行政院國家科學委員會補助專題研究計畫成果報告

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※ 台大一號心室輔助器長期動物實驗 ※
※ 及生物控制器的研發(Ⅰ) ※

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計畫類別：□個別型計畫　☑整合型計畫
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計畫主持人：朱樹勳 教授
共同主持人：王水深 教授
周迺寬 主治醫師

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□國際合作研究計畫國外研究報告書一份

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Preparation of NSC Project Reports

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計畫參與人員：徐久忠、呂啟仁、謝明國、張瀞云、潘毅豪
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一、中文摘要

目前的心室輔助器主要有隔膜型和旋轉型幫浦。隔膜式的心室輔助器體積龐大，控制系統與驅動系統的重量也對病人的行動造成很大不便；電子式離心型心室輔助器則具備了體積小、重量輕、攜帶方便、手術方式容易等優點，適合體型較纖細的東方人使用。

心室輔助器的流量控制，則可分為脈波輸出和連續輸出兩種；其中，隔膜型幫浦皆為脈波式流量控制，旋轉型幫浦則兼有之。根據現存文獻，採脈波式控制的旋轉型幫浦工作效能及目標物存活率普遍較差，因此在一般臨床應用上，仍以連續流量控制的旋轉型幫浦為主。然而在一般生物體內，血液皆經由心室以脈波的形式輸出，並透過循環系統提供維持生命所需的物質。因此，我們認為應存在一特殊的控制機制，可有效地提升脈波式心室輔助器的效能，並使實驗體之生理狀態達到最佳。

由於離心型心室輔助器在轉速過低時會造成回流(backflow)，而轉速過高時則會有過度抽吸(suction)的現象。因此幫浦在實際應用中的血液動力參數，例如心電圖、血壓、血流量、幫浦電流和轉速之間的相關性研究就顯得相當重要；必須充分了解在心臟週期中幫浦的血液動力特性，才能發展出適當而有效率的控制方法。在動物實驗中，我們觀察到對應不同轉速時，心室輔助器的流量變化及與心電圖的時序關係，並定義出最適當的控制方式，希望進而改善實驗體存活情形。

關鍵詞：心臟週期, 心室輔助器, 控制機制

Abstract

The purpose of this study is to determine the physiologic relationship between the cardiac cycle and nonpulsatile impeller centrifugal Taita No.1 left ventricular assist device (T-LVAD) in chronic animal study. The relationship of the cardiac cycle, pump flow, aortic pressure, left ventricle pressure and pump power were analyzed by five phases in four stages: the isovolumetric ventricular phase is form mitral valve closure (MVC) to aortic valve opening (AVO) and called stage 1; the ejection phase is from aortic valve opening (AVO) to aortic valve closure (AVC) and called stage 2; the isovolumetric relaxation phase is from aortic valve closure (AVC) to mitral valve closure (MVC) and called stage 3;

and the passive filling and atrial contraction phase is from mitral valve closure (MVC) to mitral valve opening (MVO) and called stage 4. Based on evidence from the physiologic volume change of left ventricle, the change of pump flow of T-LVAD in a cardiac cycle by variable voltages of pump control was evaluated using animal models. After the left posteriolateral thoracotomy via the fifth intercostal space under general anesthesia, the nonpulsatile centrifugal T-LVAD was implanted into 2 healthy calves. The inflow of T-LVAD was inserted to left ventricle through MV via left atrial appendage. The arterial blood pressure waveform was measured and recorded on the outflow of T-LVAD. The four phases of a cardiac cycle were defined as MVC-AVO (stage 1), AVO-AVC (stage 2), AVC-MVO (stage 3) and MVC-MVO (stage 4) according to the outflow pressure of the outflow of T-LVAD and differential pressure between the outflow and inflow of T-LVAD. We carried out the real-time waveform measurement for electrocardiogram (ECG), the outflow pressure, the T-LVAD flow and the speed as well as open loop and constant voltage (V). In a cardiac cycle, the sensing current of the T-LVAD was inverse to the speed. The flow of T-LVAD of the four stages were measured individually and analyzed with different control voltages from 10 to 18V. The highest flow ratio of MVC-AVC/AVC-MVC was noted when the T-LVAD worked on 14 V. By using analysis methodology of the flow ratio of a cardiac cycle, the optimal physiological effective control of T-LVAD might be achieved.

