



Original article

Relationship between time to treatment and mortality among patients undergoing primary percutaneous coronary intervention according to Korea Acute Myocardial Infarction Registry



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ABSTRACT

Background: Despite large reductions in door-to-balloon times over the period, several studies from regional and national data showed that annual mortality rates were not decreased among patients who underwent primary percutaneous coronary intervention (PCI). However, these studies mostly focused on door-to-balloon time, and there was no consideration of total ischemic time in a trend of mortality. The aim of this study was to assess the annual trend between time to treatment and 1-month mortality among patients undergoing primary PCI.

Methods and results: The study population consisted of 8040 patients who underwent primary PCI at hospitals participating in the nationwide prospective Korea Acute Myocardial Infarction Registry (KAMIR) between January 2008 and December 2011. The primary end point of this study was 1-month all-cause mortality, and time to treatment (door-to-balloon time, symptom-to-balloon time). One-month death occurred in 452 patients (5.6%) from 2008 to 2011. Additional reductions in door-to-balloon time were not translated into parallel reductions in mortality rate and total ischemic time. After adjustment using clinical risk, shorter total ischemic time was an independent predictor of 1-month mortality [adjusted odds ratio (OR) 0.78, 95% confidential interval (CI) 0.62–0.99, $p = 0.04$]. Total ischemic time could be reduced by using emergency medical services.

Conclusion: Despite improvements in door-to-balloon time, no parallel reductions in mortality rate and total ischemic time were observed. Total ischemic time was associated with mortality. The present study

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suggests that additional efforts are needed to shorten total ischemic time including patient and pre-hospital systemic delay for better prognosis after primary PCI.

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Introduction

Door-to-balloon time, time interval from hospital arrival to balloon inflation, is associated with better in-hospital and long-term survival for patients with ST-segment elevation myocardial infarction (STEMI) who received primary percutaneous coronary intervention (PCI) [1–3]. Based on these data, current guideline recommended goals of 90 min for door-to-balloon time [4]. Because of this recommendation, door-to-balloon time has been a key quality metric for primary PCI centers [5].

The previous report in Korea showed that only 51% of patients achieved this goal for reperfusion between November 2005 and January 2007 [6]. Thus, there have been institutional and national quality improvement initiatives to achieve door-to-balloon time within 90 min in Korea. But, it is unknown whether these movements are associated with better prognosis. Despite large reductions in door-to-balloon times over the period, several studies from regional and national data showed that annual mortality rates were not decreased among patients who underwent primary PCI [7,8]. However, these studies mostly focused on door-to-balloon time in Western populations, and there was no consideration of total ischemic time in a trend of mortality.

In the present study, we used large nationwide registry data from Korea to assess the annual trend between time to treatment and 1-month mortality among patients who underwent primary PCI.

Methods

Study population

The study population consisted of 8040 patients who underwent primary PCI at hospitals participating in the nationwide prospective Korea Acute Myocardial Infarction Registry (KAMIR) between January 2008 and December 2011. The KAMIR, launched in November 2005, is a prospective multi-center data collection registry reflecting real-world treatment practices and outcomes in Asian patients diagnosed with AMI. The registry consists of 50 community and teaching hospitals with facilities for primary PCI and on-site cardiac surgery. Included patients were representative of the Korean STEMI population. The first diagnosis of STEMI was established in the participating centers. Data were collected by a trained study coordinator using a standardized case report form and protocol. The study protocol was approved by the ethics committee at each participating institution. Details of the registry have been previously published in many international journals [9].

Inclusion criteria for the present study were consecutive patients aged ≥ 18 years presenting within 12 h after symptom onset, had a suggestive history with ST-segment elevation above 2 mm in two or more precordial leads, or above 1 mm in two or more limb leads, or new onset of left bundle branch block on the 12-lead electrocardiogram (ECG) with increased cardiac enzyme activity (troponin or myocardial fraction of creatine kinase), treated with primary PCI, and had completed a 1-month clinical follow-up. We excluded patients for whom time table data were not completed (symptom onset, hospital arrival, and balloon time), and the door-to-balloon times were not available due to an error value.

