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ORIGINAL RESEARCH ARTICLE

Cost-effectiveness of left ventricular assist devices for patients with end-stage heart failure: analysis of the French hospital discharge database

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Abstract

Aims Although left ventricular assist devices (LVADs) are currently approved for coverage and reimbursement in France, no French cost-effectiveness (CE) data are available to support this decision. This study aimed at estimating the CE of LVAD compared with medical management in the French health system.

Methods and results Individual patient data from the 'French hospital discharge database' (Medicalization of information systems program) were analysed using Kaplan–Meier method. Outcomes were time to death, time to heart transplantation (HTx), and time to death after HTx. A micro-costing method was used to calculate the monthly costs extracted from the Program for the Medicalization of Information Systems. A multistate Markov monthly cycle model was developed to assess CE. The analysis over a lifetime horizon was performed from the perspective of the French healthcare payer; discount rates were 4%. Probabilistic and deterministic sensitivity analyses were performed. Outcomes were quality-adjusted life years (QALYs) and incremental CE ratio (ICER). Mean QALY for an LVAD patient was 1.5 at a lifetime cost of €190 739, delivering a probabilistic ICER of €125 580/QALY [95% confidence interval: 105 587 to 150 314]. The sensitivity analysis showed that the ICER was mainly sensitive to two factors: (i) the high acquisition cost of the device and (ii) the device performance in terms of patient survival.

Conclusions Our economic evaluation showed that the use of LVAD in patients with end-stage heart failure yields greater benefit in terms of survival than medical management at an extra lifetime cost exceeding the €100 000/QALY. Technological advances and device costs reduction shall hence lead to an improvement in overall CE.

Keywords Cost-effectiveness; Left ventricular assist devices; Costs; Incremental cost-effectiveness ratio; PMSI

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Introduction

Although heart transplantation (HTx) is the optimal surgical therapy for end-stage heart failure (HF), this therapeutic option is being progressively limited. Because of the shortage of suitable donor hearts, the gap between donors and recipients is widening, along with the growing number of patients with end-stage HF. Around 10–12% of patients die during the waiting time for a donor heart, or become ineligible for transplantation because of deteriorating clinical condition.[1]

To face this shortage, left ventricular assist devices (LVADs) are being increasingly used as a bridge to transplantation (BTT) or as a destination therapy (DT) alternatively to HTx.[2–4] American data from 2005 to 2011 confirmed the LVAD use increase in clinical practice and showed that in-hospital mortality and length of stay after LVAD implantation including hospital costs have declined.[5,6] Currently, LVADs are included in the basic healthcare package in several countries, such as the USA,[7] UK,[8,9] Norway,[10] the Netherlands,[11,12] and France.[13]

Although LVAD is regarded as a life-saving therapy, its value for money remains questionable. Economic evaluations of first-generation and second-generation LVADs showed that the ratio of incremental costs vs. incremental benefits is still relatively high, ranging from £53 527 ($84 963)/quality-adjusted life year (QALY) in the UK to $201 600/QALY in the USA.[8,11,14–16]

LVADs are currently approved for coverage and reimbursement by the French healthcare system since 2012. A health technology assessment report evaluating the benefit of LVADs in terms of improved survival was published by the French authority, and their use was recommended in end-stage HF.[13] However, the health technology assessment did not provide any economic evaluation of LVAD, particularly in France due to lack of costs and effectiveness data. These data are required for the reappraisal of pricing and reimbursement expected in France in 2017.

The cost-effectiveness (CE) evaluation of LVADs appears to be essential in the context of a growing candidate population, expanding healthcare costs and falling availability of donor hearts. The aim of this study is to assess the CE of LVAD compared with medical management and to describe the routine management of patients having received LVAD since its reimbursement in French, using the exhaustive French hospital discharge database [Program for the Medicalization of Information Systems (PMSI)].

Methods

Data sources

The PMSI was used to derive the resources use and healthcare costs of LVAD recipients. The PMSI, the heart of the French financing system, is a nationwide database providing the main source of information on healthcare expenditure in all private and public hospitals. Patient level data are based on the diagnosis-related group classification. The PMSI-MCO, which includes all in-hospital outpatient and inpatient data from medical, surgical, and obstetrics wards, was used. All patients having received an LVAD were identified using the appropriate codes, and subsequently, all data (pre-LVAD and post-LVAD implantation) related to these patients were extracted from the database and analysed.

The PMSI provides demographics (sex and age), primary diagnostic for each admission, dates of admission and discharge, implanted medical devices, associated diagnostics and medical procedures, and vital status at discharge. Routine follow-ups and medications are not collected in this database, neither professional/physician fees.

The strict indication of the LVAD used as 'DT' or 'BTT' was not available in the PMSI; hence, it was not possible to analyse separately these populations. Our analysis included both conditions without distinction, reflecting so the real-life management.

A mandatory approval from Commission Nationale de l'Informatique et des Libertés (CNIL) (French data protection competent authority) was required to access PMSI database. CNIL approval was obtained prior to data extraction.

