Development of ventricular assist devices in China: present status, opportunities and challenges

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INTRODUCTION

In China, there are approximately 13 million people suffering from cardiac failure, three times the number 10 years ago. Cardiac failure treatment is a challenge to physicians and to the economics of the health-care system because it is usually a long-term therapy and is associated with high costs for society. Although cardiac transplantation is the therapy of choice for patients with drug-resistant cardiac failure, the number of donor organs cannot fulfill the demand. As in other countries, mechanical circulatory support is an alternative option for the treatment of advanced cardiac failure patients. However, the development of ventricular assist devices (VADs) in China has been so slow that, until very recently, there has been no circulatory support system available for clinical application. There is so far no programme of development of an artificial heart.

The current state of development of VADs in China is not very well known in the western world. This article is intended to address this lack of information, and will provide an overview of current progress in the development of these medical devices in China. It will then discuss the opportunities and challenges of VADs development in China.

THE PRESENT STATUS OF THE VENTRICULAR ASSIST DEVICES IN CHINA

Development of experimental programmes for mechanical circulatory support using VADs started some 30 years ago. Various devices have been developed and evaluated in animal experiments and preclinical studies. Kunxi Qian’s group at Jiansu University was the first to design mechanical circulatory support systems. They used a centrifugal pump, an axial flow pump and a magnetic suspension, which had a huge impact on the current study of VADs in China. Unfortunately, the group’s programme was discontinued after K. Qian retired. Currently, there are six main groups in China developing an active programme of VAD support. The different systems are listed in Table 1.

The first system designed in China is named the Luo-Ye pump, which was designed by Zhengxiang Luo in Guangdong Provincial Cardiovascular Institute in the early 1990s [1]. The Luo-Ye pump (Fig. 1) is a pneumatic VAD driven by a spiral vortex pump. The stroke volume of the pump is 80 ml and the pump rate is 60 bpm. Two mechanical valves are implanted at the inlet and outlet of the pump to ensure unidirectional blood flow. The dome-like asymmetrical housing, which has a conical-shaped downward convex portion at its centre together with the criss-cross conduits, facilitates a more complete emptying of the pump. The Luo-Ye pump was designed for the bypass of the native heart [2], from the left atrium to the descending aorta. The Luo-Ye pump has been available for clinical trials since 1998 [3]. About 18 patients have been supported so far with this pump. In order to meet the requirements of paediatric heart failure patients, the paediatric Luo-Ye pump was designed, in which the stroke volume of the pump is reduced to 20 ml, and the pump rate is 60 bpm [4]. Animal experiments have shown that the performance of paediatric Luo-Ye pump is similar to that of the Excor Berlin Heart [5]. Although the Luo-Ye pump achieves good clinical results, the incidence of thrombus is still a major problem, which limits its use for long-term support. In order to reduce the risk of thromboembolism, endothelial cells have been seeded and grown in the Luo-Ye pump sac to produce a monolayer endothelial cell membrane.
Although the experimental results demonstrated that this method may help prevent thrombosis, the endothelial cells were found to fall off the pump: 29.6 ± 5.9% after 4 h and 53.9 ± 6.9% after 24 h of support [6].

Nowadays, continuous-flow pumps have become the mainstream of VADs, because of the small size of the implanted pump. In China, some continuous-flow pumps have been developed. The most advanced systems using a continuous-flow pump are the FW-II axial flow pump (Fu Wai Hospital) [7], the ventricular apex axial pump (VAAP, Fu Wai Hospital) [8] and the intra-aorta pump (Beijing University of Technology).

