Mechanical Control of Coronary Artery Inflow and Vein Outflow

FUMIHIKO KAJIYA, M.D., Ph.D., KATSUHIKO TSUJIOKA, M.D., YASUO OGASAWARA, Ph.D.
KEIICHIRO MITO, B.S., OSAMU HIRAMATSU, MASAMI GOTO, M.D.
YOSHIFUMI WADA, M.D., AND SHUJI MATSUOKA, M.D.

To analyze the origin of the coronary artery inflow and the coronary vein outflow, we measured the intramyocardial artery flow and the epicardial small vein flow by means of a laser Doppler velocimeter with an optical fiber. The functional characteristics of the intramyocardial capacitance vessels were investigated by analyzing the responses of coronary vein flow after stepwise changes in coronary artery pressure during long diastole. Then the effect of the intramyocardial capacitance vessels on coronary artery inflow and vein outflow was evaluated. Intramyocardial artery flow was found to be almost exclusively diastolic with frequent systolic reverse flow, whereas peripheral coronary vein flow was almost systolic exclusively. The intramyocardial capacitance vessels have two functional components, unstressed volume and ordinary capacitance. When the unstressed volume was saturated, the intramyocardial displaceable blood volume impeded the coronary artery inflow, but promoted vein outflow.

PHASIC coronary flow is measured to determine the factors affecting coronary flow waveforms. Scaramucci (1689, cited by Porter¹) hypothesized that the deeper coronary vessels are squeezed by the contraction of the muscle fiber around them and the vessels are refilled from the aorta during diastole. To prove this hypothesis, it is necessary to investigate coronary artery inflow into and outflow from the myocardium. Since Anrep et al² investigated the circulation in the coronary artery and vein more than fifty years ago by making blood flow measurements using a hot wire method, there have been few reports^{3,4} describing artery inflow and vein outflow. This is partly because measurement of coronary vein flow using conventional

methods including the electromagnetic flowmeter has until recently been difficult, and because the vein was regarded as the only conduit of coronary artery outflow.

Our laser Doppler velocimeter (LDV) with an optical fiber is a powerful new tool for the measurement of both coronary vein flow and coronary artery flow. The most important advantage of the LDV method over conventional velocimeters is its excellent accessibility to the vessel, even when the vessel is as easily collapsible as a vein^{5,6,7}

In this paper, we would like to report on some of the results obtained by application of our LDV to three areas of study: (1) intramyocardial coronary artery and epicardial small vein flow velocity waveforms, (2) the functional characteristics of intramyocardial capacitance vessels⁸ and (3) the effect of the intramyocardial capacitance vessels on coronary artery inflow and vein outflow.

Key words:

Septal artery flow
Coronary vein flow
Intramyocardial capacitance vessels
Coronary artery pressure/flow relation
Unstressed volume

Department of Medical Engineering and Systems Cardiology, Kawasaki Medical School, Kurashiki, Japan
Grants-in-Aid for Scientific Research from the Ministry of Education, Culture and Science 62480220

Mailing address: Fumihiko Kajiya, M.D., Professor, Department of Medical Engineering and Systems Cardiology, Kawasaki Medical School, 577 Matsushima, Kurashiki 701-01, Japan

Fig.1. Schematic diagram of the laser Doppler velocimeter with an optical fiber. For velocity measurement of the septal artery, the fiber was inserted into the artery from the cardiac surface (access 1). For measurement of small vein velocity, the fiber tip was placed on the vessel wall (access 2).

METHODS

1. Laser Doppler velocimeter with an optical fiber

The laser Doppler velocimeter with an optical fiber has been described in detail elsewhere by Kajiya et al.^{9,10,11} and Nishihara et al.¹² In summary, a He-Ne laser beam is introduced onto the vascular surface or into the vascular lumen through an optical fiber (Fig. 1). Part of the light back-scattered by flowing erythrocytes is collected by the same fiber and transmitted back. The back-scattered light is detected by an avalanche photodiode and the photocurrent from the diode is analyzed by a spectrum analyzer to detect Doppler shift frequencies.

2. Animal preparation and experimental procedure

Mongrel dogs were anesthetized with sodium pentobarbital (25 mg/Kg i.v.). After intubation, they were ventilated by a Harvard respirator pump with room air, which was supplemented with 100% oxygen at a rate sufficient to maintain arterial oxygen tension at a physiological level. A left thoracotomy was performed at the 4th or 5th intercostal space. The heart was exposed and suspended in a pericardial cradle.