Time horizon and perspective

A cost-utility analysis was performed from the perspective of the healthcare system in France. This analysis encompasses the entire remainder of a patient's lifetime, to a maximum of 20 years. The economic evaluation was carried on according to the French Health Authority guideline.[17]

Decision model/Markov model

Two different Markov models were used for both treatment modalities (LVAD vs. no LVAD); transition probabilities were estimated separately. *Figure 1* shows the Markov models that were used, and *Figure 2* shows the decision model. For 'LVAD' group, we applied a previously used economic model, a semi-Markov multistate model with 1 month cycle, in which each patient exists in one of the three mutually exclusive states[8,9,18,19]: (i) alive with LVAD, (ii) alive after HTx, and (iii) dead. Each month, each state is associated with a utility value, resource use, and costs components. For 'no LVAD' group, the model includes only 'alive' and 'dead' as health states.

Transition probabilities between health states were modelled using Kaplan–Meier analyses, from the instantaneous hazard rates. Patient data were censored at the date of the last follow-up; for time to death under LVAD, patients receiving a heart transplant were censored at the date of the HTx. Probability values were modelled as time varying, where appropriate, to more accurately reflect clinical course. Thus, time-dependent transition probabilities were used for Markov cohort simulations.

Figure 1 Monthly cycle Markov models. A p12 probability of transition from left ventricular assist device (LVAD) to heart transplantation (HTx) after *t* months; p23 probability of dying *t* months after HTx; p13 probability of dying *t* months after LVAD; p11 probability of surviving with LVAD after *t* months; p22 probability of surviving with HTx after *t* months; p44 probability of surviving without LVAD every cycle; and p45 probability of dying every cycle without LVAD.

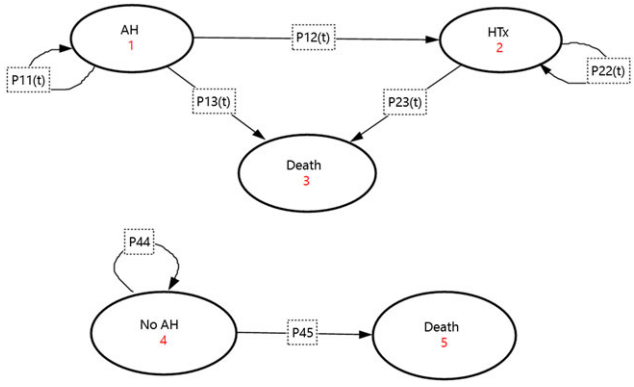
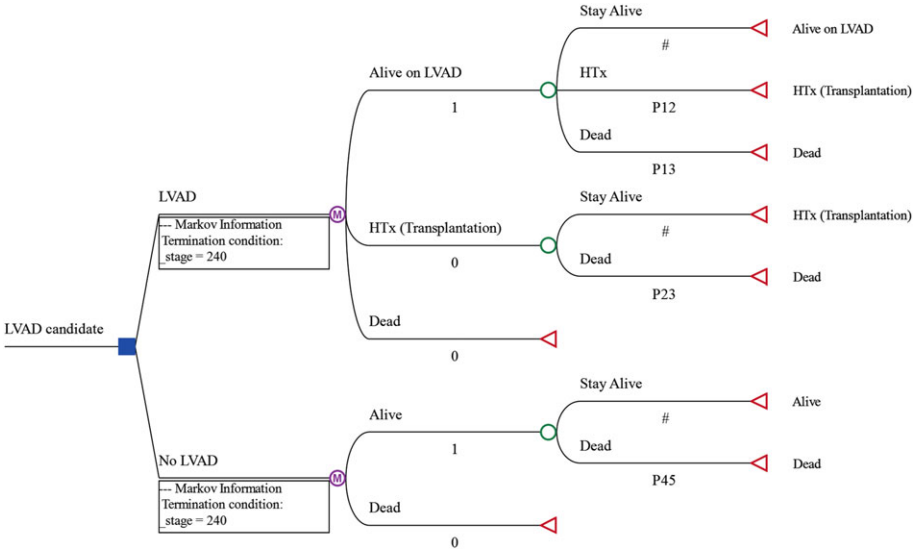


Figure 2 The decision model. HTx, heart transplantation; LVAD, left ventricular assist device.



Survival estimates for the comparator group were grounded in published data[3,4] and were provided by a clinical expert opinion. Setting a comparator group was very challenging; it was decided that the comparator group was the same patients assuming that they will not receive an LVAD (no LVAD group), but only medical management and die probably in the 3 months.

The model was developed using TreeAge Pro 2016 software. Descriptive statistics and Kaplan–Meier analyses were performed is SAS 9.4 (SAS Institute, Cary, NC).

Calculations of quality-adjusted life years

Quality-adjusted life years is the effectiveness metric used in this analysis. This measure was not available in the PMSI; therefore, utility data were obtained from literature review.[8,9] Each health state is associated with a utility value ranging from 0 to 1, where 0 represents 'death' and 1 represents 'ideal health'. Quality-adjusted life years were computed by aggregating the total time spent in each health state and applying the appropriate utility weight. The model outputs include mean life years gained (LYG), mean QALY, mean costs, mean incremental CE ratio (ICER) as €/LYG and as €/QALY.

