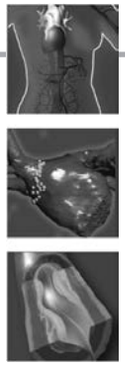

Myocardial infarctions involving acute left circumflex occlusion: are all occlusions created equally?

Compared with the right coronary and left anterior descending arteries, myocardial infarctions (MI) involving the left circumflex artery (LCx) have not been well described. Studies show an inconsistency in presentation of acute LCx occlusions leading to MI, which is thought to be due to electrocardiogram (ECG) insensitivity in this field. Acute occlusions of the LCx present as non-ST elevation MI (NSTEMI) as often as STEMI, but few studies have compared these presentations to determine whether ECG changes have an effect on outcomes and infarct size. While ECG insensitivity may play a role in the presentation of acute LCx occlusion, other factors such as myocardium at risk and overlapping blood supply also may be of importance.

KEYWORDS: ECG ■ left circumflex artery ■ NSTEMI ■ occlusion ■ outcome ■ STEMI

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The 12-lead electrocardiogram (ECG) is the initial diagnostic test used in patients presenting with symptoms suggestive of myocardial infarction (MI), and is probably the most critical component dictating initial management in these patients. Typical ST-segment elevation (STE) on ECG is indicative of a coronary artery occlusion with transmural infarction and requires immediate revascularization via cardiac catheterization and percutaneous coronary intervention (PCI) or thrombolytic therapy. MI patients with ST-segment depression (STD), nonspecific ST-segment changes or no ECG changes are generally considered to have nontransmural infarctions without vessel occlusion and are managed less aggressively in the acute setting. Occlusions involving the left anterior descending artery (LAD) and right coronary artery (RCA) are easily diagnosed by 12-lead ECG in most cases. However, the ability to diagnose acute left circumflex artery (LCx) occlusion by 12-lead ECG is often much more difficult.

While clinical outcomes and incidence of STEMI involving the RCA and LAD are well studied, less is known about MIs involving the LCx. It is subjectively viewed as having more favorable outcomes and is involved in a smaller percentage of STEMIs than the LAD and RCA [1,2]. Furthermore, studies have shown that over half of acute occlusions of the LCx present without characteristic STE on ECGs [2]. These occlusions may be poorly represented in STEMI trials due to the difficulty in diagnosing these occlusions with an ECG, but there may also be other factors that play a role in why occlusions of the LCx may not present as STEMI.

Insensitivity of ECG for LCx

It has been well documented in the literature that STE on a standard 12-lead ECG is not particularly sensitive for diagnosing acute coronary artery occlusion [3,4]. Multiple studies have suggested that the standard 12-lead ECG is least sensitive for infarcts involving acute occlusions of the LCx or inferolateral wall [3,5].

In a prospective study by Schmitt *et al.* analyzing 418 patients presenting with MI and angiographic occlusion of a coronary artery, the standard 12-lead ECG was much less sensitive for predicting acute occlusion of LCx compared with RCA and LAD. While additional ECG leads and more stringent diagnostic ECG criteria increased the sensitivity in this territory, many acute occlusions of the LCx remained undiagnosed. Table 1 summarizes the details of ECG sensitivity by the artery involved. The authors note that at least 2 mm STE in the precordial leads is most commonly used to diagnose STEMI and suggest that the most stringent ECG criteria used to increase its sensitivity for coronary occlusions would also decrease specificity, although it was not analyzed in this study [6].

Table 2 summarizes several other studies revealing a lack of sensitivity in the diagnosis of acute LCx occlusion compared with the other two major coronary arteries [6–8]. Based upon the studies reviewed, when using standard diagnostic ECG criteria, a 12-lead ECG is able to detect acute LCx occlusion in MI patients in only a third to a half of cases, compared with detection of 70–90% of acute occlusions in the other major coronaries. Data from these studies confirm what was reported in a prior 1990

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Table 1. ECG sensitivity for diagnosis of acute occlusion by artery.

