

The Prevalence of Steal-prone Coronary Anatomy in Patients with Coronary Artery Disease: An Analysis of the Coronary Artery Surgery Study Registry

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Coronary steal requires a specific anatomic arrangement of coronary occlusion, collateral vessels, and stenosis of the artery supplying the collaterals. The prevalence of this anatomic variant, steal-prone coronary anatomy, was investigated in 16,249 patients with coronary artery disease whose angiograms were carefully recorded as part of the Coronary Artery Surgery Study (CASS). Almost half of the angiograms had one or more total occlusions, and, of these, about 80% had angiographically visible collateral supply to the area distal to the occlusion. Of subjects with an occlusion and collaterals, about 60% had a hemodynamically significant stenosis of the artery supplying the collateral vessels. In summary, 23% of the patients in the CASS Registry demonstrated steal-prone coronary anatomy. Thus, coronary steal could possibly affect almost a quarter of the patients with coronary artery disease having anesthesia. Studies that seek clinical evidence of harm from coronary steal must be done in that subset of patients with coronary artery disease with steal-prone anatomy. (Key words: Complications: coronary steal. Heart: collateral circulation; coronary artery.)

THE DISCOVERY that isoflurane causes arterial vasodilation has led to concern that this inhaled anesthetic could cause a maldistribution of coronary blood flow in patients with coronary artery disease. Studies in humans have documented that isoflurane causes coronary vasodilation.^{1,2} Studies in animals have localized this dilation to the arteriolar level³ and have shown that isoflurane can cause coronary steal in dogs with chronic coronary occlusion.⁴

Only a subset of patients with coronary artery disease is likely to be subject to coronary steal. The anatomic requirements for intercoronary steal include total occlusion of a major coronary branch with collateral flow into the bed distal to the occlusion.⁵⁻⁷ In addition, the presence of a proximal stenosis of the artery supplying the collaterals enhances the conditions that cause steal and permits steal to occur with less arteriolar vasodilation.⁸

The purpose of this study was to estimate the prevalence of steal-prone coronary anatomy in patients with coronary artery disease. To this end, data from angiograms of 16,249 subjects with coronary artery disease gathered as part of the Coronary Artery Surgery Study

(CASS)⁹ were analyzed. The data provide a unique opportunity to assess the prevalence of steal-prone anatomy since the identity of the artery supplying collateral flow was coded in most cases and the presence or absence of stenosis in this artery was determined.

A surprisingly large fraction (23%) of the 16,249 subjects enrolled in the CASS Registry had the anatomic requirements for coronary steal. This finding suggests that coronary steal cannot be ignored as a public health problem and that studies designed to detect harmful consequences of coronary steal in clinical settings must be done in the correct subset of patients with coronary artery disease.

Methods

The Coronary Artery Surgery Study was initiated in 1972 by the National Heart, Lung, and Blood Institute to compare coronary bypass surgery with conventional medical therapy for coronary artery disease. Complete details of the CASS design and protocol have been published previously.⁹ The study was carried out at 15 participating medical centers in the United States and Canada (Appendix A). The CASS registry consists of consecutive patients who had coronary angiography for evaluation of suspected ischemic coronary disease at these 15 centers from 1974 to 1979. Patients were enrolled after informed consent was obtained. The current study is based on the 16,249 CASS patients enrolled between July 1975 and December 1979 who had angiographically documented coronary artery disease and who had not had previous cardiac surgery. Each angiogram was coded and the data stored in a computer. A stepwise computer search procedure was used to determine the incidence of steal-prone coronary anatomy. First, total occlusions were sought in the right coronary artery (RCA) and in the anterior descending (LAD) and circumflex (LCX) branches of the left coronary artery. For the purpose of the analysis, occlusions were sought in the proximal and mid segments of the LAD and LCX and in the RCA proximal to the origin of the posterior descending branch. Second, angiographic evidence of collateral blood supply to the zone or zones beyond the total obstruction(s) was sought. In the final step, the proportion of angiograms in which the artery supplying collaterals had a 50% or greater (diameter reduction) stenosis was determined.

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Clinical variables related to the severity and duration of coronary artery disease were tested as predictors of steal-prone anatomy in univariate analyses. Age, sex, duration of symptoms, severity of angina, and prior myocardial infarction were all highly correlated with steal-prone anatomy. Finally, these variables were entered into a logistic regression (BMDP, Version 1987)¹⁰ in order to construct a multivariate model predicting steal-prone anatomy.

Results

Almost half (7,973) of the angiograms had at least one total occlusion in these major arteries. Of these, 1,766 angiograms had two occlusions and 189 had three or more occluded vessels.

