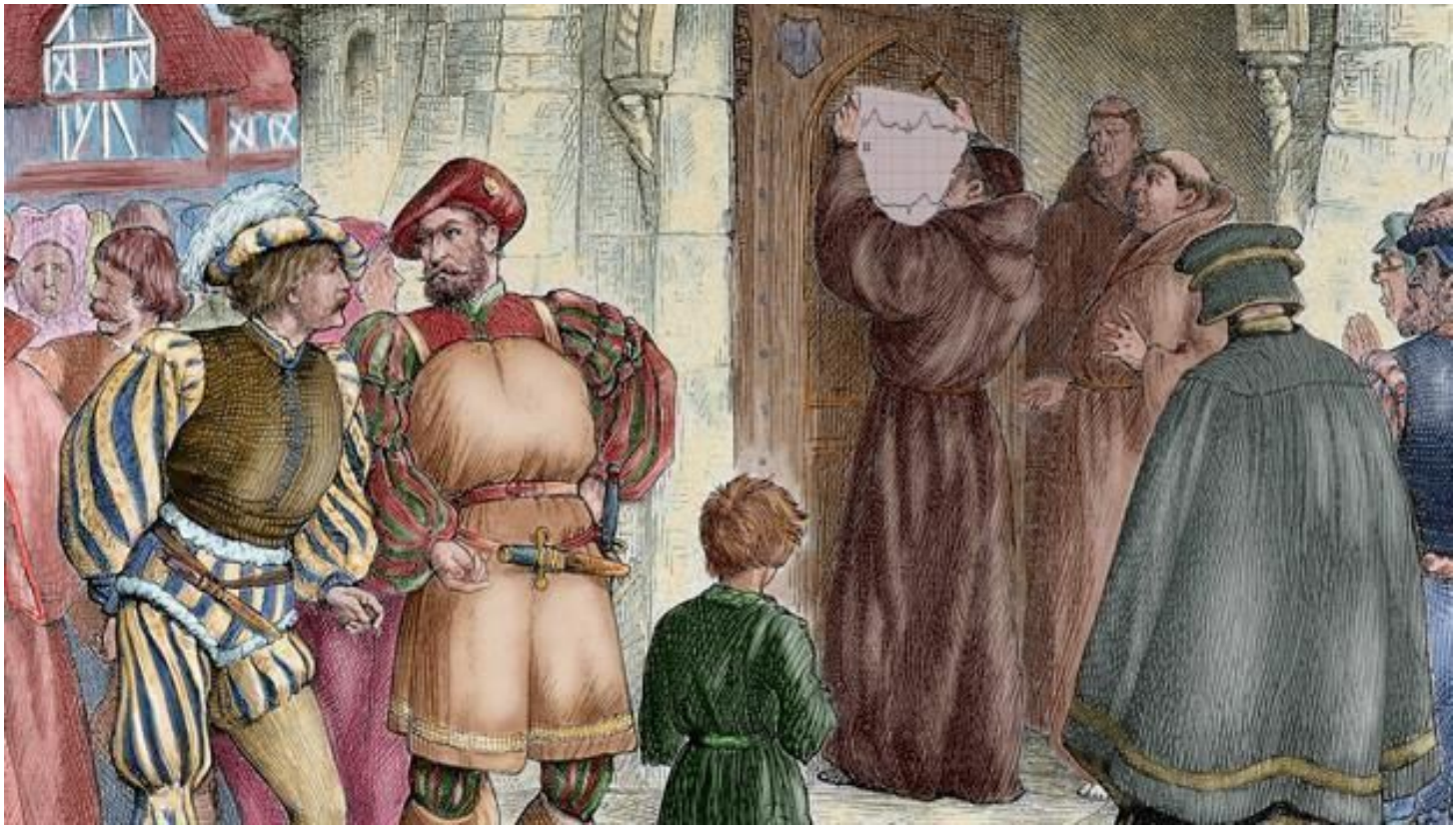
The OMI Manifesto



A collaboration by Dr. Smith's ECG Blog and EMCrit

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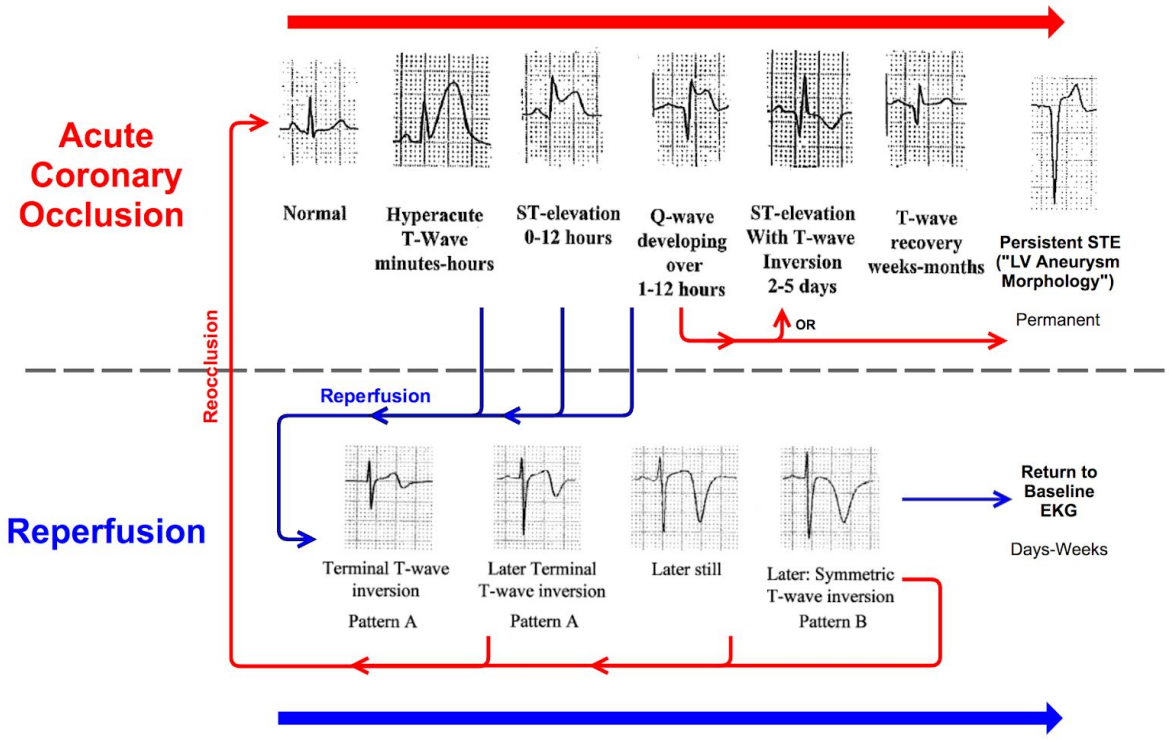
The current guideline-recommended paradigm of acute MI management ("STEMI vs. NSTEMI") is irreversibly flawed, and has prevented meaningful progress in the science of emergent reperfusion therapy over the past 25 years. Dr. Stephen Smith, my mentor and co-editor of this post, has been saying this much more eloquently for many years in his **"STEMI/NSTEMI False Dichotomy" lecture series**, but this bears repeating and needs to be reiterated as widely as possible.

Deciding which patients need emergent reperfusion therapy is complex, and our current criteria for doing so are not adequate to the task. The patients who benefit from emergent catheterization are those with acute coronary occlusion (ACO) or near occlusion, with insufficient collateral circulation, whose myocardium is at imminent risk of irreversible infarction without immediate reperfusion therapy. This is the anatomic substrate of the entity we are supposed to refer to as "STEMI." Unfortunately the term "STEMI" restricts our minds into thinking that ACO is diagnosed reliably and/or only by "STEMI criteria" and the ST segments. In reality, the STEMI criteria and widespread current performance under the current paradigm have unacceptable accuracy, routinely missing at least 25-30% of ACO in those classified as “NSTEMI”[1-9] and generating a similar false positive rate of emergent cath lab activations.[10-12]

The STEMI-NSTEMI paradigm was the best idea available in 2000, when it formally replaced the Q-wave vs. Non-Q-wave MI paradigm.[13] This paradigm shift was prompted by the Reperfusion Era, in which multiple large randomized controlled trials proved the efficacy of emergent reperfusion therapy.[14] More specifically, nearly 60,000 ACS patients were randomized to thrombolytics vs. placebo, showing an impressive mortality benefit of NNT=56 for entire cohort given thrombolytics, despite the fact that 4 of the 9 trials had no ECG inclusion criteria whatsoever, and one-third of the patients had no appreciated STE. In the subgroup with undefined STE, lytics showed an even greater mortality benefit of NNT=43. This means that STE predicted ACO (and thus mortality benefit) better than not looking at the ECG at all. However, thanks to Dr. Smith and others we have learned a great deal about expert ECG interpretation since the 1994 FTT meta-analysis, and it turns out STE is no longer our best option for predicting ACO and therefore benefit from emergent reperfusion.

To anyone who has spent time seeing patients and studying the ECGs and angiograms of acute MI, it is obvious why the STEMI criteria routinely fail in both directions. Foremost, ACO is a complex and dynamic process that doesn’t always manifest any ECG changes at all. When it does manifest ECG changes, it is an intricate and time-sensitive progression of changes, exquisitely sensitive to reperfusion and reocclusion. The earliest stages of ACO (when the benefit of intervention is maximal) routinely do not show any STE. Even if you are lucky (or wise) enough to obtain an ECG during the ST segment changes, STE is always proportional to the size of the QRS complex, which may be very small in some territories with low voltage on the surface ECG such as the high lateral wall. Furthermore, not all ACOs produce STE, some result only in changes in the QRS or T-wave, or no ECG findings at all. This may be due to a variety of causes: time of recording (including during a brief period of spontaneous reperfusion), “electrocardiographically silent” myocardial territory, small myocardial territory, and low QRS

voltage. Meanwhile, a huge proportion of controls without acute coronary syndrome have normal variant STE, or have abnormal depolarization (LVH for a common example) generating appropriate repolarization abnormalities which frequently meet STEMI criteria.



The progression of ECG findings seen during acute coronary occlusion and reperfusion.

In an attempt to spread this knowledge without challenging the deeply ingrained “STEMI vs. NSTEMI” paradigm, terms such as “STEMI equivalent” and “subtle STEMI” and “semiSTEMI” have been created and discussed for years in the literature. Sadly, these attempts have not produced widespread change in perception or management of acute MI except in the small groups of clinicians who have special interest in following such literature or the various FOAM resources that broadcast this knowledge.

For too long we have tried to keep the familiar, catchy, and beloved term “STEMI” in the name, when in reality the name itself is part of the problem. The term “STEMI” cognitively inspires us to think that only the ST segments matter, that the ST segments are reliable and don’t depend on the preceding QRS complex, and that STE on the ECG is the only necessary data point for making the reperfusion decision. If we want progress on a larger scale in the management of acute MI, we will be forced to break from the current paradigm. While some have suggested a requiem for “unstable angina” (an entity that is alive and well), we should instead nominate for a

requiem the dangerous and uniquely brainwashing term STEMI. For 25 years it has restricted our thinking, prevented further research from showing who actually benefits from emergent reperfusion, and blinded us to how much better we can do for our patients whose myocardium is actively infarcting under our care. “Is the patient having a STEMI?” must eventually be replaced with something that reminds us of the real question we should be asking: "Does the patient have an acute coronary occlusion that would benefit from immediate intervention?" To accomplish these goals, we propose the term **“OMI”** as an alternative:

OMI = Occlusion **M**yocardial **I**nfarction

To learn the history, literature, and experience that supports these views, as well as the reasons we propose OMI, read on.

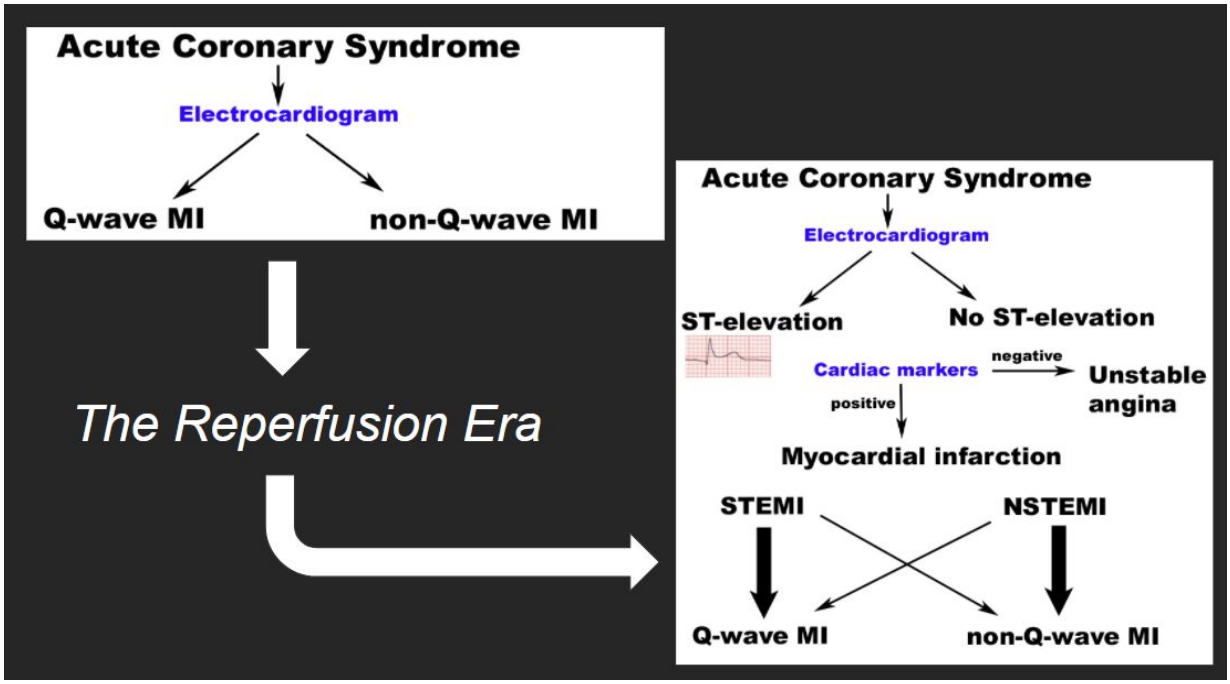
Part I: The History of STEMI and Reperfusion

In the reperfusion era we sought to answer several important questions:

Does reperfusion therapy work?

