PRESIDENT LECTURE

CORONARY COLLATERAL CIRCULATION

— Its Development and Function —

TOMOHIRO KANAZAWA, M.D.

FOR more than 3 centuries, researchers have studied the development and function of coronary collateral circulation formed by interarterial coronary anastomoses^{1,2}. As early as 1669, Lower demonstrated the existence of intercoronary arterial anastomoses in a human heart, by observing fluid injected into one coronary artery pass into another. In 1881, Cohnheim and von Schulthess-Rechberg denied the existence of interarterial communication in coronary circulation and declared that coronary arteries were anatomical endarteries. Between 1938–1941, this concept was disproved by Schlesinger, Blumgart and coworkers^{3–5} since they demonstrated that only a few, small precapillary intercoronary anastomoses pre-existed in the normal human heart, but that numerous, large intercoronary anastomoses existed in hearts with severe coronary stenosis or obstruction. They used postmortem unrolled roentgenography after injecting right and left coronary arteries with lead phosphate-agar mass. They also pointed out that these anastomoses developed as compensatory collateral circulation under conditions such as severe coronary stenosis or obstruction. Since then, many investigators have recognized experimentally or clinicopathologically that the development of collaterals formed by intercoronary arterial anastomoses is a natural compensatory and protective mechanism in the ischemic heart and that this collateral circulation is impor-

tant in reducing the extent of possible pathological ischemic myocardial damage.

Selective coronary angiography has recently permitted the accurate visualization and delineation of major coronary collateral vessels in the human heart with coronary obstruction during life⁶ and has stimulated renewed interest in the clinical and functional significance of collaterals. Many investigators have examined the clinical significance of coronary collateral circulation in coronary obstructive heart disease.

However, these studies have given rise to conflicting opinions about the functional significance of coronary collaterals. Several studies have reported that collaterals do not protect the heart from developing myocardial ischemic changes, such as myocardial infarction or abnormalities of left ventricular contraction and performance^{7–18}. On the other hand, several studies have indicated that collaterals have beneficial effects and protect against the development of myocardial ischemic changes and ventricular dysfunction^{19–30}.

For the past 30 years, my colleagues and I have studied the development and function of coronary collateral circulation formed by interarterial coronary anastomoses experimentally, clinicopathologically and clinically. This report describes the results of some of these studies.

Experimental Studies of Coronary Collateral Circulation

I. Interarterial Coronary Anastomoses in Normal Adult Dogs

Key words:

Interarterial coronary anastomoses
Coronary collateral circulation
Coronary obstruction
Myocardial infarction
Coronary collateral dysfunction/insufficiency

The Second Department of Internal Medicine, Akita University School of Medicine, Akita, Japan
Mailing address: Tomohiro Kanazawa, M.D., Nakadori 3-4-47-710, Akita 010, Japan

Fig.1. Coronary arteriogram of a dog heart soon after acute ligation of the left anterior descending coronary artery (LAD) (upper panel). Coronary arteriogram of a dog heart 5 weeks after acute ligation of the LAD (lower panel). LC: left circumflex coronary artery, R: right coronary artery, S: septal artery. Arrow indicates the point of ligation.

Inter coronary anastomoses in normal adult dogs were studied. A colored barium gelatin dye mixture was injected into the left and right ostium of coronary arteries of the isolated heart according to the modified Schlesinger's method, and the distribution and the direction of the anastomoses were studied macroscopically and roentgenologically after the heart was unrolled.

The results were as follows:

- 1) In normal adult dogs, the average number of interarterial coronary anastomoses with diameters exceeding $100\ \mu\text{m}$ was 11 per dog, but most were between $100\text{--}200\ \mu\text{m}$ in diameter, few anastomoses over $200\ \mu\text{m}$, and none were over $500\ \mu\text{m}$ in diameter.
- 2) Anastomoses to the left anterior descending coronary artery accounted for 70% of all anastomoses. Anastomoses larger than $100\ \mu\text{m}$ in diameter were found near the surface of the heart, but not in the deep layer of

Fig.2. Development of intercoronary anastomoses following acute occlusion of the left anterior descending coronary artery.

the myocardium.

