WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)
Patrick Meybohm, Aaron Wong

Date Submitted for review:
11 March 2009

Clinical question.
In patients with ACS (P) does the presence of any specific demographic factors (e.g. age, sex, race, weight) (I), compared with their absence (C), increase accuracy of prediction of delayed treatment (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis?
Prognosis.

State if this is a proposed new topic or revision of existing worksheet: New

Conflict of interest specific to this question
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? NO

Search strategy (including electronic databases searched).
PubMed “Acute Coronary Syndrome” or “Myocardial Infarction” or “Angina, Unstable” as MESH (headings) AND “age” or “demographic factors” or “race” or “sex” or “living alone” AND “treatment” or “door-to-drug time” or “door-to-balloon time” or “time-to-treatment” or “delay in seeking” or “treatment delay” or “delay in treatment” text word in abstract.
Review of references of articles (or reviews) of relevance and review of related articles linked to searched article provided by.PubMed 1965-2009.
#2 Search sex OR race OR age OR “demographic factors” OR “living alone” 1.642.870
#3 Search "door-to-drug time" OR "door-to-balloon time" OR (time AND treatment) OR (delay AND seeking) 926.615
#4 Search #1 and #2 17.454
#5 Search #1 and #3 16.679
#6 Search #4 and #3 3.355
#7 Search #4 and #3 Limit: Humans 3.323
#8 Search #4 and #3 Limit: Humans, Clinical Trial, Randomized Controlled Trial 703

State inclusion and exclusion criteria
All studies reporting delayed treatment (pre hospital and/or in hospital) in association with patients’ demographics (age, gender, race, socioeconomic status, living alone etc.) were included. The following studies were excluded: Chest pain, Stable angina, cardiac arrest, cardiogenic shock, animal studies, reports of single cases. Studies reporting differences in rates of procedures without any link to time delay. Studies with number < 200 patients were arbitrary excluded unless the studies looked at specific demographics, e.g. race or socioeconomic status.

Number of articles/sources meeting criteria for further review:
60 studies met criteria for further review. None of these were Level of Evidence (LOE) for Prognosis P1 (prospective cohort studies or meta-analyses of cohort studies), three LOE P2 (follow up of untreated control groups in RCTs or meta-analyses of follow-up studies), fifty-four LOE P3 (retrospective cohort studies), none LOE P4 (case series), and three LOE P5 (studies not directly related to the specific patient/population).

Summary of evidence

Evidence Supporting Clinical Question

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<td>Lefler 2004 (G+, R+, S+,</td>
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<th>Level of evidence for Prognosis</th>
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| Good                            | Ben-Shlomo 2008 (R) (P)  
                                   | Goff 1999 (G) (P)  
                                   | Gurwitz 1997 (S) (P)  
                                   | Grossman 2003 (G) (P)  
                                   | Johnson 1999 (R) (P) |
| Fair                            | Dracup 1997 (MJA) (A, G, R) (P)  
                                   | Khraim 2009 (A, G, R, S) (P)  
                                   | Saczynski 2008 (G, R) (P)  
                                   | Zahn 2005 (A) (I)  
                                   | Bouma 1999 (A, G) (P)  
                                   | Pellicia 2004 (A, G) (I)  
                                   | Carrabba 2004 (G) (P, I)  
                                   | Neill 2008 (G) (P, I) |
| Poor                            | Caldwell 2000 (A, G, R) (P)  
                                   | Khan 2007 (A, G, S) (P)  
                                   | Kudenchuk 1996 (G) (P)  
                                   | Moser 2005 (G) (P)  
                                   | Dracup 1997 (HL) (G, L) (P)  
                                   | Zerwic 2003 (G) (P)  
                                   | Crawford 1994 (R) (P, I)  
                                   | Banks 2007 (G) (P)  
                                   | Banks 2006 (A, G) (P) |

A=age (older), G=gender (female), R=race (non-white), S=socioeconomic status (lower SES), L=living (alone), (+)= predictor, (P)=pre hospital delay, (I)= in hospital delay, HL=Heart Lung, MJA=Med J Aus

