


## Associated Factors with Delayed Door to Balloon Time in STEMI Patients

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**Abstract**

**Introduction:** Door to balloon time is a marker of primary Percutaneous Coronary Intervention (PCI) timeliness. Door to balloon time duration, associated factors and it's relation to outcomes are not similar in various centers. Herein we aimed to define these issues in our region.

**Methods:** In this study, 188 patients with ST-Elevation Myocardial infarction (STEMI) diagnosis eligible for primary PCI were included. Demographic, clinical, and time intervals from arrival in the hospital to patients' catheterization data were recorded. Patients were followed for six-month in terms of mortality and admission.

**Results:** After excluding patients with missed data, 174 patients were entered into the study. The mean age of patients was  $60.8 \pm 11.81$  years, and 78% of patients were male. Median DBT was 70 minutes (IQR 25-75: 55-97 minute). One hundred and twenty-three patients (71%) had a timely door to balloon time. Patients with delayed door to balloon time had lower age, lower prevalence of typical chest pain, and higher prevalence of PCI on Left Circumflex Artery (LCX) than the timely group, but these differences were not significant. (P-values were 0.068, 0.074 and 0.070 respectively). Delayed DBT was evident in three segments of the door to ECG, ECG to code, and code to cath times (P-values were  $< 0.0001$ , 0.009, and  $< 0.0001$ , respectively), but the cath to balloon time was not significantly different between the two groups (P-value: 0.159). Although in-hospital mortality was higher in the delayed group than the timely group, the difference was not meaningful. (11.7% vs 4.9%, P-value: 0.103). Six-month mortality and admission rate were not different between the two groups.

**Conclusions:** Door to balloon time was acceptable in this study and was comparable to developed countries. Albeit there is room for improvement due to modifiable delayed parts.

## INTRODUCTION

Door to balloon time (DBT) is defined as the time interval from hospital arrival of ST-Elevation Myocardial Infarction (STEMI) patients to balloon catheter inflation inside epicardial coronary arteries [1]. In a meta-analysis involving 299,320 patients, patients with longer DBT had a higher risk of short and long-term mortality. STEMI patients with longer DBT are at increased risk of re-infarction, Major Adverse Cardiac Events (MACE), and mortality [2].

In a study in 4168 patients undergoing primary PCI due to STEMI, determinant factors of DBT delay were older age, female sex, the time interval between symptom onset and hospital admission, type of pre-hospital care, and time of hospital admission [3].

Due to conflicting data regarding the association of DBT door to balloon time with adverse outcomes and limited observations in our region, we aimed to evaluate the possible factors of delayed DBT door to balloon time in our center.

## MATERIALS AND METHODS

In this observational retrospective study between Sep 23, 2016, to Sep 22, 2017, in the Cardiology Department of Imam Khomeini hospital in Ardabil in the northwest of Iran, 188 patients with STEMI treated with primary angioplasty were enrolled.

Baseline, clinical and angiographic data were obtained from medical records and catheterization laboratory. Patients were followed up for six months after discharge, and six-month mortality and cardiac-related hospital admissions were also recorded. Patients with incomplete data were excluded.

DBT  $\leq$  90 min and DBT  $>$  90 min were considered as timely and delayed groups, respectively.

The patients were also categorized as DBT  $<$  60 min and DBT  $\geq$  60 min to determine the categorization outcome. The ethics committee approved this study of Ardabil University of Medical Sciences.

### Statistical Analysis

Data were analyzed using SPSS version 21 (SPSS, Inc, Chicago). Categorical data were expressed as numbers, and percentages and continuous data were presented as mean and standard deviation. Chi-square and OR tests were used for comparing categorical variables. Student's t-test for continuous variables with normal distribution and U-Mann Whitney for continuous variables without normal distribution were used. Binary regression analysis was used for defining independent predictors. P-value  $<$  0.05 was considered significant.

