

# Prehospital Activation of Hospital Resources (PreAct) ST-Segment–Elevation Myocardial Infarction (STEMI): A Standardized Approach to Prehospital Activation and Direct to the Catheterization Laboratory for STEMI

## Recommendations From the American Heart Association’s Mission: Lifeline Program

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**S**T-segment–elevation myocardial infarction (STEMI) is a high-risk condition in which survival and other clinical outcomes are significantly impacted by reducing the time from vessel occlusion to coronary blood flow restoration (total ischemic time).<sup>1–3</sup> Initiatives to reduce specific components of system delays such as the American College of Cardiology’s Door to Balloon<sup>4</sup> and American Heart Association’s (AHA) Mission: Lifeline programs<sup>5–7</sup> have been instrumental in reducing reperfusion times, with a reduction in median door to balloon time to the current level of <60 minutes.<sup>8</sup>

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Door to balloon time includes only hospital performance components; in contrast, first medical contact-to-device (FMC2D) time also encompasses the prehospital period, and therefore is a more accurate reflection of a systems performance. Consequently, efforts targeting reductions in FMC2D time provide additional opportunities for reductions in the total ischemic time.

The AHA’s Mission:Lifeline program was introduced in 2007 to develop systems of care for high-risk time-sensitive cardiovascular conditions.<sup>5</sup> Mission: Lifeline addressed the continuum of care for STEMI, including symptom onset, first medical contact, and Emergency Medical Services (EMS) transport and transfer. Its focus has been on establishing formal STEMI “systems of care” teams to improve the quality of care and outcomes of all STEMI patients by improved communication and process flows between EMS, emergency physicians, cardiologists, and other hospital staff in both referral and receiving hospitals.<sup>6,7</sup> Mission: Lifeline is a national but community-based initiative, establishing state and regional working groups to implement the national recommendations locally, in consideration of resources, geography, legislation, and regulation.

Efforts by Mission:Lifeline to reduce delays have led to a number of important strategies (Table). The strategies have been codified in the 2013 STEMI guidelines that recommended prehospital ECG to diagnose STEMI to activate the Cardiac Catheterization Laboratory (CCL) while the patient is en route to the hospital.<sup>9</sup> Pre-activation CCL is a critical component of reducing reperfusion time, allowing parallel processing in which the patient is brought to the hospital while the CCL staff is arriving. Importantly, this has been associated with decreased mortality.<sup>10</sup>

An important drawback to pre-hospital activation of CCL has been the frequent cancellation of the CCL team after EMS

**Table.** Strategies Recommended by Mission:Lifeline to Reduce Delays in Reperfusion for Primary Percutaneous Coronary Intervention for STEMI Patients

Acquiring PH-ECGs
Transmission of the PH-ECG to the emergency physician and/or cardiologist for potential activation of the CCL team before hospital arrival
Paramedic interpretation of the PH-ECG and clinical presentation to consider activation of the CCL team from the field
Establishing EMS destination policies and protocols that bypass hospitals without percutaneous coronary intervention capabilities in favor of an STEMI Receiving Center when STEMI is suspected in the field on the basis of the PH-ECG and clinical presentation
Strategies for rapid evaluation, guideline recommended therapies and transfer to STEMI receiving hospital for patients initially presenting at referral hospitals (focusing on door-in-door-out time)
Direct activation of the CCL by the Emergency Department
If STEMI is strongly suspected, consideration of taking patients directly to the CCL without prior admission to the Emergency Department, when appropriate

CCL indicates cardiac catheterization laboratory; EMS, emergency medical services; PH-ECG, prehospital ECG; STEMI, ST-segment–elevation myocardial infarction.

field activation.<sup>11–17</sup> While reasons for cancellation are numerous, a variety of patient-specific (eg, goals of care, medical comorbidities, contraindications to catheterization, etc) and system-specific factors (eg, ECG misinterpretation, ECG “STEMI-mimics,” use of ECG computer algorithm versus EMS interpretation, difficulties in ECG transmission, etc) contribute to reasons for cancellation.<sup>11–17</sup>

Incorrect activation of the CCL has a number of adverse consequences. First, unnecessary CCL activations can cause CCL staff fatigue and lead to “burn out” among physicians and the CCL staff members. There may be a loss of urgency among physicians and the CCL staff members, as they may begin to assume that STEMI protocol activation may well represent a “false alarm”. Inappropriate CCL activations are costly, as staff are often paid overtime to take calls and respond to CCL activations, regardless of whether or not the patient undergoes emergent coronary angiography.<sup>18</sup>

The 2013 STEMI guidelines indicate that consideration should be given to the development of local protocols that allow preregistration and direct transport to the CCL, bypassing the Emergency Department (ED) for patients who do not require emergency stabilization upon arrival.<sup>9</sup> Similarly, the European Society of Cardiology STEMI guidelines have recommended a strategy of ED bypass when an STEMI diagnosis is made by the EMS in the pre-hospital setting.<sup>19</sup> Use of Direct to CCL results in reductions in time to reperfusion similar to, if not greater than pre-hospital notification, despite long transport times.<sup>20</sup> If STEMI is strongly suspected, consideration of taking patients directly

to the CCL<sup>20–27</sup> without prior admission to the ED, when appropriate, can reduce the time the patient spends in the ED (“dwell time”), which is often the most variable time component, therefore potentially the most modifiable component of FMC2D time.

To successfully implement the strategy for shortening the FMC2D interval by taking the patient directly to the CCL, it is critical that the processes for field assessment accurately and reliably identify patients who are most likely having an STEMI and who are appropriate candidates for angiography. This process must be both sensitive and specific for detecting and triaging STEMI patients.

