



Driveline angle is crucial for preventing driveline infection in patients with HeartMate II device

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Abstract

We hypothesized that the externalizing direction of the driveline (the driveline angle) at the percutaneous exit site would influence the occurrence of driveline infection after left ventricular assist device implantation. From August 2013 to May 2017, 71 patients were implanted with a HeartMate II device in our center. The driveline angle was measured on anteroposterior radiography just after implantation. Risk factors for driveline infection were analyzed by uni- and multivariate analyses. Driveline infection developed in 10 (14%) patients during follow-up. Overall actual freedoms from driveline infection at 6, 12, and 24 months were 96%, 88%, and 86%, respectively. Overall number of driveline infection events per patient-year was 0.16. Receiver operating characteristic analysis determined the cut-off point of the driveline angle as 41°. The 6-, 12-, and 24-month actuarial freedoms from driveline infection in those with driveline angle more than 42° (84%, 74%, and 74%, respectively) were significantly lower than in those with driveline angle less than 41° (97%, 94%, and 90%, respectively; $p < 0.02$). The numbers of driveline infection events per patient-year were 0.16 in patients with driveline angle more than 42°, and 0.04 in patients with driveline angle less than 41°. Multivariate analysis demonstrated that driveline angle more than 42° was an independent risk factor for driveline infection (hazard ratio 4.71). Driveline angle more than 42° is an independent risk factor for driveline infection in patients with HeartMate II. Externalization of the driveline toward the horizontal direction is important to prevent driveline infection with HeartMate II.

Keywords Implantable LVAD · Driveline infection · Prevention · HeartMate II · Implant procedure

Introduction

Implantation of a left ventricular assist device (LVAD) is now a standard treatment for advanced heart failure in western countries. However, complications related to long-term LVAD support are one of the major hurdles that need to be

overcome to establish the LVAD as the destination therapy in many countries, including Japan. Major LVAD-related complications include cerebrovascular accident, hemolysis, right-sided heart failure, bleeding, device failure, and driveline infection [1–3]. Driveline infection is an unavoidable complication in the contemporary LVAD system in which the main power battery is located outside the body, and the reported prevalence of driveline infection is 0.07–0.58 events per patient-year [4, 5]. Local infection around the driveline exit site can extend to the main pump or the out-flow graft, finally developing into a fatal systemic infection.

Driveline infection of the HeartMate II device is reportedly substantially reduced when the entire driveline velour portion is left below the skin [6]. Another factor influencing the degree of driveline infection is the type of LVAD [7, 8]. Moreover, local infection around the driveline may be induced by passive movement of the driveline exit, which

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might impair firm attachment of the driveline surface to the subcutaneous tissue [9, 10]. These factors suggest that susceptibility to or extendability of driveline infection is determined by the nature of the driveline, condition of the immunologic barrier, and interaction between the driveline and the skin tissue. We hypothesized that the externalizing direction of the driveline at the percutaneous exit site would influence the prevalence of driveline infection after LVAD implantation. The present study aimed to explore the relationship between the driveline angle and driveline infection in patients with implantable LVAD.

Materials and methods

Study cohort and data collection

Data were collected from a prospective, institutional, surgical database that contained a consecutive series of 90 patients in whom a LVAD was implanted as a bridge-to-transplantation in the National Cerebral and Cardiovascular Center Hospital between August 2013 and May 2017. In this institute, HeartMate II (Abbott Laboratories, Chicago, IL, USA) had consistently been the primary choice of implantable LVAD and was implanted in 71 of the 90 patients (79%); these 71 patients comprised the cohort of the present study (Table 1). Data were collected from medical charts, operation reports, and referral letters, and were further supplemented by telephone interviews with those patients under the care of physicians outside of our institution. Data collection was performed in August 2017. The follow-up rate at July 2017 was 100%, and the mean follow-up period was 1.9 ± 1.1 years. Complications were defined according to the adverse event definitions of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) [11].

Ethical approval

All patients provided written informed consent for surgery, and for the use of their data for diagnostic and research purposes prior to the surgery. The institutional review board approved the present retrospective study and waived the need for patient consent.

