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Left Ventricular Assist Device Infections: A Systematic Review

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Abstract

Left ventricular assist devices (LVADs) are becoming a more frequent life-support intervention. Gaining an understanding of risk factors for infection and management strategies is important for treating these patients.

We conducted a systematic review and meta-analysis of studies describing infections in continuous-flow LVADs. We evaluated incidence, risk factors, associated microorganisms, and outcomes by type of device and patient characteristics.

Our search identified 90 distinct studies that reported LVAD infections and outcomes. Younger age and higher body mass index were associated with higher rates of LVAD infections. Driveline infections were the most common infection reported and the easiest to treat with fewest long-term consequences. Bloodstream infections were not reported as often, but they were associated with stroke and mortality. Treatment strategies varied and did not show a consistent best approach.

LVAD infections are a significant cause of morbidity and mortality in LVAD patients. Most research comes from secondary analyses of other LVAD studies. The lack of infection-oriented research leaves several areas understudied. In particular, bloodstream infections in this population merit further research. Providers need more research studies to make evidence-based decisions about the prevention and treatment of LVAD infections.

Keywords

heart-assist device; infection; meta-analysis

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Introduction

Although the number of patients affected by heart failure has increased over the past 2 decades, the number of heart transplants has remained relatively constant at about 3,500 to 4,000 per year because of the shortage of donor organs. This shortage has increased the use of mechanical circulatory support devices for patients with advanced heart failure refractory to treatment, particularly, left ventricular assist devices (LVADs).[1] The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) reports 5,408 such devices implanted between January 2012 and the end of the first quarter of 2014. Of these, 42.9% were considered destination therapy for patients not listed for heart transplant.[2]

As more devices have been implanted, LVAD infections, which are associated with substantial morbidity and mortality, have become an increasingly important problem. The definitive treatment, removing the device, is often not feasible, thus making LVAD infections a devastating complication for affected patients. One prospective study showed a 22% overall infection rate of LVADs and a one-year mortality 5.6 times greater in patients with infections.[3] Besides mortality, LVAD infections are associated with increased risk of pump thrombosis, bleeding complications, longer hospital stay, need for LVAD exchange, and failure to transplant.[4] As more patients have LVAD support for longer periods, developing effective prevention and treatment strategies will become even more crucial.

The International Society for Heart and Lung Transplantation (ISHLT) defines an LVAD infection as an infection occurring in the presence of an LVAD that may or may not be attributable to the LVAD, but that may warrant special consideration if an LVAD is in place. This definition includes several types of infections besides those directly associated with the device, such as catheter-related bloodstream infection or bacteremia attributable to pneumonia or urinary tract infection. LVAD infections can be further classified: driveline-related with accompanying soft tissue, pump pocket, LVAD-associated bloodstream infection, and endocardial infection with direct evidence of vegetation or infection on the internal surface of the pump.[5]

Earlier systematic reviews of LVAD infections have examined prophylactic strategies,[5,6] tools for diagnosis and management,[5] risk factors, and the microbiology of infections. The purpose of this systematic review is to analyze published studies regarding the incidence and risk factors for LVAD infections and describe the impact of each on patient-level outcomes.

Methods

Inclusion and Exclusion Criteria

Our protocol was registered with PROSPERO (Registration No. CRD2014014114). We identified studies that described either the microbiology of continuous-flow LVAD infections or outcomes of these infections (mortality, length of stay, or costs of care). We included the following epidemiologic and experimental study designs: controlled trials, quasi-experimental designs, before-and-after studies, prospective and retrospective studies, and cross-sectional studies. We excluded individual case reports; review articles; basic science papers; animal studies; case-control studies (as our outcomes of interest are epidemiologic);

studies primarily describing outcomes of right ventricular assist devices, biventricular assist devices, pneumatic LVADs (as infection rates were significantly higher in these first-generation devices) ; and pneumatic total artificial hearts. For mixed-population studies, authors were contacted to determine if a subset of data for patients who received continuous-flow devices could be obtained. Finally, pediatric studies were also excluded, as the indications and use of LVADs in adult and pediatric populations are distinct.

When a study was reported as both a preliminary and final analysis, preliminary analyses were excluded. For studies in which there was substantial, secondary data analysis reported separately for new outcomes, the results were combined for reporting purposes to minimize duplication.

Outcomes of Interest

Infections were the primary outcomes of interest in this study. We abstracted data regarding type of infection; microorganisms isolated; attempted therapies; patient-level outcomes of relapse or reinfection, or both; treatment failures; length of stay; and mortality. Infections were defined from individual studies; these definitions were abstracted and compared.

Search Strategy

With the assistance of a professional medical librarian at our institution, we determined our strategy for the literature search. We did not apply any language restrictions and searched the electronic databases of Medline (PubMed), Web of Science, EMBASE, Ovid, and CINAHL. We attempted to ensure a complete search of the health-related grey literature through searches of pertinent conference proceedings and abstracts. We manually reviewed the included references for other potentially relevant records.

Study Quality Assessment

Studies were assessed for methodologic quality by using the risk-of-bias assessment tool described in the *Cochrane Handbook for Systematic Reviews*.[7] This tool allows for subjective assessment of bias across six domains, including selection, performance, attrition, detection, and reporting. The data were summarized using Review Manager 5 software (Cochrane Collaboration, Nordic Cochrane Center).

Data Collection

Data were abstracted using a standard REDCap form (Research Electronic Data Capture, Vanderbilt University) (Supplement 1) by two independent reviewers. Disagreements were resolved by discussion. Data were synthesized qualitatively by category, and, when sufficient data were available, quantitatively using the DerSimonian and Laird random-effects method for meta-analysis and Cochrane Review Manager 5 software.

Results

Search Results

Ninety distinct studies were included in our final synthesis (Figure 1). Study characteristics, patient comorbidities, and infection data are summarized in Tables 1–3.

Definitions

Definitions for LVAD infection were not consistent among the various registries, including in INTERMACS (10 studies), J-MACS (3 studies), and ISHLT (9 studies). One study used the Centers for Disease Control/National Healthcare Network Surveillance definitions for reporting on bloodstream infection. Two studies used their own definitions for percutaneous site infection. The remaining studies did not include precise definitions for LVAD infections.

Devices and Procedure Characteristics

The most extensively studied device was the HeartMate II, with 32 studies reporting on it exclusively. Thirteen studies described the HeartWare HVAD alone. A mix of HVAD and HeartMate II data was reported in 21 studies. Other combinations of VentrAssist, HeartMate II, Evaheart, DuraHeart, and the Micromed DeBakey were reported in eleven studies. Two reported exclusively on the DuraHeart. Three studies reported results of Jarvik 2000 implantations. One study reported on the Evaheart alone. The remaining 13 studies specified continuous flow devices but did not specify the type of device.

Three studies directly compared infection rates between the HeartMate II and the HeartWare HVAD. In the first study, overall infections were significantly higher (P=.02), as were percutaneous infections (P=.01) associated with the HeartMate II.[8] The second study found the opposite, that is, a higher rate of infection for the HVAD than the HeartMate II.[9] In another study that compared the HeartMate II to the Evaheart LVAD, the HeartMate II was associated with lower infection rates.[10] These results are shown in the forest plot in Figure 2. However, the heterogeneity and small numbers of patients in these studies limited the conclusions that could be drawn from the pooled estimate. Several strategies for prophylaxis and wound dressing were discussed (Supplement 2), but none were clearly superior.

Infection Types

Driveline Infection—Fifty-two studies showed driveline infections to be the most common infection associated with LVADs, and it was the only infection described in several studies. Two studies found that the prognosis for a driveline infection was not particularly poor, and these infections were not associated with pump thrombosis or stroke.[11,12] Another study found that driveline infections tended to occur late, at a median of 190 days postoperatively.[13] In general, these infections were managed successfully with a combination of local debridement and antimicrobial therapy; LVAD removal was not necessary in most cases.

Pocket Infection—Infection of the pump pocket was the predominant infection reported in a series of patients treated with antibiotic beads plus debridement[14]. Pump pocket infection was nearly as common as driveline infection in 1 study[15] and was usually the second most common infection in studies reporting both pump pocket infection and driveline infection.[15–18] The prognosis for patients with pump pocket infection was not studied specifically in any of the included reports.

Bloodstream Infection

Although less frequently reported overall, bloodstream infections were reported in 1 study to be the most common infectious complication of LVAD implantation[19]. In addition, Aggarwal et al[20] found bloodstream infections to be associated with increased risk of both hemorrhagic and ischemic stroke; however, transient bacteremia, which was not defined, was excluded. Aldeiri et al[21] also reported an association between bloodstream infection, specifically *Pseudomonas* bacteremia, and stroke. The risk of increased mortality, stroke, and *Pseudomonas* bacteremia was also reported by Trachtenberg et al.[22]

Sources of bacteremia were not clear. Forest et al[23] reported that 43% of patients had secondary bacteremia from driveline infections. They also noted that patients with bloodstream infections were hospitalized longer than patients with driveline infections. Fungemia was not studied. Bloodstream infections were the predominant infection reported in a study by Schulman et al[24] comparing pulsatile and axial flow devices. However, they did not speculate on a reason for this finding. Starling et al[25] also reported a similar predominance of bloodstream infection in their LVAD patients. One study reported 10 cases of asymptomatic bacteremia, which were most often gram positive (90%) but had no other clearly unifying characteristics.[26]

Infection Outcomes and Treatment—Studies reporting an association between infection and mortality are summarized in figure 3. Infection incidence and mortality associated with LVAD infections appeared to decrease over time, as noted in a registry study that compared rates of complications in those who received a HeartMate II before and after the device's approval by the US Food and Drug Administration. This trend appeared to be associated with a Center's increased experience in implanting and subsequently managing the devices, as well as with the use of smaller devices with better flow dynamics.

Chamogeorgakis et al[27] noted that the most important risk factor for infection reported was a continued need for LVAD support. These authors recommended careful evaluation of the patient to ensure that support was still necessary before considering explantation followed by reimplantation.

The effect of infection on long-term patient outcomes was described in 11 studies with varying results, and two studies noted no impact of infection on long-term outcomes.[28,29] Another noted a high rate of infection-associated deaths in a cohort of patients who were substance abusers. One registry study showed LVAD infections to be significantly associated with poor survival after adjusting for age and comorbidities, with 19% of patients experiencing an LVAD infection during their first year of support.[30] However, two other studies did not find infection to be associated with increased mortality, although they did show increased hospital length of stay in patients with infection.[23,31] LVAD infections were reported as a leading cause for readmission in 5 studies.[17,32–35]

The necessity of pump exchange is not clear. One study noted a particularly poor prognosis with candidemia and concomitant implantation of a cardiac implanted electronic device (CIED), and failure to remove the device during pump exchange was associated with poor outcomes.[36] Another investigation noted good outcomes with pump exchange for treatment

of driveline infections and pump pocket infections, with no mortality and low recurrence rates.[37]

One study reported a salvage protocol where, when infection was suspected, the driveline and pocket were debrided and antibiotic beads placed, followed by subsequent debridement of all infected tissues and replacement of the LVAD.[14] When the culture no longer showed infection, the surgeons proceeded to definitive closure of the incision and possible flap coverage. This protocol was successful in clearing infection in 65% of patients. However, lower success rates were noted for *Pseudomonas* species compared with infections caused by *Staphylococcus aureus*, *Candida* species, and other gram-negative organisms, which were more likely to resolve.[14] Causative microorganisms are discussed in Supplement 3. Other demographic risk factors examined are discussed in Supplement 4.

