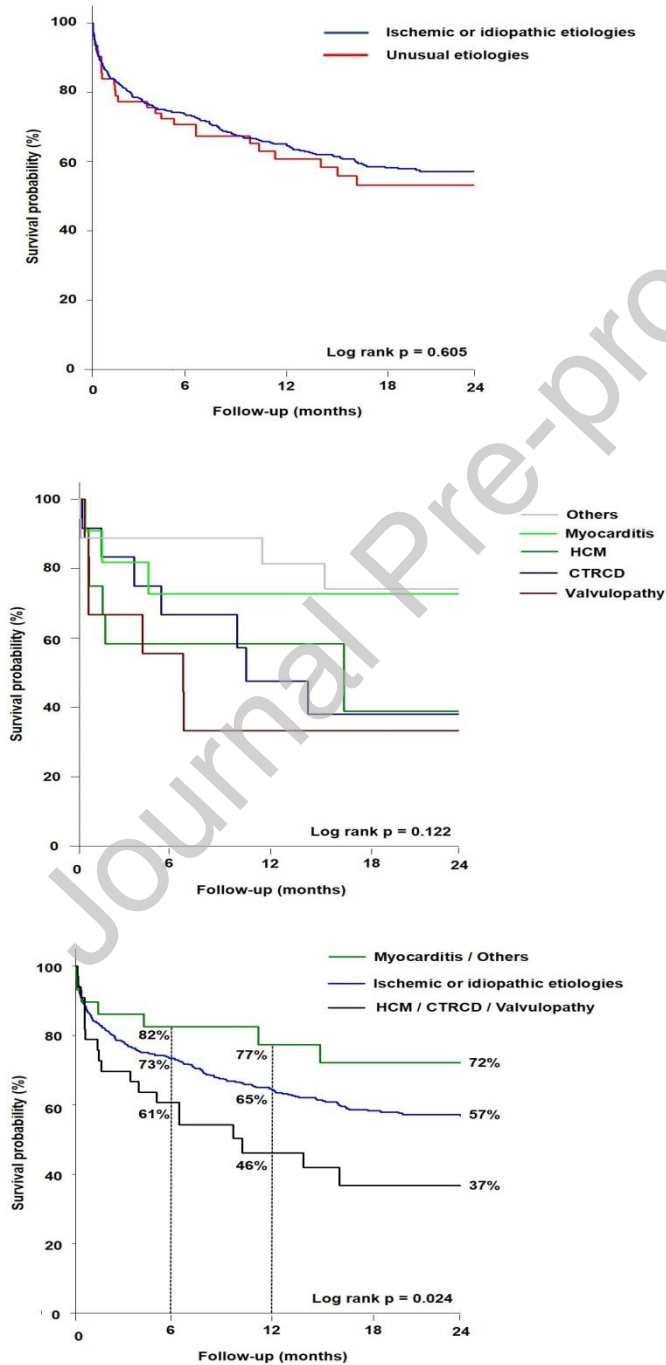


FIGURE 3: Survival curve regarding the occurrence of first LVAD-related complication among the two subgroups of uncommon etiologies.