Surgical indication and procedure

Indication for LVAD implantation was preoperatively determined by the institutional heart team comprising cardiologists, cardiac surgeons, transplant physicians, and associated co-medical staff, in accordance with current guidelines [12, 13]. As all of the patients in the present cohort were listed, transplant candidates, patients with malignancy or

Table 1 Patient characteristics

| | <i>n</i> = 71 |
|--|---------------|
| Male, no. (%) | 52 (73%) |
| Age, years | 45 ± 13 |
| Body surface area, m ² | 1.6 ± 0.2 |
| Body mass index, kg/m ² | 21.2 ± 4.3 |
| Thickness of abdominal fat (cm) | 1.7 ± 0.9 |
| Dilated cardiomyopathy, no. (%) | 42 (59%) |
| Dilated phase of hypertrophic cardiomyopathy, no (%) | 9 (13%) |
| Fulminant myocarditis | 5 (7%) |
| Ischemic etiology, no. (%) | 8 (11%) |
| Previous extracorporeal LVAD implantation, no. (%) | 11 (16%) |
| INTERMACS profile 2, no (%) | 28 (40%) |
| INTERMACS profile 3, no (%) | 42 (60%) |
| Total bilirubin (mg/dl) | 1.2 ± 1.0 |
| Creatinine (mg/dl) | 1.0 ± 0.3 |
| Albumin (g/dl) | 3.8 ± 0.5 |
| Cholinesterase (U/l) | 225 ± 73 |
| BNP (pg/ml) | 717 ± 655 |
| eGFR (ml/min/1.73 m ³) | 90 ± 105 |
| Support month | 20 ± 14 |

Data are presented as number (%) or mean ± standard deviation

BNP brain natriuretic peptide, *eGFR* estimated glomerular filtration rate, *INTERMACS* Interagency Registry for Mechanically Assisted Circulatory Support

psychiatric problems had already been excluded (Table 1). The surgical procedure of HeartMate II implantation was consistent throughout the study period, apart from the externalization point of the driveline. The driveline externalization point was determined by the heart team and was marked 1 day prior to the surgery. Until October 2015, the driveline was externalized at the right upper quadrant (*n* = 37), whereas the left upper quadrant was used from December 2015 onwards. The right-sided externalization of the drive was made via a single tunnel through the right upper rectus muscle, whereas the left-sided externalization was made using the double-tunnel technique in which the driveline penetrating the first tunnel through the right upper rectus muscle was turned horizontally into the left side through the subcutaneous tissue. The velour portion of the driveline was entirely buried under the skin in all cases.

Postoperative care

During postoperative recovery, driveline care education was given to all patients and their caregivers until they demonstrated satisfactory care skills. After discharge from the hospital, driveline care was performed by the patients themselves or their caregivers. The driveline was secured by an anchoring device such as a Foley Anchor (Centurion,

Mundelein, IL). Dressing materials were chosen in accordance with the condition of the exit site and the skin, with a dressing change performed every 2–3 days in accordance with the patients' conditions. All patients visited the institutional outpatient clinic fortnightly or monthly to be reviewed by physicians and co-medical staff, including a review of the exit site care.

Data for driveline infection were retrieved from the electrical medical chart, which included a photograph of the exit site. Driveline infection was identified based on a positive bacterial culture obtained from the skin and/or tissue surrounding the driveline, coupled with the need for antimicrobial therapy in patients with clinical evidence of infection, such as pain, fever, exudation, or leukocytosis, in accordance with the INTERMACS definition of percutaneous site infection. We made a diagnosis of driveline infection at the initiation of antimicrobial therapy or having a result of positive bacterial culture. Patients without positive bacterial culture or antimicrobial therapy, even with wet exit site and pain, were excluded from driveline infection. In addition, antimicrobial therapy, surgical debridement or driveline translocation was performed in cases with deep driveline infection in which the infection extended more than 3 cm from the exit site, as diagnosed by plain CT or Ga-67 scintigraphy. Driveline translocation is a procedure used to create a new exit site, in which the infected tissue is debrided by cutting the skin and subcutaneous tissue along with the driveline back to the intact portion of the driveline.

Measurement of the driveline angle

The driveline angle was defined as the angle between a tangential line at the driveline exit site and a horizontal line; this was measured on an anteroposterior radiography in the supine position 1 day after LVAD implantation (Fig. 1). Routine radiography showed that the driveline angle did not change throughout the study period in any patient.

