Physiology of Continuous Blood Flow in Recipients of Rotary Cardiac Assist Devices

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The beating heart and the resultant pulse wave have been a symbol of life for centuries. The development history of roller pumps for cardiopulmonary bypass shows that the human body tolerates non-pulsatile blood flow, at least for short-term support. Over the last few years, many types of rotary blood pumps have been developed for clinical use in patients requiring mid- to long-term support. Although early clinical experiences in patients with long-term support have been promising, the matter of whether pulsatile flow is needed or not remains controversial. Therefore, this review summarizes the observed clinical consequences of continuous blood flow in patients supported by rotary blood pumps and relates these consequences to underlying experimental studies. J Heart Lung Transplant 2005;24:237–45. Copyright © 2005 by the International Society for Heart and Lung Transplantation.

Because pulsatile pumping systems are complex—requiring valves, membranes and pistons—alternative concepts for pumping blood have been pursued since the early days of cardiopulmonary bypass. The first clinically applicable continuous-flow pumps were developed in the early 1950s by developers of heart–lung machines, notably DeBakey and Gibbon.[1] An integral part of these heart–lung machines has been the roller pump, developed by DeBakey in 1934.[2] The basic physiologic compatibility of short-term, non-pulsatile perfusion was demonstrated in 1956 by Weslowski.[3] However, even after promising initial results in long-term animal studies, it was not apparent that non-pulsatile flow could provide long-term support in humans.

Concerns were expressed about the effect of a diminished pulsatile pressure curve on the functions of different organs such as the kidneys, splanchnic organs and especially highly sensitive organs like the brain. Questions were also raised about the quality of life in humans during long-term circulatory support.

Carefully designed animal studies with long-term support or switch-over between pulsatile and non-pulsatile systems were carried out. These studies gave insight into general reactions as well as single organ behavior. Numerous technical developments led to a variety of blood pumps for short-, medium- and long-term applications. More recently, the first fully implantable devices became available for long-term clinical application. Clinical studies of these devices yielded new data on human patient recovery, flow adjustment and hemostasis, physical exercise, hormonal response and the mental status of the recovered recipient. Several patients were temporarily discharged, with the longest time on continuous-flow support at >400 days.

Data from these new studies may shed a different light on earlier studies and also point toward new investigations that should be undertaken. Thus, this review presents an overview of the recent clinical studies and the underlying experimental work.

HISTORIC BACKGROUND

After the first experimental studies in dogs, in the 1930s, Akutsu and Kolff[4] began work on a permanent pulsatile substitute for the heart, summarizing their experiences in 1958. The physiologic compatibility of non-pulsatile perfusion with a roller pump of the pulmonary circulation had first been demonstrated in 1953 by Weslowski et al.[5] In 1960, Saxton and Andrews published the first article on the application of centrifugal blood pumps for cardiac assist and their potential advantages (size, less moving parts, higher efficiency, no valves, no membranes).[6] Two concepts were exploited to realize small blood pumps based on the centrifugal pumping principle: In the late 1960s, Blackshear and co-workers[7] developed an impeller-based pump, which was marketed initially by Medtronic, Inc., and was available for clinical application for several years. At the same time, 1968, Kletschka and Rafferty developed a pump based on the forced vortex principle, which ultimately became known as Biomedicus "BioPump."

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Over the next several years, interest focused on hemolysis, and the toxicity of high levels of free hemoglobin within the organism. Indeglia et al[8] and Bernstein et al[9] measured erythrocyte destruction, the influence of mechanical factors on erythrocyte sub-lethal damage, and tolerance to elevated levels of free hemoglobin.