Interventional procedures and medical treatment

Loading doses of aspirin and clopidogrel were administered after patients consented to receiving PCI, and a minimum dose of 100 mg aspirin and a 300–600 mg loading dose of clopidogrel and unfractionated heparin (50–70 U/kg) were administered in order to maintain an activated clotting time above 250–300 s. The maintenance dose was 100 mg/day for aspirin and 75 mg/day for clopidogrel. Coronary artery stenting was performed using the standard technique. Performance of pre-dilation, direct stenting, post-adjunctive balloon inflation, mode of revascularization (staged or ad-hoc PCI), using intravascular ultrasound (IVUS), using thrombus aspiration device, stent type, and administration of a glycoprotein IIb/IIIa receptor blocker were at the discretion of the operator.

Statistical analysis

All analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 21.0 (IBM software group, Chicago, IL, USA). Baseline clinical and procedural characteristics were compared with the use of chi-square test for categorical variables and the analysis-of-variance F-test for continuous variables. Continuous variables are presented as mean \pm standard deviation (SD), and categorical variables as percentages. The primary end point of this study was 1-month all-cause mortality, and time to treatment (door-to-balloon time, symptom-to-balloon time). Multi-variate logistic regression analysis was performed to assess the relation between time to treatment (door-to-balloon time, total ischemic time) and 1-month mortality. Global Registry of Acute Coronary Events (GRACE) score for in-hospital mortality was used as a co-variable to adjust the relative risk [10]. All statistical tests were two-tailed, and a p -value less than 0.05 was considered significant.

Results

Baseline and procedural characteristics

A total of 9154 patients with time to presentation within 12 h who underwent primary PCI between January 2008 and December 2011 were included in this study. Patients were excluded if missing data were present in time table ($n = 668$), if they had an error value of door-to-balloon time ($n = 393$), or 1-month mortality data were not available ($n = 53$). Thus, the final study cohort consisted of 8040 patients (Fig. 1). The incidence rates of STEMI in Korea were decreased compared to NSTEMI as in a previous report [11].

The mean age was 63.9 years with 74% of male patients. Table 1 shows baseline clinical and procedural characteristics for each year. Except dyslipidemia, the prevalence of risk factors such as hypertension, diabetes, and current smoking was relatively constant. The proportion of patients with a prior MI, prior revascularization, and heart failure was remarkably lower than previous Western study (MI 2.3% vs. 18.5%, PCI 4.8% vs. 20.5%, heart failure 0.9% vs. 4.0%). Left ventricular ejection fraction was also more preserved maybe due to differences of these parameters [8]. Location of culprit artery and prevalence of multi-vessel disease were similar in each year. However, procedural factors showed some tendencies over the course of the study period.