The FW-II axial flow pump (Fig. 2A) was designed by Xiaodong Zhu of Fu Wai Hospital in 2003. The pump is 26 mm in diameter and 77 mm in length, and weighs 110 g. The diameter of the pump inlet and outlet is 13 mm. The FW-II axial flow pump consists of a rotor with four blades, a flow straightener with five blades, a flow diffuser with six blades and a housing [9]. The material of the housing and rotor is titanium alloy (TC4). The pump is driven by a 24-V DC motor, and the power rating of the pump is 10 W. The rated speed of the pump is 7500 rpm, at which the pump flow is about 4 l/min, and the pressure head of the pump is 115 mmHg. The performances of the pump have been shown to meet the requirements of blood perfusion [10]. The normalized index of haemolysis (NIH) of this pump is 0.050 ± 0.013 g/100 l, when the pump flow changes from 2 to 5 l/min. The pump is designed for short-term left ventricular assistance in an apico-descending aortic mode (Fig. 2B.). The FW-II axial flow pump has been recently approved for clinical trials by China Food and Drug Administration, for compassionate cases. Six patients have been

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![Figure 1: The structure of the Luo-Ye pump. (Reproduced from Ref. [2] with permission from Biomedical Engineering and Clinic Medicine.)](https://example.com/image1)

![Figure 2: (A) Schematic drawing of the FW-II axial flow pump. 1: motor stator; 2: flow straightener; 3: impeller; 4: magnet; 5: flow diffuser. (B) The animal experiment of FW-II axial pump. (Reproduced from Ref. [9] with permission from Chinese Journal of Biomedical Engineering.)](https://example.com/image2)
supported in the past 2 years at Fu Wai Hospital with this system for very short periods (few days).

The concept of the VAAP [11] was proposed by Guorong Li (Fu Wai Hospital) in 2007. The pump is about 20.6 mm in diameter and 65 mm in length, and weighs 50 g (Fig. 3A). In vitro experiments show that when the rotational speed is 12,000 rpm, the pump flow and pressure head are 5 l/min and 100 mmHg, respectively. The relationship between rotational speed and pump flow under various pressure heads is shown in Figure 3B. The VAAP eliminates the inlet conduit to minimize the risk of thrombosis. The flow straightener of the pump is eliminated to generate some whirling flow in the left ventricle, which is considered helpful to improve the washing of the left ventricle and to reduce thrombogenesis further [8]. The VAAP is inserted into the left ventricle through a circular cut at the ventricular apex, and the outflow conduit is connected to the descending aorta (Fig. 3C), like the Jarvick 2000. The long-term performance of the pump has been evaluated during a mean time of support of 15 days [12]. At sacrifice, a small amount of thrombus was found on the impeller. The animal experiments demonstrated that the VAAP could satisfy blood perfusion and haemocompatibility requirements.

The above-mentioned axial pumps are ‘conventional’ blood pumps similar to those developed in western countries. Consequently, they are subject to the problems of every system: they require coring of the ventricular apex. These pumps need a percutaneous wire, which has been shown to increase the incidence of local and systemic infection. In order to solve these problems, a novel blood pump, named the intra-aorta pump, has been proposed by Yu Chang at Beijing University of Technology [13]. The schematic diagram of this pump is shown in Figure 4A–C. The pump is implanted inside the ascending aorta, between the aortic root and the aortic arch, in a supravalvular position. It consists of a rotating impeller with blades, a diffuser with helically curved blades, a pair of bearings and a housing. The dynamic part of the system, which is placed outside of the body, consists of a permanent magnet and a brushless DC motor (BLDCM). The relationship between pump flow and the pressure head of the intra-aorta pump is shown in Figure 4D.

The design has some advantages compared with conventional VADs. First, because of the position of the intra-aorta pump in the ascending aorta, there is no damage to the myocardium, which may be an important issue in terms of recovery of cardiac function. Second, the percutaneous wire of the intra-aorta pump is eliminated by the paracorporeal position of the dynamic system. This change could significantly reduce the incidence of infection and improve the patient’s quality of life. Third, because there is no electronic element in the pump, there is no rise in the temperature of the intra-aortic pump. Because of the above-mentioned advantages, the intra-aorta pump is well adapted to long-term support, especially for a bridge to recovery and partial ventricular support. As the concept of the intra-aorta pump was proposed, studies have been performed on the haemodynamics of the

