

Editorial

Which is Important for Patients with ST-Segment Elevation Myocardial Infarction to Improve Prognosis, Door-to-Balloon Time or Total Ischemic Time?

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Collapse of faith on door-to-balloon (D2B: the interval from the patient's arrival at the hospital to inflation of the balloon to restore flow) time

Mesees et al. [1] showed the relationship between in-hospital mortality and shortening of door-to-balloon (D2B: the interval from the patient's arrival at the hospital to inflation of the balloon to restore flow) time until percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) using the data of the CathPCI Registry of the National Cardiovascular Data Registry (NCDR), the largest elective and emergent PCI registry, in autumn 2013. This study evaluated the data of 96,738 STEMI patients who were treated in 515 hospitals between 2005 and 2009 in which the national project for shortening of D2B time in this study. Although the patients with D2B time ≥ 180 min were excluded in this study, D2B time was significantly shortened from 83 min in 2006 to 67 min in 2009. The achievement rate of D2B time ≤ 90 min, which was recommended by the ACC/AHA guidelines [2] also significantly increased from 59.7% to 83.1%. However, the overall unadjusted in-hospital mortality was around 4.8% without significant improvement and the mortality 30 days after was also around 9% without significant improvement although significantly improved D2B time. In the group with achievement rate of D2B time ≤ 90 min, in-hospital mortality was within 4% while that in the group with D2B time ≥ 90 min was 8.9% in 2009, which was higher than the former group. This is an important study showing that the mortality of STEMI patients could not improve only by shortening D2B time and needed other strategies.

Description of D2B time on the guidelines and its campaign

The efficacy of PCI for STEMI has already been established and PCI is considered to be the standard therapy. However, the timing to begin PCI is very important. Increased D2B time is closely involved in increased in-hospital mortality although the presentation time (symptom onset-to-door time) and baseline risks

[3]. A prospective cohort study was conducted in 43,801 STEMI patients who were enrolled in the American College of Cardiology National Cardiovascular Data Registry in 2005 and 2006 and showed that delayed D2B time was related to high mortality and in-hospital mortality of the group with D2B time of 60 min was lower than that of 90 min by 0.8% [4]. The ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction specified to shorten D2B time within 90 min as much as possible and make the total ischemic time within 120 min as the Class I recommendation [2]. However, in the data of a retrospective observational study from the National Registry of Myocardial Infarction [5], the achievement rate of D2B time ≤ 90 min was approx. 3.5% in 1999 and that ≥ 120 min was similar. The rate was not improved also in 2002. On the other hand, D2B time was markedly improved in some areas and it was confirmed that the target of D2B time ≤ 90 min was attained by the effort. Therefore, the American College of Cardiology launched the national campaign, the D2B Alliance [6] on the other hand the American Heart Association started the mission named Lifeline [7], respectively.

Achievement of D2B time ≤ 90 min

Improved D2B time needs not only effort of general and interventional cardiologists but also contribution of other heart team member including emergency medicine physicians, nurses, radiographers and clinical engineering technologists. Furthermore, the spread of prehospital ECG (PH-ECG) served by emergency medical services (EMS) plays greater role for improved D2B time. The ACC/AHA guidelines on prehospital chest pain evaluation and treatment recommended to measure PH-ECG in all patients who were suspected to have acute coronary syndrome and administer aspirin to patients suspected to have STEMI [2]. In the trial of feedback reporting and quality improvement interventions in EMS, it was shown that the use of aspirin before arrival in hospital increased and the achievement rate of D2B time ≤ 90 min also increased from 27% to 67% due to increased PH-ECG without increased run time in EMS from 76% to 93% [8]. Other factors for delayed D2B time include initial transfer of STEMI patients to a hospital without PCI capability. In patients who were transferred from a hospital without PCI capability to that with PCI capability, the time from symptom onset to the door of an institution with PCI capability is extremely long, consequently, total ischemic time is also delayed. In a retrospective cohort data of 14,821 STEMI patients, 298 of them were transferred to a hospital with PCI capability and mean stay time in the first or STEMI referral hospital was 68 min. The 2008 ACC/AHA Clinical Performance Measures for Acute Myocardial Infarction [9] recommended to make the duration of time from arrival to discharge at the first hospital (i. e. , the door-in to door-out [DIDO] time) 30 min, however, this was performed only in 11% of patients. The rate of D2B time ≤ 90 min

was significantly high in the group with DIDO time ≤ 30 min and in-hospital mortality was also significantly low [10]. D2B time of STEMI patients in the United States who were reported to the Centers for Medicare & Medicaid Services markedly decreased from 96 min in 2005 to 64 min in 2010 and the achievement rate of D2B time ≤ 90 min also significantly increased from 44.2% to 91.4% owing to the effort for shortening D2B time [11]. However, the data of the Blue Cross Blue Shield of Michigan Cardiovascular Consortium showed that D2B time of STEMI patients including cardiogenic shock in 9.9 of 8771 patients markedly decreased from 103 min in 2003 to 76 min in 2008 and the achievement rate of D2B time ≤ 90 min also markedly increased from 28.5% to 62.7, however, no improved presentation time was found and in-hospital mortality remained around 4% and was not significantly improved [12]. Furthermore, Messes et al. [1] indicated that the strategy depending on D2B time alone should be reconsidered in order to decrease STEMI mortality in the United States.