II. Development and Function of Coronary Collateral Circulation

Many factors influence the development and function of coronary collateral circulation, i.e., presence of myocardial ischemia (relative or absolute), coronary obstruction (speed, location and number of obstructions), number and caliber of available anastomoses, type of anastomoses (inter-, intra-, extra-), quality of runoff beyond the point of obstruction, integrity of donor arterial tree, integrity of pre- and postanastomotic arterioles, anatomic pattern of large coronary arteries, transanastomotic pressure gradient, time, myocardial contractility (general and local), cardiac rhythm and conduction, metabolic and neurohumoral factors, viscosity of blood, drugs and possibly exercise.

Of these numerous factors, the most potent stimulus for the development of coronary collaterals is coronary obstruction itself. In this condition, the creation of a pressure gradient across the collateral vessels between the donor and recipient coronary arteries

Fig.3. The relation between the critical value of coronary blood flow for the ST elevation and the number of intercoronary anastomoses

and severe myocardial ischemia trigger collateral enlargement, growth and development.

From this standpoint, development and function of coronary collateral circulation following coronary occlusion were examined experimentally.

1. Development and Function of Coronary Collateral Circulation Following Acute Coronary Occlusion

In normal adult dogs, acute ligation was performed on the left anterior descending coronary artery. The dogs were divided into 7 groups based on survival time after ligation. From 1 to 10 weeks after ligation, the regional myocardial blood flow at the perfused area of the ligated artery was measured by the hydrogen gas clearance method, while the blood flow in the left coronary artery was measured continuously by an electromagnetic flowmeter. Direct unipolar lead electrocardiograms (ECG) of the left ventricular surface of the peripheral area of the ligated artery were recorded. A coronary arteriogram of the removed hearts was then taken by the modified Schlesinger's method and the intercoronary anastomoses which formed between the periphery of the occluded artery and the donor arteries were counted using this coronary arteriogram and the dissected hearts. They were classified by caliber into large ($>300\mu\text{m}$), middle ($300-200\mu\text{m}$) and small ($200-100\mu\text{m}$). Finally,

the myocardium was examined histologically.

The results were as follows:

1) In all of the cases that survived after coronary ligation, retrograde filling of the contrast medium was observed from the peripheral branches of the ligated artery (i.e., anastomoses) up to the occluded area. The speed of filling was faster in dogs examined 4 weeks or more after ligation than in dogs examined 1-3 weeks after ligation. On the other hand, retrograde filling of contrast medium was not observed in those that died soon after the ligation (Fig. 1).

The total number of anastomoses to the ligated artery began to increase in the 2nd week after ligation to more than that observed in normal dogs. This number continued to increase remarkably up to 5 weeks. No additional increase was found after 5 weeks. The number of small anastomoses increased until the 5th week after ligation and then decreased, while the number of middle and large anastomoses also increased until the 5th week, and increased only slightly thereafter (Fig. 2).

2) Soon after coronary ligation, the regional myocardial blood flow in the superficial layers of the peripheral area of ligation fell to nearly zero, then began to recover gradually within 1 week and returned to near-normal values 3-4 weeks after ligation. However, recovery of the blood flow in the deep layers was slow, and required about 5

Fig.4. The relation between the regional myocardial blood flow and the critical value of coronary blood flow for the ST elevation.

weeks.

A significant correlation was observed between the rate of regional myocardial blood flow recovery and the number of anastomoses that developed and the length of time survived.

3) In dogs that were observed within 1–2 weeks after ligation, the ST segment was always elevated in the ECG recorded with direct unipolar leads from the ventricular surface of the peripheral area of the ligated artery. This ST segment elevation could be eliminated by augmenting the left coronary blood inflow, but a large quantity of blood was needed. On the other hand, in dogs that survived 5 weeks or more after coronary ligation, these critical values of the coronary blood flow for ST deviation were lower than those in dogs that survived only 1–2 weeks. Similar findings were also observed in the critical values of the coronary oxygen supply and the myocardial oxygen consumption.

