ESC HEART FAILURE
ESC Heart Failure 2022; **9**: 3995–4002
Published online 23 August 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.14112

ORIGINAL ARTICLE

Pre-operative risk factors for driveline infection in left ventricular-assist device patients

Ann-Kristin Köhler[1], Hermann Körperich[1]*, Michiel Morshuis[2], Claudia Christine Freytag[3], Jan Gummert[2], Wolfgang Burchert[1], Rainer Preuss[1] and Jan Körfer[1]

[1]*Institut für Radiologie, Nuklearmedizin und Molekulare Bildgebung, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinikum der Ruhr-Universität Bochum, Bad Oeynhausen, Germany;* [2]*Klinik für Thorax- und Kardiovaskularchirurgie, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinikum der Ruhr-Universität Bochum, Bad Oeynhausen, Germany; and* [3]*Institut für Laboratoriums- und Transfusionsmedizin, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinikum der Ruhr-Universität Bochum, Bad Oeynhausen, Germany*

Abstract

Aims Implantation of left ventricular-assist devices (LVAD) to treat end-stage heart failure is of increasing relevance due to donor shortage. Infections of the driveline are common adverse events. LVAD infections can lead to high urgency listings for transplantation. However, transplantation in patients with infection leads to worse post-transplantation outcomes. This study aims to evaluate specific risk factors for driveline infections at the time of implantation.

Methods and results Four hundred forty-one patients receiving either Heartmate II or Heartware system from August 2009 to October 2013 were assessed. An expert committee sorted patients into four different groups concerning the likeliness of infection. Twenty-eight (6%) of discussed infection cases were judged as secured, 33 (7%) as likely, 18 (4%) as possible, and 20 (4%) as unlikely. The remaining 342 (78%) subjects showed either no signs of infection at all times (329 [75%]) or developed signs of infection in a second observation period within 1 year after ending of the first observation period (13 [3%]). For a better discriminatory power, cases of secured and likely infections were tested against the group with no infection at all times in a Cox proportional hazard model. Among all variables tested by univariate analysis (significance level $P < 0.15$), only age ($P = 0.07$), LVAD-type ($P = 0.12$), need for another thoracic operation ($P = 0.02$), and serum creatinine value ($P = 0.02$) reached statistical significance. These were subsequently subjected to multivariate analysis to calculate the cumulative risk of developing a drive infection. The multivariate analysis showed that of all the potential risk factors tested, only the necessity of re-thoracotomy or secondary thoracic closure had a significant, protective effect (hazard ratio [95% CI] = 0.45 [0.21–0.95]; $P = 0.04$).

Conclusion This single-centre cohort study shows that driveline infections are common adverse events. The duration of support represents the major risk factor for LVAD driveline infections.

Keywords infection; left ventricular-assist device; PET/CT; risk factor

Received: 18 February 2022; Revised: 19 July 2022; Accepted: 4 August 2022
**Correspondence to: Hermann Körperich, Herz- und Diabeteszentrum NRW, Institut für Radiologie, Nuklearmedizin und Molekulare Bildgebung, Georgstraße 11, D-32545 Bad Oeynhausen, Germany.*
Email: hkoerperich@hdz-nrw.de

Introduction

Severe heart failure is a common disease affecting 26 million patients worldwide.[1] One in five people will suffer from any stage of heart failure in their lifetime.[2] Though heart transplantation remains the gold standard in the therapy of terminal heart failure, the number of transplantations decreased in the Eurotransplant area from 2014 to 2015 due to a growing donor shortage.[3] Therefore, other therapeutic options such as the implantation of left ventricular-assist devices (LVAD) are performed more frequently.[4] Besides, patients with persistent or transient contraindications for transplantation or bridge to recovery patients can be treated with an LVAD implantation as destination therapy. Implantation improves survival and quality of life significantly.[5] Although the number of implantations as destination therapy increased, the number

© 2022 The Authors. ESC Heart Failure published by John Wiley & Sons Ltd on behalf of European Society of Cardiology.
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

of patients with LVAD listed for heart transplantation remains high.[4] After LVAD implantation, the clinical condition of patients improve and subsequently leads to a loss of the patient's high urgency status if gained before.[6] This lowers their chance for transplantation, because the majority of transplantations in Germany are performed in patients with high urgency status.[7] The duration of LVAD support is increasing, and adverse events are occurring frequently.[4] One of the most frequent adverse events in long-term use is infection.[8,9] In a prospective multicentre study, 22% of patients developed LVAD related infections.[9] The main part falls upon infections on the percutaneous driveline[9] or is caused by driveline infections. Developing an infection constitutes a severe problem for the affected patients for two reasons. First, it could be demonstrated that LVAD infection increases 1 year mortality.[9] Second, the outcome after heart transplantation worsens as well.[10–12] This shows that there is a need for identifiable risk factors that could influence heart transplantation allocation policies. High risk patients could be transplanted preferred, before a driveline infection develops. This could improve outcome of heart transplantation in general. Furthermore, existing studies dealing with driveline infections are limited by a small sample size.

