Impact of Smartphone Technology on the Early Diagnosis of Acute ST-Segment Elevation Myocardial Infarction at Non-Primary Percutaneous Coronary Intervention Capable Centres in Turkey

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ABSTRACT

Introduction: This study aimed to determine the mean time for diagnosis of acute ST-segment elevation myocardial infarction (STEMI) for both working hours (WHs) and non-WHs (NWHs) during the period that a smartphone application was in use to aid the speed of diagnosis and any significant difference in diagnosis times during NWHs with and without use of the application.

Patients and Methods: In this retrospective study, 174 patients who had been diagnosed with STEMI and transferred for primary percutaneous coronary intervention between January 2013 and April 2014 were recruited. During this period, the hospital used a smartphone application to aid diagnosis during NWHs. In addition, 58 patients who were diagnosed with STEMI during NWHs between January 2012 and November 2012, either by a cardiologist called to the emergency department or an electrocardiography being sent to the cardiologist's e-mail from a hospital computer, were enrolled.

Results: After the smartphone application was used, patients were diagnosed in a mean time of 7.9 ± 1.7 min during WHs, whereas STEMI was diagnosed in a mean time of 8.2 ± 1.4 min during NWHs. There was no statistically significant difference in diagnosis times between WHs and NWHs (p= 0.143). However, before the application was used, the mean time for the diagnosis of STEMI was 18.0 ± 3.1 min during NWHs, and consequently, there was a significant difference in STEMI diagnosis times during NWHs before and after the application began to be used (p< 0.001).

Conclusion: The application of smartphones, especially during NWHs at non-percutaneous coronary intervention-capable centres, can significantly reduce delays in STEMI treatment, which can result in improved short- and long-term clinical outcomes.

Key Words: ST elevation myocardial infarction; electrocardiography; smartphone application; percutaneous coronary intervention

Türkiyede Primer Perkütan Koroner Girişim Yapılamayan Merkezlerde Akut ST-Segment Elevasyonlu Miyokart İnfarktüsünün Erken Tanısı Üzerine Akıllı Telefon Teknolojisinin Etkisi

ÖZET

Giriş: Bu makalenin amacı akıllı telefon kullanılan dönemde çalışma ve çalışma dışı saatleri (ÇDS)'nde akut ST-elevasyonlu miyokart infarktüsü (STEMİ)'nün ortalama tanı süresini belirlemektir. Ayrıca uygulama varlığı ve yokluğunda ÇDS'deki tanı zamanları arasında önemli farklılık olup olmadığına bakılacaktır.

Hastalar ve Yöntem: Bu retrospektif çalışmaya Ocak 2013-Nisan 2014 tarihlerinde STEMİ tanısı konup primer perkütan koroner girişim (PKG) için transfer edilen 174 hasta alındı. Bu periyotta, hastanede ÇDS'de akıllı telefon kullanılmaktaydı. Ayrıca Ocak 2012-Kasım 2012 tarihlerinde ÇDS'de kardiyoloğun acile çağırılması veya hastane bilgisayarından kardiyoloğa elektronik posta ile elektrokardiyografi gönderilmesi yoluyla STEMİ tanısı konan 58 hasta alındı.

Bulgular: Uygulamanın kullanılmaya başlanılması sonrası çalışma sırasında hastaların tanı süresi ortalama 7.9 ± 1.7 dakikaydı. ÇDS'de STEMİ tanısı ortalama 8.2 ± 1.4 dakika olarak saptandı. Çalışma ve ÇDS arasında tanı zamanlarında fark görülmedi (p= 0.143). Uygulamanın kullanılmaya başlanması öncesi ÇDS'de STEMİ tanı süresi 18.0 ± 3.1 dakikaydı. ÇDS'de uygulama başlangıcı öncesi ve sonrası arasında STEMİ tanı süresi açısından anlamlı fark saptandı (p< 0.001).

Sonuç: Akıllı telefon uygulamalarının özellikle PKG yapılamayan merkezlerde ÇDS'de kullanılması STEMİ tedavisindeki gecikmeyi azaltarak kısa ve uzun dönem klinik sonuçlarda iyileşme sağlayabilir.