Study Quality

Assessments of study quality are summarized in Table 4. In general, we found a low risk for selection, performance, and detection bias. Reporting bias was more common. Attrition bias was rated as low or unclear in most studies.

Discussion

Despite substantial heterogeneity across studies, we can draw a few conclusions from the data. First, driveline infections are the most common type of LVAD infection described in the literature. This finding is consistent with what is reported in the INTERMACS database, where driveline infections in continuous-flow LVADs are reported to occur at 1.31 per 100 patient months early (first three months post implantation) and 1.42 per 100 patient months late. The most common types of infections are early pulmonary infections (4.58/100 patient months) and early urinary tract infections (3.36/100 patient months), neither of which are strictly device-related.[38]

Second, bloodstream infection is a serious complication of LVAD implantation. Two studies found an association between stroke and bloodstream infection.[20,21] Managing bloodstream infections in LVAD recipients are controversial. Most treating physicians opt for chronic, suppressive antibiotic therapy when the LVAD is clearly the source of infection; however, the best approach for managing a severe bloodstream infection from secondary sources in LVAD recipients is unclear. There is also no data to guide selection of agents for chronic suppression.

Third, and perhaps most important, we have identified a number of knowledge gaps that need to be addressed in future research. Most patients were white men; therefore, more research is needed to determine the incidence and outcomes of infections in women and minorities. The only study to specifically describe sex differences reported that women had fewer infections, but the reasons were not known.[39] Preventive strategies were also not well defined. A chlorhexidine disc and sutureless fixation device appeared promising in 1 study, but the patient cohort was too small to generalize the conclusions.[40] Likewise, the degree of detail in the study about silver dressings[41] makes it difficult to form a strong conclusion about the true benefit of this preventive strategy. Finally, demographic risk factors are poorly

understood. Hyperbilirubinemia (>6 mg/dL) was associated with 100% mortality in one study (103). The variable immunologic effects related to foreign material in the devices also complicates understanding of these effects on LVAD patients. One study, for example, found that procalcitonin values were of limited use because of the SIRS-type (systemic inflammatory response syndrome) most patients have after initial LVAD implantation.[42]

Drawing conclusions was difficult because existing data reporting standards and criteria used for defining LVAD infections are somewhat disparate. INTERMACS tracks major infections, defined as fever, drainage, or leukocytosis treated with nonprophylactic antimicrobial agents. Infections are classified into four general categories: localized non-device infection, percutaneous/pocket infection, internal pump-component infection, and sepsis. The ISHLT provides the second, most commonly used set of definitions, where infections are generally classified as VAD-specific, VAD-related, and non-VAD infections; and they further categorize infection by the area affected. However, this classification scheme does not differentiate between a bloodstream infection where a VAD is the definite source of bacteremia (LVAD-related bloodstream infection) and cases where the source of bloodstream infection in LVAD recipients is unclear (LVAD-associated bloodstream infection). More precise definitions are needed to accurately classify these complex infection syndromes.

The strategy for treating infection varied among the studies. We did not include 1 study in the review because it did not specify if pulsatile devices were used. In that study, however, transvenous lead extraction was associated with improved survival to transplant for those with bloodstream infection related to CIED infections or lead endocarditis.[43] Levy et al[44] reported that pump exchange was effective in eliminating persistent driveline infection. In this case series, antimicrobial beads were not efficacious. In general, data suggested that driveline infections can be managed in most patients with local debridement of the exit site combined with a defined course of pathogen-directed antimicrobial therapy. Device or pocket infections are typically managed with chronic, suppressive antimicrobial therapy. Emerging strategies may make more conservative local debridement with the use of negative-pressure wound dressing or other such interventions viable options in the near future. However, an LVAD exchange may be necessary if infection cannot be controlled, if relapses occur while the patient is taking suppressive antibiotic therapy or if oral suppressive therapy is not feasible (e.g., a resistant organism). There are not enough published data to make recommendations for managing bloodstream infections in patients with LVADs.

Limitations

Two important factors impacted study quality: the lack of uniform criteria to define LVAD infections and the reuse of existing data in the published literature, leading to substantial duplication of results. Study duplication is acknowledged by most investigators. In this extensive, secondary data analysis of the literature for LVAD infections, most of the published data on epidemiology and management are drawn from a relatively small number of patients. By contacting the authors and combining studies whenever duplication could be identified, we attempted to limit this effect. However, especially for the registry studies, this is a major limitation in this meta-analysis.

Conclusions

LVAD infections are a significant cause of morbidity and mortality in LVAD recipients. Most published data describe driveline infections. Bloodstream infections have not been well studied and may be linked to poorer outcomes. Current evidence is inadequate to rationally guide prevention, treatment, and chronic suppression of infections. With the approval of more continuous-flow pumps, the numbers of patients with implanted LVADs will certainly increase, as will LVAD-related and LVAD-associated infections. How to manage infectious complications definitely needs further study. Collaborative initiatives and registries that track infections and treatments may yield insights into how to address this growing problem.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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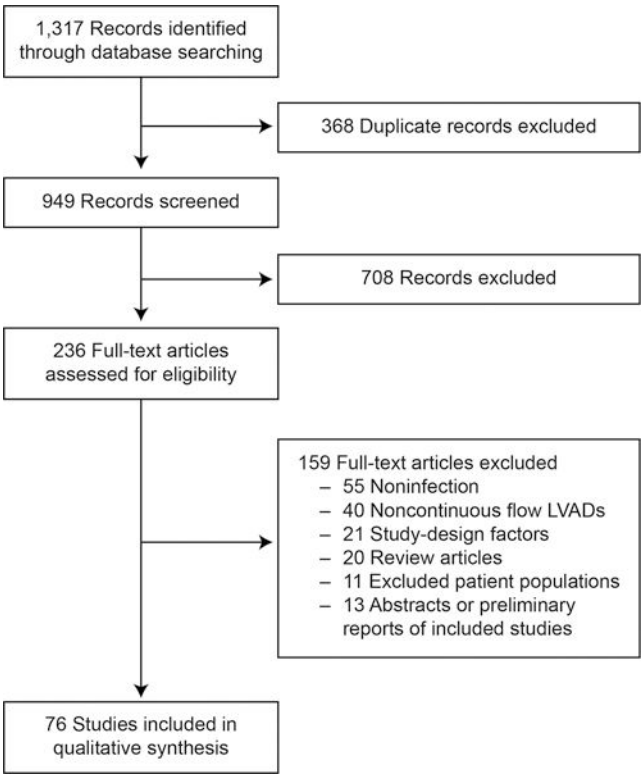

Figure 1.
PRISMA study selection flow diagram.

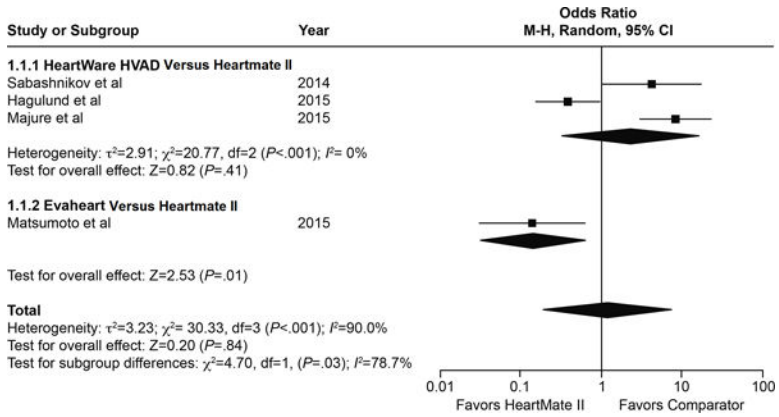

Figure 2.

Forest plot of infection rates for the HeartMate II compared with the HeartWare HVAD: data from Haglund et al[45] (all types of infections, including driveline, sternal wound, and non-LVAD infections); Majure et al[9] (rehospitalizations due to LVAD infections); and Sabashnikov et al[8] (percutaneous site infections treated only with antimicrobial agents); and the Evaheart: data from Matsumoto et al[10] (freedom-from-exit-site infection at 1 year [major endpoint], presented as number of patients with at least 1 exit-site infection in 1 year). Pooled estimates were not significant, likely because of the high degree of heterogeneity in the studies.

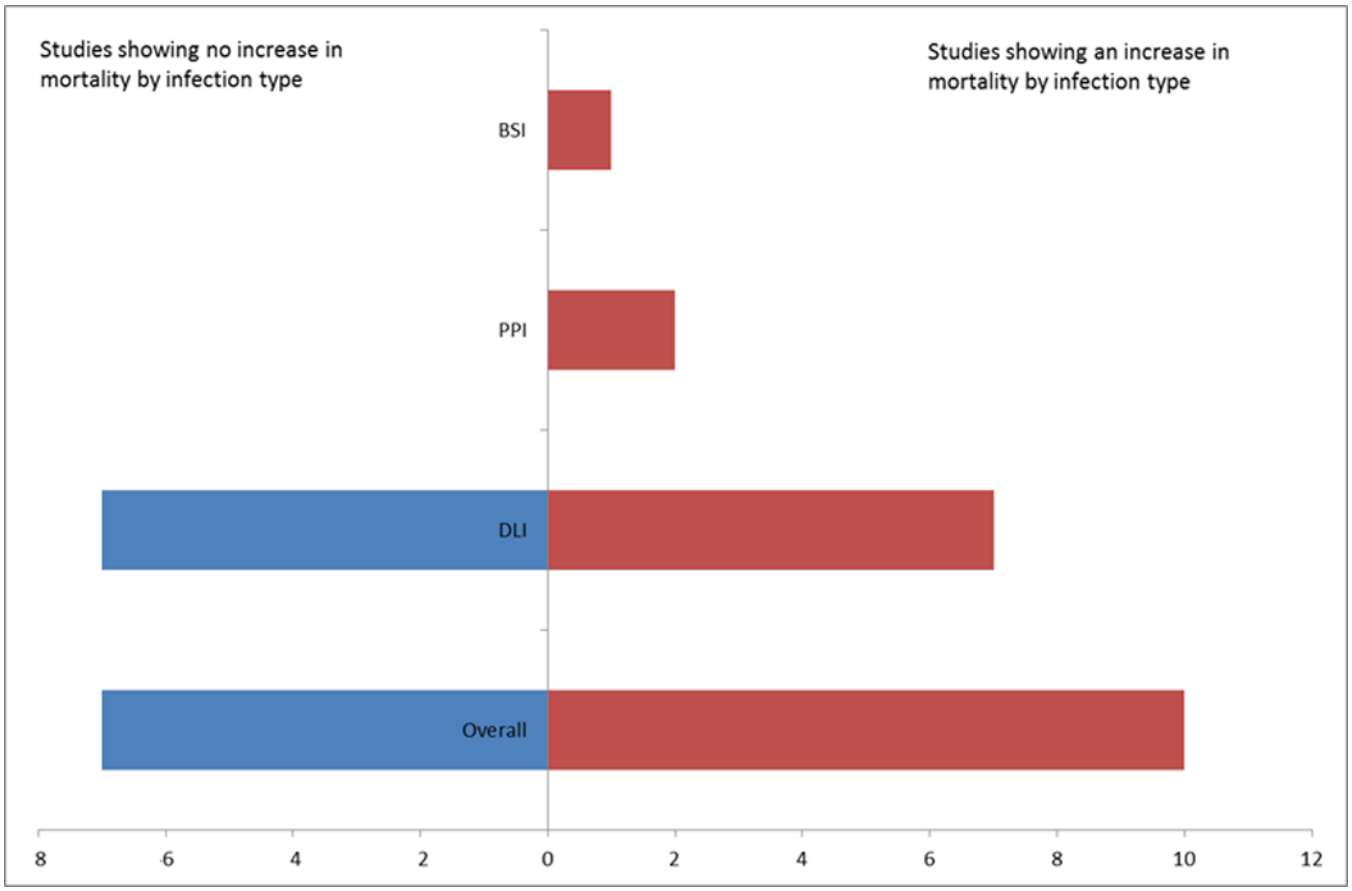

Figure 3.
Studies reporting an association between mortality by infection type

Table 1

Study Characteristics[a]

