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REVIEW

Prehospital Activation of the Catheterization Laboratory Among Patients With Suspected ST-Elevation Myocardial Infarction Outside of a Hospital

— Systematic Review and Meta-Analysis —

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Background: In the management of patients with ST-elevation myocardial infarction (STEMI), system delays for reperfusion therapy are still a matter of concern. We investigated the impact of prehospital activation of the catheterization laboratory in the management of STEMI patients.

Methods and Results: This is a systematic review of observational studies. A search was conducted of the PubMed database from inception to July 2020 to identify articles for inclusion in the study. The critical outcomes were short- and long-term mortality. The important outcome was door-to-balloon time. The GRADE approach was used to assess the certainty of the evidence. Seven studies assessed short-term mortality; 1,541 were assigned to the prehospital activation (PH) group and 1,191 were assigned to the emergency department activation (ED) group. There were 26 fewer deaths per 1,000 patients in the PH group. Three studies assessed long-term mortality; 713 patients were assigned to the PH group and 1,026 were assigned to the ED group. There were 54 fewer deaths per 1,000 patients among the PH group. Five studies assessed door-to-balloon time; 959 were assigned to the PH group and 631 to the ED group. Door-to-balloon time was 33.1 min shorter in the PH group.

Conclusions: Prehospital activation of the catheterization laboratory resulted in lower mortality and shorter door-to-balloon time for patients with suspected STEMI outside of a hospital.

Key Words: Door-to-balloon time; Mortality; Prehospital activation; ST-elevation myocardial infarction

Although improvements in the management of ST-elevation myocardial infarction (STEMI) have been achieved, including primary percutaneous coronary intervention (PCI), acute coronary syndrome (ACS) is still a major cause of death in adults worldwide. It is safe to say that, in the management of patients with STEMI, early diagnosis and reperfusion therapy are the most important steps for better prognosis.[1,2] Many efforts have been made to shorten door-to-balloon time, a key performance indicator in STEMI management. However,

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total ischemic time is emerging as a more appropriate indicator because it includes the prehospital phase, where delays can be substantial. There can be delays related to the transfer of STEMI patients from non-PCI hospitals, assessment in the emergency department (ED), or catheterization laboratory (cath lab) activation and the arrival of catheterization staff. To further improve these delays, prehospital electrocardiograms (ECGs) followed by activation of the cath lab have been reported to be effective.

The aim of this study was to clarify the effectiveness of prehospital activation of the cath lab for STEMI patients identified on the basis of prehospital ECGs.

Methods

The Japan Resuscitation Council (JRC) ACS Task Force, which was organized by the Japanese Circulation Society, the Japanese Association of Acute Medicine, and the Japanese Society of Internal Medicine, was established for the 2020 JRC guidelines. The JRC ACS Task Force established 12 clinically relevant questions that were used to conduct this systematic review.

Search Strategies

The aim of the present study was to assess all available studies to resolve the following research question: Does prehospital activation of the cath lab and the catheterization team improve prognosis among adult patients with suspected STEMI? The Population Intervention Comparator Outcome Study design and Time frame were used to guide the systematic review as follows:

P (patients): adult patients with suspected STEMI out of the hospital
I (intervention): prehospital activation of the cath lab and the catheterization team
C (comparisons, controls): ED activation of the cath lab
O (outcomes): short-term mortality (in-hospital death or 30-day mortality) and long-term mortality (>6 months) as critical outcomes; door-to-balloon time as an important outcome
S (study design): observational studies (no randomized control trials [RCTs] existed); studies without comparators, review articles, and those with pooled analyses were excluded
T (time frame): all literature published up to July 2, 2020.

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),[3,4] we undertook a systematic review and meta-analysis. We did not restrict our analysis by country, but we only included studies published in English.

A systematic search of published reports was conducted in the PubMed database to retrieve relevant articles for the review. We searched for full-text RCTs or, if RCTs were not available, observational studies in humans published before July 2020. We used a combination of key terms and established a full search strategy (**Supplementary Figure**).