How should we prospectively and noninvasively identify who receives emergent reperfusion therapy?

The good news is that we answered one of those two questions conclusively: reperfusion therapy ***does*** work. Thrombolytics were proven to save lives in almost 60,000 patients randomized to thrombolytics vs. placebo in the reperfusion era, in one of the strongest displays of evidence in the history of medicine.[14] Prior to this discovery, the previously existing paradigm had been known as “Q-wave vs. non-Q-wave” MI, in which the clinicians had few significant therapies during acute MI, and simply had to observe the patient while they completed their transmural infarct. Afterward, if the patient was still alive, they would be classified according to whether their ECG developed the Q-waves typical of transmural infarction.



Unfortunately, you will be convinced at the end of this discussion that we have not yet answered the tougher question: *Who* should receive emergent reperfusion therapy? *How* do we identify them prospectively and noninvasively?

Who benefits from potentially dangerous interventions designed to emergently open a coronary artery? *Patients with acutely occluded coronary arteries.* There is no other theory or evidence suggesting any possible benefit from emergent reperfusion therapy other than opening an acute occlusion (or near occlusion with insufficient collateral circulation such that there is significant and irreversible acute myocardial infarction). Without the beneficial part of the intervention, patients can only receive the harms.

The worst complications of coronary angiography are coronary dissections and perforations, which generally only occur from the actual coronary intervention rather than the diagnostic portion of angiography. However, all patients who undergo emergent coronary angiography (even the false positives who do not receive PCI) receive the following risks: early diagnostic closure (with possible harms depending on the actual missed/delayed diagnosis), arterial punctures with bleeding complications such as groin or retroperitoneal hematomas exacerbated by loading with multiple antiplatelet and anticoagulation drugs, contrast associated nephropathy, large cost and resource mobilization.

In the worst case scenario, there are some patients with incidental, non-acute CAD who get emergent cath and PCI *only due to* a scary-looking baseline non-ischemic ECG (for example, because the baseline features happen to meet STEMI criteria). Otherwise, these patients may not have received angiography at all, because they would have had serial negative troponins

followed by discharge or negative stress test. When these unlucky patients are cathed emergently due a false positive ECG on account of the STEMI criteria, and the interventionalist finds the baseline 70% non-culprit chronic atherosclerotic coronary stenosis, the lesion will often be intervened upon even though it is neither acute nor the cause of the ECG findings. These patients receive the full set of risks above including dissections and perforations, with no chance of benefit and rare but disastrous complications.

This seems painfully obvious, but we have to say this out loud several times during this historical journey to keep your mind grounded in reality in order to realize how far astray we have been led: **Patients with Occlusion MI (or near-occlusion with insufficient collateral circulation) are the only ones who benefit from *emergent* reperfusion therapy. And this is true no matter what their ECG shows. Those who have acute MI without occlusion (Non-Occlusion MI, or NOMI) do not need angiography emergently, although undergoing emergent reperfusion likely does not result in harm compared to urgent angiography in this subgroup. All others are exposed to the chance of harm without benefit, and do not need to be taken to the cath lab emergently.**

So in the trials designed to evaluate the efficacy of reperfusion therapy vs. placebo, how did they try to predict who had ACO and who didn't?

They *didn't*. All placebo controlled trials were in the thrombolytic era. Angiography was not employed in these studies prior to therapy, even if available. Instead of trying to figure out who had ACO (a diagnosis they couldn't make), they randomized very high risk patients with concerning acute chest pain, most with concerning but undefined ECG findings, to thrombolytics vs. placebo and observed for mortality without knowing which patients had ACO.

Before any subgroup analysis at all, the entire population of 58,600 patients on average received a significant mortality benefit of NNT=56 from lytics compared to placebo. Four of the nine component RCTs of the meta-analysis did not require any ECG changes at all for enrollment, and one-third of the patients had no appreciated STE. Despite these facts, lytics saved lives in the overall population even before ECG subgroup analysis was performed. This can only mean that the clinicians selected an initial population with a high enough prevalence of ACO that the benefit from giving lytics to the ACO patients was large enough to outweigh the harm in the patients without ACO.

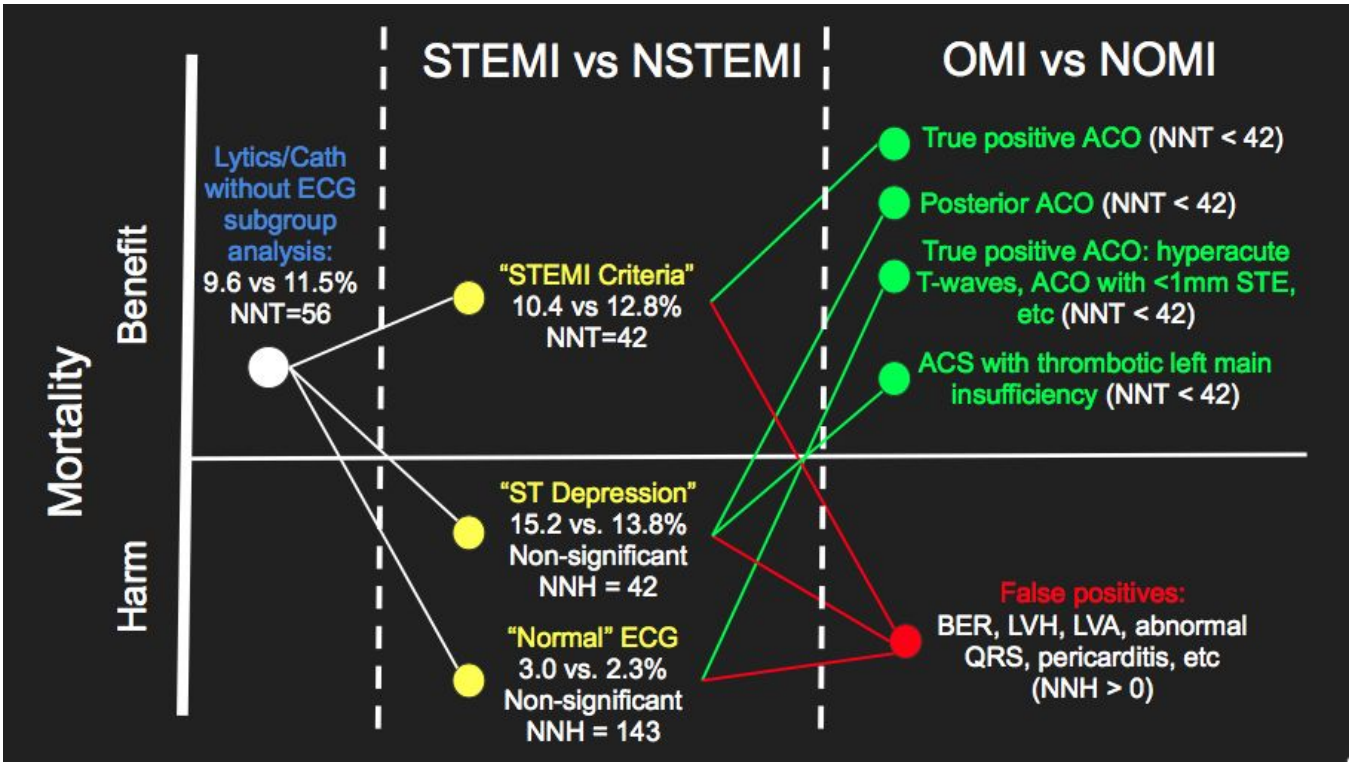
Given the enormous sample size, the next logical step was to do subset analyses to identify certain groups which had higher or lower mortality benefits (or harms) from the interventions. They discovered important trends in the timing of intervention from the onset of symptoms which are not the focus of this discussion but summarized by the eternal saying "time is muscle." Next they compared the effects of thrombolytics in all patients to the effects in subsets of patients with certain ECG findings. The subgroups included ST depression, ST elevation, and "normal." Unfortunately, only 4 of the 9 component RCTs defined their version of STE, and these 4 had

varying cutoffs and methods of measurement (usually not even specified). Compared to giving lytics to all patients regardless of ECG findings, using an undefined amount of STE as the arbiter of lytics administration produced an improvement in the NNT for short term mortality from 56 to 43. Conversely, the subgroups of ST depression and “normal” ECG showed a nonsignificant mortality *harm* (in other words, no benefit). No further subgroup analysis was performed in attempt to better define which patients received mortality benefit vs. harm. “Normal” and “ST depression” were also not defined.

Because you have not forgotten that emergent reperfusion can only be beneficial in patients with acute occlusion or near-occlusion, you realize that the subgroup of patients with STE must have had a higher proportion of patients with ACO than the groups without STE. This makes intuitive sense - if one group has all of the obvious “STEMIs” and the other group doesn’t, the group with the obvious “STEMIs” will likely have the higher proportion of ACOs and therefore the highest mortality benefit from lytics. But from your experience you realize that there are also many false positives in the STE subgroup (patients with STE but without ACO), and there are many false negatives in the non-STE group (patients without STE but with ACO), all of whom have a mortality harm by being in the wrong group.

In the STE group of the FTT meta-analysis, for example, you realize that there must be some patients with normal variant STE (“early repolarization”), LVH, LV aneurysm, takotsubo cardiomyopathy, pericarditis, appropriately discordant STE from an abnormal QRS, etc. Each of these patients in the lytics group received an approximately 1-2% risk of death from thrombolytics within the first 24 hours of treatment, without any chance of benefit because they did not have ACO.

Conversely, in the “normal” EKG and ST depression subgroups there were certainly ACO patients with hyperacute T-waves, subtle STE less than the undefined cutoff, posterior infarction manifesting as only precordial ST depression, and diffuse subendocardial ischemia with many leads with deep ST depression due to large thrombus, etc. Each of these patients in the placebo group missed out on a mortality benefit by not receiving thrombolytics.



Graphical representation of the mortality effects of subgroup analysis from the FTT Meta-analysis, with extrapolated effects showing the subdivision of patients into Occlusion vs Non-Occlusion MI rather than STEMI vs. NSTEMI.

Although STE predicts ACO better than no ECG interpretation at all, you know intuitively that there is much more room for improvement, which was unfortunately not possible in the FTT meta-analysis because they could not correlate ECG findings with angiographically proven occlusion. It is commendable that they started down the logical path of figuring out that the ECG might be a useful tool in identifying ACO quickly, easily, noninvasively, and anywhere. But remember that the FTT meta-analysis was published in *1994, and most of the studies it was based on were conducted in the 1980s*. Since then we have vastly improved our medical management and techniques for mechanical reperfusion. Naturally, you might look eagerly at the literature from 1994 onward, assuming that after 25 years with routine catheterizations they surely must have been able to perform large-scale mainstream research that helps us correlate ECG findings with ACO more accurately than when they first proved it was possible in 1994.

Inexplicably, you would be almost entirely mistaken in this assumption. Although the interventions themselves have improved, there has been almost no meaningful progress in the official worldwide approach to identifying ***who*** should get emergent intervention since 1994. Instead of 25 years of mainstream literature systematically improving our ECG criteria by correlating with angiographic evidence of occlusion, you will find 25 years of methodologically inapplicable mainstream studies and guidelines squabbling over STE millimeter criteria without demonstrating any rational thought as to what outcome they are trying to predict when they change the cutoff in V3 from 1.5 to 2.0 mm and back again.

Let us prove it to you with the following timeline of the relevant mainstream literature between 1994 and present day, which we found by following the guidelines' paper trail of references for their recommendations:

1994: Fibrinolytic Therapy Trialists' Group Meta-Analysis[14]

The FTT Meta-analysis proves that the Reperfusion Era is one of modern medicine's great success stories. No specific criteria are proposed as to what defines diagnostic STE, as most of the studies had no formal definition and the remaining studies had varying definitions.

2000: Braunwald et al, JACC: ACC/AHA Guidelines for Unstable Angina[13]

The official paradigm of of acute MI management formally changes from "Q-wave vs. non-Q-wave MI" to "STEMI vs. NSTEMI."