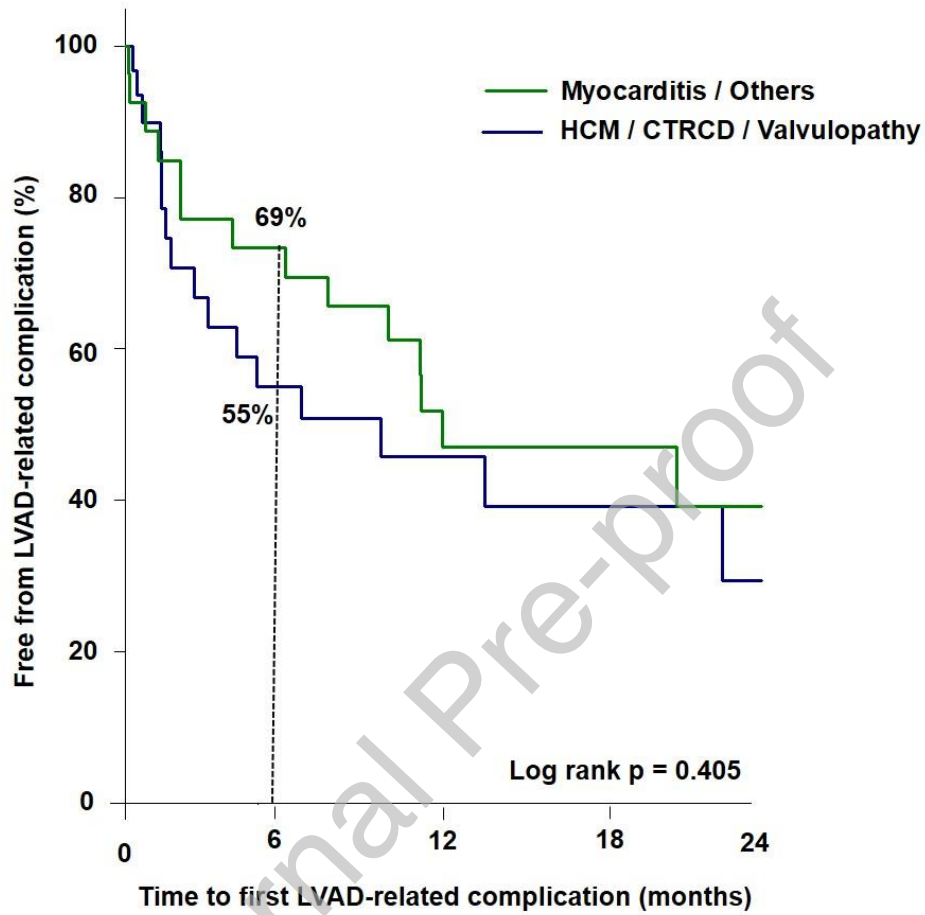


Table 1: Baseline characteristics

Values are median (interquartile range), n (%), or mean \pm standard deviation. CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; ICU = intensive care unit; LVAD = left ventricular assist device; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction.

Variable	Uncommon etiologies (HC; CTRCD; myocarditis; valvulopathy and others etiologies) (n=62)	Ischemic or idiopathic etiologies (n=590)	p Value
Age (years)	53.1 (40.3-66.1)	60.0 (52.7-66.4)	0.003
Men	43 (69%)	518 (88%)	<0.001
Body mass index (kg/m²)	24.5 (21.0-27.6)	25.3 (22.8-28.0)	0.068
Hypertension	14 (23%)	219 (37%)	0.033
Diabetes mellitus	10 (16%)	144 (24%)	0.193
Dyslipidemia*	13 (21%)	270 (46%)	<0.001
Heart failure duration (months)	82.2 (6.8-213.1)	57.4 (2.1-164.7)	0.066
LVEDD prior to LVAD (mm)	67.0 (56.5-72.0)	70.0 (64.0-75.0)	0.007
LVEF prior to LVAD (%)	20.0 (16.5-26.0)	20.0 (15.0-25.0)	0.150
Ventricular tachycardia	20 (32%)	203 (34%)	0.843
Supra-ventricular tachycardia	32 (52%)	270 (46%)	0.456
ICD prior to LVAD	31 (50%)	372 (63%)	0.061
CRT prior to LVAD	22 (35%)	176 (30%)	0.438
Drugs pre-LVAD implantation			

-Beta-blockers	39 (63%)	384 (65%)	0.840
-ACE Inhibitors / ARB	40 (64%)	380 (68%)	0.702
-MRA	38 (61%)	318 (54%)	0.328
-Diuretics	54 (87%)	475 (80%)	0.275
-Amiodarone	29 (47%)	262 (44%)	0.869
Biology Serum			
-Creatinine (µmol/L) (n=598)	106.0 (81.4-140.5)	116.0 (88.0-148.0)	0.151
-Serum sodium (mmol/L) (n=599)	136.0 (133.0-138.2)	136.0 (132.0-139.0)	0.964
-Total bilirubin (µmol/L) (n=563)	19.0 (10.0-28.0)	15.2 (10.0-27.0)	0.320
Type of LVAD			0.758
-HeartMate 2	43 (69%)	432 (73%)	
-HeartWare	13 (21%)	114 (19%)	
-Jarvik2000	6 (10%)	44 (7%)	
LVAD indication			0.014
-Bridge to transplantation	39 (63%)	348 (59%)	
-Destination therapy	18 (29%)	229 (39%)	
-Bridge to decision / recovery	5 (8%)	13 (2%)	
Combined surgery with LVAD	10 (16%)	85 (14%)	0.860
Temporary right ECLS during surgery	9 (14%)	72 (12%)	0.747
Total days in ICU	18.5 (11.0-44.0)	14.0 (9.0-56.0)	0.139
Total days in hospital	43.0 (32.0-63.5)	41.0 (30.0-58.0)	0.524