There was a significant inverse correlation between these critical values of coronary blood flow for ST elevation and the number of developed anastomoses and the length of time survived (Fig. 3). Moreover, the regional myocardial flow showed a significant inverse correlation with the critical value of coronary blood flow for ST elevation (Fig. 4).

These results indicate that the periphery of the ligated artery is nourished by the blood

flow through the collaterals which develop to the ligated artery.

4) Histologically, myocardial infarction was observed in the perfused area of the ligated artery in all cases, but the infarcted area was generally much smaller than the perfused territory of the ligated artery, and the degree of infarction was lower in the abundant-collateral group than the poor-collateral group. This natural salvage of tissue may also be related to the collateral circulation and the supply of an alternative source of arterial blood.

The above results suggest that pre-existing interarterial coronary anastomoses develop into collaterals to the occluded artery until the 5th week after coronary occlusion. In the cases that survived longer after coronary occlusion, more collaterals developed which compensated for the circulatory insufficiency, and thus limited the infarct size due to acute coronary occlusion.

2. The Collateral Source in Coronary Occlusion

One of the most important factors in the development of collaterals to the obstructive coronary artery is the existence and integrity of donor arterial trees; that is, the collateral source.

From this standpoint, coronary collateral sources were studied in dogs in which either the left anterior descending coronary artery

Fig.5. Plane coronary arteriogram and transverse slices of the left ventricle of the heart of a dog which survived for 5 weeks after ligation of the left circumflex coronary artery (LC) and which underwent acute ligation of the left anterior descending coronary artery (LAD) before 5 weeks. R: right coronary artery, S: septal artery. Arrows indicate points of points ligation.

(LAD), the left circumflex coronary artery (LC), or the right coronary artery (RC) were acutely ligated. Five weeks after coronary ligation, the formation of collaterals and collateral sources to the ligated artery were observed by postmortem arteriogram according to the previously described modified Schlesinger's method.

All of the groups showed remarkable development of collaterals. When the collateral source of each group was examined, the collateral supply to the occluded LAD was found to stem from the LC and RC, while that to the occluded LC stemmed from the LAD and RC, and that to the occluded RC from the LC and LAD.

Furthermore, we also studied the collateral sources in dogs which survived for 5 weeks after acute LC ligation and which underwent

acute LAD ligation within 5 weeks, in dogs which survived for 5 weeks after acute LAD ligation and which underwent acute RC ligation before 5 weeks, and in dogs which survived for 5 weeks after acute LC ligation and which underwent acute RC ligation before 5 weeks. All of the survivors showed abundant intercoronary and intracoronary collateral formation to the occluded arteries (Fig. 5).

These findings indicate that interarterial coronary anastomoses which develop as collaterals following coronary occlusion, when supplied with appropriate collateral sources, can form effective collateral circulation, not only for a single occluded main coronary artery, but also for two occluded main coronary arteries at different times.

Fig. 6. A comparison of max dp/dt (upper panel) and % systolic shortening (%SS) in the area of the occluded left anterior descending coronary artery (lower panel) between acute occlusion (ACO) and ACO following microsphere embolization (MSO).

3. Protective Role of Collateral Circulation During Acute Coronary Occlusion

The role of collateral circulation during acute coronary occlusion was assessed by comparing regional myocardial function and metabolism between acute coronary occlusion (ACO) and ACO following massive microsphere embolization (MSO). On open-chest dogs, the left anterior descending coronary artery (LAD) was perfused via a bypass from the carotid artery. ACO of the LAD was performed by occluding the bypass to the LAD. Two pairs of microcrystals and an epicardial ECG were instrumented in the LAD and circumflex artery areas. A tissue PCO₂ sensor was installed in the LAD area. Microspheres (100 mg of 15 μ m) were infused into the bypass to block both microcir-

ulation and collateral circulation in the LAD area.

