

ORIGINAL CONTRIBUTIONS

PREVALENCE AND INTERVENTIONAL OUTCOMES OF PATIENTS WITH RESOLUTION OF ST-SEGMENT ELEVATION BETWEEN PREHOSPITAL AND IN-HOSPITAL ECG

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ABSTRACT

Objective. To determine the prevalence and significance of ST-segment elevation resolution between prehospital and first hospital ECG. **Methods.** We examined consecutive prehospital ECGs transmitted to a single medical command center in southwestern Pennsylvania between January 1, 2009 and December 31, 2011. We included ECG cases with ST-segment elevation myocardial infarction (STEMI) and excluded cases with incomplete prehospital and/or hospital data. Our primary outcome was ST-segment resolution (STR), defined by cases no longer meeting STEMI criteria on the first in-hospital ECG. Primary variables of interest included prehospital vital signs and treatment, cardiac catheterization findings, and time intervals for diagnostics and treatment. Analysis included *t*-tests for continuous variables and chi-squared analysis for categorical variables. **Results.** We reviewed 24,197 prehospital ECGs and identified 293 cases of prehospital STEMI. Complete hospital and prehospital records were available for 83 cases (28%). Analyzed cohort was an average 62 years old and the majority were

male (67%), with a primary complaint of chest pain (93%). STR occurred in 18 cases (22%, CI 14–32%). There were no differences between STR and non-STR cases in prehospital vital signs or treatments. 95% of patients underwent cardiac catheterization with a mean door-to-needle time of 57 minutes (interquartile range 43–71). Comparing STR and non-STR cases, significant lesions ($\geq 50\%$) were found in 94 and 97% of patients ($p = 0.6$), and subtotal or total lesions ($\geq 95\%$) were found in 63 and 85% ($p = 0.1$), respectively. **Conclusions.** We found that ST-segment resolution occurred prior to catheterization in 1 of 5 patients with prehospital STEMI, emphasizing the necessity of prehospital ECG in risk stratification of patients with suspected coronary disease. Coronary lesions and intervention rates did not differ between STR and non-STR, suggesting that catheterization is warranted even when STEMI criteria are no longer met in-hospital. **Key words:**

PREHOSPITAL EMERGENCY CARE 2014;18:174–179

INTRODUCTION

The 12-lead electrocardiogram (ECG) is an essential risk stratification tool for patients with suspected acute myocardial infarction (AMI).¹ The presence of new ST-segment elevation identifies patients who benefit from urgent reperfusion via primary coronary intervention (PCI) or thrombolysis.^{2,3} Although emergency medical services (EMS) paramedics frequently acquire ECGs in the prehospital setting, the ability to activate the cardiac catheterization lab from the field is not universally adopted, and activation may depend on or be influenced by emergency physician interpretation of a repeat ECG acquired upon arrival of the patient in the emergency department (ED).

ST-segment displacement in ST-elevation myocardial infarction (STEMI) can vary over time such that the initial prehospital ECG may differ from the first emergency department ECG.^{4–6} Conversion over time from an initially nondiagnostic ECG to one

Received April 17, 2013 from the University of Pittsburgh School of Medicine (MO) and University of Pittsburgh, Department of Emergency Medicine (BS, AF, FXG, CMG), Pittsburgh, Pennsylvania. Revision received August 8, 2013; accepted for publication August 8, 2013.

Author contributions: BS, AF and MO conceived the study and designed the trial. BS, CMG, and AF supervised the conduct of the trial and data collection. CMG managed the data. MO drafted the manuscript, and all authors contributed substantially to its revision. BS takes responsibility for the paper as a whole.

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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doi: 10.3109/10903127.2013.851310

demonstrating ST-segment elevation is prognostic of poor outcomes^{7,8} and has been demonstrated to occur during out-of-hospital transport.⁹ However, there is only limited information on the prevalence and prognostic significance of ST-segment elevation resolving prior to revascularization, with most of this research based on hospitalized patients.^{10,11}

We aimed to estimate the prevalence and identify the interventional outcomes of patients who have resolution of ST-segment elevation prior to arrival in the ED. We attempt to answer the following two questions. In patients with prehospital evidence of STEMI, in what proportion of cases does ST elevation resolve between prehospital and preintervention in-hospital ECG? Also, is there a difference in the proportion of patients with subtotal or total coronary lesions ($\geq 95\%$) between groups of patients with ST-segment elevation resolution (STR) between prehospital and first in-hospital ECG versus those without STR? We hypothesized that patients with STR would have less severe intracoronary lesions than patients with persistent ST-segment elevation. We also explored whether there were differences in time to treatment between groups, hypothesizing that patients with ST-segment resolution experience decision-making delays in the emergency department, potentially resulting in delayed definitive treatment.

