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Review:

Development and current clinical application of ventricular assist devices in China*

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Abstract: Heart failure has become one of the biggest threats to human health. Transplantation remains the most effective therapy for heart failure, but because of the shortage of donors, it cannot meet the demand. Ventricular assist devices (VADs) were developed to treat heart failure, and have now been clinically applied worldwide. As the country with the largest population, China is also facing the threat of heart failure. However, the development of VADs in China is very slow and is seldom discussed. This paper first talks about the background for VAD development in China. Then several home-developed VADs in China are introduced. The current clinical application status of VADs in China is also presented. Finally the challenge and opportunity for VAD development in China are discussed.

Key words: Ventricular assist devices; Heart failure; Clinical application
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1 Introduction

Heart failure (HF) has become one of the biggest threats to human health with a prevalence of over 23 million worldwide (Bui *et al*., 2011). Medical and electrical therapies have improved outcome. However, HF commonly progresses and becomes refractory to these treatments. Cardiac transplantation remains the most effective therapy for HF, but due to the severe shortage of donors (3000 per year worldwide), it is far from satisfying all HF patients (Kumar and Phanwilkar, 2011). Numerous mechanical circulatory support (MCS) devices have been developed aimed at treating and rehabilitating patients, and among them ventricular assist devices (VADs) have seen the most rapid increase in recent years. Since the 1960s, VADs have developed from the first generation of pneumatic driven design, the second generation of axial rotary pumps, to the third generation of either hydrodynamically or magnetically suspended centrifugal blood pumps. In the USA annual VAD implants have increased from 100 in 2006 to over 2500 in 2014 (Kirklin *et al*., 2015).

As the country with the largest population, China is also facing the problem of HF. it is estimated that 4.5 million people were suffering from HF in China by 2014, and the number is still rising (Chen *et al*., 2015). However, the development of VADs in China is very slow and seldom discussed. This paper first talks about the background for VAD development in China. Then it introduces several home-developed VADs in China. The current clinical application status of VADs in China is also presented. Finally, the challenge and opportunity for VAD development in China are discussed.

2 Background

VADs have already been applied clinically worldwide. According to the Interagency Registry for

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Mechanically Assisted Circulatory Support (INTERMACS), between June 23, 2006 and December 31, 2014, 15745 patients received US Food and Drug Administration (FDA)-approved MCS devices. The annual increase of enrolled patients exceeded 2000 in the last 3 years. Ten FDA-approved adult durable devices have been registered in the INTERMACS database including 8 intracorporeal VADs, 1 extracorporeal VAD, and 1 total artificial heart (TAH) (Kirklin *et al*., 2015).

The European Registry for Patients with Mechanical Circulatory Support (EUROMACS), which collects clinical data from 21 institutes in 12 European countries, reported 741 VAD implants from January 1, 2011 to December 31, 2013. Fourteen European conformity (CE)-marked MCS systems are registered in the database, including 7 continuous flow (CF) long-term devices, 2 pulsatile extracorporeal long-term devices, 1 TAH, and 4 short-term devices (de By *et al*., 2015).

Due to device lag, implantable VADs have not been approved until very recently in Japan. Right now, Terumo DuraHeart and SunMedical EVA HEART have been approved for use in Japan after clinical trials have been completed (Sawa, 2014). By March 12, 2014, according to a report from the Japanese Registry for Mechanically Assisted Circulatory Support (J-MACS), among the registered 287 patients with VADs from 26 institutions, implantable VADs were used in 216 patients (Nishimura, 2014).

According to the 2014 Report on Cardiovascular Diseases in China, there are about 290 million patients in China suffering cardiovascular disease (CVD), which accounts for the primary cause for 44.8% and 41.9% of deaths in rural and urban areas, respectively. Among them 4.5 million patients suffer from HF, with a 0.3 million increase every year. While the HF patients account for only 20% of all hospitalized CVD patients, HF caused 40% of all deaths. Retrospective research from Beijing General Hospital of PLA shows that during the past 15 years the mortality of hospitalized chronic HF patients in 30 d could reach 5.4% (Chen *et al*., 2015).

Although heart transplantation is the most effective way to treat drug-resistant cardiac failure, the limitation of heart donors and medical resources makes it far from a sufficient treatment. From 1995 to 2015, in total 1935 patients received a heart transplant in mainland China, as shown in Fig. 1. Although the number is rising, from 177 in 2012, 232 in 2013, to 358 in 2014 (Hu *et al*., 2014b; Zhu *et al*., 2015), it is still far from the huge number of HF patients. It should also be noted that the number even fell to 319 in 2015, which was 10.9% fewer than that in 2014 (Zhao and Hei, 2016). There are 46 institutions qualified for cardiac transplantation in mainland China. Among them 13 institutions carry out 1 to 4 transplants annually, 8 do more than 10, 5 over 20, and only 2 carry out more than 30 transplants every year. The largest transplantation center in mainland China, Fu Wai Hospital (Beijing, China), did 440 transplants in total (Zhu *et al*., 2015).