About 80% (6,466) of angiograms with a total occlusion had evidence of collateral blood flow. Of these 6,466 angiograms, the source of the collaterals was not recorded in 1,106. In the remaining 5,360 angiograms, the source of the collateral vessels was identified.

Almost 60% (3,126) of the angiograms showed that arteries supplying collateral vessels had at least a 50% stenosis between the aorta and the origin of the collaterals. The distribution of these lesions by severity is shown in figure 1. It seems reasonable to assume that a similar proportion of supplying arteries would be stenosed in the 1,106 angiograms in which the source artery was not recorded. If this assumption is made, then the data indicate that 23% of the angiograms included in the CASS registry meet the criteria for steal-prone coronary anatomy. If these 1,106 cases are excluded and no other adjustments are made, then a figure of 19% can be calculated. The four anatomic variants are shown in figure 2.

The results of the logistic regression are presented in Appendix B. Each of the variables is significant at the $P < 0.0001$ level.

Discussion

The data indicate that 23% of subjects in the CASS Registry have steal-prone coronary anatomy.

ASSUMPTIONS

Data for the CASS Registry were collected between 1974 and 1979 at 15 medical centers in the United States and Canada. Data from consecutive subjects having coronary angiography during this period were entered into the Registry. Thus, although it is possible that the prevalence of steal-prone anatomy has changed in the decade since these data were collected, systematic biases in the data caused by selection criteria would appear unlikely.

The identification of collateral vessels has been a notoriously difficult procedure because collateral vessels are

small and the resolution of angiographic techniques is limited. These difficulties probably apply more to determining the source of the collaterals rather than their presence because late filling of a bed distal to an occlusion during selective injection of contrast into another artery is frequently taken as indirect evidence of collateral supply. Thus, the data probably do not seriously underestimate the frequency with which collateral vessels occur. However, the estimate of the proportion with a stenosis of the supplying artery is made somewhat uncertain by the lack of information concerning the source artery in 1,106 of 6,466 cases.

INTERPRETATION

The results of this investigation are similar to those of prior studies¹¹ in several aspects. The proportion of subjects with at least one occluded vessel (49%) is similar to that found by Elayda *et al.* (63% of 127 subjects).¹² The proportion of subjects with an occluded vessel who have collateral supply to the distal bed was 80% in the present study, in contrast to 49%,¹³ 70%,¹¹ 85%,¹⁴ and 98%¹² in other studies. The selection criteria used in these studies may account for the difference in the frequency with which collaterals were observed. In contrast, no selection criteria were applied in the present study, and the large number of angiograms reviewed in the present study enhances the precision of the estimate considerably.

Coronary steal is recognized as a cause of myocardial ischemia in patients with coronary artery disease. Evidence supporting this concept comes from observation of subjects during dipyridamole-thallium myocardial perfusion imaging. Dipyridamole (Persantin[®]) produces intense dilation of coronary arterioles but only modest decreases in systemic arterial pressure (-10 to -15%) and reflexly mediated increases in heart rate (+15 to 20%).¹⁵ Although the combination of decreased arterial pressure and increased heart rate may account for myocardial ischemia in the setting of coronary artery stenoses,¹⁶ it has been suggested that maldistribution of coronary flow also plays a role in the relatively high incidence of ischemia observed after administration of dipyridamole.¹⁷ The incidence of chest pain and/or ECG changes suggestive of ischemia after intravenous administration of dipyridamole ranges from 5¹⁷ to 42%.¹⁵ Several studies report an incidence of angina after dipyridamole (31%,¹⁸ 18%,¹⁹ 25%²⁰) similar to the 23% prevalence of steal-prone anatomy discovered in the present study.

The mechanism of coronary steal has been investigated previously.^{5,7,8,21,22} After total occlusion of the native coronary artery, blood flow into the distal bed is delivered by collateral vessels. In humans with collateral vessels visible on angiography, this flow appears sufficient to maintain cellular integrity and a moderate degree of contractile

function at rest. For example, 95% of collateral-dependent regions had normal or mildly depressed contraction and only 5% were akinetic in a study performed by Levin of 200 patients.¹³ Yet, flow through collaterals is limited; Flameng and co-workers estimated that a chronic coronary occlusion compensated by collaterals corresponds functionally to a 90% stenosis.²³

Although flow *via* collateral vessels appears sufficient at rest in most patients, collateral flow does not increase sufficiently during exercise and ischemia ensues.^{14,24,25} Eng *et al.*, for example, found that only six of 28 patients had sufficient collateral flow during exercise to avoid a perfusion defect on Thallium-201 scan.²⁵ These observations suggest that little, if any, vasodilator reserve is present in the collateral-dependent circulation and that flow into the collateral-dependent zone is thus pressure dependent.

