Pressure Measurements in the Terminal Vascular Bed of the Epimyocardium of Rats and Cats

HARALD TILLMANNS, MICHAEL STEINHAUSEN, HANS LEINBERGER, HEINZ THEDERAN, AND WOLFGANG KÜBLER

SUMMARY In order to measure pulsatile pressures in microvessels of the left ventricular myocardium, we developed a method that extends the use of the resistance servo-nulling technique to the beating mammalian heart. In 9 cats and 25 rats, we studied the terminal vascular bed of the ventricular epimyocardium by incident light in vivo microscopy, using a highly sensitive television camera tape system. Following intravenous administration of fluorescent dextrans, microvascular diameters and flow patterns could be observed continuously. Intraluminal pressures in the microvascular bed of the cat and rat heart were determined by micropuncture and a micropipet servo-nulling system. In contrast to larger coronary arterioles (diameters 160-300 μm), smaller arterioles with diameters <100 μm showed a considerable pressure drop between ascending aorta and the site of pressure recording. In venules of the epimyocardium, the pressure curve exhibited a late systolic peak, occurring just before aortic valve closure. Maximal coronary arteriolar dilatation by dipyridamole (0.5 mg/kg body weight, iv) provoked only a slight increase in systolic coronary venular pressure (controls 25 ± 3 mm Hg, dipyridamole 27 ± 6 mm Hg). On the other hand, positive inotropic intervention by intravenous infusion of dobutamine (6 μg/kg per min), as well as the application of norepinephrine, resulted in a marked rise of systolic coronary venular pressure. These data suggest that the contractile state of the myocardium and left ventricular afterload are the major determinants of systolic coronary venular pressure.

THE microcirculatory events during the cardiac cycle are governed mainly by systemic arterial pressure, changes in coronary resistance (due to vascular compression by the myocardium as well as relaxation of heart muscle), vascular cross-sectional area and capacity, and rheological properties of the blood (Gregg, 1962; Raff et al., 1972; Tillmanns et al., 1974). Until recently, only partial success has resulted from any attempts to separately identify and estimate the changes in the two variables which control hemodynamics of the coronary microcirculation, namely, extravascular support and active vasomotor changes (Gregg, 1950, 1962). Simultaneous measurements of pressures in different compartments of the coronary vascular bed, for instance in large and small coronary arteries and veins, are necessary for such an attempt.

In previous experiments, small coronary artery pressures were measured by cannulation of branches of major coronary arteries only (Gregg, 1950; Fam and McGregor, 1968; Winbury et al., 1969; Cohen and Kirk, 1973). Small coronary veins or venules were not investigated because of technical difficulties (Gregg, 1950).

The development of a transillumination technique of the left atrium of the cat heart (Tillich et al., 1971; Bing et al., 1972) and, particularly, newly developed methods of transillumination (Tillmanns et al., 1974), as well as epillumination (Steinhausen et al., 1978) of the left ventricular myocardium of rats, cats, and dogs, enable us to perform studies of the microcirculation of the beating heart in situ and add a new dimension in studying the functional determinants of the coronary microcirculation. This report describes a new technique of measuring intravascular pressures of small epimyocardial vessels of the left ventricular myocardium by means of micropuncture and a micropipet servo-nulling system according to Wiederhielm (Wiederhielm et al., 1964), applying our newly developed epillumination method (Steinhausen et al., 1978). By use of these techniques, we were able to assess functional determinants of coronary venular pressures. Furthermore, studies were performed to identify those small coronary arteries and arterioles which show a considerable pressure difference as compared to aortic pressure.