Calculations of costs

All costs for all patients having received LVAD in France since its reimbursement were derived from the real-life PMSI database. These costs include pre-LVAD and post-LVAD implantation. A micro-costing method was applied to calculate the monthly costs. Four main categories of costs were included: device costs, direct medical costs associated with the index hospitalization for LVAD implantation, direct costs for subsequent HTx if any, and direct and indirect costs for repeat inpatient and outpatient hospitalizations and follow-up inpatient/outpatient care, including related and unrelated costs as per the latest recommendations.[20] Routine follow-up costs were not available therefore were not included in the analysis. Also, professional or physician fees were not available, because the PMSI includes only patient hospital data.

The comparator group was assumed to bear the same constant costs as those who received LVAD, but prior to intervention. Direct costs, up to 1 month before the index hospitalization for LVAD implantation, were calculated.

Discounting

To estimate the present value of future costs and benefits, we adhered to the French recommendations for CE studies by using an annual discount rate of 4% (0.327374% monthly) for both costs and efficacy parameters.[17]

Sensitivity analysis

Base-case probabilistic sensitivity analysis was undertaken. The multistate probabilistic model was used to extrapolate survival, utility, and resources over the total lifetime of 1000 hypothetical patients.

Furthermore, a range of alternative assumptions was assessed using one-way sensitivity analyses:

- Reducing the time horizon to 3, 5, and 10 years to better reflect the data collection period.
- Reducing the cost of devices to 50% of their current levels.
- Reducing the HTx referrals to 1% (transplant rates) every month, as donor hearts are expected to become scarce.[21]
- Improved survival to reflect improved LVAD performance, as recent studies showed that long-term performance of LVAD had improved in the recent era.[22,23]
- Higher costs for the management of 'no LVAD' group because of prolonged intensive care unit (ICU) stay (mean ICU costs €42 000/month).
- Utility of LVAD patients at 0.81 from Month 3 and thereafter. Based on our own experience (see Supporting Information), patients who survived the implantation have a New York Heart Association (NYHA) Class I/II 3 months after LVAD transplant. The mean utility assigned to patients with NYHA Class I/II is 0.81; value derived using the standard gamble method as described elsewhere.[24]

Two-way sensitivity analysis was conducted on the device price reduction and improved performance.

Results

Patients' characteristics at the index hospitalization

All patients having received one LVAD were extracted from the PMSI. Patients excluded from the analysis were as follows: patients under 18 years old, patients having received more than one LVAD, and patients having received other than LVAD (n = 104).

There were 508 patients reported in the PMSI database as having had an LVAD implanted between 2009 and 2014 in France. Among these, 363 patients received Thoratec HeartMate, 97 HeartWare, and 48 Jarvik 2000. Almost 50% of the devices were implanted from 2012 to 2013 (*Figure 3*).

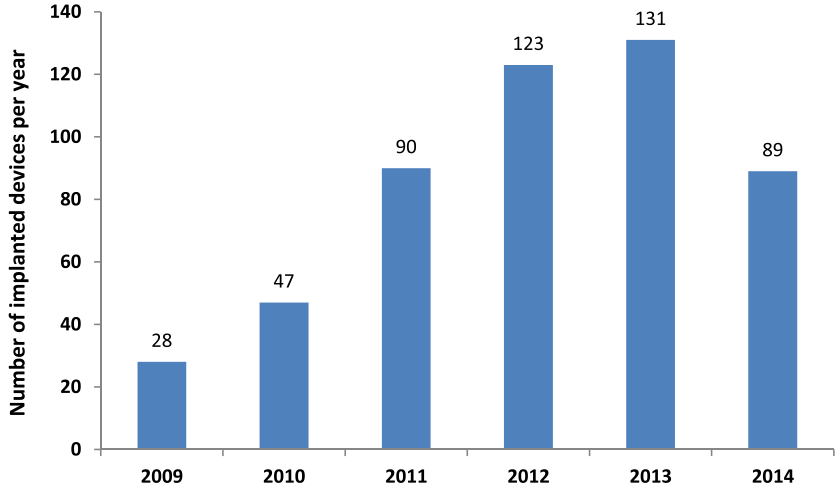
Patients' characteristics, at the index hospitalization for LVAD surgery, are summarized in *Table 1*. Patients were mostly male (83%) with a mean age of 57. The main primary

Table 1 Demographic characteristics of patients having received an LVAD between 2009 and 2014 at the index hospitalization