This large-scaled study was designed to retrospectively identify risk factors for driveline infections that might affect transplantation allocation policies and to expand existing data.

Methods

The study was performed as a single centre retrospective cohort study between August 2009 and October 2013. To generate a large study size, all patients receiving either Heartmate II or Heartware systems in the Heart and Diabetes Center North Rhine Westphalia during this time period were examined for eligibility. Patients receiving other assist devices such as biventricular assist devices or total artificial hearts were excluded because of decreasing use and relevance of these systems and their different risk profile concerning infections. The project was proved and permitted by the local ethics committee (Ethik-Kommission der Medizinischen Fakultät der Ruhr-Universität Bochum; Register number: 49/2016, EKBO/2016-120-RDA-EV) and complies with the Declaration of Helsinki.

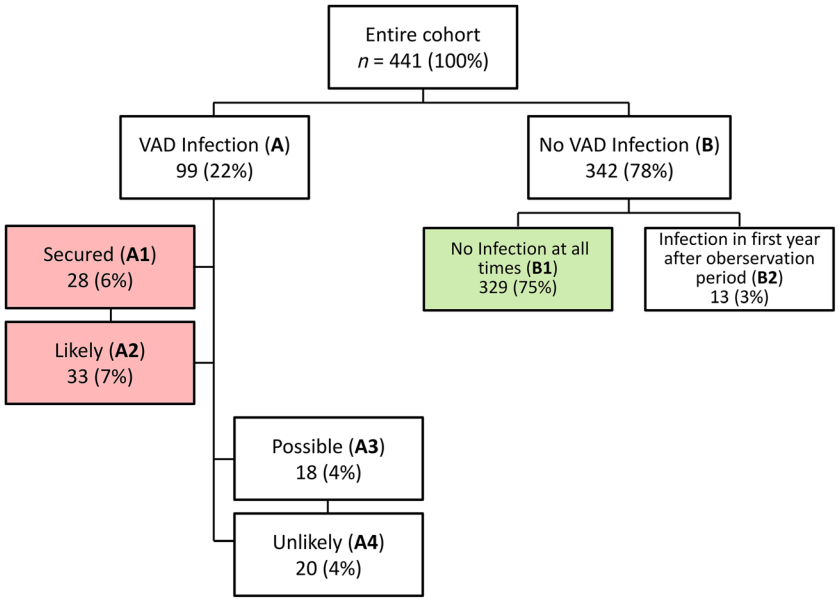
Setting and study subjects

Subjects were assessed from implantation date to the end of the observation period in March 2015. Afterwards, there was a surveillance period of 1 year. First subjects were sorted in two groups. The first group (A) include all patients showing clinical infection signs like redness, secretion or purulent discharge, fever, pain, or overheated surrounding skin. The other group (B) showed no infection signs. To create a high separation effect, patients from the first group were subsequently divided in four subgroups of likeliness of infection (A1–A4): secured infection (A1), likely infection (A2), possible infection (A3), and unlikely infection (A4). Therefore, an expert panel consisting of a microbiologist, three special ventricular assist device caregivers, a heart surgeon, a radiologist, and an intensive care specialist was formed. The criteria for grouping the subjects were the necessity of surgical debridement, microbiology in the form of culture of purulent fluid, secretion or blood, laboratory values of infection, if available confirmation by ^{18}F-fluorodeoxyglucose PET/CT imaging, and the clinical signs of infection and their development. Criteria for being allocated in the secured infection group (A1) were the necessity of surgical debridement. The probable infection group (A2) was the constellation of mentioned criteria strongly indicative of infection. In the possible infection group (A3), the patients showed altogether less reliable signs of infection, but an infection could also not be ruled out. Finally, in the unlikely infection group (A4), patients showed just discreet clinical infection signs, but no other of the mentioned criteria were indicative for an infection. The last two mentioned groups (A3 + A4) of unlikely or possible infections were censored for a higher discriminatory effect. Furthermore, it was decided that the subjects without infectious signs (B) should be also monitored 1 year after the end of the first observation period to discover newly occurring infections. Subjects showing infectious signs in this time (B2) were censored as well to improve the separation effect. This leads to group B1 including all subjects showing no infectious signs at all time. Finally tested were groups A1 + A2 against group B1. *Figure 1* gives a summary of the grouping. End point was LVAD infection. Subjects who underwent device exchange remained in the study.

Variables and data collection

The collected variables were classified into different categories. The patient-based data included age, sex, type of LVAD, operation time, and body mass index. The C-reactive protein was recorded to assess the infectious situation at implantation time. Variables to detect a low output syndrome at implantation time were cardiac index and the blood bilirubin level. We also took perioperative circumstances such as days spend on intensive care unit before implantation, days in hospital before implantation, and the necessity of re-thoracotomy or secondary thorax closure into account. Another group of variables gave information of the effects of chronic diseases. These were the creatinine level, presence of diabetes mellitus, and depression or subdepressive mood and finally the underlying disease (ischaemic cardiomyopathy vs. others). Laboratory values were usually taken on the day

Figure 1 Grouping of the entire cohort concerning likeliness of infection according to a specialist panel. For statistical analysis, the secured driveline infection group (A1 + A2) was tested against the secured non-driveline infection group (B1).



of surgery, in some cases a few days before. The cardiac index was diagnosed in a period of 12 weeks up to some days before implantation. Data were collected from electronic health records of the patients. The variables were transferred in an IBM SPSS® software chart.