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Miller et al, 2007[46]	Multi-center	HeartMate II	Prospective, observational	133	50.1	76.0	White (69) African American (23)	BTT (100) ICM (37)	126 d, median	End-stage heart failure	Severe renal, pulmonary, or hepatic dysfunction; active, uncontrolled infection; mechanical aortic valve; aortic insufficiency; other support device (except IABP)
Schulman et al, 2007[24]	New York, USA	HeartMate II, DeBakey Micro-Med	Retrospective, case series	27	55.1 (12.8)	81.5	NR	NR	NR	Implantation between October 2003 and April 2006	NR
Struber et al, 2008[16]	Hanover, Germany	HeartMate II	Retrospective, case series	101	48 (13)	NR	NR	BTT (69.3) DT (30.7)	NR	12 European centers between March 2004 and January 2007	NR
Morshuis et al, 2009[47]	Multi-center	DuraHeart	Prospective, observational	33	55.5 (12.5)	85.0	NR	BTT (100.0)	242 (243) d	Surgical contraindication to LVAD, high-risk cardiothoracic surgery within 30 days, aortic regurgitation, severe COPD, >1 week of ventilator support, active infection, end- stage renal or liver disease, primary RV dysfunction	NR
Lahpor et al, 2010[48]	Multi-center	HeartMate II	Registry review	411	51.0 (14.0)	81.0	NR	NR	236 (214) d	HeartMate II implanted in 1 of 64 European centers that contribute to the Thoratec data bank	Implantation <6 mo before study inception
Topkara et al, 2010[32]	Missouri, USA	HeartMate II, Ventr-Assist	Retrospective, case series	81	51.8 (13.7)	78.0	White (77) African American (23)	DT (29.6) BTT (70.4) ICM (46.7)	9.2 (9.2) mo	NR	NR
Wieselthaler et al, 2010[49]	Multi-center	Heart-Ware HVAD	Nonrandomized controlled trial	23	48 (12.6)	87.0	NR	ICM (30.0)	167 (143) d	Refractory end- stage heart failure with optimal medical therapy and inotropes. UNOS status 1A or 1B	Mechanical circulatory support (except IABP); cardiac transplant within 12 mo; mortality within 14 days; >72 h mechanical ventilation; PE within 2 weeks; mechanical valve; aortic regurgitation; active, uncontrolled infection; thrombocytopenia;

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
											uncontrolled coagulopathy; dialysis; liver failure
Bogaev et al, 2011[39]	Multi-center	HeartMate II	Secondary analysis of data from Heart-Mate II clinical trial and continuous access protocol	465	51.8 (13.2)	77.6	NR	BTT (100.0) ICM (44.9)	338.9 (335.9) d	At least 18 mo follow-up	HeartMate II clinical trial
Garbade et al, 2011[50]	Leipzig, Germany	HeartMate II or Heart-Ware	Retrospective, cohort	49	53 (12)	90.0	NR	DT (16.0) BTT (84.0)	138 (53) d	Implantation between 2006 and 2010	NR
John et al, 2011[25]	Minnesota, USA	HeartMate II	Retrospective, cohort	102	52.6 (12.8)	74.5	NR	BTT (100.0)	327 (286) d	BTT	Exchange for device failure or destination therapy
John et al, 2011[51]	Multi-center	HeartMate II	Registry study	1982	NR	77.2	NR	BTT (100.0)	9.7 mo	CF LVAD as BTT, data as reported to INTERMACS and from the original HeartMate II clinical trial	NR
Schaffer et al, 2011[15]	Maryland, USA	HeartMate II	Retrospective, case series	86	49.7, mean	70.9	NR	DT (33.7) BTT (66.3)	NR	Implantation between June 2000 and May 2009	NR
Starling et al, 2011[25]	Multi-center	HeartMate II	Registry review	169	NR	78.0	White (74) African American (17)	BTT (100.0)	306 (173) d	INTERMACS registry for BTT between April and August 2008	NR
Aggarwal et al, 2012[20]	Illinois, USA	HeartMate II	Retrospective, cohort	87	62 (12.8)	86.0	White (36) African American (49)	NR ICM (57.4)	923.5 (567.3) d	Consecutive patients, between 2005 and 2009	Episode of transient bacteremia
Brewer et al, 2012[52]	Multi-center	HeartMate II	Retrospective, HeartMate II BTT and DT trials	896	56.8 (14.1)	76.1	White (71.9) African American (20.2)	NR	NR	Enrollment in HeartMate II clinical trials for BTT or DT	Exchange from HeartMate XVE to HeartMate II
Bomholt et al, 2011[53]	Copen-hagen, Denmark	HeartMate II	Retrospective, cohort	31	46 (24–55)	74.0	White (100.0)	BTT (81.0) DT (19.0) ICM (26.0)	317 (93–595) d	Consecutive patients	NR
Chamogeorgakis et al, 2012[27]	Ohio, USA	HeartMate II	Retrospective, case series	135	54 (14)	78.5	NR	BTT (40.0) BTD (39.0) DT (21.0)	NR	NR	NR
Donahey et al, 2012[31]	Georgia, USA	NR	Retrospective, case series	57	NR	NR	NR	NR	NR	NR	NR
Eleuteri et al, 2012[54]	Pennsylvania, USA	HeartMate II, Heart-Ware HVAD	Retrospective, cohort	97	59 (10)	81.0	NR	BTT (33.0) BTC (21.6) DT (47.4)	3359 (340) d	Implantation between 2006 and 2011	NR
Fleissner et al, 2012[29]	Hanover, Germany	Heart-Ware HVAD	Retrospective, cohort	81	52 (16.1)	82.7	White (100.0)	ICM (45) NICM (55)	258 (531) d	Implantation in 2008, 2009, or 2011	NR

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Goldstein et al, 2012[30]	Multi-center	NR	INTERMACS registry study	2006	NR, although younger age was a risk factor for percutaneous infection	NR, although older men were at increased risk for infection	NR	NR	NR	Implantation between 6/2006 and 9/2010	NR
Guerrero-Miranda et al, 2012[55]	New Jersey, USA	HeartMate II, DeBakey Micro-Med, Centri-Mag, DuraHeart, Ventr-Assist, Heart-Ware	Retrospective, cohort	120	NR	NR	NR	NR	NR	NR	NR
Hozayen et al, 2012[56]	Minnesota, USA	Heart-Ware, Ventr-Assist, Heart-Mate II	Retrospective, cohort	63	57.5 (17.4)	68.2	NR	ICM (52.4) NICM (47.6)	NR	NR	NR
Kamdar et al, 2015[57]	Multi-center	NR	Registry study	2900	NR	NR	NR	NR	NR	All patients entered in INTERMACS registry between 6/2006 and 3/2011	NR
Krabatsch et al, 2012[58]	Berlin, Germany	Heart-Ware HVAD	Retrospective, case series	142	55.1 (15.9)	82.3	NR	NR	206 d, mean follow- up	Between 9/2009 and 10/2011	Children, patients with congenital heart disease
Maiani et al, 2012[59]	Multisite, Italy	Jarvik 2000	Registry study	65	63.0 (8.0)	89.2	NR	DT (95) ICM (53)	320 d, mean	Between 2006 and 2011	NR
Mano et al, 2012[60]	Pittsburgh, USA	CF LVAD	Retrospective, cohort	78	NR	NR	NR	NR	260 (265) d	Between 12/2006 and 6/2011	NR
Menon et al, 2012[61]	Aachen, Germany	HeartMate II	Retrospective, cohort	40	58.0 (11.0)	NR	NR	DT (22.5) BTT (62.5) BTC (15.0) ICM (72.5)	NR	NYHA IIIB or IV heart failure, between 2008 and 2011	NR
Park et al, 2012[62]	Multicenter trial	HeartMate II	Registry study	281	63.3 (12.6)	76.0	NR	DT (100.0) ICM (24.0)	1.7 y, mean	≥2 y follow-up	Prior HeartMate XVE
Popov et al, 2012[63]	Harefield, United Kingdom	Heart-Ware HVAD	Retrospective, case series	34	51.0 (10.0)	85.3	NR	NR	261 (264) d	Implantation between 2007 and 2011	NR
Schibilsky et al, 2012[64]	Tubingen, Germany	HeartMate II or Ventr-Assist	Retrospective, case series	43	55.7 (13.3)	83.7	NR	DT (25.6) BTT (74.4)	NR	Implantation between 2006 and 2010	NR
Tarzia et al, 2012[65]	Multicenter, Italy	Jarvik 2000	Registry review	65	65, median	89.2	NR	ICM (53.0)	NR	Implantation between 2006 and 2011	NR
Aldeiri et al, 2013[21]	Texas, USA	HeartMate II	Retrospective, cohort	149	55.5 (13)	75.8	NR	ICM (59.0)	NR	Implantation between 2008 and 2012	NR
Choudhary et al, 2013[28]	New York, USA	HeartMate II	Prospective, observational cohort	171	54.0 (12.4)	82.0	NR	NR	NR	Implantation between 11/2006 and 1/2013	Death within 3 mo of device explant