Anahtar Kelimeler: ST-elevasyonlu miyokart infarktüsü; elektrokardiyografi; akıllı telefon uygulaması; perkütan koroner girişim

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INTRODUCTION

Coronary artery disease is the most frequent cause of death, killing more than 7 million people worldwide in a year[1]. Acute coronary syndrome (ACS) refers to any group of symptoms attributed to obstruction of the coronary arteries. ACS occurs most often as ST elevation myocardial infarction (STEMI) (30%), non-STEMI (NSTEMI) (25%), or unstable angina (38%)[2]. Acute STEMI usually occurs when a thrombus settles on a ruptured atheromatous plaque and occludes an epicardial coronary artery.

Our hospital has used personal technology, especially smartphones, to speed up the diagnosis of patients with suspected heart symptoms in the emergency department (ED) during non-working hours (NWHs). Since late 2012, we have been using a common smartphone messenger application to send pictures of patients' electrocardiograms (ECGs) for cardiologist review, saving the time it would take a cardiologist to reach the ED. This approach enables us to begin treating heart-attack patients within the time frame when emergency care is most likely to be successful. Every minute a patient waits for the emergency doctor to arrive and study their ECG increases the risks, and this period can be especially longer during NWHs. In our hospital, when a patient complains of chest pain or any other cardiac-related symptom, an emergency doctor takes an ECG and sends the image to the cardiologist on call. Before our hospital began to use this system, either a cardiologist had to be called to the ED from home or the ECG had to be sent to the cardiologist's email from an ED computer. This process resulted in delays because the ECGs had to be scanned and transferred to the ED computer.

The early provision of therapy, particularly of reperfusion therapy, is critical to its benefit[3]. Thus, the minimisation of delays is associated with improved outcomes. If the reperfusion therapy is primary percutaneous coronary intervention (PCI), the goal should be a delay of ≤ 90 min from first medical contact (FMC) to passage of the wire into the culprit artery, and in high-risk cases with large, anterior infarcts and in early presenters within 2 h, this delay should be ≤ 60 minutes[4,5]. Both randomised studies and registries have indicated that long delays before primary PCI are associated with worse clinical outcomes. From randomised trials, it was calculated that PCI-related delays of 60-110 min may even mitigate the benefit of mechanical intervention[6].

This study aimed to determine the contributions of smartphones to the ED treatment of patients with acute STEMI in centres not capable of PCI during NWHs.

PATIENTS and METHODS

Study Population

This study was conducted at a secondary state hospital in Turkey. To select the study population, we looked at patients' files and selected patients who had been diagnosed with STEMI and transferred for primary PCI between 1st January 2013 and 30th April 2014. During this period, 174 patients were admitted to our hospital's ED with chest pain and diagnosed with STEMI. Of these, 108 subjects-50 during working hours (WHs) and 58 during NWHs-were diagnosed with STEMI between 1th January 2012 and 30th November 2012, which was the period before the hospital began to use the messenger application.

Study Protocol

The present study was an observational, retrospective study at a single centre. All the patients' ECGs were taken after they were admitted. STEMI patients were divided into two groups: 1) during WHs, defined as 8.00 am to 5.00 pm on Mondays through Fridays, and 2) during NWHs, defined as 5.00 pm to 8.00 am on Mondays through Fridays and weekends. During WHs, cardiologists are called to the ED. In contrast, after 1st January 2013, during NWHs, ED doctors would send the ECG image to the cardiologist on call through a smartphone application. Before use of this application, STEMI had to be diagnosed during NWHs by a cardiologist who was called to the ED from home or by the ECG being sent to the cardiologist's e-mail from an ED computer. In this study, the diagnosis time of STEMI was defined as the time that the cardiologist reviewed the ECG from his/her WhatsApp messenger application on their smartphone and diagnosed or arrived at the ED and assessed the ECG regarding STEMI. Moreover, the diagnosis time was defined as the time interval between admission of the patients to ED and the diagnosis of STEMI by a cardiologist.

For this study, ST-segment elevation in acute myocardial infarction was measured at the J point, was found in two contiguous leads, and was defined as being ≥ 0.25 mV in men of age < 40 years, ≥ 0.2 mV in men of ≥ 40 years, or ≥ 0.15 mV in women in leads V2-V3 and/or ≥ 0.1 mV in other leads, in the absence of left ventricular (LV) hypertrophy or left bundle branch block (LBBB)[7].

The PCI centre was informed by the cardiologist in terms of the diagnosis and clinical status of the STEMI patients. Hence, the patient was immediately taken to the catheter laboratory. This study investigated the mean time to diagnose STEMI both during WHs and NWHs after our hospital began to use the smartphone application. In addition, the study looked for any significant differences in diagnosis times in the NWHs group before and after use of the application began.