Statistical methods

First, a univariate Cox proportional hazard was used to determine associations between possible risk factors and LVAD driveline infection. LVAD driveline infection was the endpoint in the Cox proportional hazards model, and patient follow-up was censored when patients underwent heart transplantation, device explantation, or death. Variables with a significance below $P = 0.15$ were then tested in the multivariate Cox proportional hazard model to detect relevant interactions or confounding. Hazard ratios with the 95% confidence interval were calculated as well. Variables with $P < 0.05$ were defined as statistically significant. For all calculations, the IBM SPSS® software version 24 released 2016 was used.

Results

Participants

The number of subjects examined for eligibility was 442. One subject was excluded because of loss to follow up. Due to groupings described above, the number of included subjects was $n = 390$ (groups A1 + A2 + B1).

Descriptive data

Study participants were predominantly Caucasian and from every social status. The age of the participants ranged from 12 and 79 years, with a median age of 57 years and an interquartile range of 18 years [47; 65]. The majority of patients was male (340 [87%]). The Heartware system was implemented more frequently than the Heartmate II system (234 [60%]). Average operation time was 226 ± 69 min. The body mass index varied between 14 and 55 kg/m^2 with a medium of 26 ± 6 kg/m^2. About one third of the patients needed a re-thoracotomy or a secondary thoracic closure (133 [34%]). A quarter of the patients were diabetic (98 [25%]), and 140 (36%) suffered from depression or subdepressive mood. Ischaemic cardiomyopathy was the main underlying disease (186 [47.7%]). The median value of the observation time was 252 days with an interquartile range of 586 [93; 679]. The medium pre-operative cardiac index was 2.0 ± 0.7 L/min/m^2. It should be mentioned that in 98 cases, there was no cardiac index found in the electronic health record. The medium bilirubin was 2.4 ± 2.3 mg/dl. There were only two missing values. All other examined variables showed no missing data.

Outcome data

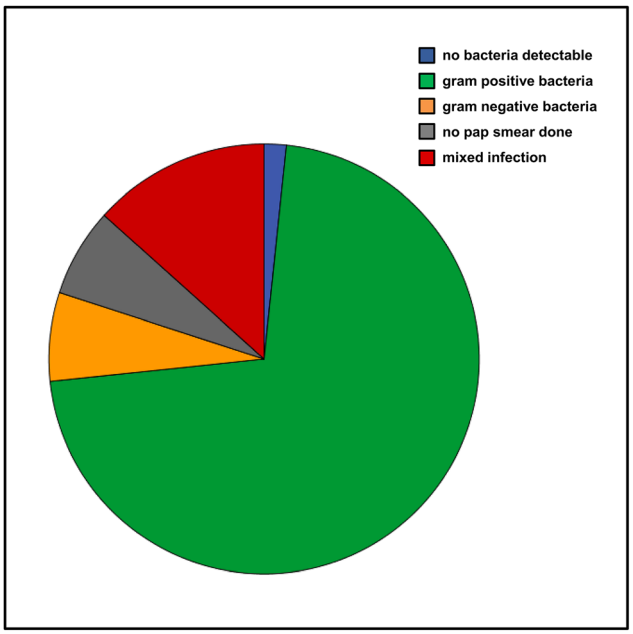
A secured or likely infection (groups A1 + A2) occurred in 61 participants corresponding to 15.6% of the censored cohort of 390 cases. The average time to develop an infection was 331 ± 273 days. The earliest infection was diagnosed 10 days after implantation. The longest period of time between

implantation and infection lasted 925 days. There was a wide range of pathogens, but the majority of driveline infections were caused by Gram-positive bacteria. Most of them were staphylococci. Nearly half of the infections were caused by *Staphylococcus aureus* (49.2%). Mixed infections are common as well. *Figure 2* shows an overview of involved bacteria. In 4% of the cohort, there was no pap smear done, and bacteria were therefore not detectable.

Univariate analysis

In the univariate analysis, younger age was a potential risk factor of developing a driveline infection. The hazard ratio was 0.98 (0.97–1.00) with a *P*-value of 0.07. Moreover, a tendency was seen that the LVAD type influences infection rates. Subjects with a Heartware system had a 53% higher risk of infection as compared with subjects with Heartmate II (P = 0.12). A need for another thoracic operation such as re-thoracotomy or secondary thoracic closure yielded a hazard ratio of 0.45 (0.21–0.94, P = 0.02). The serum creatinine value (P = 0.02) was also included in the multivariate analysis. The presence of diabetes mellitus increased the risk of developing a driveline infection to nearly 40%; however, the result was not statistically significant (P = 0.24). Also, a higher body mass index was not associated with increased infection rates (P = 0.23). In fact, cachexia rather seems to increase the rate of LVAD driveline infection. Subjects with a body mass index $<$18.49 kg/m^2 showed a LVAD driveline infection in 23.1% versus 15.1% in the group with body mass index $>$18.5 kg/m^2. All other tested variables did not show significant effects on infection rates. *Table 1* summarizes the data of the univariate analysis. As shown in *Figure 3*, the cumulative risk for developing a driveline infection increases persistently with the duration of support.