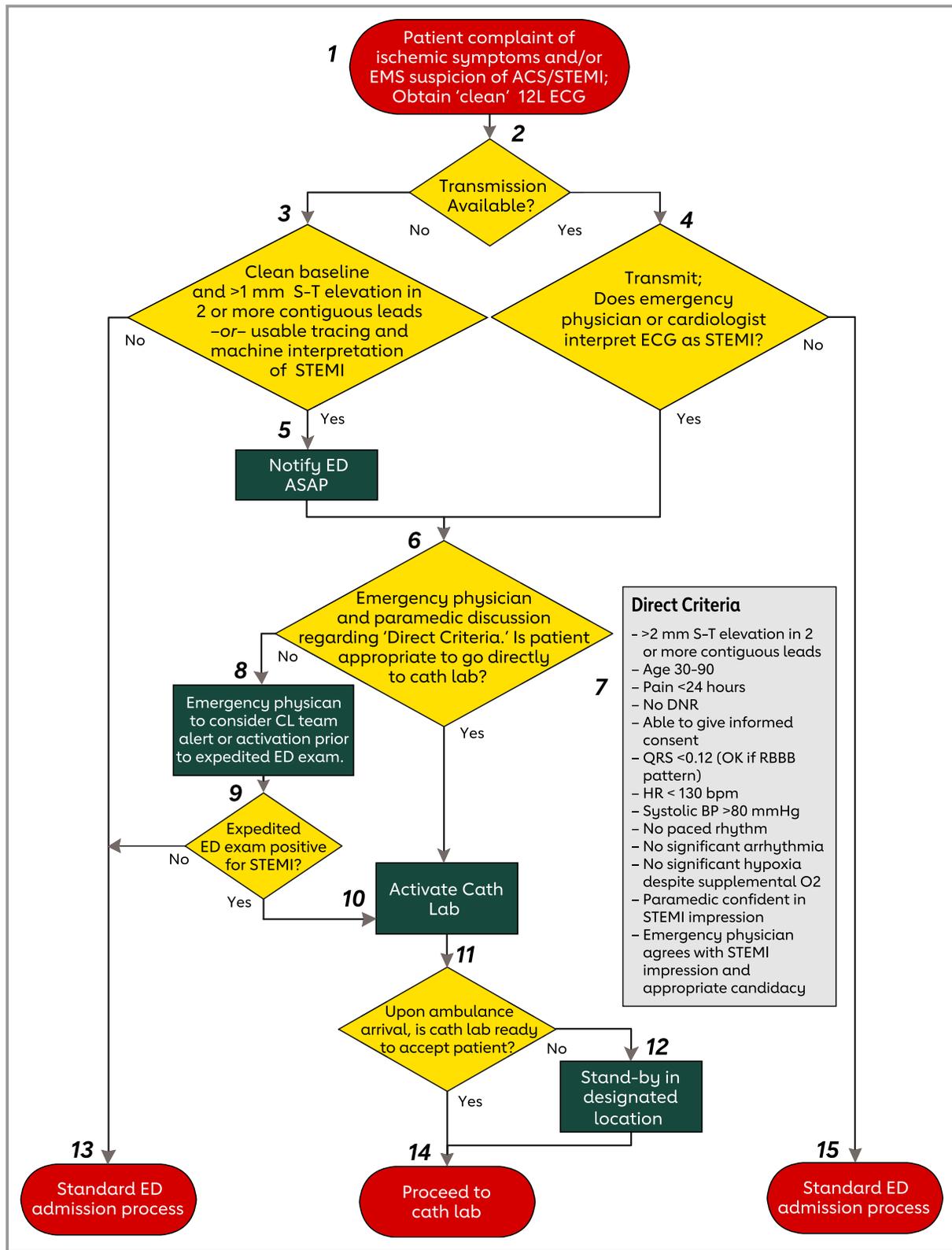
To support standardization and implementation of prehospital activation and Direct to CCL strategies, the Mission:Lifeline program established an implementation project team, which led to the development of the Mission:Lifeline Prehospital Activation of Hospital Resources (PreAct) STEMI algorithm (Figure). The PreAct STEMI algorithm outlines a process for patient triage in the field and routing upon hospital arrival. It incorporates best practices from STEMI systems of care from across the country. The PreAct STEMI algorithm is intended to:

1. Increase rates and timeliness of appropriate prehospital CCL activation and triage of patients who have ECG findings of STEMI.
2. Reduce rates of prehospital CCL activation for patients who do not have STEMI.
3. Guide decision-making for which potential STEMI patients are appropriate for: prehospital activation of the CCL; Direct to CCL routing; expedited ED exam before CCL activation; and full ED evaluation before a CCL activation decision.
4. Provide performance measures that can guide quality assurance/quality improvement efforts.

## PreAct Algorithm

The PreAct STEMI algorithm is intended to be applied to patients with ischemic symptoms and/or EMS suspicion of acute coronary syndrome/STEMI. For these patients, EMS should obtain a “clean” PH-ECG (ie, interpretable and free of artifact) (marker 1) which reduces diagnostic errors by both clinicians and software tools.<sup>28–30</sup> Standard EMS processes should apply to patients where the clinical presentation and/or ECG are not consistent with acute coronary syndrome/STEMI (markers 13, 15).

The algorithm branches depending on transmission capabilities (marker 2) and whether the ECG is consistent with STEMI. If transmission is not available and the ECG is consistent with STEMI (by EMS or machine interpretation, marker 3) or if transmission is available and the ECG is consistent with STEMI



**Figure.** The Prehospital Activation of Hospital Resources algorithm. ACS indicates acute coronary syndrome; ASAP, as soon as possible; BP, blood pressure; CCL, cardiac catheterization laboratory; DNR, do not resuscitate; ED, emergency department; EMS, emergency medical services; HR, heart rate; RBBB, right bundle branch block; STEMI, ST-segment–elevation myocardial infarction.

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(by the interpreting emergency physician or cardiologist, marker 4), EMS and the emergency physician should then confer (markers 5, 6). The discussion should focus on determining if the patient fulfills the Direct to CCL criteria (marker 7) and therefore appropriate for immediate CCL activation and direct CCL transport (marker 10). Patients who do not fulfill the Direct to CCL criteria should be transported to the ED to undergo an expedited exam (marker 9), with the goal of rapidly determining if the patient should continue to the CCL.

The emergency physician may consider cardiology and/or CCL team notification (without full activation) or full activation of the CCL (marker 8) while the patient is still in the field, depending on ECG and clinical data available.

