Experimental study of the effect of external counterpulsation on blood circulation in the lower extremities

Abstract
A bidirectional ultrasonic Doppler flowmeter with direct single sideband separation was used to measure blood flow in the femoral and dorsalis pedis arteries of 18 normal volunteers. Changes in blood-flow velocity and volume during external counterpulsation (ECP) with various sustaining times (the time for maintaining pressure) for inflation were studied. The results showed that blood-flow velocity in the femoral and dorsalis pedis arteries is increased significantly by ECP, but the change is not closely related to the duration of inflation. For a short sustaining time, the net forward blood-flow volume in arteries increased remarkably, but at longer sustaining times it dropped back significantly to a value even lower than that before ECP. The sustaining time for inflation to produce the maximum net forward flow volume (the optimal sustaining time of inflation) was found to be at one-quarter to one-third of the cardiac cycle. In a second study, changes in the calibre of the femoral artery and its collateral and anastomotic branches in the hind extremities of 5 dogs before and after ECP with an optimal sustaining time of inflation were examined by femoral arteriography. The experiments showed that the patency of collateral and anastomotic branches of the femoral artery was greater before than after ECP. The study suggests that ECP could be an effective treatment for improving the blood circulation in extremities.

Résumé
On a utilisé un débitmètre Doppler bidirectionnel à ultrasons avec séparation directe à bande latérale unique pour mesurer le débit sanguin dans les artères fémorale et dorsale du pied de 18 volontaires normaux. On a étudié les changements de la vitesse et du volume du débit sanguin au cours d’une contrepulsion externe (CPE) compte tenu de diverses périodes de maintien (de la pression) pour l’inflation. Les résultats ont montré que la CPE augmente considérablement la vitesse du débit sanguin dans les artères fémorales et dorsales du pied, mais que le changement n’est pas lié étroitement à la durée de l’inflation. Pendant une période de maintien brève, le volume net du flux sanguin à la pression dans les artères a augmenté de façon remarquable, mais lorsque les périodes de maintien se sont allongées, il est retombé considérablement, même au-dessous de la valeur antérieure à la CPE. On a constaté que la période de maintien de l’inflation nécessaire pour produire le volume net maximal du flux à la pression (la durée optimale de maintien de l’inflation) se situait encore vers le quart ou le tiers du cycle cardiaque.

© 2000 Canadian Medical Association
Introduction

External counterpulsation (ECP) is a new noninvasive technique used in the treatment of various ischemic diseases. By using the “R” wave of the electrocardiographic (ECG) signal as a trigger, the cuffs wrapped around the extremities and buttocks are inflated at diastole and apply pressure to the arteries of the extremities. This causes the diastolic pressure in the aorta to rise due to the blood flowing back into the aorta from the arteries of extremities. Therefore, the perfusion pressure of the coronary and the common carotid arteries increases and blood flow to the heart and brain is increased, as shown in animal and clinical studies. This technique has also been used in clinical trials for the treatment of coronary and cerebrovascular insufficiency and appears to be of benefit.

As part of the blood flows out of the extremities and returns to the aorta at diastole and the extremities are temporarily ischemic, some symptoms may occur during ECP therapy. Some patients complain of numbness of their extremities when the sustaining time for inflation or the treatment time is long.

It is not presently known how the blood-flow velocity and the blood volume in the arteries of the extremities change during ECP, whether ECP is capable of augmenting the blood supply to the extremities or what are the indications for ECP therapy for ischemic extremities and for ischemic extremities associated with coronary or cerebrovascular insufficiency.

This report describes experimental observations in human volunteers and animals of the change in blood-flow velocity and blood volume in peripheral arteries during ECP and the changes in collateral circulation after ECP.