Methods
Experiments were performed in 25 rats and 9 cats of both sexes (Steinhausen et al., 1973; Steinhausen et al., 1977). Wistar and Wistar-Furth rats weighing
200-400 g, and cats weighing 900-1500 g were used. Anesthesia was introduced in rats by intraperitoneal injection of Inactin (100 mg/kg body weight) and in cats by intraperitoneal injection of sodium pentobarbital (25-30 mg/kg body weight). A tracheal cannula was inserted, and the animals were ventilated by intermittent positive pressure with room air, using a small animal ventilator (Harvard). The heart was exposed by means of a bilateral thoracotomy (removal of the sternum and of ventral parts of the ribs). The animals were placed in a supine position on a heated operation table; rectal temperature was maintained at 37°C. Three small polyethylene catheters were introduced into a jugular vein for drug administration. A constant application of drugs was accomplished by a mechanical perfusion device (Braun).

Pulsatile and mean aortic as well as right atrial pressures were measured by means of polyethylene catheters, placed in the aortic arch via the carotid artery and in the right atrium via the jugular vein, respectively. Strain gauge pressure transducers (Statham P23Db) and a direct recorder (Hewlett-Packard 7) were used for pressure recording.

Reduction of excessive movement of the cardiac tissue is necessary for in vivo microscopic long-time observation of the ventricular microcirculation. We used five small needles with diameters of less than 0.2-0.3 mm each, connected to the operation table (Steinhausen et al., 1978). These needles were inserted horizontally into the ventricular myocardium, beneath the area of interest. Microscopic observation of myocardial microvasculature was accomplished by use of incident light as described in previous communications (Tillmanns et al., 1977; Steinhausen et al., 1978). Briefly, heat-filtered light originating from a pulsating xenon arc was used for illumination of the tissue, in conjunction with Ultrapak or Fluopak lens systems (Leitz, Wetzlar). Immersion objectives with up to 100x linear magnification were employed, combined with locally fabricated dipping cones. During the fluorescence microscopic studies, the application of a BG 38 and an interference filter (Schott, Mainz) resulted in a wave length maximum of 490 nm that illuminated the cardiac surface. The emitted light passed through a 530-nm filter. During micropuncture of cardiac microvessels, mostly the objective lens U011 (numerical aperture 0.25) (Leitz, Wetzlar) and/or Wild 10x (aperture 0.40) was applied. The dipping cones eliminated surface reflection; the working distance was 1.5 mm. Continuous observation and documentation of the images were accomplished by a highly sensitive silicone intensifier target image tube (Restlichtkamera, Siemens, K5B) and a television tape system (Grundig, BK 401). Contrast of the epimyocardial microvasculature was enhanced by iv injection of FITC tagged high molecular dextran (molecular weight 150,000). Thus, fluorescence microscopic observations could be obtained for a few hours at a circumscribed area of interest without damage to the cardiac tissue under study (Steinhausen et al., 1977).

Intraluminal pressures in the microvascular bed of the beating cat and rat heart were obtained by micropuncture of arterioles and venules and by applying a micropipet servo-nulling system according to the method of Wiederhielm (Wiederhielm et al., 1964; Fox and Wiederhielm, 1973), as modified by Intaglietta et al. (1970). Intramyocardial insertion of the five small steel needles rendered the epimyocardial layers to in vivo microscopic observation. Thus, arterioles (diameter 30-150 μm), small coronary arteries (diameter 150-300 μm), and venules (diameter 30-150 μm) of the beating left and right ventricular myocardium were made accessible to pulsatile intravascular pressure measurements.

Micropuncture and pressure determinations were accomplished by use of glass micropipets with tip diameters of 1-7 μm. The micropipet (Fig. 1) containing 0.6 m saline and small amounts of sulfonfluorescein, was positioned by means of a micromanipulator. After penetrating the vessel wall, the position of the pipet tip was frequently controlled by fluorescent saline injected through the pipet tip. The flushing procedure for assessing proper intubation of the microvessel was never associated with a significant variation of blood flow velocity or diameter of the vessel under study. A proper position of the pipet was identified by noticing a rapid intravascular washout of the fluorescent saline injected. Thus, adherence of the pipet tip to the vessel wall, or partial occlusion of the micropipet caused by platelets, could be detected readily by applying this technique.