For all approaches, once indications for CCL has been determined, CCL readiness is assessed (marker 11). If the CCL is adequately staffed, the patient should be transported directly to the CCL (on the ambulance stretcher and by EMS when possible). If the CCL is not adequately staffed, the patient should wait in a designated area with appropriate monitoring and supervision (usually the ED), until the CCL is ready to receive the patient (marker 12).

In systems where 12 lead ECG transmission is not utilized or when transmission is not possible, the paramedic applies the following criteria (marker 3): (1) an isoelectric baseline reasonably free of artifact and (2) at least 1 mm of ST elevation in  $\geq 2$  contiguous leads with a paramedic or machine interpretation of STEMI. If met, the receiving ED is notified as soon as possible (marker 5). The paramedic and emergency physician discuss the patient (marker 6), including Direct to CCL criteria (marker 7), with further care as outlined in the algorithm.

## Direct to CCL Criteria

Despite pre-hospital notification of STEMI patient, ED length of stay is frequently prolonged.<sup>22</sup> The purpose of the PreAct criteria (marker 7) is to identify a subset of patients who clearly have an STEMI for whom direct transfer to the CCL is appropriate, as this substantially reduces reperfusion times.<sup>20–27</sup> We use the phrase “Direct to CCL” rather than “ED Bypass” for the following reasons. First, Direct to CCL more accurately describes the intent of the efforts. Most hospital ambulance entrances flow into the ED making the path to the CCL through the ED area unavoidable. Second, in most hospitals, the process of accomplishing Direct to CCL requires participation by ED staff to coordinate CCL team communications and patient registration. At times this may require a brief “pause” or “pit stop” in the ED. Finally, Direct to CCL best describes the receiving hospitals intent with regard to its Emergency Medical Treatment and Labor Act<sup>31</sup> obligations to provide an appropriate Medical Screening Exam, since some patients who are transported directly to the

CCL may be ultimately determined to have non-cardiac conditions requiring other specialists.

Despite significantly reducing time to reperfusion, the Direct to CCL concept remains controversial. Concerns include CCL activations without a true STEMI, the difficulty in reaching consensus on Direct to CCL criteria for a standardized EMS protocol, and safety of transporting a patient to the CCL without adequate staff being present. Specific criteria were developed (marker 7) for standardized decision making for EMS and emergency physicians on appropriateness for going directly to the CCL.

However, for Direct to CCL to be successful, appropriate planning is critical.<sup>22–28</sup> Centers that have successfully implemented Direct to CCL have included additional designated in-hospital CCL activation team members who are notified by the STEMI group page to assist with patient transfer to the CCL and subsequent monitoring until the CCL team arrives.<sup>22–28</sup> Team members can vary depending on the hospital, and have included intensive care unit and/or ED nursing, in-house CICU residents, and/or dedicated transportation staff. In some centers, the team can place the patient on the procedure table, connect monitoring equipment, and confirm that all appropriate equipment is available. The success of this process is dependent on the CCL staff arriving within the recommended 30 minutes of paging.

Education of all team members is critical for patient’s safety. The transportation team members should be familiar with the location of the resuscitation equipment in the CCL and have the capability of providing immediate resuscitative treatment if required, which includes starting intravenous drips, performing defibrillation, and requesting intubation by respiratory therapy.<sup>22–28</sup>

Direct to the CCL may not be possible for all patients or all hospitals. An alternative for hospitals that do not have the resources for off hours Direct to CCL, or in situations when pre-hospital notification is short, is the establishment of a process for a short “pit stop” or “brief pause” in the ED for STEMI patients who only need to be monitored for a brief period.<sup>26</sup> If possible, patients should be kept on the EMS gurney with continued supervision by EMS and ED nursing. If time permits, admission laboratory testing can be obtained. As soon as the CCL is available, the patient should be directly transported to the CCL. The protocol should be explicit that transportation should occur promptly when the CCL is ready and should not be delayed for routine testing (eg, chest x-ray, ECG when the EMS ECG is diagnostic).

Patients who are seen at a non-percutaneous coronary intervention (PCI) hospital ED initially have the benefit of 12 lead ECGs, physician evaluation, and possibly cardiology consultation before transfer to the PCI hospital. Therefore, taking patients directly to the CCL should be standard practice for inter-facility STEMI transfers.<sup>32</sup>

## PreAct Inclusion/Exclusion Criteria

Of the Direct to CCL criteria specified, 4 are considered essential—(1) Paramedic confident in the STEMI diagnosis; (2) emergency physician and/or cardiologist confident in the STEMI diagnosis; (3) ability to provide informed consent; and (4) no “do not resuscitate” (DNR):

**Paramedic confident in STEMI diagnosis**—When EMS is uncertain about whether STEMI ECG criteria are met (in the absence of transmission) or whether the patient is having an STEMI based on the clinical presentation, initial evaluation in the ED is indicated.

**Emergency physician and/or cardiologist confident in STEMI diagnosis**—Based on the prehospital report and prehospital ECG, if the emergency physician and/or cardiologist is in doubt of the diagnosis or otherwise believes the patient needs initial ED evaluation, the patient should be evaluated in the ED initially.

**Ability to provide consent**—The patient’s mental status should be considered for ability to give informed consent. If there is doubt, direct CCL transfer is not appropriate.

**No *do not resuscitate***—Patients who have a known do not resuscitate still should be transported to an STEMI receiving center for further evaluation. Patient preference, shared-decision making, and informed consent are important and legally mandated components of the STEMI process,<sup>33,34</sup> in whom after an informed discussion emergent coronary angiography may still be performed.

## ST Elevation $\geq 2$ mm in $\geq 2$ Contiguous Leads

Using  $\geq 2$  mm as a direct criterion decreases diagnostic uncertainty and improves specificity.<sup>35</sup> This criterion is more stringent than typical criteria for STEMI diagnosis to account for technical and interpretation challenges inherent to the prehospital environment that can lead to a higher rate of over activations.<sup>35</sup> Larger extent of ST elevation also identifies patients who have greater areas at risk<sup>36</sup> and therefore more likely to benefit from accelerated reperfusion.

