







Review Article

Reperfusion Time of STEMI Patients in Indonesia and Outside Indonesia

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ABSTRACT

Background: STEMI is a medical emergency that requires quick treatment. Several problems might arise from the improper and delayed treatment of STEMI patients. **Objective:** This study aimed to examine the differences in the reperfusion time of STEMI patients in Indonesia and outside Indonesia. **Method:** Systematic Review method is used without meta-analysis. The variables to be studied in this study are Door-to-Balloon time and Total Ischemic Time. PubMed, Science Direct, and Scopus are used as search tools using the MeSH terms and keywords that have been determined to look for articles within 2017 – 2020. The selection of the literature that has been obtained was carried out according to the PRISMA algorithm. **Results:** Twelve journals were used that were relevant, compatible, and following the inclusion and exclusion criteria. It was found that the median door-to-balloon in handling STEMI in Indonesia ranged from 70 to 94 minutes, while the median total ischemic time ranged from 275 to 461 minutes. Meanwhile, the median door-to-balloon time and total ischemic time outside Indonesia ranged from 41 to 87 minutes and 112 to 273 minutes, respectively. **Conclusion:** In conclusion, the median and average door-to-balloon time and total ischemic time in Indonesia are longer than the door-to-balloon time and total ischemic time outside Indonesia in handling STEMI.

Highlights:

1. The median of door-to-ballon in handling STEMI and total ischemic time is longer in Indonesia than other countries.

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Introduction

STEMI is an emergency condition that needs to be treated as soon as possible because there is a total occlusion of blood flow in the coronary arteries. Measures to treat STEMI patients are reperfusion therapy, which can be in the form of fibrinolysis or percutaneous coronary intervention (PCI).^[1]

Fifty-two point eight percent of 31% or as many as 9.4 million deaths from the total deaths caused by cardiovascular disease are caused by Coronary Heart Disease (CHD). WHO also states that three out of four deaths caused by cardiovascular disease occur in countries with middle-lower economic levels such as Indonesia. Indonesia in 2016, cardiovascular disease caused 35% of total deaths or around 655.1 million deaths. Forty-eight point six percent of 35% or 318.8 million of the total cardiovascular deaths are caused by CHD.^[2]

Time is a very important component in the management of STEMI patients. Experiments on animals show a strong relationship between the duration of occlusion and the extent of necrosis. Cell death started after 20 minutes of occlusion and peaked after 6 hours^[3]. A study at Dr. M. Jamil Padang showed that out of 80 people who received PCI therapy, only 17 people underwent therapy less than 12 hours from the onset of the patient's chest pain. Meanwhile, 63 new patients received therapy after more than 12 hours since the onset of chest pain^[4]. The quality of service for STEMI patients

can be seen from the delay audit index that must be recorded by STEMI service providers. The results of these records need to be reviewed periodically to ensure that the service quality of the system is maintained. Delays in treating STEMI patients can be caused by several factors, including patient delays, delays in diagnosis, and delays in reperfusion therapy^[5]. Inappropriate and delayed treatment of STEMI patients can cause several complications, such as heart failure, hypotension, low cardiac output, cardiogenic shock, arrhythmias, cardiac rupture, and several other complications on hemodynamics.^[6]

This systematic review aims to examine the differences in the reperfusion time of STEMI patients in Indonesia and outside Indonesia.

Methods

The present review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020^[7]. No ethical approval was required as no patients directly participated in this study and all the used data have already been published.

Eligibility

We performed a systematic search on reperfusion time of STEMI patients in Indonesia and outside Indonesia. Studies reporting patient managed without reperfusion are excluded. The article published between 2017-2020. Any studies written

in languages other than English or Indonesian, those with no available full text and with nonhuman subjects were excluded. Duplicate articles were resolved before the title and abstract screening.

Search Strategy and Selection of Studies

We conducted a comprehensive systematic database search on July 2021 in PubMed, ScienceDirect, and Scopus. The keywords that will be used are derived from “STEMI” and “reperfusion” and “Door-to-balloon”, or “Total ischemic time” along with their related MeSH terms, synonyms, and elaboration. Review articles will be excluded but their references will be screened for potentially missed relevant studies. Titles and abstracts of the articles to identify potentially eligible studies were independently screened for full-text review.