Assessment of the Risk of Bias

The Cochrane Risk-of-Bias Tool (RevMan 5.3; The Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark) was used to appraise RCTs, non-RCTs, interrupted time series, and controlled before-and-after studies. Two experienced pairs of reviewers (K.H. and T.N.) independently appraised the risk of bias of all included studies.

Studies were categorized as having a "low", "unclear", or "high" risk of bias in each domain. The risk of bias for each element was considered "high" when bias was present and likely to affect the outcomes and "low" when bias was not present or present but unlikely to affect the outcomes.

Data Extraction and Management

The following data were extracted: author(s), title, journal name, year of publication, website (URL), and abstract. Two independent reviewers (K.H. and T.N.) screened the abstracts and titles of the studies and subsequently reviewed the full-text articles. In case of disagreements, articles were reconsidered and discussed until a consensus was reached. If no consensus could be reached, disagreements were resolved by a third reviewer (H.N.). Studies were included in the meta-analysis if they met the following criteria: (1) prehospital STEMI diagnosis followed by prehospital activation of the cath lab and catheterization team was performed as an intervention; (2) a comparison to ED activation of the catheterization team was performed; and (3) outcomes were defined as mortality or door-to-balloon time. Pilot or single-arm studies and studies with irretrievable full-text reports were excluded. We did not restrict our analysis by country, but only included studies involving human subjects.

Rating the Certainty of Evidence

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool to rate the certainty of the evidence on the effect of prehospital cath lab activation for STEMI patients.[5–7] The certainty of the evidence was assessed as "high", "moderate", "low", or "very low" by evaluating the risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Statistical Analysis

The results were summarized using a random effects model to facilitate the pooling of estimates of the treatment effects. Risk differences (RDs) and 95% confidence intervals (CIs) were used for dichotomous outcomes. Heterogeneity between trials for each outcome was evaluated using the I^2 statistic to quantify inconsistency,[8] and was considered significant if the reason for heterogeneity could not be explained and if the I^2 value was ≥50%.

We generated a funnel plot to investigate potential publication bias. The estimates for each outcome were pooled using a random effects model. The meta-analysis was performed based on all published data and data made available to us. All analyses were undertaken using Review Manager software (RevMan 5.3).

Results

Literature Search

Figure 1 shows a flow diagram of this study adapted from

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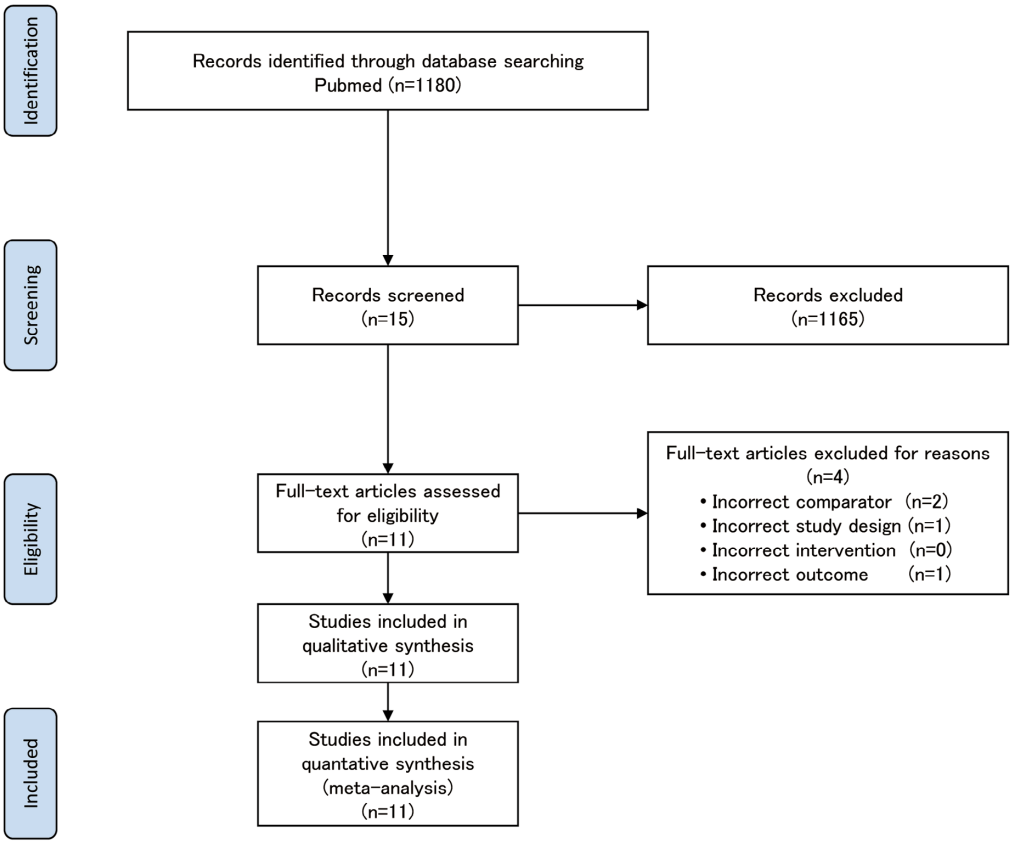