METHODS

Study Design

We examined prehospital and in-hospital records of patients with STEMI on prehospital ECGs transmitted to a single medical command center in southwestern Pennsylvania between January 1, 2009 and December 31, 2011. Approval of this study was obtained from the institutional review board (IRB) of the University of Pittsburgh.

Study Setting and Population

Patients treated by EMS agencies in southwestern Pennsylvania that receive medical command from a University of Pittsburgh Medical Center (UPMC) hospital were eligible for enrollment. This potentially could include any one of 217 EMS agencies whose catchment area spans 10 counties and who in sum respond to over 613,000 calls per year. During the study period, there was no field protocol for activation of the catheterization lab. During the period of study, participating hospitals activated the catheterization lab from the emergency department at a rate of 80–140 times per year. All ECGs were initially screened by a study investigator (MO), a trained paramedic and medical student, for any ST-segment elevations in any leads. These candidate ECGs were then reviewed with

calipers by two board-certified emergency physicians and study investigators (BS and AF). They selected ECGs that met the 2012 American Heart Association (AHA) criteria¹² for STEMI, defined as ST-segment elevation of greater than 0.1 mV in at least two contiguous precordial or adjacent limb leads. A third physician investigator reconciled any discrepancies (FXG). Investigators were blinded to automated ECG interpretation and clinical variables during this review process. ECGs with isolated T-wave inversions, ST-segment depression, or Q waves were considered nondiagnostic and excluded. Those noted to have left bundle-branch blocks (LBBB) were excluded due to the high likelihood that the LBBB would persist on follow-up ECGs and potentially affect ST-segment interpretation. Duplicate ECGs were disregarded, and if multiple ECGs existed for a given patient within a given transport, the ECG showing the greatest ST deflection from baseline was used. ECGs that met these inclusion criteria were linked to prehospital using the date, time, and EMS unit and then the in-hospital records using the patient name and date from the prehospital record. Prehospital STEMI cases with complete prehospital and in-hospital medical records, including an in-hospital ECG prior to catheterization, were included in the analysis.

Methods of Measurement

Our primary variable of interest was ST-segment elevation resolution (STR) between prehospital and first in-hospital ECG. The same diagnostic criteria for STEMI were used for the prehospital and in-hospital ECGs, and 2 categories were created to represent our primary variable of interest: STR versus non-STR. Specifically, two investigators (BS and AF) reviewed preintervention in-hospital ECGs of patients with prehospital STEMI and were blinded to automated interpretation and other clinical variables. Baseline patient characteristics, timing of ECG acquisition, initial presentation and physiologic variables, treatment, and interventional outcomes were determined for both groups. Primary intervention investigated was cardiac catheterization, as it is the primary and only treatment for STEMI within our regional hospital system. Time intervals were collected and calculated in the traditional manner for patients with findings diagnostic of STEMI on initial ECG, including prehospital ECG to first hospital ECG, hospital arrival to diagnostic catheterization (door to needle), and hospital ECG to diagnostic catheterization. Door to needle time was used instead of the traditional door to balloon time since some patients did not receive balloon angioplasty. The primary outcome of interest was the proportion of patients with $\geq 95\%$ stenosis of the primary coronary lesion, defined as the vessel with the highest percent occlusion if multiple vessels had lesions. The

secondary outcome of interest was the proportion of patients with balloon angioplasty or stent placement.

Statistical Approach

Categorical variables were presented as frequencies and percentages, whereas continuous variables were presented as medians (interquartile range [IQR]) or means (standard deviations [SD]). Data were tested for normal distribution with visual inspection of histograms and the Kolmogorov-Smirnov test. Comparisons between groups with and without STEMI resolution were made using the Pearson χ^2 test for categorical variables and the Student *t*-test or Mann-Whitney *U* test for continuous variables. All analyses were performed using STATA software (version 10, STATA, College Station, TX).