The results were as follows:

- 1) Left ventricular function, expressed as max dp/dt, and regional myocardial function, expressed as % systolic shortening in the LAD area, significantly decreased during MSO, as compared with ACO (Fig. 6).
- 2) Epicardial ST deviation and tissue PCO₂ were greater during MSO than during ACO in the LAD area.

Therefore, we concluded that collateral circulation plays a protective role during acute coronary occlusion.

4. The Functional Role of Collateral Circulation on Regional Myocardial Function and Metabolism in Acute, Subacute and Chronic Phase After Coronary Occlusion

The functional role of collateral circulation on regional myocardial function and metabolism was evaluated in dogs; in acute, subacute and chronic phase after acute coronary occlusion.

A solid plug was embolized to the left anterior descending coronary artery (LAD) using a coaxial catheter system in closed-chest dogs. Dogs were examined 3 min (A group), 1 week (S group) and 3 months (C group) after occlusion. In these groups, coronary collateral development was assessed from peripheral coronary pressure of the occluded LAD (PCP) and postmortem coronary arteriogram. Regional myocardial function was evaluated by sonomicrometry. Venous blood from the LAD area was sampled and used to assess regional myocardial metabolism.

Postmortem coronary arteriogram demonstrated well-developed collaterals in C group, poorly developed collaterals in S group and only a few collaterals in A group. The diastolic PCP increased in the following order; A group, S group, C group (19.17 ± 6.49 , 40.54 ± 17.24 , 67.61 ± 13.52 mmHg, $P < 0.001$). The systolic PCP increased in the same order; A group, S group, C group (45.71 ± 16.80 , 78.5 ± 23.04 , 96.44 ± 13.39 mmHg, $P < 0.001$). Regional myocardial function, expressed as % systolic shortening (%SS) in the LAD area, improved in the following order; A group, S group, C group (-6.0 ± 3.7 , 1.4 ± 6.8 , $9.3 \pm 5.8\%$, $P < 0.001$). There was a significant correlation

Fig. 7. The relation between % systolic shortening (%SS) in the ligated left anterior descending coronary artery (LAD) and diastolic peripheral coronary pressure of the occluded LAD (PCPd)/diastolic aortic pressure (AoPd). ■: A group, ◆: S group, ●: C group

between %SS and diastolic PCP/diastolic aortic pressure (Fig. 7). However, the %SS in C group was still less than the %SS in a normal control group ($14.3 \pm 4.4\%$). Regional myocardial metabolism also improved in the same order; O_2 uptake ratios, ΔPCO_2 and ΔpH decreased, and lactate uptake ratios increased. Histologically, the average size of myocardial infarction was 18% of the left ventricle in S group and 4% in C group ($P < 0.001$).

These results suggest that the coronary collateral circulation which develops after acute coronary occlusion plays an important role in the recovery of regional myocardial function and metabolism. It not only repairs the infarcted myocardium, but also washes out metabolic product and supplies oxygen to the ischemic myocardium, however, it does not irreversibly repair the damaged myocardium completely.

5. The Time Course of Left Ventricular Function and Coronary Collateral Development After Acute Coronary Occlusion

The time course of left ventricular function and coronary collateral development after acute coronary occlusion was studied for 4 weeks in closed-chest dogs. To produce an acute coronary occlusion, a solid plug was embolized to the left anterior descending

coronary artery using a coaxial catheter system in closed-chest dogs. In the dogs which survived for 4 weeks, serial coronary angiogram and left ventricular function were evaluated before and 1, 2 and 4 weeks after acute coronary occlusion.

Serial coronary angiographic evaluation showed that collateral development was poor 1 week after coronary occlusion, but all of the cases had good collateral development at 4 weeks (Fig. 8). One week after occlusion, left ventricular systolic pressure, max dp/dt and cardiac output were significantly lower than those before occlusion. These hemodynamic variables tended to improve 2 weeks later, and returned to nearly the level prior to occlusion at rest and during a moderate atrial pacing rate 4 weeks after acute coronary occlusion. However, left ventricular function gradually decreased as pacing rate was increased. Histologically, myocardial infarction was observed in all of the cases.