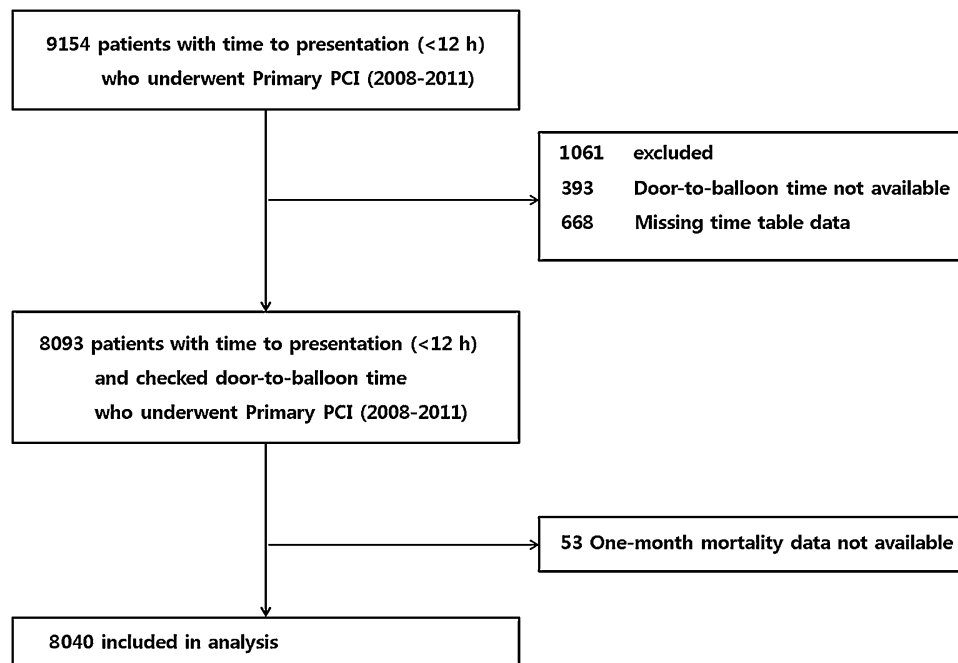


Fig. 1. Study population diagram. PCI, percutaneous coronary intervention.

Table 1

Baseline clinical and procedural characteristics.

Characteristic	Total (n = 8040)	2008 (n = 2135)	2009 (n = 2162)	2010 (n = 1890)	2011 (n = 1853)	p-Value
Age (years) ^a	63.9 ± 13.0	63.9 ± 13.1	64.0 ± 12.8	63.6 ± 13.1	64.0 ± 13.0	0.767
Age > 75 (%)	23.3	22.9	23.3	22.9	24.1	0.783
Male (%)	74.3	73.4	74.4	73.4	76.0	0.219
Clinical history (%)						
Hypertension	46.8	46.0	46.8	46.8	47.9	0.696
Diabetes mellitus	24.4	23.8	24.0	24.3	25.6	0.546
Dyslipidemia	11.2	10.7	9.2	13.5	11.7	<0.001
Current smoker	60.9	60.7	60.9	60.1	62.0	0.676
Heart failure	0.9	0.7	0.9	0.9	0.8	0.901
Stroke	5.2	5.5	5.4	4.9	5.1	0.818
Family history	7.8	6.3	8.7	8.6	7.5	0.014
Prior MI	2.3	2.4	2.3	1.9	2.8	0.320
Prior PCI	4.8	4.0	4.9	5.2	5.2	0.237
Prior CABG	0.2	0.2	0.3	0.3	0.2	0.837
Cardiogenic shock	8.4	8.1	9.7	7.4	8.5	0.078
Ejection fraction (%) ^b	52.0 ± 20.9	52.1 ± 15.4	51.8 ± 20.8	51.9 ± 24.9	51.9 ± 20.9	0.961
Procedural variables (%)						
Door-to-balloon time						
Median (min)	65	72	69	64	59	<0.001
<90 min (%)	79.9	70.3	75.4	85.7	90.2	<0.001
Total ischemic time (min)	240	257	245	227	224	0.380
Use of stent	89.9	90.8	86.8	90.7	91.6	<0.001
Drug-eluting stent	83.7	82.2	80.3	85.2	87.7	<0.001
GP IIb/IIIa inhibitor	23.3	29.2	22.0	20.6	20.9	<0.001
Thrombectomy	19.1	15.8	17.9	20.1	23.2	<0.001
Radial approach	17.4	16.8	16.6	17.6	18.8	<0.001
IVUS-guided PCI	17.4	17.9	18.5	18.4	14.4	<0.001
Target coronary artery (%)						
Left main	1.4	1.6	1.5	1.4	1.3	0.808
Left anterior descending	51.0	50.9	50.2	52.1	51.0	0.704
Left circumflex	9.3	10.2	10.1	8.4	9.3	0.253
Right coronary	38.3	37.3	39.2	38.2	38.5	0.644
Multi-vessel disease (%)	51.2	52.8	51.8	49.7	50.1	0.167
Ventricular arrhythmia (%)	3.6	4.0	3.7	3.2	3.6	0.562

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; GP, glycoprotein; IVUS, intravascular ultrasound.