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Forest et al, 2013[23]	New York, USA	NR	Retrospective, cohort	105	56 (14)	82.0	NR	DT (45.0) ICM (51.0)	NR	Implantation between 2006 and 2012	NR
Haj-Yahia et al, 2007[66]	Minnesota, USA	HeartMate II	Registry study	115	62 [53–69]	83.0	NR	DT (64.0) BTT (36.0)	NR	Survival to discharge, between 2008 and 2011	NR
Lalonde et al, 2013[67]	Toronto, Canada	HeartMate II and HeartWare HVAD	Retrospective, case series	46	50.1 (12.6)	60.8	NR	BTT (76.2) BTC (19.5) DT (4.3) ICM (26.1)	NR	Implantation between 1/2006 and 4/2012	NR
Nienaber et al, 2013[36]	Minnesota, USA	HeartMate II, Jarvik 2000, Ventr-Assist	Retrospective, case series	78	56.8 (14.9)	79.0	White (87.0) African American (7.0)	DT (62.0) BTT (38.0)	1.5 (1.0) y	Implantation between 2005 and 2011	LVAD implanted elsewhere, RVAD
Slaughter et al, 2013[68]	Kentucky, USA	Heart-Ware HVAD	Prospective, observational	332	52.8 (11.9)	71.1	White (68.7) African American (25.9)	BTT (100.0) ICM (36.7)	NR	UNOS status 1A or 1B	Other mechanical circulatory device (except IABP)
Smedira et al, 2013[17]	Ohio, USA	HeartMate II	Retrospective, case series	92	53 (14)	78.0	NR	DT (22.0) BTT (78.0)	NR	Implantation between 10/2004 and 1/2010	NR
Stulak et al, 2013[69]	Minnesota, USA	HeartMate II	Retrospective, case series	285	54, mean	51.0	NR	DT (41.0) BTT (39.0) ICM (53.0)	NR	Primary VAD implantation	NR
Tong et al, 2013[26]	Ohio, USA	HeartMate II	Retrospective, case series	254	NR	NR	NR	NR	NR	Between 2004 and 2012	NR
Wu et al, 2013[70]	Berlin, Germany	Heart-Ware HVAD	Retrospective, case review	141	51.6 (16.2)	82.5	NR	DT (28.4) BTT (71.6) ICM (44.7)	NR	Between 8/2009 and 4/2011	NR
Baronetto et al, 2014[40]	Turin, Italy	Heart-Ware HVAD	Prospective, observational cohort	23	57.5	100.0	White (100.0)	BTT (52.0) DT (48.0)	7 mo	Implant with HeartWare HVAD between 4/2013 and 11/2013	NR
Cagliostro et al, 2014[41]	New York, USA	HeartMate II (other devices unspecified)	Prospective, observational cohort	253	NR	NR	NR	NR	NR	Implantation between 2010 and 2013	NR
Chan et al, 2014[71]	Singapore, Singapore	HeartMate II or HeartWare HVAD	Retrospective, cohort	40	41.0	NR	NR	NR	NR	Implantation between 5/2009 and 9/2013	NR
Cogswell et al, 2014[72]	Minnesota, USA	HeartMate II or HeartWare HVAD	Matched cohort	60	43 (14.6)	80.0	White (73.3) African American (16.6) Asian (1.6)	BTT (95.0) DT (5.0) ICM (30.0)	NR	Age >16 y; DSM, IV substance abuse (case arm) or documented lack thereof (matched cohort)	Death in hospital, contraindications to transplantation
Dean et al, 2014[73]	Multicenter	HeartMate II	Secondary analysis of HeartMate II destination therapy clinical trial	401	60, median	NR	NR	BTT (50.0) DT (50.0)	19 (7–46) mo	Inclusion in HeartMate II registry database	NR

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Hieda et al, 2014[74]	Osaka, Japan	NR	Retrospective, case series	16	37.5 (11.9)	100.0	Asian (100.0)	BTT (100.0) ICM (18.8)	387 (228) d	BTT, between 2011 and 2013	NR
Jennings et al, 2014[75]	Detroit, USA	NR	Retrospective, case series	16	52, median	69.0	NR	DT (69.0) BTT (31.0)	NR	Between 1/2008 and 8/2011, with systemic antimicrobial agent therapy for suppression of confirmed LVAD infection	Superficial percutaneous driveline infection
John et al, 2014[76]	Multicenter	Heart-Ware HVAD	Registry study	332	52.7 (11.9)	71.1	NR	BTT (100.0) ICM (36.7)	NR	Secondary analysis of ADVANCE BTT and CAP trial with ≥6 mo follow-up	NR
Jorde et al, 2014[77]	Multi-center	HeartMate II	Registry study	380	NR	81.8	White (74.5) African American (18.7)	BTT (65.0) DT (35.0) ICM (60.0)	NR	First 247 patients who had a HeartMate II implant after FDA device approval and 133 patients in the original HeartMate II clinical trial	NR
Kimura et al, 2014[33]	Tokyo, Japan	DuraHeart Evaheart	Retrospective, case series	31	39.7 (11.7)	84.0	NR	BTT (100.0) ICM (12.9)	NR	End-stage heart failure, BTT	HeartMate II device implantation
Koval et al, 2014[78]	Ohio, USA	HeartMate II	Retrospective, case series	181	54 (13.8)	80.0	White (79.0) Other races unspecified	DT (29) BTT (71) ICM (46)	NR	Implantation between 10/2004 and 9/2011	Previous LVAD
Kretlow et al, 2014[14]	Texas, USA	CF LVAD	Retrospective, case series	26	51.3 (15.7)	81.0	NR	DT (7.7) BTT (92.3)	NR	All patients treated by the senior author for LVAD infection	NR
Masood et al, 2014[37]	Michigan, USA	CF LVAD	Retrospective, case series	328	56, median	77.0	NR	NR	NR	NR	NR
Moazami et al, 2014[79]	Multicenter	DuraHeart	Prospective, observational study	63	54 (11.3)	84.0	NR	BTT (100.0) ICM (49.0)	NR	Advanced heart failure in patients listed for transplant at 1 of 40 investigator centers	NR
Nelson et al, 2014[80]	Pennsylvania, USA	HeartMate II and Heart-Ware HVAD	Retrospective, case series	12	54.3 (19.3)	75.0	White (86.0) African American (14.0)	DT (42.0) BTT (58.0) ICM (58.0) DCM (17.0) NICM (17.0) Familial (8.0)	NR	Patients who required plastic surgery for complex wound management, between 2008 and 2013	NR
Nishi et al, 2014[81]	Osaka, Japan	Heart-Ware HVAD	Prospective, cohort	9	33.5 (7.8)	66.7	NR	BTT (100.0) ICM (0)	245 (162) d	Patients eligible for cardiac transplantation, taking maximal medical therapy	NR
Raymer et al, 2014[82]	Missouri, USA	HeartMate II Heart-Ware HVAD (35)	Retrospective case series	316	NR	78.0	NR	NR	NR	Implantation between 6/2005 and 7/2013	NR
Sabashnikov et al, 2014[8]	Harefield, United Kingdom	HeartMate II or Heart-Ware HVAD	Retrospective, cohort	139	44 (13.7)	NR	NR	BTT (100.0) ICM (11.0) DCM (83.0) PPM (1.0) HCM (5.0)	514 (481) d	Implantation between 2007 and 2013	NR

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Singh et al, 2014[83]	Wisconsin, USA	HeartMate II	Retrospective, case series	125	NR	NR	NR	NR	628 (231.1) d	Implantation between 6/2008, and 10/2011	NR
Subbotina et al, 2014[84]	Hamburg, Germany	Heart-Ware HVAD	Retrospective, case series	38	57 (12)	NR	NR	ICM 31.6	10 (7) mo	Implantation between 1/2010 and 8/2013	NR
Takeda et al, 2014[85]	New York, USA	HeartMate II, Ventr-Assist, Dura-Heart, DeBakey Micro-Med	Retrospective, case series	140	54.7 (14.4)	79.3	ICM (36.4)	DT (17.9) BTT (82.1)	NR	Implantation between 2004 and 2010	NR
Abou el ela et al, 2015[86]	Missouri, USA	HeartMate II and Heart-Ware HVAD	Retrospective, case series	363	NR	NR	NR	NR	NR	Implantation between 2009 and 2013	NR
Akhter et al, 2015[34]	Wisconsin, USA	HeartMate II (120) Heart-Ware HVAD (1) DeBakey Micro-Med (1)	Retrospective, case series	122	53 (12.9)	77.0	NR	ICM (43.6)	370 (336) d	Implantation between 2007 and 2013	NR
Birks et al, 2015[87]	Multicenter	Heart-Ware HVAD	Registry study	332	52.7 (11.9)	71.1	White (68.7) African American (26.7)	BTT (100) ICM (36.7)	NR	Secondary analysis of ADVANCE BTT and CAP trial, ≥6 mo follow-up	NR
Fried et al, 2015[11]	New York, USA	HeartMate II, Heart-Ware HVAD	Retrospective, case series	298	NR	NR	NR	NR	NR	Implantation between 2008 and 2014	NR
Fudim et al, 2015[88]	Tennessee, USA	Heart-Ware HVAD, Heart-Mate II	Retrospective, case series	161	NR	NR	NR	NR	NR	Implantation between 2009 and 2014	NR
Haeck et al, 2015[89]	Leiden, Netherlands	Heart-Ware HVAD	Retrospective, case series	16	61 (8)	81.0	NR	DT (100.0) ICM (81.0)	NR	Consecutive LVAD implants	NR
Haglund et al, 2015[45]	Tennessee, USA	HeartMate II, Heart-Ware HVAD	Registry study	81	52.6 (10.6)	78.0	NR	BTT (100.0)	NR	Patients in the Vanderbilt Advanced Heart Failure Registry	DT, died before the index hospitalization, implantation with temporary or pulsatile LVAD, RVAD, or TAH
Harvey et al, 2015[90]	Minnesota, USA	HeartMate II	Retrospective, cohort	230	57.0 (14.0)	80.4	NR	BTT (80.4) DT (19.6)	NR	Implantation between 2006 and 2013	NR
Henderson et al, 2015[91]	Illinois, USA	CF LVAD	Retrospective, cohort	56	52.4 (12.5)	NR	NR	NR	NR	Implantation between 2008 and 2014	NR
Imamura et al, 2015[13]	Japan	Evaheart, Dura-Heart, HeartMate II, Jarvik 2000, Heart-Ware HVAD	Retrospective, cohort	57	40.0 (12.0)	79.0	Asian (100.0)	BTB (9.0) ICM (5.0)	421 (325) d	NR	Driveline infection before first discharge
Krishna-moorthy et al, 2014[92]	North Carolina, USA	HeartMate II	Retrospective, case series	5	63.0 (12.2)	100.0	NR	DT (100.0) ICM (80.0)	NR	CIED lead removal after LVAD implant and ISHLT-defined LVAD infection	NR
Lushaj et al, 2015[93]	Wisconsin, USA	HeartMate II, Heart-Ware HVAD	Retrospective, case series	128	57.8	84.3	NR	DT (32.6) BTT (67.4) ICM (22.6)	NR	Between 1/2008 and 6/2014	NR