Materials and methods

According to hemodynamics, the flow volume through a blood vessel given by the Poiseuille–Hagen equation in the absence of turbulence is as follows:

$$Q = \frac{\pi R^4}{8L\eta} \cdot \Delta P,$$

$$U_{max} = \frac{R^2}{4L\eta} \cdot \Delta P,$$

Since the maximum flow velocity is:

$$Q = U_{max} \frac{\pi R^2}{2}$$

the equation for flow volume can also be written as: where flow volume ($Q$) is proportional to the 4th power of the radius of the vessel ($R^4$), the maximum flow velocity ($U_{max}$) is proportional to the square of the radius of the vessel ($R^2$) and both of them are in direct proportion to the pressure difference ($\Delta P$) between the 2 ends of the vessel. However, they are also inversely proportional to the viscosity of blood ($\eta$) and the length of the vessel ($L$). If the radius of the vessel remains unchanged, the flow is proportional to the flow velocity ($U_{max}$)

and the time duration ($t$). For a constant flow velocity, the longer the time, the larger is the blood volume. In order to increase the flow velocity and flow volume in the peripheral vessels, different pressure differences between the 2 ends of the vessel and the time duration of the blood flow have been investigated to determine empirically the optimum conditions.

Human studies

Eighteen healthy volunteers, (16 men, 2 women, mean [and SD], age 35.5 [2.3] years, ranging from 27 to 62 years) without peripheral vascular disease were studied. Blood-flow velocity was detected using a bidirectional ultrasonic Doppler flowmeter with direct single sideband separation (Model F-1, Electronic Engineering Department, Fudan University, China). The flowmeter can detect and record the forward and the reverse components of flow velocity in the same part of a vessel simultaneously. The probe of the flowmeter is attached to the point of maximum pulsation on one side of the femoral and dorsalis pedis arteries. The proximal and distal ends of the subjects’ extremities are wrapped with inflating cuffs for ECP.
The pressure in the cuffs was monitored by a pressure transducer connected to the cuffs with a special connector. The pressure, the time of compression, the duration of inflation and the degree of compression can be found from the time dependence of the pressure. The sustaining time of inflation was monitored using ear-lobe plethysmography, keeping the dicrotic (diastolic) wave higher than the percussion (systolic) wave. Heart rate was recorded from the electrocardiogram. A 6-channel physiologic recorder was used to record all the above-mentioned data.

A 10-turn potentiometer, with each turn setting of the multi-turn potentiometer representing a specific value of sustaining time of inflation, was used to set this time and to insure that a specific sustaining time for inflation could be set quickly and accurately reproduced in different experiments. The larger the number of turns, the longer the sustaining time of inflation. The turn number settings used in the experiments were 2, 4, 5, 6, 7, 8, 9, and 10, corresponding to 80, 240, 300, 380, 440, 540, 580 and 600 milliseconds respectively. The inflation pressure was controlled at either 40 kPa (300 mm Hg) or 60 kPa (450 mm Hg). For each sustaining time, counterpulsation was carried out for 5 minutes. The changes of velocity and volume of blood flow in femoral and dorsalis pedis arteries were observed. Counterpulsation experiments for the 8 different turn settings made up a single group of experiments.

Since the Model F-1 Doppler flowmeter can determine only blood-flow velocity, a Model QJI counter (Shanghai Navigation Instrumentation, Inc.) was used to determine the blood-flow volume by measuring the area (in square millimetres) under the flow-velocity curve for 5 cardiac cycles. The average area for a cardiac cycle was used as a relative measure of the flow volume. The areas taken before ECP and the areas taken during ECP with different durations of inflation were compared. A t-test was used to compare data for a given subject.

Animal studies

Five dogs (3 male, 2 female, weight 15 to 18 kg) were divided into 2 groups: 3 in the experimental group and 2 in the control group. The dogs in the experimental group were given sodium pentothal anesthesia (30 mg/kg) for bilateral femoral arteriography (Philips Diagnost-90 multifunction roentgenogram) with an injection rate of 3 mL/s. Five images were recorded automatically at 0.33, 1, 1.75, 2 and 3 minutes from the start of the bolus injection. Then ECP was done for 1 hour with an inflation pressure of 60 kPa and sustaining times of onequarter to one-third of the cardiac cycle. Bilateral femoral arteriography was repeated after ECP with the same procedures and under the same conditions. Data for 6 experiments were obtained. The same procedure was carried out for the control group, but without ECP.