Collateral vessels arise at the 50–100- μ m level of the supplying artery, thus the perfusion pressure at the origin of the collaterals is equivalent to aortic pressure minus the pressure decrease across the proximal arterial segment. Normally this pressure decrease is small, on the order of 5–15 mmHg,^{22,26–28} but with dilation of the distal bed, the pressure decrease can increase, even in the absence of a stenosis. Intense arteriolar vasodilation of the supplying artery increases flow through the proximal segment and lowers pressure at the origin of the collaterals. Because flow through the collateral system is pressure dependent, flow into the collateral-dependent zone is reduced proportionally. Thus, arteriolar dilation of the normally perfused zone increases flow to that zone at the expense of flow into the collateral-dependent zone.

Intense vasodilation is required to demonstrate intercoronary steal in the absence of a stenosis of the supplying artery. Gross and Warltier found it necessary to administer 8 mg/kg (iv) of chromonar, a dose sufficient to quadruple coronary flow to nonischemic zones, in order to produce intercoronary steal in dogs with acute coronary occlusion.⁸ In contrast, steal was demonstrated at a dose of 3 mg/kg of chromonar if a tight stenosis was applied to the supply artery. This dose of chromonar resulted in only a doubling of flow in myocardium with no flow restriction.

Gross and Warltier also demonstrated a linear relationship between coronary pressure measured distal to the stenosis and the inner:outer flow ratio of collateral-dependent myocardium. This flow ratio presumably reflects the degree of underperfusion of the zone, because decreased inner:outer ratios were observed when total collateral flow was reduced. Inner:outer ratio declined with decreases in coronary pressure whether these decreases were the result of intense vasodilation in the absence of stenosis or moderate dilation in the presence of stenosis. The lowest values were reached with intense va-

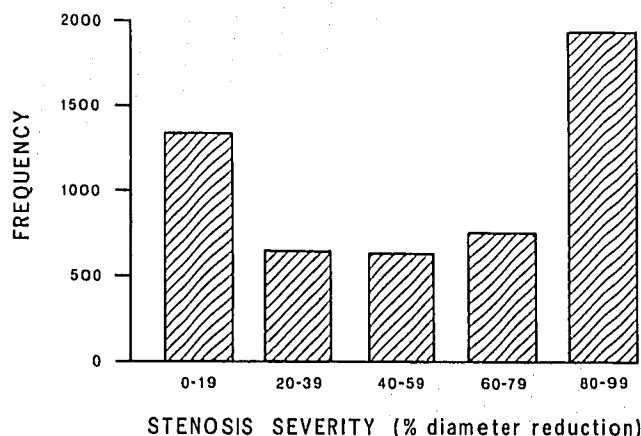


FIG. 1. The frequency distribution of stenosis severity (percentage diameter reduction) in the artery-supplying collaterals is shown. Increased severity enhances coronary steal because arteriolar dilation distal to the stenosis produces a more profound reduction in distal pressure and collateral flow.

sodilation and a tight stenosis. This observation emphasizes the central role that distal coronary pressure of the supplying artery plays in coronary steal. In addition, it illustrates that the magnitude of the resulting steal is a function of both the severity of the stenosis and the degree of arteriolar dilation.

It seems probable that a severe stenosis of the supplying artery is necessary for isoflurane to cause steal. Isoflurane decreases coronary vascular resistance by about 35% in clinically used concentrations.^{1,2} In contrast, chromonar or adenosine in adequate doses can reduce coronary resistance by 80%. This need for a severe stenosis may explain the fact that Cason and co-workers failed to demonstrate steal in a carefully performed animal study.²⁹ Their stenosis limited reactive hyperemia after a temporary occlusion to about 50% of control and corresponds to a 75–80% (diameter reduction) lesion.³⁰ In contrast, a study from our laboratory demonstrated steal in dogs in which coronary flow to the supplying vessel was held constant in order to mimic a critical stenosis (90–95% diameter reduction lesion).⁴ As figure 1 illustrates, severely stenosed supplying arteries were not infrequent in the population studied. The proportion of subjects with steal-prone anatomy and a 90% or greater diameter-reduction lesion of the supplying artery was 12%.