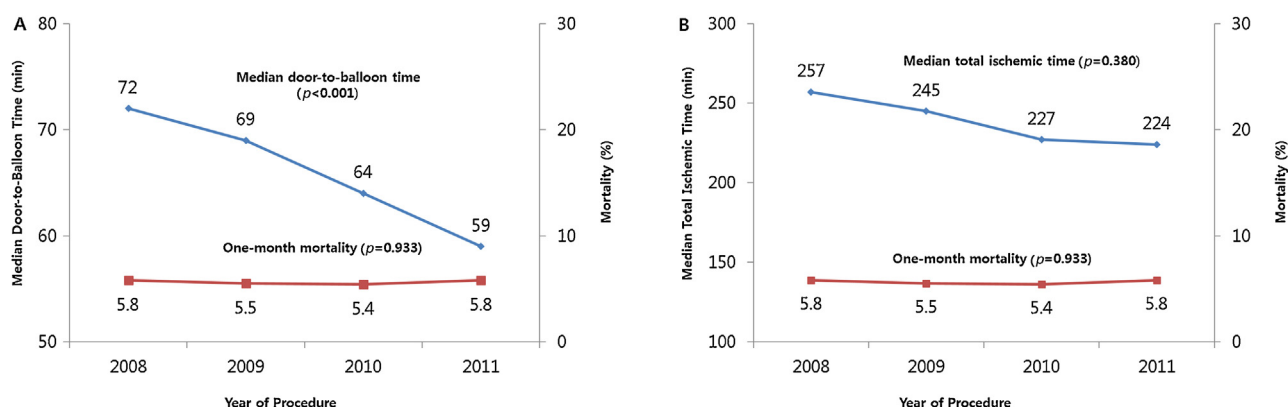
^a Plus minus values are means ± standard deviation.^b Available in 1884 patients (88.2%) in 2008, 1936 patients (89.1%) in 2009, 1684 patients (89.1%) in 2010, and 1709 patients (90.1%) in 2011.

Table 2

Door-to-balloon time and 1-month mortality in the high-risk subgroups.

Characteristic	Total	2008	2009	2010	2011	p-Value
Age >75 years (%)	23.3	22.9	23.3	22.9	24.1	0.783
Door-to-balloon time						
Median (min)	68	74	70	66	63	<0.001
<90 min (%)	77.4	68.6	72.7	81.4	88.0	<0.001
Mortality (%)	12.5	11.3	12.1	13.8	12.5	0.669
Multi-vessel disease (%)	51.2	52.8	51.8	49.7	50.1	0.783
Door-to-balloon time						
Median (min)	66	72	68	64	60	<0.001
<90 min (%)	79.4	70.7	74.9	85.8	88.6	<0.001
Mortality (%)	7.3	7.2	7.0	7.3	7.6	0.970
Cardiogenic shock (%)	8.4	8.1	9.7	7.4	8.5	0.078
Door-to-balloon time						
Median (min)	69	72	73	61	65	<0.001
<90 min (%)	76.3	69.9	67.9	90.8	80.6	<0.001
Mortality (%)	32.0	32.2	31.8	29.0	34.5	0.770
GRACE high risk (%)	66.9	67.8	68.5	64.9	66.4	0.115
Door-to-balloon time						
Median (min)	68	74	70	66	63	<0.001
<90 min (%)	79.5	71.3	74.3	85.3	89.4	<0.001
Mortality (%)	7.7	7.0	7.7	7.9	8.1	0.772

GRACE, Global Registry of Acute Coronary Events.