* Dyslipidemia is define as having a high plasma triglyceride concentration and/or a high plasma LDL cholesterol and/or a low HDL (protective) cholesterol

Table 2: Outcomes between patients with uncommon or ischemic/idiopathic cardiomyopathies

LVAD = left ventricular assist device

Variable	Uncommon etiologies (HC; CTRCD; myocarditis; valvulopathy and others etiologies) (n=62)	Ischemic or idiopathic etiologies (n=590)	p Value
Heart transplantation	20 (32%)	179 (30%)	0.867
Total of death	29 (47%)	264 (44%)	0.864
Early death (≤ 30 days)	10 (16%)	94 (16%)	0.887
Cause of death			0.324
-Cardiovascular	9 (31%)	117 (44%)	
-Non cardiovascular	19 (65%)	143 (54%)	
-Unknown etiology	1 (3%)	4 (1%)	
Major LVAD-related complications	20 (32%)	151 (26%)	0.326
-Driveline-infection	8 (13%)	76 (13%)	0.846
-Thrombosis	3 (5%)	85 (14%)	0.057
-Stroke	8 (13%)	101 (17%)	0.505
-Bleeding	4 (6%)	29 (5%)	0.826
-LVAD exchange			

Table 3: Outcomes among the patients with uncommon cardiomyopathy

LVAD = left ventricular assist device

Variable	Total (n=62)	HC / CTRCD	Myocarditis	p Value
		Valvulopathy (n=33)	Others (n=29)	
Heart transplantation	20 (32%)	5 (15%)	15 (52%)	0.005
Total death	29 (47%)	21 (64%)	8 (28%)	0.010
Early death (<30 days)	10 (16%)	7 (21%)	3 (10%)	0.312
Cause of death				0.761
-Cardiovascular	9 (31%)	6 (29%)	3 (37%)	
-Noncardiovascular	19 (65%)	14 (67%)	5 (62%)	
-Unknown	1 (3%)	1 (5%)	0	
Patients with LVAD-related complications	35 (56%)	18 (5%)	17 (57%)	0.947
Time to first LVAD-related complications, months	4.2 (1.3-11.8)	2.8 (1.3-9.6)	7.6 (1.9-14.2)	0.382
Major LVAD-related complications				
-Driveline-infection	20 (32%)	10 (30%)	10 (34%)	0.937
-Thrombosis	8 (13%)	5 (15%)	3 (10%)	0.523
-Stroke	3 (5%)	2 (6%)	1 (3%)	0.909
-Bleeding	8 (13%)	5 (15%)	3 (10%)	0.523
-LVAD exchange	4 (6%)	2 (6%)	2 (7%)	0.701

Table 4 Baseline characteristics among subgroups of uncommon etiologies

Values are median (interquartile range), n (%), or mean \pm standard deviation. CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; ICU = intensive care unit; LVAD = left ventricular assist device; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction.

	HC / CTRCD / Valvulopathy (n=33)	Myocarditis / Others (n=29)	p Value
Age (Years)	54.8 \pm 12.9	49.6 \pm 15.9	0.157
Men	20 (67)	23 (79%)	0.188
Body mass index (kg/m ²)	25.7 \pm 6.0	23.7 \pm 0.6	0.130
Hypertension	10 (30%)	4 (14%)	0.212
Diabetes mellitus	9 (27%)	1 (3%)	0.015
Dyslipidemia	9 (27%)	4 (14%)	0.323
Heart failure duration (months)	77.3 (5.7-267.8)	91.0 (6.2-172.6)	0.631
LVEDD prior to LVAD (mm)	63.5 (51.5-71.5)	69.0 (62.5-73.0)	0.079
LVEF prior to LVAD (%)	20.0 (15.0-29.5)	20.5 (20.0-25.0)	0.781
Ventricular arrhythmias	9 (27%)	11 (38%)	0.533
Supra-ventricular tachycardia	16 (48%)	16 (55%)	0.786
ICD prior to LVAD	16 (48%)	15 (52%)	1.000
CRT prior to LVAD	12 (36%)	10 (34%)	0.911
History of cardiac surgery prior to LVAD	6 (18%)	2 (7%)	0.264