Article Extraction

We independently extracted relevant articles from the included studies using a structured and standardized form. The following information was extracted: general information, research

characteristics, intervention subject characteristics, and results. Any discrepancy will be resolved by consensus between all authors involved in the data extraction process.

Quality Assessment

Risk of bias assessment will be conducted by at least two authors working independently. Disagreements will be resolved by discussion with a senior author. The tool used for assessment will be *Mixed Methods Appraisal Tool* (MMAT) 2018 version.

Data Analysis

The data analysis technique in this study used a systematic review method. Data analysis will be presented in the form of a narrative resume of the studies presented and arrive at each conclusion to explore the relationships within the studies and assess the robustness of the studies. The results of each study will be displayed in a narrative manner to become a comprehensive discussion.

Result

Study Selection

The search result in 417 records, 32 are duplicates. After title and abstract screening, 331 articles were excluded. This systematic review included 12 published articles after the full-text assessment. PRISMA flow diagram (Fig. 1) presents the process of study selection and the reasons for exclusion.

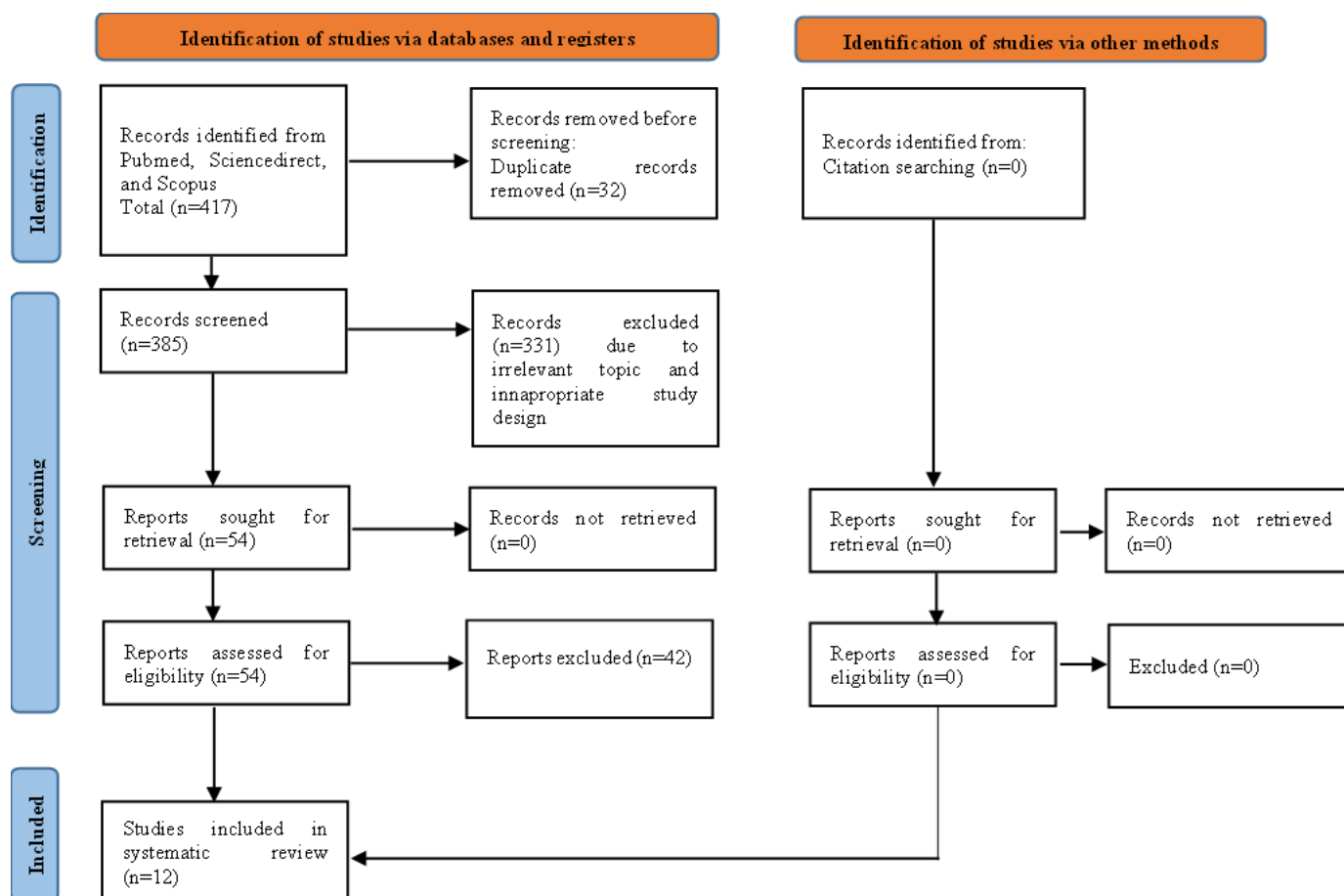


Figure 1. PRISMA flow of study selection

Quality Assessment

All included case reports were assessed using a *Mixed Methods Appraisal Tool* (MMAT) 2018 version. The summarized critical appraisal checklist shows that the risks are generally low in all articles

Discussion

PCI Therapy in Indonesia

System that was previously serial with many steps changes to be parallel can make the therapy process shorter. This parallel system is carried out by diagnosing, contacting a cardiologist, and setting up a catheterization laboratory simultaneously. The availability of an on-call cardiologist and a simplified administration system can also make the transfer process and laboratory activation faster. [8]

On the other hand, although the implementation of an integrated referral system such as CODE STEMI in Indonesia over the last 3 years has succeeded in significantly reducing the DTB duration, this system has not been able to meet the recommendation time according to international standards. In fact, every 1-minute increase in reperfusion time will affect the mortality rate 1 year after perfusion. [8]

The STEMI network which involves almost all hospitals with PCI facilities in Jakarta is showing more positive results. After 10 years of implementing the STEMI network, a significant reduction in the median DTB time was obtained to