Results

For the same inflating pressure, the forward and reverse arterial flow velocities and volumes of the lower extremities increased remarkably during ECP, but the velocities and volumes varied with the sustaining time of inflation (Fig. 1).

The effect of ECP with various turn settings on arterial blood flow velocity

For both inflation pressures of 40 and 60 kPa, the reverse blood-flow velocity increased remarkably during ECP: 5.5-fold and 15-fold, respectively, in dorsalis pedis artery ($p < 0.001$) and 1.2-fold and 1.5-fold, respectively, in the femoral artery ($p < 0.001$). However, the forward velocity increased only slightly: 49% and 65% in the dorsalis pedis artery ($p < 0.05$ and $p < 0.01$), and 13% and 32% ($p > 0.05$) in the femoral artery. Although the increase of reverse flow velocity is higher than that of forward velocity, the absolute value of the forward flow velocity was still higher than the reverse. There was no correlation between the velocity change and the duration of inflation for either the forward or the reverse flow (Fig. 2).

The effect of ECP with various turn settings on arterial blood flow volume

For inflation pressures of 40 kPa and 60 kPa, both forward and reverse blood-flow volumes increased significantly during ECP. The average forward flow volume in the femoral artery for potentiometer settings of 2 to 5 turns increased by 74% and 80% over the baseline for the 2 inflation pressures ($p < 0.05$ and $p <
The increase was less significant when the turn numbers were larger than 6 (i.e., sustaining time of 380 milliseconds). Meanwhile, the average reverse flow volume in the femoral artery increased about 1.4 fold. Despite the increase of time duration, the reverse flow volume remained unchanged or increased only slightly. Based on the algebraic sum of the forward and reverse flow volumes, the average net forward flow volumes in the femoral artery during ECP at the time settings in 2 to 5 turns were increased by 45% and 64% for the 2 inflation pressures ($p < 0.05$ and $p < 0.01$). The net forward flow volume started to decrease with increasing turn number when the turn number was larger than 5. The minimum flow volume (at 10 turns) was only about 41% of that before ECP.

The forward and reverse flow volumes in the dorsalis pedis artery increased significantly during ECP with the forward volume being higher than the reverse. No correlation was found between the change of flow volume and the sustaining time of inflation. During ECP, with a sustaining time of inflation at the 4 and 5 turn settings, the average net increase of forward flow volume was 75% and 1.3-fold, respectively, for the 2 inflation pressures used ($p < 0.05$ and $p < 0.01$, Fig. 3).

**Effect of the ratio between the sustaining time of inflation and the cardiac cycle on blood-flow volume in the extremities**

Our results showed that there is an optimal time set-

---

**Fig. 1: Forward and reverse blood-flow velocities and volumes in the femoral artery during external counterpulsion (ECP) for various turn settings (various sustaining times of inflation setting).** The top 2 curves show the qualitative changes in forward and reverse blood-flow velocities and volumes in the femoral artery during ECP for various turn settings and the same inflation pressure. The third curve shows the sustaining time of inflation in the cuffs. The time is longer for a larger number of turn settings. The bottom curve is the electrocardiogram. For small turn settings, the forward blood-flow volume is much larger than the reverse one during ECP. For larger turn settings, the forward blood-flow volume is smaller than or equal to the reverse flow velocity. For small numbers of turn setting, the forward blood-flow velocity is larger than the reverse flow velocity. For larger numbers of turn setting, the forward blood-flow velocity is almost the same as the reverse flow velocity. CM/S = centimetres/second.
ting (sustaining time of inflation) that produces the maximum net forward flow in the femoral and dorsalis pedis arteries for the same inflation pressure used. However, heart rate varied for different individuals and at different times. Therefore, the ratio between the optimal turn setting and a cardiac cycle during ECP should be used. Based on our experiments, this optimal ratio ranged from 0.25 to 0.34. This means that the optimal sustaining time of inflation is at one-quarter to one-third of the cardiac cycle. The blood-flow volume decreased when the ratio exceeded 0.34 and approached the control value. For the femoral artery, the net flow volume decreased remarkably when the ratio was larger than 0.5. The volume can be lower than that before ECP (Fig. 4).