Drugs pre-LVAD implantation

-Beta-blockers	18 (54%)	21 (72%)	0.316
-ACE Inhibitors / ARB	20 (61%)	20 (69%)	0.674
-MRA	18 (54%)	20 (69%)	0.367
-Diuretics	29 (88%)	24 (83%)	0.722
-Amiodarone	14 (42%)	15 (52%)	0.633

Biology Serum

-Creatinine (µmol/L) (n=598)	107.0 (87.0-142.0)	104.0 (68.7-137.5)	0.430
-Serum sodium (mmol/L)	135.3±5.2	135.7±4.7	0.746
(n=599)	18.0±10.3	26.5±3.4	0.039

-Total bilirubin (µmol/L)**(n=563)****Type of LVAD**

0.518

-HeartMate 2	23 (70%)	20 (69%)
-HeartWare	8 (24%)	5 (17%)
-Jarvik2000	2 (6%)	4 (14%)

LVAD indication

0.917

-Bridge to transplantation	21 (64%)	18 (62%)
-Destination therapy	9 (27%)	9 (31%)
-Bridge to decision / recovery	3 (9%)	2 (7%)

Combined surgery with LVAD

7 (21%) 3 (10%) 0.312

Temporary right ECLS during

3 (9%) 6 (21%) 0.283

surgery**Total days in ICU** 14.0 (10.2-29.5) 21.0 (11.5-51.2) 0.326**Total days in hospital** 40.0 (30.5-52.5) 46.0 (33.7-75.2) 0.432

CREDIT AUTHORS STATEMENT

Vincent Galand = Conceptualization, Methodology, Investigation, writing original draft, **Erwan Flécher** = Conceptualization, Methodology, Supervision, Writing - Review & Editing, **Céline Chabanne** = Writing - Review & Editing; **Bernard Lelong** = Writing - Review & Editing; **Céline Goéminne** = Writing - Review & Editing; **André Vincentelli** = Writing - Review & Editing; **Clément Delmas** = Writing - Review & Editing, Investigation, **Camille Dambrin** = Writing - Review & Editing, **François Picard** = Writing - Review & Editing, **Frédéric Sacher** = Writing - Review & Editing, **Michel Kindo** = Writing - Review & Editing, **Tam Hoang Minh** = Writing - Review & Editing, **Philippe Gaudard** = Writing - Review & Editing, **Philippe Rouvière** = Writing - Review & Editing, **Thomas Sénage** = Writing - Review & Editing, **Magali Michel** = Writing - Review & Editing, **Aude Boignard** = Writing - Review & Editing, **Olivier Chavanon** = Writing - Review & Editing, **Constance Verdonk** = Writing - Review & Editing, **Walid Ghodhbane** = Writing - Review & Editing, **Edeline Pelcé** = Investigation, **Vlad Gariboldi** = Writing - Review & Editing, **Matteo Pozzi** = Investigation, Writing - Review & Editing, **Jean-François Obadia** = Writing - Review & Editing, **Pierre-Yves Litzler** = Writing - Review & Editing, **Frédéric Anselme** = Writing - Review & Editing, **Gerard Babatasi** = Writing - Review & Editing, **Katrien Blanchart** = Writing - Review & Editing, **Fabien Garnier** = Writing - Review & Editing, **Marie Bielefeld** = Writing - Review & Editing, **David Hamon** = Writing - Review & Editing, **Nicolas Lellouche** = Writing - Review & Editing, **Thierry Bourguignon** = Writing - Review & Editing, **Thibaud Genet** = Writing - Review & Editing, **Romain Eschalier** = Writing - Review & Editing, **Nicolas D'Ostrevy** = Writing - Review & Editing, **Emilie Varlet** = Writing - Review & Editing, **Jérôme Jouan** = Writing - Review & Editing, **Fabrice Vanhuysse** = Writing - Review & Editing, **Hugues Blangy** = Writing - Review & Editing, **Christophe Leclercq** = Conceptualization, Methodology, Supervision, Writing - Review & Editing, **Raphaël P. Martins** = Conceptualization, Methodology, Supervision, Writing - Review & Editing, Funding acquisition.