Figure 1. Flowchart showing the study selection process regarding Clinical Question.

Table 1. Baseline Characteristics of Eligible Studies

Author, year	Study design	Country	No. sites	No. patients	PH activation vs. ED activation				
					Age (years)	Male (%)	Mortality (%)		Mean door-to-balloon time (min)
							Short-term	Long-term	
Le May et al (2006)[9]	Historical control	Canada	5	333	64.3 vs. 64.5	70.4 vs. 66.2	1.9 vs. 8.9	NA	NA
Cartensen et al (2007)[10]	Prospective	Australia	5	301	64 vs. 67	74 vs. 66	1.1 vs. 7.6	NA	NA
Brown et al (2008)[11]	Prospective	US	1	48	57 vs. 62	80 vs. 71	0 vs. 10.7	NA	73 vs. 130
Horvath et al (2012)[12]	Prospective	US	1	188	64.3 vs. 66.7	70.5 vs. 64.5	6.3 vs. 7.9	NA	NA
Squire et al (2014)[13]	Retrospective	US	NA	1,933	64 vs. 64	67 vs. 67	6.0 vs. 5.1	NA	60 vs. 73
Ong et al (2013)[14]	Prospective	Singapore	5	378	54.9 vs. 55.6	94.2 vs. 89.0	3.2 vs. 3.1	NA	NA
Savage et al (2014)[15]	Prospective	Australia	NA	281	62.0 vs. 60.8	84.1 vs. 79.8	1.6 vs. 5.0	1.6 vs. 6.4	40.4 vs. 75.6
Sørensen et al (2011)[16]	Prospective	Denmark	4	676	63 vs. 67	78 vs. 69	NA	17.8 vs. 30.6	NA
Farshid et al (2015)[17]	Prospective	Australia	1	782	62.2 vs. 62.0	75.4 vs. 77.8	NA	3.7 vs. 7.9	NA
Cone et al (2013)[18]	Prospective	US	1	85	61 vs. 67	68 vs. 62	NA	NA	37 vs. 87
Kerem et al (2014)[19]	Retrospective	US	1	31	NA	NA	NA	NA	58 vs. 79

ED, emergency department; PH, prehospital.