Group	ECG diagnostic criteria	n = diagnostic ECGs
Left circumflex artery		
Total cohort (n = 120)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1 mm STE	55 (46%) 73 (61%)
RV/posterior leads subgroup (n = 36)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1 mm STE STE V7–V9 STE V3–V6R	18 (50%) 26 (72%) 13 (36%) 2 (6%)
Right coronary artery		
Total cohort (n = 137)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1 mm STE	117 (85%) 123 (90%)
RV/posterior leads subgroup (n = 26)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1 mm STE STE V7–V9 STE V3–V6R	20 (77%) 22 (85%) 8 (31%) 16 (62%)
Left anterior descending artery		
Total cohort (n = 161)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1mm STE	137 (85%) 155 (96%)
RV/posterior leads subgroup (n = 40)	Standard 12-lead ≥2 mm STE Standard 12-lead ≥1 mm STE STE V7–V9 STE V3–V6R	34 (85%) 40 (100%) 11 (28%) 4 (10%)

ECG: Electrocardiogram; STE: ST-segment elevation; RV: Right ventricular.
Data taken from [6].

review, which stated that standard 12-lead ECG was 50% sensitive for diagnosis of acute LCx occlusion, and between 70–80% and 90% sensitive for the diagnosis of acute RCA and LAD occlusions, respectively [9].

A study by Rasoul and colleagues analyzed ECG findings in STEMI patients to compare outcomes in acute MI secondary to LCx versus RCA culprit. Despite having worse outcomes and larger infarctions, patients with LCx culprits were more likely to have a nondiagnostic ECG, less cumulative STE, and were less likely to have Q waves on ECG ($p<0.001$) [10]. These findings support the lack of sensitivity for ECGs to detect LCx related changes and indicate that ECG changes may underestimate the severity of MI in the LCx territory.

It is likely that patients with LCx occlusion, compared with occlusion of other major coronary arteries, have a tendency to present more frequently with NSTEMI because of the vessel's posterior/lateral location placing it farthest from the chest wall, with a lack of corresponding ECG leads, [3,11,12] as well as late depolarization of the lateral wall leading to less visible Q waves in this territory [3].

Table 2. Studies examining ECG sensitivity for detecting occlusion in myocardial infarction by artery.

Study	Population	Artery	n = STE	p-value	Comments	Ref.
Schmitt *et al.* (2001)	Analysis of 418 patients with MI and angiographic occlusion of a coronary artery, comparing ECG sensitivity for each artery	LCx RCA LAD	55 (46%) 117 (85%) 137 (85%)	NA	Adapted from Table 1 using standard ECG criteria of >2 mm STE	[6]
Berry *et al.* (1989)	Analysis of surface ECGs in a catheterization laboratory while transiently occluding coronary arteries during PTCA	LCx RCA LAD	19 (32%) 12 (92%) 25 (84%)	<0.01	p-value applies to LCx compared with LAD and RCA, individually	[7]
Huey *et al.* (1988)	Prospective study of 241 patients with CK-MB confirmed MI and artery occlusion to compare ECG changes by artery involvement	LCx RCA LAD	19 (48%) 76 (71%) 68 (72%)	0.012	38% with LCx occlusion had no ST changes; 21% with RCA occlusion and 20% with LAD occlusion had no ST changes (p = 0.001)	[8]

CK-MB: Creatine kinase-MB; ECG: Electrocardiogram; LAD: Left anterior descending artery; LCx: Left circumflex artery; MI: Myocardial infarction; NA: Not available; RCA: Right coronary artery; STE: ST-segment elevation.

Culprit artery distribution in STEMI & NSTEMI

ST-segment elevation myocardial infarctions involving acute occlusion of the LCx occur less often than those involving the RCA or LAD [1,3,5,6,11]. Table 3 analyzes various studies of STEMI patients and vessel involvement in each [1,5,10, 13–18]. Other studies have offered potential explanations for this difference. It is possible that plaque rupture and thrombosis resulting in artery occlusion and transmural infarction simply occur less frequently in the LCx, but the reason behind this theory has not been well explained. Differences in LCx geometry lead to changes in wall shear stress that might make plaque rupture and thrombosis less common, but this theory has not been proven [3]. A more simple explanation would be that the difference is a matter of probability. The LCx is sometimes smaller, supplying less ventricular myocardium surface area, lending itself to a lower likelihood of MI occurrence [3].