**Fig. 2.** Mortality rates according to the time to treatment, 2008–2011. The median time to treatment and 1-month mortality among patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention are shown between January 2008 and December 2011. Results between door-to-balloon time and 1-month mortality (A), and between total ischemic time and 1-month mortality (B).

Drug-eluting stent implantation tended to increase from 82.2% in 2008 to 87.7% in 2011. Thrombectomy and trans-radial approach gradually increased over the study period (thrombectomy 15.8–23.2%, radial approach 16.8–18.8%). The percentage of patients receiving IVUS-guided PCI and glycoprotein IIb/IIIa inhibitor declined annually.

Clinical outcomes

The median door-to-balloon time decreased significantly from 72 min in 2008 to 59 min in 2011. The achieved rate of goal of door-to-balloon time <90 min was significantly increased from 70.3% in 2008 to 90.2% in 2011. Similarly, no significant change in this trend was observed in any of the high-risk subgroups (Table 2). However, symptom-to-balloon time (total ischemic time) was not significantly different despite door-to-balloon time improvement ($p = 0.380$), and the rate of 1-month mortality was relatively constant over the period from 5.8% in 2008 to 5.8% in 2011 (Fig. 2). One-month death occurred in 452 patients (5.6%) from 2008 to 2011. After adjustment by GRACE score, total ischemic time below 180 min was an independent predictor of 1-month mortality [adjusted odds ratio (OR) 0.78, 95% confidential interval (CI) 0.62–0.99, $p = 0.04$]. However, lowered only door-to-balloon time

(adjusted OR 0.86, 95% CI 0.66–1.12, $p = 0.258$) or symptom-to-door time was not significantly associated with 1-month mortality (adjusted OR 0.82, 95% CI 0.63–1.06, $p = 0.136$) (Table 3).

Emergency medical services (EMS) were used in only 36.1% of patients (2902/8040). Median time of total ischemic time was significantly decreased in EMS users (202 min vs. 264 min, $p = 0.011$), but not door-to-balloon time (64 min vs. 66 min, $p = 0.223$).

Discussion

The major findings of the present study are as follows. First, door-to-balloon time had a tendency to decline during the 4 years. Second, additional reductions in door-to-balloon time were not translated into parallel reductions in mortality rate and total ischemic time. A lack of mortality benefit was also observed in high-risk subgroups. Third, total ischemic time was associated with 1-month mortality rates.

Different to many other countries, all health insurance societies were integrated into a single insurer, the National Health Insurance Program in Korea [12]. All medical institutions of Korea should claim almost all procedural costs to government (National Health Insurance Corporation). Then, government will pay the

Table 3

Door-to-balloon time, total ischemic time, and 1-month mortality.

	One-month mortality (%)		Unadjusted OR (95% CI)	p-Value	^a Adjusted OR (95% CI)	p-Value
	Achieved goal	Not achieved goal				
Door-to-balloon time <90 min	5.1	7.6	0.65 (0.53–0.81)	<0.001	0.86 (0.66–1.12)	0.258
Symptom-to-door time <90 min	4.7	6.6	0.69 (0.57–0.84)	<0.001	0.82 (0.63–1.06)	0.136
Total ischemic time <180 min	4.2	6.3	0.64 (0.53–0.78)	<0.001	0.78 (0.62–0.99)	0.040
Total ischemic time = symptom-to-balloon time.						
OR, odds ratio; CI, confidence interval.						
^a Adjusted by GRACE (Global Registry of Acute Coronary Events) risk score.						

reimbursement to hospitals after reviewing appropriateness of medical fees and health care management. The government graded the quality of care of all tertiary centers regardless of PCI-capability based on in-hospital reperfusion time (door-to-needle <30 min, door-to-balloon <90 min), and have provided incentives or reduction of reimbursement for procedural costs depending on achieving the rates of the reperfusion goal. Moreover, results are made public through the various mass media and Internet web sites. As a result, the achieved rate of goal of door-to-balloon time <90 min was dramatically increased from 70.3% in 2008 to 90.2% in 2011. One-month mortality rate was not decreased despite a large reduction in door-to-balloon time. The results were similar with previous studies [7,8]. But, it does not mean that door-to-balloon time is a useless metric for quality-improvement of PCI-capable centers [13].