Sex (n = 508)	
Male	425 (83.7)
Female	83 (16.3)
Age (n = 508)	
Mean (SD)	57.0 (10.7)
Median	59.0
Range	20–75
Implanted device (n = 508)	
Thoratec HeartMate	363 (71.5)
HeartWare	97 (19.1)
Jarvik 2000	48 (9.45)
Primary diagnosis at index hospitalization (n = 508[a])	
Heart failure	169 (33.3)
Cardiogenic shock	125 (24.6)
Dilated cardiomyopathy	70 (13.8)
Ischaemic cardiomyopathy	45 (8.8)
ST and non-ST elevation myocardial infarction	40 (7.9)
Chronic ischaemic heart disease	7 (1.4)
LOS (days) (n = 508)	
Mean (SD)	62.5 (47.4)
Median	51.0
Range	2–411
Discharge disposition (n = 508)	
Transfer	293 (57.7)
Inpatient rehabilitation unit	176 (59.9)
SSU	110 (37.4)
Long-term care hospital	7 (2.38)
Home	73 (14.4)
Death	142 (28.0)

LOS, length of stay; LVAD, left ventricular assist device; SSU, short-stay unit.
[a]Only primary diagnoses with more than 1% are presented.

Figure 3 The number of implanted left ventricular assist devices per year.



diagnoses for the LVAD implantation were HF (33%), cardiogenic shock (24%), and dilated or ischaemic cardiomyopathy (22%).

The average hospital length of stay for the LVAD surgery was 63 days. The percentage of in-hospital deaths was 28% at the index hospitalization. Among 366 patients discharged alive after the procedure, discharge destination was home in 14.4%. Among 293 patients transferred to another facility, discharge destination was rehabilitation and long-term care hospital in 62.3% or short-stay unit in 37.4%.

Clinical outcomes after LVAD implant

A total of 203 patients died on LVAD during the observed 60 month period. Of these, 142 deaths occurred during the index hospitalization. A total of 149 patients received a heart transplant. Death after HTx was observed in 29 cases.

Figure 4 illustrates survival of patients having received LVAD in France and those having received an HTx after LVAD procedure. Median survival duration with LVAD was 30 months. The 5 year survival with LVAD was quite poor, with almost 20% survival at 60 months. Median time to HTx for patients with LVAD was 24 months. Median survival duration after HTx was not reached over the observed period. The 5 year survival after HTx was good, with almost 80% survival at 60 months.

Inputs and cost-effectiveness model

The inputs to the base-case deterministic and probabilistic models are summarized in *Table 2*. *Table 3* shows the findings from the base-case deterministic and probabilistic CE analyses for the lifetime (20 years) horizon. One-way and two-way sensitivity analyses are also summarized in *Table 3*.

For the base-case deterministic lifetime model, the ICER was €123 109/QALY and €97 333/LYG. The patients treated with an LVAD have a mean survival of 1.9 years and 1.5 of QALY. The mean lifetime cost for an LVAD patient was €190 739. The majority of costs was attributable to the device implant and initial ICU and ward stay (€122 885). After the first month on LVAD support, the costs decreased. The next biggest component of cost was the transplant procedure and immediate post-transplant care (€54 164). The hypothetical 'no LVAD' patients group resulted in a fixed lifetime costs of €6178, based on a maximum of 3 months hospital care.

*Figure 5*A illustrates the probabilistic results distributed on the CE plane. Each of the 1000 iterations is represented by one data point. The hypothetical willingness to pay (WTP) threshold (WTP = €100 000/QALY) is indicated by the line passing under the scatter points. *Figure 5*B shows the CE acceptability curves for lifetime horizon in which the probability of cost-effectiveness is plotted against the health service provider's WTP for increased benefit. According to the current France threshold of €50 000–100 000/QALY adopted by the French Health Authority, LVAD cannot be considered to be cost-effective. At a WTP threshold of €120 000/QALY, LVAD could be considered appropriate taking into account the disease severity and the end-of-life setting.

One-way and two-way sensitivity analyses are presented in *Table 3*. Without exception, for all assumptions considered, patients with LVAD had higher costs and higher survival rates than patients without LVAD. These assumptions identify the device costs and survival on LVAD, as the most important drivers of the ICER. Reducing the device price by half decreases the ICER to €94 321/QALY. Also, improving device performance and patients' outcome decreases the ICER to €74 144/QALY. Two-way sensitivity analysis using both variables decreases the ICER to €62 748/QALY, which is likely to be considered cost-effective in the French context.

The ICER was also sensitive to the end-of-life care costs in patients not receiving LVAD; assuming higher costs for 'no LVAD' group, resulting from prolonged ICU stay, decreased the ICER to €96 141/QALY and thus improved the CE of the LVAD.

Discussion

We used individual patient data from the PMSI to investigate the cost-effectiveness of LVAD in patients with end-stage HF. French patients treated with LVAD had a follow-up to 60 months; to our best knowledge, this is the longest LVAD follow-up described. In the last Interagency Registry for Mechanically Assisted Circulatory Support annual report, the patients' follow-up reached the 48th month.[25]

Our findings suggest that in comparison with medical management (here no LVAD), patients with end-stage HF implanted with an LVAD had higher mean costs and higher survival benefit, delivering a probabilistic ICER of €125 580/QALY [95% confidence interval: 105 587 to 150 314] and a similar deterministic ICER of €123 109/QALY for a lifetime horizon. When the model was run for shorter time horizons (i.e. 3, 5, and 10 years), the ICER increased significantly. This could be explained by the fact that most costs are attributable to the device implant and initial ICU and ward stay (at model entry). These costs decreased with time. The next biggest component of cost was the transplant procedure and post-transplant care. According to PMSI, the probability of receiving a donor heart beyond 3 years is close to zero; we therefore set 'p12' to be 0 after 36 months. Therefore, all costs related to the heart transplant are accounted for in the first 3 years of the model.