## RESULTS

Initially, 188 patients were entered into the study, and 14 patients were excluded due to data loss. Finally, 174 patients were entered into the study. The mean age of

patients was  $60.8 \pm 11.81$  years, and 78% of patients were male. Median DBT was 70 minutes (IQR 25-75: 55-97 minute). Delayed DBT was detected in 29% of patients. Median DBT for patients without delay was 60 min (IQR 25-75: 49-72) and for patients with delayed DBT was 139 min (IQR 25-75: 104-220).

Demographic and clinical characteristics of patients were presented in Table 1. Patients' age in the timely group was higher than the delayed group, but the difference was not significant ( $60.69 \pm 11.87$  vs.  $58.21 \pm 12.21$  years, respectively, P-value: 0.068). Typical chest pain prevalence was higher in the timely group than the delayed group (79% vs. 70%, P-value: 0.074), but the difference was not meaningful. PCI of Left Anterior Descending (LAD) and Right coronary Artery (RCA) were more common in the timely group than the delayed group (47% and 35% vs. 45% and 17.6%). In comparison, the PCI on the Left circumflex artery (LCX) was higher in the delayed group (23.5% vs. 9.7%), but the difference was not significant (P-value: 0.07).

Different parts of the DBT were expressed in Table 2. Although all-time intervals from symptom onset to ballooning were lower in timely group, time intervals of the door to catheterization (cath) including Door to ECG taking (Door to ECG), ECG taking to PCI code activation (ECG to code), and PCI code activation to catheterization laboratory entrance (code to cath) times were significantly lower in the timely group (P-value:  $<$  0.0001, 0.009 and  $<$  0.0001 respectively).

In-hospital death occurred in 6.8% of patients. While in-hospital mortality in a timely group was lower than the delayed group, the difference was not significant (4.8% vs. 11.7% respectively, P-value: 0.103). In univariate and multivariate analysis, only the female gender had a significant association with in-hospital mortality. (P-Value: 0.03 and 0.005 respectively).

Admission due to cardiac disorders during six months after discharge occurred in 37.1% of patients. Although the delayed group's admission rate was slightly higher than the timely group, the difference was not significant (37.7% vs. 36.8%, P-value: 0.672). The total six-month-mortality rate was 4.3%, and there was no significant difference between the two groups (P-value: 0.415).

We also evaluated patients' outcomes based on grouping them as the door to balloon time less than 60 minutes and equal or higher than 60 minutes. In-hospital death occurred in 5.1% of the  $<$  60 min group and 7.7% of patients in  $\geq$  the 60 min group, but the difference was not significant. The 6-month mortality was lower in the  $<$  60 min group than  $\geq$  60 min, but that was not meaningful (3.6% vs. 4.6% P-value: 0.759). Six-month admission rate was also lower in  $<$  60 min group than  $\geq$  60 group without significant difference (15% vs 31%, P-value: 0.304).

**Table 1.** Demographic and Clinical Characteristics in Patients with and without the Delayed Door to Balloon Time

Characteristics	All	DBT $\leq$ 90 min	DBT > 90 min	P-value
Age, years	60.69 $\pm$ 11.87	61.95 $\pm$ 11.49	58.21 $\pm$ 12.21	0.068
Male sex	145 (77.5)	97 (79)	38 (74.5)	0.531
BMI*	27.51 $\pm$ 4.01	27.58 $\pm$ 3.84	28.05 $\pm$ 3.92	0.742
BMI < 25	25	25.5	23.8	
BMI $\geq$ 25	75	74.4	76	
Typical chest pain	133 (76)	97 (79)	36 (70)	0.074
MI $\dagger$ history	22 (12.6)	17 (13.8)	5 (9.8)	0.468
Tobacco use	96 (55)	67 (54.4)	29 (56.8)	0.131
ECG $\ddagger$ (STEMI site)				0.348
Pure Anterior	78 (45)	55 (44.7)	23 (46)	
Pure Inferior	65 (37.5)	47 (38.2)	18 (36)	
Pure lateral	4 (2.3)	1 (0.8)	3 (6)	
PCI $\S$ on				0.070
LAD//	81 (46.5)	58 (47)	23 (45)	
LCX#	24 (13.7)	12 (9.7)	12 (23.5)	
RCA**	52 (30)	43 (35)	9 (17.6)	
Transfer with				0.938
ambulance	49 (28)	35 (28.4)	14 (27.4)	
Self-transport	122 (70)	86 (70)	36 (70.5)	
In-hospital death	12 (6.8)	6 (4.9)	6 (11.7)	0.103
Education				0.175
Illiterate	70 (40)	50 (41)	20 (39)	
Literate	104 (60)	73 (59)	31 (61)	
6-month death	7 (4.3)	6 (5.1)	1 (2.2)	0.415
6-month admission $\geq$ 1	59 (37.1)	42 (36.8)	17 (37.7)	0.672