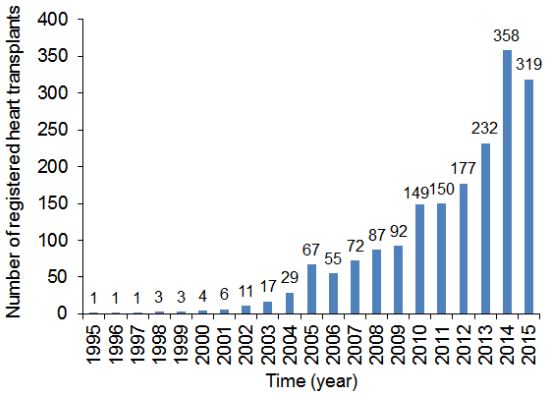

Fig. 1 Number of registered heart transplants in mainland China from 1995 to 2015 (Hu *et al*., 2014b; Zhu *et al*., 2015; Zhao and Hei, 2016)

MCS devices have been introduced into the treatment for CVD patients with 4835 cases reported in 2014. Extracorporeal membrane oxygenation (ECMO) support is the most popular technique in China. There are 703 cases supported with ECMO reported in 2014, a 30.4% increase compared to 2013 (Chen *et al*., 2015). VADs could provide long-term support to cardiac patients to make up for the shortage of transplantation. In the USA 46% of VAD implants were designated as destiny therapy in 2014 (Kirklin *et al*., 2015). The great demand from HF patients illustrates the big potential for VAD clinical application in China.

3 Development of VADs in China

Kun-xi QIAN's team in Jiangsu University, China was the first in China to develop a VAD. They

designed both a pulsatile and non-pulsatile VAD using impeller pumps (Qian, 2009). They have also studied the magnetic suspension method (Qian *et al.*, 2010) and the hemocompatibility property of the pump (Wang *et al.*, 2010). However, after QIAN retired the research discontinued. Right now, there are several groups in China aiming at VAD research, and we introduce eight groups with the most representative results.

Luo-Ye VAD is a pneumatically driven pulsatile paracorporeal circulatory support device designed by Guangdong Cardiovascular Research Institute (China) in the early 1990s (Xiao *et al.*, 2002), as shown in Fig. 2. The pump housing along with the membrane that separates blood and air is made of polyurethane with a smooth blood contact surface to increase the hemocompatibility. The entire pump is transparent so that the process of filling and emptying can be observed directly. Valves are integrated both on the inflow and outflow sides of the blood pump to prevent reverse blood flow. The pump is 85 mm in diameter, 55 mm in height, and 152.5 g in weight. The pump stroke volume is 80 ml and the frequency is selectable from 60 to 120 bpm (bpm: beat per minute). It can produce a cardiac output from 2 to 8 L/min against an afterload of 120 mmHg (1 mmHg=133.3 Pa). The Luo-Ye VAD is also available in 40 ml, and could be applied for univentricular or biventricular support (Xiao *et al.*, 2009). The pump was approved for clinical trials by the Chinese Food and Drug Administration (CFDA) in 2003. Up to April 2013, 23 patients have been supported with this pump, among whom 1 patient was waiting for heart transplantation, and the others were suffering from post-surgery low cardiac output syndrome (LCOS). Two patients were treated with biventricular support and the others with left ventricular support. Continuous intravenous heparin administration was applied to all during the early stage of the support. Eleven patients (47.8%) were weaned off the device alive, among which 8 patients (34.8%) survived until discharge. Five patients died within 30 d from discharge, and 3 patients (13.0%) achieved long-term survival. The short-term support function of the device has been proven through these trials (Huang *et al.*, 2013).

To fulfill the need from child patients, a pediatric Luo-Ye pump has also been developed. The size of the pump is similar to the ECCOR (Berlin Heart GmbH, Berlin, Germany). Its stroke volume is 20 ml and the frequency is 60 bpm. The flow rate of the pump is 1.21 L/min. Through animal trials the performance of the pediatric Luo-Ye pump has proven to be similar to the EXCOR Berlin Heart (Zhou *et al.*, 2011).

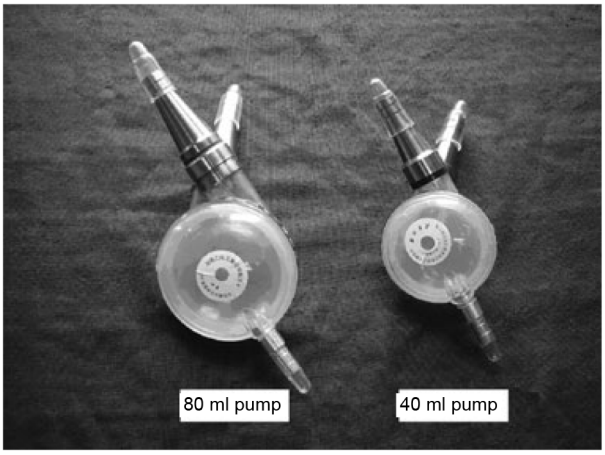

Fig. 2 Luo-Ye pumps (80 and 40 ml). Reproduced from Xiao *et al.* (2009) by permission of John Wiley & Sons Ltd.

