MEAN SYSTEMIC PRESSURE AND MEAN PULMONARY PRESSURE: THEIR EFFECTS ON THE TOTAL ARTIFICIAL HEART

Yoshitsugu Kito, M.D., Takehiko Honda, M.D., W. Harry Gibson, Ph.D., and Tetsuzo Akutsu, M.D.

Mean systemic pressure (MSP) and mean pulmonary pressure (MPP), which are mean driving pressures for venous return in the natural heart, were studied in 11 calves in which the natural heart had been replaced with a total artificial heart (TAH). They were measured simply by stopping the artificial heart pumping. Although blood translocation from the arterial to the venous side was not performed, the eventual right and left atrial pressures reached six to eight seconds after stopping the TAH would represent MSP and MPP with reasonable accuracy. The MSP varied from nine to 35 mmHg (20 ± 6 mmHg), whereas the MPP varied from nine to 39 mmHg (22 ± 7 mmHg). The MSP varied in close relation to the right atrial pressure prior to cessation of the TAH (r = 0.9124). Increases in RAP and MSP were mainly attributed to an increase in circulating blood volume. In the performance of the TAH, MSP (or MPP), proper diastolic duration and vacuum application during diastole was of prime importance in determining the end-diastolic ventricular volume.

THE importance of the concept of mean circulatory pressure (MCP) in cardiovascular dynamics has been recognized since the end of the last century. It has been called “mean systemic pressure,” “hydrostatic mean pressure,” “hydrokinetic mean pressure,” “static blood pressure,” and “mean circulatory filling pressure.” MCP is actually a measure of the degree of filling of the total circulatory system with blood. Likewise, mean systemic pressure (MSP) and mean pulmonary pressure (MPP) are measurements of the degree of filling of the systemic and pulmonary circulation, respectively.

In the natural heart, MSP and MPP are the mean driving pressures for venous return to the right and left heart, respectively. They should also be considered as important determinants of cardiac output (CO) in the total artificial heart (TAH). Measurements of these two pressures can be readily performed without any complicated procedure in the TAH model.

The purpose of the present study was to analyze the changes in the MSP and MPP during long-term TAH pumping in unanesthetized calves and to evaluate their effects on the TAH function.

MATERIALS AND METHODS

Our TAH, consisting of an inner flexible pumping chamber and outer rigid housing, was designed to be implanted orthotopically in calves after the natural heart was completely removed.

Key Words:
Total artificial heart
Mean systemic pressure
Mean pulmonary pressure
Resistance to venous return
Mock circulatory system

(Received on June 20, 1975; Accepted on March 24, 1976)
Cardiovascular Surgical Research Laboratories Texas Heart Institute P.O. Box 20269, Houston, Texas 77025, U.S.A.
* Department of Surgery University of Mississippi Medical Center Jackson, Mississippi 39216, U.S.A.
Supported by USPHS NIH Grant No. HL 18084
Reprint requests to: Tetsuzo Akutsu, M.D., Texas Heart Institute, P.O. Box 20269, Houston, Texas 77025

and was driven by compressed air. Each side of the heart, consisting of one ventricle, one atrium, one vessel, and two built-in valves, was made in one-piece construction using silicone rubber. The approximate volumes of the pumping chamber, the maximum stroke volume, and the maximum CO were 150 ml, 130 ml, and 13.0 L/min, respectively. Detailed design and construction of the device and surgical implantation techniques have been previously reported.1–3,21

Various hemodynamic tests of the present study were performed in 11 postoperative calves weighing from 70 to 98 kg (average 85 kg).

The pumping conditions were usually fixed as follows: pumping rate, 100 beats/min; systolic-diastolic ratio, 0.6 to 0.7; driving air pressure, 220 to 240 mmHg on the left side and 100 to 140 mmHg on the right side; vacuum during the diastolic phase, approximately 25 mmHg on both sides. Thereafter, the prime effort of controlling the TAH was to maintain both atrial pressures within the normal range with a CO of approximately 90/ml/kg/min.