## Aged 30 to 90 Years

Younger patients (aged <30 years) are less likely to have myocardial infarction and significantly more likely to have ECG abnormalities that mimic STEMI. Extremely elderly patients (aged >90 years) are more likely to have significant medical comorbidities or goals of care that may preclude cardiac catheterization, such that discussions of goals of care with the patient and/or their family before angiography is appropriate.

## Pain <24 Hours

Symptom duration is an important predictor of clinical outcomes in patients presenting with STEMI.<sup>9</sup> Symptoms lasting >24 hours may suggest that transmural damage had occurred—a relative contraindication to emergency catheterization.<sup>9</sup> However, prolonged symptoms should not be considered an absolute contraindication to coronary angiography, as symptom duration may be an inaccurate measure of infarct onset, such as in patients with stuttering ischemia or limited recall.

## QRS <0.12 (Unless Right Bundle Branch Block is Present)

Prolonged QRS duration is usually secondary to left bundle branch block or paced rhythm, both of which frequently obscure evidence of ischemia.<sup>37,38</sup> The presence of a right bundle branch block is an exception to this criterion.

## No Paced Rhythm

Many patients with paced rhythms have a left bundle branch block pattern, which may obscure ECG evidence of ischemia.<sup>38</sup>

## Systolic Blood Pressure >80 mm Hg

Patients with severe hypotension (eg, systolic blood pressure <70–80 mm Hg despite vasopressors) usually require stabilization before emergency coronary angiography. However, extensive delays when hypotension is due to cardiogenic shock should be avoided, as definitive treatment with PCI and/or percutaneous left ventricular support is likely to be beneficial.<sup>39</sup>

## No Significant Arrhythmias

Patients who have significant arrhythmias that require stabilization should undergo ED evaluation before being transported to the CCL. However, in situations when the arrhythmia is ischemia related, such as recurrent ventricular tachycardia or fibrillation, or heart block, proceeding rapidly to the CCL for PCI may be the most appropriate course.

## Heart Rate >130 bpm

Excessive tachycardia can indicate impending shock, hypoxia, pulmonary edema, tachyarrhythmia, or other serious conditions that would increase the risk of Direct to CCL routing, as well as obscure the interpretation of the 12-lead ECG and warrants further evaluation and stabilization in the ED before coronary angiography.

## Significant Hypoxia Despite Supplemental Oxygen

Significant hypoxia despite supplemental oxygen (eg, 100% non-rebreather) may be secondary to severe pulmonary edema or non-cardiac etiologies. Stabilization, including possible intubation before emergent angiography may be required. This is best addressed in the ED rather than in the CCL.

## Additional Considerations

The Mission: Lifeline program advocates for a consistent and standardized process for paramedics to discuss the patient with emergency physicians and/or cardiologists to determine if they meet the Direct to CCL criteria. Ideally, this should be a recorded or documented conversation for medicolegal purposes. In addition, having the Direct to CCL criteria formatted as a checklist is recommended. Patients who meet all criteria can be designated as eligible for the Direct to the CCL pathway by protocol. Monitoring with prompt feedback should be performed by the hospital STEMI quality assurance/quality improvement program to facilitate refinement of the Direct to CCL pathway based on outcomes. Open lines of communication and respectful dialogue among team members are paramount for a successful Direct to CCL program.

The PreAct STEMI algorithm provides a template that can be modified by EMS medical directors, emergency physicians, and cardiologists at a systems level based on local experience, circumstances, and resources (ie, ECG transmission, destination protocols). Similarly, systems without reliable capabilities for ED bypass may use other components of the PreAct STEMI algorithm. Mission: Lifeline encourages systems that modify criteria to measure algorithm compliance, algorithm performance, and report the results so that the Direct to CCL criteria can be refined.

Written protocols should be in place for when a patient presents for care at the hospital but not necessarily in the ED.<sup>31</sup> If patients are determined to be inappropriate for emergency angiography, the patient can be routed back to the ED, as movement of patients between 2 areas of a hospital or facility that share the same Medicare provider number is acceptable under the Emergency Medical Treatment and Active Labor Act regulations and is not considered a transfer.<sup>31</sup> It is critical to have written policies that guide processes for the Emergency Medical Treatment and Active Labor Act screening exams in the CCL and how patients are handled if they are not found to be appropriate for emergency angiography and PCI.

## Quality Metrics

Definitions for false positive (overactivation) and false negative (under-activation) activations from EMS have varied.<sup>11–17</sup>

Without standardized definitions that are widely used, comparison between agencies and systems is difficult. Because the terminology of “false positive” and “false negative” are often perceived pejoratively, particularly by EMS, the terms “overcall,” “undercall,” and “correct call” are recommended.

For EMS, an overcall is defined when EMS declares a “STEMI Alert” (eg, EMS notifies the hospital of their field impression of STEMI) but the patient does not undergo emergency angiography and is not diagnosed with myocardial infarction. Emergency angiography was specifically selected as the discriminating factor. If the interventional cardiologist thought emergency angiography was indicated, it should be sufficient to support the decision leading to an EMS STEMI Alert. Exclusions can be made for cases where symptoms and/or ECG changes resolved after the STEMI Alert was declared.

An EMS undercall is defined as cases where the patient diagnosed with STEMI who arrived by ambulance and underwent emergency angiography who met PreAct criteria, but EMS did not declare a STEMI Alert before arrival at the ED.

An EMS correct call is defined as cases where there is an STEMI Alert with subsequent emergency angiography or emergency thrombolytic administration (true positive); or, where there is not an STEMI Alert and neither emergency angiography nor emergency thrombolytic administration is performed (true negative).

Similar definitions for over-, under- and correct calls should be applied to the ED CCL activations.

Feedback on all STEMI activations should be provided in a timely manner, typically within 24 to 48 hours after CCL activation. Summary statistics on over-, under-, and correct calls should be provided to each EMS agency on a regular basis (eg, monthly, quarterly). More granular determination of reasons for overactivation can be useful to identify common reasons with the potential for protocol modification.