The FW-II pump is an axial blood pump designed by the Fu Wai Heart Hospital in 2003. The pump is 26 mm in diameter and 77 mm in length. The rotor and the housing are both made of titanium alloy. The power supply of the direct current (DC) brushless driven motor is 10 W. The rolling bearings which support the rotor are made of ruby. In vitro tests show that when the pump rotates at 7500 r/min, a flow rate of 4 L/min can be produced against an afterload of 115 mmHg. With the rotation speed rising to 8500 r/min, a flow rate of 4 L/min can be generated against an afterload of 145 mmHg. In vitro tests show that when the flow rate rises above 2 L/min, the normalized index of the hemolysis (NIH) value of the pump is (0.050±0.013) g/100 L, which demonstrates good hemocompatibility. As the flow rate reaches 4.5 L/min, the NIH value decreases to (0.043±0.024) g/100 L (Chen, 2011). The FW-II pump was approved for clinical trials by CFDA in 2013. Five patients who had trouble in removing MCS after surgery for severe coronary heart disease were chosen to be subjects of a clinical trial. FW-II pumps were implanted into the selected patients with a supporting time of (24.0±2.6) h. The maximum flow rate reached 3.2 L/min during the trial. The pumps worked at the rotation speed of 7000–9000 r/min and acquired a flow rate of 1.9–3.0 L/min. No mechanical failure occurred during the trial. Despite one patient who died from acute renal

failure 7 d after the operation, the other four patients all survived till discharge with a good prognosis (Hu *et al.*, 2014a).

Ventricular Apex Axial Pump (VAAP) is a micro axial flow pump also developed by the Fu Wai Heart Hospital, as shown in Fig. 3. The pump is implanted in the ventricular wall and the outflow conduit is connected to the descending aorta. The inlet conduit is eliminated to reduce thrombosis risk. Because of the lack of a straightener, a whirling flow is produced inside the ventricle, which could wash the ventricle and prevent thrombosis formation. The pump has a diameter of 20.6 mm and a length of 70 mm (Li *et al.*, 2010). Tail guideline vanes are designed to improve pump efficiency. At the rotation speed of 11 000 r/min, a flow rate of 5 L/min can be produced against an afterload of 100 mmHg. In vitro tests showed that the NIH value of the pump is 0.023 g/100 L at the designed working point (Li *et al.*, 2015). The animal tests showed that VAAP could satisfy blood perfusion and hemocompatibility requirements (Li *et al.*, 2010).

BJUT-II is an intra-aorta axial flow pump designed by the artificial heart research group in Beijing University of Technology (Beijing, China), as shown in Fig. 4. It has a length of 25 mm, a maximum diameter of 18 mm, and a weight of 40 g (Gu *et al.*, 2014a). The pump is implanted between the aortic root and the aortic arch to avoid damaging the heart or the aortic valve. An extracorporeal dynamic system placed 150 mm away from the pump is applied as the driving force, which eliminates the use of transcutaneous wires to significantly reduce infection risk (Gu *et al.*, 2014b). The hemodynamic effect of the pump on the ventricle and the aorta has been studied (Chang and Gao, 2010). Different support strategies have also been evaluated and compared (Xuan *et al.*, 2012). Animal tests were conducted to evaluate the biocompatibity and stability of the pump. The mean support time was 11 d. During the support, all the physiological parameters of the experimental animals stayed in the normal range (Zhang Q. *et al*., 2014).

The ChinaHeart VAD (also known as CH-VAD) is a third-generation magnetically suspended centrifugal blood pump developed by Suzhou Tongxin Medical Instrument Co., Ltd. (Suzhou, China), as shown in Fig. 5. The pump is 31 mm in height and 56 mm in diameter, and has a volume of 45 ml. The weight of the pump is 350 g. The maximum pump flow can reach 10 L/min. The power of the pump is 15 W. In vitro tests show that the working point of the pump is 2500 r/min, 6 L/min, and 80 mmHg, and the NIH index under such a working condition is 0.0076 g/100 L (Liu *et al.*, 2012; Xu *et al.*, 2012). A case study reported 6 cases of animal experiments using sheep models to evaluate the properties of the pump. Warfarin was chosen as the anti-coagulate. All the experimental sheep were executed after the test. The longest survival time of the sheep was 38 d. Dissection showed that thrombosis was not generated in the pump except in one case. No thrombosis was found in any sheep ventricle (Li *et al.*, 2013; Lin *et al.*, 2013). According to Chen C., chairman of Tongxin