Keywords: Cardiac cycle, Centrifugal left ventricular assist device, Pump control

二、緣由與目的

Because centrifugal blood pumps have great potential as new ventricular assist devices, control of these pumps is of great interest to many researchers (1, 2). Normal cardiac cycle is consisted of five phases: the isovolumetric contraction phase is between mitral valve closures (MVC) and aortic valve opening (AVO); the ejection phase is between AVO and mitral aortic valve closure (AVC). The isovolumetric phase is between AVC and mitral valve open (MVO). The passive filling and atrial contraction phase is between MVO and MVC. In this study, we divided the five phases of the cardiac cycle to four stages according to the movement of aortic valve and mitral valve. The stage 1 is as same as the isovòlumetric contraction phase, the stage 2 as the ejection phase, the stage 3 as the isovolumetric relaxation phase and the stage 4 as the passive filling phase and atrial contraction phase. When using a centrifugal blood pumps for an LVAS, the arterial blood pressure waveform changes with the LVAD condition because of the LVAD produces nonpulsatile flow and the native produces a pulsatile flow. From less detailed reports. The relationship of the cardiac cycle, pump flow, aortic pressure, left ventricle pressure and pump power were analyzed physiologically. The purpose of this study was to analyze the physiologic effects and the performance of T-LVAD in terms of the four stages of the cardiac cycle of the calves in chronic study. In addition, we attempted to learn how to recognize the optimal control of T- LVAD by the analysis methodology to achieve the effective ventricular assistance.

三、研究報告應含的內容

Materials and Methods

Two calves, were weighing around 80 kg, were used for experiments. Under endotracheal general anesthesia (Thiamylal induction, Halothane maintenance), left posterolateral thoracotomy was then performed to expose the heart and the descending aorta. A 3/8 inches polyurethane tube with polytetrafluoroethylene cuff was sutured to the descending aorta as the outflow tube of T-LVAD. A 32-French polyurethrane tube was inserted into the left ventricle via the left auricle through the mitral valve. The T-LVAD was fixed on the back just beneath the scapula for close observation. The blood pressure waveform of the outflow of T-LVAD was monitored by Hewelett -Packard oscilloscope. The ultrasonic flow probes

(T206 Transonic System Inc., Ithaca, NY, USA) ware attached to the inflow of T-LVAD. (Fig.1) The T-LVAD was set to function. The calf was extubated after it was completely awake, and it was then allowed to stand up and to eat as early as possible.

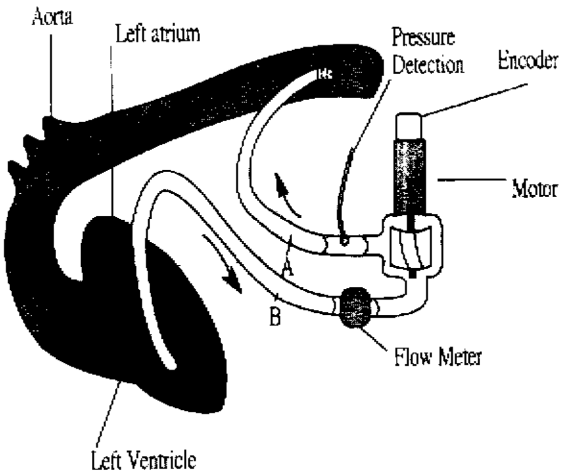


Fig. 1 The inflow tube of T-LVAD is inserted into the left ventricle via the left auricle cross mitral valve and the outflow of T-LVAD is end-to-side anatomosis on the descending aorta. The clamped point A is on the outflow tube near the descending aorta and the clamped point B is on the inflow tube near the left ventricle.

