The Human Myocardial Stain as Mitigated by Coronary Collaterals

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If the human coronary artery tree were an end-arterial system, i.e., one without interarterial anastomoses, as stated in 1881 by Cohnheim et al on the basis of canine studies, permanent total upstream occlusion of an epicardial branch would invariably result in the necrosis of the downstream myocardium. So far, data from less historical works have, however, indicated an absence of myocardial infarction in 50% of patients with chronic coronary artery occlusion. One of the concluding remarks of the study by Choi and coworkers published in the present issue of Circulation is that “most patients with chronic coronary artery occlusions show evidence of prior myocardial infarction.” Are we on the way back to Cohnheim’s paradigm? Maybe not, because Choi et al reassure the reader that it is the presence of coronary collaterals that mitigates the transmural extent of myocardial scar and regional wall-motion abnormalities (Figure 1).

Prevalence of Myocardial Scar and Collateral Flow: The Present Study

The careful work by Choi et al has shown convincingly that increasingly sensitive detectors of myocardial scar raise its prevalence from a mere quarter of the population with chronic occlusion as defined by ECG Q waves to 42% by the history of prior ischemic symptoms suggestive of myocardial infarction, 69% based on the presence of regional left ventricular (LV) wall-motion abnormalities as assessed by cardiac magnetic resonance imaging, and 86% as defined by myocardial late gadolinium enhancement. In the context of the population of interest and compared with other clinical studies in the field, the present study is well powered, the fact of which renders the mentioned figures reliable. The data shown are well anchored in existing knowledge by illustrating a direct link between infarct size and the occurrence of ECG and LV functional signs of scar. Additionally, the data support the concept of infarct size and its electric and LV functional consequences being limited by the collateral supply to the area at risk for necrosis. In the study by Choi et al, well-developed collaterals were defined angiographically as those that showed a continuous branchlike connection between the collateral and the chronically occluded artery, with respectively complete retrograde filling of the collateral receiving artery (Figure 1). It remains unclear whether both angiographic criteria or either criterion alone had been fulfilled to establish the tag of “good” versus “poor” collateral flow. The term flow is a misnomer, because it was just qualitative arterial contrast filling and not flow in milliliters per minute that was determined. To obtain actual flow would have been feasible with positron emission tomography, myocardial perfusion contrast echocardiography, or coronary pressure-derived collateral function measurement in the context of recanalization of the chronic occlusion (Figure 2). The measurement of flow would have allowed assessment of collateral function as a continuous instead of a dichotomous parameter and, as such, would have permitted comparison of qualitatively equivalent methods: Late gadolinium enhancement LV scar volume versus quantitative collateral function.

(F)Utility of Collaterals in Chronic Coronary Occlusions?

Knowledge of the frequency of well-developed collaterals in the study by Choi et al would facilitate interpretation of the main study finding of an 86% prevalence of scar despite the beneficial effect of collaterals. It would allow insight into how futile or utile the collaterals had been at the time of acute myocardial infarction in this particular versus other study populations with chronic total occlusions. The (f)utility of coronary collaterals depends on their functional absence or presence at the time of acute coronary occlusion. The development of functionally absent, although structurally preformed, collaterals requires 1 to 2 weeks’ time and is thus useless for myocardial salvage. Structural growth of small preformed collateral vessels, that is, collateral arteriogenesis, is initiated physically by the coronary perfusion pressure gradient between the (potentially) collateral-supplying contralateral and the occluded collateral-receiving artery. The pressure gradient induces or augments flow across preformed anastomoses, and the molding force of
arteriogenesis is endothelial tangential fluid shear force.\textsuperscript{10} The instantaneous response to augmented vascular shear force is flow-mediated dilation of collateral vessels, which in the case of small preformed anastomoses may not be sufficient for myocardial salvage. Because arteriogenesis occurs irrespective of ischemia, coronary collaterals can grow during the process of myocardial necrosis. Previous investigations have observed collateral vessels at the onset of acute myocardial infarction in \( \approx 40\% \) of patients.\textsuperscript{11} Waldecker et al\textsuperscript{12} detected angiographic collaterals to myocardium distal to an acutely occluded coronary artery in 334 (53\%) of 626 patients during the acute infarct phase, whereas the prevalence was shown to increase between 3 and 6 hours after symptom onset (from 66\% to 75\%), and the absence of collaterals was related to the early occurrence of cardiogenic shock. Collaterals that develop late after infarction into an area of necrotic myocardial tissue may exert a beneficial effect on LV dilatation or aneurysm expansion.\textsuperscript{13} Conversely, residual blood flow carried by collaterals at the time of acute myocardial infarction implies reduced infarct size and improved residual LV ejection fraction.\textsuperscript{14}

The ultimate test of the futility or utility of the coronary collateral circulation relates to the question of whether it reduces mortality. In the context of acute myocardial infarction, this has not been investigated very frequently, and the answer seems to still be controversial.\textsuperscript{15–17} Given the numerous variables that influence the relevance of collateral supply in acute coronary syndrome, such as the time window of study inclusion after symptom onset, the mode of revascularization (none, thrombolysis, percutaneous coronary intervention), the distinction between preformed and subsequently grown collaterals, and the mode of collateral assessment, the debate is not unexpected. Recently, Steg et al\textsuperscript{17} documented in 2173 patients with subacute myocardial infarction that
angiographic presence of coronary collaterals was associated with a lower cumulative 60-month rate of death ($P=0.009$), class III and IV heart failure ($P=0.0001$), or either end point ($P=0.0002$) but had no association with the risk of reinfarction. However, by multivariate analysis, collateral flow was not an independent predictor of death or of the primary trial end point of death, reinfarction, or class IV heart failure. In the setting of chronic stable coronary artery disease including chronic total coronary occlusion, well-developed collaterals, as defined by a collateral flow index $\geq 0.25$ (Figure 2), have been found to significantly lower the risk of both all-cause and cardiac mortality. $^{18}$ In a meta-analysis that also included trials with qualitative angiographic assessment, $^{19}$ the risk ratio for death of any cause for high versus low or absent collateralization in patients with stable coronary artery disease was 0.59 (95% confidence interval, 0.39–0.89; $P=0.012$).

## Clinical Implication

Because the study by Choi and coworkers $^3$ was not intended to provide a longitudinal but rather a cross-sectional view of patients with chronic coronary artery occlusion, the question of whether the omnipresence of myocardial scar is relevant may be raised. It could be argued that the lower one fourth to one third of LV necrotic volume as detected seismographically by late gadolinium enhancement magnetic resonance imaging is structural noise (or human myocardial stain) without functional relevance. When we consider the vertical compared with the horizontal plus vertical dimension of infarct size, the present study has documented that in normally functioning myocardial regions subtended by the occluded artery, there has been no transmural scar. Functional relevance was defined by the present study as LV regional wall-motion abnormalities, that is, a score based on visual grading of myocardial thickening during systole versus diastole, the fact of which may render their reported existence in more than two thirds of the patients debatable. As a consequence, we approach the frequency reported before the study by Choi et al $^3$ of one half may render their reported existence in more than two thirds

## Disclosures

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## References


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