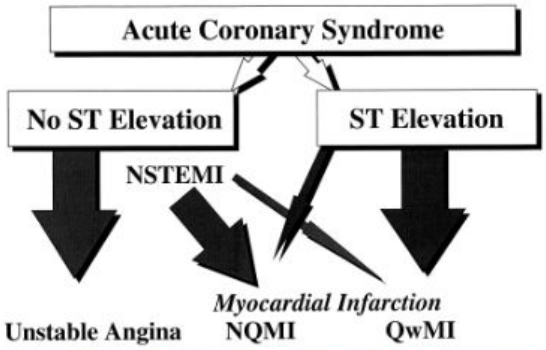


Figure 1. Nomenclature of ACSs. Patients with ischemic discomfort may present with or without ST-segment elevation on the ECG. The majority of patients with ST-segment elevation (large arrows) ultimately develop a Q-wave AMI (QwMI), whereas a minority (small arrow) develop a non–Q-wave AMI (NQMI). Patients who present without ST-segment elevation are experiencing either UA or an NSTEMI. The distinction between these 2 diagnoses is ultimately made based on the presence or absence of a cardiac marker detected in the blood. Most patients with NSTEMI do not evolve a Q-wave on the 12-lead ECG and are subsequently referred to as having sustained a non–Q-wave MI (NQMI); only a minority of NSTEMI patients develop a Q-wave and are later diagnosed as having Q-wave MI. Not shown is Prinzmetal's angina, which presents with transient chest pain and ST-segment elevation but rarely MI. The spectrum of clinical conditions that range from US to non–Q-wave AMI and Q-wave AMI is referred to as ACSs. Adapted from Antman EM, Braunwald E. Acute myocardial infarction. In: Braunwald EB, ed. Heart disease: a textbook of cardiovascular medicine. Philadelphia, PA: WB Saunders, 1997.

2000: Menown et al, European Heart Journal: Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction[15]

Menown performs a case-control study of 1190 subjects. 149 healthy controls plus 1041 patients with acute chest pain (335 of which had acute MI diagnosed by biomarkers including CK-MB) were combined and then divided into "training" and "validation" groups. Logistic regression using various millimeter cutoffs in different leads was performed on the training group, then tested in the validation group. They concluded that the best cutoff was $\geq$2 mm STE in at least one of the anteroseptal leads, or $\geq$1mm in any of the other leads. This correctly

classified 83% of the patients as acute MI or no acute MI, with 56% sensitivity and 94% specificity. This is referenced throughout the future guidelines. The outcome was MI by biomarkers (CK-MB), not angiography, so cases without occlusion are included in the MI group.

Even if the sensitivity were adequate, they unfortunately fail to recognize that "acute MI" diagnosed by biomarkers is not the outcome we are trying to predict. We are trying to predict ACO or near ACO because that's who benefits from emergent vs. urgent reperfusion. Certainly ACO causes elevated biomarkers, but no one has ever advocated that positive biomarkers alone identifies a subgroup with ACO and/or benefit from emergent reperfusion. Like many other studies you will see in this arc of literature, this study does not include angiographic findings and does not make any mention of other ECG findings other than STE.

2000: First Universal Definition of MI[16]

In 2000 the American College of Cardiology and the European Society of Cardiology published their first combined "STEMI criteria" referencing the FTT meta-analysis and Menown et al. They are identical to Menown's derived criteria above.

Table 3. ECG Changes Indicative of Myocardial Ischemia That May Progress to MI

1. Patients with ST segment elevation:
   New or presumed new ST segment elevation at the J point in two or more contiguous leads with the cut-off points ≥0.2 mV in leads V_1, V_2, or V_3 and ≥0.1 mV in other leads (contiguity in the frontal plane is defined by the lead sequence aVL, I, inverted aVR, II, aVF, III).
2. Patients without ST segment elevation:
   a. ST segment depression
   b. T wave abnormalities only

New or presumed new ST segment depression or T wave abnormalities, or both, should be observed in two or more contiguous leads. Also, new or presumed new symmetric inversion of T waves ≥1 mm should be present in at least two contiguous leads.

2001: Macfarlane et al: Age, Sex, and the ST Amplitude in Health and Disease[17]

Macfarlane argues that normal healthy people have differing amounts of STE on their baseline ECGs, and this seems to differ by age and sex. 1338 healthy patients' ECGs are reviewed and age/sex-specific normal cutoffs are presented for each of the 12 classic leads, showing how the amount of STE on baseline ECGs changes by age and sex. He concludes "It is clear that any diagnostic criteria for ST abnormality must be based on a knowledge of these changes."

	Precordial Leads					
	V1 STj	V2 STj	V3 STj	V4 STj	V5 STj	V6 STj
Male	0.06 ± 0.04	0.16 ± 0.07	0.15 ± 0.06	0.09 ± 0.05	0.05 ± 0.04	0.03 ± 0.03
18-29 yr	0.00–0.15	0.03–0.33	0.05–0.31	0.00–0.20	−0.01–0.15	−0.02–0.10
Female	0.02 ± 0.02	0.05 ± 0.04	0.04 ± 0.03	0.02 ± 0.03	0.01 ± 0.02	0.01 ± 0.02
18-29	−0.02–0.07	−0.01–0.14	−0.03–0.11	−0.04–0.08	−0.04–0.06	−0.03–0.05
Male	0.05 ± 0.04	0.13 ± 0.07	0.11 ± 0.06	0.07 ± 0.05	0.04 ± 0.04	0.03 ± 0.03
30-39	−0.02–0.13	0.00–0.30	0.00–0.25	−0.03–0.17	−0.03–0.13	−0.03–0.08
Female	0.02 ± 0.02	0.05 ± 0.04	0.04 ± 0.04	0.01 ± 0.03	0.01 ± 0.03	0.01 ± 0.02
30-39	−0.02–0.06	−0.03–0.14	−0.04–0.12	−0.05–0.10	−0.04–0.06	−0.04–0.05
Male	0.05 ± 0.03	0.11 ± 0.06	0.09 ± 0.05	0.05 ± 0.04	0.03 ± 0.03	0.02 ± 0.02
40-49	0.00–0.11	0.02–0.27	0.01–0.22	−0.01–0.13	−0.03–0.09	−0.03–0.07
Female	0.03 ± 0.02	0.05 ± 0.03	0.03 ± 0.03	0.01 ± 0.03	0.01 ± 0.03	0.00 ± 0.02
40-49	−0.01–0.08	−0.02–0.14	−0.03–0.10	−0.04–0.07	−0.05–0.06	−0.04–0.06
Male	0.05 ± 0.03	0.10 ± 0.06	0.08 ± 0.06	0.04 ± 0.04	0.02 ± 0.02	0.01 ± 0.03
≥50	−0.01–0.12	0.01–0.24	−0.02–0.20	−0.05–0.13	−0.06–0.10	−0.05–0.07
Female	0.03 ± 0.02	0.05 ± 0.03	0.03 ± 0.03	0.01 ± 0.03	0.00 ± 0.02	0.00 ± 0.01
≥50	−0.01–0.09	−0.02–0.13	−0.05–0.09	−0.05–0.08	−0.06–0.05	−0.05–0.04

Note: these values are in millivolts (mV). 0.1 mV = 1 millimeter (mm)

Macfarlane has explored one particular ECG finding (STE) in healthy patients with normal conduction who presumably do not have ACO. From this we see that widespread ST segment elevation is in fact common, and varies widely even among particular age/sex groups. Unfortunately it cannot speak to the ECG findings of patients who actually do have ACO, and he does not characterize other important aspects of the healthy normal ECG (R-wave amplitude, QT interval, T-wave size relative to QRS complex, area under the ST segment and T-wave, presence of pathologic Q waves, QRS amplitude, QRS fragmentation/distortion, J-waves, etc).

2003: Wu et al, International Journal of Cardiology. Normal limits of the electrocardiogram in Chinese subjects.[18]

Similarly, Wu and colleagues collected ECGs from 5,360 apparently healthy Chinese adults (3,614 men and 1,746 women from ages 18 to 84). Upper and lower limits of various ECG measurements were recorded, and age/sex differences were analyzed. They confirmed that STE is common, with 2% of males aged 18-40 having 3mm or more of J-point elevation in leads V1 and V2 at baseline. They conclude that “some of these findings are at odds with established diagnostic ECG criteria.”

Again, the reason these findings are at odds with the criteria is because the any ST segment elevation criteria are imprecise at differentiating normal STE from abnormal. This study is nevertheless cited throughout the future guidelines.

2004: ACC/AHA STEMI Guidelines[19]

ACC/AHA instead recommends STE of >1mm in any 2 contiguous leads as a Class 1A recommendation for fibrinolytic therapy.

Pharmacological reperfusion

Indications for Fibrinolytic Therapy

Class I

1 **In the absence of contraindications, fibrinolytic therapy should be administered to STEMI patients with symptom onset within the prior 12 hours and ST elevation greater than 0.1 mV in at least 2 contiguous precordial leads or at least 2 adjacent limb leads.** (*Level of Evidence: A*)

2004: Macfarlane et al., Journal of Electrocardiology: Age, Sex, and the ST Segment in Health and Disease[20]

Macfarlane and colleagues hypothesize that age and sex-based cutoffs will better predict myocardial infarction than current 1st Universal Definition criteria. They used logistic regression techniques to derive revised STEMI criteria from a training set of 2285 patients (789 with chest pain and 1496 normal adults). They then tested the derived criteria on 1220 separate patients with chest pain (248 with acute MI by *biomarkers*, 972 without; since this cohort was from the 1980s, the "biomarker" used was CK-MB, not troponin). No angiographic outcomes are included. The derived criteria below are almost impossible to decipher, not to mention the fine print "certain other restrictions apply." With this added complexity they were only able to increase the sensitivity from 42 to a *whopping 47%* and the specificity from 96 to 99%.

Table 2. Outline of proposed criteria for ST elevation MI

1. For any one lead, for males ≥35 years and females ≥40 years.
   a) ST_j amplitude >age/sex dependent limit and $|S/ST| < 8.0$.
   b) $ST/T > 0.23$ for aVL, I
      or $ST/T > 0.35$ for II, aVF, III
      or $ST/T > 0.25$ for V1 - V4
   c) $|T-| < 100\ \mu V$

Certain other restrictions apply

If any two contiguous leads meet the above criteria, then ST elevation MI is reported unless these are V1, V2 or V2, V3 in the presence of LVH with secondary repolarisation abnormalities.

OR

2. For any age/sex
   a) ST_j amp $> 80\ \mu V$ and $ST/T > 0.55$ and $|S/ST| < 8$
   b) $ST > 200\ \mu V$ in any limb lead and $|S/ST| < 8$
   c) $ST > 400\ \mu V$ in any chest lead and $|S/ST| < 8$

If any 2 contiguous leads meet criterion (a) or any one lead meets criterion (b) or (c), then ST elevation MI is reported.

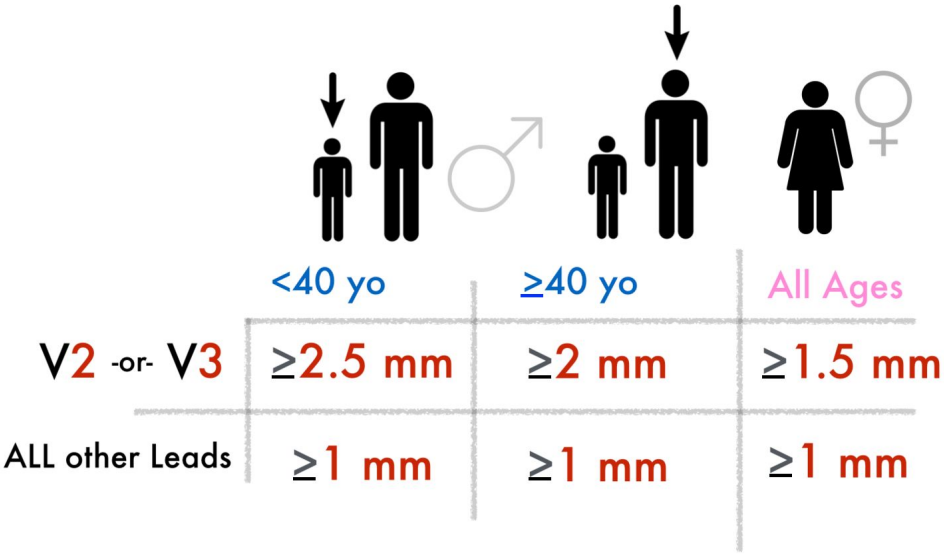
Once again, lack of angiographic outcomes leaves the reader wondering if the authors even understood that STEMI is supposed to predict ACO and mortality benefit from emergent reperfusion. We are not trying to correlate ECG findings with elevated biomarkers, we are trying to correlate with ACO so that we know whom to take to the lab emergently to prevent the cell death that results in the release of biomarkers. Even if the authors had used angiographic outcomes, it still demonstrates the constricted thinking that only the ST segments matter - despite amazingly complex criteria proposed, no ECG findings other than STE are considered. Although these criteria never show up again in any literature I have found, this study is referenced throughout the future guidelines.

2007: 2nd Universal Definition of MI[21]

International guidelines now recommend 2 contiguous leads with at least 1.0 mm STE, except leads V2-V3 which require 1.5 mm in women and 2.0 mm in men.

2009: AHA/ACCF/HRS Standardization and Interpretation of the Electrocardiogram[22]

Chief authors Galen Wagner and Peter Macfarlane introduce for the first time the current "STEMI criteria", citing former guidelines, Macfarlane et al, and Wu et al, recommending 2 contiguous leads meeting STE criteria pictured here:



2012: 3rd Universal Definition of MI[23]

The criteria are identical to the 2009 AHA/ACCF/HRS criteria above and are the currently recommended criteria worldwide. Like the other criteria above, they do pay some minor lip service to other possible ECG findings such as hyperacute T waves as possibly representing acute MI, but they do not seem to understand that these findings might equally represent acute

coronary occlusion or benefit from emergent cath, and they give no formal recommendation as to how they should be diagnosed or treated.