The measuring and analysis of the pressure waveform and pump flow waveform was performed one month after the T-LVAD implanted. At first, the T-LVAD was stopped for a while by clamping the outflow tube on A in fig. 1 or the inflow tube on B in fig. 1. The pressure waveform revealed the blood pressure of descending aorta and pointed out the AVO and AVC when the outflow tube was clamped completely on point A. Another pressure waveform showed the pressure of the left ventricle and pointed out the MVC and MVO. Then, the clamp was released and T-LVAD was set to function again. The ECG, blood pressure waveform and pump flow were divided to four stages according to the pressure waveform of descending aorta and left ventricle pressure. The pump flow of the four stages in a cardiac cycle was calculated individually by the equations.

$$F_{Stage1} = \frac{1}{N}\sum_{n=1}^{N}\frac{1}{t_2 - t_1}\int_{t1}^{t2} F(t)dt \qquad (1)$$

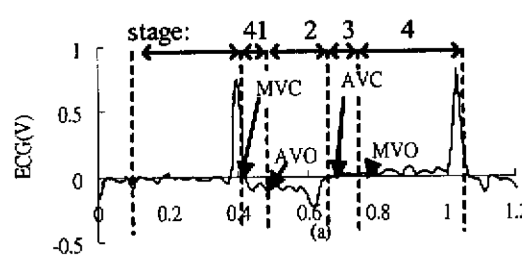
$$F_{Stage2} = \frac{1}{N}\sum_{n=1}^{N}\frac{1}{t_3 - t_2}\int_{t2}^{t3} F(t)dt \qquad (2)$$

$$F_{Stage3} = \frac{1}{N}\sum_{n=1}^{N}\frac{1}{t_4 - t_3}\int_{t3}^{t4} F(t)dt \qquad (3)$$

$$F_{Stage4} = \frac{1}{N}\sum_{n=1}^{N}\frac{1}{t_5 - t_4}\int_{t4}^{t5} F(t)dt \qquad (4)$$

Under the open loop and constant voltage control mode, the T-LVAD was driven by 10, 11,12,13,14,15,16,17, and 18 V each for five minutes. The ECG, the outflow pressure and the pump flow waveform were synchronously collected and recorded by 16 bits analog digital convert DAQ card 6035E (National Instrument Inc, San Jose, CA) in 250 Hz. The data was analyzed by Lab View software. The flow of the T-LVAD was calculated and recorded individually. The flow index of stage 1/(stage 2+ stage 3+ stage 4), stage 2/(stage 1+ stage 3+ stage 4), stage 3/(stage 1+ stage 2 + stage 4), stage 4/(stage 1+ stage 2+ stage 3), (stage 1+ stage 2+ stage 3)/ stage 4, (stage 1 + stage 2)/(stage 3+ stage 4), (stage 2+ stage 3)/(stage 1+ stage 4), stage 2/ stage 4 were separately calculated and made of the plot. All data are expressed as mean ± SD.

Results



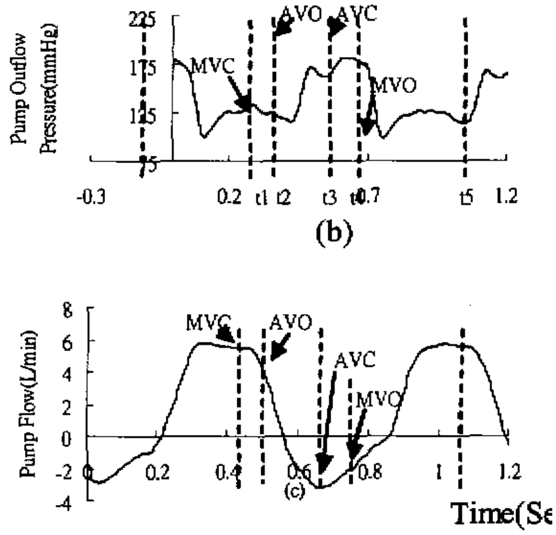


Fig. 2 The ECG (a), outflow pressure (b) and pump flow (c) waveform were divided to four stages by MVC, AVO, AVC and MVO.

