Editorial

Collateral Flow to the Territory of the Occluded Infarct-Related Artery

Percutaneous Coronary Intervention or No Percutaneous Coronary Intervention: Why Does the Gold Not Always Glitter?

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Time and time again, randomized clinical trials have demonstrated what is conceptually logical and should be right is not always right. Randomized large clinical trials are often undertaken on the basis of this logical hypothesis. Very often, small clinical trials also show encouraging results. However, when large randomized clinical trials are performed, they not infrequently reveal rather disappointing and unexpected results. The study by Steg et al, “Impact of Collateral Flow to the Occluded Infarct-Related Artery on Clinical Outcomes in Patients with Recent Myocardial Infarction: A Report From the Randomized Occluded Artery Trial,” reported in this issue of Circulation, proves this again.

The investigators of the Occluded Artery Trial (OAT) studied the influence of presence or absence of collateral blood flow to the territory of the infarct-related artery on long-term clinical outcomes including death, reinfarction, and reverse remodeling and the development of Stage C heart failure. The effect of recanalization of the occluded artery by percutaneous coronary intervention (PCI) and medical therapy was also compared to that of medical therapy alone.

The OAT study enrolled 2201 patients; 1087 and 1086 patients were randomized, respectively, to PCI and medical therapy and to medical therapy alone. The collateral blood flow was estimated semiquantitatively on the basis of accepted angiographic criteria. The degree of collateral blood flow was then correlated to the long-term outcome including death, reinfarction, and class III or IV heart failure. The impact on ventricular reverse remodeling was not assessed.

The results of this study demonstrate that the absence of collateral blood flow is associated with worse prognosis in relation to death and systolic heart failure. Furthermore, the study also reports that the higher the extent of collateral blood flow, the lower the rate of death and severe heart failure; but no effect was observed on the incidence of reinfarction. In the OAT study, the investigators also performed a semiquantitative assessment of total flow (ie, the sum of collateral flow from the noninfarcted coronary arteries and the residual Thrombolysis In Myocardial Infarction flow in the infarct-related artery). A higher total flow was associated with lower long-term mortality and lower incidence of New York Heart Association class III or IV heart failure.

However, the multivariate analysis in this study revealed that when the other risk factors were incorporated, collateral blood flow or total blood flow was neither an independent predictor of death and reinfarction nor of severe heart failure. PCI also did not provide any additional benefit compared to medical therapy alone. Thus, issues remain as to whether it is advisable to recanalize the infarct-related artery late after the onset of myocardial infarction.

It is now well documented that in patients with acute coronary syndromes, whether ST-elevation myocardial infarction or non–ST-elevation myocardial infarction/unstable angina, early recanalization of the culprit artery soon after the onset of myocardial ischemia/infarction is associated with a better immediate and long-term prognosis, improved left ventricular function, and reduced risk of arrhythmogenic death. Indeed, it is a 1A indication for the management of acute coronary syndrome. Thus, there is no controversy about recanalization of the infarct-related artery when patients present within a few hours of the onset of symptoms. Usually, in these patients there is no or inadequate collaterals in the territory supplied by the occluded infarct-related artery.

The angiographically visible collateral vessels are present predominantly in the epicardium. They are muscular arteries, and their anatomic composition is similar to those of epicardial coronary arteries. The collateral arteries function as conduit arteries like the epicardial coronary arteries and connect the territory of one epicardial artery to that of another (contralateral). The collateral arteries may also connect the proximal to the distal segment of the same epicardial coronary artery across severely or totally occluded segments (ipsilateral). A number of stimuli have been recognized that influence development of collateral vessels. The severity of coronary artery stenosis, as determined by the transtenotic pressure gradient, is an important stimulus, and a substantial pressure gradient is required for the formation of collateral arteries. The duration and severity of myocardial ischemia are also a major stimulus for the development of collateral vessels. The collateral vessels are more likely to be...
present when myocardial ischemia develops gradually, as in patients with subacute or chronic coronary artery obstruction. When severe ischemia occurs suddenly after total occlusion of an epicardial coronary artery, as in patients with ST-elevation myocardial infarction, the collateral vessels are usually absent in the territory of the infarct-related artery. It should be appreciated that the magnitude of collateral blood flow in the territory of the obstructed coronary artery is usually inadequate when myocardial oxygen demand is increased. Coronary blood flow per gram of myocardium provided by the collateral arteries is reduced compared to normally perfused myocardium. In the OAT study, well-developed collaterals (grade 2) were present in 374 patients, and, on the basis of the pathophysiological mechanisms of development of collaterals, it is very likely that, in these patients, ischemia developed gradually because of “subacute or chronic” obstruction of the culprit artery and the collateral vessels provided adequate blood flow at rest to the territory of the occluded artery. Indeed, in this trial, the time elapsed from symptom onset to coronary angiography was longer in patients with collaterals than in patients without.