$\S$ Door to balloon time; \*Body Mass Index;  $\dagger$ Myocardial Infarction;  $\ddagger$ Electrocardiography;  $\S$ Percutaneous coronary intervention; //Left anterior descending (artery); #Left circumflex (artery); \*\*Right coronary (artery)

Data in the table are presented as mean  $\pm$  SD or No. (%).

**Table 2.** Different Segments of Door to Balloon Time in Minute

Component segments of DBT, min	All (n = 174)	DBT* $\leq$ 90 min (n = 123)	DBT > 90 min (n = 51)	P-value
Symptom onset to door time	120 (63-276)	120 (64-225)	126 (60-411)	0.449
Door to ECG $\dagger$ time	25 (12-43)	29 (20-41)	68 (30-110)	< 0.0001
ECG to code time	10 (5-20)	10 (5-18)	15 (5-31)	0.009
Code to cath $\ddagger$ time	10 (7-20)	10 (6-15)	17 (10-30)	< 0.0001
Cath to ballooning time	15 (10-20)	15 (10-20)	15 (10-25)	0.159

\*: Door to balloon time,  $\dagger$ : Electrocardiography,  $\ddagger$ : Catheterization

Data are presented as median (IQR), IQR: Interquartile range

## DISCUSSION

DBT is associated with myocardial ischemic damage and could be considered a modifiable risk factor in contrast to non-modifiable risk factors like demographic and clinical characteristics. Although the more extended door to balloon time has been associated with worse outcomes, the direct causal effect is unclear. A focus on improving DBT door to balloon time may lead to overtreatment of patients with primary PCI. In a study, about 25% of activated catheterizations for suspected STEMI were false positive [4].

Meanwhile, there are conflicting data regarding the association of DBT with mortality. Some studies have not found a significant relationship between improving DBT and reduction of mortality [5]. Another point is that, despite improvement in DBT, the in-hospital mortality rate has not reduced [5-8]. Regarding these facts, it seems reasonable to further evaluate the pros and cons of efforts for improving the door to balloon time. The 2013ACC/AHA guideline-recommended treating STEMI patients with the goal of time within 90 minutes [9].

Due to the decreasing slope of DBT time in recent years, 2017 [10] European society of cardiology and the

European association of cardiothoracic surgery changed their recommendation regarding DBT to within 60 minutes after STEMI diagnosis for primary PCI-capable centers [11].

The reported data from developed [12-14] and even some developing countries [15, 16] indicate acceptable DBT despite some concerns regarding collecting data like excluding patients with cardiogenic shock and cardiac arrest [17].

Selection bias might be evident in some studies, for instance, in a study, although the self-transport group had longer DBT but had lower mortality than Emergency Medical Services (EMS) group. The cause may be due to younger age and lower risk factors of mortality like old age and higher killip classification in the self-transport group [18].

In our study, the median door to balloon time was 70 minutes, and the majority of patients (71%) had on-time DBT door to balloon time (DBT  $\leq$  90 min). This result is comparable with some studies of developed countries in recent years [19].

In a study comparing door to balloon times in Asia, delayed DBT was detected in most countries. The median door to balloon times was between 71 and 135

minutes, albeit with regarding that the dates of studies were between 2002 and 2013 [20].