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Majure et al, 2015[9]	District of Columbia, USA	HeartMate II, Heart-Ware HVAD	Retrospective, case series	141	54.6 (13.6)	74.0	African American (61.7) Other races not specified	DT (36.1) BTT (63.9) ICM (35.0)	NR	Implantation between 2011 and 2014	Death before discharge
Maltais et al, 2015[94]	Multicenter	Heart-Ware HVAD	Registry study	382	NR	NR	NR	NR	NR	Secondary analysis of ADVANCE BTT and CAP trial	NR
Matsumoto et al, 2015[10]	Osaka, Japan	Evaheart, Heart-Mate II	Retrospective, cohort	39	NR	NR	NR	NR	NR	Implantation between 2007 and 2014	NR
McCandless et al, 2015[95]	Utah, USA	HeartMate II	Retrospective, cohort	57	56 (14.6)	87.7	NR	DT (25.0) BTT (75.0)	302 (302) d	Utah Artificial Heart Program Database, between 2008 and 2012	NR
McMenamy et al, 2015[96]	Sydney, Australia	CF LVAD	Retrospective, cohort	85	NR	NR	NR	NR	NR	Implantation between 2010 and 2014	NR
Nishinaka et al, 2015[18]	Japan	Evaheart	Registry review	108	42.0 (19)	NR	NR	NR	NR	Advanced heart failure, J-MACS registry	NR
Ono et al, 2015[97]	Japan	HeartMate II	Registry review	104	41.7	76.0	NR	BTT (100)	299.2 d	J-MACS registry between 2013 and 2014	NR
Potapov et al, 2015[98]	Europe	HeartMate II	Retrospective, cohort	479	NR	NR	NR	ICM (46.6) DCM (49.5)	610 (592) d	Implant done at 1 of 3 high-volume European centers between 2006 and 2014	NR
Trachtenberg et al, 2014[22]	Texas, USA	HeartMate II	Retrospective, case series	149	55.4 (13)	76.0	NR	ICM (59.1)	642 (531) d	Implantation between 2008 and 2012	NR
Tsiouris et al, 2015[99]	Connecticut, USA	HeartMate II (136) Heart-Ware HVAD (13)	Retrospective, cohort	149	53.7 (12.1)	74.0	White (59.0) African American (41.0)	BTT (54.3) DT (45.7) ICM (37.0) NICM (63.0)	435.7 (392.2) d	Implantation between 2006 and 2013	NR
Van Meeteren et al, 2015[12]	USA	NR	Registry review	734	57, median	78.6	NR	NR	NR	Hospital in Mechanical Circulatory Support Registry Network, between 2004 and 2014	NR
Wus et al, 2015[100]	Pennsylvania, USA	HeartMate II	Retrospective, case series	68	57 (11.4)	80.9	White (60.3) Other races not specified	NR	NR	First implant	No ICU-intermediate care–discharge pathway, implant at outside hospital, OHT during index hospitalization, never left ICU, had pump exchange
Yoshioka et al, 2014[101]	Osaka, Japan	Jarvik 2000	Retrospective, case series	9	57 (11.0)	77.8	NR	DT (22.8) BTT (77.2)	725 d, median	NR	NR

First Author, Year	Location	Device	Study Design	No. of Patients	Patient Age, Years	% Men	Race/ Ethnicity (%)	Indication for LVAD (%)	Duration of Support	Inclusion Criteria	Exclusion Criteria
Yost et al, 2015[19]	Illinois, USA	NR	Retrospective, case series	134	58 (13.1)	73.1	NR	NR	NR	Implantation between 2012 and 2014	NR

Abbreviations: ADVANCE, Ventricular Assist Device for the Treatment of Advanced Heart Failure; BTB, bridge to bridge; BTC, bridge to candidacy; BTD, bridge to destination therapy; BTT, bridge to transplant; CAP, continuous-access protocol; CF, continuous flow; CIED, cardiovascular implantable electronic device; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; DT, destination therapy; HCM, hypertrophic cardiomyopathy; IABP, intraaortic balloon pump; ICM, ischemic cardiomyopathy; ICU, intensive care unit; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; ISHLT, International Society for Heart and Lung Transplant; IV, intravenous; J-MACS, Japanese Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; NICM, nonischemic cardiomyopathy; NR, not recorded; OHT, orthotopic heart transplant; PE, pulmonary embolus; PPM, peripartum cardiomyopathy; RV, right ventricular; RVAD, right ventricular assist device; TAH, total artificial heart.

[a]Data presented as mean (standard deviation) or median (interquartile range)

Table 2

Patients' Comorbidities[a]

Study	BMI (kg/m^2)	INTERMACS Score	Cardiac Resynchronization Device, %	Diabetes Mellitus, %
Miller et al, 2007[46]	26.8 (5.9)	NR	NR	NR
Schulman et al, 2007[24]	NR	NR	NR	37.0
Struber et al, 2008[16]	NR	NR	NR	NR
Morshuis et al, 2009[47]	NR	NR	CRT, 82	NR
Lahpor et al, 2010[48]	NR	NR	NR	NR
Topkara et al, 2010[32]	28.0 (5.6)	NR	NR	33.3
Wieselthaler et al, 2010[49]	27.6, mean	NR	69.6	NR
Bogaev et al, 2011[39]	NR	NR	CRT, 49.4 ICD, 76.3	NR
Garbade et al, 2011[50]	NR	1.7 (0.74)	NR	NR
John et al, 2011[25]	28.7 (6.8)	3.6 (1.7)	NR	28.4
John et al, 2011[51]	28.4 (9.1)	2.5 (2.9)	NR	NR
Schaffer et al, 2011[15]	28.3 (7.0)	2.6 (1.0)	80.2	NR
Starling et al, 2011[25]	NR	NR	NR	NR
Aggarwal et al, 2012[20]	27.26 (6.4)	NR	NR	NR
Brewer et al, 2012[52]	26.5 (5.9)	NR	53.1	NR
Bomholt et al, 2011[53]	24.2 (21.1–27.3)	NR	CRT, 83.9 (ICD, 25/31; CRT-P, 1)	16.1
Chamo-georgakis et al, 2012[27]	NR	NR	NR	NR
Donahey et al, 2012[31]	NR	NR	NR	NR
Eleuteri et al, 2012[54]	NR	NR	NR	NR
Fleissner et al, 2012[29]	26.9 (4.6)	NR	ICD, 100.0	14.8
Goldstein et al, 2012[30]	NR	NR, although noted not to be a significant predictor of infection risk	NR	NR, although noted not to be a significant predictor of infection risk
Guerrero-Miranda et al, 2012[55]	NR	NR	NR	NR
Hozayen et al, 2012[56]	29.5 (6.1)	NR	NR	39.7
Kamdar et al, 2015[57]	NR	NR	NR	NR
Krabatsch et al, 2012[58]	NR	NR	NR	NR
Maiani et al, 2012[59]	NR	NR	NR	NR
Mano et al, 2012[60]	NR	NR	NR	NR
Menon et al, 2012[61]	NR	NR	NR	NR
Park et al, 2012[62]	NR	NR	NR	NR
Popov et al, 2012[63]	26.0 (6.0)	NR	NR	21.0
Schibilsky et al, 2012[64]	NR	NR	NR	NR
Tarzia et al, 2012[65]	NR	3.1	NR	NR
Aldeiri et al, 2013[21]	28.5 (7.0)	NR	NR	46.3

Study	BMI (kg/m^2)	INTERMACS Score	Cardiac Resynchronization Device, %	Diabetes Mellitus, %
Choudhary et al, 2013[28]	NR	NR	NR	NR
Forest et al, 2013[23]	NR	NR	NR	NR
Haj-Yahia et al, 2007[66]	NR	NR	NR	34.0
Lalonde et al, 2013[67]	24.1 (5.1)	3.2 (0.7)	NR	23.9
Nienaber et al, 2013[36]	29.4 (6.1)	NR	87.0	39.0
Slaughter et al, 2013[68]	28.2 (6.1)	3 (2–3)	NR	NR
Smedira et al, 2013[17]	27 (6.0)	NR	NR	38.0
Stulak et al, 2013[69]	NR	NR	NR	21.0
Tong et al, 2013[26]	NR	NR	NR	NR
Wu et al, 2013[70]	25.8 (5.1)	2 (1–3)	54.6	28.4
Baronetto et al, 2014[40]	24.4	Median 3 (range, 2–4)	78.2	13.0
Cagliostro et al, 2014[41]	NR	NR	NR	NR
Chan et al, 2014[71]	>25, 81% overweight	NR	NR	NR
Cogswell et al, 2014[72]	30 (7.5)	3.6 (1.9)	NR	15.0
Dean et al, 2014[73]	NR	NR	NR	NR
Hieda et al, 2014[74]	NR	NR	0	NR
Jennings et al, 2014[75]	NR	NR	NR	NR
John et al, 2014[76]	28.2 (6.1)	NR	NR	NR
Jorde et al, 2014[77]	NR	NR	NR	44.2
Kimura et al, 2014[33]	NR	2.2 (0.8)	NR	NR
Koval et al, 2014[78]	28 (5.9)	2.5 (3.3)	NR	NR
Kretlow et al, 2014[14]	NR	NR	NR	NR
Masood et al, 2014[37]	NR	NR	NR	NR
Moazami et al, 2014[79]	NR	NR	NR	NR
Nelson et al, 2014[80]	29.3 (8.0)	NR	NR	58.3
Nishi et al, 2014[81]	NR	2.3 (0.5)	NR	NR
Raymer et al, 2014[82]	NR	NR	NR	NR
Sabashnikov et al, 2014[8]	26.0 (5.0)	2.4 (1.1)	46.0	13.0
Singh et al, 2014[83]	NR	NR	NR	NR
Subbotina et al, 2014[84]	NR	NR	NR	NR
Takeda et al, 2014[85]	NR	NR	82.9	31.4
Abou el ela et al, 2015[86]	NR	NR	NR	NR
Akhter et al, 2015[34]	NR	3.0, median	NR	26.7
Birks et al, 2015[87]	28.2 (6.1)	NR	NR	NR
Fried et al, 2015[11]	NR	NR	NR	NR
Fudim et al, 2015[88]	NR	NR	NR	NR
Haeck et al, 2015[89]	NR	3.4 (1.3)	75.0	25.0
Haglund et al, 2015[45]	28.8 (5.5)	2.9 (1.0)	NR	41
Harvey et al, 2015[90]	NR	NR	NR	34.2

Study	BMI (kg/m^2)	INTERMACS Score	Cardiac Resynchronization Device, %	Diabetes Mellitus, %
Henderson et al, 2015[91]	NR	NR	NR	NR
Imamura et al, 2015[13]	20.5 (2.9)	2.5 (0.6)	42.0	3.5
Krishna-moorthy et al, 2014[92]	31 (6.3)	NR	100.0	60.0
Lushaj et al, 2015[93]	28.2 (5.6)	2.7	81.3	40.6
Majure et al, 2015[9]	28.3 (5.9)	NR	NR	37.5
Maltais et al, 2015[94]	NR	NR	NR	NR
Matsumoto et al, 2015[10]	NR	NR	NR	NR
McCandless et al, 2015[95]	26.8 (5.0)	NR	NR	NR
McMenamy et al, 2015[96]	NR	NR	NR	NR
Nishinaka et al, 2015[18]	NR	NR	NR	NR
Ono et al, 2015[97]	NR	NR	NR	NR
Potapov et al, 2015[98]	NR	2 (1–3)	NR	NR
Trachtenberg et al, 2014[22]	28.4 (7.1)	NR	NR	46.3
Tsiouris et al, 2015[99]	28.4 (5.6)	2.8 (1.1)	25.3	45.0
Van Meeteren et al, 2015[12]	NR	NR	NR	NR
Wus et al, 2015[100]	28.6 (5.9)	NR	NR	39.0
Yoshioka et al, 2014[101]	NR	1.8 (0.35)	NR	NR
Yost et al, 2015[19]	NR	NR	NR	NR

Abbreviations: BMI, body mass index; CRT, cardiac resynchronization therapy; CRT-P, cardiac resynchronization therapy, with pacemaker; ICD, implantable cardioverter-defibrillator; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; NR, not reported.