![Figure 3: (A) Ventricular apex axial pump; (B) the relationship between rotational speed and pump flow under various pressure head; and (C) the schematic diagram of the VAAP implantation. (Reproduced from Ref. [12] with permission from Chinese Journal of Biomedical Engineering.)](https://academic.oup.com/ejcts/article-abstract/46/2/179/361163)
pump [14], the haemodynamic effect of the pump on the left ventricle and aorta [15, 16], and pump-control strategies for various purposes [17–21]. These studies have given good results. Animal experiments have been performed to evaluate the biocompatibility of the pump and the stability of the control system, and to determine the optimal non-invasive surgical protocol for its implantation. The mean time on support is 11 days. Every physiological parameter remained within the normal range. This short-term implantation demonstrates good hydraulic characteristics and biocompatibility of the pump and the stability of the control system.

Although the axial flow pumps have performed well in clinical applications, thrombosis remains a critical issue and permanent antithrombotic therapy is mandatory. One of the most critical problems is the risk of thrombosis at the shaft bearing and shaft axle. In order to overcome this problem, bearing-free pumps using a magnetic suspension are being developed in China. Two programmes are developing pumps based on this concept: the Magnetic-Liquid Suspension Blood Pump (MLSBP; TEDA International Cardiovascular Hospital, Tianjin) and the ChinaHeart VAD (Suzhou Tongxin Medical Instrument Co. Ltd).

The MLSBP is designed by Xiaocheng Liu of TEDA International Cardiovascular Hospital and Wei Wang of the China Academy of Launch Vehicle Technology (Fig. 5A) [22]. Surgical and aerospace industry technologies are then being used together (Fig. 5B). The pump consists of a housing, an impeller with four blades and a magnetic levitation system. The impellers of the pump utilize magnetic-liquid suspension technology, which combines magnetic suspension technology with hydraulic suspension. According to the results of in vitro experiments, the pump can achieve a pump flow range of 3–7 l/min, when the pressure head of the pump is changed from 60 to 180 mmHg. The relationship between flow

![Figure 4:](A) Schematic diagram of the intra-aorta pump; (B) the intra-aorta pump; (C) the dynamic part of the system comprising a permanent magnet and a brushless DC motor; and (D) the relationship of flow and pressure head of the intra-aorta pump. (Reproduced from Ref. [14] with permission from American Society of Artificial Internal Organs Journal.)
rate and pressure head for different rotational speeds is shown in Figure 5C. Until now, the MLSBP has been evaluated in 21 cases of in vitro haemolysis tests and 18 cases of animal experiments. The NIH value is about 0.002 g/100 l. The longest survival time of animals on support was 108 days; the maximum value of plasma-free haemoglobin (FHb) during animal experiments was 44.276 mg/l, which is in the normal range. The change in FHb during the days of the experiments is shown in Figure 5D.

The ChinaHeart is another centrifugal pump that utilizes magnetic suspension technology (Fig. 6). It was designed by Chen at Suzhou Tongxin Medical Instrument Co. Ltd. The pump is 56 mm in diameter and 31 mm in height, and weighs 350 g. Its volume is about 45 ml. The maximum pump flow under 100 mmHg is about 10 l/min. The power rating is 15 W [23]. The ChinaHeart has been used so far in 2 cases of chronic animal experiments. The mean survival time was 38 days, in which the mean FHb value was about 0.0846 g/l [24].

Besides the above-mentioned circulatory support systems, other programmes are being developed in China, by Shanxi Juian Artificial Heart Co. Ltd and Zhongshan Heart Co. Ltd. However, these programmes mainly borrow the concept of X. Zhu and G. Li at Fu Wai. Both have reached the preclinical testing stage.