**Evidence Neutral to Clinical question**
A=age (older), G=gender (female), R=race (non-white), S=socioeconomic status (lower SES), L=living (alone), (P)= pre hospital delay, (I)= in hospital delay, HL=Heart Lung, MJA=Med J Aus

Evidence Opposing Clinical Question

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Level of evidence
Initial observational human studies revealed prolonged delay time from onset of symptoms to arrival at the hospital for black patients compared with historical studies including white patients. A subsequent large prospective follow-up study revealed that African-Americans with acute myocardial infarction tended to delay seeking care compared with whites (median times to presentation after onset, 6 versus 3 hours, respectively), and were less likely to be admitted to the hospital (39 versus 59%). However, this difference did not reach statistical significance, and once admitted, both African-Americans and whites were equally likely to be admitted to the coronary care unit and to undergo cardiac catheterization. Following large retrospective analyses emphasized prehospital time delay in seeking care (symptom-to-door) in non-black minorities (Hispanics, Asian-Pacific islanders, and native Americans), however there were no significant differences in hospital mortality for non-black minorities compared with whites. In addition, further demographic factors, such as older age, female gender, socioeconomic status, and living alone were independently associated with delayed presentation to the hospital after the onset of symptoms of acute myocardial infarction. Some theoretical reasons suggested by some investigators were inherent morbidity and accessibility to medical services (age, socioeconomic factors, living alone).

Since early reperfusion therapy for patients with evolving myocardial infarction is essential, it is important to analyze not only the effect of different demographic, cultural, and socioeconomic factors on the prehospital delay, but also, once admitted, on both probability of early reperfusion and door-to-treatment/reperfusion times (in hospital delay). Numerous large retrospective studies have shown that ethnicity minority experiences significantly longer times to fibrinolytic therapy (door-to-drug times), longer times to percutaneous coronary intervention (door-to-balloon times), less likelihood to undergo coronary bypass surgery, and increased mortality even when high-risk specific coronary anatomy subgroups were examined, thus, raising concerns of health care disparities.

Acknowledgements:
Nil.
Citation List


14. LOE P3. Good (n=40,000). Supportive (A+, G+, R+) (I). Forty thousand patients from NRMI (1994 to 2000). Median door-to-balloon time was assessed and delayed in-hospital treatment defines as > 2 hour. In multivariated analysis, older age, female sex and non-white were associated mean increase of 5 to 6 min of delay.

15. LOE P3. Good (n=275,046). Supportive (A+, G+, R+) (I). Non-black minorities (Hispanics, Asian-Pacific islanders, and native Americans) presented later to the hospital after the onset of symptoms (135 vs 122 minutes) than whites. Also, non-black minorities were less likely to present later than patients who delay longer.


17. LOE P2. Poor (underpowered; n=61). Neutral (G) (P). Median delay time in seeking medical care for symptoms of acute myocardial infarction tended to be longer for women compared to men (4.4 hours vs 3.5 hours; not significant).

18. LOE P5. Good. Supportive (A+, G+, R+) (I). Large registry with specifically looked at patient > 65 years old. Advanced age, women and non-white population were predictors for longer door-to-needle time.

19. LOE P3. Poor (n=51,991). Supportive (S+) (I, P). In this population-based cohort study, socioeconomic status had pronounced effects on access to specialized cardiac services in Ontario's universal health care system, as well as on mortality one year after acute myocardial infarction. Progressive increases in neighborhood median income levels predicted greater rates of use of coronary angiography, shorter waiting times for catheterization, and lower mortality one year after acute myocardial infarction.

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21. LOE P3. Fair. Supportive (G+) (P). Single centre study from 1988 to 1997 with 1737 patients looking specifically at gender and outcomes post AMI. Crude analysis showed women had significant longer symptom onset to hospital arrival and door-to-balloon time.

22. LOE P3. Poor (n=275,046). Supportive (S+) (I, P). In this population-based cohort study, socioeconomic status had pronounced effects on access to specialized cardiac services in Ontario's universal health care system, as well as on mortality one year after acute myocardial infarction. Progressive increases in neighborhood median income levels predicted greater rates of use of coronary angiography, shorter waiting times for catheterization, and lower mortality one year after acute myocardial infarction.