Figure 2 Overview of the bacteria involved leading to left ventricular-assist devices driveline infections



Multivariate analysis

The four variables, age, LVAD type, necessity of re-thoracotomy or secondary thoracic closure as well as creatinine level, had a $P < 0.15$ and were therefore tested in the multivariate analysis. The results are summarized in *Table 2*. The necessity of re-thoracotomy or secondary thoracic closure and the creatinine level were significant, however as protective rather than as risk factors. *Figures 4* and *5* illustrate the negative correlations. The necessity of another thoracic operation lowered the risk of driveline infection by 55%. A 1 mg/dl higher creatinine level lowers risk for driveline infection by 36%.

Discussion

This retrospective cohort study dealing with risk factors for LVAD driveline infection stands out by the large sample size of 441 subjects. Among these, 15.6% of the subjects developed a LVAD driveline infection, which is less than described in other studies.[9,10,13] As the study was performed retrospectively, it was challenging to decide whether participants have had a driveline infection or not. To address this problem, an expert consent was formed. Criteria for classification were based on the criteria of M. Hannan and colleagues, who developed standardized definitions of driveline infection.[14] It should be mentioned that criteria could not be adopted completely, because of some missing data such as histopathological examinations. Nevertheless, experts stuck to theses definitions as close as possible. As Hannan and colleagues suggested,[14] subgroups of likeliness of infection were developed. Cases of infection, which could not be evaluated with less than highly likelihood, were excluded for better discriminatory power. Because our definition of a driveline infection was strict, the infection rate was slightly lower compared with other studies.[9,10,13] In addition to the standardized definitions, the temporal development of the driveline infection was included in our statistical treatment. If infectious signs were described more than one time, the expert committee classified the infection as more likely. To ensure that non-infection subjects have been indeed free of driveline infection during the observation period, an additional year of follow up after ending of regular observation time was implemented. This not only led to a high separation effect but also reduced the sample size.

Table 1 Characteristics of study subjects and univariate Cox proportional hazards model

Entire cohort	Driveline infection group	No driveline infection group		Hazard ratio (95% CI)	*P*
n=390	61	329			
Patient based data					
Age (year)	54.2 (14.1)	51.0 (17.2)	54.8 (13.4)	0.98 (0.97–1.00)	0.07
Sex (male)[a]	340 (87.2)	53 (86.9)	287 (87.2)	0.75 (0.35–1.57)	0.44
LVAD type (Heartware)[a]	243 (60.0)	40 (65.6)	194 (59.0)	1.53 (0.90–2.61)	0.12
BMI (kg/m^2)	26.2 (5.6)	26.1 (5.9)	26.2 (5.5)	1.02 (0.97–1.07)	0.55
Infectious situation at implantation					
CRP (mg/L)	7.7 (6.5)	7.9 (7.8)	7.7 (6.3)	1.00 (0.97–1.04)	0.89
Low output syndrome at implantation/perioperative circumstances					
Cardiac index (L/min/m^2)	2.0 (0.7)	2.1 (0.8)	1.9 (0.7)	1.25 (0.86–1.80)	0.24
Bilirubin level (mg/dl)	2.4 (2.3)	2.1 (1.9)	2.4 (2.3)	0.99 (0.86–1.14)	0.93
Days on intensive care unit (day)	5.5 (11.5)	5.3 (11.5)	5.5 (11.5)	1.01 (0.99–1.04)	0.39
Days in hospital (day)	17.3 (21.5)	18.4 (23.8)	17.2 (21.1)	1.00 (0.99–1.01)	0.85
Re-thoracotomy or secondary thoracic closure[a]	133 (34.1)	8 (13.1)	125 (38.0)	0.45 (0.21–0.94)	0.02
OP time (min)	226.7 (68.7)	213.7 (64.8)	229.1 (69.2)	1.00 (1.00–1.00)	0.94
Chronic diseases					
Creatinine level (mg/dl)	1.7 (0.8)	1.4 (0.6)	1.8 (0.9)	0.63 (0.42–0.93)	0.02
Diabetes mellitus[a]	98 (25.1)	19 (31.1)	79 (24.0)	1.39 (0.81–2.39)	0.24
Depression or subdepressive mood[a]	140 (35.9)	23 (37.7)	117 (35.6)	0.99 (0.68–1.45)	0.96
Underlying disease (ICM vs. others)[a]	186 (47.7)	30 (49.2)	156 (47.4)	0.98 (0.59–1.62)	0.94

Note: Values as mean ± standard deviation.
BMI, Body mass index; CI, confidence interval; ICM, ischaemic cardiomyopathy; LVAD, left ventricular assist device; SD, standard deviation.
[a]Number of subjects, in parentheses (%, related to entire cohort).