THE OPPORTUNITIES FOR DEVELOPING VENTRICULAR ASSIST DEVICES IN CHINA

The recent report of the National Center of Cardiovascular Diseases shows that there are about 500 000 new cases of cardiac failure every year in China. Of them, 46% are related to ischaemic cardiomyopathy, and 19% to valvular diseases. There are 230 million people facing the problem of myocardial ischaemia and 2.9 million new cases per year of acute myocardial infarction. These already high figures are increasing progressively, probably because of poor control of risk factors: sedentariness is observed in 67% of the population. There are 240 million people facing obesity.

Like everywhere in the world, cardiac failure is one of the leading causes of death, and the numbers are increasing. This might be the consequence of ageing of the population (the number of people >65 years of age is projected to increase from 7% in 2000 to 16% in 2030 [25]). The prevalence of risk factors of heart–brain diseases is also growing, such as hypertension, metabolic syndrome, smoking, sedentariness and urbanization of the Chinese population as they move from rural areas to the cities [26]. Recent policy has permitted stabilization in smoking habits, but impact on the epidemiology of cardiac failure is still not visible. Finally, progress in cardiology and cardiovascular surgery, as in western countries, should lead to an increase in the number of patients reaching an advanced age and therefore the stage of advanced chronic cardiac failure.

Access to modern active treatments remains difficult for the vast majority of Chinese people. Despite the rise in recent years in the number of major cardiac centres (600 centres for cardiac surgery in China in 2009), only a few of them are actually very active: fewer than 20 perform cardiac surgery in more than 1000 cases a year. Of these active centres, five perform cardiac surgery more than 6000 times a year and two perform less than 10 000 times a year. The vast majority of the centres, however, perform cardiac surgery less than 100 times a year. However, their

Figure 5: (A) Hybrid suspension blood pump; (B) the diagram of the hybrid suspension blood pump; (C) the relationship between flow rate and pressure head of the MLS blood pump; and (D) the change in FHb of the MLS blood pump over time. (Reproduced from Ref. [23] with permission from Journal of Biomedical Engineering Research.)
development is quite rapid, with an 18% rise in the number of procedures per year. The heterogeneity of the geographical location of the centres is another unique characteristic of Chinese cardiac surgery: most of the centres are located in the big cities of the eastern part of the country. However, the situation is improving quite rapidly, facilitated by the spectacular growth of the economy, a strong commitment of the authorities to reduce the disparities between western and eastern provinces and the recent development of both the social security system and private insurance.

Cardiac transplantation, the ultimate treatment for end-stage cardiac failure, is also facing a difficult situation. The impact of transplantation, which gives spectacular results for individuals, remains trivial from an epidemiological point of view. The number of transplantations performed every year remains very low and is not rising significantly: in 2010, 147 cases in 15 centres; 148 in 2011; and 104 in August 2012 [27]. The most active centre is Fu Wai Hospital [28]: 60 in 2010, 52 in 2011 and 46 in 2012. There are only three centres doing more than 5 cases per year, and 13 centres doing less than 5. The 2007 reorganization of transplantation in China has not actually improved the situation, and organ procurement is still quite slow. Religious, societal and also practical issues account for this situation and do not allow much optimism about the possibility of transplantation becoming an effective response to the issue of cardiac failure.

This leaves a unique opportunity for the development of mechanical circulatory support systems. Nine clinical centres have been working in this field since 1998. Extracorporeal membrane oxygenation (ECMO) support is the most popular technique. The numbers remain quite low: the total activity at the most active centre, Fu Wai Hospital, is 192 cases, despite the fact that this unit has more than 10 000 cases of cardiac surgery per year. The mean duration of ECMO is only 2.1 days. The results are quite gratifying, as 60% of patients can be weaned off ECMO, and 54% are discharged from the hospital [29].

