Multislice Computed Tomography After Left Main Drug-Eluting Stenting
Are We Putting the CarT Before the Horse?

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Coronary stenting has become the dominant therapy for patients referred for coronary revascularization. Because of their documented efficacy in reducing in-stent restenosis (ISR),1–3 drug-eluting stents (DES) are used for this purpose in most percutaneous revascularization procedures. Although intended primarily for use in native, de novo stenoses in coronary vessels 2.5 to 3.5 mm in diameter, DES currently are implanted in a diverse array of patients and lesions, including total occlusions, large and small vessels, acute myocardial infarction, and saphenous vein grafts, despite the absence of convincing trial efficacy data in some of these circumstances.

Despite the growing perception by cardiac interventionalists of their ability to percutaneously address increasingly complex patient subsets, the diseased left main coronary artery (LM) generally has been regarded as the exclusive purview of the cardiac surgeon. This rationale has centered around older trials documenting enhanced survival and reduced symptoms in surgically treated symptomatic patients with LM disease compared with patients randomized to medical therapy, which generally did not include percutaneous coronary intervention (PCI).4 Surgical referral of symptomatic patients with LM disease was subsequently corroborated by results from interventional studies in the balloon angioplasty and bare metal stenting eras.5,6 Retrospective analysis of data from the Unprotected Left Main Trunk Investigation Multicenter Assessment (ULTIMA) registry suggested that unprotected LM stenting might be successfully performed if guided by a simple patient risk stratification, limiting treatment to younger individuals not exhibiting shock who have relatively preserved left ventricular systolic function.6

Given the deliverability and low restenosis rates of currently available DES, the plausibility of percutaneous therapy targeting unprotected LM stenoses has resurfaced and has initially been addressed in a series of single-center reports and collected registries, most of which suggest improved outcomes compared with bare metal stents7,8 and acceptable results when contrasted with similar risk surgical patients.9,10 Although clearly not a mainstream therapy—yet, DES, when implanted in unprotected LM lesions, are subject to the cascade of vascular responses noted after implantation in other locations within the coronary circulation, albeit at some incremental increase in risk given the location of the device. Concerns related primarily to LM stent restenosis, a phenomenon reported to be associated with sudden cardiac death,11 suggest a need for clinical vigilance and have led to directives from expert consensus documents for follow-up coronary angiography within 6 months after stent implantation.12

In This Issue
In this issue of Circulation, Van Mieghem and colleagues13 report an initial experience comparing high-resolution multislice CT (MSCT) with quantitative coronary angiography and intravascular ultrasound (IVUS) in detecting restenosis after LM DES. Over almost 2 years, they identified 74 eligible patients from a group of 91 individuals scheduled for coronary angiography after LM stenting and performed MSCT in close proximity to follow-up angiographic/IVUS examination.

The main finding of these investigators was that, using coronary angiography as the gold standard with usual definitions for restenosis, in the majority of patients with technically adequate scans, MSCT correctly identified all patients with ISR, a finding noted in 14% of patients. The specificity of MSCT in documenting ISR was 80% (in contrast to the sensitivity of 100%) because of a false-positive rate of 7%, the majority of which occurred in patients undergoing complex bifurcation stenting.

MSCT and IVUS correlated well in determining the arterial reference diameters and minimal lumen diameters with the potentially important finding of a threshold value of 1 mm of neointimal hyperplastic tissue (corresponding to a 30% stenosis by quantitative coronary angiography) that would be reliably detected by MSCT. This finding requires verification in future studies. A potentially troubling finding was the apparent overestimation of stent diameter by MSCT-compared with IVUS-collected data.

As the authors note, these patients represent the best-case scenario for MSCT. Given current technological limitations, MSCT can be expected to perform well only in relatively large, less mobile segments of the coronary tree. The authors’ conclusion that a negative MSCT rules out LM ISR and may be an acceptable first-line alternative to coronary angiography.
phy appears reasonable from their data. Aside from the usual concerns relating to the generalizability of initial reports in a small number of patients, several other caveats bear mentioning.

**Specific Concerns**

Although the suggestion has been made that LM ISR is occasionally associated with sudden cardiac death, late acute decompensation related to DES most often is associated with acute thrombosis at the site of stenting, which has been shown to be linked to inflammation and delayed/reduced neointimalization rather than its profusion. Consequently, MSCT might not be expected to eventuate in mortality reductions in groups of patients subjected to routine follow-up. In addition, in clinical practice, interventionalists are called on to treat patients with ISR caused by an unacceptable severity of anginal symptoms. However, as Table 5 reveals, only 20% of patients with ISR had Canadian Cardiovascular Society class III anginal symptoms, and almost half were asymptomatic. These data might call into question the benefit (and cost-effectiveness) of using MSCT as a screening test. Although certainly beyond the scope of this study, clinicians need to wonder what should be done with such data if a $\geq 50\%$ stenosis is seen in an asymptomatic patient after LM DES. PCI has inherent risks, and the benefits of intervening (MSCT-facilitated occluostenotic reflex) in such a population are not currently known.

MSCT might have further utility in screening patients who undergo LM DES for a late stent malapposition. This phenomenon has been noted to occur more commonly after DES implantation than was previously reported in bare metal stenting and could conceivably presage late stent thrombosis.