meet the recommended time according to international standards. The adoption of this system also led to a change in the majority of reperfusion strategy choices. The choice of invasive strategies has significantly increased in the management of STEMI patients after the adoption of these systems. This improvement can be achieved by integrating administrative systems in the emergency department, increasing the number of interventional cardiologists, and providing cardiologists and nurses in the catheterization laboratory with a special guard schedule. [9]

Most study in Indonesia reported door-to-balloon (DTB) has been able to meet the international recommendation with median range between 70-94 minutes. Even though, there is a study that reported DTB between 158-288 minutes. [8]

After implementing integrated network to minimize the time needed to treat STEMI patients, there's significant decrease in DTB up to 45% decrease in median DTB compare to before the integrated network. [9]

Table 1. Door-to-balloon in Indonesia

Author	Door-to-Balloon
	DTB median after implementation of CODE STEMI
Ginanjari <i>et al.</i> (2020)	decrease significantly, 130 minutes (45%) compared to before implementation (158 [66-640] vs. 288 [120-1376] minutes, $p < 0.01$)
Dharma <i>et al.</i> (2018)	DTB median decrease after implementing STEMI network (94 [72-122] vs. 82 [67-103] minutes, $p < 0.001$).
Sunjaya, Sunjaya dan Priyana (2019)	DTB median fluctuate every year even after implementing iSTEMI (104 [45-474], 101.5 [25-344], 115 [30-562] minutes).
Dakota <i>et al.</i> (2019)	DTB median STEMI patients is 70 [58-88] minutes.

The problems currently being faced in the STEMI patient management system in Indonesia include traffic congestion, especially in the capital city, which often causes large delays in reperfusion time; PCI centers that do not provide 24/7 services, limitations in peripheral areas that are still far from PCI centers, low proportion of catheterization laboratories compared to the general population, and limited number of interventional cardiologists compared to systems in developed countries. [9]

A good management system is needed not only to shorten the transfer process and achieve optimal reperfusion time in STEMI patients, but also to provide the best choice of therapeutic strategy for each patient. Good collaboration is needed between medical personnel in primary health facilities, emergency ambulance services, call centers for

STEMI patients, and interventional cardiologists to work in a protocol that has been mutually agreed upon, so that the quality of therapy choices can be improved for each STEMI patient in Indonesia. [9]