2018: Sadly, that bring us up to present day. As you can see, the mainstream literature and development of guidelines from 1994 to 2018 has been almost completely devoid of critical thought and methodologic rigor despite millions of ACOs and catheterizations during that time. None of the guidelines seem to realize that acute MI diagnosed by biomarkers is not the outcome by which we should be evaluating ECG findings. It seems as though no guideline author has considered whether there might be more to identifying ACO on the ECG than ST segments alone. Meanwhile, Dr. Smith and many others have continued to produce textbooks, studies, and FOAM resources showing how to improve our ECG interpretation beyond this rudimentary level, but despite this there is ongoing mainstream ignorance of these advances.

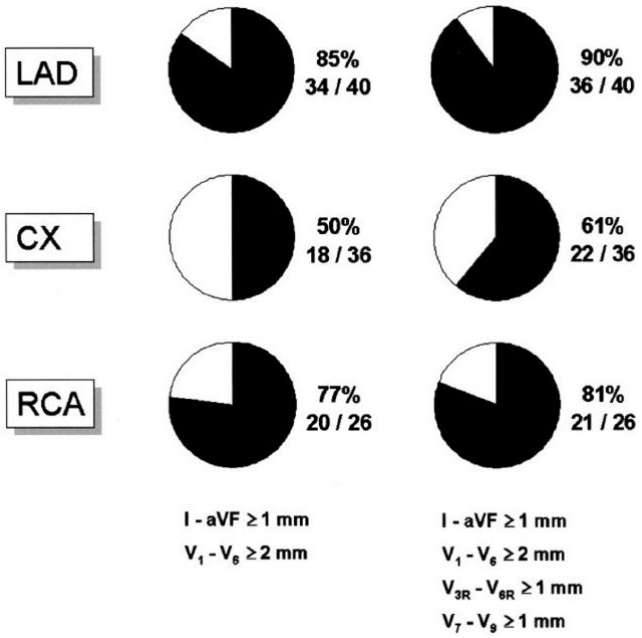
Now that you see the development of the STEMI criteria after 1994 is simplistic and uncritical, you might speculate that there exists evidence confirming your suspicion that STEMI criteria are inaccurate in identifying ACO. You'd be correct.

Part II: How and Why "STEMI Criteria" Fail

#1: Under the current "STEMI" paradigm, 25-30% of the patients we classify as "NSTEMI" are consistently found to have missed acute coronary occlusion.

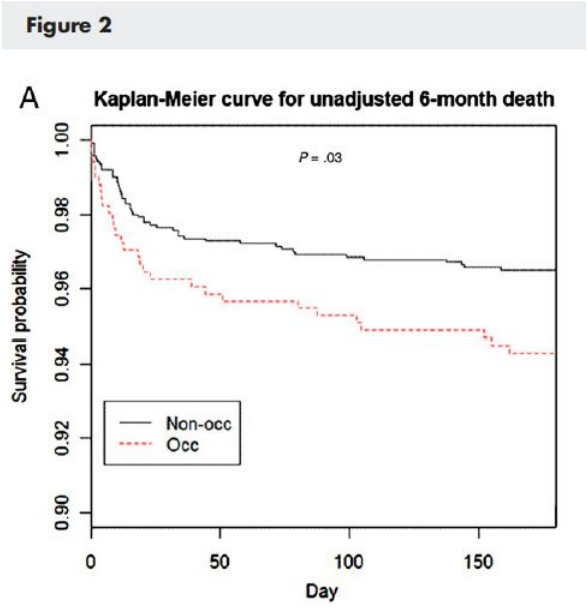
Schmitt et al. Diagnosis of acute myocardial infarction in angiographically documented occluded infarct vessel: limitations of ST-segment elevation in standard and extended ECG leads. Chest 2001.[1]

1788 patients with acute MI (diagnosed by clinical symptoms and positive CK-MB) were prospectively enrolled and all underwent emergent coronary angiography. 418 of these 1788 (23%) had acute coronary occlusion. Of the 418 patient with ACO, 29% did not meet "STEMI criteria." The highest miss rate (50%) was recorded in patients with acute left circumflex occlusion. In the graphic below you can see the proportion of coronary occlusions which were identified by the STEMI criteria subdivided by coronary artery and presence of extended leads.



Wang et al. Incidence, distribution, and prognostic impact of occluded culprit arteries among patients with non-ST-elevation acute coronary syndromes undergoing diagnostic angiography. American Heart Journal 2009.[2]

Post-hoc analysis of the PARAGON-B randomized controlled trial. Of 1,957 patients with NSTE-ACS (those who were prospectively negative for STEMI criteria), 528 (27%) had completely occluded culprit vessels. There was no difference in the time from admission to angiography between the groups (both about 3 days), but the coronary occlusion group had larger infarct size (higher troponins) and higher 6 month risk-adjusted mortality.



From AM et al. Acute myocardial infarction due to left circumflex artery occlusion and significance of ST-segment elevation. The American Journal of Cardiology 2010.[3]

1,500 consecutive patients with complete occlusion or near occlusion ($\geq$90% stenosis with TIMI <3) were identified post-hoc from a prospective PCI database. Their ECGs were then re-read to determine whether they met STEMI criteria (in this study $\geq$1mm in 2 contiguous leads). Even with the formidable bias of knowing that these patients all had occlusion or near occlusion prior to ECG review, only 1,077 (72%) patients met STEMI criteria, while 423 (28%) did not. This is particularly remarkable considering that only 1 mm was used as criteria even for anterior MI. The recommended value for V2 and V3 is now 1.5 mm for women, 2.0 mm for men > age 40, and 2.5 mm for men under age 40.

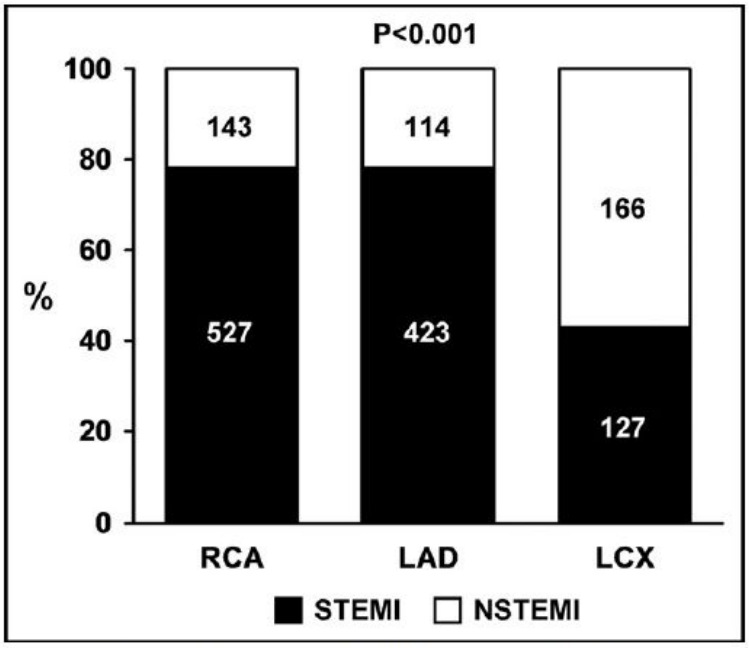


Figure 1. Relative frequency of STEMI versus NSTEMI presentation according to culprit artery.

Pride et al. Angiographic and clinical outcomes among patients with acute coronary syndromes presenting with isolated anterior ST-segment depressions. JACC 2010.[4]

Post hoc analysis of the TRITON-TIMI-38 randomized controlled trial comparing prasugrel with clopidogrel among ACS patients undergoing cardiac catheterization. Of 13,608 patients, 1,198

(8.8%) were identified based on isolated anterior ST segment depressions (who therefore did not meet their current STEMI criteria). 314 (26.2%) of these 1,198 patients had completely occluded culprit arteries (defined as TIMI flow 0 or 1) at the time of cardiac cath. Because only ~¾ of the original 13,608 patients actually had MI, the 314 patients with occlusion actually represents closer to one-third of the group, rather than one-fourth as presented. The left circumflex artery was the most frequent culprit artery in those with occlusion (48%).

Abbas et al. Acute angiographic analysis of non-ST-segment elevation acute myocardial infarction. American Journal of Cardiology 2004.[5]

Post-hoc analysis of the Primary Angioplasty for Acute Myocardial Infarction study. Of 1,531 patients in the study, there were only 61 patients without STE or LBBB who received immediate angiography. 29 patients (45.8%) of this "NSTEMI" group had TIMI=0 (acute occlusion) found upon angiography. In the group with STE or LBBB, only 61.5% had TIMI=0.

TABLE 1 Baseline Clinical, Demographic, and Angiographic Criteria

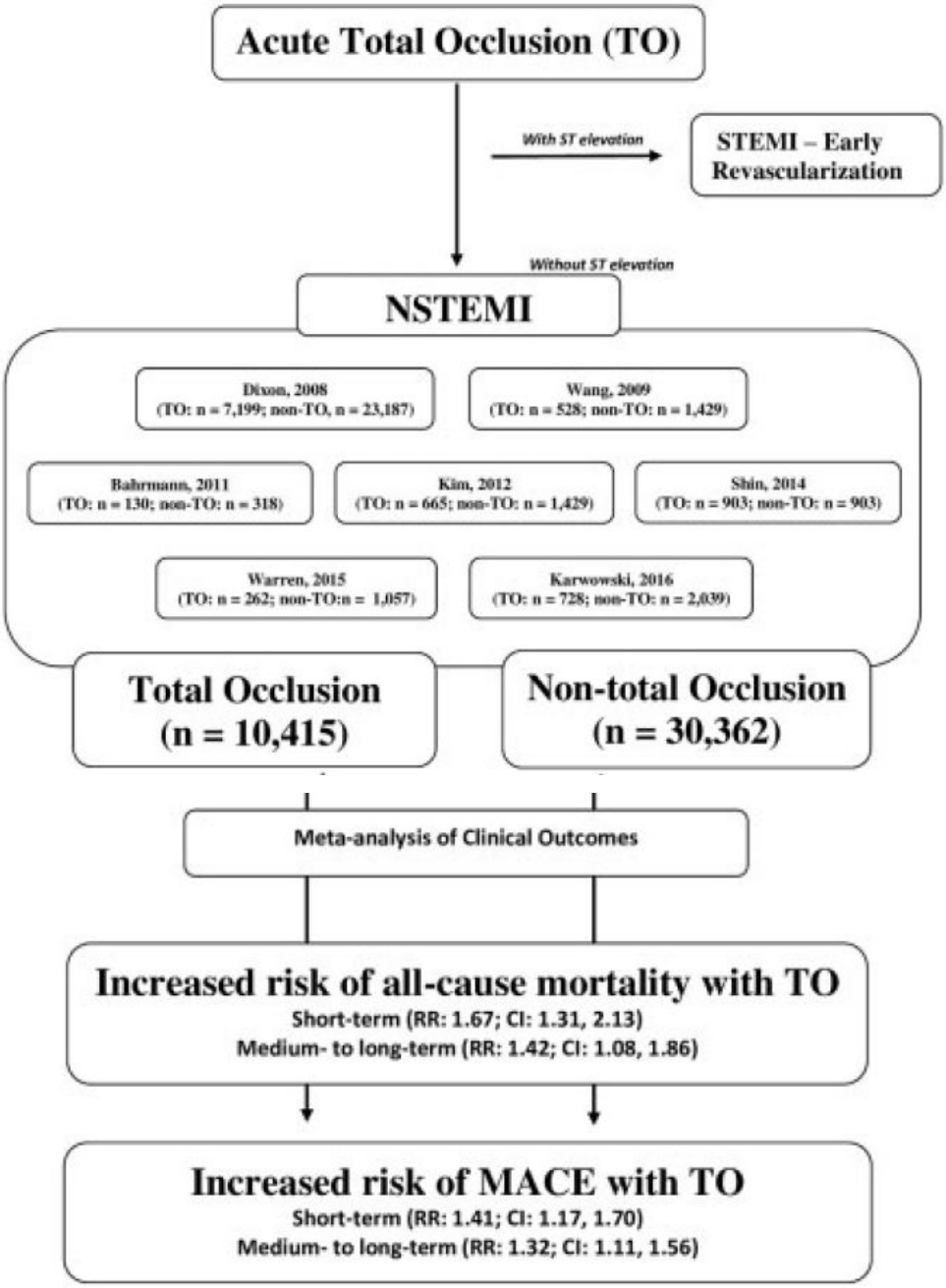
Criteria	STE or LBBB AMI (n = 1,470)	Non-STE AMI (n = 61)	p Value
Clinical and demographic			
Age (yrs)	61 ± 13	60 ± 11	0.36
Killip class >I	132 (9%)	4 (7%)	0.43
Women	387 (26%)	15 (25%)	0.76
Diabetes mellitus	243 (17%)	7 (12%)	0.31
Previous myocardial infarction	196 (13%)	14 (23%)	0.036
Hypertension	657 (45%)	26 (43%)	0.7
Ever smoked	989 (67%)	49 (80%)	0.033
Previous coronary bypass surgery	52 (3.6%)	8 (13%)	0.002
Angiographic criteria and procedural outcome			
Emergency room to balloon time (min)	143 ± 192 (110)	230 ± 176 (185)	<0.0001
Infarct-related coronary artery			
Right	610 (42%)	19 (31%)	0.16
Circumflex	202 (14%)	18 (30%)	0.0003
Left anterior descending	595 (40%)	18 (30%)	0.13
Other	63 (4%)	6 (9%)	
Percutaneous coronary intervention	1,366 (93%)	54 (89%)	0.2
Multivessel disease	742 (50%)	28 (46%)	0.48
Initial percent stenosis	97.3% ± 6.3 (100)	97% ± 4.4 (99)	0.012
Initial TIMI score >0	566 (38.5%)	32 (54.2%)	0.011
Ejection fraction (%)	48.6 ± 12	45.4 ± 14	0.010
Catheter laboratory complications*	260/1,067 (24%)	7/44 (16%)	0.2
Procedural success	1,226/1,366 (90%)	56/59 (95%)	0.43
Final TIMI score = 3	1,247/1,363 (91.5%)	52/54 (96%)	0.31

*Includes bradycardial and ventricular arrhythmias, intubation, hypotension, death, and cardiopulmonary resuscitation.
Values are numbers (percentages) or mean ± SD (median).
STE = ST-segment elevation.