Based on these results, we concluded that collateral development after acute coronary occlusion plays an important role in the recovery of left ventricular function by repairing the infarcted myocardium and restoring blood flow in the ischemic area, but does not irreversibly repair the damaged myocardium completely.

Fig.8. Serial coronary angiogram of a dog following acute occlusion of the left anterior descending coronary artery (LAD).
Upper panels: before occlusion (left), 30 min after occlusion (right). Lower panels: 2 weeks after occlusion (left), 4 weeks after occlusion (right). CX: left circumflex coronary artery, PL: embolized solid plug

6. Collateral Function in Acute and Subacute Coronary Occlusion

The functional role of coronary collateral development in relation to ventricular function was evaluated in dogs with acute coronary occlusion (ACO) and subacute coronary occlusion (SCO), and the findings were compared with that in normal dogs.

A solid plug and a hollow plug were embolized to the left anterior descending coronary artery to cause acute coronary occlusion and subacute coronary occlusion in closed-chest dogs, respectively, using a coaxial catheter system. The hole of the hollow plug was occluded within 24–48 h after embolization by thrombus formation. Left ventricular function (left ventricular systolic pressure, left ventricular diastolic pressure, max dp/dt and cardiac output) was measured at rest and during stress, such as during an increase in heart rate, in ACO dogs and

SCO dogs which survived for 8 weeks after embolization, and in normal dogs. There was no significant difference in left ventricular function at rest between normal dogs and either ACO dogs or SCO dogs.

However, under the condition of a high heart rate, moderate or distinct depression of left ventricular function was observed in the ACO group, while only slight depression was observed in the SCO group, as compared to normal dogs.

Postmortem coronary arteriogram demonstrated good development in both ACO dogs and SCO dogs which survived for 8 weeks after embolization. However, histological examination revealed that the average size of the myocardial infarction was 11.5% of the left ventricle in the ACO group and 6.0% in the SCO group ($P < 0.01$).

These results suggest that the protective and compensatory function of coronary col-

Fig.9. Coronary arteriogram of a dog 8 weeks after simultaneous implantation of Ameroid constrictors around the left circumflex and the right coronary arteries.

laterals is more effective in subacute coronary occlusion than in acute coronary occlusion. Thus, the process of gradual coronary obstruction stimulates collateral development, and once complete occlusion is attained, these collaterals form a more effective collateral circulation than that in abrupt coronary occlusion.

7. Collateral Function in Chronic Multiple Coronary Artery Occlusion

To create a slowly developing coronary artery occlusion, Ameroid constrictors were simultaneously placed around the left circumflex and the right coronary arteries of dogs.

Eight weeks after Ameroid closure, marked coronary collateral development (Fig. 9), and an absence of myocardial infarction or only focal areas of fibrosis, were observed in all 8 survivors by postmortem coronary arteriogram and histological examination. Moreover, left ventricular systolic pressure, left ventricular diastolic pressure, max dp/dt and cardiac output were not significantly different than those in normal control dogs.

These results indicate that the process of gradual coronary obstruction provides adequate opportunities for the formation of an extensive collateral circulation which can

adequately protect function following cessation of antegrade perfusion.

Clinical and Clinicopathological Studies of Coronary Collateral Circulation

1. Clinical and Hemodynamic Evaluation of The Role of Coronary Collateral Circulation in The Protection of Left Ventricular Function

The clinical significance of coronary collateral circulation which has evolved from interarterial coronary anastomoses has been the subject of intensive study for several decades. Nevertheless, there has been some controversy concerning the functional importance of these collateral vessels and their ability to protect the myocardium against ischemia, as previously described.

Since controversy exists over what effect collateral vessels have on various clinical expressions and on left ventricular function in coronary heart disease, a consecutive series of patients with obstructive coronary artery disease was studied.