23. LOE P3. Poor (n=40.000). Supportive (A+, G+, R+) (I). Forty thousand patients from NRMI (1994 to 2000). Median door-to-balloon time was assessed and delayed in-hospital treatment defines as > 2 hour. In multivariated analysis, older age, female sex and non-white were associated mean increase of 5 to 6 min of delay.


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likely to receive beta-blocker therapy at discharge (odds ratio 0.86) than whites, but they were generally as likely to receive intravenous thrombolytic therapy and undergo both coronary arteriography and revascularization procedures as their white counterparts. National registry of myocardial infarction II database.


LOE P3. Fair. Neutral (G) (P, I). AMI registry of 6 hospitals in Florence from 2000 to 2001 with 920 patients looking at outcomes of women compared to men. Non-adjusted median pre hospital delay and door-to-balloon time for women were not statistically different from men.


LOE P3. Fair. Supportive (A+, G+) (P). Database from 2708 patients enrolled into GUSTO-I in Canada. Univariate analysis showed longer prehospital delay in women and elderly. Age was an independent predictor of longer door-to-drug time with multivariated analysis.


LOE P3. Poor (n=2030). Neutral (R) (P, I). Blacks and Whites were equally likely to seek and receive care based on a telephone interview in inner-city Boston.


LOE P3. Fair. Supportive (A+, G+) (I). A single centre study with 1791 patients with STEMI treated with primary PCI, looking at relationship of ischemic time (delayed treatment) and 1 year mortality. Age > 70 years old and women were associated with longer door-to-balloon time in unadjusted analysis.


LOE P3. Fair. Supportive (S+) (P)/ Neutral (A,G, R) (P). 317 patients with AMI enrolled in 3 hospitals in Sydney. Lower income and year of education were found to be associated with longer prehospital delay but only year of education was found to be independent predictor on logistic regression analysis.

19. Dracup K, Moser DK: Beyond sociodemographics: factors influencing the decision to seek treatment for symptoms of acute myocardial infarction. Heart Lung 1997; 26: 253-62

LOE P3. Poor. Supportive (A+, S+)/ Neutral (G, L). Enrolled patients from GUSTO Trial in North America from multiple sites with total of 277 patients. Crude analysis showed elderly and lower income had significantly longer pre hospital delay.


LOE P3. Good. Supportive (S+) (P). Neighborhood income was specifically looked at for association with pre hospital delay and was found to be independent predictor of long delay in 9700 patients in this community surveillance study.


LOE P3. Good. Supportive (A+, G+, R+, L+) (P, I). Combining GUSTO-I and III studies data with total of 27849 patients. Pre hospital delay was significantly associated with older age, female and black. Longer door-to-treatment time was associated with elderly, female and black using a step wise regression model. Higher socioeconomic status (higher educational levels, professional and health insurance) was also found to be associated with shorter pre hospital delay in GUSTO III database.


LOE P2. Good (n=3783). Supportive (A+, R+) (P)/ Neutral (G) (P). The Rapid Early Action for Coronary Treatment (REACT) is a multicenter, randomized community trial designed to reduce patient delay. During a 4-month baseline data collection period, the overall median prehospital delay time was 2 hours, with substantially longer delays of 30 to 45 minutes for the mean for several important subgroups, including women, Hispanics, non-Hispanic blacks, the elderly, the disabled and homemakers.


LOE P3. Supportive. Fair (A+, G+, R+) (P). Duration of prehospital delay was analysed in a large (n=364,131) cross-sectional sample of patients included in the second National Registry of Myocardial Infarction (USA). Elderly patients, women, and minorities, such as african americans, hispanics, american indians, and asians were more likely to delay seeking medical care of longer than 3 hours.

LOE P3. Fair. Supportive (A+, G+) (P). Using the Global Registry of Acute Coronary Events (GRACE) project elderly age and women were associated with prehospital delay > 2 hours in the STEMI patients only.


LOE P3. Fair (n=1000). Supportive (A+) (P). Mean and median intervals from chest pain onset to emergency department arrival were longer in elderly (>70 years) people (P = 0.05).


LOE P3. Good. Supportive (A+) (P)/ Neutral (G) (P). Both age and gender were looked at in this 374 patients single centre study with univariate and multiple regression analyses. Only age was found to be independent predictor for lag time of > 12 hours.