In addition to standard definitions, results of ^{18}F-fluorodeoxyglucose PET/CT were included into our evaluation. Inflamed tissue has a higher metabolism. Therefore, a higher uptake of ^{18}F-fluorodeoxyglucose can be visualized in an ^{18}F-fluorodeoxyglucose PET. Combining this examination with a low dose CT allows the correct anatomical mapping of the inflammatory process. In contrast, CT alone can only show morphological signs of infection, such as an abscess. For this reason, hybrid imaging is the first choice for detecting infections in patients with implants.[15,16] *Figure 6* gives an example of a LVAD driveline infection detected in an ^{18}F-fluorodeoxyglucose PET/CT. In our study, 54 subjects underwent PET/CT to detect suspected infection. If a higher uptake of ^{18}F-fluorodeoxyglucose surrounding the driveline has been seen in the PET/CT, the presence of a driveline infection was supposed to be more likely. This information was of great importance while the experts sorted subjects into the different groups of likeliness of infection. An advantage in using the results of ^{18}F-fluorodeoxyglucose PET/CT especially in the diagnosis of driveline infections can be assumed.[15,16] Another major difference to the standard definitions was that the local position of infection was not divided in deep or superficial, as the aim of the study was to detect risk factors for driveline infection in general.

As expected, staphylococci are the most common pathogens. These results are in accordance with prior studies.[9,10,17] Only in one patient that *Candida lusitaniae* was involved in driveline infection. The patient died shortly after diagnosis of the driveline infection. Other authors found a high mortality within patients with fungal LVAD driveline infections as

Figure 3 Cumulative hazard for developing a LVAD driveline infection dependent on length of time after implantation

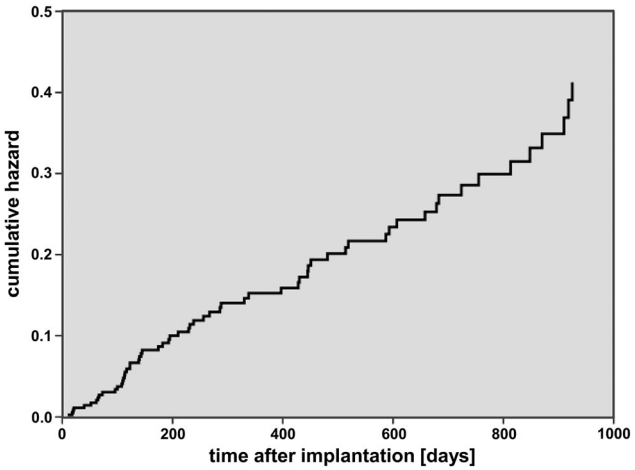
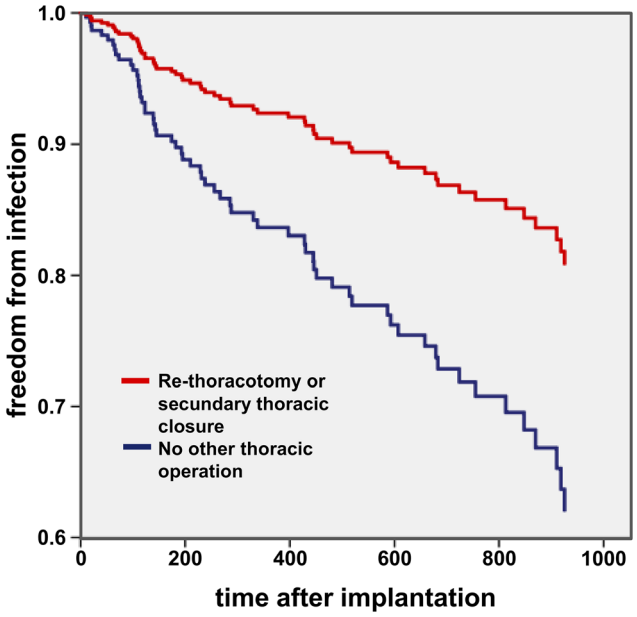


Table 2 Multivariable Cox proportional hazards model describing risk factors for driveline-infection in left ventricular assist device recipients (*n* = 390)

Variable	Hazard ratio	95% CI	*P*
Age (year)	0.99	0.97–1.01	0.21
LVAD type (Heartware)[a]	1.65	0.95–2.84	0.07
Re-thoracotomy necessary or secondary thoracic closure[a]	0.45	0.21–0.95	0.04
Creatinine level (mg/dl)	0.64	0.43–0.95	0.03

Note: Values as mean ± standard deviation.
Abbreviations: CI, confidence interval; LVAD, left ventricular assist device.
[a]Number of subjects, in parentheses (%, related to entire cohort).

Figure 4 Negative correlations between the necessity for another thoracic operation immediately or a few days after implantation and LVAD driveline infections during the time period (excluded major surgical complications or those who may have been lost)



well.[18] However, it should be recognized that there are doubts whether the pap smear, which in this study was mostly done to detect involved bacteria, is an appropriate diagnostic tool. It was mentioned by the microbiologist that, if available, the examination of some millilitre of purulent discharge or blood cultures would be more suitable in the diagnosis of driveline infections and detecting of involved bacteria.