Pressure measurements in microvessels were made using the resistance servo-nulling technique of Wiederhielm (Wiederhielm et al., 1964; Fox and Wiederhielm, 1973), as modified by Intaglietta (Intaglietta et al., 1970). In this system, the conductivity of the saline solution within the pipet considerably exceeded that of the surrounding plasma. Pressure alterations in small punctured vessels cause a dislocation of the plasma-saline interface within the pipet tip, bringing about a change in the electrical impedance of the micropipet tip, as determined by a Wheatstone bridge circuit (Wiederhielm et al., 1964). Thus, the resistance between the shank of the pipet and the tissue was continuously monitored. The balance of the bridge circuit provides a means of monitoring the interface location and thereby the intravascular pressure. Zero pressure was established prior to each pressure recording by immersing the micropipet in a small beaker containing Ringer’s solution.

The frequency response characteristics of the commercially available servo-nulling system used in our experiments correspond to the data published by Intaglietta et al. (1970). The evaluation of the pressure measurement system established its ability to follow rapid pressure changes, as for example, the monitoring of systolic...
FIGURE 1  A: In vivo microphotograph of a micropipet used for pressure measurements in microvessels of the ventricular myocardium. The pipet is inserted into the lumen of an epicardial venule of the rat heart. The picture was obtained by means of incident light microscopy. In close proximity to the dark venule, myocardial capillaries can be recognized showing a predominantly parallel pattern. B: In vivo fluorescence microphotograph of a micropipet used for microvascular pressure measurements in the beating mammalian heart. The pipet was inserted into an epicardial venule in the same way as shown in Figure 1A; the fluid within the micropipet is stained with FITC. On the left side of this picture, the oscilloscope tracings of aortic pressure (upper panel) and simultaneously measured pulsatile pressures in the small epicardial venule being investigated by micropuncture (lower panel) are recorded.
and diastolic pressures within the coronary microvasculature. The servo null system permitted registration of fast pressure variations in the same magnitude as the systemic arterial pressure simultaneously measured by means of a Statham P23Db strain gauge transducer. This statement is based upon simultaneous pressure measurements in carotid artery (Statham P23Db) and in a small coronary vessel (micropipet servo-nulling system). The statement also holds for recordings derived from the same pressure source, but obtained by the two different methods.

Artifacts of the pressure recordings generated by contact with the vessel wall could easily be recognized in a marked pressure rise within the servo-nulling system (>300 mm Hg), as discussed in the original report of this method (Wiederhielm et al., 1964). Thus, damped or erratic signals of the pressure measurement system indicated an improper position of the pipet. This facilitated control of its position which was particularly helpful during positive inotropic or chronotropic interventions.

**Results**

Micropuncture of larger and small coronary arterioles, or venules of the beating mammalian heart reveals reliable and reproducible pressure recordings. Thereby, the functional behavior of different compartments of the terminal vascular bed of the myocardium can be described. Due to anatomical arrangement, larger and small arterioles of the cat heart were more accessible to in vivo micropuncture compared to arterioles of the rat heart. In rats, most of the coronary arterial branches are embedded firmly in the myocardial tissue. Only few small coronary arteries of the rat heart branch within the epimyocardial layer and can thus be detected by incident light microscopy. In the cat heart, most arteries branch within the epimyocardial. Thus, larger coronary arterioles with diameters ranging from 150 to 300 \( \mu m \) can be punctured and made accessible to in vivo microscopy. Arterioles with diameters of less than 100 \( \mu m \) occasionally have been studied, but the observation period is more limited due to cardiac contraction. The above-mentioned reduction of the excessive movement of the cardiac tissue does not inhibit myocardial contraction, which in some instances may interfere with the maintenance of proper positioning of the micropipet within a small vessel lumen for a long period of time.

On the other hand, in both species, micropuncture of small veins and venules of superficial myocardial layers was facilitated by their topographical arrangement. Venules could easily be differentiated from arterioles because of the direction of flow at areas of bifurcation. Furthermore, in line with the observation of Ludwig (Ludwig, 1971), we also noticed that, prior to the confluence of capillaries and postcapillaries to form a venule, the capillary network becomes denser (Tillmanns et al., 1974).