RESULTS

Baseline Characteristics

We reviewed 24,197 prehospital ECGs, of which 293 (1.2%) met STEMI criteria. We excluded 180 cases, including 49 (27%) without prehospital records and 131 (73%) who were delivered to non-UPMC hospitals. Additionally, we excluded 30 cases without a hospital ECG prior to cardiac catheterization, resulting in 83 complete records for analysis (Figure 1). Among 83 cases of prehospital STEMI, we identified 18 patients who had STR, resulting in a prevalence estimate of 22% (95% CI 0.14–0.32). The median time between prehospital and first in-hospital ECG was 31 minutes (IQR 23–52) for patients with STR and 24 minutes (IQR 19–31) for the non-STR group. Patient characteristics and prehospital physiology are shown in Table 1. Overall, patients were a mean age of 62 years old, with the ma-

TABLE 1. Patient characteristics and prehospital physiology

	ST resolution (n = 18)	ST nonresolution (n = 65)	p-value
Male, n (%)	13 (72)	43 (66)	0.6
Symptoms, n (%)			
Chest pain	16 (89)	61 (94)	0.6
Shortness of breath	3 (17)	15 (23)	0.8
Weak/dizzy/ lightheaded	3 (17)	8 (12)	0.7
Pain rating, median (IQR)	6 (4–8)	8 (4–10)	0.8
Age, mean (SD)	63 (13)	60 (12)	0.7
Initial prehospital vital signs			
Heart rate (beats/min)	71 (22)	74 (20)	0.6
Heart rate >100 beats/min, n (%)	0	4 (6)	0.6
Respiratory rate (rpm), median (IQR)	20 (18–20)	18 (16–20)	0.5
Respiratory rate > 25 rpm, n (%)	1 (6)	5 (8)	0.9
Systolic blood pressure (SBP: mmHg)	134 (50)	136 (35)	0.9
Hypotensive (SBP \leq 90 mm Hg), n (%)	3 (17)	6 (9)	0.4
Hypoxemia (saturation <95%), n (%)	2 (11)	9 (14)	0.9
Abnormal mental status (GCS < 15), n (%)	2 (11)	6 (9)	0.9

majority being men (67%) and 93% with a chief complaint of chest pain. There were low rates of tachycardia (5%), tachypnea (7%), hypotension (11%), hypoxemia (13%), and depressed mental status (10%), with no significant differences between groups.

Treatment and Interventional Outcomes

During prehospital transport, 98% of patients received supplemental oxygen, 87% received aspirin, 80% received sublingual nitroglycerin, and 30% received analgesia with intravenous morphine, with no differences in treatment between groups (Table 2). Overall, 95% of patients underwent diagnostic coronary catheterization, with a median time of hospital arrival to diagnostic catheterization of 57 minutes (IQR 43–71 minutes). Time from in-hospital ECG to diagnostic catheterization was a median 56 (IQR 40–65) minutes for patients with STR versus 37 (IQR 25–58) minutes for patients with non-STR (*p* = 0.04). Two significant delays exist in the STR group (16 hours 15 minutes and 9 hours 38 minutes), whereas the longest time for the non-STR group was 3 hours 57 minutes.

Among the 79 patients who underwent diagnostic coronary catheterization, significant lesions (>50% occlusion) were found in the left main or left anterior descending branch (30 patients, 38%), circumflex (16 patients, 20%), and the right coronary artery or its branches (41 patients, 52%), as shown in Table 3. Two patients had lesions in 3 vessels and 9 patients had lesions in 2 vessels (all in the non-STR group).

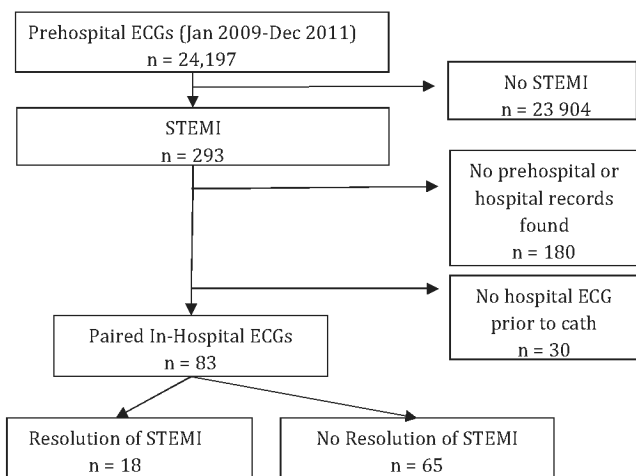


FIGURE 1. Patient selection.