Figure 5 Negative correlations between creatinine level >1.3 mg/dl and LVAD driveline infections during the time

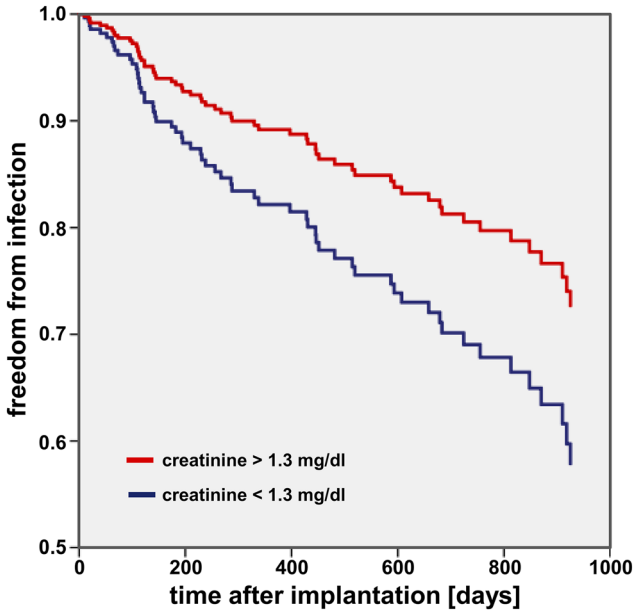
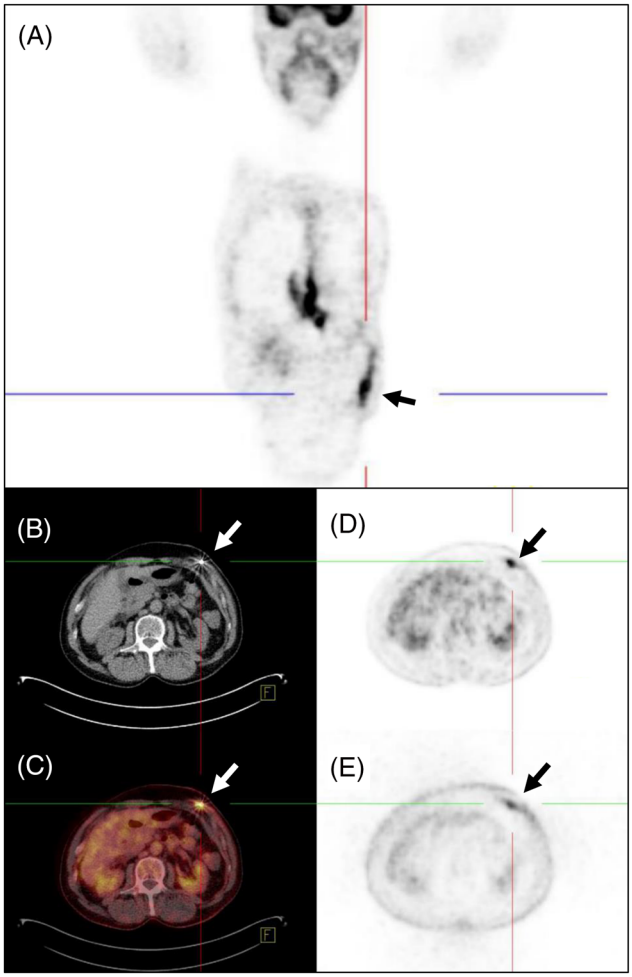


Figure 6 Exemplary images of a LVAD driveline infection (arrow) in a 59-year-old male patient detected by ^{18}F-fluorodeoxyglucose PET (A) coronal and (D, E) axial layering) and after image fusion with a low dose CT ((C) axial layering). A higher uptake of ^{18}F-fluorodeoxyglucose can be seen around the driveline in the abdominal wall. (B) low dose CT. (D) attenuation corrected ^{18}F-fluorodeoxyglucose PET. (E) non-attenuation corrected ^{18}F-fluorodeoxyglucose PET



In the present study, a higher pre-operative creatinine level is associated with a decreased rate of infection. This is in contrast to other studies in which a positive correlation was found,[8,9] possibly related to a compromised immune system.[19] A probable explanation for our findings could be a higher rate of dialysis in the LVAD driveline infection group. Although the patients in the LVAD driveline infection group might have a worse renal function, a lower creatinine level could be found due to dialysis recently performed before determining the laboratory values. Another reason could be a