## Discussion

Current guidelines recommend an FMC2D time of  $\leq 90$  minutes.<sup>26</sup> Use of prehospital ECGs decreases time-to-revascularization, with or without transmission to the STEMI receiving center.<sup>40,41</sup> These time savings translate into improved patient outcomes.<sup>6,7,42</sup> The premise of the PreAct STEMI program is that a consistently applied process including routine, timely prehospital ECGs with prehospital notification will improve the accuracy and decision-making of activation of the CCL for STEMI patients, leading to expedited patient evaluation and routing upon hospital arrival, including taking patients direct to the CCL. Application of a consistent process should increase the appropriateness of patients undergoing cardiac catheterization, reducing delays, and improving outcomes.

## Prehospital Barriers to EMS Prehospital Acquisition, Interpretation, and Transmission

Prehospital identification of STEMI has been successfully implemented in many regions by training EMS personnel to make STEMI-focused interpretations of 12-lead ECGs. However, universal adoption of prehospital ECG acquisition with CCL activation remains limited. Barriers include funding for ECG transmission equipment and interpretation training, and issues with hospital acceptance of a broader EMS role in STEMI care.

One barrier to widespread use of prehospital ECGs is funding to train and equip EMS personnel to acquire, interpret, and transmit the prehospital ECG. At present, there are no standards defining the education required to achieve and maintain competence in STEMI-focused prehospital 12-lead ECG interpretation.

The AHA recommends 3 modes of prehospital ECG interpretation: paramedic interpretation, computerized algorithm diagnosis, and ECG transmission for remote interpretation.<sup>35</sup> Paramedics can be trained to acquire and interpret prehospital ECGs accurately in the absence of confounding ECG factors, with high sensitivity and specificity.<sup>6,35,42–46</sup> An alternative to reliance on paramedic ECG interpretation is to use the computerized interpretation technology. This process is rapid, easy, requires minimal training, is readily available and accessible regardless of geographic location, and is not dependent on a wireless network.<sup>35</sup> However, compared with physician interpretation, computer-based ECG interpretation results in more false-positive and false-negative ECGs.<sup>35</sup>

The results of EMS programs for STEMI recognition have been mixed. In some communities, EMS can recognize STEMI with good sensitivity and specificity.<sup>6,47–49</sup> In others, there have been high percentages of EMS-initiated CCL activations for patients who did not ultimately have STEMI.<sup>11–17</sup> The expense and inconvenience of these cases, particularly in off-hours, can be considerable, and has contributed to under-use and decreased adoption of prehospital CCL activation.

The third method for pre-hospital STEMI identification is ECG transmission.<sup>47–49</sup> Novel wireless technologies have simplified the ability to transmit ECGs from the field to receiving hospitals<sup>49</sup> or even to physician mobile devices,<sup>47,49</sup> for physician interpretation (ie, emergency physician, cardiologist, or both). The availability of rapid ECG interpretation can be invaluable in situations in which some but not all of the ECG criteria for STEMI are met, avoiding significant delays in diagnosis and triage. Conversely, over-activation for patients who have ECG STEMI mimics (left ventricular hypertrophy, early repolarization) may be decreased. However, a significant number of barriers limit Routine use of 12-lead ECG transmission.<sup>50</sup> ECG transmission programs require training and education, reliable acquisition and receiving equipment,

adequate wireless network coverage for consistent successful transmission, and 24/7 physician availability, all of which may vary greatly between communities.<sup>49</sup> Although  $\approx 90\%$  of EMS systems in large metropolitan areas have PH-ECG capability, transmission decreases to only 43% in rural areas.<sup>50</sup> Even when available, additional barriers to transmission include variations and incompatibility in transmitting and receiving equipment among hospitals and EMS agencies, even within the same system.

An additional barrier to pre-hospital STEMI recognition is that frequently rural EMS units operate with basic life support personnel, and often does not include PH-ECG protocols. A potential solution is to train basic life support personnel to perform the ECG, in those not previously trained to do so, and relay or transmit the machine interpretation, and determine if there is significant artifacts that might limit the interpretation validity.

STEMI systems should determine which PH-ECG interpretation process is most appropriate for their system. All systems should work to ensure a mechanism for verbal communication between the paramedic and emergency physician when discussion is needed for the Direct to CCL criteria, especially with equivocal cases. Consistent implementation of the PreAct algorithm can standardize pre-hospital communication of the critical information that could increase the success of pre-hospital activation and early ED assessment, leading to direct CCL transportation for the appropriate patient.

## PreAct Validation

Lange et al retrospectively applied the PreAct algorithm to 957 PH-ECG CCL activations at a single Los Angeles County STEMI receiving center.<sup>11</sup> Of the 957 patients, 746 (78%) would not have been activated based on the PreAct algorithm. Patients who would have been activated appropriately had significantly higher median peak troponin I values, were more likely to receive emergency cardiac catheterization and undergo PCI and were less likely to have CCL cancellation than patients who did not meet the algorithm criteria.<sup>12</sup> Subsequently, the PreAct STEMI algorithm was integrated into the CCL team activation algorithm at the same STEMI Receiving Center (SRC), resulting in a significant reduction in the CCL cancellation rate, from 57% to 16%.<sup>51</sup> Importantly, nearly half of the CCL cancellations were related to protocol deviation in which the PreAct STEMI algorithm inclusion criteria were not met. Door-to-balloon times for patients who did not meet the PreAct STEMI criteria but were found to have STEMI after evaluation in the ED were only an average of 15 minutes longer than PreAct STEMI patients (58–73 minutes). These early data indicate that consistent use of the PreAct algorithm is promising.<sup>51</sup>

## Future Goals

Currently, no national database tracks the rates of CCL STEMI cancellations. Contemporary estimates are primarily limited to single centers or systems, with marked variability in CCL cancellation rates.<sup>11–17</sup> In addition, definitions of appropriate CCL activation and cancellation vary greatly. One goal of the PreAct STEMI algorithm is to standardize reporting and definitions, resulting in more accurate national data.

There are similar challenges and rationale for guiding prehospital activations for other time sensitive conditions, such as stroke, cardiac arrest, massive pulmonary embolism, and aortic dissection. Implementing systems of care can be beneficial, as has been seen for cardiac arrest,<sup>52</sup> and more recently aortic dissection.<sup>53</sup> The PreAct STEMI algorithm and definitions may provide a useful model for application to these high-risk time-sensitive conditions to guide hospital destination decisions, field activation of hospital resources, routing on hospital arrival, and standardized definitions for false positives and false negatives.