Perhaps a more likely reason for the relative decreased incidence of STEMIs in the LCx is related to the insensitivity of ECGs. In the Krishnaswamy *et al.* study, the authors surmise that the low percentage of STEMIs involving the LCx is a representation of the low sensitivity of ECG for detecting occlusions in this territory, implying that many MIs related to LCx occlusion are being misdiagnosed as NSTEMIs [5]. Multiple large studies of non-ST elevation acute coronary syndrome (NSTE-ACS) have analyzed artery involvement and culprit lesion characteristics (Table 4) [3,5,11,19,20]. In most cases, the culprit lesion is equal among vessels, and acute occlusion appears to be undetectable on ECGs in about one in four cases. These NSTE-ACS studies, when isolating occlusions by arteries or location of infarcts, have shown that the LCx or its territory is more commonly involved, suggesting that occlusions of the LCx are more likely to be missed by standard 12-lead ECG, thereby supporting the argument that the low incidence of STEMI in LCx is related to misdiagnosis as NSTEMI.

Outcomes in MI involving the LCx

The clinical outcomes most studied in patients presenting with any coronary artery occlusion include mortality and re-infarction. Multiple studies have addressed these outcomes to determine if there are differences among MI patients with and without culprit vessel occlusion (Table 5) [3,11]. Each of these studies indicates that these clinical outcomes are worse in NSTE-ACS patients with occlusion compared with those without occlusion, but these studies do not analyze outcomes in those with LCx occlusion individually. Nevertheless, patients with infarcts involving typical LCx territories (inferolateral or posterolateral) were significantly more likely to have an occluded culprit than nonoccluded culprit [3,11], and in the study by Wang *et al.*,

Table 3. Culprit lesion distribution in multiple studies of ST-segment elevation myocardial infarction.

Study	Population	Artery (%)			Total	Ref.
		LCx	*LAD*	*RCA*		
Krishnaswamy *et al.* (2009)	Review including analysis of five major STEMI trials to examine frequency with which each artery is involved:					[5]
	HORIZONS-AMI	15.8	40.1	42.0	3559	
	CLARITY-TIMI 28	14.7	39.8	45.1	3066	
	On-TIME 2	11.5	41.7	45.8	907	
	Tadel-Kocjancic *et al.*	15.5	40.3	42.1	1666	
	Grines *et al.*	13.7	41.6	44.3	900	
	Total:	14.8	40.3	43.3	10,098	
Yip *et al.* (2002)	Prospective study of patients having PCI for MI (typical CP with STE or LBBB, or typical chest pain >30 min with STD and +markers) to analyze clinical features, outcomes, prognostic determinants in LCx occlusion	8.1	56.3	35.5	819	[1]
		Note: 84.4% of all patients had TIMI ≤1 flow on angiography with no significant difference between groups				
Wang *et al.* (2004)	Prospective evaluation of patients with STEMI to map location of artery occlusion	15.9	38.9	44.2	206	[13]
Rasoul *et al.* (2007)	Prospective evaluation of patients with STEMI or persistent symptoms with signs of ischemia to assess culprit artery and compare outcomes of LCx and RCA related MI	14	47	36	1657	[10]
		Note: 19 patients had left main culprit and 23 patients had CABG culprit				

+markers: Abnormal cardiac markers; CABG: Coronary artery bypass graft; CP: Chest pain; LAD: Left anterior descending artery; LBBB: Left bundle branch block; LCx: Left circumflex artery; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; RCA: Right coronary artery; STD: ST-segment depression; STE: ST-segment elevation; STEMI: ST-segment elevation myocardial infarction; TIMI: Thrombolysis in myocardial infarction.

Table 4. Culprit lesion distribution and incidence of occlusion in studies of non-ST elevation-acute coronary syndrome.