This study excluded patients admitted to the ED between 1st December 2012 and 30th December 2012 and who were diagnosed with STEMI because this period was a time of transition to using the smartphone application. In addition, the study excluded patients who had STEMI but who were not transferred for PCI because of special conditions.

Statistical Analysis

Descriptive statistics are presented herein as the mean ± SD for continuous variables and as numbers and percentages

for categorical variables for comparing groups. Variables were checked using the Shapiro-Wilk test to determine whether the variables showed a normal distribution. Homogeneity of the variances was analysed using the Levene test. An independent samples t-test was used to compare two groups of data that fitted a normal distribution. The Mann-Whitney U test was used to compare non-normally distributed data. An overall 5% type-I error level (95% confidence interval) was used to infer statistical significance and a two-sided p value of < 0.05 was considered significant. Statistical analyses were performed using the statistical package for social sciences version 15 (SPSS Inc.; Chicago, IL, USA).

RESULTS

Between January 2013 and April 2014, the ratio of impels for STEMI to all impels was 22.98%. During this period, STEMI was diagnosed in 174 patients (122 men and 52 women). The number of patients diagnosed with STEMI during WHs was 70 and during NWHs was 104.

Between January 2012 and November 2012, the ratio of impels for STEMI to all impels was 23.16%. During this period, 108 patients were diagnosed with STEMI. The number of patients diagnosed with STEMI during WHs was 50 and during NWHs was 58. During WHs, 78% were males, while during NWHs, 83% were males. The mean age of STEMI patients during WHs (57 ± 14) was not significantly different than that during NWHs (59 ± 11) ($p > 0.254$).

Between January 2013 and April 2014, patients admitted to the ED with STEMI were diagnosed in a mean time of 7.9 ± 1.7 min during WHs. In these patients, STEMI was diagnosed by a cardiologist in the ED. During NWHs, the mean time for diagnosis was 8.2 ± 1.4 min, and STEMI was diagnosed after an emergency doctor sent the ECG image to the cardiologist on call using the smartphone application. There was no significant difference in diagnosis time between WHs and NWHs ($p > 0.05$) (Table 1), indicating that transmitting patients' ECGs to cardiologists' smartphones during NWHs caused no delay in diagnosis (Table 2).

However, from January 2012 to November 2012, the mean time to diagnose STEMI was 9.0 ± 1.5 min during WHs and 18.0 ± 3.1 min during NWHs, indicating a significant difference in diagnosis time between WHs and NWHs ($p < 0.001$). During this time period, STEMI was diagnosed during NWHs either by a cardiologist being called to the ED from home or by the ECG being sent to the cardiologist's e-mail from an ED computer. This caused significant delays in diagnosis during NWHs compared with that during WHs (Table 1).

In addition, this study investigated any difference in diagnosis times during NWHs before (NWH2) and after (NWH1) our hospital began to use the smartphone application. There was a significant difference between these two groups, with the application shortening the time to diagnosis ($p < 0.001$).

DISCUSSION

The main findings of the present study were as follows: 1) The diagnosis time for acute STEMI was similar between WHs and NWHs when using the smartphone messenger application. 2) A significant difference in STEMI diagnosis times before and after this application began to be used was found.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischaemia in association with persistent ECG ST elevation and a subsequent release of biomarkers of myocardial necrosis. Diagnostic ST elevation in the absence of LV hypertrophy or LBBB is defined by the European Society of Cardiology/ACCF/AHA/World Heart Federation Task Force for the Universal Definition of Myocardial Infarction as new ST elevation at the J point in at least two contiguous leads of ≥ 2 mm (0.2 mV) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2-V3 and/or of ≥ 1 mm (0.1 mV) in other contiguous chest leads or limb leads[8]. New or presumably new LBBB is considered a STEMI equivalent. In addition, ST depression in two or more precordial leads (V1-V4) may indicate transmural posterior injury; multilead ST depression with coexistent ST elevation in lead aVR has been described in patients with left main or proximal left anterior descending artery occlusion[9]. At present, STEMI accounts for approximately 25%-40% of all myocardial infarction presentations[10].