Blood pressures in both atria, aorta and pulmonary artery were measured with Statham pressure transducers through attached side tubes. The CO was measured by means of an electromagnetic flow meter (Carolina Medical Electronics). These variables were continuously recorded on a Hewlett Packard recorder. The zero reference point for atrial pressures was set at the midpoint of the right atrium.9

To measure the MSP and MPP, the TAH was stopped at the end of the systolic phase by simultaneously occluding both compressed air lines. All measurements were performed when the calves were sitting quietly in a normal prone position without anesthesia or sedative and after they had recovered from implantation surgery. The circulating blood volume (CBV) was periodically measured using a IHSs-11.32 and a model 132 B analyzer computer (Nuclear-Chicago Corporation).

Effects of the MSP on the TAH were also measured in a mock circulatory system designed for this purpose. The system included adjustable peripheral resistance and venous return determined by the height of an inflow reservoir.

Fig. 2. The arterial pressure (AP) at its lowest point was approximately 10 mmHg higher than the right atrial pressure (RAP) at its highest value reached when arterial blood was not withdrawn (A). When 70 ml of arterial blood was withdrawn immediately following the stop of the TAH pumping, both AP and VP reached approximately the same value within six to eight seconds. CO: Cardiac output. LAP: Left atrial pressure. PAP: Pulmonary artery pressure. VP: Venous pressure.

RESULTS

Repeated Measurements of the Mean Systemic Pressure:

Pressure recordings, when TAH pumping was repeatedly stopped for a short period of time following systole, are shown in Fig. 1. When the TAH stopped beating, the arterial pressure (AP) fell rapidly and the right atrial pressure (RAP) rose reaching near plateau levels six to eight seconds before activation of the autonomic nervous reflex took place. These two pressures, however, did not always reach complete equilibrium within that time. Eventual values of each AP and RAP, measured repeatedly under relatively constant circulatory conditions, never varied more than one mmHg. A critique of this method will be discussed later.

Effect on the Arterial Pressure after Rapid Withdrawal of Blood from the Arterial Circuit:

Changes in AP and RAP, when the TAH was stopped with no withdrawal of blood are shown in Fig. 2-A. The arterial pressure at its lowest point was approximately 10 mmHg higher than the venous pressure at its highest value. When blood was rapidly withdrawn from the arterial system with a syringe immediately following the stop of TAH pumping, both the AP and the RAP reached the same value in six to eight seconds (Fig. 2-B).

The additional decrease in arterial pressure by a rapid withdrawal of 70 ml of blood from the arterial side was 7.5 mmHg with a rate of 0.107
mmHg/ml. The average rate of decrease was 0.074 ± 0.028 mmHg/ml (mean ± S.D.). Since the purpose of this study was to find a simple way of measuring MSP, the involvement in any extra pump setup for blood relocation was not intended. After finding the possibility of bringing the AP and the RAP to an equilibrium within eight seconds by a rapid withdrawal of arterial blood, it was necessary to investigate the possibility that the same amount of blood, when injected into the venous side, might have some effect on the RAP. For this purpose almost twice as much blood (130 ml) as that withdrawn from the arterial side was rapidly infused into the venous system during temporary cessation of TAH pumping. In fact, 130 ml of blood was the maximum amount that could be infused with a syringe within eight seconds. The infusion, however, did not cause any measurable increase in RAP. In other words, when the RAP as well as the venous pressure was obtained in such a manner, it could be considered as an equilibrated value with reasonable accuracy. The equilibrated value in the pulmonary circuit was estimated in the same manner.

**Daily Hemodynamic Changes:**

The daily average hemodynamic changes in five calves, surviving longer than one week, are shown in Fig. 3. The arterial, pulmonary and left atrial pressures as well as the CO stayed within the normal range. However, the RAP had a tendency to increase toward the end of the experiment. The MSP varied from nine to 35 mmHg (20.3 ± 6.3 mmHg), whereas the MPP varied from nine to 39 mmHg (22.3 ± 7.2 mmHg) and remained 2.0 ± 2.9 mmHg higher than MSP. Changes in MPP were proportional to those in

*Japanese Circulation Journal Vol. 40, September 1976*
Fig. 4. Relationship between MSP and right atrial pressure (RAP). The MSP varied in close relation to the value of RAP prior to the stop of TAH pumping; RAP increased one mmHg for each one mmHg of increase in MSP.