Study	Population	Group	Culprit artery		Comments	Ref.
			Occluded	*Non-occluded*		
Dixon *et al.* (2008)	A total of 30,386 NSTEMI patients undergoing PCI in NCDR database	Total	7199 (24%)	23,187 (76%)	Study did not define incidence of LCx occlusion; infarcts due to occlusion more likely in posterolateral territory (40 vs 32%, p < 0.0001)	[11]
		LCx	28%	28%		
		LAD	38%	38%		
		RCA	34%	34%		
Wang *et al.* (2009)	1957 NSTE-ACS patients from PARAGON-B trial who had diagnostic angiography	Total	528 (27%)	1429 (73%)	Infarcts due to occlusion more likely to occur in inferolateral territory (63 vs 45%, p < 0.0001)	[3]
		LCx	25%	23%		
		LAD	37%	54%		
		RCA	38%	24%		
Krishnaswamy *et al.* (2009)	Review, including major NSTE-ACS trials to examine incidence of artery involvement (ISAR-REACT 2, ACUITY and PRISM PLUS)	Total	1541 (14%)	9709 (86%)	Study did not define incidence of LCx occlusion; incidence of each artery involved also includes data of 3838 patients from Mauri *et al.*	[5]
		LCx	32.8%	32.8%		
		LAD	37.2%	37.2%		
		RCA	32.2%	32.2%		
VANQWISH trial (2002)	Patients with non-Q wave MI who had angiography to identify characteristics of culprit lesions	Total	46 (21%)	127 (79%)	Data include the 173 patients for which single culprit lesion was found; incidence of culprit occlusion by vessel includes those with multiple culprits	[19]
		LCx	38%	31.7%		
		LAD	27%	33.1%		
		RCA	35%	36.2%		

LAD: Left anterior descending artery; LCx: Left circumflex artery; MI: Myocardial infarction; NCDR: National Cardiovascular Data Registry; NSTE-ACS: Non-ST elevation-acute coronary syndrome; NSTEMI: Non-ST-elevation myocardial infarction; PCI: Percutaneous coronary intervention; RCA: Right coronary artery.

artery occlusion occurred in patients with inferolateral involvement more frequently than occlusion occurred in the other territories. Those with inferolateral occlusion had increased risk adjusted 6-month mortality compared with all other groups (HR: 1.93; 95% CI: 1.13–3.28). Owing to a similarity in 6-month mortality in the group with occluded culprit arteries to recently published data of 6-month mortality rates in STEMI patients, Wang *et al.* termed these cases 'STEMI equivalents' [3], suggesting that acute occlusions (even in absence of typical ECG changes) confer a risk similar to STEMI.

Lindahl *et al.* analyzed 1142 NSTE-ACS patients from the FRISC-II trial who had angiography to determine possible mechanisms for prognostic value of troponin T (TnT). Higher values of TnT were associated with worse 12-month outcomes. Of those with LCx culprits, the proportion of patients with occlusion increased from 4 to 22% as TnT value increased from <0.01 to >0.63 µg/l (p<0.001). There was not a similar increase in proportions of occluded culprits as TnT increased in the LAD (8–12%, p = 0.62) or RCA (7–9%, p = 0.48). Furthermore, a disproportionate

Table 5. Outcomes in myocardial infarction patients with occluded versus nonoccluded culprit lesions.

Study	Population	Significant outcomes	Culprit		p-value	Comments	Ref.
			Occluded	*Non-occluded*			
Dixon *et al.* (2008)	30,386 NSTEMI patients undergoing PCI in NCDR database	Mortality (hospital)	2.5%	1.4%	<0.001	In posterolateral MI (40% occluded vs 32% nonoccluded; p<0.0001)	[11]
		Cardioshock	1.6%	1.0%	<0.001		
		CHF	1.8%	1.3%	0.0002		
Wang *et al.* (2009)	1957 NSTE-ACS pts from PARAGON-B trial with diagnostic angiography	Mortality (6 month)	5.5%	3.5%	0.03	In inferolateral MI (63% occluded vs 45% nonoccluded; p<0.0001)	[3]
		LV dysfunction	20%	10%	<0.0001		
		Median peak CK-MB × ULN	4.3 ng/ml	2.1 ng/ml	<0.0001		

Cardioshock: Cardiogenic shock; CHF: Congestive heart failure; CK-MB: Creatine kinase-MB; MI: Myocardial infarction; NCDR: National Cardiovascular Data Registry; NSTE-ACS: Non-ST-elevation-acute coronary syndrome; NSTEMI: Non-ST elevation myocardial infarction; PCI: Percutaneous coronary intervention; ULN: Upper limit of normal.

number of patients in the group with highest TnT had occlusions, particularly in the LCx [21].