Patients with STEMI typically do not seek medical care for approximately 1.5-2 h after symptom onset, and there has been little change in this interval over the past 10 years[11,12]. One of the reasons patients may delay seeking care is because their symptoms differ from those of a heart attack as they do not present dramatically with severe, crushing chest pain[13]. Although more than 98% of the U.S. population is covered by the 911 service[14], U.S. patients with STEMI often do not call an EMS or 911 and are thus not transported to the hospital by ambulance. A 2011 observational study found that EMS transport was used for only 60% of 37.643 patients with STEMI[15], although patients with possible ischaemic symptoms should be transported to the hospital by ambulance rather than by friends or relatives. The use of pre-hospital ECGs, particularly when coupled with the communication of STEMI diagnosis and preferential transport to a PCI-capable hospital, has been shown to result in rapid reperfusion times and excellent clinical outcomes[16-18]. However, unfortunately, in Turkey, public ED (112) ambulances do not have 12-lead ECG machines. Therefore, patients do not receive ECGs until they are admitted to the ED. This means that STEMI patients are diagnosed in EDs, and if the hospital is PCI capable, are then taken to the catheter laboratory. However, if they are initially taken to a non-PCI-capable centre, they must be transferred to a PCI-capable one.

Reperfusion therapy should be administered to all eligible STEMI patients who have had symptom onset within the first 12 h[19,20]. Primary PCI is the recommended method of reperfusion when it can be performed in a timely manner by experienced

operators[20-22]. Immediate transfer to a PCI-capable hospital for primary PCI is the recommended triage strategy for STEMI patients who initially arrive at or are transported to a non-PCI-capable hospital, with an FMC-to-device time system goal of ≤ 120 min[21-24]. In the absence of contraindications, fibrinolytic therapy should be administered to STEMI patients at non-PCI-capable hospitals when the anticipated FMC-to-device time at a PCI-capable hospital exceeds 120 min because of unavoidable delays[19,25,26]. However, our hospital does not use fibrinolytic therapy because of its proximity to PCI-capable centres.

Any regional medical system must seek to enable the rapid recognition and timely reperfusion of STEMI patients as systemic delays to reperfusion are correlated with higher rates of mortality and morbidity[27-30]. Consideration should be given to the development of local protocols that allow preregistration and direct transport to the catheterisation laboratory of a PCI-capable hospital (bypassing the ED) for patients who do not require emergent stabilisation upon arrival.

Several trials have suggested the benefit of transferring STEMI patients from a non-PCI-capable hospital to a PCI-capable one for primary PCI[23,31]. In many communities, a significant percentage of STEMI patients who present initially to a non-PCI-capable hospital cannot physically be transferred to a PCI-capable one and achieve an FMC-to-device time treatment goal of ≤ 90 min. A DANAMI-2 trial showed that a reperfusion strategy involving the transfer of STEMI patients from a non-PCI-capable hospital to a PCI-capable one for primary PCI was superior to the use of fibrinolysis at the referring hospital, primarily because of a reduction in the rate of reinfarction in the group treated with primary PCI[21,23]. In that study, the average first door-to-device time delay was approximately 110 min[23]. Efforts are needed to reduce the delay between arrival to and transfer from a non-PCI-capable hospital (door-in-door-out). Among a subset of 14.821 patients in the NCDR ACTION-GWTG registry, the median door-in-door-out time was 68 min (interquartile range, 43-120 min). A door-in-door-out time of ≤ 30 min, achieved in only 11% of patients, was associated with shorter delays to reperfusion and a lower in-hospital mortality rate[32].

A smartphone is a mobile phone with more advanced computing capability and connectivity than phones with basic features. Early smartphones typically combined the features of a mobile phone with those of another popular consumer device, such as a personal digital assistant, a media player, a digital camera or a GPS navigation unit. Modern smartphones include all of those features plus the features of a touchscreen computer, including web browsing, Wi-Fi and third-party applications. Messenger applications are cross-platform, mobile-messaging applications that allow users to exchange messages without having to pay for a short message service. Such applications enable users to send and receive location information, images, video, audio and text messages in real time to individuals and groups at no cost. For suspected medical cases, practitioners can use smartphone messaging applications to share ECGs with specialists.