It is not surprising that the long-term prognosis in patients with grade 2 collaterals was better and that the rate of development of severe systolic heart failure in these patients was lower. In patients with grade 2 collaterals, left ventricular ejection fraction was normal, which is usually not associated with postinfarction left ventricular remodeling. In the OAT study, the relationship between the magnitude of stress-induced myocardial ischemia and collaterals has not been studied. It is conceivable that, in patients with grade 2 collaterals, stress-induced ischemia is less severe than in patients with grade 0 or 1 collaterals. Because the severity and the extent of myocardial ischemia, whether at rest or during stress, is the major determinant of prognosis and the risk of developing heart failure, the patients with grade 2 collaterals had a better prognosis and less risk of developing severe heart failure. It is surprising, however, that the collateral blood flow did not influence the incidence of reinfarction. It will be interesting to know the mode of death of patients in the OAT study. Whether sudden cardiac death, which can occur during ischemia without evidence of myocardial necrosis, was the predominant mechanism or not is unclear. It should be also appreciated that, in the OAT study, patients with severe ischemia on stress testing along with patients with left main or 3-vessel coronary artery disease, patients with angina at rest, and patients with New York Heart Association class III or IV heart failure were excluded. Thus, the patients investigated in the OAT study had lower risks of mortality and of developing severe heart failure. In these low-risk patient populations, it is also unlikely that PCI with optimal medical therapy should provide any benefits compared with medical therapy alone.

The primary objective of reperfusion therapy, whether by PCI or by coronary artery bypass graft surgery, is to provide coronary blood flow to the ischemic myocardium and to minimize the risks of adverse cardiovascular events. Ischemia results from an imbalance between myocardial oxygen demand and supply. The imbalance can be reduced either by decreasing myocardial oxygen demand or by increasing coronary blood flow. In the OAT study, the pharmacological agents used to decrease myocardial oxygen demand, such as β-blockers, nitrates, and calcium channel blockers, have not been detailed, but it can be presumed that it was similar in both the PCI and the medical groups. In the absence of significant myocardial ischemia, it is not expected that late recanalization of the infarct-related artery will provide any advantages over medical therapy. Thus, result of the present trial—that the routine PCI was not better than the adequate medical therapy—is not surprising. It is also well documented that revascularization treatments alone do not prevent reinfarction and other adverse cardiovascular events. An aggressive treatment for reduction of the risks of atherothrombotic cardiovascular diseases such as dyslipidemia, hypertension, diabetes mellitus, and obesity is necessary. It is presumed that such therapy was implemented in a similar fashion in both the PCI and medical therapy groups. It is therefore neither unexpected nor surprising that PCI was no better than medical therapy.

The investigators of OAT postulated that recanalization of the recanalized infarct-related artery may offset the potential benefit of PCI. The recanalization of a totally occluded artery is associated with a rapid regression of the functional collateral vessels. Thus, the consequences of abrupt reocclusion may cause more extensive myocardial infarction. The recanalization of the recanalized occluded infarct-related artery by PCI is not infrequent.

It should be appreciated that a number of recent studies have reported results contrary to those reported by the OAT study in this issue of Circulation. A meta-analysis of 10 randomized trials included 3560 patients. There were 648 patients with total occlusion of the infarct-related artery. The results of this meta-analysis showed that late recanalization of the infarct-related artery by PCI was associated with improved survival and less left ventricular remodeling. Recanalization of totally occluded infarct-related arteries by PCI 12 hours or longer after the onset of infarction was associated with reduced adverse cardiovascular events including left ventricular remodeling and heart failure. There was a significant increase in left ventricular ejection fraction and a reduction of left ventricular end-systolic and end-diastolic volumes. Thus, presently it remains uncertain when PCI is indicated in postinfarction patients who present late after onset of infarction.

The OAT study concluded that collateral blood flow has the potential to improve left ventricular function, but it is not an independent predictor of long-term prognosis. The study also concluded that routine recanalization by PCI of the infarct-related artery is not indicated in patients presenting late after the onset of myocardial infarction. It should be remembered from past experience that routine application of any therapy or procedure may be not only lacking in benefits but actually harmful. Routine placement of balloon flotation catheters was associated with higher adverse complications in patients with acute coronary syndromes, in patients with acute lung injury, and in patients with chronic heart failure, but there are still residual indications for the use of balloon flotation catheters. Similarly, although there is no indication for routine late PCI of totally occluded infarct-related arteries.
in selected patients with severe residual myocardial ischemia, late recanalization of infarct-related arteries by PCI may be beneficial and may be indicated.

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**Disclosures**

None.

**References**


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