Mean age of our patients was about 60 years, which was slightly younger than the majority of other studies [21]. In our study, patients with delayed DBT had lower age, lower prevalence of typical chest pain, and higher prevalence of PCI on LCX artery, although these differences were not significant. It seems that patients with delayed DBT had atypical symptoms and probably lower suspicion of myocardial infarction in the point of view of health care providers that make the diagnosis pathway more complicated and leads to delayed times. Three parts of DBT, including door to ECG, ECG to code, and code to cath times, were significantly higher in the delayed group. Although the cath to ballooning time was lower in a timely group than the delayed group, the difference was not meaningful. Similar to our findings, the most common factors related to longer DBT in a study in Asia were delay in the emergency department, atypical clinical presentation, and unstable medical condition [22].

Although DBT usually assesses primary PCI timeliness, several factors are in close relation with DBT [23]. In this study, in-hospital mortality, six-month mortality, and cardiac-related hospitalization were no significant differences between timely and delayed groups. In univariate analysis, none of the variables had a significant association with DBT > 90 min. It could be explained in this way that patients with delayed DBT had a lower probability of myocardial infarction regarding lower age, atypical symptoms, and probably lower risk factors that neutralize the adverse effects of delayed DBT. Regarding these facts, delayed DBT should be interpreted along with other factors. In other words, the associated factors leading to delayed DBT should be determined and analyzed appropriately.

Previous studies showed that the direct relation of DBT with the outcome is questionable due to the existence of several confounders and unavailability of these factors assessment in most studies [7, 24]. Pre-hospital delays, day-time, and institutional factors are examples of these confounders. On the other hand, multiple meta-analyses have shown a consistent link between DBT and adverse outcomes despite these confounders' existence.

Like previous studies, in our study, the female gender was an independent predictor of in-hospital mortality [25]. As shown in our study, time from hospital arrival to STEMI diagnosis and activation of the catheterization laboratory or time to activation time has a substantial impact on DBT. Recommendations for reducing DBT are autonomous emergency physicians, activation of the cardiac catheterization team, and a centralized paging system for simultaneous activation of the involved groups [26].

Another strategy for reducing DBT is taking pre-hospital 12 lead ECG by EMS personnel for patients suspicious of STEMI [27]. Pre-hospital ECG could omit the door's delay to ECG time, which was a

significant factor in increasing DBT in our study. Some centers have developed an alerting system for rapidly identifying and treating STEMI patients with PCI, which leads to the achievement of DBT  $\leq$  90 min in most patients. Still, these protocols need training, careful preparation, and interdepartmental collaboration [28].

## CONCLUSION

Multiple related and several confounding factors have an association with DBT. Although patients with delayed DBT have an increased risk of adverse events, improving DBT does not necessarily lead to mortality reduction. Due to other related factors that have a direct impact on outcomes regardless of DBT itself. Reducing DBT in our study seems to be achievable due to modifiable factors, including ECG taking as soon as possible in patients with suspected acute coronary syndrome and on-time triage of eligible patients with STEMI to the catheterization laboratory.

### Limitations of the Study

The retrospective nature of our study might have an impact on unknown confounding factors. The small sample size and incomplete data of some patients were other limitations of our research.

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### Financial Disclosures

None

### Author Contributions

Study conception and design: B Zamani, Amirajam, Acquisition of data: Ghadimi, N zamani, Analysis and interpretation of data: Chenaghlou, Abazari, Drafting of the manuscript: Chenaghlou, Separham, Abbasnezhad, Critical revision: Chenaghlou

## REFERENCES

- Peterson MC, Syndergaard T, Bowler J, Doney R. A systematic review of factors predicting door to balloon time in ST-segment elevation myocardial infarction treated with percutaneous intervention. *Int J Cardiol.* 2012;157(1):8-23. doi: 10.1016/j.ijcard.2011.06.042 pmid: 21757243
- Foo CY, Bonsu KO, Nallamothu BK, Reid CM, Dhippayom T, Reidpath DD, et al. Coronary intervention door-to-balloon time and outcomes in ST-elevation myocardial infarction: a meta-analysis. *Heart.* 2018;104(16):1362-9. doi: 10.1136/heartjnl-2017-312517 pmid: 29437704
- Schuehlen H, Maier B, Behrens S, Schoeller R, Theres H. Determinants of Door-to-balloon time in STEMI Patients: data from the Berlin Myocardial Infarction Registry (BMIR). *Europe Heart J.* 2013;34(suppl 1):P5315-P. doi: 10.1093/eurheartj/eh310.P5315
- Butala N, Yeh R. Is Door-to-Balloon time a misleading metric?: Expert Analysis; 2015.
- Flynn A, Moscucci M, Share D, Smith D, LaLonde T, Changezi H, et al. Trends in door-to-balloon time and mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Arch Intern*