confounding effect between cachexia and creatinine level. Cachectic patients in principle have a reduced creatinine level, because mass of muscle tissue is lower. We suppose that cachexia leads to impaired immune system and, therefore, a higher rate of LVAD driveline infections. As explained before, cachectic patients have a lower creatinine level, which might have led to a confounding effect. Defining cachexia with a body mass index below 18.49 kg/m^2, indeed more LVAD driveline infections were detected in this patient group compared with the group with patients having a body mass index >18.5 kg/m^2. Though cachexia on its own is not a statistically significant risk factor, the assumption that cachexia is a confounder could explain why a positive correlation between increasing creatinine and the appearance of LVAD driveline infection could not be observed in our study. It is to be recognized that maybe other laboratory values such as the glomerular filtration rate might have given a better statement to renal function than one pre-operative creatinine value. Unexpectedly, the performance of another thoracic operation such as a re-thoracotomy or a secondary thoracic closure is not associated with a higher infection rate. This supports the findings of Stulak and colleagues as well as Tambe and colleagues.[20,21] It can be suggested that these early post-operative events do not increase the risk for driveline infections, because these kinds of infections are mainly developing depending on the duration of support. Hypothetically, surgical standards during re-thoracotomy or secondary thoracic closure could lead to lower infection rates. For example, the extended disinfection of the surgical site. Also, removing little blood clots or hematomas in the chest cavity or surrounding the exit site which otherwise can represent a good growing medium for bacteria could decrease the probability of infection. Another explanation could be the longer lasting immobilization of patients undergoing re-thoracotomy or secondary thoracic closure. Longer bedrest could lead to a better healing and attachment of the driveline. In the study of Gordon and colleagues, a history of depression significantly increased the risk for developing a driveline infection[9]; thus, this variable was also examined in our study. All subjects had a psychiatric consultation evaluating patients' mental status. Although 36% suffered from depression or subdepressive mood, this issue did not represent a risk factor for driveline infection in our study. Therefore, former findings could not be supported. Other tested probable risk factors such as age, sex, body mass index, type of LVAD, ischaemic cardiomyopathy as underlying disease, length of hospitalization, and stay on intensive care unit before implantation showed no significant effects on developing a driveline infection which is in accordance to the findings of Zierer and colleagues.[10] Simon and colleagues discovered that presence of diabetes mellitus increased risk for blood stream infection in LVAD patients.[17] In our study, the presence of diabetes mellitus also seems to increase risk for driveline infections (hazard ratio 1.39) but was not significant (P = 0.24), which is in accordance with the findings of Gordon and colleagues.[9] Our study demonstrates that the duration of support increases the cumulative risk and represents the major risk factor for driveline infections.

The major aim of this study was to detect risk factors for driveline infections and to discuss possible effects on transplantation allocation policies. If identifiable, high-risk patients should be transplanted before developing a driveline infection. However, the duration of support is the only detectable risk factor. Therefore, the development of a driveline infection cannot be predicted at implantation time. Also, near term post-operative conditions such as necessity for re-thoracotomy or secondary thoracic closure are no risk factors and cannot help to predict driveline infections. Except for the duration of support the examined risk factors in the present study could not earlier identify high risk patients for driveline infection, which would justify an increased priority for heart transplantation. Nevertheless, the results of Simon and colleagues, who also report that the duration of support is a risk factor for driveline infection,[17] can be confirmed. According to Komoda and colleagues, it should be taken into account awarding bridge to transplant patients with high urgency status for heart transplantation after a certain period of time.[6]

Our study has some limitations. Bias or confounding cannot be excluded completely, because of the retrospective character of the study. A confounding effect between cachexia and creatinine level is possible as explained above. However, there are no other indications for bias or confounding effects. The difficulty to define a driveline infection for sorting patients into the corresponding cohort may be another weakness. Through using a prospective study design, the standardized definitions for driveline infections could have been applied in a better way. However, the large sample size may allow some generalization of our results. In order to clarify about the controversial potential risk factors pre-operative creatinine level and depression, a large prospective study would be needed. Including the glomerular filtration rate should be considered as an alternative option to assess renal function in future studies.

In conclusion, LVAD driveline infections were slightly less frequent in our patients than in prior studies. The microbiological findings are similar to results of other researchers.[9,10,17] The duration of support is the most important risk factor for driveline infections. Altogether, the development of a driveline infection is not predictable at implantation time. However, awarding bridge to transplant patients with high urgency status for heart transplantation after a certain period time should be considered. There were no other conclusive risk factors for driveline infection that could influence transplantation allocation policies found in this study.

DOI: 10.1002/ehf2.14112

Acknowledgements

We thank Ellen von Rössing for the assistance in data collection. We acknowledge support by the Open Access Publication Funds of the Ruhr-Universität Bochum.

Open Access funding enabled and organized by Projekt DEAL.

Conflict of interest

There are no conflicts of interest to declare.

