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Letter to the Editor

Effect of door-to-balloon time on in-hospital mortality in patients with myocardial infarction: A meta-analysis

Hong-Lin Chen [a], Kun Liu [b,*]

[a] Nantong University, Nantong City, PR China
[b] Department of Cardiothoracic Surgery, Affiliated Hospital of Nantong University, Nantong City, PR China

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Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are two important methods for reperfusion for acute myocardial infarction (MI) patients. Surgical time is also important for these two operations. Our pervious study used dose–response meta-analysis, and found that early CABG leads to more in-hospital mortality than late CABG, especially in the first two weeks after acute MI [1]. For PCI, the traditional view believes that longer time to reperfusion is not only associated with worsened left ventricular systolic function and new-onset heart failure [2], but also associated with higher mortality [3]. However, some researchers analyzed annual trends in door-to-balloon (DTB) times and in-hospital mortality, and found that reduced DTB time did not decrease the mortality as expected [4,5]. It is still controversial whether DTB time is related with prognosis for MI patients. In this paper, we also used dose–response meta-analysis to assess the effect of DTB time on in-hospital mortality in patients with MI.

In this meta-analysis, we searched PubMed and ISI databases up to 12 December 2014. The search terms included myocardial infarction, door-to-balloon, and mortality. We also supplemented our searches by manually reviewing the references of all relevant studies. The search was limited to English-language articles. To be included, studies had to meet the following criteria: (1) investigated the effect of DTB time in patients with MI after PCI; (2) outcomes must included in-hospital mortality, if in-hospital mortality was not found, 30 day mortality used as substitutes; (3) provided data comparing in-hospital mortality between the early reperfusion group (DTB < 90 min) and late reperfusion group (DTB ≥ 90 min), or provided data comparing in-hospital mortality between different time intervals of DTB time; and (4) provided odds ratio (OR) and 95% confidence interval (CI) between early reperfusion and late reperfusion, or provided OR between different DTB time intervals, or the ORs can be calculated from the raw data.

We followed a standard protocol for data extraction. For each study, the following data were recorded: first author, year of publication, country, enroll year, study design, patient's number, the in-hospital death and survival patients' number in different time group, and the ORs. The quality of articles was assessed according to the Newcastle–Ottawa Scale (NOS) [6]. The NOS contains eight items, categorized into three dimensions including Selection (4), Comparability (1), and Exposure (3). The NOS ranges between zero up to nine stars. Data extraction and article quality assessment were carried out independently by two reviewers. Disagreements were resolved by discussion together.

We analyzed the data by the following processes: First, we assessed the in-hospital mortality difference between early reperfusion and late reperfusion. Fixed effect model or random effect model was chosen according to heterogeneity. Overall effects were determined using the Z test. Visual inspection of a funnel plot, the Egger test, and Begg test were performed to assess publication bias. Sensitivity analyses were performed by only including prospective cohorts, or by excluding the study with the largest sample. Second, we examined the relationship between different DTB time intervals and in-hospital mortality of MI patients after PCI. Dose–response meta-analysis proposed by Greenland and Longnecker [7] and Orsini et al. [8,9] was used for assessing the relationship. Sensitivity analyses were performed by excluding the study with the largest sample. All statistical analyses were performed with Stata software, version 13.0 (Stata Corp, College Station, Texas). Two-sided $P < 0.050$ was considered statistically significant.

We identified 15 studies with 189,904 patients for meta-analysis [4,10–23]. The flow diagram for selecting studies was shown in Appendix Fig. 1. Among 15 studies, 6 were conducted in the United States, 2 in Japan, 1 in UK, Canada, Singapore, and India, and the rest of 3 were multicenter studies. The studies included 7 prospective cohorts, 3 retrospective cohorts, 2 randomized trials, and the rest of 3 didn't report the study design. The quality rating of the included studies ranged from 7 to 8 stars on the scale of nine. Table 1 showed the characteristics of the identified studies.

All 15 studies with all 189,904 patients were included in the analysis for in-hospital mortality difference between the early reperfusion group

* Corresponding author.
E-mail address: pphss@126.com (K. Liu).

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Table 1
Characteristics of the included studies assessing door-to-balloon (DTB) time on in-hospital mortality in patients with myocardial infarction.