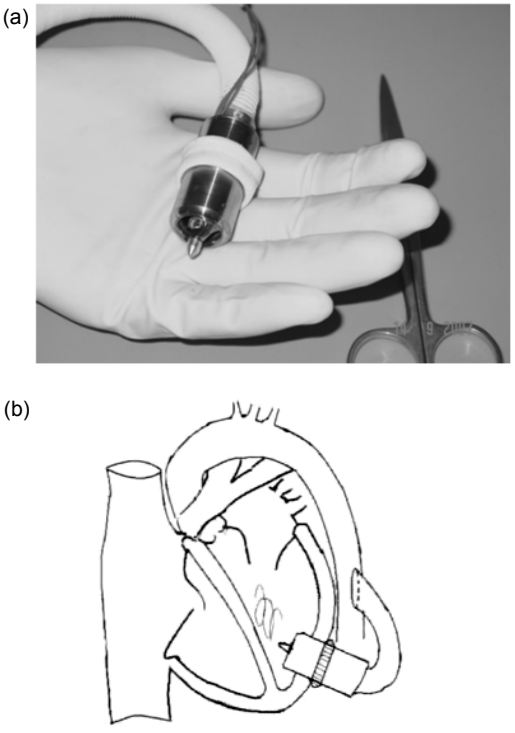

Fig. 3 Picture of VAAP (a) (Li *et al.*, 2010) and installation of VAAP (b) (Li *et al.*, 2015)

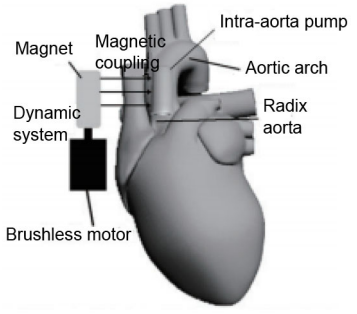

Fig. 4 Illustration of BJUT-II pump (Chang *et al.*, 2013)

Co., the newest version of the pump is only 50 mm in diameter, 26 mm in height, and 186 g in weight, which makes it one of the smallest third-generation implantable VADs worldwide. By July 2016, nearly 30 cases of animal experiments have been conducted in total, and the dissection results indicated good hemocompatibility (Chen, 2016).

An implantable Magnetic-Liquid Suspension Blood Pump (MLSBP) has been developed by TEDA International Cardiovascular Hospital (Tianjin, China) and the China Academy of Launch Vehicle Technology (Beijing, China), as shown in Fig. 6. The pump is made of titanium alloy which has good hemocompatibility. The magnetic levitation method is applied to suspend the rotor inside the pump housing. In addition, a hydraulic suspension bearing is placed on the upper side of the impeller to prevent touchdown. The pump has a diameter of 49 mm and a weight of 177 g. In vitro tests showed that the NIH value of the pump was (0.0038±0.0008) g/100 L (Zhang W. *et al.*, 2014). When the rotor rotates at 3200 r/min, the pump can generate a flow rate of 5 L/min against an afterload of 100 mmHg. Animal tests using sheep models have evaluated the pump. The longest survival time of the sheep is 120 d, while the pump worked at a rotation speed of 2400 r/min and flow rate of 3.0 L/min. All hematologic and biochemical parameters of the sheep were within normal ranges during the test except for a slightly higher myocardial enzyme. The sheep could walk freely carrying the lithium battery and the controller after the implantation. The battery could provide a 4-h support after each charge. Neither mechanical wearing nor thrombus formation was observed in inflow and outflow conduits or the pump interior (Liu *et al.*, 2015). The research team has realized batch production of the device, and the corresponding animal tests started in December 2014. The researchers planned to launch clinical trials after at least 6 batches of animal tests.

Han *et al.* (2012) in Zhejiang University (Hangzhou, China) designed a hydraulic suspension centrifugal blood pump using a novel spiral groove bearing (SGB), which is mounted on the motionless upper plate of the pump, with the mating surface of the rotor rotating with a direction facilitating the outward flow, as shown in Fig. 7. Contrary to conventional design, the applied groove has a width decreasing with increasing spiral radius. This design guarantees a convergent inward flow, which keeps the

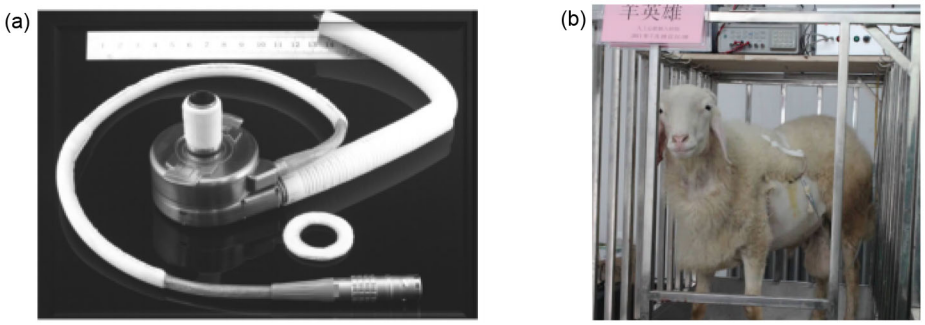

Fig. 5 Pictures of CH-VAD pump (a) and a sheep 20 d after the implantation of CH-VAD pump (b) (Li *et al.*, 2013)