A worrisome finding in this report is the reduced diagnostic accuracy of MSCT in the group undergoing complex stenting involving the distal LM. Specific lesion location within the LM is not clear from the report by Van Mieghem et al; however, 34% of their population underwent complex bifurcation stenting. Prior reports of DES for LM disease have documented a distal location in an overwhelming segment of LM-diseased patients, raising the possibility that MSCT will have diminished utility for most candidates for LM DES.

It also would be interesting to know what percent of the patients reported on had significant LM calcification. Was the so-called “blooming effect” responsible for the systematic overestimation of MSCT-derived stent diameter noted by the authors? If not, how will MSCT perform in stented, calcified vessels?

Although “less invasive” than conventional coronary angiography, MSCT is limited by its inability to study patients who are routinely studied in the angiographic laboratory. The exclusions for performing MSCT listed in Table 1 (obesity, heart rate >70 bpm, breathing artifact, atrial fibrillation, etc) are patient characteristics routinely encountered in the catheterization laboratory. In addition, intervention can follow diagnostic imaging in the catheterization laboratory, minimizing delays and patient apprehension. In contrast to MSCT, coronary angiography can study the entire coronary tree and collect hemodynamic data, qualities that MSCT is unlikely to duplicate in the foreseeable future. One must also be cognizant of the fact that LM coronary angiography using current technology can be accomplished at a radiation exposure of $\approx 1$ mSv, a dose significantly lower than the 15.2 to 21.4 mSv reported by the authors as associated with image acquisition with 64-slice MSCT.

**General Concerns**

When the clinical outcome of an intervention is assessed, it can be useful to broaden the discussion to consider whether the procedure itself is appropriate. Van Mieghem et al have correctly noted that recent consensus guidelines “strongly recommend” coronary angiography as follow-up to LM stenting. However, that same document generally regards PCI in this location as a class III procedure (general agreement that the procedure is not useful/effective and in some cases may be harmful), reserving a class IIb indication for LM PCI only for highly symptomatic patients who are not surgical candidates.

Some reasons underpinning the lack of endorsement of LM PCI at this time bear reiteration. Most patients with LM disease have multivessel disease, and complete revascularization (most often associated with the surgical approach) has been documented to eventuate in more effective symptom relief and reduced mortality, especially in higher-risk patients, including those with LM disease. It is important to remember that in most patients with LM disease, the diseased segment is distal, a location associated with higher rates of restenosis, especially when multiple stents are used. Consequently, complex bifurcation disease is an important prognostic indicator for the interventionalist but not for the surgeon.

Although low death and restenosis rates generally have been reported initially after LM DES, there have been signals that such outcomes are not universal. One registry reported an 11% one-year cardiac mortality after LM DES; however, the long-term mortality rate was less than half of this in patients receiving elective intervention. A 44% overall restenosis rate at 9 months was reported by Price et al in patients undergoing unprotected LM DES; almost one quarter of restenoses involved the ostia of both the left anterior descending and left circumflex arteries. It is reasonable to assume, however, that clinical restenosis rates in patients undergoing LM DES will likely be lower than reports to date, given the mandated angiographic follow-up in reported series.

It can be noted that the ingrained concept of survival benefit attendant to surgical revascularization for LM CAD is generally based on data accrued in an era before the widespread adoption of medications now known to be of vital importance (eg, statins, ACE inhibitors for left ventricular dysfunction). On the other hand, the interventional community previously has shown a willingness to embrace a technique or device as a significant therapeutic advancement, subsequently abandoning it or relegating it to niche status after a randomized trial is performed. The experience relating to coronary atherectomy illustrates this point. The ongoing DES versus surgery trials in LM/multivessel coronary artery disease patients will be important to define the relative...
benefits of competing strategies in important patient populations. We can hope that the results from these trials will define specific groups in whom a particular strategy is preferred or in whom a certain technique should not be used. For example, we may learn that patients with ostial and mid LM lesions do as well with a percutaneous approach as they do with the more invasive surgical technique, and that complex bifurcation stenting (eg, culotte, crush, “T”) techniques should not be used or perhaps these patients should be referred for surgery or a hybrid therapy.

If patients with LM disease are ultimately treated percutaneously, how long and at what dose should thienopyridine therapy be prescribed? Some have suggested that because thrombosis is seen most often with distal LM lesions, these patients should receive double the usual dose of clopidogrel. Adoption of LM stenting may be hampered in the United States by the lack of commercial availability of DES >3.5 mm in diameter. Studies in patients referred for evaluation of LM lesions have shown that the average vessel diameter is >4.0 mm. This would raise concerns relating to device undersizing and the need for overdilation with potential adverse events related to stent malapposition, polymer disruption, strut fracture, etc.

In summary, Van Mieghem and colleagues are to be congratulated for a well-executed study that suggests that MSCT may be an adequate surrogate for conventional angiography in patients undergoing LM DES. Their intriguing findings relating to whether LM, particularly unprotected LM, interventional techniques should not be used or perhaps these patients should be referred for surgery or a hybrid therapy.

Disclosures

None.

References


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