(i) Measurements of coronary artery and vein flow velocities

The targets of measurements in this study were the septal artery and the small branch of the interventricular vein. For blood velocity measurement of the septal artery, the optical fiber was inserted into the artery from its origin (access 1 in Fig. 1).¹³ The measurements were obtained at a depth of 10–20 mm from the entrance of the artery. The position of the fiber tip was changed by monitoring the Doppler signal. When a maximum and steady signal was obtained, the fiber was fixed with a drop of cyanoacrylate on the cardiac surface. For measurements of the small branch of the interventricular vein, vessels with an outer diameter of about 150–500 μ m were chosen so that their vascular walls were transparent to the laser light. The fiber tip was positioned and fixed on the vessel wall (access 2 in Fig. 1) to measure the blood flow velocity.

(ii) Analysis of functional characteristics of intramyocardial capacitance vessels⁸

The peripheral portion of the great cardiac vein (GCV) in A-V node blocked dogs was isolated and the optical fiber tip was inserted into the vessel. Both the left main coronary artery (LM) and the left anterior descending coronary artery (LAD) were cannulated and connected to

Fig.2. The experimental protocol. Coronary inflow was shut off and then great cardiac vein flow decreased. Fifteen seconds after inflow cannula occlusion, a long diastole was induced. Two seconds later, the cannula was reopened and the perfusion pressure was increased stepwise. The response of the vein outflow was analyzed. Redrawn from Kajiya et al.⁸

Fig.3. A typical example of the blood flow velocity in the deep portion of the septal artery with other hemodynamic variables. AoP: aortic pressure. IMP: intramyocardial pressure. LAD: left anterior descending coronary artery.

a reservoir to regulate perfusion pressure. Coronary inflow and perfusion pressure were measured at the peripheral portion of the cannula inserted into the LAD. During continuous infusion of adenosine into the coronary artery, the cannulae were occluded to shut off the LAD flow (Fig. 2). The blood velocity in the GCV decreased and reached a minimal steady value within 15 sec. Then a long diastole was induced by the cessation of pacing. Two seconds after the cessation of

pacing, the cannulae were reopened and the perfusion pressure was increased stepwise to a preset target pressure. The time course of the GCV flow velocity was analyzed after the initiation of reperfusion.

(iii) Evaluation of the effect of the intramyocardial capacitance vessels on coronary artery inflow and vein outflow

To investigate the effect of the intramyocardial capacitance vessels on coronary vein outflow, the initial part of the protocol shown in Fig. 2 was used; The time course of the GCV flow velocity was analyzed after occlusion of the cannulae. The GCV velocities before the cannulae occlusion were altered to various values by changing the perfusion pressure and vasomotor tone to determine the relation between the GCV velocities before occlusion and the squeezed out process of the blood after occlusion.

To evaluate the effect of the intramyocardial capacitance vessels on coronary artery inflow, the last part of the protocol in Fig. 2 was used. The target pressure after the reopening of the cannulae was changed at 7 different levels. The pressure flow (P/F) relation was analyzed for different conditions in the intramyocardial capacitance vessels.

RESULTS

(i) Coronary artery and vein blood flow velocities.

Figure 3 shows a typical example of the blood flow velocity in the deep portion of the septal

Fig. 4. A representative tracing of the blood flow velocity in small branches of the interventricular vein with left ventricular pressure.

Fig. 5. A representative tracing of variables recorded during a trial. the coronary vein flow was absent for about 1 second (dead time) and increased with the first order time delay after reperfusion. CPP: coronary perfusion pressure. CBF: coronary artery blood flow (LAD). GCV-V: great cardiac vein velocity. Redrawn from Kajiya et al.⁸

artery (15–20 mm depth from its origin). The velocity waveform in the septal artery displays a diastolic-predominant pattern which is characteristic of the phasic pattern of left coronary artery blood flow. Unlike proximal epicardial artery flow, a reverse flow was almost always observed in the septal artery and a systolic forward flow was negative or negligibly small.