Patients with complete proximal obstruction of either the left anterior descending coronary artery or the right coronary artery with or without angiographically documented collaterals were compared clinically, elec-

Fig.10. Effect of coronary collaterals on clinical, electrocardiographic, hemodynamic findings and exercise stress test in patients with isolated left anterior descending coronary artery obstruction (upper panel) and in patients with isolated right coronary artery obstruction (lower panel). CRT: cardiothoracic ratio, CHF: congestive heart failure, ECG: electrocardiographic signs of Q wave infarction, CI: cardiac index, LVEDP: left ventricular end-diastolic pressure, EF: ejection fraction

trocadiographically, hemodynamically, and left ventriculographically to appraise the functional significance of the collateral vessels.

The results were as follows:

1) Among 31 patients (mean age of 54.3 years) with total obstruction of the left anterior descending coronary artery, good collateral vessels to the distal portion of this vessel were observed in 16 patients (group A), and poor collateral vessels were observed in 15 patients (group B). All of the patients were male and there was no significant difference in age between groups A and B.

The frequencies of single, double and triple coronary vessel disease were similar in groups A and B.

There was no significant difference in the cardiothoracic ratio between groups A and B. However, the frequency of congestive heart failure and transmural anterior myocardial infarction was significantly lower in group A than in group B. This significance was not altered by taking into account the number of vessels involved with significant coronary artery disease. The frequency of abnormal left ventriculogram was also significantly lower in group A than in group B. The incidence of ventricular aneurysm tended to be higher in group B than in group A (7 cases vs. 3 cases). Furthermore, rupture of the interventricular septum was observed in 2 patients in group B. The cardiac index was significantly higher in group A than in group B. Furthermore, left ventricular end-diastolic pressure was lower in group A than in group B. In addition, left ventricular ejection fraction was larger in group A than in group B. However, there was no significant difference in left ventricular systolic pressure, max dp/dt, or the number of positive stress exercise tests by the treadmill method between groups A and B. The above results are summarized in Fig. 10.

2) Among 23 patients (mean age of 55.2 years) with total obstruction of the right coronary artery, good collateral vessels to the distal portion of this vessel were observed in 13 patients (groups C) and poor collateral vessels were observed in 10 patients (group D). All of the patients were male and there was no significant difference in age between groups C and D. The frequencies of single, double and triple vessel disease were similar in groups C and D. However, the average number of diseased vessels was significantly higher in patients with right coronary obstruction than in those with left anterior descending coronary artery obstruction (2.30 ± 0.17 vs. 1.68 ± 0.15 , $P < 0.01$).

There was no statistically significant difference in cardiothoracic ratio or the frequency of congestive heart failure between groups C and D. The frequency of transmural inferior myocardial infarction tended to be lower in group C than in group D, but this difference was not significant. The frequency of abnor-

Fig.11. Postmortem coronary arteriogram of case 1. Arrow indicates the completely occluded portion of the main stem of the left coronary artery (see text). LAD: left anterior descending coronary artery, LC: left circumflex coronary artery, R: right coronary artery, S: septal artery

mal ventriculogram tended to be higher in group C than in group D, but again, this difference was not significant. There was no statistically significant difference between groups C and D in cardiac index, left ventricular end-diastolic pressure, left ventricular ejection fraction, left ventricular systolic pressure, max dp/dt, the frequency of abnormal left ventriculogram, or the frequency of positive stress exercise test. The above results are summarized in Fig. 10.

All of the above results indicate that collaterals to the obstructed left anterior descending coronary artery play a significant protective role against the development of myocardial ischemic changes or abnormalities of left ventricular contraction. In addition, well-functioning coronary collateral circulation may prevent the development of transmural myocardial infarction and heart failure, and may be an important factor in the ability of some patients to survive an attack of myocardial infarction.