In 1976, Johnston et al[10,11] reported prolonged pulsatile and non-pulsatile left ventricular bypass with a centrifugal pump. Four of the 9 animals in the complete bypass group reached the pre-set end-point (14 days) without complications. Based on favorable clinical results of temporary ventricular support with a centrifugal pump in 1979,[12] Golding and colleagues started a series of long-term experiments in calves, using Medtronic impeller pumps as left and right ventricular-assist devices to a fibrillating heart.[13] These calves survived up to 34 days (and in later experiments up to 99 days[10]) with totally non-pulsatile perfusion and "at no time in the course of this experiment was there any evidence of neurologic damage, subcutaneous edema or ascites. The animal was doing well with good appetite and was intermittently exercised in treadmill tests."[14] One essential observation in these early experiments was an increase of circulatory blood flow to a value 20% above that expected with physiologic levels of pulsatile perfusion. However, after 6 weeks, these flow rates returned to normal.

These reports of successful use of centrifugal pumps encouraged numerous investigators to develop a wide variety of continuous-flow blood pumps, based on centrifugal and axial pumping mechanisms, including systems with sealed bearings, blood-immersed bearings and magnetically levitated systems. The increased activity triggered workshops on rotary blood pumps, which were first held in Austria in 1988 and 1991,[15–17] and then in Houston in 1992. These meetings led in turn to the foundation of the International Society for Rotary Blood Pumps (ISRBP).

However, it was not until much more recently that non-pulsatile cardiac prostheses became available for long-term clinical use. These include the MicroMed DeBakey axial flow pump, the Jarvik 2000 axial pump, the AB-180 centrifugal pump and the HeartMate II axial pump (or Nimbus pump). From these preliminary experiences[18–21] it became clear that rotary devices are suitable for long-term use and are able to revive patients in very severe pre-operative conditions. Although the number of patients is still limited, and major randomized studies have not yet been undertaken, a first discussion of the clinical effects of low arterial pulsatility and a preliminary comparison to the data obtained in animals can be made.

OVERALL CARDIAC OUTPUT

The pathophysiology and major metabolic changes in animals perfused by non-pulsatile flow have been important topics in cardiac surgical research for many years. Apart from the long-term effects of continuous flow to the organism, investigators also evaluated the immediate effect of a switch between pulsatile and non-pulsatile circulation. Studies in the early 1980s by Golding et al[22] and Yada et al[23] reported that a certain period of time was required for a mammal to accommodate to non-pulsatile flow. During their experiments in 1983, Yada and co-workers did not find any physiologic differences between a pulsatile and a non-pulsatile group when using a 20% higher cardiac output during non-pulsatile perfusion for the first 6 weeks. Taenaka and colleagues[24] from Osaka re-examined the physiologic reactions of awake animals to an immediate switch of flow pattern from pulsatile to non-pulsatile. Based on experiences at The Cleveland Clinic, the Osaka group tried to eliminate possible adverse effects by anesthesia and surgical intervention. They designed their experiment without the need for anesthesia and surgery at the time of the switch between pulsatile and rotary systems. They did not find any deviations in hemodynamics, oxygen consumption or blood catecholamines. Thus, they believed they had proved that a mammal accommodates well and immediately to systemic non-pulsatile circulation. This led to the conclusion that earlier experimental observations were influenced by the clinical management, and probably also by the specific effects of these early devices.

In recent clinical experience, no increases of required pump flows over that required for pulsatile systems were observed.[25,26] In contrast, some centers assist patients even with low pump output only.[27] From our clinical experience, we believe strongly that such a device must have the capability to replace the full cardiac output, especially in the early post-operative phase and during potential episodes of increased flow and metabolic demand (such as infection and vasoplegia). However, we also believe that, after cardiac recovery and remodeling, a lower flow rate, with partial support only, is acceptable in many patients.

"LOW PULSATILITY" FLOW PATTERNS

No rotary pump has yet been driven in a pulsatile fashion (which may increase blood trauma and add additional pressure load to the ventricle). However, ventricular action can impose considerable pulsatility, particularly after an initial period of cardiac recovery.[26,27] Therefore, a comparison of continuously assisted circulation must consider the percentage of unloading or the type of heart failure. Proposals to quantify pulsatility—beyond simple observation of the