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TABLE 2. Prehospital and in-hospital treatments

	STEMI resolution (n = 18)	STEMI nonresolution (n = 65)	p-value
Prehospital treatments			
Oxygen	18 (100)	63 (97)	0.9
Aspirin	16 (89)	56 (86)	0.9
Nitrates	15 (83)	51 (78)	0.8
Morphine	6 (33)	19 (29)	0.8
In-hospital treatments			
Diagnostic coronary catheterization	16 (89)	63 (97)	0.2
Hospital arrival to diagnostic catheterization, median (IQR) (min)	62 (45–75)	56 (42–70)	0.5
≤60 minutes from hospital arrival to catheterization	6 (33)	31 (48)	0.3
Hospital ECG to diagnostic catheterization, median (IQR) (min)	56 (40–65)	37 (25–58)	0.04
≤60 minutes from hospital ECG arrival to catheterization, n (%)	6 (33)	31 (48)	0.3
Primary percutaneous coronary intervention (PCI)	12 (75)	58 (92)	0.1
Hospital arrival to PCI, median (IQR) (min)	65 (43–77)	69 (55–87)	0.7
Door-to-balloon time ≤ 90 minutes	5 (42)	35 (60)	0.4
Primary PCI with stenting	12 (75)	55 (87)	0.2
Coronary artery bypass graft surgery	0	3 (5)	0.9

Results are presented as n (%) unless otherwise noted.

Overall, the primary lesion resulted in a ≥95% occlusion in 80% of patients, with a nonsignificantly higher proportion among the non-STR group (85%) than STR group (63%).

DISCUSSION

The present study provides the first published estimate of the prevalence and interventional outcomes

TABLE 3. Cardiac catheterization outcomes

	STEMI resolution (n = 16)	STEMI nonresolution (n = 63)	p-value
Vessels with ≥50% stenosis on diagnostic catheterization n (%)			
Left main or left anterior descending	8 (50)	22 (35)	0.3
Circumflex	3 (19)	13 (21)	0.9
Right coronary and branches	7 (44)	34 (55)	0.4
Percent stenosis n (%)			
99–100%	9 (56)	50 (81)	0.1
≥95%	10 (63)	53 (85)	0.1
≥90%	13 (81)	55 (89)	0.4
≥70%	15 (88)	58 (90)	0.7
≥50%	15 (94)	60 (97)	0.6

in patients with resolution of ST-segment elevation between prehospital and first in-hospital ECG. We found that one-fifth of patients meeting STEMI criteria based on the prehospital ECG experience resolution of diagnostic ST-segment elevation between prehospital and first in-hospital ECG. Contrary to our hypothesis, we found that patients with resolution of ST-segment elevations prior to catheterization have similar rates of coronary lesions and receive percutaneous coronary interventions at a similar rate as patients without STR. We found, however, that there may be delays in primary coronary intervention among some patients with STR.

Previous studies have reported the prevalence of ST-segment resolution in hospitalized patients, with estimates ranging from 4 to 27%.^{5,6,10,11} Two studies by Terkelson et al. have reported on the prevalence of ST-segment resolution and used ECGs extending from the prehospital setting to the inpatient setting.^{5,6} Additionally, Verbeek et al. documented STEMI progression through serial ECGs in the prehospital setting.⁹ Our findings contribute to existing literature by generating estimates of the phenomenon of STR from prehospital to initial hospital ECG and identifying the interventional outcomes of patients with this phenomenon.

Prior studies have indicated that resolution of ST-segment elevation is associated with better clinical outcomes and less myocardial damage.^{10,11} Rimar et al. noted that patients with resolution prior to definitive treatment have improved clinical outcomes, including decreased mortality at various time points up to 1 year.¹¹ Additionally, examining ST-segment resolution compared with angiographic evidence of reperfusion, Baine et al. note that patients with STR on ECG (or STR plus angiographic evidence of reperfusion) had better clinical outcomes than those who exhibited reperfusion only via angiography (no STR), indicating that the ECG may be an effective risk-stratification tool prior to intervention.¹⁰ Terkelson et al. included prehospital ECGs when monitoring ST segments for resolution prior to cardiac catheterization.^{5,6} They found that patients with resolution prior to cardiac catheterization had lower peak troponin levels and improved left ventricular ejection fraction at 3 months when compared to patients with persistent ST-elevation.⁵ In subsequent research they report that patients with STR prior to intervention had smaller infarct sizes on SPECT at 30 days.