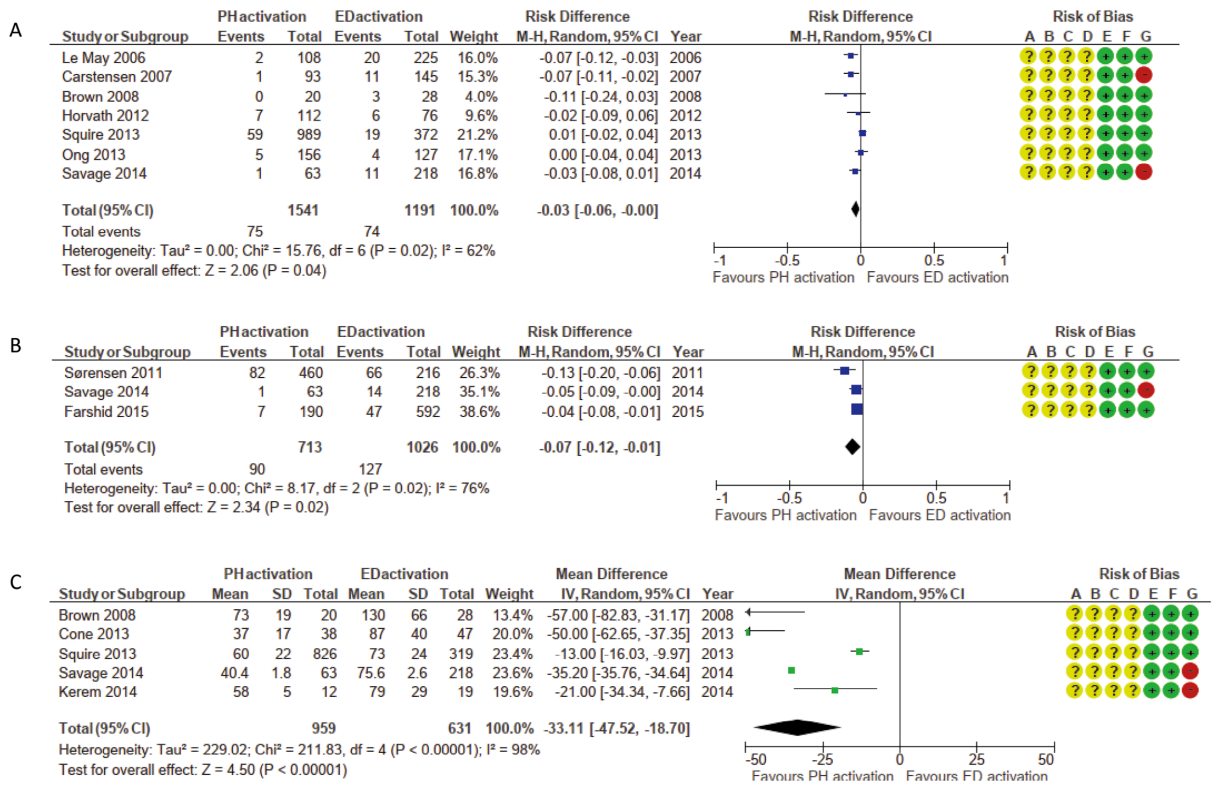

Figure 2. Forest plot for each outcome separately: (**A**) short-term mortality, (**B**) long-term mortality, and (**C**) door-to-balloon time. ED, emergency department; PH, prehospital.

the PRISMA statement (2009).[4]

A search of the PubMed database returned 1,180 articles. We excluded 1,165 articles because their designs did not meet the inclusion criteria. Of the 15 included articles, 4 were excluded because of no outcomes of interest. Thus, 11 articles were retained for review in the final analysis.[9–19]

Study Characteristics

All 11 studies were observational studies.[9–19] The detailed characteristics of the individual studies are presented in **Table 1**, and the forest plot of outcomes with the risks of bias evaluated for each of the studies are shown in **Figure 2**.

Outcomes

For the critical outcome of short-term mortality (in-hospital death or 30-day mortality), 7 studies[9–15] included 2,732 patients, 1,541 of whom were assigned to the prehospital activation (PH) group and 1,191 to the ED activation group. There were 6 fewer deaths per 1,000 patients (95% CI from 43 fewer to 19 more) among the PH than ED activation group. For the critical outcome of long-term mortality (>6 months), 3 studies[15–17] included 1,739 patients, 713 of whom were assigned to the PH group and 1,026 to ED activation group. There were 54 fewer deaths per 1,000 patients (95% CI from 71 fewer to 33 fewer) among the PH than ED activation group.