O'Keefe *et al.* evaluated whether patients with high risk MI involving the inferior wall, with RCA or LCx occlusion on angiography, would benefit from urgent reperfusion, regardless of ECG changes. This multicenter trial of 120 patients who had urgent reperfusion included 78 (65%) patients who had RCA occlusion and 42 (35%) patients who had LCx occlusion. Each of the patients with RCA occlusion had diagnostic STE on ECG, while ten (24%) of patients with LCx occlusion were without STE. When comparing these three groups (RCA with STE, LCx with STE and LCx without STE), there was no significant difference in left ventricular area at risk or the proportion of myocardium salvaged with urgent reperfusion, suggesting that those with LCx occlusion and no STE benefited from urgent reperfusion as much as those who presented with STEMI [2].

The aforementioned study by Rasoul *et al.* examining patients with STEMI to compare outcomes in those with acute MI secondary to LCx compared with RCA culprits found that those with infarcts involving the LCx were larger by peak CK-MB ($p<0.001$), were more likely to have a left ventricular ejection fraction less than 45% ($p < 0.01$), and had higher 30-day ($p = 0.03$) and 1 year ($p = 0.04$) all-cause mortality compared with infarcts involving the RCA. This study contradicts prior assumptions that infarcts involving the LCx are lower risk. These findings occurred in the presence of less ECG abnormalities, but the study did not identify presence or absence of artery occlusion on angiography. Those with LCx related MI had less collateral circulation with smaller LCx diameter [10].

Two small studies have compared outcomes in patients with and without ECG changes who had MI involving the LCx system. In a retrospective analysis of 56 MI patients presenting with LCx or obtuse marginal (OM) occlusion comparing outcomes in those presenting with NSTEMI compared with STEMI, those with STEMI had significantly larger infarcts ($p < 0.001$), higher rates of in-hospital mortality ($p = 0.017$), cardiogenic shock ($p = 0.019$), and in-hospital CHF ($p = 0.008$), as well as worse long-term outcomes. This study also found that patients with left or mixed coronary dominance were more likely to present with STE ($p = 0.037$) [22]. A recently published study included 96 patients with MI who were eventually found to have a significant LCx lesion to compare clinical characteristics and outcomes in those with and without ST-T changes. Patients without ST-T changes had lower creatine kinase ($p = 0.037$) and CK-MB ($p = 0.017$), and fewer patients without ST-T changes had Killip class III/IV. While patients with ST-T changes had higher overall and 30-day mortality, these differences were not statistically significant ($p = 0.28$ and 0.35, respectively). Similar to the prior study, ST-T changes were less likely to occur in patients with right or mixed dominance ($p = 0.05$). Furthermore, proximal lesions were more likely to lead to ST-T changes [23].

Three subgroups of LCx MI patients

It has previously been suggested that patients presenting with NSTEMI have better outcomes because they inherently have less myocardium at risk and the infarcts are subendocardial rather than transmural. However, more recent data have suggested that this assumption may not be true. Terkelsen *et al.* performed a review of 654 patients presenting with acute MI. Patients with STEMI had a 1-year mortality rate of 21% compared with a 1-year mortality rate of 31% in NSTEMI patients, with this difference remaining statistically significant after multivariate analysis. NSTEMI patients in this study and in other studies tend to have more comorbidities. While it was not the case in this study, other studies have also shown that NSTEMI patients have more multivessel disease [24]. Also addressed in this study by Terkelsen *et al.* is the difference in treatment strategies among these two groups, with STEMI patients having acute reperfusion. This difference in treatment strategy cannot be ignored when comparing these two groups. While the long-term risk may be greater in NSTEMI, the acute risk is inherently much higher for STEMI, which is why these patients require acute reperfusion and why acute identification of LCx occlusion may be important. If a significant proportion of LCx occlusions are not being detected by 12-lead ECG as suggested by multiple studies, improved detection of these infarcts may result in better patient outcomes.