Despite the huge clinical needs, the use of VADs is even more exceptional: 6 cases of short-term support (3.5 days) at Fu Wai Hospital over recent years, using home-made devices. Shanghai Eastern Hospital has had 6 cases in the past 10 years, using imported VADs (mostly Medos, and in 1 case an InCor VAD system). There have been a few cases at the Guangzhou General Hospital (20 cases using a home-made pulsatile pump) and at TEDA International Cardiovascular Hospital. Fewer than 30 Abiomed paracorporeal pneumatic VADs have actually been used in China since this foreign device was approved by the China Food and Drug Administration.

**THE CHALLENGES OF DEVELOPING VENTRICULAR ASSIST DEVICES IN CHINA**

The lack of approved foreign and local VADs in the country obviously accounts for the very slow pace of clinical development of mechanical circulatory support in China. Nevertheless, there might be other reasons: the high cost of the devices and the problem of reimbursement; the organization of health care in most centres, with the lack of integration of medical and surgical treatments in specialized, patient-centred units; and lack of adequate financial support. In China, studies on mechanical circulatory systems usually depend on governmental funding, which is not enough to promote its development. There is almost no support at all from private industry.

One of the big issues for the development of VAD therapy in China will be the cost of the procedure and the lack of significant official and private coverage. Cardiac surgery in China is much less expensive than in western countries. Charges for routine coronary artery bypass graft surgery are in the range of 10 000–20 000 RMB (1200–2400 Euro), which is paid in full by the patient and is rarely and only partly reimbursed by insurance companies. The cost of resynchronization devices is one of the major limiting factors for the development of clinical practice. Only a very limited part of the population can afford a VAD at western prices, i.e. about 85 000 Euro (705 000 RMB). This problem could be solved by the approval of cheap domestic VADs. However, the huge preference of Chinese patients for western medical devices may lead to some surprises and open the market up to western VADs in China: western-made artificial valves cost at least three times more than domestic ones, yet the demand is great.

Despite the present situation, the future of mechanical circulatory support in China may be exceptionally bright if we consider the needs and the present development of active research, which has been detailed previously. Extrapolating from the figures in the USA, where there are 20 cases of long-term circulatory support per million inhabitants, in Germany (10 per million) and in France (2 per million), the potential number of candidates ranges from 2700 to 27 000 per year. Current needs may, in fact, be greater than these figures, because the contribution of cardiac transplantation to the treatment of cardiac failure is much lower in China than in western countries and will probably remain quite anecdotal.

It may be assumed that, in the immediate future, one of the leading research programmes in China will reach the level of safety and efficacy required for the approval by the local authorities. Thereafter, these authorities will obviously play a major role in the development of circulatory support. They have already issued rules for the approval of clinical programmes: the centre has to include both cardiac surgery and cardiology; be equipped with at least 40 ICU beds, echocardiography and CT scanning and a cath lab; should have 10 years of experience in cardiac surgery and invasive cardiology. The staff must include academically qualified senior surgeons and cardiologists, and 2 senior experts.
trained for such procedures must be present in the department 2 h a day, 7 days a week. The authorities are also currently reviewing the procedures for device registration. Clarification and simplification of current procedures are to be expected: 8 years were required for the registration of the only western device authorized in China.

Besides the regulatory issues, education of surgeons and cardiologists is improving rapidly: meetings on cardiac failure management are more and more frequent. Symposia on the clinical use of mechanical circulatory support are now being organized, with wet labs to train surgeons in the technique, and acute implantations in animal models to permit surgeons to become familiar with the management of patients on support. The success of the first HeartMate II symposium in 2012, in Beijing, organized by the third Hospital of Peking University, reflects the huge interest of the Chinese surgical community. Another such meeting should be organized, with the participation of cardiac failure cardiologists.

A good example of the potentially rapid growth in the use of circulatory support is the recent approval of the Impella Pump (Abiomed Europe GmbH in China) by the China Food and Drug Administration [30]. It should accelerate the procedures for approval of other home-made and/or western-made devices. Subsequently, Chinese manufacturers and investors, stimulated by the huge potential market, will increase their support in this rapidly developing field.

LIMITATION

Some data cited in this article are unpublished and were obtained at meetings and from group leaders.

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