In the study by Gross and Warltier,⁸ a micrometer-driven vessel occluder was used to create the supply artery stenosis. The degree of obstruction was carefully controlled and probably relatively unaffected by the experimental procedure. In contrast, a large proportion of patients with coronary stenoses have flexible lesions that are subject to active and passive forces that change the caliber of the orifice and thus stenosis resistance.^{31,32} Arteriolar dilation can decrease downstream pressure, cause passive

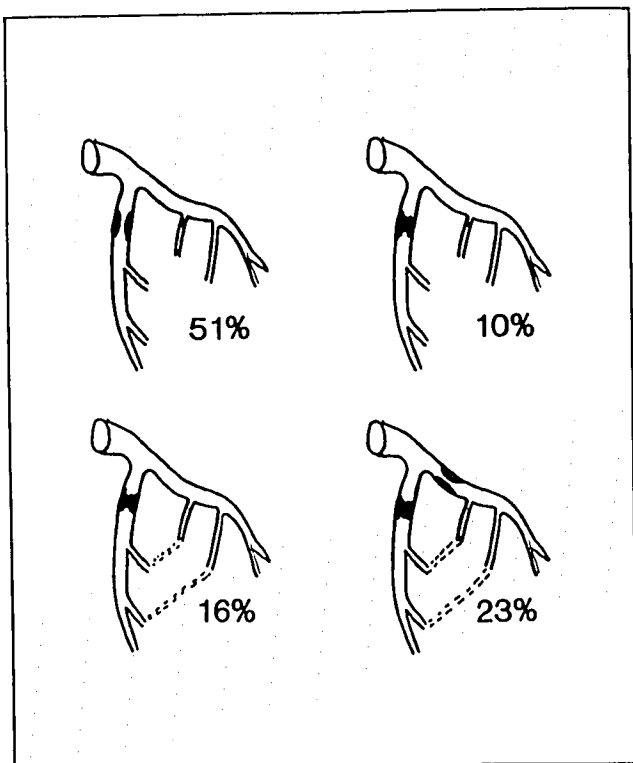


FIG. 2. Angiograms in the CASS Registry were sorted into these four anatomic variants. A schematic diagram of the left coronary artery is shown, but collateral connections with the right coronary artery were included in the analysis as well. Just more than half of the 16,249 angiograms surveyed had one or more stenoses but no occluded vessels (top left). Ten percent had a total occlusion but no collateral supply to the distal bed (top right). Of those angiograms with a total occlusion and intercoronary collaterals (shown as dashed lines), about 60% had a hemodynamically significant stenosis of the artery supplying the collateral vessels (lower right) and about 40% did not (lower left). (For the purposes of this study, any stenosis with a 50% or greater diameter reduction of the artery was considered "hemodynamically significant".) Intercoronary steal is most likely to occur in the anatomic variant at lower right because arteriolar dilation decreases pressure distal to the stenosis and reduces flow through the high-resistance collateral network. This variant was present in 23% of 16,249 angiograms examined.

collapse of the stenosis, and lead to an increase in the relative severity of the stenosis.³³ On the other hand, vasodilator drugs such as nitroglycerin that preferentially affect epicardial coronary arteries tend to dilate these dynamic stenoses and reduce stenosis resistance.³⁴ The net effect of a vasodilating drug would thus appear to depend on its balance between arteriolar and large vessel dilation. In terms of drugs commonly used in anesthesia, nitroglycerin predominantly affects large coronary arteries.³⁴ Nitroprusside dilates both large and small vessels³⁴ and adenosine predominantly affects arterioles. Halothane relaxes epicardial vessels³⁵ and causes a mild, dose-dependent arteriolar dilation.³⁶ Isoflurane does not relax epicardial vessels *in vivo*,³ although it antagonizes con-

striction induced by phenylephrine, serotonin, and prostaglandin F_{2α} (PGF_{2α}) in the presence of intact endothelium *in vitro*.³⁷ Isoflurane causes a moderate degree of arteriolar dilation, reducing coronary resistance by about 35% at 1 MAC.^{1,2}

CLINICAL CORRELATES OF STEAL-PRONE ANATOMY

Clearly, not all patients with coronary artery disease who are scheduled for surgery will have recently had coronary arteriography. Thus, it would be useful to be able to predict, from easily obtained clinical data, which patients are most likely to have steal-prone anatomy. A univariate analysis of data concerning the clinical history of subjects in the CASS Registry determined that subjects with steal-prone anatomy tended to be elderly men with severe angina (as scaled by the Canadian Heart Classification).³⁸ Angina had been present for a long time before catheterization in these subjects. Because a total occlusion is a necessary component of steal-prone anatomy, it was not surprising that steal-prone anatomy was found more frequently in subjects with a clinical history of prior myocardial infarction.