Total ischemic time is related to long-term clinical outcomes especially in high-risk subgroups [14,15]. Clinical study using cardiovascular magnetic resonance showed that shorter ischemic time in patients with primary PCI was associated with smaller infarct size and micro-vascular obstruction, and larger salvage myocardium [16]. As mentioned above, shorter door-to-balloon time is associated with reduced mortality. But, the effect of door-to-balloon time reduction could be varied across the subgroups of patients. Early presenter (≤ 3 h) after symptom onset and high-risk patients appear to benefit the most after achieved door-to-balloon time goal [17]. Pooled analysis from two randomized trials also showed that patients with later presentation (> 3 h) had no significant 1-year mortality reduction despite short door-to-balloon time (≤ 90 min) [18]. Also in Asian data, the benefit of short door-to-balloon time was limited to patients who presented early [14]. A recent study showed that total ischemic time was a better predictor than door-to-balloon time for 1-month mortality and infarct size [19].

However, there have been no special attentions or regulations except door-to-reperfusion time in Korea. In-hospital reperfusion time should be continuously used as a performance measure at the PCI center. But, it may not be an ideal goal for the general health care system. Total ischemic time including patient and systemic delay might be a more suitable target for national quality improvement program. For reduction of patient delay, education about STEMI symptoms and rapid contact with EMS are needed [20]. In the present study, EMS was associated with reducing total ischemic time. Several reports showed that EMS-based pre-hospital network to hospitals or interventional cardiologist reduced systemic delay and improved outcomes [21–24]. For non-PCI capable centers, telemedicine and establishment referral system to PCI centers could be helpful to decrease systemic delay [25,26]. Several subgroups of patients such as older age, female gender, hypertension, diabetes mellitus, and stroke should be focused to minimize treatment delay [27].

There were several limitations to this study. First, the non-randomized nature of the registry data could result in selection bias. There were several clinical and procedural differences over the study period. Unmeasured changes in the patient population could affect the 1-month mortality. It is also possible that low-risk patients are being treated more quickly, and higher-risk patients are being delayed. Second, this study included 1-month follow-up period. It could be possible that shorter door-to-balloon time translates into reduction of long-term mortality and heart failure. Third, there were not enough data about detailed information of pre-hospital system delay in KAMIR. It is insufficient to evaluate the relationship between mortality and systemic delay in primary PCI.

Conclusion

The present study showed that there was a trend of significant decline of door-to-balloon time during 4 years. Despite these improvements, no parallel reductions in mortality rate and total ischemic time were observed. After adjustment using clinical risk, total ischemic time was associated with 1-month mortality rates. Door-to-balloon time should probably become only one of a number of metrics instead of the sole quality metric. Additional efforts are needed to reduce total ischemic time including patient and pre-hospital systemic delay for better prognosis after primary PCI.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Appendix A

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Jung han Yoon, Bon Kwon Koo, Byung Ok Kim, Myoung Yong Lee, Kee Sik Kim, Jin Yong Hwang, Seok Kyu Oh, Nae Hee Lee, Kyoung Tae Jeong, Seung Jea Tahk, Jang Ho Bae, Seung Woon Rha, Keum Soo Park, Kyoo Rok Han, Tae Hoon Ahn, Moo Hyun Kim, Joo Young Yang, Chong Yun Rhim, Hyeon Cheol Gwon, Seong Wook Park, Young Youp Koh, Seung Jae Joo, Soo Joong Kim, Dong Kyu Jin, Jin Man Cho, Wook Sung Chung, Yang Soo Jang, Jeong Gwan Cho, Ki Bae Seung, and Seung Jung Park.