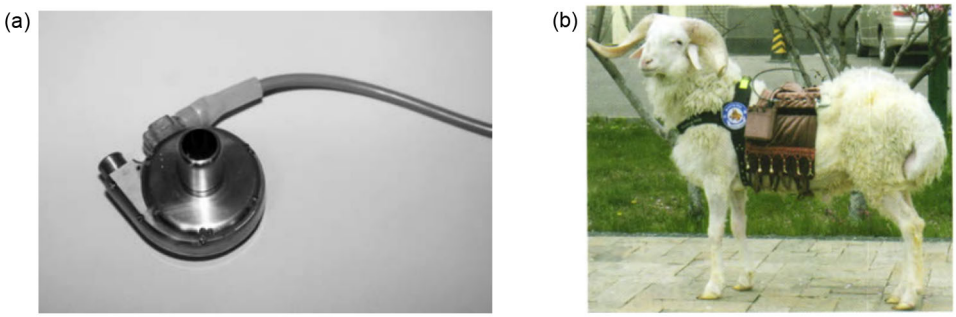

Fig. 6 Pictures of MLSBP pump (a) (Zhang W. *et al.*, 2014) and a sheep after the implantation of MLSBP pump (b) (Liu *et al.*, 2015)

load-carrying capacity of the bearing at a high level and stabilizes the rotor suspension (Han *et al.*, 2012). The pump has a diameter of 52 mm. In vitro tests showed that at 3000 r/min, the pump flow rate can reach 5 L/min against an afterload of 104.7 mmHg. Fu *et al*. (2015) have also presented a coil-coupling-based transcutaneous energy transmission system (TETS) for wirelessly powering the implanted blood pump. The TETS is designed based on a class-E power amplifier (E-PA), whose efficiency is over 95% when its load is kept in a certain range (Fu *et al.*, 2015). However, the reliability of the pump needs further in vivo testing.

Luo Y. at Shanghai Jiao Tong University (Shanghai, China) designed a novel injection suspension blood pump which utilized the centrifugal forces generated by the high-speed impeller rotation to suspend the rotor, as shown in Fig. 8a (Wu *et al*., 2017). The suspension method is to lead injection streams generated by the impeller rotation into the gap between the blade tip surfaces and the pump casing. This method is passively controlled. The injection flow produces localized high pressure in the gap region to levitate the rotor. Both axial and radial levitation forces are produced due to the conical shape of the pump casing. The pump has a diameter of 75 mm and a height of 30 mm. In vitro tests have been conducted, which showed that at 2000 r/min, the flow rate of the pump can reach 5 L/min against an afterload of 100 mmHg. At such a working point the minimum bearing gap reached 280 μm, which was much larger than that of conventional hydrodynamic bearings (usually the gap is less than 100 μm), and would probably reduce the risk of blood damage (Zhu *et al.*, 2016). Results showed that the NIH value of the pump was 0.016 g/100 L, which proved good hemocompatibility. Further tests are needed to evaluate the reliability and safety of the pump.

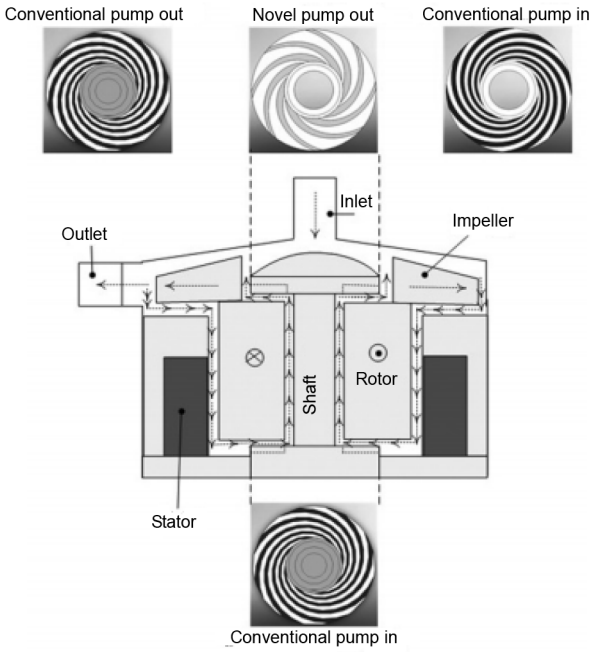

Fig. 7 Schematic drawing of the blood pump and SGB. Reproduced from Han *et al.* (2012) by permission of John Wiley & Sons Ltd.