In seven cats, micropuncture of 15 larger coronary arterioles with diameters ranging from 150 to 300 \( \mu m \) was performed. Under control condition, only a minute difference in systolic, diastolic, or mean pressures was observed between ascending aorta and the site of micropuncture \( (P < 0.005, \text{Tables } 1 \text{ and } 2) \). On average, the large coronary arteriolar:aortic pressure ratio during systole amounted to 0.97 (Table 2). Occasionally, no consistent pressure difference was noted between the aortic root and the measurement site in larger cor-

**Table 1**

<table>
<thead>
<tr>
<th>Peak systolic pressure (mm Hg)</th>
<th>100 ± 9</th>
<th>98 ± 7</th>
<th>67 ± 12</th>
<th>24 ± 0</th>
<th>23 ± 4</th>
</tr>
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<tr>
<td>Diastolic pressure (mm Hg)</td>
<td>71 ± 8</td>
<td>68 ± 8</td>
<td>45 ± 9</td>
<td>5 ± 2</td>
<td>4 ± 2</td>
</tr>
<tr>
<td>Mean pressure (mm Hg)</td>
<td>80 ± 8</td>
<td>73 ± 9</td>
<td>53 ± 9</td>
<td>11 ± 2</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>Vessel diameter (mean) (( \mu m ))</td>
<td>200 ± 49</td>
<td>209 ± 49</td>
<td>59 ± 32</td>
<td>148 ± 36</td>
<td>68 ± 15</td>
</tr>
</tbody>
</table>

Pulsatile and mean small vessel pressures are presented as mean ± 1 SD. \( \phi = \) vessel diameter (mean).

**Table 2**

<table>
<thead>
<tr>
<th>Arteriolar</th>
<th>Aortic Pressure Ratio in the Ventricular Myocardium of the Rat Heart</th>
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<tbody>
<tr>
<td>Large arterioles (150–300 ( \mu m ))</td>
<td>0.97 ± 0.03 (( n = 15 ))</td>
</tr>
<tr>
<td>Small arterioles (25–100 ( \mu m ))</td>
<td>0.71 ± 0.12 (( n = 7 ))</td>
</tr>
<tr>
<td>Coronary arteriolar: aortic pressure ratio</td>
<td>0.96 ± 0.03 (( n = 15 ))</td>
</tr>
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The pulsatile and mean coronary arteriolar: aortic pressure ratio is presented as mean ± 1 SD. This table contains only those small vessel pressures simultaneously recorded with aortic pressure. \( \phi = \) vessel diameter (mean).
Simultaneous recordings of pulsatile pressures in the ascending aorta (BP, upper panel) and in a large epimyocardial arteriole (diameter 150 μm) of the cat heart (CA, lower panel). Aortic pressure was determined with a strain gauge transducer; coronary arteriolar pressure was measured by means of the resistance servo-nulling device. Regarding both pressure curves, no consistent pressure difference can be noted. Furthermore, following application of norepinephrine, a parallel pressure rise can be recognized.

On coronary arterioles (Fig. 2). Coronary arteriolar pressure curves closely resembled aortic pressure tracings, during control periods as well as during pharmacological intervention. The intravenous application of norepinephrine (5–50 μg/min) (Fig. 2), nitroglycerin (20–30 μg/kg), or dipyridamole (0.5 mg/kg), respectively, failed to enhance the minimal pressure drop from aorta to the site of micropressure recording.

In recent experiments, we succeeded in measuring pulsatile pressures in smaller coronary arterioles (range of diameters 50–100 μm) (Tables 1 and 2). These smaller arterioles consistently showed a considerable pressure difference between aortic root and the site of micropuncture (Fig. 3) (P < 0.001, Table 1). The small coronary arteriolar:aortic pressure ratio during systole averaged 0.71 (Table 2).