Figure 4 shows a representative tracing of the vein flow velocity waveform in a small branch of the interventricular vein. The small peripheral vein flow exhibited a systolic-predominant flow which is the characteristic of coronary vein flow. However, the onset of the flow was earlier, the flow acceleration was higher and the diastolic flow component was much smaller than those in the GCV and the coronary sinus flows.^{14,15} Therefore, the difference in the phase of the velocity waveforms was more prominent between the septal artery and the peripheral coronary vein than those in the large epicardial artery and vein.

(ii) The function characteristics of intramyocardial capacitance vessels⁸

The time course of the coronary hemodynamic data along the protocol shown in Fig. 2 is displayed in Fig. 5. After occlusion of the coronary inflow, the GCV decreased and reached a minimal value. Then it fell to zero with the cessation of pacing. After reopening the inflow, it was still absent for a few seconds (dead time). Then it reappeared and increased with the first order time delay. The presence of the dead time indicates the existence of unstressed volume in the intramyocardial vascular compartment which is defined as the volume of the blood in a vessel at zero transmural pressure. The time constant of the first order delay relates to the product of resistance and capacitance of the diastolic coronary circulation with minimal vasomotor tone. The unstressed volume was estimated from the coronary artery inflow during the dead time and resulted in a value of 5.2 ml/100 gLV (Fig. 6). The value of capacitance was obtained by di-

Fig.6. Mechanical lumped model representing the characteristics of the intramyocardial capacitance vessels and estimated values of the unstressed volume, the capacitance and the resistance. Redrawn from Kajiya et al.⁸

Fig.7. A typical example of the decaying process of the coronary vein flow velocity after coronary inflow occlusion. The great cardiac vein flow decreased exponentially. GCV: great cardiac vein.

viding the time constant by the resistance. The estimated capacitance value was 0.08 mg/mmHg/100 gLV.

(iii) Effect of intramyocardial capacitance on coronary artery inflow and vein outflow

Figure 7 shows the decaying process of the GCV flow velocity after coronary inflow occlusion. It should be noted that the GCV flow decreased exponentially. Thus, the process can be expressed as

$$\tilde{V}_{GCV} = V_{GCV} e^{-\frac{t}{\tau}} \quad \dots \dots \dots (1)$$

where $\tilde{V}_{GCV}$ is the decaying velocity after the inflow occlusion, V_{GCV} is the initial velocity before occlusion and τ is the time constant. Integration of Eq. (1) with respect to time t gives

$$\int_0^{\infty} V_{GCV} e^{-\frac{t}{\tau}} dt = V_{GCV} \cdot \tau \quad \dots \dots \dots (2)$$

The value of $V_{GCV} \cdot \tau$ implies the total squeezable (displacable) volume V_0 stored in the intramyocardial capacitance vessel before occlusion:

$$V_0 = V_{GCV} \cdot \tau \quad \dots \dots \dots (3)$$

It follows

Fig.8. The relationship between the great cardiac vein and the total squeezable (displacable) blood volume in the intramyocardial vessels and that between the vein flow and the time constant. The former relationship showed a significant correlation, but the latter did not.

Fig.9. Responses of the great cardiac vein flow for different perfusion pressures. The left anterior descending coronary artery flow appears to be greater before the appearance of the great cardiac vein flow. CPP: coronary perfusion pressure. CBF: coronary artery blood flow (LAD). GCV-V: great cardiac vein velocity.

$$V_{GCV} = V_0/\tau \quad \dots\dots\dots (4)$$

Then, the problem is "which parameter is more sensitive to the change in V_{GCV} , τ or V_0 ?" Fig. 8 shows the relations between V_{GCV} and V_0 and between V_{GCV} and τ . The correlation coefficient between the total squeezable (displacable) volume and the coronary vein flow was

significantly high ($p < 0.01$), whereas the relation between the time constant and the vein flow was not statistically significant.

Figure 9 shows an example of the GCV responses following stepwise increase in the perfusion pressures. Recall that the intramyocardial capacitance vessels functionally consist of unstressed volume (UV) and ordinary capacitance. The delayed onset of the GCV flow indicates an initially unfilled condition of the unstressed volume (UVunfill) and the resumption of the GCV flow implies a filled condition (UVfill). Fig. 10 shows a typical example of the pressure flow (P/F) relations before and after resumption of the GCV flows. The LAD velocities for given coronary artery pressures were always higher when the GCV flows were absent, i.e., the UV was unfilled. The slope of the P/F relation for UVunfill was steeper than that for UVfill, whereas there was no difference in the zero flow pressure intercept between the two.