Luo Y. has also discussed the possibility of applying the double-suction structure in blood pump design. A double-suction centrifugal blood pump utilizing the injection suspension method was designed and analyzed, as shown in Fig. 8b (Wu *et al*., 2017). The advantages of double-suction design include auto-balanced axial thrust force due to the axial symmetric structure (Lobanoff and Ross, 2013). In addition, the shear stress of the double-suction pump is relatively low compared to a single-suction design, and could be beneficial to blood cells (Zhuang *et al.*, 2010). Numerical analysis revealed that the NIH value of the double-suction pump was 0.008 g/100 L, which was almost half the value of the aforementioned single-suction pump. However, this design needs further experimental validation and evaluation.

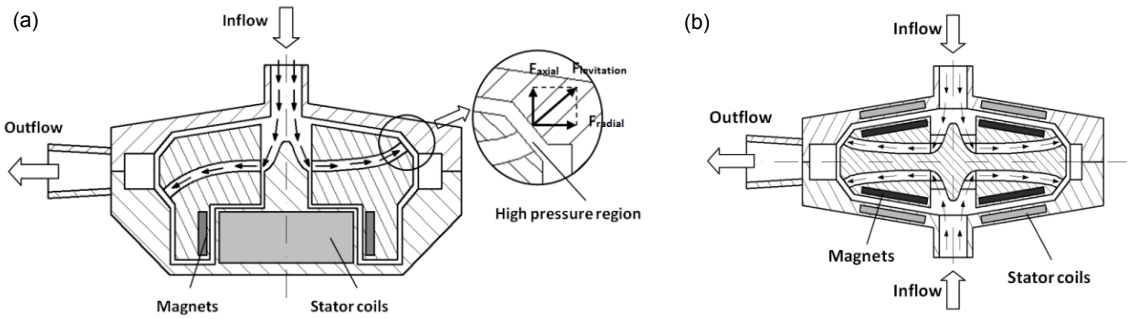

Fig. 8 Schematic drawing of the injection suspension pumps with single-suction (a) and double-suction (b). Reproduced from Wu *et al.* (2017) by permission of John Wiley & Sons Ltd.

4 Current clinical status of VAD in China

Among the Chinese-made devices, Luo-Ye pump and FW-II pump have been approved for clinical trials by the CFDA in 2003 and 2013, respectively. As described above, clinical trials have proven the reliability of the two pumps as short-term ventricular support devices. Third-generation pumps, for example CH-VAD and MLSBP, are still being tested in animal trials to validate their safety and reliability.

Several Western-made VADs have already been imported into China for clinical application. Three extracorporeal VADs have been registered for clinical use by the CFDA: Medos Deltastream VAD in 2004, AbioMed BVS5000 in 2005, and Jostra Rotaflow blood pump in 2005. The approvals of the latter two devices expired in 2009. Impella is a percutaneous VAD approved for clinical use by CFDA in 2013. It is a temporary (≤6 h) ventricular support device indicated for use during high risk percutaneous coronary interventions (PCI) performed in patients with severe coronary artery disease and a depressed left ventricular ejection fraction. A few other devices which have been approved in the USA or Europe also went through several clinical trials in China. Only a few clinical applications of VADs have been reported in China, as illustrated below, so statistics are unavailable.

The first successful intracorporeal VAD implantation in China was carried out on March 21, 2001 in Fu Wai Hospital using the NOVACOR N100 device. The patient was suffering from severe HF with an ejection fraction of 20%. The implantation was successful and the circulation of the patient was improved. Warfarin and heparin were used for anticoagulation. Seven hundred and sixty-three days after the surgery the patient received a heart transplant and the blood pump was removed. The patient recovered well after the transplantation and was later discharged from hospital (Wu *et al*., 2004).

Fu Wai Hospital reported 12 patients supported with AbioMed BVS5000 from February 2004 to April 2006. The selected patients were all males with an average age of (55.2±9.6) years and an average body surface area of (1.76±0.10) m^2. BVS5000 was inserted for the treatment of post-cardiotomy shock after coronary artery bypass graft in 11 patients (92%) and in 1 dilated cardiomyopathy patient for acute cardiogenic shock. Heparin was applied to maintain an activated blood clotting time (ACT) of 180 to 200 s. The median duration of support was 5 d (3 to 43 d), with a flow rate of 3.8 to 4.5 L/min. Nine patients (75%) were weaned from support and eight patients (67%) were discharged from the hospital. Four (33%) patients died. The most common morbidity was adverse neurological events (Hu *et al*., 2008; Luo *et al*., 2008b).

Fu Wai Hospital has also supported one patient with Medos VAD as bridge to transplant (BTT) therapy. The support lasted for 26 d. As the renal dysfunction of the patient was not improved during the support, hemofiltration was consistently applied. Plasmapheresis was conducted three times to recover liver function. Combined heart and kidney transplantation was finally conducted and the VAD was removed. The patient died 6 months after the transplant due to infection (Luo *et al*., 2008a).