## Conclusions

Total ischemia time interval is the principal determinant of outcome in STEMI, with FMC2D time a major component of that interval. Two of the most successful strategies to reduce that component have been (1) PH-ECG acquisition to allow field activation of the CCL before hospital arrival and (2) transport of patients directly to the CCL upon hospital arrival for selected cases. Reluctance to broader use of both strategies has been based on over activations from the field. The PreAct STEMI algorithm provides a framework of process flow and eligibility criteria to inform both the field activation and Direct to CCL decisions. It can be readily modified based on locality specific criteria to address specific circumstances and preference of the local EMS, emergency medicine, and cardiology communities. More consistent prehospital CCL activation for STEMI patients by use of standardized criteria such as those outlined have the potential to significantly reduce ischemia times, improve outcomes and decrease mortality for the acute STEMI patient.

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## References

1. Denktas AE, Anderson V, McCarthy J, Smalling RW. Total ischemic time: the correct focus of attention for optimal ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv.* 2011;4:599–604.
2. Stone GW, Selker HP, Thiele H, Patel MR, Udelson JE, Ohman EM, Maehara A, Eitel I, Granger CB, Jenkins PL, Nichols M, Ben-Yehuda O. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. *J Am Coll Cardiol.* 2016;67:1674–1683.
3. Nielsen PH, Terkelsen CJ, Nielsen TT, Thuesen L, Krusell LR, Thayssen P, Kelbaek H, Abildgaard U, Villadsen AB, Andersen HR, Maeng M; Danami-2 Investigators. System delay and timing of intervention in acute myocardial infarction (from the Danish Acute Myocardial Infarction-2 [DANAMI-2] trial). *Am J Cardiol.* 2011;108:776–781.
4. Bradley EH, Nallamothu BK, Herrin J, Ting HH, Stern AF, Nembhard IM, Yuan CT, Green JC, Kline-Rogers E, Wang Y, Curtis JP, Webster TR, Masoudi FA, Fonarow GC, Brush JE Jr, Krumholz HM. National efforts to improve door-to-balloon time results from the Door-to-Balloon Alliance. *J Am Coll Cardiol.* 2009;54:2423–2429.
5. Jacobs AK, Antman EM, Faxon DP, Gregory T, Solis P. Development of systems of care for ST-elevation myocardial infarction patients: executive summary. *Circulation.* 2007;116:217–230.
6. Jollis JG, Granger CB, Henry TD, Antman EM, Berger PB, Moyer PH, Pratt FD, Rokos IC, Acuna AR, Roettig ML, Jacobs AK. Systems of care for ST-segment-elevation myocardial infarction: a report from the American Heart Association's Mission: Lifeline. *Circ Cardiovasc Qual Outcomes.* 2012;5:423–442.
7. Jollis JG, Al-Khalidi HR, Roettig ML, Berger PB, Corbett CC, Doerfler SM, Fordyce CB, Henry TD, Hollowell L, Magdon-Ismail Z, Kochar A, McCarthy JJ, Monk L, O'Brien P, Rea TD, Shavadia J, Tamis-Holland J, Wilson BH, Ziada KM, Granger CB. Impact of regionalization of ST-segment-elevation myocardial infarction care on treatment times and outcomes for emergency medical services-transported patients presenting to hospitals with percutaneous coronary intervention: Mission: Lifeline Accelerator-2. *Circulation.* 2018;137:376–387.
8. Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, Gurm HS. Door to balloon time and mortality among patients undergoing primary PCI. *N Engl J Med.* 2013;369:901–909.
9. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso JE, Tracy CM, Woo YJ, Zhao DX. CF/AHA Task Force: 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *Circulation.* 2013;127:529–555.
10. Shavadia JS, Roe MT, Chen AY, Lucas J, Fanaroff AC, Kochar A, Fordyce CB, Jollis JG, Tamis-Holland J, Henry TD, Bagai A, Kontos MC, Granger CB, Wang TY. Association between cardiac catheterization laboratory pre-activation and reperfusion timing metrics and outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a report from the ACTION Registry. *JACC Cardiovasc Interv.* 2018;11:1837–1847.
11. Lange DC, Conte S, Pappas-Block E, Hildebrandt D, Nakamura M, Makkar RR, Kar S, Torbati S, Geideman J, McNeil N, Cercek B, Tabak SW, Rokos I, Henry TD. Cancellation of the catheterization lab after activation for STEMI: frequency, etiology and clinical outcomes. *Circ Cardiovasc Qual Outcomes.* 2018;11:e004464.
12. Baran KL, Lange D, Ajoku A, Kabian JA, Hildebrandt D, Kontos MC, Gunderson M, French W, Henry TD. Prospective assessment of the Mission:Lifeline PREACT-STEMI algorithm to reduce false activation of the cardiac catheterization laboratory. *J Am Coll Cardiol.* 2018;71(11 Supplement): A1171.
13. Barnes GD, Katz A, Desmond JS, Kronick SL, Beach J, Chetcuti SJ, Bates ER, Gurm HS. False activation of the cardiac catheterization laboratory for primary PCI. *Am J Manag Care.* 2013;19:671–675.
14. Garvey JL, Monk L, Granger CB, Studnek JR, Roettig ML, Corbett CC, Jollis JG. Rates of cardiac catheterization cancellation for ST-segment elevation myocardial infarction after activation by emergency medical services or emergency physicians: results from the North Carolina Catheterization Laboratory Activation Registry. *Circulation.* 2012;125:308–313.