Figure 4 Time to event analyses using the Program for the Medicalization of Information Systems database. LVAD, left ventricular assist device.

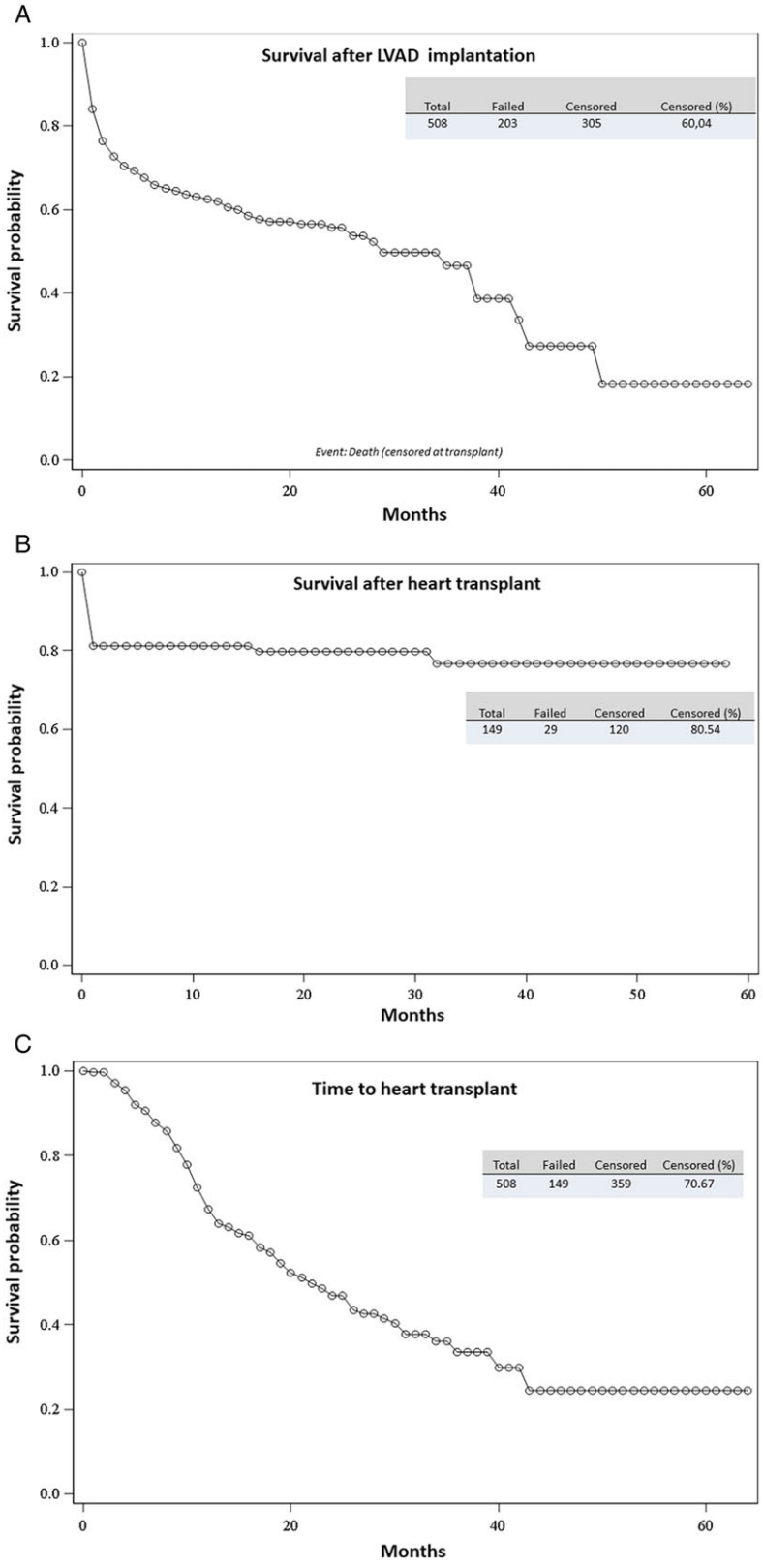


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Table 2 Summary of the base-case model inputs