Statistical analysis

Data are presented as the mean \pm standard deviation for continuous variables, and as percentages for categorical variables. Differences between groups were analyzed with the χ^2 test or the Student's *t* test, with $p < 0.05$ considered statistically significant. Uni- and stepwise multivariate analyses based on the Cox proportional hazard model were used to determine associations between pre- or intraoperative factors and driveline infection. The cut-off point for the driveline angle was determined by receiver operating characteristics (ROC) analysis. Freedom from driveline infection was evaluated via Kaplan–Meier actuarial analysis; comparisons between groups were made using the log-rank test. Statistical analyses were performed with EZR (Saitama Medical

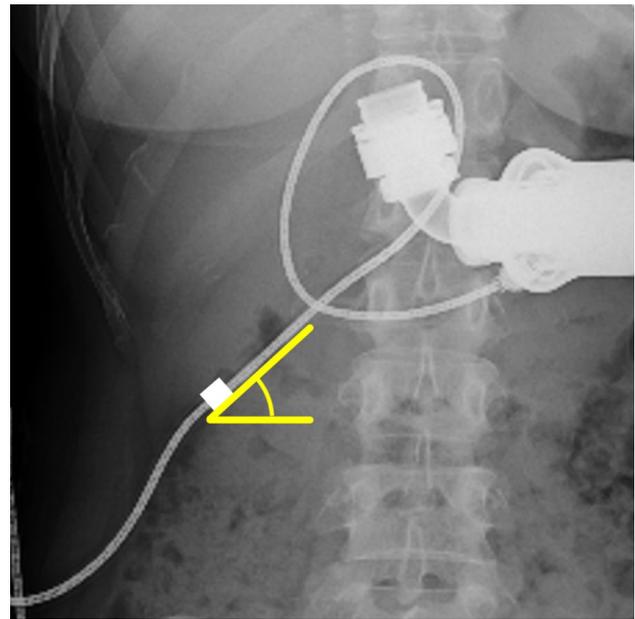


Fig. 1 Illustration of the driveline angle as the angle between a tangential line at the driveline exit site and a horizontal line, measured on anteroposterior radiography

Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing).

Results

Early results of HeartMate II implantation

A HeartMate II device was implanted in 71 patients as a bridge-to-transplantation between August 2013 and May 2017. There was one in-hospital death due to multiple organ failure attributed to severe right-sided heart failure. In-hospital major complications related to HeartMate II implantation included chest re-exploration for bleeding in 11 patients (15%), cerebrovascular accidents in 11 (15%), driveline infection in two (3%), major hemolysis in two (3%), right-sided heart failure in two (3%), and rapid progression of aortic insufficiency in one (1.4%).

Long-term results of HeartMate II implantation

Clinical follow-up was completed in all 71 patients who underwent HeartMate II implantation. Fifteen patients successfully underwent cardiac transplantation at 25 ± 8 months post-HeartMate II implantation, while 54 patients were awaiting cardiac transplantation at the end of July 2017. The remaining two patients died prior to transplantation, due to right-sided heart failure

or cerebrovascular accident at 41 days and at 3.1 years after HeartMate II implantation, respectively. By the end of follow-up, 53 patients (76%) had experienced major complications, such as driveline infection, major bleeding, cerebral vascular accident, major hemolysis, major device malfunction, right-sided heart failure, and/or aortic insufficiency.

Driveline infection: frequency and treatment

Overall, 10 (14%) patients developed driveline infection during follow-up. Bacterial culture of the exit site identified methicillin-sensitive *Staphylococcus aureus* in four patients, and methicillin-resistant *S. aureus* in five, despite preoperative decolonization by nasal mupirocin ointment. Of these ten patients, two developed the driveline infection in hospital, while the average interval between LVAD implantation and diagnosis of the first driveline infection in the remaining eight patients was 9.4 (1.0–26.8) months. Overall actual freedom from driveline infection was 96% at 6 months, 88% at 12 months, and 86% at 24 months (Fig. 2).

Of the 10 patients with driveline infection, five (50%) underwent surgical debridement for deep driveline infection in hospital after intensive systemic and local antibiotic treatments. Of these five patients, two underwent surgical translocation of the driveline; the infected exit site tissue was debrided, and then a longitudinal skin incision was made along the driveline until the intact portion of the driveline appeared, where a new exit site was created. As

a result, no patient required LVAD exchange for pump pocket infection extending from driveline infection.