From January 1999 to December 2006, Shanghai East Hospital (Shanghai, China) supported 21 patients with the Jostra Rotaflow system, 3 patients with the Berlin Heart VAD, 5 patients with the Medos VAD, and 1 patient with the Berlin Heart INCOR. For the 21 patients supported with Jostra Rotaflow, their circulation function was all improved. Eleven patients were weaned from the support after an average duration of 24.4 h (3 to 135 h). The other ten patients died during support due to irreversible refractory HF, multiple organ failure (MOF), or bleeding. For the other nine patients, their cardiac function was prominently improved. Three patients died early after the implantation, with two dying from MOF and one from severe immune hemolysis. Two patients recovered cardiac function, then were weaned off the device and discharged from hospital. One patient discharged with the VAD died while waiting for a transplant. One patient received heart transplantation after 451 d of support, and died 15 d after the transplant due to cerebral infarction (Lu *et al*., 2007; Fan *et al*., 2008).

From 2011 to 2013 the Hospital of Zhengzhou University supported six patients who were suffering from severe bleeding during ECMO with the Medos pneumatic system. Five of the patients were males and one was female. Two patients died after 1 and 2 d of VAD support, respectively. Three patients were supported with Medos for 16, 35, and 37 d, respectively,

till recovery, then weaned off the device and discharged from the hospital. One patient received a transplant after 35 d of VAD support and recovered well (Rong *et al*., 2013).

From September to November 2014, four patients received the Impella 2.5 implantation in the Fu Wai Hospital. Three patients aged 50, 50, and 63 years, respectively, were suffering from severe coronary HF with an ejection fraction of 28%, 20%, and 26%, respectively. Impella 2.5 was applied to support them during PCI. One patient aged 20 years was suffering from dilated cardiomyopathy with an ejection fraction of 20%. Cardiac shock attacked him while he was waiting for a donor heart. Impella 2.5 was applied immediately to reduce the burden on his heart. The transplant succeeded and the Impella device was removed 8 h later (Xie *et al*., 2015; Yan and Liang, 2015).

5 Challenge and opportunity

VADs have three main clinical applications: BTT, bridge to recovery (BTR), and destination therapy (DT) (Hunt and Frazier, 1998; Rose *et al*., 2001). Because of the severe limitation in the number of heart donors, the BTT application is limited. BTR is also limited and depends on the extent of myocardial damage and the etiology. The greatest potential for VAD therapy is to become DT for the HF patients who are not heart transplant candidates, have not recovered myocardial function, and may benefit from long-term VAD support.

Despite the huge demand from a vast number of HF patients, China has obviously fallen behind in the clinical application of VADs in comparison to the USA, EU, or Japan. No statistics have been collected due to the very limited clinical experiences. From the reported clinical applications in China, it can be observed that in most cases VAD support was applied as BTR. Only a few cases applied VAD as BTT. No case has been reported to use VAD as DT. The reason lies in the limitation of the clinical approvals of VADs. Despite Impella, all the other registered devices are extracorporeal VADs which could only be applied for short-term support. No implantable VADs have so far been approved for clinical use in China.

The relatively slow development of VADs in China is partially due to the high cost of the devices. The acquisition cost of the most popular long-term implantable VAD in America, Thoratec HeartMate II (HM II), is £78500 ($112000, tax not included) in 2011 (Moreno *et al*., 2012). According to the National Bureau of Statistics of China, in 2015 the annual per capita disposable incomes of all the residents, urban residents, and rural residents are 21966 CNY ($3367), 31195 CNY ($4794), and 11422 CNY ($1755), respectively (National Bureau of Statistics of China, 2016). Obviously, it is hard for most Chinese patients to afford a VAD. According to the current health care policy in Beijing, the coverage ceiling for an artificial organ is 32400 CNY ($4980), which only accounts for 4.3% of the device cost of HM II and can do little help in reducing the burden on patients. As for short-term support devices, the device cost of Impella ranges from $20000 to $25000, which is much less expensive than the implantable VADs, yet would still lay a heavy burden on recipients.

The shortage and imbalance in medical and nursing resources could also be a potential limiting factor for the application of VADs in China. According to statistics from the Chinese Biomedical Engineering Society, in 2014, a total of 209737 cardiac surgeries were conducted in 733 hospitals. Among them 53003 (25.3%) operations were completed by the Top 10 (1.4%) hospitals. Five hundred and twenty-six (71.8%) hospitals conducted fewer than 200 cardiac surgeries annually (Zhu *et al*., 2015). According to Rules for Approval of Clinical Application of VADs issued by the Ministry of Health of the People's Republic of China in 2010, institutes qualified for the clinical application of VADs should have at least 10 years' experience in cardiovascular medicine and surgery, more than 1000 cardiac operations annually and experts with over 10 years of cardiology clinical experience. The unbalanced distribution of medical resources would limit the number of hospitals that can perform VAD implantation and replacement. As the patients might probably need to move to another province for the treatment, their costs would rise even higher.