Fig. 5. Relationship between the resistance to venous return (RVR) and the total peripheral resistance (TPR). RVR varied from 0.06 to 0.1 mmHg/ml/sec (0.05 ± 0.02 mmHg/ml/sec), whereas TPR varied from 0.29 to 1.28 mmHg/ml/sec (0.70 ± 0.20 mmHg/ml/sec). No significant correlation between TPR and RVR was observed.

MSP (r = 0.8025, y = 1.0x + 1.8), and MSP varied in close relation to the value of the RAP prior to cessation of TAH pumping; MSP increased one mmHg for each one mmHg increase in RAP (r = 0.9124, y = 1.0x + 7.3) as shown in Fig. 4. No apparent correlation between MPP and LAP was observed because LAP was maintained between 0 and 10 mmHg to control TAH pumping.

Resistance to Venous Return:

The resistance to the venous return (RVR) was calculated by the following equation where VR is venous return:

\[
RVR = \frac{MSP \text{ (or MPP)} - \text{ rap (or LAP)}}{\text{VR}}
\]

The pressure gradient between MSP and RAP was 6.7 ± 2.7 mmHg. Despite a tendency for MSP to increase, the pressure gradient did not change significantly throughout the experiment. The RVR varied from 0.06 to 0.1 mmHg/ml/sec (0.05 ± 0.02 mmHg/ml/sec). The relationship between the total peripheral resistance (TPR) and RVR is shown in Fig. 5. No significant correlation between the TPR and RVR was observed (r = 0.584). The TPR varied from 0.29 to 1.28 mmHg/ml/sec (average 0.70 ± 0.20 mmHg/ml/sec) and had a tendency to decrease toward the end of the experiment. The resistance to the VR to the left atrium varied from 0.05 to 0.20 mmHg/ml/sec (average 0.13 ± 0.05 mmHg/ml/sec).

Circulatory Blood Volume (CBV), MSP, and MPP:

The relationship between CBV and MSP is shown in Fig. 6. The MSP was measured each time immediately after CBV was measured. The MSP increased 0.35 mmHg for each one ml/kg increase in CBV (r = 0.8774, y = 0.35x - 5.27), and the compliance of the vascular system calculated under normal pumping conditions was approximately 2.9 ml/mmHg/kg. On the other hand, when the blood volume was rapidly altered.

*Japanese Circulation Journal Vol. 40, September 1976*
by transfusion, MSP increased 0.64 mm Hg for each one ml/kg increase in blood volume ($r = 0.6948, y = 0.64x + 0.24$) as shown in Fig. 7. The compliance calculated after changing the blood volume by transfusion was approximately 1.6 ml/mmHg/kg. It should be noted that each measurement was performed before the stress relaxation mechanism occurred. The effect of the changes in CBV on RAP showed an increase in RAP on 0.6 mmHg for each ml/kg increase in CBV ($r = 0.7000$).

The correlation between the increase in MPP and the increase in CBV was not significant. The correlation coefficient with the change in CBV was 0.6594 during normal pumping and 0.6850 when the CBV was rapidly changed by blood transfusion.

**Effects of Vasomotor Tone on MSP and MPP:**

The effects of the vasomotor tone on MSP and MPP were studied before and after administration of Levophed or Isuprel. The driving condition was not altered throughout the studies unless the hemodynamic parameters reached a critical level. The MSP increased 14 percent one minute after intravenous administration of 0.2 mg of Levophed, whereas, MPP increased 90 percent (Fig. 8). The CO decreased 40 percent due to a relative lowering of the driving air pressure. The LAP increased to 30 mmHg, but no apparent increase in RAP was observed.

Fig. 9 shows recordings of pressure changes after the injection of Isuprel (0.1 mg). Although arterial and pulmonary artery pressures decreased 40 percent and 20 percent, respectively, no significant changes in MSP and MPP were observed.