DISCUSSION

The capacitance effect of epicardial coronary arteries and veins may lead to a misinterpretation of the actual inflow pattern to and outflow pattern from the myocardium. To avoid and/or to minimize the effect of epicardial coronary vessels, we measured the septal artery flow velocity and the small peripheral vein flow velocity by our LDV with an optical fiber.

Fig.10. A typical example of the pressure/flow relations before and after resumption of the great cardiac vein (GCV) flows. The left anterior descending coronary artery flow was smaller when the GCV flow reappeared.

The velocity waveform in the septal artery was characterized by (1) a forward flow which was almost exclusively diastolic and (2) a reverse flow in most cases, although the velocity waveform in the proximal coronary artery includes considerable systolic forward flow. These observations are in agreement with the report by Chilian and Marcus.¹⁶ Carew et al¹⁷ reported that the diastolic-predominancy existed in the septal artery as measured by an electromagnetic flowmeter, although a significant forward flow was recognizable in their original tracing. The systolic forward flow in their data may be the result of zero-flow instability of the electromagnetic flowmeter and/or vascular stenosis due to application of the cuff around the septal artery. Small peripheral vein flow was characterized by a systolic predominant pattern. The diastolic forward flow component was much smaller than that in great cardiac vein flow and coronary sinus flow. Therefore, the phase opposition between artery inflow and vein outflow was much clearer between the septal artery flow and the small peripheral coronary vein flow.

The phase opposition between coronary artery and vein flow can only be explained by the intramyocardial capacitance vessels,¹⁸ which store the artery inflow during diastole and squeeze it out to the coronary vein during systole. We investigated the functional characteristics of the intramyocardial capacitance vessels and found that

they functionally consist of "unstressed volume" and "ordinary capacitance".⁸ With vessels embedded in tissue as intramyocardial vessels, transmural pressure at a volume less than the unstressed volume may be negative. To return the vessels from a collapsed to cylindrical configuration requires only a small change in the intraluminal pressure. This characteristic of the vessels may contribute to the unstressed volume. This volume may be attributable to veins and also to capillaries. The unstressed volume is approximately 5% of the myocardium and the time constant in relation to ordinary capacitance is about 1 second.

Coronary vein flow before coronary inflow occlusion was related closely to the total displaceable blood volume after occlusion, but no significant correlation with the time constant was observed. This indicates that the coronary vein flow is mainly dependent on the total displaceable blood volume stored in the intramyocardial capacitance vessels, i.e., the more intramyocardial blood volume, the more coronary vein flow. Although the real reason for the close correlation between the intramyocardial blood volume and the coronary vein flow is unclear, the relationship is of interest, especially in analogy with the "Starling law" of the heart. The Gregg effect⁷ may be partly related to this relationship.

The filled state of the unstressed volume in the intramyocardial vessels can be estimated by

the presence of the GCV flow velocity and inversely, the unfilled state can be judged by absence of the flow. This is because when the unstressed volume is not saturated, its intraluminal pressure is less than or equal to the GCV pressure and the flow remains at zero level, but when it is filled with blood, the inside pressure exceeds the outflow pressure and the GCV flow resumes. The LAD flows for the given LAD pressures were smaller for the filled state of the unstressed volume. This is interesting as it indicates negative mechanical feedback to the coronary artery inflow due to the condition of the intramyocardial capacitance vessels, i.e., the increase in the blood volume in the intramyocardial vessels decreased the coronary artery inflow. Since the P/F relation was linear ($r = 0.97-0.99$), we simply estimated the slope of the relation and the zero-flow intercept by a linear regression. The slope was steeper when the unstressed volume was not filled, but the zero-flow intercept was unchanged under both conditions, filled and unfilled. However, it could not be concluded that the major determinant of the difference in the coronary inflow as a result of the change in the state of unstressed volume is the resistance rather than the back pressure, since we did not examine the linearity of the P/F relation for very low flow regions or the pressure dependent change in the resistance.

In summary, we observed the following. (1) The velocity waveform in the intramyocardial artery was almost exclusively diastolic, while that in the small peripheral epicardial vein was systolic. (2) The intramyocardial capacitance vessels have two functional components, unstressed volume and ordinary capacitance. (3) The systolic coronary vein outflow is closely related to the total displacable blood volume in the intramyocardial capacitance vessels. (4) When the unstressed volume was saturated, the diastolic coronary inflow was decreased significantly by reducing the slope of the linear regression of the pressure/flow relationship.