As complications such as bleeding, infections, mechanical failure, and neurological events may happen with an implanted VAD and without rapid or proper response, the complications could probably develop to be a death event, it is very important that the care givers should be aware of any possible complication, and in case of an emergency, the patients

should be sent immediately to hospitals, which could provide treatment and VAD replacement if needed. If VADs could be applied as DT in China, which means that the patients could be discharged from hospitals with implanted VADs, proper nursing would be required not only inside the hospital but also during discharge. Much training for both hospital and community nursing is needed to reach this goal. The general lack of quantity and quality of community care in China makes the effort even harder.

However, due to the high mortality of HF and the increasing demand for quality of life from HF patients, we believe that VADs still have great potential in China. A very good proposition would be the development of Chinese-made VADs, which would greatly reduce the cost of the device. Right now, several implantable VADs have entered animal tests, including the CH-VAD from Tongxin Co. According to Tongxin Co., it is estimated that their product could be at least 50% cheaper than a similar Western-made pump, which would make it more affordable for the HF patients not only in China but also in other parts of the world.

Implantable VADs are life-support devices classified as Class III medical devices, of which the safety and reliability are strictly controlled by the Chinese government. According to the Regulations for Supervision and Management of Medical Devices issued by the State Council of China (2014), clinical trials of high-risk Class III medical devices should be conducted with approval from CFDA, and highly risk Class III medical devices could not be registered without clinical trials completed in China proving their effectiveness and reliability. Implantable VADs are listed in this menu. According to Jie-min Zhang, a joint developer of MLSBP, at least six batches of animal tests need to be conducted for the approval of clinical trials, and the survival time of each experimental animal with implanted VADs should exceed 3 months. This procedure would probably take 3 to 5 years. Although the number of clinical trials needed for registration is not restricted in China, the effectiveness, safety, and reliability of VADs could not be proven without clinical trials of long term and large quantity. This could last for more than 10 years. According to Regulations for Quality Management on Clinical Trials of Medical Devices issued by CFDA in 2016, subjects recruited in the clinical trials should not be charged any fee, which means that the device developer could hardly earn any profit during the trials. This long period of animal tests and clinical trials without profit is a big challenge for the development of Chinese-made VADs.

The Chinese government now pays strong attention to the development of the domestic medical device industry, and supports Chinese-made VAD development in both policy and finance. Rules for Registration of Medical Instruments were modified by CFDA in 2014. The period of validity for medical instruments has been extended from 4 to 5 years, and after the registration expires, the company could simply extend the registration instead of registering again as before. In 2014, CFDA also issued a Specialized Approval Procedure for Innovative Medical Devices. It indicated that medical devices which apply international leading technology and have high clinical practice value could be approved as innovative medical devices after completing certain approval procedures. The innovative medical devices would go through accelerated approval procedures in the registration process. This specialized procedure is released to shorten the approval cycle of innovative medical devices and promote their development, from which Chinese-made VAD developers could benefit. Tongxin Co. has applied for the specialized procedure, and received approval of CH-VAD as an innovative medical device by July 2016.

The Chinese government also provides financial support for the development of Chinese-made VADs directly. The Ministry of Science and Technology of the People's Republic of China released two 863 Programs aimed at developing implantable blood pumps in 2007 and 2009. The programs supported research on implantable blood pumps with 3 million and 5 million CNY, respectively, during a three-year period. VAD researchers in universities could apply for the funding supported by the National Natural Science Foundation of China, which could support the research with 500000 to 1200000 CNY during a three-year of four-year period. Local government provides financial support for the development of high-tech medical industry as well. Lots of industry parks have been built all around the nation. High-tech medical companies joining the industry parks could benefit from various preferential policies, including rent relief, tax reduction, financial support, etc.

The "Made in China 2025" plan was revealed in 2015 by the State Council of the People's Republic of China. The plan has drawn up a blueprint for the development of Chinese manufacturing over the next 10 years. The high-tech medical device is listed as one of the ten key developing fields. To promote Chinese-made medical devices, the reformed health care policy requires priority use of Chinese-made medical devices in public hospitals. Development of Chinese-made VADs would very possibly benefit from such favorable policies in the upcoming years. As the Chinese-made devices enter clinical use, the cost of VADs could probably be further covered by health care to assist HF patients financially.

Compliance with ethics guidelines

Yue WU, Liang-fan ZHU, and Yun LUO declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

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中文概要

题　目：心室辅助装置在中国的发展和临床应用现状

概　要：由于人口基数巨大，我国存在大量心力衰竭病人急需治疗，但心脏供体的数量远远无法满足要求。因此，心室辅助装置在我国有广阔的市场需求和应用前景。目前我国心室辅助装置的发展相比发达国家较为滞后，临床应用也数量很少，其高昂的价格是重要制约因素，我国医疗资源的不平衡也是影响因素。我国现已制定各种政策和法规鼓励国产心室辅助装置的发展，也有科研经费和地方财政进行支持。国产心室辅助装置的价格预计会大大低于进口心室辅助装置，一旦投入临床应用，可以使更多的心力衰竭病人受益。

关键词：心室辅助装置；心力衰竭；临床应用