LOE P3. Good (n=2409). Supportive (A+, G+, L+) (P)/ Neutral (S) (P). Advanced age (>=85 years; odds ratio 1.40) and female sex (odds ratio 1.24) were significantly associated with delayed presentation to the hospital for more than 6 hours after the onset of symptoms of acute myocardial infarction.


LOE P3. Fair. Supportive (G+) (P). In this study specifically looked at gender and delay in 3 time intervals (door to ECG, ECG to treatment and door to treatment). Female gender was associated with longer (23 min) door-to-treatment time in multivariate analysis.


LOE P3. Good (n=78,254). Supportive v. Compared with men, women were less likely to receive early aspirin (adjusted OR=0.86) and beta-blocker treatment (adjusted OR=0.90), reperfusion therapy (adjusted OR=0.75), or timely reperfusion (door-to-needle time <=30 minutes: adjusted OR=0.78; door-to-balloon time <=90 minutes: adjusted OR=0.87) based on the 'Get With the Guidelines-Coronary Artery Disease database'.


LOE P2. Good (n=3031). Neutral (R) (P). African-Americans with acute myocardial infarction tended to come to the emergency department at a later time after their chest pain began to subside compared with whites (median times to presentation after onset, 6 hours and 3 hours, respectively (P = 0.08)), and were less likely to be admitted to the hospital (39 versus 59 %). Once admitted, both African-Americans and whites were equally likely to be admitted to the coronary care unit and to undergo cardiac catheterization. However, African-Americans were less likely to undergo coronary artery bypass surgery with an odds ratio of 0.36 [CI, 0.16 to 0.80].


LOE P3. Poor. Neutral (A, G, S) (P). In this Pakistan study, age and gender were not associated with delay in presentation (> 6 hour) after AMI.


LOE P3. Poor. Neutral (G) (P). There was no difference in pre hospital delay between men and women. Although acute reperfusion therapies for AMI were more commonly used in men in this study, this did not mean longer door-to-treatment time.


LOE P3. Poor. Supportive (A+) (I). This small study looked specifically at age and door-to-balloon delay and was found to a positive association.

LOE P2. Fair (underpowered). Supportive (R+) (P). Mean time for prehospital delay with clinical symptoms of myocardial infarction differed significantly between blacks and whites (16 hours vs. 8.8 hours, p <0.05).


LOE P2. Fair (n=1,051,382; meta-synthesis of 48 reports). Supportive (G+, R+, S+, L+). Female gender, African American race, low socioeconomic status, and living alone contribute to prehospital delay seeking medical treatment for symptoms of an acute myocardial infarction.


LOE P3. Good. Supportive (A+, G+) (P). 5469 patients were randomized to receive either pre-hospital thrombolytic treatment, followed by placebo in hospital (pre-hospital group), or pre-hospital placebo, followed by thrombolytic treatment in hospital (hospital group) in the European Myocardial Infarction Project trial (EMIP). A post hoc analysis of these data was performed to correlate components of the interval between symptom onset and treatment with baseline patient characteristics. The delay between onset of symptoms and calling for an ambulance was significantly longer for female patients (P<0.001) and older patients (>65 years old; P<0.001).


LOE P3. Good. Supportive (A+, G+) (P, I). NRMI database from 1990 to 1994. Pre hospital delay was analyzed in 212,990 patients and predictors for delay were advanced age and female gender. In 59,802 patient receiving thrombolytic therapy, multivariate analysis showed advance age and female gender were predictors for longer door-to-drug time.


LOE P3. Fair (n=4500). Supportive (A+, G+) (P). Advance age and female gender was associated with pre hospital delay in multivariate analysis.


43. Moser DK, McKinley S, Dracup K, Chung ML: Gender differences in reasons patients delay in seeking treatment for acute myocardial infarction symptoms. Patient Educ Couns 2005; 56: 45-54

LOE P3. Poor. Neutral (G). This small study (n=194) looking at gender showed no difference in median delay time between men and women.


LOE P3. Fair (n=663). Neutral (G) (P, I). There was no difference in pre hospital and in hospital time delay demonstrated in this study.