- Med. 2010;170(20):1842-9. doi: 10.1001/archinternmed.2010.381 pmid: 21059978
6. Wang TY, Fonarow GC, Hernandez AF, Liang L, Ellrodt G, Nallamothu BK, et al. The dissociation between door-to-balloon time improvement and improvements in other acute myocardial infarction care processes and patient outcomes. *Arch Intern Med.* 2009;169(15):1411-9. doi: 10.1001/archinternmed.2009.223 pmid: 19667305
  7. Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, et al. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med.* 2013;369(10):901-9. doi: 10.1056/NEJMoa1208200 pmid: 24004117
  8. Ho YC, Tsai TH, Sung PH, Chen YL, Chung SY, Yang CH, et al. Minimizing door-to-balloon time is not the most critical factor in improving clinical outcome of ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention. *Crit Care Med.* 2014;42(8):1788-96. doi: 10.1097/CCM.0000000000000329 pmid: 24717469
  9. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Jr., Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;127(4):529-55. doi: 10.1161/CIR.0b013e3182742c84 pmid: 23247303
  10. Gibson CM, Pride YB, Frederick PD, Pollack CV, Jr., Canto JG, Tiefenbrunn AJ, et al. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. *Am Heart J.* 2008;156(6):1035-44. doi: 10.1016/j.ahj.2008.07.029 pmid: 19032997
  11. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 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(2):119-77. doi: 10.1093/eurheartj/ehx393 pmid: 28886621
  12. Krumholz HM, Herrin J, Miller LE, Drye EE, Ling SM, Han LF, et al. Improvements in door-to-balloon time in the United States, 2005 to 2010. *Circulation.* 2011;124(9):1038-45. doi: 10.1161/CIRCULATIONAHA.111.044107 pmid: 21859971
  13. Traj, van der Wulp I, de Bruijne MC, Wagner C. Exploring the treatment delay in the care of patients with ST-elevation myocardial infarction undergoing acute percutaneous coronary intervention: a cross-sectional study. *BMC Health Serv Res.* 2015;15:340. doi: 10.1186/s12913-015-0993-y pmid: 26292969
  14. Ikemura N, Sawano M, Shiraishi Y, Ueda I, Miyata H, Numasawa Y, et al. Barriers Associated With Door-to-Balloon Delay in Contemporary Japanese Practice. *Circ J.* 2017;81(6):815-22. doi: 10.1253/circj.CJ-16-0905 pmid: 28228609
  15. Victor SM, Gnanaraj A, S V, Pattabiram S, Mulasari AS. Door-to-balloon: where do we lose time? Single centre experience in India. *Indian Heart J.* 2012;64(6):582-7. doi: 10.1016/j.ihj.2012.09.007 pmid: 23253411
  16. Akimbaeva Z, Ismailov Z, Akanov AA, Radisauskas R, Padaiga Z. Assessment of coronary care management and hospital mortality from ST-segment elevation myocardial infarction in the Kazakhstan population: Data from 2012 to 2015. *Medicina (Kaunas).* 2017;53(1):58-65. doi: 10.1016/j.medic.2017.01.006 pmid: 28256299
  17. Salarifar M, Askari J, Saadat M, Geraiely B, Omid N, Poorhosseini H, et al. Strategies to Reduce the Door-to-Device Time in ST-Elevation Myocardial Infarction Patients. *J Tehran Heart Cent.* 2019;14(1):18-27. doi: 10.18502/jthc.v14i1.651 pmid: 31210766