In contrast, no definite protective role of the collateral circulation against inferior myocardial infarction or asynergy of the left ventricle was demonstrated in patients with total obstruction of the right coronary artery. This may partly be due to the fact that the average number of diseased vessels was sig-

nificantly higher in patients with obstruction of the right coronary artery than in those with obstruction of the left anterior descending coronary artery. Another possible reason for this difference is that obstruction of the right coronary artery may have less of an effect on left ventricular performance than that of the left anterior descending coronary artery, and thus the protective role of collateral vessels may not become manifest.

In this study, there was no significant difference in positive stress exercise between patients with and without good collaterals in patients with left anterior descending coronary artery or right coronary obstruction. This suggests that the function of coronary collateral circulation is adequate at rest, but inadequate to meet the increased myocardial oxygen demand during stress exercise.

2. Clinicopathological Evaluation of The Role of Coronary Collateral Circulation

As mentioned earlier, many factors influence the development and function of coronary collateral circulation. When these factors are not favorable, the development of collaterals can be restricted. Moreover, even when collaterals develop to the highest possible grade, there are many factors which influence collateral function. When these fac-

Fig.12. Postmortem coronary arteriogram of case 2. Black circles show completely occluded portions. Hatched portions represent old myocardial infarction and double hatched portions represent summation of infarcts (see text). LAD: left anterior descending coronary artery, LC: left circumflex coronary artery, R: right coronary artery, S: septal artery

tors are not satisfactory, the function of the collateral circulation will be limited and disturbed. This condition produces coronary collateral dysfunction/insufficiency, which results in such conditions such as angina, fresh myocardial infarction, intractable arrhythmia, cardiogenic shock and even sudden death in coronary heart disease.

Although most of these factors are interrelated, the integrity of the donor arterial tree and perfusion pressure are the most important factors in collateral function. For example, old coronary occlusions may be at least partially compensated by collaterals originating from another coronary artery, however, if a fresh occlusion occurs in this donor artery, the transc collateral blood supply will be cut off and fresh infarction is inevitable. The infarction in these cases is often referred to as "infarction at a distance" or "summation of infarcts".

On the other hand, an abrupt drop in perfusion pressure, such as aortic pressure, reduces the coronary flow and may further diminish collateral flow, or during increased myocardial oxygen demand, collaterals may become flow-limiting in the sense of a steal

phenomenon. In these situations, coronary collateral dysfunction/insufficiency may occur and develop into a vicious cycle which leads to angina, infarction, arrhythmia and/or sudden death.

Presented below are clinical cases of patients with coronary heart disease who died after signs of acute myocardial infarction. Postmortem examination of their hearts revealed that they died from coronary collateral dysfunction/insufficiency.

Case 1. 59-Year-Old Man

This patient had been suffering from attacks of effort angina for 2 years and was admitted to our clinic with typical signs of acute myocardial infarction. The ECG showed fresh antero-septal infarction. He died suddenly in the middle of the night 5 weeks after admission.

Fig. 11 shows a postmortem coronary arteriogram of his heart. The main stem of the left coronary artery was completely occluded by organized old thrombus. However, despite this fact, the left anterior descending coronary artery and circumflex coronary artery were well-demonstrated by

the injection of contrast medium into the right coronary artery. Numerous anastomoses larger than 500–1,000 μm were found between the right and left coronary arteries. Old myocardial infarction was present at the left anterior and lateral walls. Moreover, summation of old and fresh infarction was seen at the apex area of the left ventricle.

Based on these findings, the natural history of this case may be explained as follows:

The rate of left main coronary artery occlusion might have been so slow that enough time was available for the development of interarterial coronary anastomoses between the left and right coronary arteries; left coronary circulation was well-maintained and compensated by this collateral circulation. In other words, the left coronary circulation may have been completely replaced by collateral circulation, with the right coronary artery as the sole source. Therefore, his heart was functioning on a single coronary artery.

This condition would spread the perfused area of the donor artery (the right coronary artery in this case) and reduce the coronary reserve. In this condition, when a fall in blood pressure, an increase in the heart's workload, or both, occur, the peripheral perfused area will be predisposed to myocardial ischemia and fresh myocardial infarction will occur without fresh coronary occlusion. Therefore, this patients ultimately died from coronary collateral dysfunction/insufficiency.