**MSP and MPP, and TAH Function:**

In relation to MSP and CO in animal experiments, relationships among venous pressure, diastolic duration, and grade of suction during diastole were also studied in our mock circulatory system. When the inflow reservoir height, systolic duration, and driving air pressure were fixed as indicated in Fig. 10, the CO increased somewhat, in proportion to the increase in di-
Fig. 8. Hemodynamic recordings indicating the effect of Levophed® on MSP and MPP. The MSP increased approximately 14 percent one minute after intravenous administration of 0.2 mg of Levophed, whereas the MPP increased approximately 90 percent. CO: Cardiac output. RAP: Right atrial pressure. LAP: Left atrial pressure. AP: Atrial pressure. PAP: Pulmonary artery pressure.

astolic duration, with various degrees of vacuum pressures. These data suggested that optimal diastolic durations to achieve complete ventricular filling under these fixed conditions were 275, 300, 350, 375, and 400 msec, with −100, −80, −60, −40, and −20 mmHg of vacuum pressure, respectively.

Fig. 11 presents optimal diastolic durations at different inflow reservoir heights when systolic duration, vacuum pressure and driving air pressure were fixed at a constant level. The optimal diastolic durations were 300, 325, 350, 375, and 400 msec at 40, 30, 20, 10, and 0 cm of inflow reservoir height, respectively.

DISCUSSION

It has been impossible to measure MSP by conventional means in conscious animals because the heartbeat must be stopped. The other major factor contributing to the difficulty of measuring MSP is the requirement of a special pump setup for rapid translocation of blood from the arterial side to the venous side since the autonomic nervous reflex will begin eight seconds after the heartbeat is stopped. In the present study, however, translocation of blood using a special pump setup was not performed.

Fig. 12 presents the theoretical pressure change when translocation of blood from the arterial side to the venous side is or is not performed during the induced cessation of the heartbeat. In this figure the compliance ratio of the arterial system to that of the venous system is considered to be approximately 1 to 8. Both arterial and venous pressures will reach equilibrium point A within eight seconds, if the blood is redistributed rapidly within the circulatory system after the heartbeat ceases.

In the TAH, when the pumping was stopped by simply clamping both air pressure lines and no other procedures were carried out, usually the arterial and venous pressures did not reach equilibrium point A. Instead, the eventual arterial pressure was somewhere close to point B and the
increased venous pressure was somewhere close to point C. The pressure difference between these two points varied from 0 to 20 mmHg. But, whatever the difference, less than 100 ml of blood withdrawal from the arterial side successfully brought both pressures to equilibrium. In fact, the difference between points C and A was less than one mmHg.

The effects of the changes in blood volume on MSP and MPP (Fig. 6) presented similar characteristics as observed in dog experiments.\textsuperscript{12,13,17}

Stimulation of the alpha receptor by Levoephed yielded a more significant effect on MPP than on MSP. The MPP increased 90 percent while the MSP increased 14 percent one minute after administration of Levoephed. These data suggest that the driving air pressure on the left side became relatively low in relation to the marked increase in TPR; the driving air pressure on the right side was sufficient to overcome the increased pulmonary resistance. Consequently, a certain amount of additional blood was temporarily accumulated in the pulmonary circuit causing a high MPP and a high LAP. Such a discrepancy in the cardiac output between the right and left sides continued until a new equilibrium was established. Stimulation of the beta adrenergic receptor by administration of Isuprel did not yield increases in MSP and MPP (Fig. 8). These data suggest that stimulation of the alpha receptor causes a significant rise in the peripheral resistance increasing both the MSP and MPP; stimulation of the beta receptor causes no apparent changes in MSP and MPP. It may be concluded that changes in compliance of the total systemic circulation and pulmonary circulation were mainly caused by the alpha receptor, not by the beta receptor.

One of the major problems encountered in our experiments was a progressive increase in RAP or venous pressure.\textsuperscript{4,6,15,16} The RAP increased in proportion to the increase in MSP.