However, DTB timing cannot be used as the sole reference for evaluating the quality of treatment in STEMI patients. In this case, the total ischemic time can better represent the main problem that must be overcome to reduce reperfusion time, so reperfusion time reduction must focus primarily on total ischemic time. [10]

Delay in reperfusion time is not always the result of failure of the referral system. Unclear signs, symptoms, and ECG results indicating the presence of STEMI can be one of the causes of delays in reperfusion time in STEMI patients, due to doubts in

establishing the diagnosis of STEMI in the initial contact.^[9]

Although most of the study in Indonesia has succeeded in achieving DTB <90 minutes, all median of total ischemic time in Indonesia still far from meeting the recommended time of <120 minutes. A

study in Indonesia found that median of total ischemic time in Indonesia range between 275-330 minutes, more than double the recommended time^[11]. Another study even reported that median of total ischemic time in Indonesia is 461 minutes, that is almost 4 times the recommended time.^[10]

Table 2. Total ischemic time in Indonesia

Author	Total Ischemic Time
Sunjaya, Sunjaya dan Priyana (2019)	Median of total ischemic time for STEMI patients decreasing every year after iSTEMI network implementation (330 [75-750], 330 [65-710], 275 [90-780] minutes).
Dakota <i>et al.</i> (2019)	Median of total ischemic time for STEMI patients is 461 [359-572] minutes.

Technological developments in the last decade have contributed to the improvement of digital health systems. Telecardiology technology has helped improve the quality of the pre-hospital treatment system by reducing diagnosis time, improving the quality of diagnosis in STEMI patients, reducing the prevalence of false diagnosis of angina, and reducing readmission rates with post-operative monitoring and post-discharge monitoring services.^[11]

The higher prevalence of PCI in interhospital referral patients could be due to earlier risk identification and stratification in referred patients so that they still meet the recommended time for

PCI action. Having carried out risk identification and stratification before the patient arrives at the PCI center also helps shorten the patient's DTB time, by shortening the time for administration and activation of the catheterization laboratory. In referring hospitals, generally education and requests for approval have been carried out regarding plans for PCI action so that patients already have a decision regarding PCI action to be carried out when they arrive at the referral hospital. Inter-hospital referral for PCI action is relevant because of the expected superior clinical outcomes compared to fibrinolytic therapy, even with the time delay that occurs for this reason.^[9]

PCI therapy outside Indonesia

All Study in outside of Indonesia found succeeded in achieving DTB median <90 minutes, range from 41 minutes, all the way to 89 minutes.

Table 3. Door-to-balloon outside Indonesia

Author	Door-to-balloon
Yu <i>et al.</i> (2019)	DTB median for patients which utilizes media social are significantly shorter than the patient without utilizing media social (52.61 ± 42.20 vs. 78.40 ± 50.64 minutes, $p=0.003$).
Mallidi <i>et al.</i> (2018)	DTB median of direct admission patients is shorter than transfer patients (71 vs. 124 minutes, $p<0.001$).
Yoshioka <i>et al.</i> (2020)	Rapid response car unit tend to have shorter DTB than emergency service or referral between hospital (51.0 [43-57] vs. 61.0 [52-68] vs. 59.5 [48-72] minutes, $p=0.130$).
Kawecki <i>et al.</i> (2017)	DTB median of transfer patients is significantly shorter than direct admission (41 [30-63] vs. 45 [30-72] minutes, $p<0.001$).
Callachan <i>et al.</i> (2017)	DTB median of direct admission patients, emergency service, and transfer patient (81 [64-105] vs. 70 [48-89] vs. 62 [46-77] minutes, $p<0.001$).

The shorter ECG-to-call lab time on the use of social media facilities in the referral process indicates that shortening the activation time of the catheterization laboratory can be achieved because the cardiologist has been able to confirm the presence of STEMI as an indication of laboratory activation even before the patient arrives at the referral hospital. ^[12]

The importance of lifestyle modification and consumption of routine medicines according to

clinical indications must also be prioritized to improve the clinical condition of STEMI patients, so that it will not only improve outcomes when patients experience attacks, but can also prevent attacks from occurring and improve the patient's overall quality of life.