15. Larson DM, Menssen KM, Sharkey SW, Duval S, Schwartz RS, Harris J, Meland JT, Unger BT, Henry TD. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. *JAMA*. 2007;298:2754–2760.
16. Lu J, Bagai A, Buller C, Cheema A, Graham J, Kutryk M, Christie JA, Fam N. Incidence and characteristics of inappropriate and false-positive cardiac catheterization laboratory activations in a regional primary percutaneous coronary intervention program. *Am Heart J*. 2016;173:126–133.
17. Kontos MC, Kurz MC, Roberts CS, Joyner SE, Kreisa L, Ornato JP, Vetrovec GW. 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.
18. Henry TD, Younger L, Derekhshan A, Conte S, Pappas-Block E, Makkar R, Kar S, Spiegel B, Geiderman J, Torbati S, Lange D. Economic impact of false ST-segment elevation myocardial infarction (STEMI) cardiac catheterization laboratory (CCL) activations at a major Los Angeles county STEMI-receiving center (SCR). *J Am Coll Cardiol*. 2016;67(13 Supplement):635.
19. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kasrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P; ESC Scientific Document Group. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119–177.
20. Bagai A, Jollis JG, Dauerman HL, Peng SA, Rokos IC, Bates ER, French WJ, Granger CB, Roe MT. Emergency department bypass for ST-segment-elevation myocardial infarction patients identified with a prehospital electrocardiogram: a report from the American Heart Association Mission: Lifeline Program. *Circulation*. 2013;128:352–359.
21. Carstensen S, Nelson GC, Hansen PS, Macken L, Irons S, Flynn M, Kovoov P, Soo Hoo SY, Ward MR, Rasmussen HH. Field triage to primary angioplasty combined with emergency department bypass reduces treatment delays and is associated with improved outcome. *Eur Heart J*. 2007;28:2313–2319.
22. Bagai A, Al-Khalidi HR, Muñoz D, Monk L, Roettig ML, Corbett CC, Garvey JL, Wilson BH, Granger CB, Jollis JG. Bypassing the emergency department and time to reperfusion in patients with prehospital ST-segment-elevation: findings from the reperfusion in acute myocardial infarction in Carolina Emergency Departments Project. *Circ Cardiovasc Interv*. 2013;6:399–406.
23. Parikh SV, Treichler DB, DePaola S, Sharpe J, Valdes M, Addo T, Das SR, McGuire DK, de Lemos JA, Keeley EC, Warner JJ, Holper EM. Systems-based improvement in door-to-balloon times at a large urban teaching hospital: a follow-up study from Parkland Health and Hospital System. *Circ Cardiovasc Qual Outcomes*. 2009;2:116–122.
24. Lee CH, Ooi SB, Tay EL, Low AF, Teo SG, Lau C, Tai BC, Lim I, Lam S, Lim IH, Chai P, Tan HC. Shortening of median door-to-balloon time in primary percutaneous coronary intervention in Singapore by simple and inexpensive operational measures: clinical practice improvement program. *J Interv Cardiol*. 2008;21:414–423.
25. Khot UN, Johnson ML, Ramsey C, Khot MB, Todd R, Shaikh SR, Berg WJ. Emergency department physician activation of the catheterization laboratory and immediate transfer to an immediately available catheterization laboratory reduce door-to-balloon time in ST-elevation myocardial infarction. *Circulation*. 2007;116:67–76.
26. Baran KW, Kamrowski KA, Westwater JJ, Tschida VH, Alexander CF, Behrs MM, Biggs TA, Koller PT, Mahoney BD, Murray ST, Raya TE, Rusterholz PK, Valeti US, Wiberg TA. Very rapid treatment of ST-segment-elevation myocardial infarction: utilizing prehospital electrocardiograms to bypass the emergency department. *Circ Cardiovasc Qual Outcomes*. 2010;3:431–437.
27. Cheskes S, Turner L, Foggett R, Huiskamp M, Popov D, Thomson S, Sage G, Watson R, Verbeek R. Paramedic contact to balloon in less than 90 minutes: a successful strategy for ST-segment elevation myocardial infarction bypass to primary percutaneous coronary intervention in a Canadian emergency medical system. *Prehosp Emerg Care*. 2011;15:490–498.
28. Chase C, Brady WJ. Artifactual electrocardiographic change mimicking clinical abnormality on the ECG. *Am J Emerg Med*. 2000;18:312–316.
29. Drew BJ. Pitfalls and artifacts in electrocardiography. *Cardiol Clin*. 2006;24:309–315.
30. Bosson N, Sanko S, Stickney RE, Niemann J, French WJ, Jollis JG, Kontos MC, Taylor TG, Macfarlane PW, Tadeo R, Koenig W, Eckstein M. Causes of prehospital misinterpretations of ST elevation myocardial infarction. *Prehosp Emerg Care*. 2017;21:283–290.
31. Zibulewsky J. The Emergency Medical Treatment and Active Labor Act (EMTALA): what it is and what it means for physicians. *Proc (Bayl Univ Med Cent)*. 2001;14:339–346.
32. Miedema MD, Newell MC, Duval S, Garberich R, Handran C, Larson DM, Mulder S, Wang YL, Lips D, Henry TD. Causes of delay and associated mortality in patients transferred with ST-elevation myocardial infarction. *Circulation*. 2011;124:1636–1644.
33. Whitney SN, McGuire AL, McCullough LB. A typology of shared decision making, informed consent, and simple consent. *Ann Intern Med*. 2004;140:54–59.
34. Fendler TJ, Spertus JA, Kennedy KF, Chen LM, Perman SM, Chan PS; American Heart Association's Get With the Guidelines-Resuscitation Investigators. Alignment of do-not-resuscitate status with patients' likelihood of favorable neurological survival after in-hospital cardiac arrest. *JAMA*. 2015;314:1264–1271.
35. Ting HH, Krumholz HM, Bradley EH, Cone DC, Curtis JP, Drew BJ, Field JM, French WJ, Gibler WB, Goff DC, Jacobs AK, Nallamothu BK, O'Connor RE, Schuur JD; American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research, Emergency Cardiovascular Care Committee; American Heart Association Council on Cardiovascular Nursing; American Heart Association Council on Clinical Cardiology. Implementation and integration of prehospital ECGs into systems of care for acute coronary syndrome. A scientific statement from the American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research, Emergency Cardiovascular Care Committee, Council on Cardiovascular Nursing, and Council on Clinical Cardiology. *Circulation*. 2008;118:1066–1079.
36. Rodríguez-Palomares JF, Figueras-Bellot J, Descalzo M, Moral S, Otaegui I, Pineda V, Del Blanco BG, González-Alujas MT, Evangelista Masip A, García-Dorado D. Relation of ST-segment elevation before and after percutaneous transluminal coronary angioplasty to left ventricular area at risk, myocardial infarct size, and systolic function. *Am J Cardiol*. 2014;113:593–600.
37. Sgarbossa EB, Pinski SL, Barbagelata A, Underwood DA, Gates KB, Topol EJ, Califf RM, Wagner GS. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. *N Engl J Med*. 1996;334:481–487.
38. Kozlowski FH, Brady WJ, Aufderheide TP, Buckley RS. The electrocardiographic diagnosis of acute myocardial infarction in patients with ventricular paced rhythms. *Acad Emerg Med*. 1998;5:52–57.
39. van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, Kilic A, Menon V, Ohman EM, Sweitzer NK, Thiele H, Washam JB, Cohen MG; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232–e268.
40. Diercks DB, Kontos MC, Chen AY, Pollack CV Jr, Wiviott SD, Rumsfeld JS, Magid DJ, Gibler WB, Cannon CP, Peterson ED, Roe MT. Utilization and impact of pre-hospital electrocardiograms for patients with acute ST-segment elevation myocardial infarction: data from the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry. *J Am Coll Cardiol*. 2009;53:161–166.
41. Rokos IC, French WJ, Koenig WJ, Stratton SJ, Nighswonger B, Strunk B, Jewell J, Mahmud E, Dunford JV, Hokanson J, Smith SW, Baran KW, Swor R, Berman A, Wilson BH, Aluko AO, Gross BW, Rostykyus PS, Salvucci A, Dev V, McNally B, Manoukian SV, King SB III. Integration of pre-hospital electrocardiograms and ST-elevation myocardial infarction receiving center (SRC) networks: impact on door-to-balloon times across 10 independent regions. *JACC Cardiovasc Interv*. 2009;2:339–346.
42. Jollis JG, Roettig ML, Aluko AO, Anstrom KJ, Applegate RJ, Babb JD, Berger PB, Bohle DJ, Fletcher SM, Garvey JL, Hathaway WR, Hoekstra JW, Kelly RV, Maddox WT Jr, Shiber JR, Valeri FS, Watling BA, Wilson BH, Granger CB; Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE) Investigators. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. *JAMA*. 2007;298:2371–2380.
43. Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy and clinical effect of out-of-hospital electrocardiography in the diagnosis of acute cardiac ischemia: a meta-analysis. *Ann Emerg Med*. 2001;37:461–470.
44. Le May MR, Dionne R, Maloney J, Trickett J, Watpool I, Ruest M, Stiell I, Ryan S, Davies RF. Diagnostic performance and potential clinical impact of advanced care paramedic interpretation of ST-segment elevation myocardial infarction in the field. *CJEM*. 2006;8:401–407.
45. Feldman JA, Brinsfield K, Bernard S, White D, Maciejko T. Real-time paramedic compared with blinded physician identification of ST-segment elevation myocardial infarction: results of an observational study. *Am J Emerg Med*. 2005;23:443–448.
46. Cantor WJ, Hoogveen P, Robert A, Elliott K, Goldman LE, Sanderson E, Plante S, Prabhakar M, Miner S. Prehospital diagnosis and triage of ST-elevation