Fig. 9. Hemodynamic recordings indicating the effect of Isuprel\textsuperscript{©} on MSP and MPP. Although arterial and pulmonary artery pressure (AP and PAP) decreased 40 percent and 20 percent respectively, no significant changes in MSP and MPP were observed. CO: Cardiac output. RAP: Right atrial pressure. LAP: Left atrial pressure. AP: Atrial pressure. PAP: Pulmonary artery pressure.
Fig. 10. Relationship between cardiac output (CO) and duration of diastole with various vacuums applied during diastole under the pumping condition indicated. Note the steep increase in CO at the duration of diastole between 250 and 300 msec leveling off after 400 msec.

Fig. 11. Relationship between cardiac output (CO) and duration of diastole with various inflow reservoir heights used under the pumping condition indicated. Note the steep increase in CO in proportion to the increase in the inflow reservoir height when the duration of diastole became longer than 250 msec.
Mean Systemic Pressure and Mean Pulmonary Pressure

**Fig. 12.** The theoretical pressure changes with or without the translocation of blood from the arterial to the venous circuit following the stop of the heartbeat. The arterial and venous pressures would reach equilibrium point A within eight seconds if blood was rapidly redistributed in the circulatory system after stopping the heartbeat. In TAH experiments, the arterial pressure decreased somewhere close to point B, and the venous pressure increased somewhere close to point C when the TAH pumping was simply stopped, and equilibrium point A was reached by withdrawal of 70 ml of blood from the arterial side.

(Fig. 4). The pressure gradient between the MSP and RAP, and RVR remained $6.7 \pm 2.7$ mmHg and $0.05 \pm 0.02$ mmHg/ml/sec, respectively. Although the venous return curve shifted to the right, venous return to the ventricle remained unchanged and the CO did not change significantly implying that the pressure gradient to produce a normal CO (90 ml/kg/min) always remained at approximately 7 mmHg. From this observation it may be concluded that if the RAP is 0 mmHg and the CO is normal, the MSP should be maintained at approximately 7 mmHg. Among the factors having significant effects on the MSP in TAH calves were changes in circulating blood volume, vasomotor tone and interstitial fluid volume. It should be noted that similar symptoms are observed in the failing natural heart.

In the natural heart it is generally agreed that MSP, RAP, and RVR are three major determinants of venous return to the atrium, and it is also well known that preload, contractility and afterload are three major determinants of stroke volume. The correlation among these factors has also been evidenced in the TAH. An increase in end-diastolic volume (EDV) implies rises in both right atrial pressure and end-diastolic fiber length (preload), increasing myocardial fiber shortening (Frank-Starling's mechanism). The EDV is essentially the same as the blood volume returning to the atrium in each cardiac cycle as long as the inflow valve is intact. Since filling of the ventricle is only achieved during diastole, the main determinants of ventricular filling in the TAH are MSP and diastolic duration. However, since the resilience of the artificial heart ventricle is considerably less than the natural heart, a sufficient amount of vacuum pressure is required for filling. Effects of the MSP on the performance of the TAH have been presented in our mock circulatory system (Figs. 9 and 10). Low MSP and subsequent low venous return must be compensated either by long diastolic duration or strong vacuum, or by both.

**SUMMARY AND CONCLUSIONS**

In TAH experiments, the right and left atrial pressures measured following the stop of the TAH may represent the MSP and MPP with reasonable accuracy. The measuring technique is not difficult and values obtained by repeated measurements never varied considerably.

In calves with an implanted TAH, increases in RAP and MSP are mainly attributed to an increase in circulating blood volume. In the performance of the TAH, MSP, MPP, proper duration of diastole, and proper vacuum pressure during diastole are prime determinants of the end-diastolic ventricular volume.

Since the pumping fashion of the TAH can be readily altered at will, it will be a useful tool for various studies of cardiovascular physiology in unanesthetized, conscious animals.

**Acknowledgement**

We express our sincere appreciation to Elvin E. Smith, Ph.D. (Associate Professor, Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson Mississippi) for his indispensable advice during experiments and valuable comments in the preparation of this paper.

**REFERENCES**