REFERENCES

1. PORTER WT: The influence of the heart-beat on the flow of blood through the walls of the heart. *Am J Physiol* 1: 145, 1898
2. ANREP GV, CRUICKSHANK EWH, DOWNING AC, SABBA RA: The coronary circulation in relation to the cardiac cycle. *Heart* 14: 111, 1927
3. CHILIAN WM, MARCUS ML: Coronary venous outflow persists after cessation of coronary arterial inflow. *Am J Physiol* 247: H984, 1984
4. SPAAN JAE: Intramyocardial compliance studied by venous outflow at arterial occlusion (abstr). *Circulation* 66 (Suppl II): 42, 1982
5. KAJIYA F, TSUJIOKA K, GOTO M, WADA Y, TADAOKA S, NAKAI M, HIRAMATSU O, OGASAWARA Y, MITO K, HOKI N, TOMONAGA G: Evaluation of phasic blood flow velocity in the great cardiac vein by a laser Doppler method. *Heart and Vessels* 1: 16, 1985
6. KILPATRICK D, LINDERER T, SIEVERS RE, TYBERG JV: Measurement of coronary sinus blood flow by fiber-optic laser Doppler anemometry. *Am J Physiol* 242: H1111, 1982
7. HELLENBRAND WK, KLASSEN GA, ARMOUR JA, SEZERMAN O, PATON B: Automatic nervous system regulation of epicardial vein systolic and diastolic blood velocity as measured by a laser Doppler velocimeter. *Can J Physiol Pharmacol* 46: 1463, 1986
8. KAJIYA F, TSUJIOKA K, GOTO M, WADA Y, CHEN X-L, NAKAI M, TADAOKA S, HIRAMATSU O, OGASAWARA Y, MITO K, TOMONAGA G: Functional characteristics of intramyocardial capacitance vessels during diastole in the dog. *Circ Res* 58: 476, 1986
9. KAJIYA F: Laser Doppler blood velocimetry with optical fiber. Digest of 2nd International Conference on Mechanics in Medicine and Biology p 16, 1980
10. KAJIYA F, HOKI N, TOMONAGA G, NISHIHARA H: A laser-Doppler-velocimeter using an optical fiber and its application to local velocity measurement in the coronary artery. *Experientia* 37: 1171, 1981
11. KAJIYA F, HIRAMATSU O, MITO K, OGASAWARA Y, TSUJIOKA K: An optical fiber laser Doppler velocimeter and its application to measurements of coronary blood flow velocities. *Med Prog Tech* 12: 77, 1987
12. NISHIHARA H, KOYAMA J, HOKI N, KAJIYA F, HIRONAGA M, KANO M: Optical fiber laser Doppler velocimeter for high-resolution measurement of pulsatile blood flow. *Appl Optics* 21: 1785, 1982
13. MITO K, OGASAWARA Y, HIRAMATSU O, WADA Y, GOTO M, TADAOKA S, TSUJIOKA K, KAJIYA F: Evaluation of velocity waveform in a intramyocardial small artery and vein by laser Doppler method. *Circulation* 76 (Suppl IV): 386, 1987
14. SCHOLTHOLT J, LOCHNER W: Systolischer und diastolischer Anteil am Coronarsinusaussfluß in Abhängigkeit von der Größe des mittleren Ausflusses. *Pflügers Arch* 290: 349, 1966
15. STEIN PD, BADEER HS, SCHUETTE WH, GLASER JF: Pulsatile aspects of coronary sinus blood flow in closed-chest dogs. *Am Heart J* 78: 331, 1969
16. CHILIAN WM, MARCUS ML: Phasic coronary blood flow velocity in intramural and epicardial coronary arteries. *Circ Res* 50: 775, 1982
17. CAREW TF, COVELL JW: Effect of intramyocardial pressure on the phasic flow in the interventricular septal artery. *Cardiovasc Res* 10: 56, 1976

18. SPAAN JAE, BREULS NPW, LAIRD JD: Diastolic-systolic coronary flow differences are caused by intramyocardial pump action in the anesthetized dog. *Circ Res* 49: 584, 1981
19. GREGG DE: Effect of coronary perfusion pressure or coronary flow on oxygen usage of the myocardium. *Circ Res* 13: 497, 1963