In Turkey, the knowledge of ECGs in medical personnel other than cardiologists is very inadequate. Therefore, diagnosing STEMI is a significant problem. In addition, during NWHs, the delays in receiving primary PCI that are experienced by patients who initially present at non-PCI-capable centres worsen the prognosis of those patients. Misdiagnosis or delays occur frequently if there is no cardiologist present at the hospital. There are two ways to prevent this. One is the greater education of practitioners about ECGs. The other is enabling practitioners to consult with cardiologists about ECGs by means of smartphone applications. The second option is easier, more suitable and more cost-effective for Turkey. In this case, if the hospital does not have a cardiologist, it can send the ECG to a cardiologist at another hospital. A cardiologist can evaluate the ECG from any location, including from home, and if there is STEMI, the patient can be transferred for primary PCI without delay.

The present study found no difference in diagnosis times between WHs and NWHs. Another benefit of using such an application is preventing impels caused by initial misdiagnosis at non-PCI-capable hospitals. Some hospitals without cardiologists send patients to our hospital for the diagnosis of NSTEMI. Before the use of smartphone applications, 30%-35% of these patients were diagnosed with STEMI in our hospital and sent to PCI-capable centres for primary PCI. However, there were significant delays until a true diagnosis was made. Our hospital has remediated this situation by using smartphone consultations regarding ECGs before taking patients with suspected NSTEMI for impellation, and if there is STEMI, we offer to transfer the patient to a PCI-capable hospital directly. In one case example, a specialist wanted us to accept a patient in our non-PCI-capable hospital for coronary care, but thanks to the use of a smartphone

Table 1. Diagnosis times for WH1 and NWH1 in the period between January 2013 and April 2014 and WH2 and NWH2 in period between January 2012 and November 2012

Category	Mean time (min)	N	Std. deviation
WH1	7.9	70	1.7
NWH1	8.2	104	1.4
WH2	9.0	50	1.5
NWH2	18.0	58	3.1

NWH: Non-working hours, WH: Working hours.

Table 2. Comparison between WHs and NWHs in the period of January 2013 and April 2014

	N	Z	P
WHs	70	-1.467	0.143
NWHs	104		

NWH: Non-working hours, WH: Working hours.

messenger application, our cardiologist was able to see the patient's ECG and diagnose acute inferior myocardial infarction with bradycardia instead. Therefore, the patient was transferred to a PCI-capable centre directly rather than to our hospital, avoiding a probable delay before appropriate treatment.

Study Limitations

This study was performed using a relatively limited number of patients. In addition, the patients' door-to-balloon times were not known. Furthermore, the time from admission to ED to ECG varied and may have depended on the severity of the symptoms. For example, elderly female patients or diabetics may have fewer symptoms, and their ECGs might not have been taken immediately.

CONCLUSION

We demonstrated a significant difference in diagnosis times during NWHs between before and after the smartphone messenger application began to be used in patients with STEMI. The use of such applications may minimise delays and improve clinical outcomes in this setting. In addition, the use of smartphone messenger applications can assure that the catheterisation laboratory is prepared while the ambulance transfer is occurring, so that the patient can be transferred directly to the catheterisation laboratory table upon arrival.

The present study showed that during the NWHs, the direct transmission of a 12-lead ECG by a smartphone messenger application from an ED to a cardiologist's smartphone was extremely beneficial. In addition, during NWHs, the use of an appropriate smartphone application may indirectly lead to a reduced infarction size and limited reduction of the ejection fraction by decreasing the diagnosis time for acute STEMI.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: KC, HAC
Analysis/Interpretation: EY, KC
Data Acquisition: HAC, EY
Writing: HAC, KC
Critical Revision: EY, KC
Final Approval: All of authors