Risk factors associated with driveline infection

The results of the uni- and multivariate analyses of risk factors associated with driveline infection are summarized in Table 2. Driveline angle was identified as an independent risk factor for driveline infection (hazard ratio 1.03, $p=0.03$). The side that the exit site was located on (covariate or double-tunnel technique) and the period during which the operation was performed (early: April 2014–September 2015, or late: October 2015–March 2017) were not independent risk factors for driveline infection. The ROC analysis determined the cut-off point of the driveline angle as 41° (Fig. 3a). The respective 6-, 12-, and 24-month actuarial freedoms from driveline infection in the patients with a driveline angle more than 42° (84%, 74%, and 74%, respectively) were significantly lower than those of the patients with a driveline angle $<42^\circ$ (97%, 94%, and 90%, respectively; $p<0.016$) (Fig. 3b). The numbers of driveline infection events per patient-year were 0.16 in patients with a driveline angle more than 42° , and 0.04 in patients with a driveline angle less than 41° . Further uni- and multivariate analyses based on the Cox proportional hazard model demonstrated that driveline angle more than 42° as a categorical value was an independent risk factor for driveline infection (hazard ratio 4.71).

Discussion

We reviewed a consecutive series of 71 patients who had undergone HeartMate II implantation as a bridge-to-transplantation in a single institution since 2013, which was when this device was approved for marketing in Japan. Major adverse events post-HeartMate II implantation included major bleeding in 43 patients, cerebrovascular accidents in 15, device malfunction in seven, device-related major hemolysis in five, right-sided heart failure in six, and driveline infection in ten. Of the ten patients with driveline infection, five underwent surgical debridement of the infected exit site. Driveline angle was the sole independent risk factor for driveline infection in the present series, and the cut-off value of the driveline angle was 41° .

Although HeartMate II was implanted only as a bridge-to-transplantation in Japan, the very long waiting time in Japan for transplantation time dependently worsens patient quality of life during HeartMate II support due to a variety of complications represented by driveline infection. A previous study evaluating the INTERMACS registry reported that the prevalence of driveline infection was 19% at 12 months after LVAD implantation [8]. The present results (12%

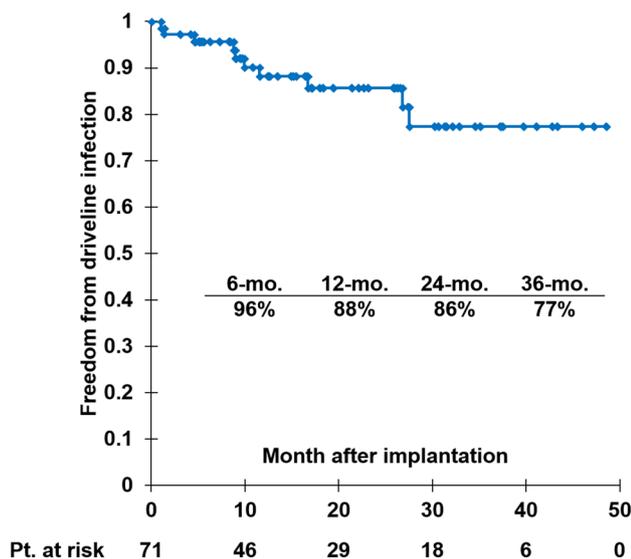


Fig. 2 Overall actual rates of freedom from driveline infection at 6, 12, and 24 months were 96%, 88%, and 86%, respectively

Table 2 Uni- and multivariate Cox proportional hazard analyses of variables associated with driveline infection

| Covariate | Univariate | | | Multivariate | | |
|------------------------------------|--------------|-----------|----------------|--------------|-----------|----------------|
| | Hazard ratio | 95% CI | <i>p</i> value | Hazard ratio | 95% CI | <i>p</i> value |
| Age (years) | 0.98 | 0.93–1.03 | 0.35 | | | |
| Sex male | None value | 0–Inf | 0.99 | | | |
| INTERMACS profile | 2.08 | 0.45–9.53 | 0.35 | | | |
| BMI (kg/m ²) | 1.01 | 0.88–1.17 | 0.89 | | | |
| BSA (m ²) | 9.56 | 0.34–270 | 0.19 | | | |
| Albumin (g/dl) | 1.09 | 0.29–4.19 | 0.9 | | | |
| Abdominal fat (cm) | 1.13 | 0.56–2.31 | 0.73 | | | |
| Cholinesterase (U/l) | 0.99 | 0.99–1.01 | 0.36 | | | |
| Creatinine (mg/dl) | 1.91 | 0.32–11.4 | 0.48 | | | |
| eGFR (ml/min/1.73 m ³) | 0.99 | 0.98–1.01 | 0.61 | | | |
| Total bilirubin (mg/dl) | 1.33 | 0.71–2.48 | 0.37 | | | |
| BNP (pg/ml) | 0.99 | 0.99–1.00 | 0.33 | | | |
| Double-tunnel technique | 0.24 | 0.03–1.98 | 0.18 | | | |
| Late period (2015/10–2017/3) | 0.2 | 0.02–1.68 | 0.14 | | | |
| Right side exit site | 4.2 | 0.51–35 | 0.18 | | | |
| Driveline angle (°) | 1.03 | 1.00–1.06 | 0.03 | 1.03 | 1.00–1.06 | 0.04 |
| Re-exploration for bleeding | 3.2 | 0.9–11.4 | 0.07 | 2.77 | 0.78–9.85 | 0.12 |