Health state transition probabilities	*P* (95% CI)	Source of information
LVAD group		PMSI
LVAD support until death (p13)		
Month 1	0.17 (0.13 to 0.21)	
Month 2	0.09 (0.06 to 0.13)	
Months 3+	0.05 (0.03 to 0.08)	
Transition from LVAD to HTx (p12)		
Months 1 and 2	0.002 (0 to 0.006)	
Months 3–6	0.03 (0.01 to 0.04)	
Months 7–12	0.05 (0.02 to 0.08)	
Months 13–24	0.04 (0 to 0.09)	
Months 25–36	0.01 (0 to 0.02)	
Months 37+	0	
Transition from HTx to death (p23)		
Month 1	0.20 (0.13 to 0.28)	
Month 2	0.01 (0 to 0.05)	
No LVAD group		Sharples *et al.*[9] expert opinion
Survival without LVAD (p44)		
Months 1–3	0.1	
Months 4+	0	
Health state utilities	***U* (95% CI)**	**Source of information**
Patients without LVAD (all months)	0.55 (0.50 to 0.60)	Clarke *et al.*[8]; Sharples *et al.*[9]
Post-LVAD		
Months 1 and 2	0.55 (0.50 to 0.60)	
Months 3+	0.74 (0.59 to 0.88)	
Post-HTx (all months)	0.83 (0.82 to 0.84)	
Costs (€)	**Mean cost (€) (SD)**	**Source of information**
LVAD group		PMSI
LVAD implant procedure (including LVAD device + associated devices + hospitalization)	122 885 (11 854)	
LVAD device	86 388 (5115)	
Post-LVAD implant		
Month 1	6320 (18 957)	
Month 2	2930 (4054)	
Month 3	3830 (5774)	
Month 4	3257 (4638)	
Month 5	3274 (4509)	
Month 6	4065 (5688)	
Months 7–24	3011(4707)	
Months 25+	2576 (3444)	
HTx procedure + associated hospitalization	54 164 (12 995)	
Post-HTx		
Month 1	3008 (2695)	
Month 2	2891(4333)	
Month 3	1890 (1910)	
Month 4	2179 (2429)	
Month 5	2443 (6008)	
Month 6	2214 (3563)	
Months 7+	1706 (1741)	
No LVAD group		PMSI
Support on medical management		
All months	5563 (6022)	

CI, confidence interval; HTx, heart transplantation; LVAD, left ventricular assist device; PMSI, Program for the Medicalization of Information Systems.

Because the database does not provide information about medication, the impact of a new medical therapy could not be studied. However, other CE studies confirmed that the main cost drivers in this population are the devices, the procedure and the post-procedure complications costs.[26] In the Oslo University experience, medical therapy represented 1% of total costs during the pre-LVAD and the LVAD phase and was insignificant during the post-LVAD phase.[10] Therefore, it is unlikely that new medical therapy could be a significant cost driver in LVAD patients.

Our ICER was found consistent with other countries' ICER ranging from $84 963/QALY in the UK to $201 600/QALY in the USA. It was close to the Netherland's ICER (€107 600–€112 000/QALY).[11,27] However, French ICER was

Table 3 Summary of base-case results and sensitivity analyses

Base-case deterministic analysis–lifetime model			
	Mean costs (€)	Mean LYG	Mean QALY
LVAD	190 739	1.905	1.504
No LVAD	6178	0.009	0.005
Difference	184 561	1.896	1.499
ICERs (€/LYG)		97 333	
ICER (€/QALY)		123 109	
Base-case probabilistic analysis–lifetime model–Monte Carlo simulation			
	Mean costs (€) (95% CI)	Mean LYG (95% CI)	Mean QALY (95% CI)
LVAD	191 174 (12 453)	1.905 (0.000)	1.48 (0.078)
No LVAD	5927 (6 932)	0.009 (0.000)	0.005 (0.000)
Difference	185 247	1.896	1.475
ICERs (€/LYG)		97 695 (83 219–111 804)	
ICER (€/QALY)		125 580 (105 587–150 314)	
One-way sensitivity analysis			
	ICER (€/QALY)	Difference in QALYs	Difference in costs (€)
3 year time horizon	217 658	0.761	165 667
5 year time horizon	172 890	0.995	171 940
10 year time horizon	137 882	1.304	179 739
Reduction in device price (mean price = €43 194, half price)	94 321	1.499	141 367
Reduction in HTx referrals (p12 = 0.01 all months)	150 471	1.14	171 525
Increased survival because of improved device performance; p13 = 0.1 (Month 1) and 0.01 (Months 2+)	74 144	3.79	281 036
Higher costs for the management of 'no LVAD' group because of prolonged ICU stay; mean costs €42 000/month	96 141	1.499	144 094
Utility of LVAD patients at 0.81 from Month 3 (as patients in the single-centre study have NYHA I/II—utilities are derived using the standard gamble method as described[24])	119 520	1.544	184 561
Two-way sensitivity analysis			
	ICER (€/QALY)	Difference in QALYs	Difference in costs (€)
Reduction in device price (mean price = €43 194, half price) + improved device performance: p13 = 0.1 (Month 1) and 0.01 (Months 2+)	62 748	3.79	237 842

CI, confidence interval; HTx, heart transplantation; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; LVAD, left ventricular assist device; LYG, life years gained; NYHA, New York Heart Association; QALY, quality-adjusted life year.

