Competitive Coronary Flow between the Native Left Anterior Descending Artery and Left Internal Mammary Artery Graft: Is It a Surrogate Angiographic Marker of Over-or-Unnecessary Revascularization Decision in Daily Practice?

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Abstract

Overdiagnosis and overtreatment are often thought of as relatively recent phenomena in modern medicine, influenced by a contemporary combination of technology, specialization, payment models, marketing, and supply-related demand. Several investigators have reported discrepancies between the angiographic and functional severity of coronary angiographic stenosis. However, the visual anatomic assessment of the coronary lesion severity continues in daily practice.

We evaluated the consecutive all coronary angiograms performed between January 2015 and December 2015 and examined only patients who had previous coronary artery bypass grafting (CABG) to analyze the cases with regard to presence of the competitive flow (CF) between the native left anterior descending coronary artery (LAD) and left internal mammary artery (LIMA) graft.

A total of 8,248 diagnostic coronary angiographies were performed between January 2015 and December 2015 at our facility. Of these, 886 coronary angiographies of CABG patients were detected. Whereas LIMA graft occlusion detected in 19 patient (2.1%), the LIMA-LAD CF rate was found in 86 (9.7%) CABG patients. The angiographic severity of the LAD stenosis in CF group evaluated as mild in 20 (25%), moderate in 61 (70%), and severe coronary artery disease in 4 (5%) patients.

Our results showed that there is 9.7% rate of LIMA-LAD CF. Therefore, some unnecessary coronary stenting or CABG procedures might have been performed due to limited use of functional testing for clinical decision making. The functional angiography should play a more prominent role in catheterization laboratories as recommended by current revascularization guidelines to prevent overdiagnosis, misdiagnosis, or incorrect treatment decisions.

Keywords

- competitive coronary flow
- unnecessary revascularization
- functional angiography

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Overdiagnosis and overtreatment are often thought of as relatively recent phenomena in modern medicine, influenced by a contemporary combination of technology, specialization, payment models, marketing, and supply-related demand. A study by the American College of Cardiology analyzed 140,000 heart procedures and concluded 12% were unnecessary, with another 38% deemed questionable.¹ Indeed, the invasive coronary angiography has been accepted as the reference method for the angiographic assessment of severity of coronary artery disease (CAD). However, the management of intermediate coronary lesions, defined by a diameter stenosis of 40 to 70%, continues to be a therapeutic dilemma for cardiologists and cardiovascular surgeons. Although the accuracy with which individual angiographic lesions are assessed visually is imperfect, the visual assessment of the coronary lesion severity continues in daily practice probably due to high cost, intense work pressure, or time issues.² Indeed, interventionalists' visual estimation of coronary lesion severity is highly variable and results in overestimating or underestimating in about one-quarter of cases.³ Therefore, the changes that have occurred in patient evaluation throughout the last 2 decades have important implications for the new cardiac catheterization laboratory. Intravascular ultrasound and fractional flow reserve index (FFR) which provide anatomic and functional information have been recommended in the catheterization laboratories to designate patients to the most appropriate revascularization decision.^{4,5} Although it appears to be increasing in catheter laboratories, it is still not adequate level in terms of the use of FFR. Fewer than half of all patients are evaluated noninvasively for myocardial ischemia before revascularization in real-world practice.⁶ Only 50% of percutaneous coronary interventions (PCI) on stable CAD patients has been found to be appropriate according to a study looked at data from more than half a million procedures submitted by 1,091 United States hospitals.¹ It has also been reported that some coronary artery bypass (CABG) surgery procedures might have been performed unnecessarily.^{7,8} Medico-legal and ethical aspect of unnecessary revascularization is out of this topic.

The left internal mammary artery (LIMA) is the choice for graft of the left anterior descending coronary artery (LAD). The LIMA patency is mainly determined by the progression of atherosclerosis and intimal hyperplasia within the graft as well as technical failures.⁹ However, the CABG to mild to moderately stenotic LAD vessels due to over-assessment of the LAD lesion may lead to competitive coronary flow (CF) between the LIMA graft that is considered to be one of the major factors affecting early LIMA patency and causing the graft to constrict and fail.¹⁰ Therefore, ischemia should be identified more precisely and revascularization decision should be applied more logically. Routine use of functional methods such as the FFR to improve the accuracy of lesion measurement may reduce unnecessary PCI or CABG and improve arterial graft patency. The objectives of this study were to delineate the frequency of the CF between the native LAD and LIMA graft as an angiographic surrogate marker of unnecessary revascularization decision in real-world settings.