According to the Fig. 2(a), the pump flow waveform was divided to four stages. The pump flow of each stage was calculated in equations (1), (2), (3) and (4). The pump flow was linearly raised by increasing motor voltage from 10 to 18 V in each stage. The average flow of stage 1 was the highest, the stage 4 was second, the stage 2 was third and the stage 3 was fourth. (Fig. 3)

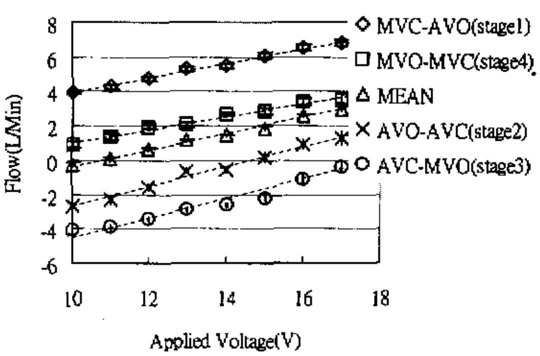


Fig. 3 The pump flow of each stage was calculated in different motor voltages. The highest pump flow was noted at stage 1 between MVC and AVO when the blood volume of left ventricle was full. The lowest pump was noted at stage 3 between AVC and MVO when the blood volume of left ventricle was near empty.

The back flow effect was noted at stage 2 when the motor voltage was less than 14 V, and the suction effect noted at stage 3 when the motor voltage was more than 18 V. The summation of the pump flow of stage 3 and stage 4 was near zero when the motor voltage set 14 V and pumps speed at 3200 rpm. The optimal motor control voltage was specified by the highest flow index of (stage 1+stage 2) /(stage3+stage4). (Fig.4)

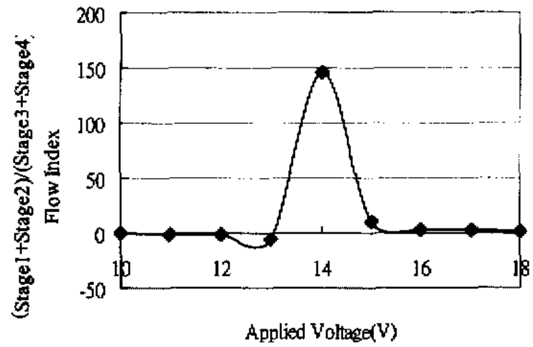


Fig. 4 The highest flow index of (stage 1+ stage 2)/ (stage 3+ stage4) occurred when the motor voltage was set 14 V because of the summation of pump flow of (stage 3 + stage 4) was near zero. The flow index of (stage 1+ stage 2)/ (stage 3 + stage 4) were negative when the motor voltage was less than 13 V.

Discussion

The motor current waveform is correlated with the bypass flow through the centrifugal LVAD so that power spectral analysis of the motor current wave could provide information useful in determining the performance of centrifugal LVAD. (l) Some studies revealed the current index of systole/diastole and flow index of systole /diastole which will be a useful monitoring parameter. (7,8) The systole phase is from AVO to AVC which is as well as stage 3, and the diastole phase is from AVC to MVO to MVC then to AVO which is same as (stage 1 + stage 2 + stage 3). In this study, the relationship between the outflow pressure waveform and valvular movement in the cardiac cycle are divided clearly by temporarily clamping the inflow tube to get the arterial blood pressure waveform which the AVO is pointed out on the trough and the AVO on the diacrotic notch. Then, the MVC is pointed on the first trough of left ventricle pressure waveform which is get by temporarily clamping outflow tube and the MVO on the second trough. The sucking effect that occurs at higher centrifugal speeds and regurgitating effect at lower speeds will create the deformed aortic pressure waveform. In the stage 3, the sucking effect and backflow effect reaches the maximum immediately after the AVC. The optimal motor control voltage will be obtained on the peak in the specific plate form of the flow index of (stage1+stage2) / (stage3+stage4). (Fig.5)