For the important outcome of door-to-balloon time, 5 studies[11,13,15,18,19] included 1,590 patients, 959 of whom were assigned to the PH group and 631 to the ED activation group. The door-to-balloon time was 33.1 min shorter (95% CI from 47.5 to 18.7 min shorter) in the PH than ED activation group.

Certainty of Evidence

We assessed the certainty of evidence for each outcome and present a summary of the evidence profile in **Table 2**. For the critical outcome, the certainty of the evidence was rated as very low for the effect of prehospital activation of the cath lab and catheterization staff on short- and long-term mortality because of the serious risk of bias. For the important outcome, the certainty of the evidence was rated as low for the effect of prehospital activation of the cath lab and catheterization staff on door-to-balloon time because of the risk of bias. A visual inspection of the funnel plots suggested no publication bias (**Figure 3**).

Discussion

This systematic review demonstrated that prehospital activation of the cath lab and catheterization team is associated with statistically significant lower long-term mortality and a tendency for lower short-term mortality compared with ED activation. Prehospital activation was also associated with a statistically significant shorter door-to-balloon time.

In the previous (2015) JRC guideline, prehospital activation was shown to have a beneficial effect only on 30-day mortality. The 2017 European Society of Cardiology guidelines for STEMI state that when a STEMI diagnosis is made

Table 2. Evidence Profile

No. studies	Certainty assessment					
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Short-term mortality[9–15]						
7	Observational studies	Not serious	Serious[A]	Not serious	Serious[B]	None
Long-term mortality[15–17]						
3	Observational studies	Not serious	Not serious	Not serious	Serious[C]	None
Door-to-balloon time[11,13,15,18,19]						
5	Observational studies	Not serious	Not serious	Not serious	Not serious	None

No. studies	No. patients		Effect		Certainty	Importance
	PH activation	ED activation	Relative (95% CI)	Absolute (95% CI)		
Short-term mortality[9–15]						
7	75/1,541 (4.9%)	74/1,191 (6.2%)	OR 0.56 (0.28 to 1.12)	26 fewer per 1,000 (from 43 fewer to 19 more)	⨁◯◯◯ Very low	CRITICAL
Long-term mortality[15–17]						
3	90/713 (12.6%)	127/1,026 (12.4%)	OR 0.47 (0.34 to 0.66)	54 fewer per 1,000 (from 71 fewer to 33 fewer)	⨁◯◯◯ Very low	CRITICAL
Door-to-balloon time[11,13,15,18,19]						
5	959	631	–	MD 33.11 min lower (from 47.52 to 18.70 min lower)	⨁⨁◯◯ Low	IMPORTANT

[A]I^2 >50% and variation in point estimation. [B]The 95% confidence interval (CI) crosses the threshold. [C]Does not reach the optimal information size (n=1,579 for both groups). CI, confidence interval; ED, emergency department; MD, mean difference; OR, odds ratio; PH, prehospital.