Data are presented as number (%) or mean ± standard deviation

BNP brain natriuretic peptide, BMI body mass index, BSA body surface area, eGFR estimated glomerular filtration rate, INTERMACS Interagency Registry for Mechanically Assisted Circulatory Support

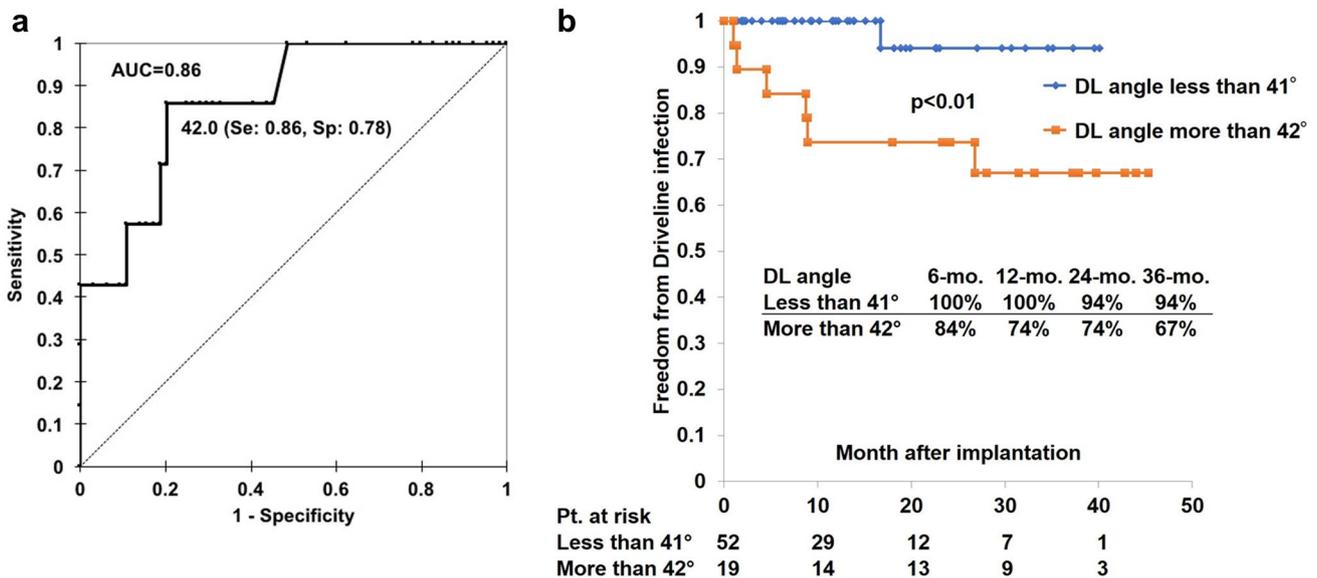


Fig. 3 a Receiver operating characteristics analysis determined that the cut-off point of the driveline angle was 41°. The area under the curve was 0.86 (sensitivity 0.86, specificity 0.78). b The respective 6-, 12-, and 24-month actuarial rates of freedom from driveline

infection in the patients with a driveline angle more than 42° (84%, 74%, and 74%, respectively) were significantly lower than those of the patients with a driveline angle less than 41° (97%, 94%, and 90%, respectively; *p* = 0.016)

prevalence of driveline infection at 12 months) were consistent with this previous report [8], despite the differences in characteristics or postoperative care of the cohorts, suggesting that the surgical and medical treatment protocols of the

contemporary LVAD have nearly been standardized. However, our contemporary method of driveline externalization, in which the driveline exits horizontally at an angle of less than 42°, led to a driveline infection prevalence of only 6% at

12 months. Moreover, our method led to a driveline infection prevalence of 10% at 24 months, which is substantially better than the previously reported driveline infection prevalence after LVAD implantation [8]. This noticeable improvement in the prevalence of driveline infection may be explained by the theory that the attachment of the driveline at the exit site is the major determinant of driveline infection [6, 9]. We consider that horizontal externalization towards the left using the double-tunnel technique would be the most consistent method with which to achieve immobilization of the driveline at the exit site, which is a prerequisite to wound healing along the subcutaneous route [9].

