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EDITORIAL COMMENT

Guilty as Sin

Revisiting Sutton's Law in ST-Segment Elevation Myocardial Infarction*

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Compared with complete revascularization (CR), incomplete revascularization of coronary artery disease is associated with a greater risk of future cardiac events, including death (1). It has long been held, however, that primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) should limit itself to the infarct-related artery (IRA) only. Simply stated, because "that's where the lesion is," to paraphrase Willie Sutton† (2). This recommendation makes sense, because an unforeseen complication during intervention in the non-IRA territory would add insult to injury by transforming a single-territory event into a multiple-territory one: at the very least, more widespread myocardial stunning, and at the worst, greater myocardial necrosis at a time of looming instability during an acute syndrome. It simply does not appear reasonable to take this added risk. After all, the decision to proceed with multiple-vessel coronary angioplasty in chronic coronary artery disease is typically multifaceted, taking into consideration symptom burden, response to medical therapy, ischemia burden, cardiac function, coronary anatomy, lesion features, and comorbidity/overall risk.

In the setting of primary PCI, most of these features are unknown, and the decision to perform multiple-vessel PCI becomes guided primarily by coronary anatomy and lesion features. Although counterintuitive and at odds with the thoughtful approach usually mandated by coronary intervention, the different nature of an acute coronary syndrome as compared with stable disease may warrant a different approach. In effect, patients with STEMI are at a greater risk of suffering from an additional myocardial infarction and events (3). Furthermore, post-infarction cardiac remodelling impacts a slew of key prognostic determinants including function, volumes, and arrhythmogenic milieu. Although remodelling depends greatly on successful revascularization of the IRA, the field is increasingly recognizing the contribution of neighboring vessels through collateralization of the IRA but also through the influence non-IRA territories have on global cardiac geometry.

The historical aversion to multiple-vessel PCI in STEMI rests, not only on common sense, but also on observational studies. In one such analysis, the performance of multivessel PCI at the time of primary PCI was associated with greater in-hospital mortality compared to primary PCI of the IRA only when unstable patients were excluded (mortality differences were lost at 24 and 42 months) (4). However, some interesting additional findings emerged as staged PCI (non-IRA PCI performed in a second procedure within 60 days) led to decreased mortality at 12 months compared with PCI of the IRA alone (mortality differences also lost at further time points). Potential mortality benefit of staged multivessel PCI for STEMI was recently confirmed in a second contemporary registry (5). Such key studies opened the door to newer questions surrounding the timing of multivessel PCI for STEMI. Large meta-analyses supplemented these

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†When asked by a judge why he robbed banks, Willie Sutton reportedly replied: "Because that's where the money is!" Although later refuted by Sutton himself, the diagnostic strategy of going for the obvious is referred to as Sutton's law, on occasion leading to cognitive error.

observational studies, by further suggesting that staged multivessel PCI in STEMI could reduce mortality, as long as primary PCI focused only on the IRA, and non-IRA vessel intervention was performed at a second time (whether in-hospital or following discharge) (6). Faced with such evidence suggesting potential benefit, the question of multivessel PCI in STEMI was cited as an important area of research by the 2013 ACCF/AHA Guideline for the Management of STEMI (7).

Since 2013, randomized controlled trials have begun to better inform decisions towards multivessel PCI in STEMI. The PRAMI (Preventive Angioplasty in Myocardial Infarction) study reported data from 465 patients with STEMI with multivessel stenosis (defined as 50% diameter stenosis visually); randomization was performed following successful IRA angioplasty, where one-half were randomized to IRA PCI only, and one-half to immediate CR (8). Over 2 years follow-up, the CR strategy significantly reduced cardiac death and nonfatal infarction (number needed to treat [NNT] of 14) and combined cardiac death, nonfatal infarction, and refractory angina (NNT 7). The CvLPRIT trial studied 296 patients with STEMI with multivessel stenosis; randomization was performed following angiography but before IRA angioplasty, where one-half underwent IRA PCI only, and one-half had non-IRA PCI performed preferentially during the same procedure, but at the very least during the same hospitalization (9). CR led to a significant reduction of combined all-cause mortality, nonfatal infarction, heart failure, and ischemia-driven revascularization (NNT 9) at median follow-up of 1 year.

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In this issue of the *Journal*, McCann et al. (10) further examine the impact of multivessel versus IRA-only PCI in the setting of STEMI. They perform cardiovascular magnetic resonance (CMR) to compare early infarct characteristics, late infarct characteristics, and late ischemic burden in a sample of the CvLPRIT (Complete Versus Lesion-Only Primary PCI Pilot Study) population. The role of CMR here is unique in providing highly detailed infarct characteristics that were previously inaccessible: Necrosis size is now measured with greater precision and with a much lower limit for detection compared with earlier imaging modalities, and the precise mapping of infarct distribution reveals non-IRA infarcts that were before ignored by enzyme rise alone. The finding that total infarct size did not differ between CR and IRA-only PCI is reassuring to those who were concerned that multivessel PCI may increase myocardial necrosis, either in territories remote from the STEMI by distal embolization or main vessel/side-branch compromise, or in the STEMI territory itself by compromise of collateral branches. Arguably, the strongest predictor of major adverse cardiovascular events following STEMI has repeatedly been shown to be infarct size by CMR. CMR has previously informed us on periprocedural injury in PCI by identifying as little as 1% to 2% necrosis, and the current study reports similarly impressive reliability. Keeping this in mind, McCann et al. (10) suggest that there may be a trade-off when performing CR for STEMI, because a greater percentage of patients presented multiple-territory acute necrosis (CR 17.1% vs. IRA-only 4.8%, $p = 0.004$). Although the size of such acute non-IRA infarcts was small (CR 2.5% vs. IRA-only 2.1% of LV mass, $p = 0.004$), prior studies suggest that even so-called "small" infarcts may have important effects on malignant arrhythmia and death. Despite these impactful short-term findings, an important feature of the current study was to perform follow-up CMR, confirming that total necrosis size remained similar for CR versus IRA-only at 9 months. The apparent discordance between an increased percentage of multiple territory infarcts and the absence of increase in total infarct size remains to be explained; because there is little mechanistic evidence to support such a discrepancy, these findings would benefit from corroboration in a larger sample. Furthermore, although the presumed benefit of CR has long been decreased ischemic burden, this study fails to identify any difference in residual ischemic burden between CR and IRA-only at 9 months. Such unexpected findings highlight important gaps in our knowledge and the importance of future trials to better inform clinical decisions.

Clinicians are looking forward to clarity on: 1) whether multiple-vessel PCI during STEMI may benefit specific subpopulations and not others; 2) what the optimal timing for intervention on the non-IRA vessel(s) may be; 3) whether specific interventional strategies, devices, and medications should be favored; and 4) whether lesion characteristics help inform the decision, for instance, whether ischemia testing—either during the index procedure by fractional flow reserve, or early after initial IRA-only PCI by timely noninvasive imaging—may guide tailored revascularization of non-IRAs where residual ischemia remains. Among current ongoing efforts, the international multicenter COMPLETE (Complete vs. Culprit-Only Revascularization to Treat Multi-Vessel Disease After Primary PCI for STEMI) randomized control trial (NCT01740479) aims to further inform on several of these questions in a cohort of 3,900

patients, of which nearly one-half have been recruited to date. At the present time, our decisions are made on partial and sometimes contradictory data, but efforts such as the CvLPRIT CMR substudy are essential in helping move the field forward. As our understanding of acute coronary syndromes improves alongside technical success rates in percutaneous intervention, we may need to question old ways and embrace new ideas for the benefit of the patient.

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