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REVIEW

Artificial Heart (Clinical)

Patient management important for long-term support beyond 5 years in the BTT: republication of the article published in the *Japanese Journal of Artificial Organs*

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Abstract
Heart transplantation is considered to be the best treatment for severe heart failure refractory to medical therapy, improving patients' survival and quality of life (QOL). However, the number of donors is smaller than the number of registered applicants for heart transplantation, which increases every year, and the waiting period for heart transplantation has been extended to more than 1700 days by 2022. Since 2011, reimbursement for the implantable left ventricular assist device (iLVAD) was established. The numbers of the iLVAD patients have been increasing year by year. Patients are managed at home with an iLVAD and can live with their families and even return to work, depending on the situation. On the other hand, self-management at home, including caregivers, is important for a safe life. Home management beyond 5 years is becoming more common due to long waiting time for transplant. This article outlines the important aspects of patient management for long-term support. This review was created based on a translation of the Japanese review written in the *Japanese Journal of Artificial Organs* in 2023 (Vol. 52, No. 1, pp. 62–66), with some modifications.

Keywords Home management · Implantable LVAD · Quality of life

Introduction

Heart transplantation is considered to be the best treatment for severe heart failure refractory to medical therapy, improving patients' survival and quality of life (QOL). More than 20 years have passed since the Organ Transplant Law was enacted in 1997 and heart transplantation began. After the revision of the Organ Transplant Law in 2010, the number of organ donations has gradually and steadily increased. However, the number of donors is smaller than the number of registered applicants for heart transplantation, which increases every year, and the waiting period for heart transplantation has been extended to more than 1700 days by 2022 [1]. In 2011, reimbursement for the implantable left ventricular assist device (iLVAD) was introduced. Patients on the transplant waiting list are now waiting for a transplant at home, whereas previously they had to wait in the hospital with an external ventricular assist device and wait years for a transplant. Patients are managed at home with an iLVAD and can live with their families and even return to work, depending on the situation. On the other hand, self-management at home, including caregivers, is important for a safe life.

With the extension of the waiting time for heart transplantation [1], home management beyond 5 years is becoming more common. This article outlines the important aspects of patient management for long-term support.

Complications of iLVAD home management

Potential complications during home implantable left ventricular assist device (iLVAD) therapy include device failure, serious infection (bacteremia, sepsis, mediastinitis, driveline infection, pocket infection), neurological dysfunction (cerebral infarction, cerebral hemorrhage), bleeding, right

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heart failure, arrhythmia, hemolysis, gastrointestinal complications, and more.

From the latest J-MACS (Japanese registry for Mechanically Assisted Circulatory Support) Statistical Report (published May 6, 2022) [2], we will focus on complications that become problematic after 5 years (1825 days).

(1) Survival rate

Through the efforts of each institution, 1-, 2-, and 3-year iLVAD survival rates in Japan are significantly higher than in other countries [3, 4].

The 5-year survival rate analyzed from the survival rate curve is significantly higher than that of other countries, about 77%. The 5-year survival rate is not a large decrease compared with the 4-year survival rate (about 80%), but it is about 9% lower than the 3-year survival rate (about 86%), and it is likely that some factor affects survival.

(2) Device failure

Pump failure is one of the most common adverse events. Device failure is defined by J-MACS as "a failure of one or more components of the mechanical circulatory support system that directly causes or threatens to cause inadequate circulatory support (low cardiac output) or death." Driveline disconnection is one of the most common causes of pump failure in the mid-remote stage and has been reported overseas to occur in approximately 3% of cases after HeartmateII (HMII) (Abbott) implantation and to be the cause of 46% of pump replacements [5]. In our hospital, it occurred in 19% (10/54) of cases after HMII implantation, and all cases required pump replacement.

The incidence of driveline disconnection in Japan is higher than that in other countries, approximately 20% to 30%, and the incidence in our hospital is similar. We investigated the causes of driveline disconnection in our hospital. We speculated that the cause might be excessive weight gain, stress on the driveline due to excessive exercise, or a problem with the triple line driveline penetration method used in our hospital (pulling the subfascial line from the left side to the right side and then back to the left side), but we could not identify the cause because there was no consistency in the area where the driveline was disconnected.

Since the introduction of the HeartMate 3 (HM3, Abbott), a magnetically levitated centrifugal pump, the driveline has been improved and the incidence of driveline disconnection has decreased, resulting in fewer device failures and pump replacements3). Our hospital has not experienced any driveline disconnects or device failures with the HM3. According to the J-MACS Statistical Report (2022) [2], the incidence of device failures due to causes other than thrombus was approximately 40% over a 5-year period, which is higher than the incidence of failures due to intra-device thrombus, which is approximately 10%. Because driveline disconnection is an unpredictable factor in device failure, it is important to know how to respond after it occurs. Our policy is to switch to battery power as soon as a driveline disconnect is suspected on the HMII and to perform a semi-emergency pump replacement within 1 to 2 weeks. Driveline fractures can occur even after 5 years of HMII, so patients with HMII should be closely monitored.