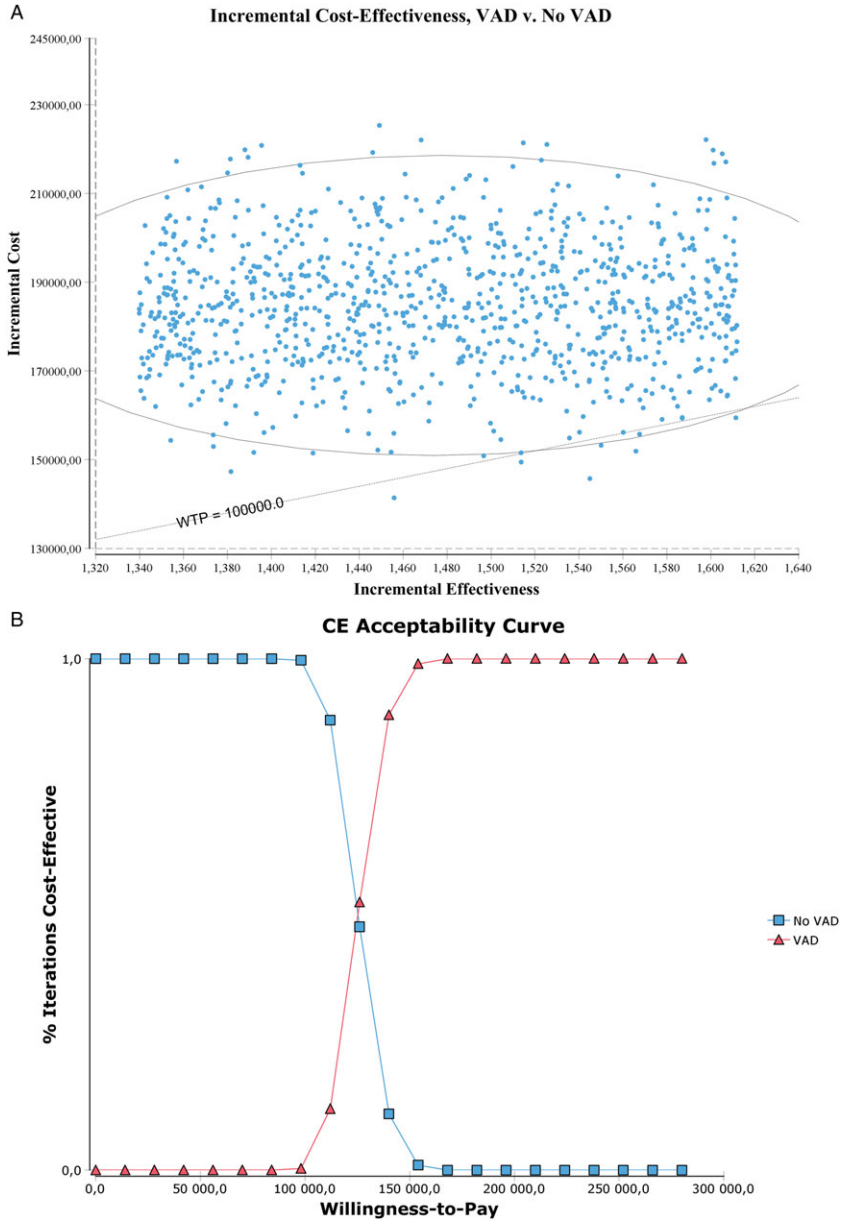
significantly lower than published estimates coming from the USA.[14,15] Obviously, the USA has a less parsimonious approach than France, with healthcare expenditure per capita in 2014 almost twice the French level. The favourable ICER observed in the UK, which is mostly a result of the efficiency (mean 5.4 LYG), could be explained by less severe cases included in the model: only 58.1% of patients presented with severe cardiovascular disease (NYHA IV), 38.7% moderately severe (NYHA III), and 13.2% (NYHA II) minimal.[8] Of note, based on our own experience, all patients had a NYHA of Class IV at LVAD implantation, which reflects the clinical practice in France.

The sensitivity analysis demonstrates that our estimates of the ICERs were reasonably robust to changes in the base case. Reduction in the LVAD price along with improvements in the health-related quality of life both has the potential to make its use more cost-effective, as described above and elsewhere.[9,18] Also, assumption based on maximum of 3 months in ICU for the 'no LVAD' group resulted in a significant improvement in ICER. Of note, there were no signs in cost savings over time (i.e. between the period 2009–2011 and 2012–2014) (data not shown).

The CE estimate is critically dependent on the choice of comparator population. The main difficulty in modelling CE of LVADs remains the lack of adequate comparison data. In reality, these patients might be not eligible for transplantation or more acutely ill than those waiting for a donor, hence making comparison with heart transplant inadequate. In the absence of the LVAD, we might expect these patients to receive a mixture of optimal management with prolonged ICU stay and worst clinical outcomes, which explains the uncertainty around the cost and effects of end-of-life care in this group.