Khan et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. European Heart Journal 2007.[6]

Meta-analysis including all available prospective observational studies or post-hoc analyses of RCTs in which NSTEMI patients were prospectively enrolled and assessed for the prevalence of totally occluded culprit arteries. They found 7 studies (only 1 of which we discussed above,

Wang et al), including a total of 40,777 NSTEMIs, 10,415 (25.5%) of which had total coronary occlusions found on angiography an average of 24 hours after presentation. Those with unrecognized acute total occlusion had higher short and long-term risk of MACE and mortality.



Koyama et al. Prevalence of coronary occlusion and outcome of an immediate invasive strategy in suspected acute myocardial infarction with and without ST-segment elevation. The American Journal of Cardiology 2002.[7]

This is an amazing study documenting the results one hospital found when they underwent a "radical shift from a noninvasive to an invasive strategy available 7 days/week, 24 hours/day...available to all patients with non-ST elevation acute coronary syndromes if symptoms and/or electrocardiographic abnormalities did not respond to anti-ischemic treatment within ~20 minutes and acute myocardial infarction was suspected by clinicians." STEMI was defined in this study by STE $\geq$1mm in at least 2 consecutive limb leads and/or $\geq$ 2mm in at least 2 consecutive precordial leads. During the initial transition period they enrolled 279 patients with STEMI and 125 with NSTEMI. Of the 125 NSTEMIs, 59 (47%) had TIMI 0 flow (complete occlusion). In fact, closer inspection of Table 3 below shows that the rates of each TIMI flow grade recorded in "NSTEMI" were shockingly similar to that found in the "STEMI" patients, confirming that STE does not differentiate occlusions from non-occlusions (OMI from NOMI). Rather than a 3 day delay to catheterization as in the retrospective studies above, 93% of all patients in this study underwent cath within 6 hours of presentation. Not surprisingly, given both groups had similar rates of occlusion and similar time to angiography, there was no difference in any measured in-hospital or 6 month clinical outcomes.

TABLE 3 Angiographic Findings

	STEMI (n = 279)	NSTEMI (n = 125)	p Value
Culprit coronary			
Left anterior descending	122 (44%)	27 (22%)	<0.001
Left circumflex	31 (11%)	33 (26%)	<0.001
Right	96 (34%)	33 (26%)	0.14
Left main	3 (1.1%)	3 (2.4%)	0.56
No coronary artery disease	17 (6.1%)	13 (10%)	0.19
Not identified	10 (3.6%)	16 (13%)	0.001
TIMI flow grade			
0	160 (57%)	59 (47%)	
1	9 (3.2%)	5 (4.0%)	
2	39 (14%)	15 (12%)	
3	71 (25%)	46 (37%)	0.12
No. of coronary arteries with >50% luminal narrowing			
1	123 (44%)	36 (29%)	0.005
2	70 (25%)	38 (30%)	0.32
3	76 (27%)	38 (30%)	0.28
None	17 (6.1%)	13 (10%)	0.19

TABLE 5 Cumulative Event Rates

	STEMI (n = 279)	NSTEMI (n = 125)	p Value
All-cause mortality			
In-hospital	13 (4.7%)	7 (5.6%)	0.91
6 mo	19 (6.8%)	11 (8.8%)	0.62
Nonfatal myocardial infarction			
In-hospital	8 (2.9%)	1 (0.8%)	0.35
6 mo	12 (4.3%)	3 (2.4%)	0.52
Nonfatal stroke			
In-hospital	4 (1.4%)	2 (1.6%)	0.75
6 mo	5 (1.8%)	2 (1.6%)	0.78
Post-coronary artery bypass surgery	2 (0.7%)	2 (1.6%)	0.78
Unrelated to coronary artery bypass surgery	2 (0.7%)	0 (0.0%)	0.86
Target lesion revascularization			
In-hospital	6 (2.2%)	5 (4.0%)	0.47
6 mo	13 (4.7%)	9 (7.2%)	0.42

Marti D et al. Incidence, angiographic features, and outcomes of patient presenting with subtle ST-elevation myocardial infarction. American Heart Journal 2014.[8]

Prospective observational study of 504 patients with acute “persistent ischemic symptoms not responding to nitrates plus any ST elevation [who] were admitted for emergent coronary angiography.” These patients were grouped into those with “subtle STE” defined as 0.1 to 1mm of STE, and those with “marked STE” defined as 1mm or more of STE in any one lead. The primary outcome of the study was the preprocedural incidence of occlusion defined as an acute culprit with TIMI 0 or 1 flow, which was recorded in 86% of the 504 patients. Of those with occlusion, 18% had not even a single lead with 1mm STE (much less 2 consecutive leads with 1-2.5mm as is required in certain leads in our current criteria).

Smith et al. Electrocardiographic differentiation of early repolarization from subtle anterior ST-segment elevation myocardial infarction. Annals of Emergency Medicine 2012.[9]

Retrospective case-control study comparing 143 electrocardiographically “subtle” proven acute LAD occlusions compared against 70 controls with acute chest pain and ST segment elevation in the emergency department who ruled out by serial biomarkers and cardiology evaluation. 31 (22%) patients with subtle LAD occlusion (9% of all 355 LAD occlusions identified) had mean STE less than or equal to 1 mm. 19 patients had no lead with more than 1mm, and 8 patients had less than or equal to 1 mm in only 1 lead. The LR+ and LR- of the guideline-recommended STEMI criteria performed pitifully in this population. Low R-wave amplitude was a better

predictor of LAD occlusion in this group than was STE. A 3-variable logistic regression formula using computerized QTc, R-wave amplitude in lead V4, and ST Elevation at 60 ms after the J-point in lead V3 performed far better than any ST elevation criteria at differentiating normal variant ST Elevation from Subtle LAD Occlusion.

Table 4. Diagnostic utility of various STEMI voltage criteria in subtle myocardial infarction versus early repolarization, derivation group and validation group combined (n=314; 143 STEMI, 171 ER).*

At Least 2 Consecutive Leads With STE	Location of STE Measurement	LR+ (95% CI)	LR– (95% CI)
1) ≥1 mm V1–V6	STEJ	1.0 (0.7–1.5)	0.9 (0.5–1.4)
	STE60	1.0 (0.9–1.0)	5.0 (0.6–45)
2) ≥2 mm in any of V1–V3 or ≥1 mm V4–V6[19]	STEJ	1.4 (1.1–1.6)	0.7 (0.5–0.9)
	STE60	1.2 (0.9–1.5)	0.6 (0.4–0.9)
3) ≥1 mm V1 or V4–V6, or ≥2 mm in V2–V3	STEJ	1.3 (1.0–1.5)	0.7 (0.6–0.9)
	STE60	1.2 (0.9–1.5)	0.5 (0.3–0.8)
4) ≥1 mm V1 or V4–V6, or ≥2 mm in V2–V3 (men) or ≥1.5 mm in V2–V3 (women)	STEJ	1.3 (1.0–1.6)	0.7 (0.5–0.9)
	STE60	1.1 (0.8–1.5)	0.5 (0.3–0.8)
5) ≥1 mm in V1 or V4–V6, or ≥2 mm in V2–V3 (men) or ≥2.5 mm in V2–V3 (men <40 y) or ≥1.5 mm in V2–V3 (women)[18]	STEJ	1.5 (1.2–1.7)	0.6 (0.3–0.8)
	STE60	1.2 (0.9–1.6)	0.3 (0.2–0.6)
6) ≥1 mm in V5–V6 or ≥2 mm in V1–V4	STEJ	1.7 (1.4–2.0)	0.7 (0.5–0.9)
	STE60	1.3 (1.0–1.6)	0.5 (0.4–0.8)
ECG criterion: STEMI if >23.4: (1.196×STE60 V3)+(0.059×QTc)–(0.326×RA V4)		**9.2 (8.5–10)**	**0.1 (0.08–0.3)**

*Data for LR+ approaching 10 and LR– approaching 0.1 have been bolded.

Counter-argument: ***"Haven't there been RCTs showing no benefit for early vs. delayed intervention for NSTEMI patients? If so, why didn't the subtle ACOs in these NSTEMI cohorts generate a benefit for the early intervention groups?"***

There is a moderately-sized body of literature which has been mistakenly used to claim that there is no difference in outcomes between immediate vs. urgent invasive treatment for NSTEMI, explained in detail below. Even if this were an accurate representation of the literature, it would not disprove the theory that the subgroup of NSTEMI patients with ACO benefit from emergent invasive management. If the percentage of patients with ACO is low in the study population of NSTEMIs, even a large mortality benefit (for those with ACO) will not be observable in a small RCT. If you randomize five patients with ACO as well as 300 without ACO, you may not detect a difference in outcomes even if all five ACO patients were saved by emergent intervention. If you use expert ECG interpretation to successfully select out those few patients with ACO, however, the benefit will be obvious (because acute occlusion is who benefits). **There has never been any prospective interventional study using expert ECG interpretation to examine the effects of immediate vs. non-immediate cardiac catheterization.** We hope to change this in the future.

Nevertheless, we must inoculate ourselves with the literature concerning immediate vs. urgent invasive treatment for NSTEMI because it is frequently used as an objection to the idea that any subgroup of NSTEMI patients might need emergent intervention. The misconceptions in the

following studies generally stem from the fact that "early" intervention was not actually performed emergently, and that NSTEMI patients with ischemia refractory to maximal medical therapy were excluded from the trials (as they already have an indication for emergent [<2 hours] angiography according to both the European Society of Cardiology guidelines and the ACC/AHA guidelines.[24,25]

Mehta et al. Early versus delayed invasive intervention in acute coronary syndromes. The TIMACS (Timing of Intervention in ACS) Trial. NEJM 2009.[26]

3031 NSTEMI patients were randomized to "early" intervention (</=24 hours) vs. delayed (>/=36 hours) intervention. The median time from presentation to coronary angiography was 14 vs. 50 hours in the "early" vs. delayed groups, respectively. Because the "early" intervention was not actually early, the study cannot be used to inform the decision to pursue emergent (generally considered < 2hrs) invasive intervention on NSTEMI patients, let alone on ACO patients without obvious STE. Unsurprisingly, there was no difference in the rates of death, MI, or stroke in these two groups. Although not stated in the methods, personal communication between the lead author and Dr. Smith revealed that patients with refractory ischemia were (appropriately) excluded from the trial altogether. When effects of early intervention were stratified by GRACE risk score, a significant reduction in the primary outcome (composite of death, MI, or stroke) was found in the group with GRACE score more than 140 (13.9% vs. 21.0%, P=0.006).

Hoedemaker et al. Early Invasive Versus Selective Strategy for Non-ST-Segment Elevation Acute Coronary Syndrome: The ICTUS Trial. JACC 2017.[27]

The ICTUS trial randomized 1,200 NSTEMI patients with elevated troponin T to "early invasive" ("within 24 to 48 hours after randomization") vs. "selectively invasive" groups. There was no difference in 1-year mortality (2.5% in both groups) or spontaneous MI, but there was a 5% absolute increase (15 vs. 10%) in myocardial infarction in the early invasive group which was ascribed to procedure-related MI. At 10-year follow up there was again no statistical difference in death or spontaneous MI (34 vs 29%). Notably, patients were excluded for "an indication for reperfusion therapy, hemodynamic instability or overt congestive heart failure," which by the current guidelines includes refractory ischemia. Prevalence of angiographic occlusion and detailed ECG analysis are not reported. Although this study has no bearing on any question regarding emergent reperfusion therapy, the 5% absolute increase in peri-procedural MI (NNH=20) does reinforce the significant harms of emergent catheterization for those without benefit (those without ACO).

van't Hof et al. A comparison of two invasive strategies in patients with non-ST elevation acute coronary syndromes: results of the Early or Late Intervention in unStable Angina (ELISA) pilot study. European Heart Journal 2003.[28]

220 patients with non-ST elevation ACS were randomized to "early" vs. "late" (median time to angiography 6 vs. 50 hours). There was no difference in clinical outcomes at 30 days follow up. Refractory ischemia was excluded. Although 6 hours is certainly sooner than 24-48, it is still not soon enough to qualify as emergent reperfusion therapy. No detailed ECG analysis performed, and no angiographic occlusion data reported. **Remember this important fact:** refractory chest pain was excluded. Patients with OMI with persistent occlusion generally have refractory pain; thus, such patients would have been excluded.