(3) Infection

Depending on the patient's preoperative severe heart failure status, iLVAD patients are often complicated by hepatic dysfunction, renal dysfunction, poor nutritional status, and severe edema, and are therefore at higher risk for postoperative infection complications than patients undergoing conventional open-heart surgery. In the acute postoperative period, the risk of catheter-related bloodstream infection is also high, and the incidence of sepsis up to 30 days after surgery is approximately 10%. Catheter-related skin infections occur in approximately 10–30% of cases [6]. According to the J-MACS Statistical Report (2022) [2], the driveline infection-free rate is 94% within 90 days (6% incidence), 87% within 180 days (13% incidence), 78% within 1 year (22% incidence), 68% within 2 years (32% incidence), 61% within 3 years (39% incidence), and approximately 57% within 5 years (43% incidence), a significant complication that is increasing every year. For pump pocket and pump infections, the incidence is 99% (1%) within 90 days, 99% (1%) within 180 days, 98% (2%) at 1 year, 98% (2%) at 2 years, 96% (4%) at 3 years, and approximately 94% (6%) at 5 years. Driveline infections are approximately 7 times more common than pump pocket and internal pump infections over a 5-year period, making them an important factor in long-term home management.

Prevention of driveline infections

After receiving certification as an implantable ventricular assist device (iLVAD) implantation center in 2013, our hospital has performed iLVAD treatment in 97 cases (54 HMII, 42 HM3, and 1 HVAD), including replacements. Initially, the HMII was mainly used, and the driveline was made by creating a loop in the pocket from the pocket on the left perineum under the heart, adjusting the length, and then penetrating directly to the outer edge of the right rectus abdominis muscle (Fig. 1A-a) [7]. This method was adopted because it is a technique I learned