[a]Data presented as mean (standard deviation) or median (IQR).

Table 3

Infection and Outcome Data

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Miller et al, 2007[46]	19 LVAD infections	DLI, 100.0%	NR	NR	NR	Pacemaker lead-related infections occurred later in the course of treatment
Schulman et al, 2007[24]	11 LVAD infections	DLI, 18.8% BSI, 63.6% Endocardial infection, 9.1%	NR	NR	NR	NR
Struber et al, 2008[16]	24 LVAD infections	0.37 DLI/patient y	Of 21 DLI, 6 recurred; no mortality associated with DLI	NR	NR	NR
Morshuis et al, 2009[47]	24 infections 18 LVAD infections	DLI, 72% PPI, 28%	NR	NR	NR	NR
Lahpor et al, 2010[48]	NR	0.19–0.61 DLI/patient y 0.07–0.09 PPI/patient y	0.13–0.62 deaths attributable to infection	NR	NR	Combined results of 3 studies
Topkara et al, 2010[32]	42 patients with at least 1 episode of infection (number of infections not specified)	PPI, 78.0% DLI, 22.0% 8.6% developed *Clostridium difficile* infection	Sepsis (18.5%) associated with decreased survival Overall mortality from LVAD infections, 19.7%	1 patient required LVAD explantation	DLI: MRSA (27.2%) *Pseudomonas aeruginosa* (18.1%) MSSA (9%) *Serratia marcescens* (9%) *Citrobacter koseri* (9%) *Enterobacter cloacae* (9%) *Stenotrophomonas maltophilia* (9%) *Klebsiella pneumonia* (9%) PPI: MRSA, 1 (16.6%) CoNS, 2 (33.3% *P aeruginosa*, 1 (16.6%) *C koseri*, 1 (16.6%) *N sicca*, 1 (16.6%)	Infection was associated with greater length of hospital stay and mortality
Wieselthaler et al, 2010[49]	16 infections 8 LVAD infections	DLI, 100%	NR	7 treated with antimicrobial agents alone; 1 treatment failed and debridement required	NR	NR
Bogaev et al, 2011[39]	89 patients with at least one infection (number of infections not specified)	20 LVAD infections; subtypes not specified	NR	NR	NR	Excluded transient bacteremia
Garbade et al, 2011[50]	6 LVAD infections	Only DLI reported	NR	NR	NR	NR
John et al, 2011[25]	22 LVAD infections	DLI, 100.0%	NR	NR	NR	Before FDA device approval, the rate of driveline infection

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
						was 26.3%, which decreased to 18.8% after FDA approval
John et al, 2011[51]	1,113 infections in 556 patients	303 LVAD infections: PPI, 33 BSI, 233 Endocardial, 5 Line sepsis, 41 Other, 386	NR	NR	NR	NR
Schaffer et al, 2011[15]	140 infections 68 LVAD infections	DLI, 30.0% PPI, 28.0% Sternal wound, 2%	NR	NR	NR	NR
Starling et al, 2011[25]	142 infections	DLI, 31.7% PPI, 2.8% BSI, 33.1% Line sepsis, 1.4% Other, 60.5%	NR	NR	NR	NR
Aggarwal et al, 2012[20]	30 infections	BSI only	BSI was associated with increased risk of hemorrhagic and ischemic stroke	NR	CoNS, 47.1% *Candida* spp, 8.8% *Enterococcus faecalis*, 8.8% *Achromobacter xylosoxidans*, 5.9% MRSA, 5.9% MSSA, 5.9% *Bacillus* spp, 2.9% *Corynebacterium* spp, 2.9% *E cloacae*, 2.9% *P aeruginosa*, 2.9% *Streptococcus mitis*, 2.9% Other *Streptococcus* spp, 2.9%	The study aim was to show sex differences in LVAD complications; higher strokes and fewer infections were reported for women
Brewer et al, 2012[52]	230 LVAD infections	NR	NR	NR	NR	Sepsis and device-related infections increased as BMI increased to >35
Bomholt et al, 2011[53]	55 infections in 12 patients	DLI, 55 No BSI, PPI, or others reported	All patients treated with antibiotics alone; no LVAD explantations	Patients had 1–8 relapses, but none required device explantation	*Staphylococcus aureus* (33%) *Corynebacterium* spp (15%) *E faecalis* (13%) *E coli* (14%) *Klebsiella* spp (7%) *E cloacae* (3%) *Proteus* spp (3%)	Infection rates were low, and those that occurred were easily managed
Chamogeorgakis et al, 2012[27]	34 infections	DLI, 26 (67.0%) PPI, 8 (21.0%)	2 deaths, both in patients with infections managed with medical therapy	5 patients had device exchange; 2, device removal; 1, recurrence; 6 infections required surgical débridement	*S aureus* (33%) CoNS (7%) *Pseudomonas* spp (27%) *Klebsiella* spp (7%) *Serratia* spp (7%) *Proteus* spp (7%) *Candida* spp (7%)	Major risk factor for recurrence was continued device need; recommended a workup to determine if device reimplantation was necessary after explantation in all cases

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Donahey et al, 2012[31]	17 MDRO LVAD infections	NR	Infections were associated with longer length of stay but not mortality	NR	MRSA was the most common MDRO	Risk factors for MDRO included exposed driveline, hospital length of stay, and age
Eleuteri et al, 2012[54]	23 infections	DLI, 100%	NR	NR	NR	Study included implementation of a driveline grading system–based approach to site care, with a significant drop in driveline infection rate (36.3% to 16.0%)
Fleissner et al, 2012[29]	20 infections	DLI, 100%	No association was observed between LVAD infections and mortality	11 infections were treated medically, with 3 treatment failures requiring device explantation	37 isolates in 20 DLI *S aureus* (6/37) *Staphylococcus epidermidis* (7/37) *Staphylococcus warneri* (1/37) *Staphylococcus lugdunensis* (1/37) *Staphylococcus haemolyticus* (1/37) *S mitis* (1/37) *Staphylococcus dysgalactieae* (1/37) *Proteus mirabilis* (4/37) *Proteus vulgaris* (1/37) *Corynebacterium* spp (8/37) *Granulicatella* spp (1/37) *Enterococcus* spp (3/37) *Pseudomonas* spp (1/37) *Escherichia* spp (1/37)	Increased rates of infection associated with obesity, very low ejection fraction, use of fresh frozen plasma during surgery, and not double tunneling the driveline
Goldstein et al, 2012[30]	239 infections in 197 patients	DLI, 100% (percutaneous site)	23 deaths, 6 with sepsis In multivariate analysis, LVAD infection was associated with younger age and did negatively impact survival	20% of infections were associated with sepsis; pneumonia was the most common nondevice-associated infection	NR	Prolonged LVAD use was positively associated with infection, with 19% of patients developing an LVAD infection by 12 mo of support
Guerrero-Miranda et al, 2012[55]	9 LVAD infections in patients with axial-flow LVADs; 0 in patients with centrifugal flow devices	NR	NR	NR	NR	Infections decreased (LVAD and non-LVAD–related) with the later generation of continuous-flow devices (vs pulsatile and axial devices)
Hozayen et al, 2012[56]	9 LVAD infections	DLI, 100.0%	NR	NR	NR	Foam dressing was noninferior to gauze for preventing infection and was associated with higher caregiver satisfaction
Kamdar et al, 2015[57]	294 LVAD infections	DLI, 80.0% PPI, 6.8% BSI, 12.6%	NR	NR	NR	Younger age and prior bypass grafting were risk factors for infection

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Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Krabatsch et al, 2012[58]	37 LVAD infections	DLI, 75.7% BSI, 24.3%	5.3% of infections progressed to sepsis	NR	NR	NR
Maiani et al, 2012[59]	3 episodes of sepsis in the first 12 mo after device implantation	NR	NR	NR	NR	INTERMACS score correlated with mortality and infection
Mano et al, 2012[60]	Rates of infection varied from 19%–25% among groups (stratified by body surface area)	NR	NR	NR	NR	Lower BMI was associated with more nondevice-related infections
Menon et al, 2012[61]	2 LVAD infections	DLI, 100%	1 death	1 successful débridement, device retained	*S aureus* 2 (100%)	NR
Park et al, 2012[62]	383 infections 257 LVAD infections	DLI, 27% PPI, 7% BSI, 28% Other LVAD, 30% non-LVAD, 45%	NR	NR	NR	Risk of infection decreased midtrial vs early
Popov et al, 2012[63]	5 infections	DLI, 100%	NR	NR	NR	NR
Schibilsky et al, 2012[64]	7 LVAD infections	DLI, 100%	NR	NR	NR	Fewer superficial, late DLI in the double-tunnel group compared with the conventional group
Tarzia et al, 2012[65]	NR	DLI, 5	NR	NR	NR	Postauricular gable and intraventricular pump appeared to be associated with reduced local and systemic infections compared with prior studies of LVAD infections
Aldeiri et al, 2013[21]	33 infections, 19 LVAD-related	NR	*P aeruginosa* BSI associated with stroke	NR	NR	NR
Choudhary et al, 2013[28]	56 LVAD-related infections	DLI, 91% PPI, 5%	Survival not impacted by infection	NR	15 *Pseudomonas* organisms	*S aureus* infections tended to occur earlier than infections of other organisms, particularly *Pseudomonas* spp
Forest et al, 2013[23]	27% of patients had at least 1 episode of infection (some recurrent)	DLI, 30% 43% of patients with DLI had bacteremia	Bacteremia did not impact long-term survival, but BSI was associated with longer hospital stay	NR	41% of organisms were *Staphylococcus* spp	NR
Haj-Yahia et al, 2007[66]	32 infections, 6 LVAD-associated	DLI or PPI, 100%	Infection was a leading cause of readmission	NR	NR	NR
Lalonde et al, 2013[67]	1.2 (1) infections/patient, including 16 episodes of	DLI, 11 episodes BSI, 5 episodes	30-day mortality from LVAD infections, 10.9%	NR	NR	Infection rates were comparable between HeartWare HVAD and HeartMate II