A multivariate logistic regression was performed as a second step in this analysis. By use of this formula (Appendix B), it can be calculated that a 75-yr-old man with Canadian Heart Class III angina who has had angina for 10 yr as well as a prior myocardial infarction has a 48% probability of steal-prone anatomy. In contrast, a 40-yr-old woman with mild angina (Canadian Heart Class I) for 2 months and no prior infarction, has only a 9% probability of steal-prone anatomy.

The variables selected for this analysis of the clinical correlates of steal-prone anatomy were chosen *a priori* from the voluminous data collected for the CASS registry.⁹ It is possible that other variables might provide a more accurate estimate of the likelihood of steal-prone anatomy. The results of this analysis should apply reasonably well to the United States population with coronary artery disease because consecutive cases from multiple centers were collected to form the Registry. Although the validity of the regression model should be tested in another data set before it is widely applied, it seems unlikely that a comparably large and detailed collection of coronary angiograms exists.

LIMITATIONS

The CASS registry includes only patients with sufficiently severe symptoms of coronary artery disease to warrant angiography, so these findings should not be extrapolated to all patients with symptoms of coronary artery disease.

This study has been limited to the anatomic arrangements requirements for intercoronary steal, that is, a maldistribution of blood flow in which flow to one artery

increases at the expense of flow into another artery. A second type of steal has been described that involves redistribution across the myocardial wall in the distribution of a single, stenosed vessel. Dilation of the arteries in the epicardial layer results in a decrease in flow to the sub-endocardial layer under critical conditions.^{39,40} None of the anesthetic agents has been shown to cause transmural steal.

Angiography is not an exact science, and significant interobserver variability may exist in the estimates of stenosis severity.^{41,42} This variability might cause angiograms to be wrongly classified as "steal prone." A special effort was made by the CASS investigators during the course of the study to improve the quality of angiograms and standardize the reading of cine films.⁴³

CONCLUSIONS AND IMPLICATIONS

Steal-prone coronary anatomy was found in 23% of 16,249 subjects with coronary artery disease enrolled in the CASS Registry.

Judging from experiments in animals, the magnitude of flow redistribution caused by a coronary vasodilator in a patient with steal-prone anatomy will depend on the severity of the stenosis of the supplying artery and the intensity of arteriolar dilation caused by the drug. Dilation of epicardial vessels at the site of a dynamic stenosis will reduce the gradient across the stenosis, increase distal coronary pressure, and thus counteract steal.

The surprisingly high incidence of steal-prone anatomy suggests that coronary steal may be an important consideration for anesthesiologists, given the larger number of patients with coronary artery disease who have anesthesia and surgery each year. It also seems clear that studies seeking a harmful effect from coronary steal must be performed in patients with steal-prone anatomy. Inclusion of outcome data from subjects with coronary disease who do not have steal-prone anatomy would likely bias the results toward the conclusion of "no effect."

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Appendix A

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Appendix B

The logistic regression formula estimates the probability of coronary steal as $\frac{1}{1 + e^{-\kappa}}$ where $\kappa = X_1 + 0.5485X_2 + 0.0011X_3 + 0.0134X_4 - 0.5129X_5 - 3.1982$ and

$$X_1 = \begin{cases} 0 & \text{if no angina} \\ 0.8409 & \text{if Canadian Heart Class I or II}^\dagger \\ 0.9781 & \text{if Canadian Heart Class III or IV} \end{cases}$$

[†] Canadian Heart Classification for Angina Pectoris: Anginal symptoms are grouped into four categories of severity, according to criteria established by the Canadian Cardiovascular Society: Class I: "Ordinary physical activity does not cause . . . angina, such as walking and climbing stairs. Angina with strenuous or rapid or prolonged exertion at work or recreation." Class II: "Slight limitation of ordinary activity. Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Walking more than 2 blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions." Class III: "Marked limitation of ordinary physical activity. Walking one to two blocks on the

level and climbing one flight of stairs in normal conditions and at normal pace." Class IV: "Inability to carry on any physical activity without discomfort—anginal syndrome may be present at rest."

$$X_2 = \begin{cases} 0 & \text{if no prior myocardial infarction} \\ 1 & \text{if prior myocardial infarction} \end{cases}$$

X_3 = duration of chest pain (weeks)

X_4 = age (years)

$$X_5 = \begin{cases} 0 & \text{if male} \\ 1 & \text{if female} \end{cases}$$

Each of the variables is significant ($P < 0.0001$). This logistic regression analysis excluded 1,106 angiograms in which the source artery was not recorded (see Methods). The constant has been adjusted to give an overall incidence of 23% for steal-prone anatomy. The validity of this adjustment is based on the assumption that the distribution of supply artery stenoses is the same in the 1,106 angiograms with missing data as in the 5,960 angiograms in which the identity of the supply artery was recorded.