We did not distinguish between DT and BTT setting, as we do not have the information. Moreover, decision seems very tricky in practice because patient eligibility for

Figure 5 (A) Incremental cost-effectiveness (CE) chart [left ventricular assist device (LVAD) vs. no LVAD] and (B) CE acceptability curve for lifetime model. WTP, willingness to pay.



transplantation could change over time, and choices rely heavily on the patient survival to transplant. It is worth noting that published data showed that the initial device strategy did not necessarily correspond to the final use of the device; BTT and DT are unlikely to be mutually exclusive categories.[25,28,29] For example, in the randomized controlled trial of LVAD (continuous-flow device vs. pulsatile-flow device), 13% of DT patients received a donor heart within 2 years after implantation.[30] On the other hand, less than 50% of BTT patients had received a donor heart 2 years after LVAD implantation.[31] Moreover, Interagency Registry for Mechanically Assisted Circulatory Support report showed that the device strategy was uncertain for approximately 40% of patients who received an implant, and assignment is generally difficult.[29] Although LVAD therapy is often highly effective regardless of the device strategy, with 1 year survival reaching 86% for BTT and 78% for DT (compared with 25% for medical therapy), neither BTT nor DT meet the traditional CE target yet.[28]

Data from PMSI showed that 30% of LVAD patients received a heart transplant and their survival after transplantation was very good. Indeed, it was argued that

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LVAD not only increases patient survival while implanted, but its benefit might be also carried forward once the patient receives a donor heart (in form of less deteriorated organs function vs. conventionally treated patients).[32]

It is worth mentioning that although ICER was comparable with other countries, effects in terms of mean QALY and LYG were better in previously published articles compared with our results.[8,9,19] This inconsistency could be explained by several assumptions: (i) the observed transition probabilities, in particular from LVAD to death (p13), were lower in those studies than in our study. The PMSI showed that patients are at a 17% risk of death in the first month after LVAD implantation, and at 9% the month after; these probabilities were obviously lower in the UK cited studies. (ii) Another topic to highlight is that all these studies were conducted to evaluate the LVAD in BTT settings, suggesting that patients were in a better health status than those who receive LVAD as a DT. In Clarke *et al*.,[8] 13.2% of patients presented with minimal heart failure and slight limitation of physical activity (NYHA II) at the implantation. In our analysis, BTT and DT patients were pooled; no distinction in the database was possible. (iii) The third issue to be highlighted is the discount rates. The French discount rate recommended by the authorities is among the highest (4%), while it ranges between 1.5% and 3.5% in other countries. In the latest recommendations, 3% was considered as the most appropriate real discount rate for CE analyses.[20] However, as our aim is to inform decision makers in France, we used the rate required by the French Health Authority.[17]

Although CE studies became part of market access requirements in France for drug and medical devices, the lack of an ICER threshold stands as a real issue in using ICER to inform decision making. The French threshold exists intuitively but not as a hard value. It ranges from €50 000/QALY to as high as €300 000/QALY for some rare conditions or oncology drugs. There is a clear perception that the French informal threshold may be outstandingly higher than that of other countries.

Main study limitations include uncertainties arising (i) from the lack of comparator group outcomes (which were assumed), (ii) from the lack of non-health sector data to conduct an analysis based on societal perspective,[20] (iii) from the lack of routine follow-up and medication costs, and (iv) from the health state utilities (derived from available secondary data and not from the studied population). Interestingly, all the available CE studies rely on the same UK studies for utility data. Actually, EuroQol five dimensions questionnaire utility scores for LVAD patients were derived from the NYHA Functional Classification using the relationship between EuroQol five dimensions questionnaire and NYHA for HF patients, as described elsewhere.[33] Because there are uncertainties around the utility values, we performed one-way sensitivity analysis using the assumptions derived from our single-centre cohort to test robustness of the model; the sensitivity results showed that our estimates of the ICERs were reasonably robust to changes in the utility assumptions. These utility estimates need to be updated with actual primary data.

These limitations will continue to hamper economic evaluations of LVAD in France until direct health-related quality of life measures (to derive specific utilities) and all direct and non-direct costs form health and non-health sectors are collected in a prospective trial. However, in the absence of such data, it is appropriate to use individual patient data from the French PMSI database to derive transition probabilities and costs.

To our best knowledge, this is the first CE evaluation of LVAD performed in France. The ICER exceeds the minimal WTP threshold adopted in France (€50 000/QALY), but is significantly lower than that adopted for some rare conditions or oncology drugs (€300 000/QALY). Our findings should be carefully considered in light of the disease burden, available funding and future supply of donor hearts.

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Conflict of interest

None declared.

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Supporting information

Additional Supporting information may be found online in the supporting information tab for this article.

Appendix S1. Main hospitalisation categories following the LVAD index hospitalization, using the DRG system (n = 5146).

Appendix S2. Survival curve - Survival with a VAD; Survival curve - Survival after heart transplant; Survival curve – Time to heart transplant; Costs (€) after VAD transplantation (n = 508).

Appendix S3. Survival curve - Survival with a VAD; Survival curve - Survival after heart transplant ; Survival curve – Time to heart transplant; Costs (€) after VAD transplantation (*n* = 508).

Table S1. Clinical characteristics and clinical outcomes of the 14 patients having received LVAD in Hopital Marie Lannelongue.

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