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
	pneumonia, 10 episodes of urinary tract infection					
Nienaber et al, 2013[36]	101 LVAD infections in 78 patients	DLI, 36.6% PPI, 4.0% BSI, 35.6% Cannula infection, 10.9% Mediastinitis, 5.0% CIED, 3.9%	NR	14% of infections required débridement; only 3 required device explant	NR	Candidemia was associated with poor outcome DLI was associated with prolonged therapy and destination therapy. Most superficial infections did not progress to deep infection Outcomes improved with CIED removal for concomitant LVAD/CIED infection
Slaughter et al, 2013[68]	145 LVAD infections	DLI, 51.7% Sepsis, 48.3%	NR	NR	NR	NR
Smedira et al, 2013[17]	68 infections 51 LVAD infections	DLI, 55.0% PPI, 19.6% Septic emboli (device), 7.8% BSI, 5.8%	Infection was the leading cause of readmission	NR	NR	NR
Stulak et al, 2013[69]	NR	DLI, 41 infections 7 infections required device exchange	NR	NR	NR	Study compared prophylactic antibiotics to reduce DLI; no effect noted
Tong et al, 2013[26]	47 LVAD infections	PPI ± DLI, 23.4% DLI, 76.6%	NR	8 pump exchanges, 11 irrigation and debridement of the driveline or pump	10 patients had isolated bacteremia of no clinical significance; 90% were GPC; 43% of infections were gram positive, 43% gram negative, and 15% anaerobic	Study of late onset infection; late infections occurred in 20% of patients and were associated with worse survival
Wu et al, 2013[70]	66 infections	DLI, 27.3%	NR	NR	NR	NR
Baronetto et al, 2014[40]	None	NR	NR	NR	NR	Primary purpose was to evaluate the use of a stat-lock and chlorhexidine disc to prevent infection
Cagliostro et al, 2014[41]	NR	NR	NR	NR	NR	76.3% of patients with a standard dressing did not have a driveline infection vs 88.6% with silver dressing
Chan et al, 2014[71]	11 infections	DLI, 100%	NR	All patients treated medically, 4 relapses	MSSA (27.6%) CoNS (20.7%)	Pus or discharge was present in 89% of patients
Cogswell et al, 2014[72]	11 infections	DLI, 100%	Mortality was higher in patients who abused substances	NR	NR	Odds ratio was 5.4 for driveline infection in patients who were substance abusers
Dean et al, 2014[73]	39 infections	DLI, 100%	NR	NR	NR	Leaving the velour portion of the driveline was associated with fewer infections compared

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
						with data from the original HeartMate II DT trial
Hieda et al, 2014[74]	27 LVAD-associated infections	DLI, 55.6% BSI, 44.4%	No deaths	No medical therapy failed; no transplants required	MRSA, 48 (11.9%) MSSA, 39 (9.7%) *Staphylococcus anginosus*, 5 (1.2%) *Staphylococcus capitis*, 10 (2.5%) *Staphylococcus caprae*, 5 (1.2%) *S epidermidis*, 45 (11.1%) *S haemolyticus*, 4 (1.0%) *S lugdunensis*, 26 (6.4%) α-*Streptococcus* spp 9 (2.2%) *Staphylococcus* spp 14 (3.5%) *Corynebacterium* spp 28 (6.9%) *K pneumonia*, 39 (9.7%) *E coli*, 38 (9.4%) *E aerogenes*, 16 (4.0%) *S maltophilia*, 7 (1.7%) *E faecalis*, 22 (5.4%) *M morganii*, 18 (4.5%) *C freundii*, 18 (4.5) *P fluorescens*, 4 (1.0%) *S marcescens*, 9 (2.2%)	Gram-negative bacilli were rarely isolated from the exit site
Jennings et al, 2014[75]	17 infections in 16 patients	DLI, 13 PPI, 1 BSI, 3	NR	Chronic suppression with antibiotics failed in 5 patients; 3 devices had to be explanted	MRSA, 3 (12%) MSSA, 5 (20%) *S marcescens*, 3 (12%) *P mirabilis*, 1 (4%) *P aeruginosa*, 1 (4%) *Staphylococcus maltophilia*, 2 (8%) *Klebsiella* spp, 4 (16%) *Acinetobacter* spp, 1 (4%) *Achromobacter* spp, 2 (8%) *Citrobacter* spp, 1 (4%) *Actinomyces* spp, 1 (4%) *Corynebacterium* spp, 1 (4%)	*C difficile* infection, 2 patients
John et al, 2014[76]	113 infections	DLI, 49.6%	NR	NR	*S aureus* was the most common microorganism in DLI	DLI was associated with diabetes mellitus and higher BMI. Sepsis was associated with decreased survival
Jorde et al, 2014[77]	192 LVAD infections	Before FDA approval, 35%; after approval, 19%	NR	NR	NR	NR
Kimura et al, 2014[33]	17 LVAD infections	DLI, 94.1% BSI, 5.9%	34% of readmissions were attributed to	NR	*S aureus* predominated (6 of 8 culture-positive sepsis episodes)	NR

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
			infection; 8 episodes progressed to sepsis			
Koval et al, 2014[78]	89 LVAD infections	DLI, 100% (study was of DLI only)	DLI was associated with a decreased rate of survival	1/3 of superficial infections progressed despite conservative therapy	*S aureus* and *Pseudomonas* spp were responsible for 1/3 of infections	When there was recurrent infection with a new organism, gram-positive infections occurred after gram-negative infections and vice versa
Kretlow et al, 2014[14]	26 patients with at least 1 LVAD infection	DLI, 42.3% PPI, 50.0% Endocardium, 8.0%	Successfully treated infections had 29% mortality compared with 67% mortality of treatment failures	1 device was explanted; the patient survived	*P aeruginosa*, 9 (19.6%) *E coli*, 5 (10.9%) VRE, 4 (8.7%) *S marcescens*, 4 (8.7%) *S maltophilia*, 4 (8.7%) CoNS, 3 (6.5%) *E cloacae*, 2 (4.3%) MSSA, 2 (4.3%) MRSA, 1 (1.0%) *Acinetobacter baumannii*, 1 (2.2%) *Actinomyces* spp, 1 (2.2%) *Candida albicans*, 1 (2.2%) *C koseri*, 1 (2.2%) *Eikenella corrodens*, 1 (2.2%) *K pneumonia*, 1 (2.2%) *M morganii*, 1 (2.2%) *N sicca*, 1 (2.2%) *P mirabilis*, 1 (2.2%) GBS, 1 (2.2%) Viridans group streptococci, 1 (2.2%) No growth, 1 (2.2%)	Antibiotic bead and repeat debridement was associated with infection clearance in most patients (65.3%)
Masood et al, 2014[37]	59 LVAD infections	Exclusively DLI and PPI	NR	0% mortality with pump exchange	NR	Pump exchange with omental transposition for confirmed PPI; had a 75% (21%) freedom from recurrence of device-related infections
Moazami et al, 2014[79]	33 LVAD infections	DLI, 30.0% PPI, 6.0% BSI, 13.0%	NR	NR	NR	NR
Nelson et al, 2014[80]	12 patients with at least 1 LVAD infection	DLI, 50.0% Mediastinitis and LVAD exposure/ erosion, 50.0%	Multidisciplinary surgical approach achieved salvage achieved in all cases	50% mortality noted at follow-up (post hospital discharge)	MSSA, 1 MRSA, 1 *Pseudomonas* spp, 4 *Parvimonas* spp, 1	Complex wounds were associated with greater mortality, even after attempted surgical salvage
Nishi et al, 2014[81]	2 LVAD infections	DLI, 1 BSI, 1	NR	NR	NR	NR
Raymer et al, 2014[82]	NR	NR	NR	NR	NR	BMI >35 was associated with increased risk of infection

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Sabashnikov et al, 2014[8]	73 infections 37 LVAD infections	DLI, 95.0% PPI, 5%	NR	NR	27 organisms isolated *S aureus* (70%) *Enterobacter* spp (15%) Coliform spp (44%) *Pseudomonas* spp (48%) *Enterococcus* spp (15%) *Klebsiella* spp (22%) *S maltophilia* (19%) *Proteus* spp (19%) *Bacteroides* spp (7%) *Citrobacter* spp (15%) *S marcescens* (4%) *A baumannii* and *calcoaceticus* (4%) *Pantoea* spp (4%) *Chryseobacterium indologenes* (4%) VRE, 1/27 (4%) Anaerobic spp, 1/27 (4%) MRSA, 1/27 (4%) *Prevotella* spp, 1/27 (4%) *Peptostreptococcus* spp, 1/27 (4%) Group B β-hemolytic *Streptococcus*, 1/27 (4%) *Morganella morganii*, 1/27 (4%)	Double tunnel was not associated with fewer driveline infections HeartMate II was associated with more infections than the HeartWare HVAD
Singh et al, 2014[83]	NR	NR	NR	NR	MRSA and MSSA were the most commonly isolated organisms	DLI decreased with exposure of only the silicone velour portion of the driveline
Subbotina et al, 2014[84]	6 infections 2 LVAD infections	NR	Infection was associated with 33% mortality	NR	NR	NR
Takeda et al, 2014[85]	NR	DLI, 21	NR	NR	NR	NR
Abou el ela et al, 2015[86]	98 infections	DLI, 100%	NR	22% of those with a primary revision needed a second revision	*Pseudomonas aeruginosa*, 26% MSSA, 19% MRSA, 22%	The combination of driveline relocation into the rectus muscle, velour removal, and wound- vacuum therapy had better outcomes
Akhter et al, 2015[34]	32 readmissions for infection; 21 were LVAD infections	DLI, 100%	NR	NR	NR	Infection was a leading cause of readmission in this cohort
Birks et al, 2015[87]	113 infections	DLI, 49.6%	NR	NR	*S aureus* was the most common organism isolated in DLI	DLI rates in white vs nonwhites were similar
Fried et al, 2015[11]	38 LVAD infections	DLI, 100%	NR	NR	NR	DLI was not associated with an increased risk of stroke or device thrombosis

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Fudim et al, 2015[88]	18 infections	DLI, 100%	NR	NR	NR	DLI was more common in those with external anchoring sutures, but this was not statistically significant after multivariate adjustment
Haeck et al, 2015[89]	2 LVAD infections	DLI, 100%	NR	NR	NR	Both patients with DLI required hospitalization
Haglund et al, 2015[45]	11 infections 5 LVAD infections	Sternal wound infection, 60% DLI/pump pocket infection, 40%	NR	NR	NR	More infections occurred in HeartMate II patients than in HeartWare HVAD patients (0.49 [0.70] vs 0.17 [0.68]; *P*=.001) Infection was the second most common cause of readmission after cardiac causes
Harvey et al, 2015[90]	60 infections	DLI, 100%	NR	NR	NR	Risk of stroke was increased with infection and with postoperative sepsis
Henderson et al, 2015[91]	27 infections	DLI, 100%	NR	NR	NR	Higher BMI was associated with an increased risk of infection
Imamura et al, 2015[13]	24 LVAD infections	DLI, 23 PPI, 3	NR	1 pump exchanged (HeartMate II to Jarvik 2000) due to PPI	NR	Higher BMI was a predictor of readmission for infection
Krishnamoorthy et al, 2014[92]	5 LVAD infections	BSI, 80%	NR	After lead extraction, 4 patients had a relapse of the BSI	*S aureus*, 20% *Enterococcus* spp, 40% *Pseudomonas* spp, 20% *Klebsiella* spp, 20% 40% were MDRO	CIED removal for LVAD infection is still associated with high rates of relapse of the infection and patient mortality
Lushaj et al, 2015[93]	4 LVAD infections	NR	NR	NR	NR	BTT vs DT did not show a significant difference in infection rates
Majure et al, 2015[9]	66 infection-related readmissions 27 LVAD-infection–related readmissions	DLI, 39 infections	NR	NR	NR	Patients with an HVAD had a significantly higher rate of hospitalization than patients with a HeartMate II for LVAD-related infections (HR, 2.90 (95% CI, 1.03–8.13, *P*=.04)
Maltais et al, 2015[94]	NR	NR	NR	NR	NR	Infection overall decreased after 30 days, with 4.23 events/patient y in the first 30 d, and 1.06 events from 30–180 d, 0.97 events from 180–365 d. DLI did not change significantly over time
Matsumoto et al, 2015[10]	NR	NR	NR	NR	NR	Freedom from infection at 12 mo was better with the