Neumann et al. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. The ISAR-COOL Study. JAMA 2003.[29]

410 patients with Non-STE ACS but with either ST depression or elevated troponin T levels were randomized to antithrombotic pretreatment for 3-5 days or to early intervention with <6hrs of pretreatment. The two groups received catheterization with a median time of 2.4 vs. 86 hours from presentation. All patients received aspirin, clopidogrel, heparin, and tirofiban. There was significantly higher rate of death or "large" MI in the delayed strategy group compared to the early invasive group (11.6% vs. 5.9%, P=0.04). This difference was driven by an excess of 3 deaths and 10 large MIs in the delayed strategy group which all occurred before delayed angiography. Incredibly, the authors' conclusion is spun as the following: "In patients with unstable coronary syndromes, deferral of intervention for prolonged antithrombotic pretreatment *does not improve the outcome* compared with immediate intervention accompanied by intense antiplatelet treatment." Stated more appropriately to their opening metaphor, it appears the supposed "cooling-off" period was more of a smoldering burn period, during which the patients' myocardium was sizzling on the back-burner. No angiographic occlusion data or detailed ECG analysis was reported.

Thiele et al. Optimal timing of invasive angiography in stable non-ST-elevation myocardial infarction: the Leipzig Immediate versus early and late PercutaneouS coronary Intervention triAl in NTSEMI (LIPSIA-NSTEMI Trial). European Heart Journal 2012.[30]

201 patients with NSTEMI were randomized to receive immediate (<2 hours, median 1.1 hour) catheterization, while 200 patients were randomized to an receive 10-48 hour (median 18.6 hours) catheterization. There was no difference in death or MI within 6 months. Exclusion criteria appropriately featured refractory ischemia. No detailed ECG analysis available, and no angiographic occlusion outcomes available. With a truly short time to catheterization in the immediate group, the most likely explanation for lack of benefit is that the patients with subtle occlusion (who were more likely to have refractory ischemic symptoms) were correctly excluded in the first place.

Montalescot et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. JAMA 2009.[31]

352 patients with non-STE ACS, TIMI score 3 or greater, but without refractory ischemia were randomized to receive immediate or next working day intervention (between 8 and 60 hours). Actual average time from randomization to sheath insertion was 70 minutes vs. 21 hours between the two groups. Median peak troponin I values did not differ between the two groups (2.1 vs. 1.7 ng/mL). There was no difference in the secondary endpoint composite of death, MI, or revascularization at 1 month follow up (13.7 vs 10.2%). Prevalence of angiographic occlusion is not available, nor is detailed expert ECG analysis. Again, lack of benefit likely confirms that patients with subtle occlusion were correctly excluded from the study based on refractory symptoms.

Reuter et al. Early invasive strategy in high-risk acute coronary syndrome without ST-segment elevation. The Sisca randomized trial. International Journal of Cardiology 2015.[32]

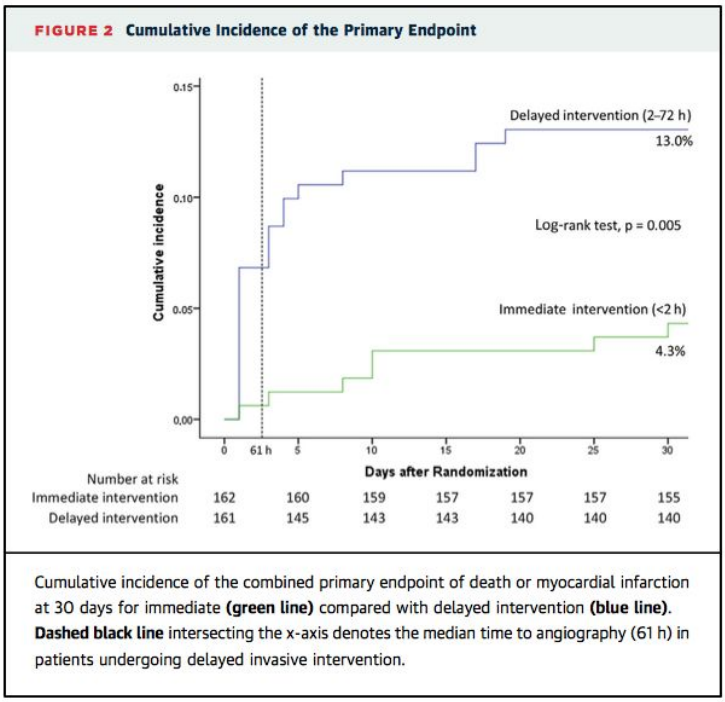
170 patients were enrolled primarily in the pre-hospital setting based on NSTE-ACS and at least one of three ECG findings in at least two contiguous leads: “(1) T-wave inversion of more than 3 mm, (2) a ST segment depression of at least 0.5 mm and/or (3) a transient ST-segment elevation of at least 1 mm.” These patients were randomized to either an early invasive strategy (angiography within 6 hours) or a delayed invasive strategy (angiography within 6 hours not advised but per physician discretion). Notably, because these patients were enrolled pre-hospital, “refractory angina” could not be excluded as the patients had not yet received maximal medical management. The median time from randomization to sheath insertion was 2.8 hours in the early invasive strategy group compared to 20.9 hours in the delayed invasive strategy group.

The primary endpoint (composite outcome including death, MI, or urgent revascularizations at 30 days) was significantly lower for early invasive strategy group (2% vs. 24%, $P<0.01$). However, closer inspection reveals that this difference was largely driven by 14 patients in the delayed strategy group who received urgent revascularization before the sixth hour after randomization. Twenty one (24%) patients in the delayed invasive strategy group had their randomized strategy overridden by treating physicians due to development of STEMI (n=2), persistent chest pain (n=13), recurrent pain (n=3), arrhythmia (n=2), and undocumented (n=1); 14 of those patients received PCI, which was then counted in the composite 30-day outcome as an urgent revascularization. There was a trend toward reduction in index visit MIs in the early invasive group (1 vs 10 MIs, 1% vs. 12%) which did not reach statistical significance given the very small sample size. Long term mortality was 16% in both groups after 4.1 years median follow up. There was no detailed ECG analysis available, and no angiographic occlusion data is

provided.

Milosevic et al. Immediate versus delayed invasive intervention for non-STEMI patients: the RIDDLE-NSTEMI Study. JACC Cardiovascular Intervention. 2016.[33]

323 patients without STEMI but with elevated cardiac troponin I and "new ST-segment depression at least 1mV and/or T-wave inversion in >/=2 contiguous leads" were randomized to immediate intervention (<2hrs) and delayed intervention groups (2 to 72 hours). Refractory angina was excluded, as well as "posterior MI" (no criteria stated). Median time from randomization to angiography was 1.4 vs. 61.0 hours. The primary endpoint (occurrence of death or new MI at 30-day follow up) was less frequent in the immediate intervention group compared to the delayed intervention group (4.3% vs. 13%, P=0.008). This difference was almost entirely accounted for by an excess of adverse outcomes occurring in the delayed intervention group prior to catheterization (0 deaths and 0 MIs in the immediate intervention group vs. 1 death and 10 MIs in the delayed intervention group before catheterization). At 1 year, all cause death was nonsignificantly lower in the immediate intervention group (4.9 vs. 5.6%), but the significant reduction in MI persisted (3.1% vs. 13.8%, P=0.002), as well as the significant reduction in the composite outcome of death or MI (6.8% vs. 18.8%, P=0.002). No detailed ECG analysis was performed, and the incidence of angiographic occlusion is not reported.



#2: Physicians across all specialties have poor accuracy and poor inter-rater reliability for detecting ACO under the current paradigm.

McCabe et al, Journal of the American Heart Association. Physician accuracy in interpreting potential ST-segment elevation myocardial infarction electrocardiograms.[34]

A cross-sectional survey was performed by having emergency medicine physicians, cardiologists, and interventional cardiologists review 36 ECGs from the Activate-SF database of prospective STEMI activations. 12 (33%) of the 36 cases had no culprit lesion (defined as no STEMI), whereas the other 24 (66%) were true positives with total acute occlusion (defined as STEMI). This corresponded well with the actual overall rate of false positive STEMI activations in the entire registry of 36% which was recorded from prospective practice. For each ECG clinicians were asked, “based on the ECG above, is there a blocked coronary artery present causing a STEMI?” 124 physicians interpreted a total of 4392 ECGs. Overall kappa value of interreader agreement was only 0.33, reflecting poor agreement. Overall sensitivity and specificity for true positive STEMI (occlusion) was only 65% (95%CI 63-67%) and 79% (95%CI 77-81%). There was a 6% increase in the odds of successful interpretation with every 5 years of experience since medical school graduation. After adjusting for experience there was no difference in the odds of overall accurate interpretation between specialties. However, interventional cardiologists had the highest group specificity at 89%, while emergency medicine attendings had the highest group sensitivity at 74%. This excellent study is supported by many others showing poor inter-rater reliability.[35-37]

#3: Physicians cannot agree on where and how to measure the ST segment, and even when they can agree the interrater reliability of ST segment measurement remains poor.

Carley et al. What’s the point of ST elevation? Emergency Medicine Journal 2002.[38]

Cross sectional study in which 63 clinicians who commonly prescribe thrombolytics for acute MI were asked to identify and quantify the degree of STE present in 3 sample ECG complexes. They were also asked to mark the ECG where they identified the J-point. Overall, STE was not identified in 23 (12%) cases. For figures 1-3 below, the percentage of doctors who correctly identified the J-point correctly was 29%, 61%, and 13%.

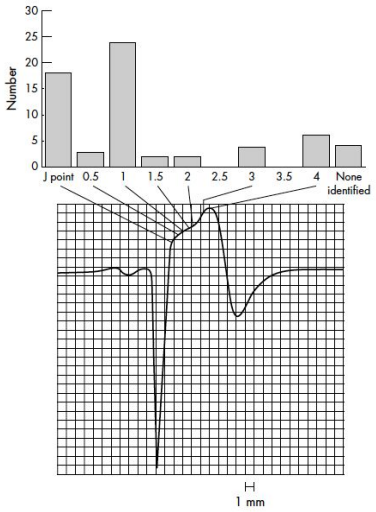


Figure 1 ECG 1. Point of measurement of ST elevation above baseline (in mm past J point).

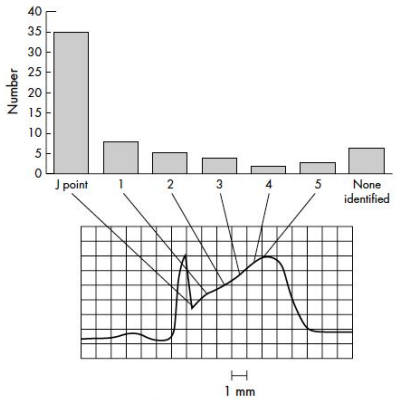


Figure 2 ECG 2. Point of measurement of ST elevation above baseline (in mm past J point).

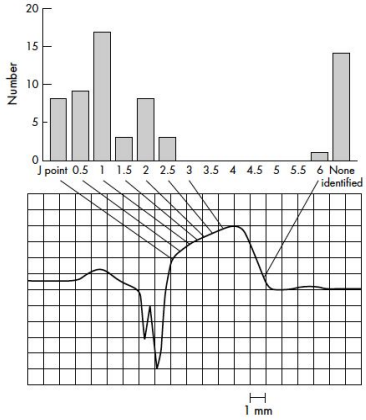


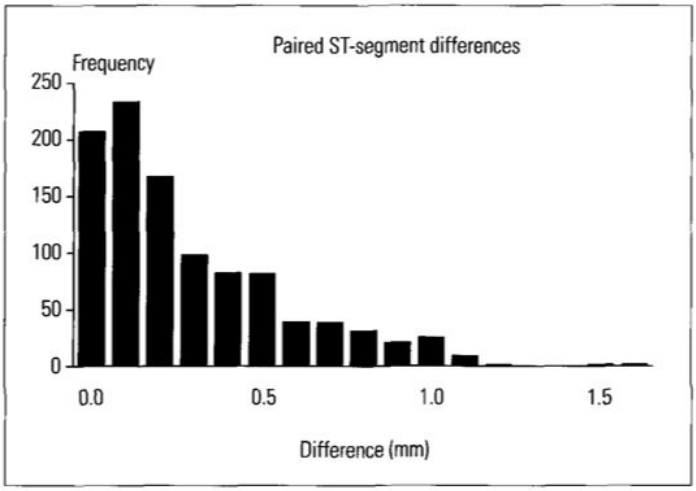
Figure 3 ECG 3. Point of measurement of ST elevation above baseline (in mm past J point).

Tandberg et al. Observer variation in measured ST-segment elevation. Annals of Emergency Medicine 1999.[39]

A blinded, paired-sample survey was administered to 52 subjects including emergency physicians, emergency medicine residents, and senior medical students. They were given a packet of 40 ECGs, blinded to the fact that it actually consisted of a random order of identical pairs of only 20 ECGs from patients with “enzymatically proven myocardial infarction.” They were asked to measure all ECGs, then the difference between the each reader’s two measurement of the same ECG was studied. The average difference in segment height among all groups was 0.28 mm. Overall statistical agreement between paired ST-segment measurements was very good (K=0.85). However, “one fifth of the time, intraobserver measurements of paired ST-segment elevations differed by more than half a millimeter.” When specifically asked whether the ST-segment elevation was greater than or equal to 2.0 mm, readers disagreed with themselves in 14% of cases.

Figure.

Histogram showing the frequency distribution of the 1,035 paired ST-segment estimation differences (larger minus the smaller). The positive difference (in millimeters) is shown on the horizontal axis. Frequency is shown on the vertical axis.



#4: The name "STEMI" itself is a powerful cognitive roadblock against improving the management of acute MI.