References

- [1] Lambert L, Brown K, Segal E, Brophy J, Rodes-Cabau J, Bogaty P. Association between timeliness of reperfusion therapy and clinical outcomes in ST-elevation myocardial infarction. *JAMA* 2010;303:2148–55.
- [2] McNamara RL, Wang Y, Herrin J, Curtis JP, Bradley EH, Magid DJ, Peterson ED, Blaney M, Frederick PD, Krumholz HM, NRM Investigators. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2006;47:2180–6.
- [3] 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.
- [4] American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, O'Gara PT, Kushner FG, Ascheim DD, Casey Jr DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum 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. *J Am Coll Cardiol* 2013;61:485–510.
- [5] Jacobs AK, Antman EM, Ellrodt G, Faxon DP, Gregory T, Mensah GA, Moyer P, Ornato J, Peterson ED, Sadwin L, Smith SC, American Heart Association's Acute Myocardial Infarction Advisory Working Group. Recommendation to develop strategies to increase the number of ST-segment-elevation myocardial infarction patients with timely access to primary percutaneous coronary intervention. *Circulation* 2006;113:2152–63.
- [6] Song YB, Hahn JY, Gwon HC, Kim JH, Lee SH, Jeong MH. The impact of initial treatment delay using primary angioplasty on mortality among patients with acute myocardial infarction: from the Korea Acute Myocardial Infarction Registry. *J Korean Med Sci* 2008;23:357–64.
- [7] Flynn A, Moscucci M, Share D, Smith D, LaLonde T, Changezi H, Riba A, Gurm HS. Trends in door-to-balloon time and mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Arch Intern Med* 2010;170:1842–9.
- [8] Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, Gurm HS. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med* 2013;369:901–9.
- [9] Kim HK, Jeong MH, Lee SH, Sim DS, Hong YJ, Ahn Y, Kim CJ, Cho MC, Kim YJ. The scientific achievements of the decades in Korean Acute Myocardial Infarction Registry. *Korean J Intern Med* 2014;29:703–12.
- [10] Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, Van De Werf F, Avezum A, Goodman SG, Flather MD, Fox KA, Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. *Arch Intern Med* 2003;163:2345–53.
- [11] Kook HY, Jeong MH, Oh S, Yoo SH, Kim EJ, Ahn Y, Kim JH, Chai LS, Kim YJ, Kim CJ, Cho MC. Korea Acute Myocardial Infarction Registry Investigators. Current trend of acute myocardial infarction in Korea (from the Korea Acute Myocardial Infarction Registry from 2006 to 2013). *Am J Cardiol* 2014;114:1817–22.
- [12] Ebrahim S, Sung J, Song YM, Ferrer RL, Lawlor DA, Davey Smith G. Serum cholesterol, haemorrhagic stroke, ischaemic stroke, and myocardial infarction: Korean national health system prospective cohort study. *BMJ* 2006;333:22.
- [13] Nallamothu BK, Normand SL, Wang Y, Hofer TP, Brush Jr JE, Messenger JC, Bradley EH, Rumsfeld JS, Krumholz HM. Relation between door-to-balloon times and mortality after primary percutaneous coronary intervention over time: a retrospective study. *Lancet* 2015;385:1114–22.
- [14] Shiomi H, Nakagawa Y, Morimoto T, Furukawa Y, Nakano A, Shirai S, Taniguchi R, Yamaji K, Nagao K, Suyama T, Mitsuoka H, Araki M, Takashima H, Mizoguchi T, Eisawa H, et al. 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.
- [15] De Luca G, Suryapranata H, Zijlstra F, van't Hof AW, Hoorntje JC, Gosselink AT, Dambink JH, de Boer MJ, ZWOLLE Myocardial Infarction Study Group. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2003;42:991–7.