Materials and Methods

We evaluated all consecutive coronary angiograms performed between January 2015 and December 2015 and examined only patients who had previous CABG surgery to analyze the cases with regard to presence of the CF between the LIMA and LAD. Clinical information was collected from patient files. Dominant flow direction was graded as antegrade, competitive, and no-flow (occlusion). A patent graft meant that the graft had a complete continuity of the graft lumen in the overall length from the subclavian artery to the anastomotic site with the coronary branch, irrespective of the flow direction. Normal antegrade flow was defined as a situation in which antegrade graft flow (i.e., from the in situ graft to the target coronary branch) was found in most of the multiplane LIMA angiography. When the continuity of the graft lumen from an in situ LIMA graft to the anastomosis with the target coronary branch was interrupted at any level, it was defined as LIMA occlusion, which was regarded as a no-flow situation with closure of the lumen of the bypass graft. The CF was defined as a situation in which the target vessel was barely opacified from the LIMA graft injection and the bypass graft was filled by retrograde flow from the native coronary injection. The reverse flow was defined as the lack of opacification of a distal anastomotic site during graft angiography, but clear retrograde graft opacification during native coronary angiography. The difference between CF and reverse flow was whether the contrast medium from the in situ LIMA finally reached the target branch in the best frame of multiplane examinations. The CF in bypass grafts probably contributed to the coronary perfusion, but the durability of graft patency was considered uncertain because the retrograde flow from the native coronary branch was almost comparable with that of reverse flow grading.¹¹ Therefore, the reverse flow was included in CF group in this study.¹¹ The angiographies in CF group were also evaluated with regard to angiographic severity as follows: mild (<30% luminal narrowing), moderate (30–70% luminal narrowing), and severe (>70%).

Results

A total of 8,248 diagnostic coronary angiographies were performed between January 2015 and December 2015 at our facility. Of these, 894 patients who had undergone CABG had coronary angiography, however, 5 CABG patients had two diagnostic coronary angiographies and 1 CABG patient had four diagnostic coronary angiographies during the study period; a total of 886 coronary angiographies of CABG patients were evaluated with regard to presence of the CF. Patients' mean age was 65 years, and 79% were men. The mean interval of coronary angiography following CABG was 8.5 years. There were 19 patients (2.1%) with LIMA occlusion, 38 patients (4.3%) with CF, and 48 patients with reverse flow (5.4%). Total 86 patients (9.7%) were found to have CF between the LAD and LIMA graft (► **Table 1**). The angiographic severity of the patients in CF group evaluated as mild in 20 (23%), moderate in 62 (72%), and severe CAD in 4 (5%) patients.

Table 1 Basal clinical and angiographic features of CABG patients

	CABG patients (n = 886)
Age (y)	64.7 ± 9.2
Sex (male)	34/49 (69%)
Diabetes mellitus (%)	44
Hypertension (%)	75
Hyperlipidemia (%)	79
Current smoking (%)	31%
CABG to angiogram time (y)	8.5 ± 5.0
CABG graft number	2.35 ± 0.94
LVEF (%)	67 ± 7
LIMA occlusion (%)	2.1%
Reverse flow (%)	5.4
Isolated CF (%)	4.3
Total CF (%)	9.7

Abbreviations: CABG, coronary artery bypass grafting; CF, competitive flow; LIMA, left internal mammary artery; LVEF, left ventricular ejection fraction.

Discussion

Our results showed that there is 9.7% rate of LIMA-LAD CF and this high rate of CF may indirectly reflect the unnecessary revascularization decisions in real-world settings. This rate is compatible with the sub-analysis of the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study thoroughly evaluated the “visual-functional mismatch” of CAD.¹² Of the patients with three-vessel disease as assessed by visual estimation, only 14% had three-vessel disease after FFR measurement, whereas 9% had no functionally significant stenosis.

The LIMA is the choice for graft of the LAD coronary artery. Unlike saphenous veins, LIMA grafts rarely develop arteriosclerosis (4%), and only 1% develops important arteriosclerotic luminal narrowing. However, there are some other factors than arteriosclerosis that influence graft patency. An important factor affecting early arterial graft patency is native coronary artery blood flow. When performed CABG to hemodynamically unimportant moderately stenotic LAD vessels due to overassessment of the LAD lesion, this may lead to CF between the native LAD and LIMA graft resulting in anatomically or functionally LIMA occlusion or reverse flow.¹¹ Therefore, the CF can be efficiently avoided by appropriate graft arrangement and patients' selection.^{13,14} However, the CF is a multifactorial phenomenon, and even an estimate of its impact is difficult, especially if based on preoperative coronary angiography alone.¹⁵ Some authors recommend a few intraoperative techniques to evaluate the CF that allows us to make informed intraoperative decisions regarding anastomotic quality, vessel runoff, and competing native coronary blood flow.¹⁶ A revascularization strategy for distal lesions

should be discussed separately from that for proximal lesions. For distal lesions, more severe stenosis is necessary to avoid graft failure, compared with proximal lesions.¹⁷ Because the bypass grafts with reverse flow do not contribute to the coronary perfusion in the grafted territory, the efficacy of CABG might be unpromising, even when the bypass graft is anatomically patent.¹¹

There are some possible mechanisms or explanations for unnecessary coronary stenting and/or CABG decisions in daily practice. First, catheter-induced left main coronary artery (LMCA) vasospasm is a rare complication of coronary angiography; but, it has been reported that the inability to distinguish vasospasm from obstructive disease of the LMCA can lead to inappropriate referral for CABG surgery.^{18–20} Moreover, referring these patients for CABG may cause occlusion of LIMA grafts from CF from patent native LMCA.²¹ Edris et al reported two patients with LMCA vasospasm who were referred for CABG, and repeat coronary angiography showed a normal LMCA after 6 years in the first patient and after just 2 days in the second patient.¹⁹ Attempts to ameliorate possible catheter-induced spasm by using intra-coronary nitroglycerin seems like a reasonable routine practice in hemodynamically stable patients with significant LMCA stenosis or even three-vessel disease.²⁰