**Effect of ECP on arterial collateral and anastomotic branches in the hind extremities of dogs**

In the control group, the results of a second arteriography after a 1-hour interval are similar to those of the previous one. No increase in patency of collateral and anastomotic branches of the femoral artery was noted. For dogs under ECP for 1 hour, a significant increase in patency of collateral branches of the lower extremities was noted (Fig. 5). The volume of blood-flow was greater than that before ECP (Fig. 6).

---

**Fig. 2: Effect of external counterpulsation (ECP) with various turn settings on blood-flow velocity in the arteries of the lower extremities during ECP (values are mean [and standard error of the mean]).** For ECP with various turn settings, the reverse (R, squares) flow velocity in the femoral artery (FA) and the forward (F, diamonds) and R flow velocities in the dorsalis pedis artery (DPA) increase significantly at 40 kPa (300 mm Hg) and 60 kPa (450 mm Hg) ($p < 0.05$ and $p < 0.01$), but the F flow velocity in the FA increases only slightly. Blood-flow velocity is not closely related to the turn setting.

_Clin Invest Med • Vol 23, no 4, August 2000_
hind extremities was seen on arteriography. Arteriograms obtained at 1 second and 1.75 seconds showed increasing patency of collateral branches of the proximal segment (above the puncture point) of the femoral artery, indicating increased patency of anastomotic branches (Fig. 5).

**Discussion**

Under normal physiological conditions, there are 3 phases of blood flow in the femoral and dorsalis pedis arteries: forward flow, reverse flow and the second forward flow. The first forward flow is caused by the ejection of blood during systole. The reverse flow is due to the sudden closure of the aortic valve and the drop of impulse force and a reactive force caused by filling expansion of the distal vessel wall in the extremities. The second forward flow is due to the force of contraction of the aortic arch in expansion in diastole. However, in a small number of patients, the second forward flow is minimal or even undetectable, possibly due to the poor elasticity of vessel wall. Therefore, the blood flow in the lower extremities is affected by both myocardial contraction and...
the 2 reactive forces.

Under our experimental conditions, arterial blood flow in the lower extremities was mainly determined by the following force components:

• The effective force of ECP, that is, the compressive force on the arteries of the lower extremities produced by cuff inflation during ECP, causing the blood in the lower extremities to flow back into the aorta.

• The negative force produced by the sudden expansion of arteries due to the release of compression following a rapid deflation of the cuffs, causing blood to flow to the arteries in the lower extremities from the aorta.

• The reactive force produced by the resistance of aortic blood flow to the force of arterial blood in the lower extremities, resulting in pressure on the aorta, and the reactive force produced by obstruction of blood flow from overexertion of pressure on arteries and the filling expansion of arteries in the lower extremities, rendering blood flow back to aorta.

• The contractile force of myocardium and aorta; that is, the force produced by contraction of the heart during systole and contraction of the aortic arch during diastole, ejecting the blood from the left ventricle and aorta distally.

In routine ECP, the action of ECP, the negative force produced by it and the myocardial contractile force are basically stable, except that the reactive force varies in accordance with the sustaining time of inflation. However, the change of sustaining time of inflation changes the algebraic sum of the negative force, the contraction force by myocardium and aorta, and the reactive force.