While patients with STR may have improved clinical outcomes compared to those without STR, we found similarities when examining intracoronary lesions. Specifically, we found that a significant proportion of patients with STR and non-STR have ≥95% occlusion in the primary lesion, with no significant differences between groups. We found no difference in the distribution of lesions between groups, though a higher proportion of patients without STR have multivessel

disease. This supports the belief that STR likely indicates a reperfusion of the affected myocardium from nonaffected secondary or ancillary coronary vessels. If this is the case, it remains unclear whether emergently opening a lesion in which distal myocardium flow has already been restored will actually improve outcomes.

We found procedural delays in some patients who experience STR between prehospital and first in-hospital ECG. Specifically, there was a median of 19 minutes greater delay from in-hospital ECG to diagnostic catheterization. Delays in care of STEMI patients are associated with increased mortality.^{13,14} Large multicenter studies have investigated the value of early intervention in non-ST-elevation MI (NSTEMI) patients,¹⁴⁻¹⁶ and based on these studies the AHA guidelines recommend early intervention for high-risk NSTEMI patients.¹⁷ Our findings suggest that resolution of STEMI may complicate decision-making, speed of catheterization lab activation, or time to patient transport to the catheterization lab.

LIMITATIONS

Given the exploratory nature of this study, there are several limitations worth discussing. First, the strict inclusion criteria for this study resulted in a small sample size, resulting in wide confidence intervals on prevalence estimates and being underpowered to detect differences in outcomes between patients with and without STR. For example, the prevalence estimates of STR patients with a primary lesion with $\geq 95\%$ stenosis ranged from 35 to 85%. However, it is reasonable to argue that even if the true prevalence is 35% this is high enough to justify the risks of cardiac catheterization.¹⁸ To achieve an 80% power to detect a difference between patients with a primary lesion with $\geq 95\%$ stenosis at an alpha of 0.05 would require 71 patients per group, which would require review of around 96,000 prehospital ECGs. Second, our screening of ECGs was limited by lack of specific record keeping, where we may have inadvertently "screened out" cases that should have been included. Third, we had an overall low yield of cases included in the analysis, despite a large number of prehospital ECGs screened. This could have resulted in selection bias, either resulting in noninclusion of cases of more severe disease when data were missing or noninclusion of less severe cases that the paramedics did not identify as at risk for coronary disease. This bias must be considered in the context of a system where ECG transmission is encouraged on a routine basis for indications including shortness of breath, altered mental status, and syncope. Finally, we defined ST-segment resolution dichotomously, as opposed to quantitatively. Although this may have resulted in underidentifying more subtle ST-segment displacement

changes, we believe it is more clinically relevant in risk stratification as occurs in the acute care setting.

SUMMARY

These findings suggest that prehospital ECGs are critical in identifying patients with AMI. In EMS systems without prehospital ECG capabilities, up to one-fifth of acute STEMI cases could be missed. Also, our findings suggest that those patients with STR between prehospital and first in-hospital ECG should be considered at similar risk for having actionable coronary lesions as patients with persistent ST elevations. EMS systems with prehospital ECG capabilities have the opportunity to identify these cases and provide appropriate risk stratification. Whether an early intervention strategy improves outcomes for these patients cannot be assessed from the current data.