Patients with MI involving the LCx can be divided into three groups: NSTEMI secondary to a non-occlusive culprit artery; NSTEMI secondary to occluded culprit; and STEMI. Given our relative lack of knowledge about MIs involving the LCx, low sensitivity of ECG for diagnosing LCx occlusions, and the frequency with which these occlusions occur in the setting of NSTE-ACS, it seems prudent to analyze and

compare outcomes in these three subgroups. The findings on 12-lead ECG may represent risk in the acute setting, as they do for other coronaries, or they may represent a special circumstance for which the 12-lead ECG is less representative of risk and outcomes, in which case analysis of other diagnostic strategies should be entertained.

ST-elevation myocardial infarction is higher risk than NSTEMI in the acute setting so group 3 represents the highest acute risk of MI of the LCx, and group 1 represents the lowest acute risk. The acute risk and outcomes of group 2 (NSTEMI secondary to occluded LCx as culprit) are less clear. The MI risk in these patients may be equivalent to group 3, as proposed by Wang *et al.* [3] or may be equivalent to group 1, as conventional knowledge would suggest. Alternatively, these patients may represent an intermediate risk group, whereby the MI risk lies somewhere between groups 1 and 3.

In many of the aforementioned NSTE-ACS studies, patients with acute occlusions have larger infarcts and worse outcomes than those without occlusions, when analyzing all arteries. Although none of the large studies specifically isolated the LCx, indirect evidence and smaller studies suggest that larger infarcts and worse outcomes may occur (and also may be more significant) in the LCx alone. These studies imply that group 2 has worse outcomes than group 1. One potential explanation for this discrepancy is that many of the aforementioned studies analyzed all vessels with occlusions. Inclusion of patients with acute occlusions of the RCA and LAD who have NSTEMI selects patients who are less likely to have nondiagnostic ECGs in acute MI (owing to a much higher sensitivity for ECG to detect acute occlusions) and selects vessels which are usually larger, supplying more myocardium, often without overlapping blood supply. The inclusion of these patients drives the clinical outcomes to be worse than patients presenting with STEMI.

Even less clear is whether occlusion of the LCx is actually a 'STEMI-equivalent'. The study by O'Keefe *et al.* compares patients with LCx occlusion and NSTEMI to those with STEMI involving the LCx, showing similar outcomes. This would imply that NSTEMI involving an occluded LCx culprit is of equal risk to STEMI. However, this was a small group of patients and results are based upon myocardial salvage rather than clinical outcomes. All NSTEMI patients underwent urgent revascularization within 6 h, which is not standard of care. There was no comparison group of NSTEMI patients with LCx occlusion who did not have urgent revascularization, and the lower risk NSTEMI patients were not included. Our recent retrospective study contradicts the O'Keefe study, indicating that occlusions of the LCx in NSTEMI are not 'STEMI-equivalents' [22]. Similarly, the Chua *et al.* study found that infarcts are larger if ST-T wave changes are present, also indicating that the lack of ECG changes may be representative of less myocardium involvement [23]. Some recently obtained, unpublished data involving over 150,000 MI patients with LCx or OM occlusion from the National Cardiovascular Data Registry (NCDR) CathPCI Registry suggests that STEMI patients have larger infarcts and worse short-term outcomes compared with NSTEMI patients.

We favor the hypothesis that NSTEMI with acute LCx occlusion (group 2) is of intermediate risk, resulting in larger infarcts and worse outcomes than NSTEMI involving LCx culprit without occlusion (group 1), but smaller infarcts and better outcomes than LCx resulting in STEMI (group 3). In actuality, patients in group 2 probably lie on a continuum between groups 1 and 3, with some approaching risk of STEMI and others approaching risk of NSTEMI without occlusion.

Myocardium at risk and effect of overlapping blood supply

There is little doubt that ECG insensitivity plays a major role in the high incidence of nondiagnostic ECGs in acute LCx occlusion, but we believe there is enough evidence in the aforementioned outcomes studies to suggest that other factors, such as myocardium at risk, also contribute to the high incidence of nondiagnostic ECGs in acute LCx occlusion. Myocardium at risk is a reflection of multiple factors, including area of ischemic myocardium and degree of overlapping blood supply. It is well known that the LCx supplies less myocardium than the LAD and if nondominant, the RCA as well. In a pathologic study of fatal infarcts, size of infarcts involving the RCA and LCx occupied respective means of 18 and 20% of the left ventricular myocardium, compared with a mean of 40% of the left ventricular myocardium in infarcts involving the LAD [25].