Why, then, do flow velocity and flow volume change with the sustaining time of inflation for the same pressure? In our experiment, the deflation time was changed to change the sustaining time of inflation. According to our experimental studies, for the same sustaining time of inflation, the key factor that affects the flow volume in the lower extremities is the phase when the deflation is applied (i.e., the phase in which a negative force is produced in the arteries of lower extremities). Our experiments have shown that optimal results can be obtained when the inflation starts in the reverse flow period and the start time of deflation is near the end of the second forward flow of diastole. In this condition, the active force from the aortic wall during diastole, the negative force of the femoral artery and the myocardial contraction force are in the same direction and applied in sequence, resulting in a strong and steady active force to create rapidly a massive flow of blood from the aorta into the femoral artery. On the other hand, an earlier or later start of the deflation time makes the sustaining time of inflation too short or too long, so that the 3 force components are activated at a disordered pace and may overlap in time. Therefore, the effects of the force components may be cancelled, resulting in a less efficient effect so that the flow velocity and flow volume in the forward direction are close or equal to the reverse ones, or even result in a negative effect (i.e., transient ischemia in the lower extremities). The duration of blood flow in the arteries of extremities is reduced with larger sustaining time of inflation within a cardiac cycle. The blood volume in the extremities is, therefore, reduced. On the contrary, the duration of blood flow in the arteries of extremities is increased, causing increased blood volume in these arteries. In the treatment of ischemic heart disease,
Fig. 5: Arteriographic changes in the femoral artery before and after external counterpulsation (ECP) in dogs. Top left — control dog, top right — control dog 1 hour later. Bottom left — study dog before ECP, bottom right — study dog after 1 hour of ECP.
ischemic cerebrovascular disease and eye disease, longer sustaining time of inflation equivalent to 50% to 60% of the cardiac cycle is often used. In these cases, blood-flow volume in the extremities is likely lower than that before ECP. This may result in a transient ischemia of the extremities, causing limb numbness in some patients.

Generally, most of the collateral and anastomotic branches of the lower extremities are closed. However, during vigorous exercises or when the arteries of lower extremities are stenosed, part of collateral and anastomotic branches might open reflexly to augment blood supply to the extremities. Once insufficient blood supply occurs as a result of the loss of or an inadequate compensative mechanism, some degree of ischemia will occur, leading to related symptoms, such as feeling cold, pallor, pain, intermittent claudication or even necrosis. Femoral arteriography in dogs showed that patency of collateral and anastomotic branches of the femoral artery after ECP increases remarkably, which could result in a greater blood supply to the extremities, including the ischemic tissue covered by the stenosed or obliterated arteries, leading to the relief of the extremity ischemia.

We conclude that, with an adequate sustaining time of inflation, ECP is capable of augmenting blood supply to the extremities. The mechanism of the augmentation can be explained as follows. Vessels of the extremities are compressed and released alternately with the inflation and deflation of the cuffs. This results in the increase of intravascular pressure difference, which, in turn, increases significantly the velocity and volume of forward and reverse blood flow passing through the vessels. This has an impact on the stenosed or obliterated vessels and makes them dilated or even recanalized. For optimal sustaining time of inflation (in the range of one-quarter to one-third of the cardiac cycle), the forward flow volume greatly surpasses the reverse one, resulting in a significantly increased net forward flow volume in a cardiac cycle. Furthermore, there is increased patency in the collateral and anastomotic branches of the lower extremities after ECP, greatly increasing the blood flow in the extremities. Our study suggests that external counterpulsation could be an effective modality in the treatment of arterial obstructive diseases of extremities, such as atherosclerosis, Buerger’s disease, delayed healing of long-bone fractures and peripheral circulatory insufficiency.

References


7. Ruch TC, Fulton JF. Medical physiology and biophysics. vol 2. Beijing (China): Science Publisher; Correspondence to: Dr. Dawei Cai, External Counterpulsation Laboratory, The Clinical Medical College, Shanghai Medical University, 85 Wu Jin Rd., Shanghai 200080, People’s Republic of China; fax 011 86 21 63240825, kjcsfph@public9.sta.net.cn