Second, several investigators have reported discrepancies between the severity of visual estimation of coronary angiographic stenosis and the severity of functional coronary stenosis.^{3,4,22} Compared with quantitative coronary angiography, visual assessment by clinicians tends to overestimate lesion severity in patients undergoing PCI.²³ Visual assessment of the coronary lesion stenosis has a high degree of inter- and intraobserver variability, which may lead to inadequate lesion treatment and coverage or alternatively to overcoverage.³ Many factors conspire to produce this effect, including limited or inadequate angiographic views of the lesion, lack of definite knowledge of the true reference diameter of any chosen vessel and the unknown nature and pattern of flow abnormality within the vessel for a particular area of myocardium which it supplies. FAME trials have established the clinical utility of FFR, which is now accepted as a standard of care.^{24,25} Despite the apparent benefits, the adoption of FFR into daily clinical practice has been limited due to habit, bias, training experience, practical pressures of patient throughput, financial incentives, misconceptions by patients, a perception by referring physicians of the need to stent coronary stenosis, cumbersome set-up time, and reimbursement for pressure wires.²

Cardiologists are still very prone to make decisions about an intermediate stenosis purely on the basis of its angiographic appearance in almost three quarters of all cases, even when noninvasive proof of ischemia is missing, and even when the use of additional invasive diagnostic tools is not restricted by financial limitations.²² Results of a recent web-based survey suggest that most interventional cardiologists rely on visual assessment alone when deciding whether to revascularize intermediate lesions in stable patients.²² Toth et al reported that no physician requested FFR in all cases as would have been expected based on the guidelines, and

speculated that these practice habits might lead to unnecessary stenting or inappropriate deferral in about a third of all cases.²² Mohammed et al also reported that 33.3% patients had occluded LIMA conduits to the LAD artery, likely from similar physiology.^{20,22} Thus, it is rational to think that unnecessary stenting might be higher than these unnecessary surgery rates.^{1,26}

This topic is particularly important in the light of the current scientific knowledge. Previous studies, like Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), FAME 1 to 3, and DEFER, suggested that revascularization by either PCI or CABG did not improve survival or myocardial infarction rates except in patients with severe or unstable CAD presentations (e.g., three-vessel/LMCA or ST elevation myocardial infarction).^{4,12,24,25,27} While PCI for most stable patients is not generally a life-saving procedure, the FAME studies guide us on who will benefit most from revascularization over continued optimal medical therapy.^{5,12,24,25} However, recent advances in drug eluting stents and adjuvant pharmacological agents might have been reduced the threshold for revascularization therapy in the absence of firm evidence of objective ischemia.² Thus, consideration is sometimes given to treating stenosis of intermediate degree without consideration of their functional significance in clinical practice.²⁸ However, FAME study revealed that angiography is inaccurate in assessing the functional significance of a coronary stenosis when compared with the FFR, not only in the 50 to 70% category but also in the 70 to 90% angiographic severity category.¹² On the other hand, most surgical recommendations for patients with multivessel CAD are to bypass all lesions with diameter stenosis of > 50% for complete revascularization, the patency rate of vein grafts on vessels with functionally insignificant proximal stenosis has been in question.⁸ Therefore, ischemia should be identified more precisely and revascularization decision should be applied more logically. Otherwise, these practice habits might continue to lead the unnecessary coronary stenting²⁹ or CABG surgery,^{22,30} or conversely, might cause to functionally significant stenosis remains unrevascularized.

As with any retrospective study, there are a few limitations that must be kept in mind. First, we could not evaluate prebypass coronary angiograms and therefore possible functional evaluation rates. It would be nice to perform FFR to these patients to evaluate the effect of the CF on distal native LAD territory. Second, if any patient has got a mild type LAD, a dominant right coronary artery or a circumflex artery, then the huge amount of myocardium is in jeopardy because of right coronary artery and circumflex stenosis, and may warrant surgery even if LAD is moderately stenosed. Thus patient may warrant surgery for non-LAD indications and if there is moderate (>50%) stenosis in LAD, then according to guidelines, it is mandatory that a graft is placed to LAD also. However, this non-LAD surgery indication is very exceptional. Third, the regression of a previous lesion or some other neighboring graft also is speculated as rare causes of this phenomenon and may not be related to the unnecessary revascularization decision.

In conclusion, routine use of functional methods such as the FFR to improve the accuracy of lesion measurement may reduce unnecessary revascularization decision and medical costs, and improve function of arterial grafting and patient's clinical outcomes. So-called functional angiography will and should play a more unpleasant role in catheterization laboratories in the future.

Conflict of Interest

There are no any potential conflicts of interest, including related consultancies, shareholdings, and funding grants.

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