- myocardial infarction by paramedics without advanced care training. *Am Heart J*. 2012;164:201–206.
47. Adams GL, Campbell PT, Adams JM, Strauss DG, Wall K, Patterson J, Shuping KB, Maynard C, Young D, Corey C, Thompson A, Lee BA, Wagner GS. Effectiveness of prehospital wireless transmission of electrocardiograms to a cardiologist via hand-held device for patients with acute myocardial infarction (from the Timely Intervention in Myocardial Emergency, NorthEast Experience [TIME-NE]). *Am J Cardiol*. 2006;98:1160–1164.
  48. Bosson N, Kaji AH, Niemann JT, Squire B, Eckstein M, French WJ, Rashi P, Tadeo R, Koenig W. The utility of prehospital ECG transmission in a large EMS system. *Prehosp Emerg Care*. 2015;19:496–503.
  49. Sanchez-Ross M, Oghladian G, Maher J, Patel B, Mazza V, Hom D, Dhruva V, Langley D, Palmaro J, Ahmed S, Kaluski E, Klapholz M. The STAT-MI (ST-segment analysis using wireless technology in acute myocardial infarction) trial improves outcomes. *JACC Cardiovasc Interv*. 2011;4:222–227.
  50. O'Connor RE, Nichol G, Gonzales L, Manoukian SV, Moyer PH, Rokos I, Sayre MR, Solomon RC, Wingrove GL, Brady WJ, McBride S, Lorden AL, Roettig ML, Acuna A, Jacobs AK. Emergency medical services management of ST-segment elevation myocardial infarction in the United States—a report from the American Heart Association Mission: Lifeline Program. *Am J Emerg Med*. 2014;32:856–863.
  51. Lange D, Conte S, Pappas-Block E, Hildebrandt D, Nakamura M, Makkar R, Kar S, Henry TD. Validation of the AHA Mission Lifeline PreAct algorithm to reduce false activation of the CCL. *J Am Coll Cardiol*. 2018;71(11 Supplement):A1170.
  52. McCarthy JJ, Carr B, Sasson C, Bobrow BJ, Callaway CW, Neumar RW, Ferrer JME, Garvey JL, Ornato JP, Gonzales L, Granger CB, Kleinman ME, Bjerke C, Nichol G; American Heart Association Emergency Cardiovascular Care Committee; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; and the Mission: Lifeline Resuscitation Subcommittee. Out-of-hospital cardiac arrest resuscitation systems of care: a scientific statement from the American Heart Association. *Circulation*. 2018;137:e645–e660.
  53. Graham KJ, Strauss CE, Boland LL, Mooney MR, Harris KM, Unger BT, Tretinyak AS, Satterlee PA, Larson DM, Burke MN, Henry TD. Has the time come for a national cardiovascular emergency care system? *Circulation*. 2012;125:2035–2044.

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