In 25 rats and 7 cats, coronary venules were studied. Figure 4 shows the typical pressure curve of a coronary venule (diameter 50 μm); the simultaneously recorded aortic pressure is shown in the upper panel. In venules of the epimyocardium, the pressure curve exhibited a late systolic peak, occurring later than in aorta or coronary arterioles, just before aortic valve closure. Thereafter, venular pressure decreased and reached its minimum simultaneously with the aortic pressure.

Pulsatile and mean pressures were measured in 23 large coronary venules (diameter 100–200 μm) and in 19 small coronary venules (diameter 50–100 μm). Diastolic and mean small coronary venular pressures slightly exceeded diastolic and mean pressures in larger coronary venules (Table 1). During systole, no significant pressure difference was noted; systolic large and small coronary venular pressures averaged 24.4 or 22.8 mm Hg, respectively (Table 1).

In contrast to intramyocardial venules, an increase in coronary venular pressure in superficial venules was accompanied by an increase in vessel diameter, as shown in Figure 5. However, the graph represents only the correlation of peak systolic venular pressure to the largest diameter within the cardiac cycle. It does not represent a pressure volume diagram at steady pressure flow conditions. Therefore, the graph does not indicate the pressure volume characteristics of small coronary veins and venules.

Maximal coronary arteriolar dilation by intravenous injection of dipyridamole (in doses which af...
Small coronary venular pressures were determined by means of the resistance servo-nulling technique. Vessel diameters were obtained from television tape recordings following iv injection of FITC labeled dextran. In each experiment, small coronary venular pressure rise during systole was accompanied by an increase in vessel diameter.

In additional experiments, the effect of a positive inotropic intervention on coronary venular pressures of the rat heart was investigated. Following intravenous administration of the primarily β1-stimulating agent dobutamine (6 μg/kg per min) (Fig. 7), aortic pressure (upper panel) did not change significantly, whereas systolic coronary venular pressure increased (lower panel).

An increase in myocardial contractile force in conjunction with a rise of total peripheral resistance as caused by norepinephrine, also provoked a marked rise of systolic and mean coronary venular pressures (Fig. 8, upper panel); in the lower panel, aortic pressure is registered. The increase in coronary venular pressures following application of nor-epinephrine considerably exceeded the rise of coronary venular pressure observed after administration of dobutamine.

Discussion

The data reported here confirm that by means of the resistance servo-nulling system according to Wiederhielm (Wiederhielm et al., 1964; Intaglietta et al., 1970; Fox and Wiederhielm, 1973), pulsatile microvascular pressures can be reliably determined. This report extends the applicability of the micropipet servo-nulling system to the coronary microvasculature. Using our newly developed epillumination technique (Tillmanns et al., 1977; Steinhausen et al., 1978), microvessels of the ventricular myocardium could be visualized. By means of the resistance servo-nulling system, in arterioles and venules of the beating cat and rat heart, constant and reproducible pressure tracings were obtained. Simultaneously with our first data on pulsatile pressures in small vessels of the left ventricular myocardium of the rat heart (Tillmanns et al., 1977), other investigators (Nellis et al., 1977) also reported on pressure measurements in the microvasculature of the right heart. These authors used a transillumination technique similar to that previously described by our group (Tillmanns et al., 1974).

At this moment, an influence of our experimental conditions—reduction of cardiac tissue movement—on the data concerning pressure differences between aorta and large coronary arterioles cannot be completely excluded. On the one hand, the pressure drop along small coronary arteries and larger arterioles theoretically could be minimized by diminution of arteriolar kinking as well as by arteriolar dilation due to manipulative trauma (Lindbom et al., 1977). However, the latter, to some extent, is ruled out by the marked residual dilatory capacity of coronary arterioles under study following application of dipyridamole or nitroglycerin. On the other hand, any experimentally induced distortion or compression of the vessels studied would have resulted in a major pressure difference between aorta and the site of micropuncture, even in larger coronary arterial branches. This, however, was never observed in our experiments. Regarding coronary venular pressures, diastolic venular pressure in general was in the same range as right atrial and central venous pressures, indicating absence of venous outflow obstruction in the myocardial region under study. In only two cats was diastolic coronary venular pressure considerably higher than central venous pressure. In these experiments, more vigorous cardiac contraction necessitated a tighter restriction of cardiac movement. During all experiments included into this study, the lack of inflow and outflow disturbance was checked by monitoring capillary and venular blood flow velocity. Unphysiological compression resulted in a diminution of microvascular blood flow velocity, even in stasis.