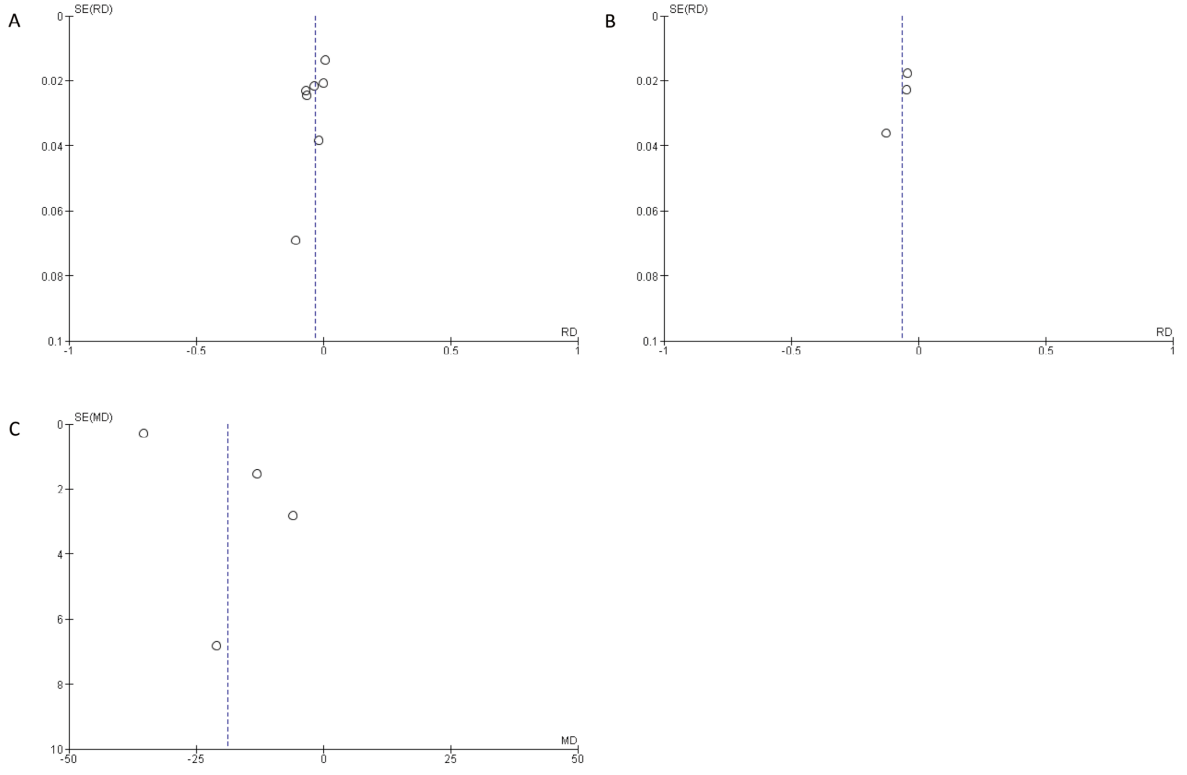

Figure 3. Funnel plots for each outcome separately: (**A**) short-term mortality, (**B**) long-term mortality, and (**C**) door-to-balloon time.

in the prehospital setting, immediate activation of the cath lab, ED bypass, and direct transfer to the cath lab reduces treatment delay.[2] Class 1B and Class 1C recommendations are given for prehospital 12-lead ECGs and ED bypass, respectively, based on several observational studies.[2]

In this systematic review, prehospital ECGs followed by activation of the cath lab improved clinical outcomes in STEMI patients. Prehospital activation of the cath lab and catheterization team resulted in a tendency for lower short-term mortality, significantly lower long-term morality, and shorter door-to-balloon time. Our findings support and further confirm the previous recommendations mentioned above.

This study has several limitations. First, this review was performed using only the PubMed database, and it is possible that other important reports on this topic were missed. Second, no RCTs were found related to this topic; thus, only observational studies were included in the present systematic review. Third, prehospital ECGs are not available nationwide in Japan. There are some areas where emergency medical services are not equipped with 12-lead ECG recorders. In addition, all the studies included in this systematic review are from Western countries, and it is not clear whether those findings are applicable to Japan.

Conclusions

Prehospital activation of the cath lab and catheterization staff results in lower mortality and shorter door-to-balloon time for patients with suspected STEMI outside of hospitals.

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Disclosures

T. Matoba is a member of *Circulation Reports*' Editorial Team. The remaining authors have no conflicts of interest to disclose.

Author Contributions

All authors were involved in the study design. K.H. and T.N. identified the studies included in the meta-analysis and analyzed the data. K.H. drafted the manuscript. Y.T., M.K., T. Matoba, and H.N. reviewed the manuscript. All authors were involved in data interpretation and discussion. All authors had full access to all data (including statistical reports and tables) in the study and take responsibility its integrity and the accuracy of the analysis, and read and approved the final manuscript.

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Supplementary Files

Please find supplementary file(s);
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