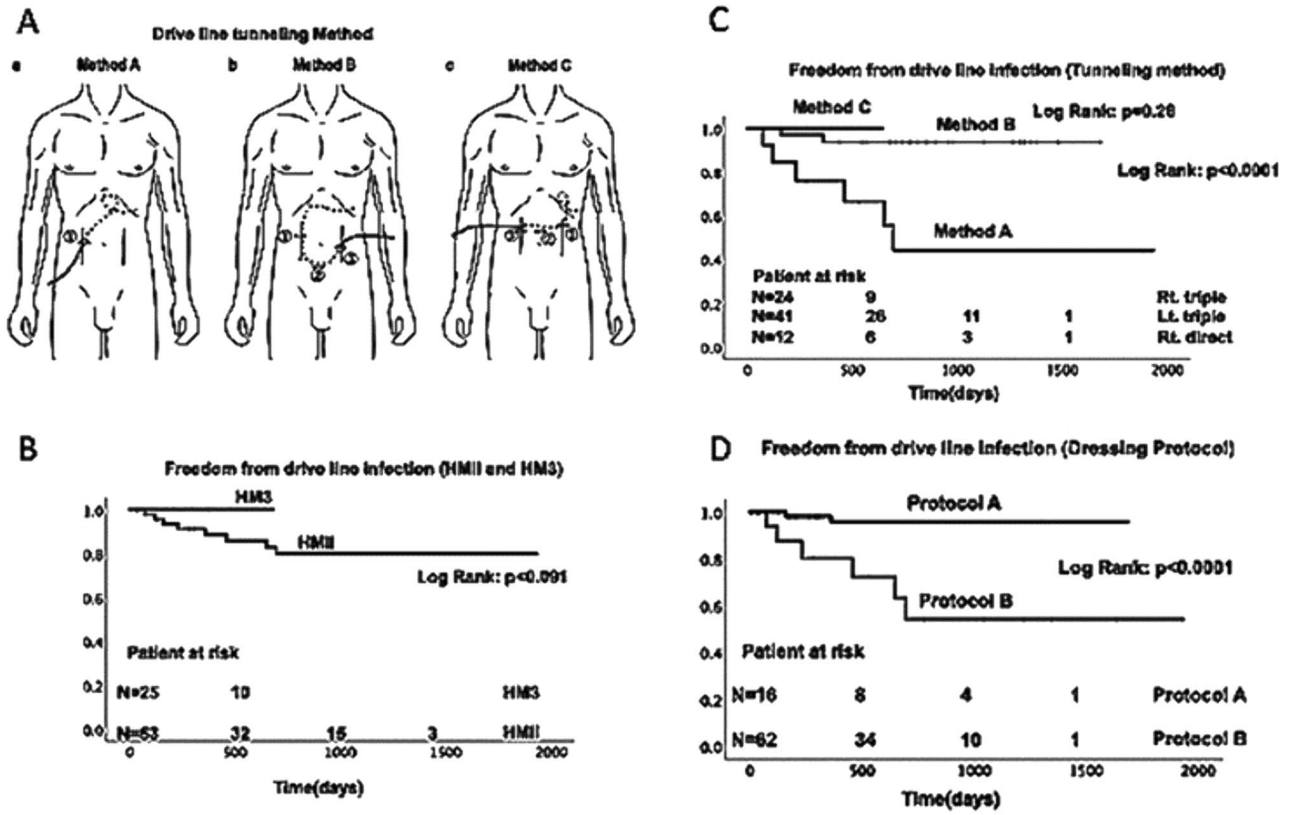

Fig. 1 Driveline penetration method (**A**), comparison of driveline infection between HMII and HM3 (**B**), comparison of infection by the driveline penetration method (**C**), and comparison of shower protocols (**D**)

at the Department of Cardiac Surgery at the University of Alberta, Canada, and because it is a common method in other countries. However, it was found that this technique has the disadvantage that once infection occurs, the infected area becomes closer to the artificial heart as attempts are made to control the infection with debridement, despite the presence of the rectus abdominis muscle. In fact, we had one patient whose VAD was about 5 cm away from becoming infected, and we were afraid every time we disinfected his driveline. This patient was able to get a heart transplant with no recurrence of infection. The driveline infection rate with this procedure was as high as 46% (6/13 patients).

Next, we modified the method of driveline penetration to pass from the pocket to the right side of the rectus abdominis fascia, under the fascia in the middle below the umbilicus, and out to the outer edge of the rectus abdominis muscle on the left side (Fig. 1A-b). We chose this method because we believed that repeated debridement would prevent pocket infection even if infection occurred due to the long distance through the subfascia.

Because the drive line was close to the body, it was easy to fix, and there was no drive line twitching during mobilization, which significantly reduced the infection rate. The driveline infection rate with this technique was 5% (2/42 patients).

After the change to HM3, the driveline became slightly shorter, requiring a change in the method of subcutaneous driveline implantation. We used a method in which the driveline was routed from the pocket to the right side of the rectus abdominis muscle, from the left side through the subperitoneal fascia in the middle above the umbilicus, and out to the outer edge of the rectus abdominis muscle (Fig. 1A-c). There were no infected cases for two consecutive years [0% (0 cases/25 cases), Fig. 1B]. We consider this change in the method of penetration of the driveline to be one of the methods that significantly reduced the infection rate (Fig. 1C).

Another change was the use of showers for iLVAD patients. When the facility first opened, showering directly into the driveline was prohibited. However, showering protocols from academic societies and the International Society for Heart and Lung Transplantation either assumed that showering would not cause contamination from tap water, or there was no clear protocol [6, 8]. Based on our experience with showering directly on the wound in patients with wound infections, we attempted to clean the driveline by applying the shower directly to the driveline in some patients. However, we experienced three cases of Pseudomonas

aeruginosa infection of the driveline. These three patients did not improve after several months of driveline debridement and translocation procedures and had to have their pumps replaced, but since then there has been no recurrence of infection, two have received heart transplantation and one is on the transplant waiting list. Of the three cases, two were infected during hospitalization; Pseudomonas aeruginosa was detected in showerheads in the patients' rooms and was suspected to be the cause. After that, the method was changed to the fully protected method. The driveline infection rate was significantly reduced to 38% (6/17) before the fully protected method (protocol A) and 3% (2/62) after the fully protected method (protocol B) (Fig. 1D).

Other institutions are attempting to reduce driveline infections by various methods (e.g., placing the fibrous portion of the driveline in the subcutaneous tunnel [9] and using silver-ion-containing wound dressings with antimicrobial activity to prevent infection [10]), but since infection control is a personal management issue for each patient, the key factor is how quickly the patient can get to the hospital to prevent the infection from worsening. If the infection is treated early, it is likely that many cases will resolve with antimicrobial administration and drainage alone.

(1) Neurological dysfunction

Among the neurological dysfunctions that may occur during home management of iLVAD, cerebral complications including infarction and hemorrhage are important, and the frequency of cerebral infarction has been reported to be bimodal, with a high incidence in the acute phase, followed by a decrease and then an increase in the remote phase [11]. However, according to the J-MACS Statistical Report (2022) [2], the non-incidence rate of stroke among neurological dysfunction is 89% (11% incidence) within 90 days, 84% (16% incidence) within 180 days, 78% (22% incidence) at 1 year, 72% (28% incidence) at 2 years, 69% (31% incidence) at 3 years, and about 65% (35% incidence) at 5 years, implying a smaller increase in the remote period. Practically speaking, in long-term management, if a patient is registered for heart transplantation at the age of 64 years, regardless of the underlying disease, after 5 years he or she will be 69 years old and then enter his or her 70 s, so the risk of atherosclerotic stroke and cerebral hemorrhage is likely to be increased as in patients not on the transplant waiting list. In our hospital, the incidence of atherosclerotic cerebral infarction in iLVAD patients aged 60 years or older was 6% (1/16 patients). Treatment includes endovascular thrombolysis and endovascular therapy, both of which carry a risk of bleeding and require caution [12, 13].