In our studies, configuration of small coronary
Figure 6 Effect of intravenously administered dipyridamole on coronary venular pressure \( (P_{cv}, \text{vessel diameter } 135 \mu m) \) of the rat heart. Pulsatile coronary venular pressure (upper panel) was measured using the servo-nulling technique; aortic pressure \( (BP, \text{lower panel}) \) was determined by means of a strain gauge transducer. The application of dipyridamole resulted in a rise of aortic pressure pulse, whereas aortic mean pressure did not change significantly. On the other hand, a slight increase in systolic coronary venular pressure can be noted.

artery and arteriolar pressure curves closely followed aortic pressure, during control condition as well as during pharmacological interventions. In larger coronary arterioles (diameter 150-300 \( \mu m \)), neither the onset of pressure rise nor peak pressure was delayed compared to aortic pressure. In smaller arterioles (diameter 25-100 \( \mu m \)) of the left ventricular myocardium, however, peak pressures occurred 15-25 msec later than in the ascending aorta.

As already mentioned, larger arterioles (diameter 150-300 \( \mu m \)) of the left ventricular epimyocardium showed only minimal and inconsistent pressure differences between the ascending aorta and the site of micropuncture. The small pressure difference did not change following variations of arteriolar diameters induced by dipyridamole, nitroglycerin, or norepinephrine. A small pressure difference of about 5 mm Hg between the ascending aorta and relatively large branches (diameter 500-1000 \( \mu m \)) of major coronary arteries was reported by other authors (Fam and McGregor, 1968; Winbury et al., 1969; Cohen and Kirk, 1973), applying a differential pressure-amplifying system. This pressure drop was diminished by nitroglycerin (Cohen and Kirk, 1973). It is most likely that the differential pressure amplifier system used in those studies is more apt to elucidate variations of such minute pressure differences between the aorta and small coronary arteries or larger coronary arterioles, respectively, compared to the two different transducer systems used in our own experiments.

In contrast to small coronary arteries and larger arterioles, smaller arterioles (diameter 25-100 \( \mu m \)) of the left ventricular epimyocardium showed a consistent and considerable pressure drop compared to aortic pressure. In coronary arterioles with diameters of approximately 30 \( \mu m \), for example, the pressure difference amounted to 30% of aortic mean pressure. In agreement with previous results of other authors (Gregg, 1962; Burton, 1972), we were
able to demonstrate that, in the coronary vasculature, too, the greatest drop of pressure occurs in the arterioles. Our data on the magnitude of pressure differences compared to aortic pressure clearly elucidate that most of the vascular resistance to flow and the largest variability of vascular resistance are confined to small coronary arterioles, with diameters of less than 100 μm.

Small coronary venous and venular pressures have not been measured previously due to technical difficulties. In 1950, great cardiac vein pressure recordings were published (Gregg, 1950) which were of a shape similar to our coronary venular pressure tracings. In the great cardiac vein and in veins of the peripheral circulation, however, systolic pressure and pressure pulse did not reach the high values that were observed in small coronary veins. A marked variation of coronary sinus pressure due to respiration was described (Bostroem et al., 1965). In our experiments, however, coronary venular pressure did not change with respiration, but was markedly influenced by myocardial contraction. In each study, small coronary vein or coronary venular pressure was characterized by a late systolic peak, just before aortic valve closure.