45. Oka RK, Fortmann SP, Varady AN: Differences in treatment of acute myocardial infarction by sex, age, and other factors (the Stanford Five-City Project). Am J Cardiol 1996; 78: 861-5

LOE P3. Poor (n=3016). Supportive (G+, R-) (P). Women were less likely than men to undergo angiography but were equally likely to undergo revascularization and thrombolysis. Hispanics and whites were equally likely to receive angiography and thrombolysis, but Hispanics were less likely than whites to undergo revascularization (Stanford Five-City Project during the years 1986 to 1992).


LOE P3. Poor. Supportive (G+) (P). Pre hospital delay of > 2 hours was more common in women as compared to men.

LOE P3. Fair. Supportive (G+) (P). Female gender had significant longer physician, transportation and total pre hospital delay in multivariate analysis.


LOE P3. Good. Supportive (A+, G+) (P). A group of 6676 consecutive patients with acute myocardial infarction from 1990 to 1992 were studied. In a multivariate logistic regression analysis, a greater than 2 h patient delay was independently associated with male gender and increased age.


LOE P3. Fair (n=4,843). Neutral (A, G) (P). Comparison between older (>65 years) and younger (<=65 years) revealed no significant differences during their stays in the emergency departments, in the use of continuous 12-lead ST-segment monitoring, in door-to-thrombolysis time and door-to-balloon time.


LOE P3. Good (n=4,760). Supportive (R+) (I). Black patients were less likely than white patients to receive thrombolytic therapy at the time of arrival (32.4% vs. 48.2%; P <0.01), and were less likely to undergo bypass surgery (6.9% vs. 12.5% by 90 days; P <0.001) even when high-risk specific coronary anatomy subgroups were examined, although there was no difference in the percentage of patients who refused coronary artery bypass graft surgery. In contrast, black patients were equally likely to receive beta-blockers and angiotensin converting enzyme inhibitors and more likely than white patients to receive aspirin at the time of discharge.


LOE P3. Fair. Supportive (A+, G+, R+) (I). Door-to-balloon time of this large registry were analyzed and longer delay was seen in older patient, women and non white.


LOE P3. Fair (n=5,967). Supportive (A+) (P)/ Neutral (G, R) (P). Older age and female gender were found to have longer prehospital delay but only older age were found to be associated with longer delay after controlling for confounding factors. Gender and race were not found to be predictors.


LOE P3. Fair. Supportive (A+, G+, S+) (P). In this Turkish study (n=439), female, age > 55 and total education < 9 years were independent predictors for prolonged pre hospital delay.


LOE P5. Fair. Supportive (G+, R+) (I). Based on a computerized survey of 720 of primary care physicians women (odds ratio, 0.60) and blacks (odds ratio, 0.60) were significantly less likely to be referred for cardiac catheterization than men and whites, respectively.


LOE P5. Fair (n=1,796). Supportive (R+) (I). Reluctance by African-American patients to undergo invasive cardiac procedures (surgery or percutaneous transluminal coronary angioplasty) was significantly higher compared with Caucasian patients (15.4% versus 8.3%; odds ratio 2.026).


LOE P3. Fair. Supportive (A+, G+, R+, S+) (P). In this large AMI population of age > 65 years, female, black and SES were risk factors for delayed hospital presentation.


LOE P3. Poor (n=1416). Supportive (A+, G+) (I). Crude analysis showed older patients and women had longer symptom-to-door and symptom-to-balloon but similar door-to-balloon time as compared to younger patients and men, respectively.


LOE P3. Good. Supportive (A+, R+) (P, I). Black race and age > 60 years were independent predictors for pre hospital delay and longer door-to-balloon time.

LOE P3. Fair (n=4815). Supportive (G+) (I)/ Neutral (A) (I). Female sex was independently associated with longer door to angiography times (OR 1.21, 95% CI 1.01 to 1.45) based on the german registry of percutaneous coronary interventions in acute myocardial infarction.


LOE P3. Poor (n=212). Supportive (R+) (P)/ Neutral (G, L) (P). African Americans delayed significantly seeking treatment longer than non-Hispanic Whites (3.25 hours vs. 2.0 median hours).