  18. Kodama N, Nakamura T, Yanishi K, Nakanishi N, Zen K, Yamano T, et al. Impact of Door-to-Balloon Time in Patients With ST-Elevation Myocardial Infarction Who Arrived by Self-Transport- Acute Myocardial Infarction-Kyoto Multi-Center Risk Study Group. *Circ J.* 2017;81(11):1693-8. doi: 10.1253/circj.CJ-17-0083 pmid: 28637970
  19. Noguchi M, Ako J, Morimoto T, Homma Y, Shiga T, Obunai K, et al. Modifiable factors associated with prolonged door to balloon time in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Heart Vessels.* 2018;33(10):1139-48. doi: 10.1007/s00380-018-1164-y pmid: 29736558
  20. Li L, Wu MY, Zhang F, Li SF, Cui YX, Hu D, et al. Perspective of delay in door-to-balloon time among Asian population. *J Geriatr Cardiol.* 2018;15(12):732-7. doi: 10.11909/j.issn.1671-5411.2018.12.001 pmid: 30675145
  21. Jayawardana S, Salas-Vega S, Cornehl F, Krumholz HM, Mossialos E. The relationship between off-hours admissions for primary percutaneous coronary intervention, door-to-balloon time and mortality for patients with ST-elevation myocardial infarction in England: a registry-based prospective national cohort study. *BMJ Qual Saf.* 2020;29(7):S41-9. doi: 10.1136/bmjqs-2019-010067 pmid: 31831635
  22. Sim WJ, Ang AS, Tan MC, Xiang WW, Foo D, Loh KK, et al. Causes of delay in door-to-balloon time in south-east Asian patients undergoing primary percutaneous coronary intervention. *PLoS One.* 2017;12(9):e0185186. doi: 10.1371/journal.pone.0185186 pmid: 28934306
  23. Krumholz HM, Bradley EH, Nallamothu BK, Ting HH, Batchelor WB, Kline-Rogers E, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention: Door-to-Balloon: An Alliance for Quality. *JACC Cardiovasc Interv.* 2008;1(1):97-104. doi: 10.1016/j.jcin.2007.10.006 pmid: 19393152
  24. Foo CY, Andrianopoulos N, Brennan A, Ajani A, Reid CM, Duffy SJ, et al. Re-examining the effect of door-to-balloon delay on STEMI outcomes in the context of unmeasured confounders: a retrospective cohort study. *Sci Rep.* 2019;9(1):19978. doi: 10.1038/s41598-019-56353-7 pmid: 31882674
  25. Scholz KH, Maier SKG, Maier LS, Lengenfelder B, Jacobshagen C, Jung J, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. *Eur Heart J.* 2018;39(13):1065-74. doi: 10.1093/eurheartj/ehy004 pmid: 29452351
  26. McCabe JM, Armstrong EJ, Hoffmayer KS, Bhavne PD, MacGregor JS, Hsue P, et al. Impact of door-to-activation time on door-to-balloon time in primary percutaneous coronary intervention for ST-segment elevation myocardial infarctions: a report from the Activate-SF registry. *Circ Cardiovasc Qual Outcomes.* 2012;5(5):672-9. doi: 10.1161/CIRCOUTCOMES.112.966382 pmid: 22949494
  27. Shi O, Khan AM, Rezai MR, Jackevicius CA, Cox J, Atzema CL, et al. Factors associated with door-in to door-out delays among ST-segment elevation myocardial infarction (STEMI) patients transferred for primary percutaneous coronary intervention: a population-based cohort study in Ontario, Canada. *BMC Cardiovasc Disord.* 2018;18(1):204. doi: 10.1186/s12872-018-0940-z pmid: 30373536
  28. Levis JT, Mercer MP, Thanassi M, Lin J. Factors Contributing to Door-to-Balloon Times of  $\leq$ 90 Minutes in 97% of Patients with ST-Elevation Myocardial Infarction: Our One-Year Experience with a Heart Alert Protocol. *Perm J.* 2010;14(3):4-11. doi: 10.7812/tpj/10-027 pmid: 20844699