References

- OGara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby KL, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo J, Zhao DX. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61(4):485-510.
- De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation*. 2004;109:1223-5.
- Shiomi H, Nakagawa Y, Morimoto T, Furukawa Y, Nakano A, Shirai S, Taniguchi R, Yamaji L, Nagao K, Suyama T, Mit-suoka H, Araki M, Takashima H, Mizoguchi T, Eisawa H, Sugiyama S, Kimura T. Association of onset to balloon and door to balloon time with long term clinical outcome in patients with ST elevation acute myocardial infarction having primary percutaneous coronary intervention: observational study. *BMJ*. 2012;344:e3257.
- Bouwmeester S, van Hellemond IE, Maynard C, Young D, Bethea C, Gorgels A, Wagner G. The stability of the ST segment estimation of myocardial area at risk between the prehospital and hospital electrocardiograms in patients with ST elevation myocardial infarction. *J Electrocardiol*. 2011;44:363-9.
- Terkelsen CJ, Norgaard BL, Lasssen JF. Potential significance of spontaneous and interventional ST-changes in patients transferred for primary percutaneous coronary intervention: observations from the ST-MONitoring in acute myocardial infarction study (The MONAMI study). *Eur Heart J*. 2006;27(3):267-75.
- Terkelsen CJ, Kaltoft AK, Norgaard BL, Bottcher M, Lassen J, Clausen K, Nielsen SS, Thuesen L, Nielsen TT, Botker HE, Andersen HR. ST changes before and during primary percutaneous coronary intervention predict final infarct size in patients with ST elevation myocardial infarction. *J Electrocardiol*. 2009;42:64-72.
- Fesmire FM, Bardoner JB. ST-segment instability preceding simultaneous cardiac arrest and AMI in a patient undergoing

- continuous 12-lead ECG monitoring. *Am J Emerg Med.* 1994;12:69–76.
8. Johnson SM, Mauritsen DR, Winniford MD, Willerson JT, Firth BG, Cary JR, Hillis DL. Continuous electrocardiographic monitoring in patients with unstable angina pectoris: identification of high-risk subgroup with severe coronary disease, variant angina, and/or impaired early prognosis. *Am Heart J.* 1982;103:4–12.
 9. Verbeek PR, Ryan D, Turner L, Craig A. Serial prehospital 12-lead electrocardiograms increase identification of ST-segment elevation myocardial infarction. *Prehosp Emerg Care.* 2012;16:109–14.
 10. Bainey KR, Fu Y, Wagner GS, Goodman SG, Ross A, Granger CB, de Werf F, Armstrong PW. Spontaneous reperfusion in ST-elevation myocardial infarction: comparison of angiographic and electrocardiographic assessments. *Am Heart J.* 2008;156(2):248–55.
 11. Rimar D, Crystal E, Batter A, Gottlieb S, Freimark D, Hod H, Boyko V, Mandelzweig L, Behar S, Leor J. Improved prognosis of patients with clinical markers of spontaneous reperfusion during acute myocardial infarction. *Heart.* 2002;88:352–6.
 12. Thygesen K, Alpert JS, Jaffe AS, Maarten SL, Chaitman BR, White HD. Third universal definition of myocardial infarction. *Circulation.* 2012;126:2020–35.
 13. Rathore SS, Curtis JP, Chen J, Wang Y, Nallamothu BK, Epstein AJ, Krumholz HM, Hines HH Jr. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. *BMJ.* 2009;338:b1807.
 14. McNamara RL, Wang Y, Herrin J, Curtis JP, Bradley EH, Magid DJ, Peterson ED, Blaney M, Frederick PD, Krumholz HM. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol.* 2006;47(11):2180–6.
 15. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, Afzal R, Chrolavicius S, Jolly SS, Widimsky P, Avezum A, Rupprecht HJ, Zhu J, Col J, Natarajan ML, Horsman C, Fox K, Yusuf S. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med.* 2009;360:2165–75.
 16. Montalescot G, Cayla G, Collet JP, Elhadad S, Beygui F, Le Breton H, Choussat R, Leclercq F, Silvain J, Duclos F, Aout M, Dubois-Rande JL, Barthelemy O, Ducrocq G, Bellemain-Appaix A, Payot L, Steg PG, Henry P, Spaulding C, Vicaut E. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. *JAMA.* 2009;302(9):947–54.
 17. Wenger NK. 2011 ACCF/AHA focused update of the guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction (Updating the 2007 guideline): highlights for the clinician. *Clin Cardiol.* 2012;35:2–8.
 18. Singh M, Holmes DR Jr, Dehmer GJ, Lennon RJ, Wharton TP, Kutcher MA, Aversano T, Rihal CS. Percutaneous coronary intervention at centers with and without on-site surgery: a meta-analysis. *JAMA.* 2011;306(22):2487–94.