Furthermore, Elsman and colleagues have demonstrated that increased collateral flow in acute MI is associated with smaller infarct size and lower incidence of Killip class 2 or above [26]. Therefore, due to the fact that the LCx often supplies less myocardium with high incidence of collateralization from the RCA, the likelihood

of having significant STE on ECG is reduced. Similarly, Christian *et al.* determined that while a higher degree of STE was associated with myocardium at risk and infarct size, there was a stronger correlation with radionuclide measure of collateral flow [27]. In other words, STE were less prominent as amount of collateral flow increased. Although smaller studies, Stribling *et al.* and Chua *et al.* indicated that ECG changes are greatly dependent on coronary dominance such that those with right dominance, and potential dual blood supply to the LCx territory, are less likely to present with STEMI [22, 23]. By comparison, patients who have acute occlusions of a nondominant, small RCA do not have typical STE on inferior ECG leads representative of left ventricular myocardial injury [28,29].

Diagnostic testing

Multiple prior studies have suggested using improved diagnostic strategies in order to detect acute LCx occlusion in patients presenting with symptoms consistent with MI. Simply adding posterior and right ventricular (RV) leads have been shown to increase sensitivity for detection of the LCx territory [6]. Other potential diagnostic strategies suggested the inclusion of emergent angiography in high-risk patients, urgent transthoracic echocardiography to detect wall motion abnormalities for MIs involving LCx occlusion not detected by ECG [6,11,30], and acute coronary computed tomography [11]. Full body 80-lead ECG has also been shown to increase detection of STEMI compared with 12-lead ECG [31,32]. Its use in clinical practice has not been fully established, but it could potentially improve detection of acute LCx occlusions.

Other than posterior and RV leads in high-risk patients, these other potential solutions to diagnose acute LCx occlusion are not routinely recommended in clinical practice, and in some cases may be cumbersome, time consuming, and costly. We feel that high-risk patients with continuous, typical symptoms suggestive of ischemia without STE on 12-lead ECG should have additional posterior and RV leads with low threshold for immediate catheterization. This strategy would increase the likelihood of detecting acute LCx occlusions that may result in larger infarcts and poor outcomes. Less clear is the management strategy for patients with MI but lesser symptoms that are initially managed medically. It is likely that these patients, even with occlusion of LCx, are lower risk with smaller infarcts approaching risk of NSTEMI patients involving nonocclusive lesions.

Conclusion

The relative insensitivity of standard 12-lead ECG for the LCx makes the detection of artery occlusions in patients presenting with acute coronary syndrome difficult and has contributed to a lower incidence of STEMIs involving the LCx as compared with other major coronary arteries. Obviously, outcomes and management of NSTEMI without occlusion and STEMI involving the LCx or any other coronary artery has been well studied and should be managed as suggested by clinical guidelines. However, outcomes and management related to NSTEMI secondary to LCx occlusion are not well established. It has been assumed that acute occlusions of the LCx are similar to acute occlusions of other coronary arteries, despite the absence of STE on ECG, leading to the proposal to use other diagnostic strategies in order to detect acute LCx occlusion and potentially improve outcomes related to acute LCx occlusion.

As LCx occlusion is not detected as frequently by ECG, many patients with LCx related MI and occlusion are likely medically managed and never have coronary angiography. Therefore, there is a subset of patients who are never fully analyzed in studies. Many of these patients may have LCx occlusion without high-risk features, and their lack of inclusion selects for a higher risk group, potentially leading to an overestimation of risk in NSTEMI patients who are included in studies. For this reason, it is extremely difficult to determine the exact prognosis in patients with LCx occlusion.