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
						HeartMate II (85%) than the Evaheart (46.2%)
McCandless et al, 2015[95]	4 LVAD infections	DLI, 100%	NR	NR	*S aureus*, 2 *Achromobacter* spp, 1 *S marcescens*, 1	Fewer infections with silicone than with velour
McMenamy et al, 2015[96]	No LVAD infections	N/A	N/A	N/A	N/A	No DLIs, even in patients with a BMI >35
Nishinaka et al, 2015[18]	NR	0.36 DLI/patient year 0.04 PPI/patient year	NR	NR	NR	NR
Ono et al, 2015[97]	NR	43% of those with BSA <1.5 and 16% of those with ≥1.5 BSA had DLI	NR	NR	NR	Smaller BSA was associated with more DLI
Potapov et al, 2015[98]	NR	0.08 DLI/patient year	NR	NR	NR	Authors concluded that the HeartMate II has an acceptable associated complication and infection rate
Trachtenberg et al, 2014[22]	45 infections	22 BSI originated from DLI 4, catheter-related BSI 4, UTI-related BSI	Persistent bacteremia, particularly *Pseudomonas*, was associated with all-cause mortality and stroke	62% of BSI persisted after treatment with appropriate antibiotics and required chronic, lifelong oral suppression	*Pseudomonas* spp, 12 *S aureus*, 11 *E faecalis*, 5 *Candida* spp, 3 *E coli*, 1 *K pneumoniae*, 1 Other, 12	NR
Tsiouris et al, 2015[99]	41 LVAD infections	DLI, 9 PPI, 1 BSI, 31	NR	1 patient required a device exchange; all others treated with 6 wk of antibiotics without need for chronic suppression	DLI: *S aureus*, 5 CoNS, 2 *Pseudomonas* spp, 1 *Serratia* spp, 1 PPI: CoNS, 1 BSI: CoNS, 16 *S aureus*, 5 *Enterobacter* spp, 3 *Klebsiella* spp, 2 *Serratia* spp, 1 *Candida* spp, 2 Viridans group streptococci, 2	DLI infection did not alter risk of death
Van Meeteren et al, 2015[12]	81 LVAD infections	DLI, 100% (other infections not included)	NR	DLI did not adversely affect survival or increase risk of pump thrombosis or stroke	NR	NR
Wus et al, 2015[100]	NR	DLI, 0	NR	NR	NR	Driveline dressing changes varied from daily to weekly without any significant impact on DLI

Study	Incidence of Infection	Type of Infection	Outcome of Infection	Outcome of Treatment	Microorganisms	Comments/Limitations
Yoshioka et al, 2014[101]	1 LVAD infection	DLI, 100%	NR	NR	NR	DLI was late onset (2 y post implant)
Yost et al, 2015[19]	34 LVAD infections	DLI, 32.3% PPI, 8.8% BSI, 39.1%	NR	NR	NR	Infection rates in patients with and without delayed sternal closure were not statistically different

Abbreviations: BMI, body mass index; BSI, bloodstream infection; CIED, cardiovascular implantable electronic device; CoNS, coagulase-negative *Staphylococcus*; CRI, cardiac resynchronization device; DLI, driveline infection; DT, destination therapy; GPC, gram-positive cocci; MDRO, multidrug resistant organisms; MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *Staphylococcus aureus*; NA, not applicable; NR, not reported; PPI, pump pocket infection; UTI, urinary tract infection; VRE, vancomycin-resistant enterococcus; ±, with or without.

[a]Study reported both incidents.

Table 4

Quality Assessments and Risk of Bias[a]

Study	Risk of Selection Bias	Risk of Performance Bias	Risk of Detection Bias	Risk of Attrition Bias	Risk of Reporting Bias
Miller et al, 2007[46]	Low	Low	Low	Low	Low
Schulman et al, 2007[24]	Low	Low	Unclear	Low	Low
Struber et al, 2008[16]	Low	Low	Low	Low	High
Morshuis et al, 2009[47]	Low	Low	Low	Low	Unclear
Lahpor et al, 2010[48]	Low	Low	Low	Low	Unclear
Topkara et al, 2010[32]	Low	Low	Low	Low	Low
Wieselthaler et al, 2010[49]	Low	Low	Unclear	Low	Low
Bogaev et al, 2011[39]	Low	Low	Low	Low	Unclear
Garbade et al, 2011[50]	Low	Low	Low	Low	Low
John et al, 2011[25]	Low	Low	Low	Low	Low
John et al, 2011[51]	Low	Low	Low	Low	Low
Schaffer et al, 2011[15]	Low	Low	Low	Low	Low
Starling et al, 2011[25]	Low	Low	Low	Low	Low
Aggarwal et al, 2012[20]	Low	Low	Low	Low	Low
Brewer et al, 2012[52]	Low	Low	Low	Low	Low
Bomholt et al, 2011[53]	Low	Low	Low	Low	High
Chamogeorgakis et al, 2012[27]	Unclear	Unclear	Unclear	Unclear	Unclear
Donahey et al, 2012[31]	Unclear	Unclear	Unclear	Unclear	Unclear
Eleuteri et al, 2012[54]	Low	Low	Low	Low	Low
Fleissner et al, 2012[29]	Low	Low	Unclear	Low	Low
Goldstein et al, 2012[30]	Low	Low	Low	Unclear	Unclear
Guerrero-Miranda et al, 2012[55]	Unclear	Unclear	Unclear	Unclear	High
Hozayen et al, 2012[56]	Low	Low	Low	Low	Low
Kamdar et al, 2015[57]	Low	Low	Unclear	Unclear	Unclear
Krabatsch et al, 2012[58]	Low	Low	Low	Unclear	High
Maiani et al, 2012[59]	Low	Unclear	Unclear	Unclear	High
Mano et al, 2012[60]	Unclear	Unclear	Unclear	Unclear	Unclear

Study	Risk of Selection Bias	Risk of Performance Bias	Risk of Detection Bias	Risk of Attrition Bias	Risk of Reporting Bias
Menon et al, 2012[61]	Low	Low	Low	Low	Unclear
Park et al, 2012[62]	Low	Low	Low	Low	Unclear
Popov et al, 2012[63]	Low	Low	Low	Low	Unclear
Schibilsky et al, 2012[64]	Unclear	Unclear	Unclear	Unclear	Unclear
Tarzia et al, 2012[65]	Unclear	Low	High	Low	High
Aldeiri et al, 2013[21]	Low	Unclear	Unclear	High	Unclear
Choudhary et al, 2013[28]	Low	Low	Low	High	Unclear
Forest et al, 2013[23]	Low	Low	Low	Low	High
Haj-Yahia et al, 2007[66]	Low	Low	Low	Low	Low
Lalonde et al, 2013[67]	Low	Low	Low	Low	Low
Nienaber et al, 2013[36]	Low	Low	Low	Low	Low
Slaughter et al, 2013[68]	Low	Low	Unclear	Unclear	Unclear
Smedira et al, 2013[17]	Low	Low	Low	Low	Low
Stulak et al, 2013[69]	Low	Low	Low	High	High
Tong et al, 2013[26]	Low	Low	Low	Low	Low
Wu et al, 2013[70]	Low	Low	Unclear	Low	Low
Baronetto et al, 2014[40]	Unclear	Unclear	Unclear	Unclear	Unclear
Cagliostro et al, 2014[41]	Unclear	Low	High	Low	Unclear
Chan et al, 2014[71]	High	High	High	Low	Low
Cogswell et al, 2014[72]	High	Unclear	Unclear	Low	Unclear
Dean et al, 2014[73]	Low	Low	Low	Low	Low
Hieda et al, 2014[74]	Low	Unclear	Unclear	Low	Low
Jennings et al, 2014[75]	Low	Low	Low	Low	Low
John et al, 2014[76]	Low	Low	Low	Low	Low
Jorde et al, 2014[77]	Low	Low	Low	Low	High
Kimura et al, 2014[33]	Low	Low	Low	Low	Low
Koval et al, 2014[78]	High	High	Unclear	Unclear	Unclear
Kretlow et al, 2014[14]	Low	Low	Unclear	Unclear	High
Masood et al, 2014[37]	Low	Low	Low	Low	Low
Moazami et al, 2014[79]	Low	Low	Low	Low	Low

Study	Risk of Selection Bias	Risk of Performance Bias	Risk of Detection Bias	Risk of Attrition Bias	Risk of Reporting Bias
Nelson et al, 2014[80]	Low	Low	Unclear	Unclear	High
Nishi et al, 2014[81]	Unclear	Unclear	Unclear	Unclear	Unclear
Raymer et al, 2014[82]	Low	Low	Low	Low	High
Sabashnikov et al, 2014[8]	Low	Low	Low	Low	Unclear
Singh et al, 2014[83]	Low	Low	Low	Low	High
Subbotina et al, 2014[84]	Low	Low	Unclear	Unclear	Unclear
Takeda et al, 2014[85]	Low	Unclear	Unclear	Unclear	High
Abou el ela et al, 2015[86]	Low	Low	Low	Low	Low
Akhter et al, 2015[34]	Low	Low	Unclear	Unclear	High
Birks et al, 2015[87]	Low	Low	Unclear	High	Unclear
Fried et al, 2015[11]	Low	Low	Unclear	Low	High
Fudim et al, 2015[88]	Low	Low	Unclear	Low	Low
Haeck et al, 2015[89]	Low	Low	High	Low	High
Haglund et al, 2015[45]	Unclear	Unclear	Unclear	Unclear	Unclear
Harvey et al, 2015[90]	Unclear	Unclear	Low	Low	Low
Henderson et al, 2015[91]	High	Low	Low	Low	Low
Imamura et al, 2015[13]	Low	Unclear	Unclear	Low	High
Krishna-moorthy et al, 2014[92]	Low	Low	Low	Low	Low
Lushaj et al, 2015[93]	Low	Low	High	Low	High
Majure et al, 2015[9]	Unclear	Low	Unclear	Low	Unclear
Maltais et al, 2015[94]	Low	Low	Unclear	Unclear	Unclear
Matsumoto et al, 2015[10]	Low	Low	Unclear	Unclear	Unclear
McCandless et al, 2015[95]	High	High	Unclear	Low	Low
McMenamy et al, 2015[96]	Low	Low	Low	Unclear	High
Nishinaka et al, 2015[18]	Low	Low	High	Low	High
Ono et al, 2015[97]	Low	Low	Unclear	Low	Low
Potapov et al, 2015[98]	Low	Low	Low	Low	Low
Trachtenberg et al, 2014[22]	Low	Low	Unclear	Low	Unclear
Tsiouris et al, 2015[99]	Unclear	Low	Low	Unclear	High
Van Meeteren et al, 2015[12]	Unclear	Low	Low	Unclear	Unclear

Study	Risk of Selection Bias	Risk of Performance Bias	Risk of Detection Bias	Risk of Attrition Bias	Risk of Reporting Bias
Wus et al, 2015[100]	Low	Low	Low	Low	Low
Yoshioka et al, 2014[101]	Low	Low	Low	Low	Low

[a] Risk of bias was assessed using the tool in the *Cochrane Handbook for Systematic Reviews*[7].