D2B time in Japan

Also in Japan, the importance of D2B time is specified by the guidelines of the Japanese Circulation Society [13], however, nationwide achievement rates remain unknown due to no national registry in Japan. In addition, it is unclear whether or not the objective of the achievement of D2B time ≤ 90 min is appropriate for current conditions in Japan. No large-scale study was conducted in Japan to evaluate the effect of improved D2B time on mortality while most studies in Japan were observational studies using registry. The Japan Acute Myocardial Infarction registry (J-AMI registry) was conducted in 2030 patients in 213 institutions who were enrolled from May to July 2011. Median presentation time was 135 min and mean D2B time was 42 min achieving ≤ 90 min. In-hospital cardiac death was 3.2% that significantly increased when D2B time was longer without difference between regular and after hours. Median total ischemic time was 190 min that did not achieve ≤ 120 min. No significant correlation was found in in-hospital mortality, however, the lowest time was 5 hr showing bimodal peaks [14]. The reason may be that severe STEMI patients with cardiogenic shock resulting in death were admitted to hospital earlier, consequently, the mortality of patient with short total ischemic time was high. An ongoing prospective, multicenter cohort study in Kanto District includes STEMI patients who underwent PCI within 24 hr after symptom onset were enrolled in the Japan Cardiovascular Database (JCD) -KICS from September 2008 to 2011. Patients with cardiogenic shock or cardiopulmonary arrest were excluded and a study in the remaining 214 patients was conducted [15]. Median presentation time was 196 min and mean D2B time was 104 min not achieving ≤ 90 min. However, in-hospital mortality was low (3.3%) without difference in in-hospital mortality between the groups with D2B time ≤ 90 min and ≥ 90 min. No difference in in-hospital mortality was found between the group with presentation time ≤ 2 hr and the group with that ≥ 2 hr, i. e., 2 to 24 hr. No difference in mortality was probably found by presentation time or D2B time in moderate STEMI patients because severe STEMI patients were excluded in this study. On the other hand, a study of long term prognosis, the Coronary Revascularization Demonstrating Outcome Study in Kyoto (CREDO-Kyoto) acute myocardial infarction registry was published [16]. This is an observational study of 3-year prognosis in 3391 patients in 26 institutions in which PCI was performed

within 24 hr after symptom onset that was registered from January 2005 to December 2007. Median total ischemic time was 4.2 hr, median presentation time was 2.4 hr and median D2B time was 90 min, respectively. Composite of death and congestive heart failure in the group with presentation time ≤ 3 hr was significantly lower than that with that ≥ 3 hr, on the other hand, the longer presentation time significantly frequently induced composite of death and congestive heart failure. However, no significant difference in composite of death and congestive heart failure between the long (≥ 90 min) and short (≤ 90 min) D2B time groups was found. The group with presentation time ≤ 2 hr in the short D2B group showed significant difference in composite of death and congestive heart failure while other groups had no significance. If presentation time is shortened and D2B time reaches within 90 min, the long-term prognosis may be improved.

Problems in D2B time

The major problem about studies of D2B time is the difference in study patients. Subjects differed, to be specific, patients with cardiogenic shock and out-of-hospital cardiac arrest were excluded in some studies, patients with D2B time ≥ 180 min were excluded in others, and patients with total ischemic time ≥ 24 hr, i. e., patients who underwent PCI 24 hr after onset were also included. Longer presentation time generally induces higher severity, in contrast, patients with severe disease including cardiogenic shock have earlier presentation time and in studies in many patients with severe disease, in-hospital mortality may be higher in patients with earlier presentation time and total ischemic time. With regard to D2B time, moderate patients are likely to have short D2B time and severe patients spend long time for circulatory and respiratory care, resulting in longer D2B time. Therefore, D2B time should be examined by severity. Based in animal experiments and clinical studies using various modality, it is known that myocardial salvage is successfully performed by reperfusion within several hours after onset. As described by Kimura et al. [16], in-hospital mortality may not be improved when ischemic time is several hours or longer although presentation time and D2B time are shortened. Therefore, it is necessary to decide an indicator appropriate specific to each disease to reduce STEMI mortality.

Conclusion

Recent data not only in the United States [1] but also in Japan [16] have shown that in-hospital mortality was not improved by D2B time ≤ 90 min in accordance with the ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction [2] and the objectives cannot be attained unless total ischemic time including D2B time is reduced. In addition, extension of myocardial necrosis due to delayed ischemic time may have effects on long-term prognosis; therefore, endpoints in these studies should include not only in-hospital mortality but also long-term prognosis.

Thus, it is important to make efforts to enhance educational campaign for acute myocardial infarction more positively and reduce presentation time. Another important approach for shortening presentation time are to fully record and transmit PH-ECG in EMS, establish the system to directly transfer STEMI patients into an institution with primary PCI and attain mean stay time (DIDO time) ≤ 30 min in the first or STEMI referral hospital.

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