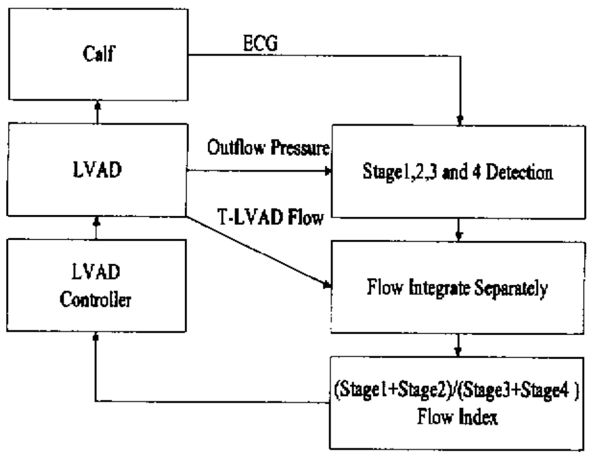


Fig. 5 Shown is our optimal motor control algorithm about the use of the flow index of (stage 1+ stage2) / (stage 3 + stage 4).

In the future study, the definition of four stages will be achieved by the ECK and outflow pressure wave and the flow index of (stage1+stage2) / (stage3+stage4) will be calculated immediately. Then, the optimal motor control voltage will be set on the peak of the waveform of the flow index of (stage1+stage2) / (stage3+stage4). The T-LVAD is a centrifugal pump that has no valves. The T-LVAD is advantageous in terms of simplicity and decreased thrombogenicity. However, when such a valveless pump will have sucking and backflow effects which can lead to damage the blood cells and even the failing heart. The optimal motor voltage control will be achieved by such analysis of the cardiac cycle to reduce the sucking and backflow effect.

Conclusion

For the implantalbe impeller centrifugal T-LVAD to be driven with a high flow without backflow and sucking effects, the flow index of (stage 1+ stage 2)/(stage 3+stage4) is the optimal motor control parameter.

四、參考文獻

1.Wang SS, Chu SH, Chou NK, Qian KX. The pulsatile impeller pump for left ventricular assist. Artif Organs 1996; 20(12): 1310-1313
2.Nosé Y, Kawahito K, Nakazawa T. Can we develop a nonpulsatile permanent rotary blood pump? yes, we can. Artif Organs 1996; 20(6): 467-74
3.Iijima T, Inamoto T, Nogawa M, Takatani S,. Control of centrifugal pump based on motor current. Artif Organs 1997; 21(7): 655-660
4. Yokokawa M, Nosé Y. A new control method that estimates the backflow in a centrifugal pump. Artif Organs 1999;23(6):538-541
5. Waters T. Allaire P. Tao G. Adams M. Bearnson G. Wei N. Hilton E. Baloh M. Olsen D Khanwilkar P. Motor feedback physiological control for a continuous flow. Artif Organs 1999; 23(6): 480-6
6. Fukuju T, Uchida N, Tabayashi K. Spectral analysis of hemodynamics during left ventricular assistance. Int J Artif organs 1996;19(6):367-71
7. Yuhki A, Hatoh E, Noggawa M., Miura M, Shimazaki, Takatani. Detection of suction and regurgitation of the implantable centrifugal pump based on the motor current waveform analysis and its application to optimization of pump flow. Artif Organs 1999 23(6): 532-537
8. Kameneva MV, et al. Rotary blood pump flow spontaneously increases during exercise under constant pump speed: results of a chronic study. Artif Organs 1999;23(8):797-801

Legends