"STEMI" has to be one of the catchiest and most popularized acronyms in all of medicine. What a perfect acronym - the letters perfectly spell out the name and form a short, audibly pleasing word that rolls off the tongue with unmistakable ease and sheer fun. Like the persuasive words of an effective movie villain, this helps to explain how successful the term has been in blinding us from the truth and cognitively inspiring us to fail at the reperfusion decision.

When you define an entire management paradigm around the ST segment, it should come as no surprise that the vast majority of clinicians have no idea that something other that the ST segment matters. It's not called "hyperacute T-wave MI," and thus the vast majority of those making the emergent reperfusion decision cannot identify a hyperacute T-wave. Even if the ST segments were the only thing that mattered in predicting ACO, the term "STEMI" does not suggest that the amount or morphology of the ST segment deviation might depend on the preceding QRS complex. Experienced ECG interpreters know that everything on the ECG is proportional, and no ST segment or T-wave can ever be interpreted without considering it in the context of the preceding QRS complex. Abnormal depolarization always results in abnormal repolarization, which usually follows the pattern of "appropriate discordance," whereby the ST segment and T-wave deviation should generally be opposite the biggest and most abnormally conducted portion of the QRS complex. This knowledge (paired with practice) results in a huge decrease in false positives and false negatives, as the dramatic ST-T changes of LVH become

frankly boring to the trained eye, and the subtle increased area under a T-wave in lead aVL becomes terrifying in the context of a small normal QRS. As you would predict, the STEMI paradigm crumbles into total uselessness at the extremes of abnormal QRS complexes, such as LBBB or paced rhythm, where the expert ECG interpreter must rely on specially derived and validated rules to quantify the amount of expected vs. observed discordance and concordance.

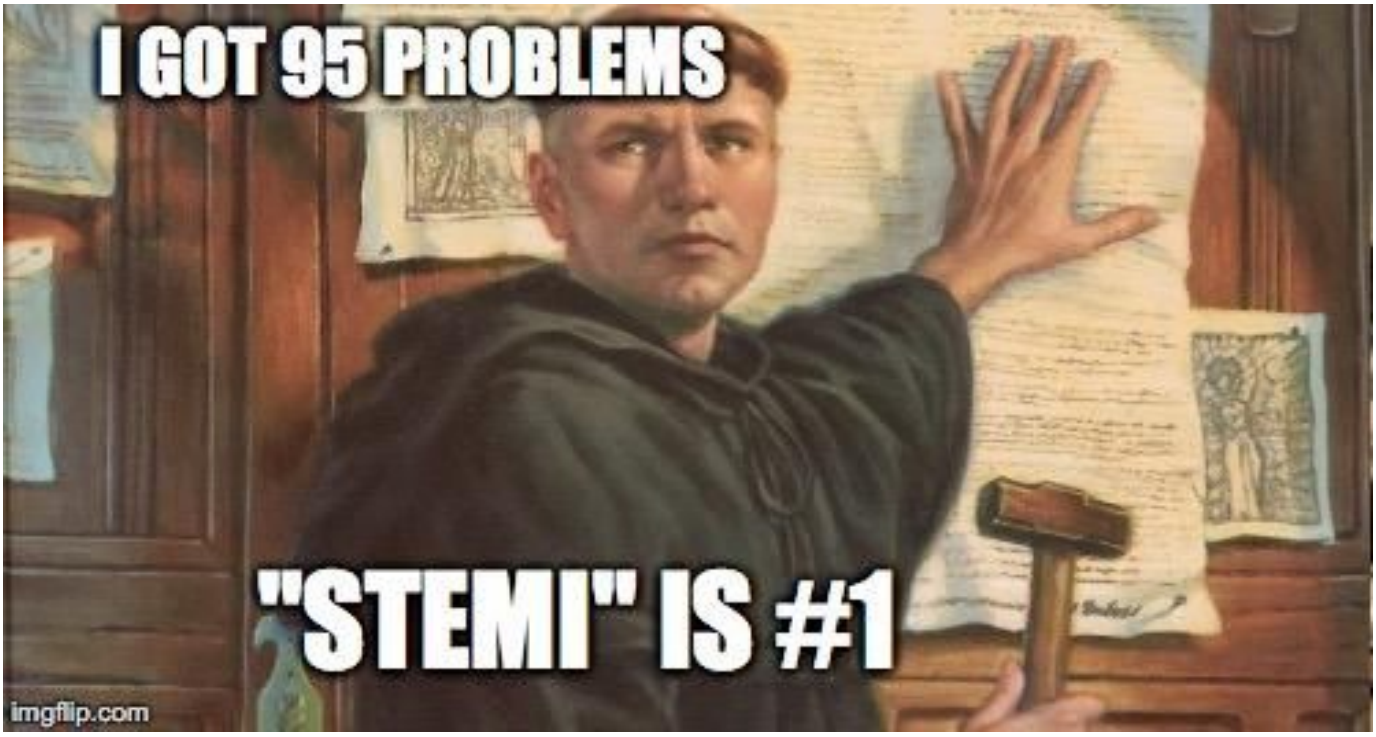
Let's submerge to the next deepest level of brainwashing inspired by the term "STEMI." Calling it "STEMI" prevents you from ever saying out loud what you're actually trying to identify: acute coronary occlusion. When you look at an ECG in the setting of possible ischemia you are first and foremost looking for any pattern which reliably predicts ACO, because these are the patients who benefit from emergent reperfusion. But when you look for "STEMIs" you lose touch with what you're actually looking for; you even start to forget that STEMI was supposed to be a predictor of ACO in the first place. How else can we explain that 25 years of mainstream literature and guidelines have failed to improve guideline-based ECG criteria based on angiographic outcomes? And all this in spite of all the literature cited above which shows the weakness of the criteria. There seems to be no other logical explanation except that they have forgotten what they are actually looking for; they are looking for STEMIs instead of acute coronary occlusions (OMIs).

Focussing on STE as the diagnostic criteria for ACO leads to some amazing examples of the human brain's proclivity to see what it expects to see rather than what is there, and to ignore unexpected findings, unconsciously warping them into expected findings. The human eye is remarkably good at detecting even submillimeter deviations of a line especially a thin black line on a contrasted background with the help of gridlines (just ask the mother of a young child with a laceration through the vermillion border how close she would like the approximation of wound edges in your lac repair). Yet consider 1.0 mm deviation, now on the ECG of a young healthy man who presented for some unrelated complaint but also mentions some extremely vague atypical chest pain, and watch your colleagues struggle internally as the higher brain functions reject the objective visual input that the ECG does in fact show the dreaded STE. They believe consciously or subconsciously that if they find ST segment deviation, they are obligated to consider it in the context of the STEMI criteria and paradigm. They know from years of experience that this STE in a scenario with extremely low clinical suspicion for ACS is nondiagnostic, and is actually a normal variant. But the guidelines and STEMI paradigm imply so strongly that ST segment deviation must be considered abnormal that it becomes easier to deny the existence of the meaningless ST deviation than it is to admit that it's present, confront it cognitively, and figure out whether it's normal or abnormal. In other words, if you show an ECG with normal variant ST elevation ("early repolarization") to a physician, they deny the existence of ST elevation; to most, just voicing "ST Elevation" means only STEMI.

This is what happens when the brain subconsciously knows the futility of a concept but does not yet know why or how to accept it's futility - the brain simply bends perceived reality to avoid the conflict altogether. Another example: ask a room full of physicians to recite the STEMI criteria. They can't. They don't have it memorized, and few of them actually explicitly use it in practice,

though most of them will reference this as the guideline-approved practice and teach it to medical students. From experience they know intuitively that we shouldn't learn the STEMI criteria, yet their education has provided them with nothing better to say, and so they pass it on to the next generation.

Finally, STEMI Criteria suggests that a patient requires ECG findings to warrant emergent cath lab activation. This is wrong in many ways. Acute coronary occlusion with large resulting transmural MI may sometimes present with absolutely normal serial ECGs even in the hands of experts. In addition to a clinical history with extremely high pretest probability for acute coronary occlusion, there are other clinical features that may require emergent cath lab activation. These include ischemia refractory to maximal medical management, ischemia with cardiogenic shock, ischemia with electrical instability, and others. The name STEMI degrades the emergency of these other conditions and falsely reassures us that the ECG identifies all patients who need emergent cath lab activation. Remember, in the 1970s-1980s before the term STEMI existed, they still showed a mortality benefit of NNT=56 in the primary analysis of 60,000 patients using thrombolytics even before ECG subgroup analysis, with 4 of the 9 trials enrolling patients without any ECG criteria.

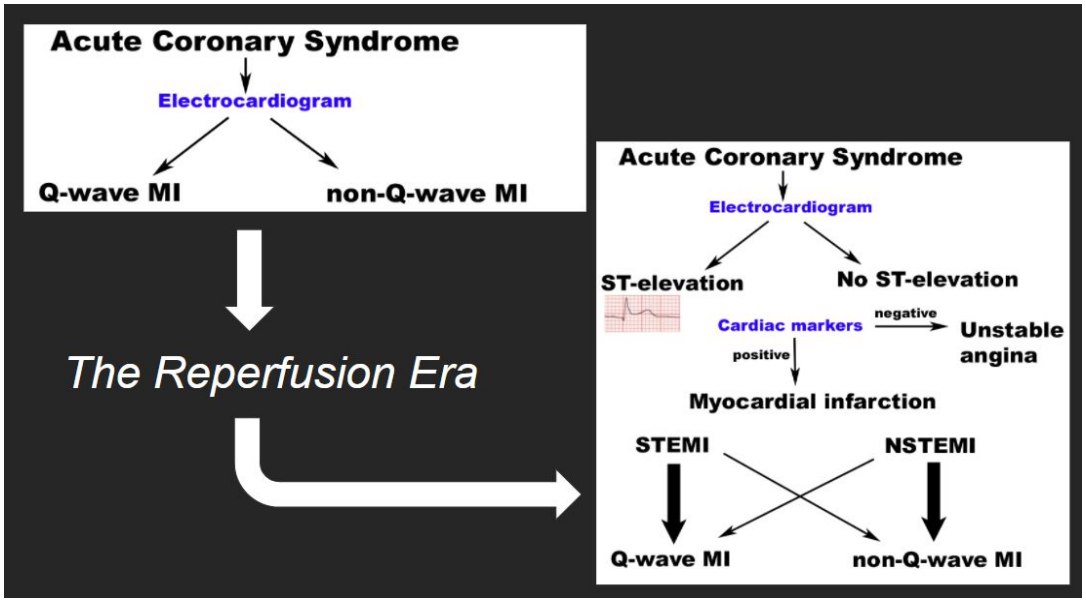


Part III: Occlusion MI (OMI)

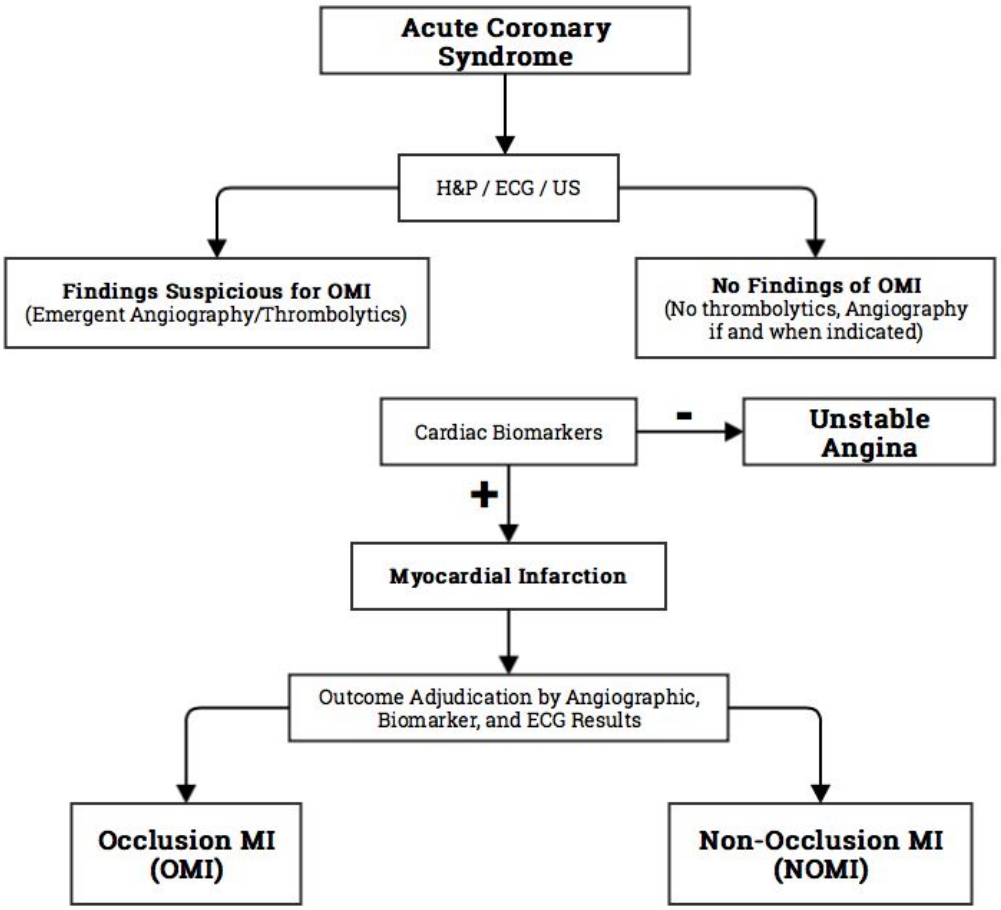
For these reasons, it has long been time that we must exorcise the word STEMI from our vocabulary. Too long has it clouded our ability to see the true objective and prevented further research from improving the acute care of myocardial infarction. While some authors have suggested a requiem for the term “unstable angina,” you know that this entity will likely always exist (transient occlusion and reperfusion may be so rapid or with such good collateral circulation that there is no troponin leak, no test is ever perfect, etc). Instead, we believe the term “STEMI” should be nominated for a requiem for all the reasons given above. We are not the first to suggest this, nor is this a suggestion that only comes from outside the field of cardiology.[40] This is an enormously difficult task given the beloved nature of the term and the depth to which STEMI vs. NSTEMI has been ingrained in our training, culture, and research. We have attempted to beat around this bush for years by inventing terms such as “STEMI equivalent,” “subtle STEMI,” and “semi-STEMI,” but sadly these terms have not produced widespread change in understanding except for the small groups of clinicians who follow the literature on this topic or the various FOAM resources that broadcast this knowledge. While these invented terms were correctly designed, they have not been able to correct the problems made by STEMI. In our best attempt to create an appropriate replacement, we bring to you:

OMI = Occlusion MI
NOMI = Non-Occlusion MI

Notice that the name doesn’t say anything about the ST segment. It doesn’t brainwash you into thinking that ST segments are the only way to diagnose ACO. It also doesn’t imply that the ECG is the only way to make the reperfusion decision. Most importantly, it reminds you what you’re actually trying to identify, treat, and research: a dangerous acute thrombotic occlusion that needs to be opened immediately. Instead of the false dichotomy of STEMI vs. NSTEMI, we propose the true dichotomy of OMI vs. NOMI as the next logical step in the ongoing progression of acute MI paradigm. Please join us as we go forward into to the ***Occlusion-Reperfusion Era***.