Longer reperfusion times, which were independently associated with higher mortality rates, were independent of the type of patient admission. This higher mortality rate is associated

with a lower left ventricular ejection fraction (LVEF) and a larger area of myocardial infarction at a longer reperfusion time. Studies that do not show a difference in mortality rates between direct admissions and interhospital referrals may be due to late patient presentation, or onset-to-FMC time that exceeds the recommended time of 60-20 minutes. [13]

The prolonged waiting time at the emergency department of a referral hospital can be caused by several things. This delay can be caused by delays in the activation of the catheterization laboratory, especially on holidays and outside working hours up to two times; and delays in EKG examination services at the referral hospital emergency unit,

resulting in increased service effectiveness even on holidays and outside working hours, both with in-home call facilities and limiting the maximum response time in the emergency department, as well as improving chest pain triage by adding special officers to serve and interpret EKG results, are important steps to take to reduce the length of waiting time in the emergency department. Patients with chest pain should be prioritized while estimating reperfusion time even before the diagnosis is known. On the other hand, delays in the emergency department can also be caused by the patient's unstable condition upon arrival and the patient's co-morbidities, so resuscitation is necessary before PCI is performed. [14]

Table 4. Total ischemic time outside Indonesia.

Author	Brief Explanation of <i>Total Ischemic Time</i>
Kawecki <i>et al.</i> (2017)	Median of total ischemic time for transfer patients are longer than direct admission (270 [180-420] vs. 235 [158-385] minutes, $p < 0.001$).
Callachan <i>et al.</i> (2017)	Longer total ischemic time was found on transfer patients compared to patients from emergency service and direct admission (4.5 [3.0-7.5] vs. 3.1 [1.8-4.3] vs. 3.2 [2.1-5.3] hours, $p < 0.001$).
Wenner <i>et al.</i> (2020)	53-67% PCI patients failed to receive PCI on the recommended time frame.
Roe, Banka dan Mooney (2019)	Median of total ischemic time is 96 (30-940) minutes with average of 118 minutes. 67% of patients receive PCI treatment in less than 120 minutes.

The integrated STEMI network program is currently the main strategy of choice in shortening reperfusion time in STEMI patients. In addition to increasing the effectiveness and quality of services by increasing the knowledge and skills of medical personnel as well as improving the transportation system and health facilities, increasing efficiency in the economic sector must also be considered. In compiling, developing, and integrating this system, it is necessary to consider the amount of loyalty to related companies, such as transportation service providers and telecommunications network service providers. It is also necessary to consider inter-company market share and patent agreements with contributor companies both in the same or different fields. This integrated system also needs a good and structured allocation of funds so that it can run well [15]. This is expected to increase the commitment of contributing companies in improving service quality and developing new alternatives so as to improve the quality of management of STEMI patients as a whole.

Conclusion

In conclusion, this study shows that there are differences in the reperfusion time of STEMI patients in Indonesia and outside Indonesia, the median door-to-balloon time in Indonesia ranges from 70 to 288 minutes, while the median door-to-balloon time outside Indonesia ranges from 41 to 124 minutes, and the median total ischemic time in

Indonesia ranges from 275 to 461 minutes, while the median total ischemic time outside Indonesia ranges from 96 to 270 minutes.

Study Limitation

The results of the analysis in this systematic review should be interpreted with clinical considerations found in the field at each health facility where clinicians work. This study has several limitations in evaluating the overall management process of STEMI patients both in Indonesia and outside Indonesia. In this systematic review, there was no justification for the number of samples, research settings, and research methods in comparing the outcomes of each study, so that bias might occur due to differences in these matters. In future studies, it is necessary to carry out a more detailed selection with the main considerations on these three things.

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Ethical Consideration

None

Conflict of Interest

None

Funding Disclosure

None

Author Contribution

The idea and review of the literature involved input from Yudi Her Oktaviono. To the study's methodology and design to gather the data, Muhammad Fachriyan Romadhona. Sundari Indah Wiyasihati contributed to the result. The discussion of the results of this study was assisted by Rosi Amrilla Fagi. All authors approved the final version of the work.