We consider that the most substantial factor affecting the driveline angle at the driveline exit site is the stability of the local site. A wider driveline angle (a driveline angled in a vertical and caudal direction) tends to enable the driveline to move in and out of the exit site, or to be interfered with by the lower part of the body or waist during somatic movements (such as sitting up, bending down, crouching, sitting on a chair or bed, and taking off and putting on trousers), which are common actions performed during daily activity; in contrast, a smaller driveline angle (a driveline externalized in a horizontal direction) can remain relatively immobile during the abovementioned body motions. Furthermore, the point at which the side of the body contacts the surface of the driveline at the exit site can be difficult to see with a vertically directed driveline; subsequently, this area may not be completely cleaned during daily care, whereas with a horizontally directed driveline, this area is visible to the patient, and can be more easily cleaned. Therefore, the smaller driveline angle (horizontally directed driveline) would lead to stability of the driveline exit site and facilitation of adequate topical care, resulting in a lower incidence of driveline exit site infection, even in our relatively young population.

We also tried to figure out other factors potentially related to driveline infection, such as wound care method, frequency of dressing change, frequency of medical consultation, outpatient clinic visits and body weight gain. We consistently managed wound in dry condition, utilizing moisture-permeable film dressing in all patients in this study. In case of wet wound condition with or without evidence of driveline infection, patients were advised to increase frequency in dressing change. We encouraged frequent dressing change in warm and sweaty season to keep wound dry. In cases with unfavorable wound condition, regardless of reasons, frequency of outpatient clinic increased. Therefore, we could not conclude relationship between driveline infection and exit site care method, frequency of dressing change or outpatient clinic visit. Among ten patients with driveline infection, only one patient developed driveline infection subsequently to body weight gain. Although patients with increased body weight

and abdominal fat tend to develop instable or wet exit site, fortunately little patients in our cohort developed to positive bacterial culture.

It should be noted that the use of the double-tunnel technique with a left-side exit site did not significantly influence driveline infection in the present study. However, we still consider that the current double-tunnel technique with a left-side exit site is the most effective method to prevent driveline infection for two reasons. First, Japanese patients generally have a relatively small body size, which makes it difficult to achieve a driveline angle of less than 42° when using a right-side exit site. Second, compared with a right-side exit site, a left-side exit site would be easier to access and care for in right-handed patients, which comprise the great majority in the Japanese population. Additionally, a longer subcutaneous attachment in the left-side exit site may contribute to better stability of the exit site. However, according to multiple analyses including the side of exit site, the left-side exit site was excluded by stepwise multivariate Cox proportional hazard analysis. We did not measure the length of the buried portion of driveline. Therefore, independent impact of the length of the buried portion of the driveline should be investigated in further large-size study.

Our population had a lower incidence of driveline infection compared with that reported in the INTERMACS registry. Apart from the driveline angle, the good long-term outcome in the present series may have been influenced by our excellent care protocol, including patient education for self-care of the exit site, management of anticoagulant therapy using CoaguCheckR (Roche Diagnostics International, Basel, Schweiz), handling of the device, and how to deal with device alarms. Our good results might also have been influenced by our use of antibiotic prophylaxis for methicillin-resistant *S. aureus*, Gram-negative bacteria, and fungi [14].

The present study was limited by its retrospective nature in a single institute, with a small cohort of patients only implanted with HeartMate II devices. Furthermore, the reproducibility of the influence of the driveline angle on the disruption of tissue ingrowth at the exit site was not proven histologically. Further investigation to verify the mechanism is warranted. We could not figure out the impact of frequency of dressing change, medical consultation and side of exit site. Sole influence of such factors should be investigated. Moreover, the present findings should be confirmed with other implantable LVADs.

In conclusion, driveline angle more than 42° was an independent risk factor for driveline infection in patients with HeartMate II. Externalization of the driveline toward the horizontal direction is important to prevent driveline infection of HeartMate II devices. The concept of driveline stability with adequate externalization at the exit site is very important for long-term durable driveline care.

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Compliance with ethical standards

Conflict of interest Authors declare that they have no conflict of interest.

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