References

1. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, Jaarsma T, Krum H, Rastogi V, Rohde LE, Samal UC, Shimokawa H, Budi Siswanto B, Sliwa K, Filippatos G. Heart failure: Preventing disease and death worldwide. *ESC Heart Fail*. 2014; **1**: 4–25.
2. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. *Nat Rev Cardiol*. 2011; **8**: 30–41. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3033496/pdf/nihms261324.pdf Accessed June 14, 2017.
3. Eurotransplant. Annual Report 2015. https://www.eurotransplant.org/cms/mediaobject.php?file=AR_ET_20153.pdf. Accessed June 14, 2017.
4. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, Miller MA, Baldwin JT, Young JB. Seventh INTERMACS annual report: 15,000 patients and counting. *The Journal of heart and lung transplantation: the official publication of the International Society for Heart Transplantation*. 2015; **34**: 1495–1504.
5. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med*. 2001; **345**: 1435–1443.
6. Komoda T, Drews T, Hetzer R, Lehmkuhl HB. New prioritization of heart transplant candidates on mechanical circulatory support in an era of severe donor shortage. *J. Heart Lung Transplant*. 2010; **29**: 989–996. 20570532 Accessed October 30, 2014.
7. Eurotransplant Statistical Report 2017. https://www.eurotransplant.org/cms/mediaobject.php?file=803150+020288+Statistical+Report+2017+(online)13.pdf. Accessed November 08, 2018.
8. Holman WL, Park SJ, Long JW, Weinberg A, Gupta L, Tierney AR, Adamson RM, Watson JD, Raines EP, Couper GS, Pagani FD, Burton NA, Miller LW, Naka Y. Infection in permanent circulatory support: Experience from the REMATCH trial. *J Heart Lung Transpl*. 2004; **23**: 1359–1365.
9. Gordon RJ, Weinberg AD, Pagani FD, Slaughter MS, Pappas PS, Naka Y, Goldstein DJ, Dembitsky WP, Giacalone JC, Ferrante J, Ascheim DD, Moskowitz AJ, Rose EA, Gelijns AC, Lowy FD. Prospective, multicenter study of ventricular assist device infections. *Circulation*. 2013; **127**: 691–702. 23315371 Accessed October 02, 2014.
10. Zierer A, Melby SJ, Voeller RK, Guthrie TJ, Ewald GA, Shelton K, Pasque MK, Moon MR, Damiano RJ, Moazami N. Late-onset driveline infections: The Achilles' heel of prolonged left ventricular assist device support. *Ann Thorac Surg*. 2007; **84**: 515–520. http://www.annalsthoracicsurgery.org/article/S0003-4975(07)00695-9/pdf Accessed November 09, 2014.
11. Schulman AR, Martens TP, Russo MJ, Christos PJ, Gordon RJ, Lowy FD, Oz MC, Naka Y. Effect of left ventricular assist device infection on post-transplant outcomes. *J Heart Lung Transplant*. 2009; **28**: 237–242.
12. Healy AH, Baird BC, Drakos SG, Stehlik J, Selzman CH. Impact of ventricular assist device complications on posttransplant survival: An analysis of the united network of organ sharing database. *Ann Thorac Surg*. 2013; **95**: 870–875. 23218024 Accessed October 30, 2014.
13. Gordon RJ, Quagliarello B, Lowy FD. Ventricular assist device-related infections. *Lancet Infect Dis*. 2006; **6**: 426–437.
14. Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, Schueler S, Holman WL, Lawler LP, Gordon SM, Mahon NG, Herre JM, Gould K, Montoya JG, Padera RF, Kormos RL, Conte JV, Mooney ML. Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. *J Heart Lung Transpl*. 2011; **30**: 375–384. 21419995 Accessed April 14, 2015.
15. Kanapinn P, Burchert W, Körperich H, Körfer J. 18F-FDG PET/CT-imaging of left ventricular assist device infection: A retrospective quantitative intrapatient analysis. *J Nucl Cardiol*. 2018.
16. Dell'Aquila AM, Mastrobuoni S, Alles S, Wenning C, Henryk W, Schneider SRB, Deschka H, Sindermann JR, Scherer M. Contributory role of fluorine 18-Fluorodeoxyglucose positron emission tomography/computed tomography in the diagnosis and clinical management of infections in patients supported with a continuous-flow left ventricular assist device. *Ann Thorac Surg*. 2016; **101**: 87–94 discussion 94.
17. Simon D, Fischer S, Grossman A, Downer C, Hota B, Heroux A, Trenholme G. Left ventricular assist device-related infection: Treatment and outcome. *Clin Infect Dis*. 2005; **40**: 1108–1115.
18. Aslam S, Hernandez M, Thornby J, Zeluff B, Darouiche RO. Risk factors and outcomes of fungal ventricular-assist device infections. *Clin Infect Dis*. 2010; **50**: 664–671.
19. Hauser AB, Stinghen AEM, Kato S, Bucharles S, Aita C, Yuzawa Y, Pecoits-Filho R. Characteristics and causes of immune dysfunction related to uremia and dialysis. *Perit Dial Int*. 2008; **28**: S183–S187.
20. Tambe SP, Kimose H-H, Raben Greisen J, Jakobsen C-J. Re-exploration due to bleeding is not associated with severe postoperative complications. *Interact Cardiovasc Thorac Surg*. 2017; **25**: 233–240.
21. Stulak JM, Romans T, Cowger J, Romano MA, Haft JW, Aaronson KD, Pagani FD. Delayed sternal closure does not increase late infection risk in patients undergoing left ventricular assist device implantation. *J Heart Lung Transplant*. 2012; **31**: 1115–1119.