First author, year	Country	Enroll year	Study design	NOS	Patients number	DTB < 90 min			DTB ≥ 90 min			OR [95% CI]
						In-hospital death	In-hospital survival	In -hospital mortality	In-hospital death	In-hospital survival	In-hospital mortality	
Cannon (2000) [10]	USA	1994–1998	Prospective cohort	8	27,080	355	7609	4.5%	1302	17,814	6.8%	1.57 (1.39–1.77)
Brodie 2001 (SPAMIT) [11]	Multicenter	NR	Randomized trial	NA	1232	18	389	4.4%	24	805	2.9%	0.64 (0.5–1.20)
Brodie, 2006 (CADILLAC)	Multicenter	NR	Randomized trial	NA	2082	7	472	1.5%	31	1399	2.2%	1.49 (0.65–3.42)
Brodie (20060	USA	1984–2003	Prospective cohort	8	2322	19	365	4.9%	172	1744	9.0%	1.89 (1.16–3.08)
Rathore, 2009 (national cohort)	USA	2005–2006	Prospective cohort	8	43,801	891	24,468	3.5%	1108	17,334	6.0%	1.76 (1.60–1.92)
Rathore, 2009 (>65 years)	USA	1994–1996	Retrospective cohort	8	1932	49	420	10.4%	246	1217	20.2%	1.73 (1.25–.40)
Kong (2009)	UK	2005–2008	Retrospective cohort	7	459	13	272	4.6%	20	154	11.5%	2.72 (1.32–5.61)
Lee (2009)	Singapore	2007–2008	Prospective cohort	8	297	8	191	4.0%	13	85	13.3%	3.65 (1.46–9.14)
Hannan (2010)	USA	2004–2006	NR	8	5092	97	2271	4.1%	177	2547	6.5%	1.63 (1.26–2.10)
Lambert (2010)	Canada	2006–007	Retrospective cohort	8	1287	14	403	3.4%	53	817	6.7%	1.87 (1.02–3.41)
Hudson (2011)	17 countries	2004–2006	NR	8	5745	73	2352	3.0%	125	2823	4.2%	1.43 (1.06–1.91)
Victor (2012)	India	2008–2009	Prospective cohort	7	85	2	63	3.1%	2	18	10.0%	3.50 (0.46–26.62)
Shiomi (2012)	Japan	2005–2007	Prospective cohort	7	1538	28	855	4.3%	50	605	5.7%	2.52 (1.57–4.05)
Kodaira (2013)	Japan	2008–2011	Prospective, multicenter cohort	8	214	3	102	2.8%	4	105	3.7%	1.30 (0.28–5.93)
Menees (2013)	USA	2005–2009	NR	8	96,738	2642	68,751	3.7%	1850	23,495	7.3%	2.05 (1.93–2.18)

SPAMIT: Stent Primary Angioplasty in Myocardial Infarction Trial; CADILLAC: Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications trial; NOS: Newcastle–Ottawa Scale; OR: odds ratio; NR: not report; NA: not applicable.

and late reperfusion group. The in-hospital mortalities ranged from 1.5% to 10.4% in the early reperfusion group, and 2.2% to 20.2% in the late reperfusion group. Table 1 also showed the in-hospital mortality between two groups of the identified studies. There was substantial heterogeneity in the studies ($I^2 = 65.2\%$). The OR of in-hospital mortality between two groups was 1.745 (95% CI 1.546 to 1.968; Z = 9.05, P = 0.000).

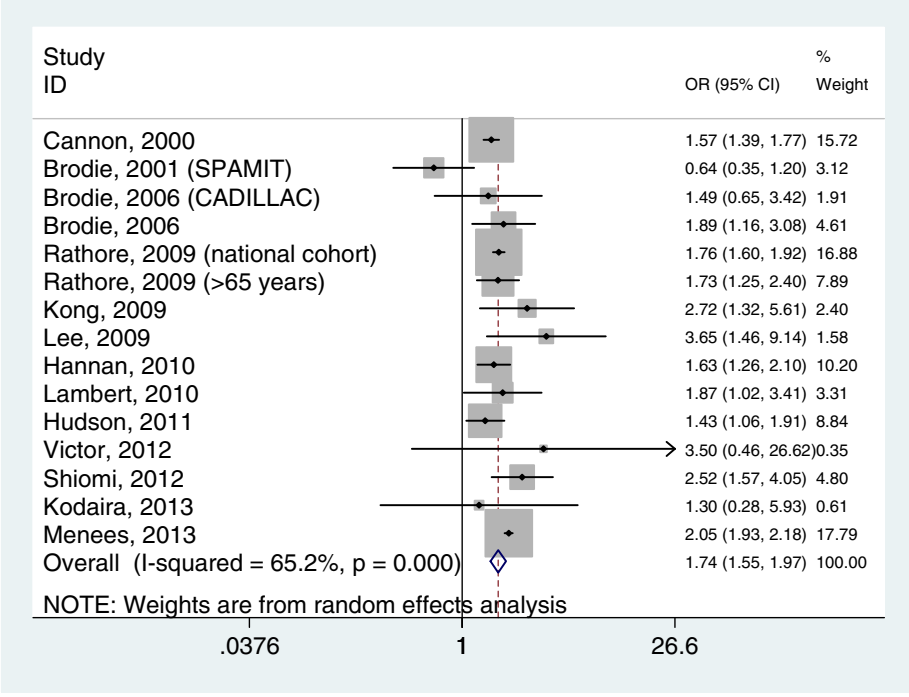

Fig. 1. In-hospital mortality difference between early DTB (<90 min group) and late DTB (≥90 min) group.