REFERENCES

1. WHO Factsheet N8310, updated June 2011. Available from: http://www.who.int/mediacentre/factsheets/fs310/en/index.html.
2. Torres M, Moayedi S. "Evaluation of theacutely dyspneic elderly patient". Clin Geriatr Med 2007;23:307-25.
3. Luepker RV, Raczynski JM, Osganian S, Goldberg RJ, Finnegan JR Jr, Hedges JR, et al. Effect of a community intervention on patientdelay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. JAMA 2010;304:763-71.
4. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation 2003;108:2851-7.
5. Pinto DS, Kirtane AJ, Nallamothu BK, Murphy SA, Cohen DJ, Laham RJ, et al. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. Circulation 2006;114:2019-25.
6. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneus coronary intervention and in-hospital fibrinolysis in acute miyocardial infarction patients. Eur Heart J 2006;27:779-88.
7. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. Eur Heart J 2007;28:2525-38.
8. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. Circulation 2012;126:2020-35.
9. Go AS, Barron HV, Rundle AC, Ornato JP, Avins AL. National Registry of Myocardial Infarction 2 Investigators Bundle-branch block and in-hospital mortality in acute myocardial infarction. Ann Intern Med 1998;129:690-7.
10. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. N Engl J Med 2010;362:2155-65.
11. Goldberg RJ, Spencer FA, Fox KA, Brieger D, Steg PG, Gurfinkel E, et al. Prehospital delay in patients with acute coronary syndromes (from the Global Registry of Acute Coronary Events [GRACE]). Am J Cardiol 2009;103:598-603.
12. Spencer FA, Montalescot G, Fox KA, Goodman SG, Granger CB, Goldberg RJ. Delay to reperfusion in patientswith acute myocardial infarction presenting to acute care hospitals: an international perspective. Eur Heart J 2010;31:1328-36.
13. Finnegan JR Jr, Meischke H, Zapka JG, Leviton L, Meshack A, Benjamin-Garner R, et al. Patient delay in seeking care for heart attack symptoms: findings from focus groups conducted in five U.S. regions. Prev Med 2000;31:205-13.
14. 2013 ACCP/AHA Guideline for the management of ST-Elevation myocardial Infarction.
15. Mathews R, Peterson ED, Li S, Roe MT, Glickman SW, Wiviott SD, et al. Use of emergency medical service transport among patients with ST-segment-elevation myocardial infarction: findings from the National Cardiovascular Data Registry Acute Coronary Treatment Intervention Outcomes Network Registry-Get With The Guidelines. Circulation 2011;124:154-63.
16. Sørensen JT, Terkelsen CJ, Nørgaard BL, Trautner S, Hansen TM, Bøtker HE, et al. Urban and rural implementation of pre-hospital diagnosis and direct referral for primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction. Eur Heart J 2011;32:430-6.
17. Le May MR, So DY, Dionne R, Glover CA, Froeschl MP, Wells GA, et al. A city wide protocol for primary PCI in ST-segment elevation myocardial infarction. N Engl J Med 2008;358:231-40.
18. Rokos IC, French WJ, Koenig WJ, Stratton SJ, Nighswonger B, Strunk B, et al. Integration of pre-hospital electrocardiograms and ST-elevation myocardial infarction receiving center (SRC) networks: impact on door-to-balloon times a cross 10 independent regions. JACC Cardiovasc Interv 2009;2:339-46.
19. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardia linfarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994;343:311-22.
20. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003;361:13-20.
21. Andersen HR, Nielsen TT, Vesterlund T, Grande P, Abildgaard U, Thayssen P, et al. Danish multicenter randomized study on fibrinolytic therapy versus acute coronary angioplasty in acute myocardial infarction: rationale and design of the DANish trial in Acute Myocardial Infarction-2 (DANAMI-2). Am Heart J 2003;146:234-41.

22. Dalby M, Bouzamondo A, Lechat P, Montalescot G. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. Circulation 2003;108:1809-14.

23. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, et al. DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003;349:733-42.

24. Nielsen PH, Terkelsen CJ, Nielsen TT, Thuesen L, Krusell LR, Thayssen P, et al. 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;108:776-81.

25. Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything? Am J Cardiol 2003;92:824-6.

26. Pinto DS, Kirtane AJ, Nallamothu BK, Murphy SA, Cohen DJ, Laham RJ, et al. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. Circulation 2006;114:2019-25.

27. Rathore SS, Curtis JP, Chen J, Wang Y, Nallamothu BK, Epstein AJ, et al. National Cardiovascular Data Registry. 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.

28. Terkelsen CJ, Jensen LO, Tilsted HH, Trautner S, Johnsen SP, Vach W, et al. Health care system delay and heart failure in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: follow-up of population-based medical registry data. Ann Intern Med 2011;155:361-7.

29. 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.

30. Terkelsen CJ, Sørensen JT, Maeng M, Jensen LO, Tilsted HH, Trautner S, et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 2010;304:763-71.

31. Widimský P, Budesínský T, Vorác D, Groch L, Zelízko M, Aschermann M, et al. 'PRAGUE' Study Group Investigators. Long distance transport for primary angioplasty vsim mediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. Eur Heart J 2003;24:94-104.

32. Wang TY, Nallamothu BK, Krumholz HM, Li S, Roe MT, Jollis JG, et al. Association of door-in to door-out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. JAMA 2011;305:2540-7.