Much of the literature analyzed in this review comes from studies including a selection of patients with acute coronary syndromes. Perhaps the real prognosis for LCx-related MI comes from registries in which all patients are included. However, based on all of the available data in the MI population with LCx culprits, we feel that NSTEMIs involving acute LCx occlusion have a risk profile in-between that of NSTEMI without occlusion and STEMI, with some infarcts approaching risk of STEMI and some approaching risk of NSTEMI without occlusion. The best explanation for the variable presentations of MIs secondary to LCx occlusion involves the extent of myocardium at risk. Those presenting with STEMI or high-risk symptoms likely have dominant LCx systems supplying a large percentage of left ventricular myocardium, leading to larger infarcts and more obvious ECG changes, while those with NSTEMI and low risk clinical features likely have RCA dominance with collateral blood supply to the LCx

territory, leading to smaller infarcts, inability of the ECG to capture electrical changes, and better outcomes. Currently, use of additional posterior and RV ECG leads, along with monitoring of signs and symptoms and clinical judgment should be used to determine where patients with acute coronary syndrome potentially related to the LCx lie on this continuum. Those with evidence of STE on additional leads or high-risk patients with ongoing clinical evidence of ischemia likely approach risk of STEMI and should be managed accordingly, while those without significant ECG changes or ongoing symptoms are likely to approach risk of NSTEMI and may be managed more conservatively.

Future perspective

Myocardial infarction secondary to acute LCx occlusion continues to be difficult to diagnose with the standard 12-lead ECG, leading to consideration of other modalities to acutely identify these infarctions. Though we have made inferences and predictions regarding outcomes in patients with MI secondary to LCx occlusion, no large, published studies have isolated MI patients with LCx occlusion to determine risk profile in those presenting with NSTEMI compared with STEMI and to identify potential reasons for variations in ECG findings.

If patients with acute LCx occlusion presenting with NSTEMI have outcomes similar to those NSTEMI patients with LCx lesions without culprit occlusion, it obviates the need to undergo further testing to acutely identify an occlusion in this territory. Only if patients with LCx occlusion and NSTEMI are determined to have risks similar to STEMI patients (or at least greater than NSTEMI patients), should other noninvasive acute testing be established and standardized in order to better recognize LCx occlusion and improve outcomes. Potential diagnostic modalities would include urgent angiography or coronary computed tomography, transthoracic echocardiography, nuclear imaging, 80-lead ECG, or other yet-to-be determined diagnostic strategies. These testing modalities would then need to be studied rigorously to determine the best strategy for this group of patients.

We feel that patients with NSTEMI secondary to culprit LCx occlusion who are clinically stable without significant ECG changes will approach risk of all other NSTEMIs and may be managed accordingly, while those who are clinically unstable with recurrent symptoms or ischemic ECG changes will approach risk of STEMI. Analysis of angiographic findings in these patients will also find that left dominance will predict STEMI in LCx occlusion while right dominance will predict NSTEMI. If our predictions are correct, there will be less of an emphasis on other diagnostic modalities to acutely and non-invasively identify acute LCx occlusion.

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Executive summary

ECG sensitivity for acute left circumflex artery occlusion
- ECG sensitivity for the diagnosis of left circumflex artery (LCx) occlusion is less than 50%.
- ECG sensitivity for the diagnosis of right coronary artery or left anterior descending artery occlusion is more than 70%.

Incidence of myocardial infarction in major coronary arteries
- ST-elevation myocardial infarction (STEMI) and non-ST elevation-acute coronary syndrome (NSTE-ACS) occur least often in the LCx.
- Occlusions in NSTE-ACS are more likely to occur in LCx or its territory.
- ECG insensitivity is often considered to be the reason for differences.
- More studies are needed to better define reasons for differences.

Comparison of outcomes in myocardial infarction secondary to left circumflex artery occlusion based upon ECG findings
- When analyzing all coronaries, outcomes are worse in NSTE-ACS patients with occlusion compared with those without occlusion.
- STEMI has a higher risk and worse outcomes than non-STEMI (NSTEMI) when isolating LCx occlusion myocardial infarction patients.
- Risk of NSTEMI with LCx occlusion may fall on a continuum between STEMI and NSTEMI without occlusion.
- Larger, more directed studies are needed to compare outcomes.

Role of myocardium at risk
- Right coronary dominance may predispose to NSTEMI.
- Amount of myocardium supplied by LCx may be directly related to STEMI presentation.

Management strategies
- Noninvasive strategies in addition to standard ECG have shown promise in diagnosing acute LCx occlusion.
- These modalities are only necessary if the diagnosis of acute LCx occlusion without traditional ECG changes is proven to improve outcomes.

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