Occlusion-Reperfusion Era



Hopefully your next question based on the diagram above is: “so now how am I actually supposed to figure out which patients have OMI and need immediate intervention?” We have been answering that question for years, so come on over to our resources:

Dr. Smith’s ECG Blog (nearly 1,000 cases and counting of instructive ECGs in EM clinical context)

Hot off the press: Dr. Smith’s New Article: New Insights Into the Use of the 12-Lead Electrocardiogram for Diagnosing Acute Myocardial Infarction in the Emergency Department, Canadian Journal of Cardiology 2018

EMCrit Podcast 146 – Who Needs an Acute PCI with Steve Smith (Part I)

EMCrit Podcast 147 – Who Needs an Acute PCI with Steve Smith (Part II)

PDF Summary: Who Needs Acute PCI?
One-Page Cheat Sheet: Who Needs Acute PCI?

Rule Name	Population	Rule Description	Sensitivity (for OMI)	Specificity (for OMI)
Modified Sgarbossa-1 (41)	LBBB	Any 1 of 3 criteria, in at least one lead: 1) Concordant STE at least 1mm 2) Concordant STD V1-V3 at least 1mm 3) Excessively discordant STE defined by ST/S ratio >25% 3) Excessively discordant STE defined by ST/S ratio >20%	80% 84%	99% 94%
Modified Sgarbossa-2 (41)	LBBB	Any single lead with excessively discordant STE or STD defined by >30% of preceding R or S wave	64%	98%
Modified Sgarbossa for Paced Rhythm (42)	Right Ventricular Paced Rhythm	Any 1 of 3 criteria, in at least one lead: 1) Concordant STE at least 1mm 2) Concordant STD V1-V6 at least 1mm 3) Excessively discordant STE defined by ST/S ratio >25%	67%	99%
Terminal QRS Distortion (43)	Differentiating normal STE from ischemic STE from LAD occlusion	Absence of S wave and J wave in either of V2 or V3	20%	100% (95%CI 98-100)
3-Variable Formula for normal STE vs. LAD Occlusion (44)	Differentiation of normal STE from LAD occlusion Exclude (obvious LAD occlusion): STE>5mm Any convex ST segment V2-V6 Any STD (inferior or anterior) Terminal QRS distortion Any Q waves V2-V4	Components: (in milliseconds or millimeters) QTcB = computerized QTc (Bazette) STE60V3 = STE (from PR to point 60ms after J point) in V3 RAV4 = R wave amplitude in V4 Formula: (1.196 x STE60V3) + (0.059 x QTcB) - (0.326 x RAV4) Most accurate cutpoint: 23.4; >23.4 very likely represents LAD occlusion, AUC = 0.9538 Cutpoint of 22.0 (any value >22.0 should prompt close evaluation)	86% 96%	91% 81%
4-Variable Formula (45)	Same as 3-Variable Formula, not validated	Same as 3-Variable Formula, but adds total amplitude of the QRS in V2 (QRSV2) Formula: (0.052 x QTcB) - (0.151 x QRSV2) - (0.286 x RAV4) + (1.062 x STE60V3) Most accurate cutpoint: 18.2; >18.2 very likely LAD occlusion; AUC = 0.9686	89%	95%
Anterior Left Ventricular Aneurysm (Persistent STE after Prior Anterior MI) (46)	STE in V1-V4 that could be either acute occlusion or old MI with persistent STE Q waves (usually QS waves) present in V1-V4	If there is a single lead among V1-V4 with T wave amplitude to total QRS amplitude ratio of >0.36, the ECG represents acute occlusion False negative results occur with prolonged chest pain (subacute MI)	92%	69%
STD in aVL (47)	ECG with any STE in II, III, aVF, considering inferior acute MI Exclude: LVH, LBBB, delta wave, paced rhythm	With any amount of STD in aVL, any STE in inferior leads is MI until proven otherwise Cannot differentiate old MI with persistent STE from acute MI	99%	100% (95%CI 91-100)

References

1) Schmitt et al. Diagnosis of acute myocardial infarction in angiographically documented occluded infarct vessel: limitations of ST-segment elevation in standard and extended ECG leads. Chest. 2001 Nov;120(5):1540-6. (PMID: 11713132)

2) Wang et al. Incidence, distribution, and prognostic impact of occluded culprit arteries among patients with non-ST-elevation acute coronary syndromes undergoing diagnostic angiography. Am Heart J. 2009 Apr;157(4):716-23.

3) From AM et al. Acute myocardial infarction due to left circumflex artery occlusion and significance of ST-segment elevation. The American journal of cardiology 2010;106:1081-5.

4) Pride et al. Angiographic and clinical outcomes among patients with acute coronary syndromes presenting with isolated anterior ST-segment depressions. JACC Cardiovasc Interv. 2010 Aug;3(8):806-11.

5) Abbas et al. Acute angiographic analysis of non-ST-segment elevation acute myocardial infarction. Am J Cardiol 2004;94;907-909.

6) Khan et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. European Heart J, 2007. 38, 3082-3089.

7) Koyama et al. Prevalence of coronary occlusion and outcome of an immediate invasive strategy in suspected acute myocardial infarction with and without ST-segment elevation. The American journal of cardiology 2002;90:579-84.

8) Marti D et al. Incidence, angiographic features, and outcomes of patient presenting with subtle ST-elevation myocardial infarction. Am Heart J 2014; 168:884-90.

9) Smith et al. Electrocardiographic differentiation of early repolarization from subtle anterior ST-segment elevation myocardial infarction. Ann Emerg Med. 2012;60:45-56.

10) McCabe et al. Prevalence and factors associated with false-positive ST-segment elevation myocardial infarction diagnoses at primary percutaneous coronary intervention-capable centers: a report from the Activate-SF registry. Arch Intern Med. 2012;172:864–871.

11) Larson et al. “False-positive” cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. JAMA. 2007;298:2754–2760.

12) Kontos et al. An evaluation of the accuracy of emergency physician activation of the cardiac catheterization laboratory for patients with suspected ST-segment elevation myocardial infarction. Ann Emerg Med. 2010;55:423–430.

13) Braunwald et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol. 2000 Sep;36(3):970-1062.

14) Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet. 1994 Feb 5;343(8893):311-22.

15) Menown et al. Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction. European Heart J. 2000 Feb;21(4):275-83. (PMID: 10653675)

16) Alpert et al. Myocardial infarction redefined - a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000 Sep;36(3):959-69. (PMID: 10987628)

17) Macfarlane et al. Age, sex, and the ST amplitude in health and disease. J Electrocardiol. 2001;34 Suppl:235-41. (PMID:11781962)

18) Wu et al. Normal limits of the electrocardiogram in Chinese subjects. Int J Cardiol. 2003 Jan;87(1):37-51.

19) Antman et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction - executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2004 Aug 4;44(3):671-719.

20) Macfarlane et al. Modification of ACC/ESC criteria for acute myocardial infarction. J Electrocardiol. 2004;37 Suppl:98-103. (PMID: 15534817)

21) Thygesen et al. Universal definition of myocardial infarction. Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. J Am Coll Cardiol. 2007 Nov 27;50(22):2173-95. (PMID: 18036459)

22) Wagner et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction. J Am Coll Cardiol. 2009 Mar 17;53(11):1003-11. (PMID: 19281933)

23) Thygesen et al. Third universal definition of myocardial infarction. J Am Coll Cardiol. 2012 Oct 16;60(16):1581-98. (PMID: 22958960)

24) Roffi et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European heart journal 2016;37:267-315.

25) Amsterdam et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;130:e344-426.

26) Mehta et al. Early versus delayed invasive intervention in acute coronary syndromes. The New England journal of medicine 2009;360:2165-75. The TIMACS (Timing of Intervention in ACS) Trial.

27) Hoedemaker et al. Early Invasive Versus Selective Strategy for Non-ST-Segment Elevation Acute Coronary Syndrome: The ICTUS Trial. J Am Coll Cardiol. 2017 Apr 18;69(15):1883-1893.

28) van't Hof et al. A comparison of two invasive strategies in patients with non-ST elevation acute coronary syndromes: results of the Early or Late Intervention in unStable Angina (ELISA) pilot study. 2b/3a upstream therapy and acute coronary syndromes. Eur Heart J. 2003 Aug;24(15):1401-5.

29) Neumann et al. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. The ISAR-COOL Study. JAMA 2003 Sep 24;290(12):1593-9.

30) Thiele et al. Optimal timing of invasive angiography in stable non-ST-elevation myocardial infarction: the Leipzig Immediate versus early and late PercutaneouS coronary Intervention triAl in NTSEMI (LIPSIA-NSTEMI Trial). Eur Heart J. 2012 Aug;33(16):2035-43.

31) Montalescot et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. JAMA 2009 Sep 2;302(9);947-54.

32) Reuter et al. Early invasive strategy in high-risk acute coronary syndrome without ST-segment elevation. The Sisca randomized trial. Int J Cardiol. 2015 Mar 1;182:414-8.

33) Milosevic et al. Immediate versus delayed invasive intervention for non-STEMI patients: the RIDDLE-NSTEMI Study. JACC Cardiovasc Interv. 2016 Mar 28;9(6):541-9.

34) McCabe et al. Physician accuracy in interpreting potential ST-segment elevation myocardial infarction electrocardiograms. Journal of the American Heart Association 2013;2:e000268.

35) Jayroe et al. Differentiating ST elevation myocardial infarction and nonischemic causes of ST elevation by analyzing the presenting electrocardiogram. The American Journal of Cardiology 2009;103:301-6.

36) Tran et al. Differentiating ST-elevation myocardial infarction from nonischemic ST-elevation in patients with chest pain. The American journal of cardiology 2011;108:1096-101.

37) Turnipseed et al. Electrocardiogram differentiation of benign early repolarization versus acute myocardial infarction by emergency physicians and cardiologists. Academic emergency medicine: official journal of the Society for Academic Emergency Medicine 2006;13:961-6.

38) Carley et al. What's the point of ST elevation? Emerg Med J. 2002;19:126-128.

39) Tandberg et al. Observer variation in measured ST-segment elevation. Ann Emerg Med. 1999 Oct;34(4 Pt 1);448-52.

40) Phibbs et al. Differential classification of acute myocardial infarction into ST- and non-ST segment elevation is not valid or rational. Ann Noninvasive Electrocardiol 2010;15(3):191-199.

41) Meyers et al. Validation of the modified Sgarbossa criteria for acute coronary occlusion in the setting of left bundle branch block: a retrospective case-control study. Am Heart J 2015;170:1255-64.

42) Dodd et al. Performance characteristics of the modified Sgarbossa criteria for diagnosis of acute coronary occlusion in emergency department patients with ventricular paced rhythm and symptoms of acute coronary syndrome. Acad Emerg Med 2017;24(S1): S36.

43) Lee et al. Terminal QRS distortion is present in anterior myocardial infarction but absent in early repolarization. Am J Emerg Med 2016;34:2182-5.

44) Smith et al. Electrocardiographic differentiation of early repolarization from subtle anterior ST-segment elevation myocardial infarction. Ann Emerg Med 2012;60:45-56.e2.

45) Driver et al. A new 4-variable formula to differentiate normal variant ST segment elevation in V2-V4 (early repolarization) from subtle left anterior descending coronary occlusion: adding QRS amplitude of V2 improves the model. J Electrocardiol 2017;50:561-9.

46) Klein et al. Electrocardiographic criteria to differentiate acute anterior ST-elevation myocardial infarction from left ventricular aneurysm. Am J Emerg Med 2015;33:786-90.

47) Bischof et al. ST depression in lead aVL differentiates inferior ST-elevation myocardial

infarction from pericarditis. Am J Emerg Med 2016;34:149-54.