Case 2. 70-Year-Old Man

This patient had had no previous attacks of myocardial infarction, but had been suffering from repeated congestive heart failure. He was admitted to our clinic with typical signs of acute myocardial infarction with shock. The ECG showed old posterolateral infarction and fresh antero-septal infarction. He died with shock on the 3rd day after admission.

Fig. 12 shows a postmortem coronary arteriogram of his heart. The left anterior descending coronary artery, the left circumflex coronary artery and the right coronary artery were completely occluded by organized old thrombus. However, the territories of all of these vessels were filled with

contrast medium through the collaterals distal to the points of occlusion. Old myocardial infarction was found at the peripheral areas which were perfused by the respective occluded arteries. Moreover, summation of old and fresh infarction was seen at the apex of the left ventricle without fresh coronary occlusion. The collaterals were formed by septal branches which originated from the left anterior descending coronary artery and by the atrial branches which originated from the left circumflex coronary artery.

Based on these findings, the natural history of this case may be explained as follows:

The first coronary occlusion may have been well-compensated by the enlargement of pre-existing anastomoses as collaterals from the remaining two coronary arteries. The second coronary occlusion may have partially cut off some of these collaterals from their donor arteries, which would have been again compensated by a second development of collateral vessels. The third coronary occlusion may have also cut off most of the collaterals. Finally, only the septal branches and atrial branches would have remained as collateral sources. In other words, the myocardium may have been nourished by very poor collaterals through septal and atrial branches, and presumably by non-coronary collateral circulation, such as Tebesian vessels, arterioluminal channels and/or extracardiac collateral arteries.

These may have been inadequate to nourish the myocardium, which could easily result in coronary collateral dysfunction/insufficiency, when either the blood pressure dropped, the heart's workload increased, or both. This patient's final condition, i.e., fresh infarction without fresh coronary occlusion and power failure, indicate that this was the case. Therefore, this patient ultimately died from coronary collateral dysfunction/insufficiency.

CONCLUSION

All of the above experimental results and clinical and clinicopathological findings indicate that compensatory and protective anastomotic coronary collateral circulation develops when and where it is needed. This is surely a very important self-defense mechanism in the living body. This self-defense

mechanism, however, is not always sufficient, and the natural history and clinical outcome of coronary obstructive heart disease depends largely upon the conditions in which the collateral circulation develops and functions.

After coronary obstruction, the jeopardized myocardium can be supplied with oxygen and nutrients only by collateral channels. The coronary circulation of coronary obstructive hearts is partly, and sometimes completely, replaced by collateral circulation. This collateral can protect the myocardium against the deleterious effects of ischemia.

Natural history and clinical outcome of coronary heart disease is very hard to predict. The time from the first attack of myocardial infarction to death may vary between a few minutes to more than ten years.

Acute myocardial infarction is generally caused by coronary obstruction superimposed on thrombosis in a region of critical coronary narrowing, although coronary vasospasm or platelet aggregation have also been implicated. When the obstruction strikes an unprepared collateral system, i.e., when pre-existing anastomoses are small, the collaterals may only help make the infarct somewhat smaller than the perfused area of the obstructed artery. However, if the patient survives the first attack of acute coronary obstruction, the collaterals develop on a daily basis as functional compensatory circulation in both single-vessel obstruction and multiple obstructions which may occur at different times. Moreover, gradual progression of a coronary lesion to total obstruction provides adequate opportunities for the formation of an extensive collateral circulation which can help prevent myocardial infarction and ventricular dysfunction following coronary obstructions.

However, although a well-developed collateral circulation can deliver sufficient nutritional blood and oxygen during normal and even slightly elevated oxygen demand, function is restricted by many critical factors. Such conditions can be defined as coronary collateral dysfunction/insufficiency.

Finally, the ability of the coronary obstructive heart to exploit its collateral circulation may determine the natural history and prognosis in a given individual.

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