- [16] Francone M, Bucciarelli-Ducci C, Carbone I, Canali E, Scardala R, Calabrese FA, Sardella G, Mancone M, Catalano C, Fedele F, Passariello R, Bogaert J, Agati L. Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST-segment elevation myocardial infarction: insight from cardiovascular magnetic resonance. *J Am Coll Cardiol* 2009;54:2145–53.
- [17] Brodie BR, Hansen C, Stuckey TD, Richter S, Versteeg DS, Gupta N, Downey WE, Pulsipher M. Door-to-balloon time with primary percutaneous coronary intervention for acute myocardial infarction impacts late cardiac mortality in high-risk patients and patients presenting early after the onset of symptoms. *J Am Coll Cardiol* 2006;47:289–95.
- [18] Brodie BR, Gersh BJ, Stuckey T, Witzentichler B, Guagliumi G, Peruga JZ, Dudek D, Grines CL, Cox D, Parise H, Prasad A, Lansky AJ, Mehran R, Stone GW. When is door-to-balloon time critical? Analysis from the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) and CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) trials. *J Am Coll Cardiol* 2010;56:407–13.
- [19] Solhpour A, Chang KW, Arain SA, Balan P, Loghin C, McCarthy JJ, Vernon Anderson H, Smalling RW. Ischemic time is a better predictor than door-to-balloon time for mortality and infarct size in ST-elevation myocardial infarction. *Catheter Cardiovasc Interv* 2016;87:1194–200.
- [20] Bates ER, Jacobs AK. Time to treatment in patients with STEMI. *N Engl J Med* 2013;369:889–92.
- [21] Dhruva VN, Abdelhadi SI, Anis A, Gluckman W, Hom D, Dougan W, Kaluski E, Haider B, Klapholz M. ST-Segment Analysis Using Wireless Technology in Acute Myocardial Infarction (STAT-MI) trial. *J Am Coll Cardiol* 2007;50:509–13.
- [22] Ortolani P, Marzocchi A, Marrozzini C, Palmerini T, Saia F, Baldazzi F, Silenzi S, Taglieri N, Bacchi-Reggiani ML, Gordini G, Guastaroba P, Grilli R, Branzi A. Usefulness of prehospital triage in patients with cardiogenic shock complicating ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. *Am J Cardiol* 2007;100:787–92.
- [23] Diercks DB, Kontos MC, Chen AY, Pollack Jr CV, Wiviott SD, Rumsfeld JS, Magid DJ, Gibler WB, Cannon CP, Peterson ED, Roe MT. Utilization and impact of pre-hospital electrocardiograms for patients with acute ST-segment elevation myocardial infarction: data from the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry. *J Am Coll Cardiol* 2009;53:161–6.
- [24] Bagai A, Jollis JG, Dauerman HL, Peng SA, Rokos IC, Bates ER, French WJ, Granger CB, Roe MT. Emergency department bypass for ST-segment-elevation myocardial infarction patients identified with a prehospital electrocardiogram: a report from the American Heart Association Mission: Lifeline program. *Circulation* 2013;128:352–9.
- [25] Rasmussen MB, Frost L, Stengaard C, Brorholt-Petersen JU, Dodt KK, Søndergaard HM, Terkelsen CJ. Diagnostic performance and system delay using telemedicine for prehospital diagnosis in triaging and treatment of STEMI. *Heart* 2014;100:711–5.
- [26] Wilson BH, Humphrey AD, Cedarholm JC, Downey WE, Haber RH, Kowalchuk GJ, Rinaldi MJ, Miller DA, Sarafin JL, Garvey JL. Achieving sustainable first door-to-balloon times of 90 minutes for regional transfer ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv* 2013;6:1064–71.
- [27] Chandrasekhar J, Marley P, Allada C, McGill D, O'Connor S, Rahman M, Tan R, Hosseiny AD, Shadbolt B, Farshid A. Symptom-to-balloon time is a strong predictor of adverse events following primary percutaneous coronary intervention: results from the Australian Capital Territory PCI Registry. *Heart Lung Circ* 2016 [Epub ahead of print].