(2) Massive bleeding

The most important massive bleeding event is gastrointestinal bleeding.

According to the J-MACS Statistical Report (2022) [2], the non-incidence rate of gastrointestinal bleeding among massive bleeding is 97% (3% incidence) within 90 days, 96% (4% incidence) within 180 days, 95% (5% incidence) at 1 year, 93% (7% incidence) at 2 years, 91% (9% incidence) at 3 years, and about 87% (13% incidence) at 5 years, suggesting that the increase in remote periods is not so great. The incidence in Japan is thought to be low, as foreign reports have shown up to 40% [14–16] of such cases. The mechanisms of gastrointestinal bleeding include anticoagulation therapy, acquired von Willebrand syndrome associated with changes in von Willebrand factor, and platelet suppression, and it is said that the effect of von Willebrand factor differs among devices, and reports are awaited.

(3) Right ventricular failure

According to the J-MACS Statistical Report (2022) [2], the incidence of right ventricular failure was 95% (5% incidence rate) within 90 days, 94% (6% incidence rate) within 180 days, 93% (7% incidence rate) at 1 year, 91% (9% incidence rate) at 2 years, 88% (12% incidence rate) at 3 years, and approximately 83% (17% incidence rate), suggesting that the increase in the remote period is not so great. Right ventricular failure that does not occur in the early postoperative period but develops in the remote period is called late-onset right ventricular failure (RVF). The cause of RVF is thought to be the deformation of the septum and the change in the morphology of the right ventricle as a result of left ventricular aspiration by the LVAD.

In our hospital, the rigid ring has been used for the past 7–8 years. Tricuspid valve ring suture is incorporated into the basic technique, and there is little change in right heart morphology in the remote postoperative period, and the incidence of right ventricular failure is low. Overt right ventricular failure developed in 2% of cases (2/99), and all patients reached heart transplantation. All cases were treated within the first 5 years of the institution's establishment. One patient had not undergone tricuspid valve annuloplasty. The other had undergone tricuspid valve annuloplasty. The patient also had worsening right ventricular failure due to worsening aortic insufficiency. The small ring was selected, and there were left ventricular morphological changes due to worsening aortic insufficiency, and tricuspid regurgitation was exacerbated by apex retraction

and pacing leads, and right ventricular heart failure was also exacerbated.

(4) Aortic insufficiency

If moderate or severe aortic insufficiency is present before LVAD surgery, aortic valve replacement, aortic valve surgery such as Park's Stitch, or Aortic Valve Closure should be performed. There are de novo cases in which aortic insufficiency is newly exacerbated in the mid-remote period, even in cases in which aortic insufficiency is not present preoperatively. In such cases, it is possible to temporarily increase cardiac output by increasing the rotation rate, but in many cases the aortic insufficiency worsens in the long-term. J-MACS Statistical Report (2022) [2] data do not include aortic insufficiency, so we present data from our institution. The avoidance rate for moderate or worse aortic insufficiency was 98% at 1 year (incidence 2%), 89% at 2 years (incidence 11%), 78% at 3 years (incidence 22%), and 67% at 5 years (incidence 33%), with remote stage deterioration. Avoidance of aortic valve surgery is 100% at 1 year (0% incidence), 100% at 2 years (0% incidence), 91% at 3 years (9% incidence), and 91% at 5 years (9% incidence), which does not mean that more patients will undergo surgery. Some patients with moderate or severe aortic insufficiency have an open aortic valve. In these cases, BNP levels are often low. It has been reported that aortic insufficiency is less likely to occur in patients whose aortic valve is closed at rest but open during exercise [17, 18]. Risk factors for de novo aortic insufficiency include females, large body surface area, age > 60 years, and preoperative mild aortic insufficiency [19, 20]. If an increase in the proportion of aortic valve interventions is observed in certain patients over a 10-year period, the strategy of treating moderate or severe aortic insufficiency as an indication for surgery may need to be changed. However, the strategy may need to be modified.

Conclusion

We have outlined the important aspects of patient management for long-term home care for more than 5 years. Driveline disconnection, driveline infection, and de novo aortic insufficiency in HMII increase with time, and the management team must be cautious in long-term management. Of these, driveline infection can be improved by reviewing insertion methods and protocols, and de novo aortic insufficiency can be addressed if the cardiac team performs periodic echocardiography and right heart catheterization to confirm hemodynamic changes.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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