It is most likely that this late systolic peak of coronary venular pressure is generated by the systolic contraction of the myocardium. The late systolic occurrence of peak pressure, compared to aortic and coronary arteriolar pressures, probably rules out the likelihood that systolic venular pressure originates from direct compression of the collecting vessels. Furthermore, the same pressure curve was noted in superficial venules of the epicardium, not even surrounded by any muscle fibers. On the other hand, data from our previous studies (Tillmanns et al., 1974) revealed a marked reduction of microvascular diameters during systolic contraction. These findings were confirmed later by other authors (Reus-Blom and Platteborse, 1974). All these data combined suggest the idea that systolic coronary venular pressure results from a pressure and volume wave generated by systolic compression of myocardial capillaries. In our experiments, this is confirmed by the observation of a concomitant systolic increase in diameters of the most superficial epicardial venules. Furthermore, our own data on microvascular blood flow patterns in the intact beating turtle and dog heart revealed a marked increase in capillary and venular cell velocity during ejection phases (Tillmanns et al., 1974). These data obtained from the terminal vascular bed of the ventricular myocardium are in good agreement with the macro-observations of enhanced coronary sinus outflow during systole, as previously described by other authors (Johnson and Wiggers, 1937; Gregg, 1962).

In line with the literature (Gregg, 1950; Burton, 1972), however, from these results it cannot be concluded that coronary venules constitute a significant proportion of total coronary resistance. The magnitude of the late systolic pressure in small coronary veins and venules is merely a function of the rhythmic contraction of the heart which, during systole, acts on the coronary vascular bed like a pump, restricting arteriolar inflow and propelling venular outflow. Consequently, a rise of left ventricular systolic and end-diastolic pressure due to an increase in afterload, as well as a faster and stronger myocardial contraction due to positive inotropic drugs, should enhance systolic coronary venular pressure. In agreement with this hypothesis, positive inotropic intervention by administration of the predominantly β1-stimulating agent, dobutamine (Robie et al., 1974; Vatner et al., 1974a; Tuttle and Mills, 1975; Gillespie et al., 1977; Goldberg et al., 1977; Loeb et al., 1977; Jewitt et al., 1978), as well as a rise of total peripheral resistance in conjunction with an increase in myocardial contractile force caused by norepinephrine (Berne et al., 1958; Pitt et al., 1967; Krayenbühl, 1969; Vatner et al., 1974b), resulted in a marked rise of systolic coronary venular pressure. The increase in mean coronary venular pressure was less marked. When
dobutamine in doses that did not provoke a systemic response (3–12 μg/kg per min) was used, a constant and considerable enhancement of systolic coronary venular pressure was observed. The increase in coronary venular pressures caused by norepinephrine considerably exceeded the coronary venular pressure rise following application of dobutamine. The more pronounced response to norepinephrine is easily explained by the combined effect of the drug on myocardial contractile force and on peripheral vascular resistance. 

On the other hand, the potent coronary vasodilator drug, dipyridamole, known to enhance total coronary flow by 360–400% (Bretschneider et al., 1959; Elliott, 1961; Bretschneider, 1963; de Graff and Lyon, 1963; Winbury et al., 1969) and to provoke only a slight reduction of left ventricular afterload, on average caused only a very small increase in systolic coronary venular pressure. In some experiments, during administration of this drug, systolic coronary venular pressures remained unchanged. This indicates that the contractile state of the myocardium and left ventricular afterload are major determinants of systolic coronary venular pressure. Therefore, the latter seems to be primarily a parameter of extravascular coronary support. However, further experiments will be necessary to quantify these observations. 

Pulsatile pressures in coronary arterioles and venules can be measured reliably by our above-described methods. This is an essential precondition for any attempt to evaluate and estimate the determinants of coronary pressure and flow. Simultaneous measurements of coronary microvascular blood flow velocities and microvessel diameters by means of fluorescent dextrans and fluorescent particles, using a method recently developed in our laboratory (Steinhausen et al., 1981), facilitate further investigation of the pharmacological response of the different compartments of the coronary vascular bed.

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