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Supplementary Data

Table 1. Distribution of studies in Indonesia

Author, Year of Publication	Setting	Sample Characteristic, n	Intervention, n	Comparison, n	LoE
Sunjaya <i>et al.</i> , 2019 ^[11]	West Jakarta, Indonesia. Cengkareng General Hospital through the iSTEMI Network database.	Patients diagnosed with STEMI who received reperfusion measures, n = 437	Referrals from non-PCI health facilities in the first year of implementing the iSTEMI network, n=147	Referrals from non-PCI health facilities in the third year of implementation of the iSTEMI network, n=95	4
Dharma <i>et al.</i> , 2018 ^[9]	Jakarta, Indonesia. Tertiary educational hospital in the Jakarta Acute Coronary Syndrome (JAC) registry.	Total patients diagnosed with STEMI before and 5 years after implementing STEMI network, n= 1676	Referrals from non-PCI health facilities 5 years after the implementation of the STEMI network (Jakarta Cardiovascular Care Unit)	STEMI patients before STEMI network implementation, n= 624	4
Ginanjjar <i>et al.</i> , 2020 ^[8]	Jakarta, Indonesia. Cipto Mangunkusumo National General Hospital.	Patients diagnosed with STEMI who received primary PCI, n=207	Patients who received PCI after implementing CODE STEMI, n = 135	The patient received PCI action before the implementation of CODE STEMI, n = 72	4
Ermiami <i>et al.</i> , 2017 ^[16]	Manado, Indonesia. RSUP Prof. Dr. R.D. Kandou Manado.	Patients diagnosed with STEMI who received primary PCI reperfusion at the referral hospital, n = 41	Patients with PCI ≤90 minutes, n=8	Patients with PCI >90 minutes, n = 33	5
Dakota <i>et al.</i> , 2019 ^[10]	Jakarta, Indonesia. The largest tertiary education hospital in Indonesia through the Jakarta Acute Coronary Syndrome (JAC) registry.	Patients diagnosed with STEMI who received PCI and were referral patients, n=1076	Referrals from non-PCI health facilities, n=1076	N/A	5

Table 2. Distribution of studies outside Indonesia

Author, Year of Publication	Setting	Sampe Characteristic, n	Intervention, n	Comparison, n	LoE
Yu <i>et al.</i> , 2019 ^[12]	Taiwan, China. China Medical University Hospital	Patients diagnosed with STEMI who received primary PCI in a teaching hospital, n = 140	Referrals use LINE social media to send patient ECG results before departure, n=51	Conventional reference, n=89	4
Mallidi <i>et al.</i> , 2018 ^[15]	Massachusetts, USA. Baystate Medical Center and University of Massachusetts Memorial Hospital (UMass).	Patients diagnosed with STEMI who received primary PCI at 2 regional referral hospitals, n=1236	Conventional referrals from non-PCI health facilities, n=426	Non-referral, n=810	3
Yoshioka <i>et al.</i> , 2020 ^[17]	Komatsushima, Japan. Tertiary emergency referral center in Komatsushima.	Patients diagnosed with STEMI who received primary PCI in tertiary hospitals during working hours and days, n=121	Referrals using the rapid response team facility, n=33	Conventional referral, n=68, and emergency services, n=20	4
Wenner <i>et al.</i> , 2020 ^[14]	Vancouver, USA. Within the Vancouver Coastal Health Authority (VCHA).	Patients diagnosed with STEMI who received primary PCI at a regional referral hospital, n=1936	FMC-to-PPCI over time according to guideline recommendations (90 minutes in health facilities with PCI, 120 minutes in health facilities without PCI), n=1099	FMC-to-PPCI on time according to the guideline recommendation n=837	4
Roe <i>et al.</i> , 2019 ^[18]	Irlandia. RS tersier di 3 wilayah administratif.	Pasien terdiagnosis STEMI yang mendapat tindakan PCI primer di RS tersier, n=105	FMC- <i>to</i> -PPCI >120 min, n=35	FMC- <i>to</i> -PPCi ≤120 min, n=70	3
Kawecki <i>et al.</i> , 2017 ^[13]	Polandia. Dalam <i>Polish registry of Acute Coronary Syndromes (PL-ACS), nationwid.</i>	Pasien terdiagnosis STEMI yang mendapat tindakan PCI primer <12 jam setelah onset gejala, n=70093	Non-referral, n=39144	Referrals from non-PCI health facilities, n=30947	3
Callachan <i>et al.</i> , 2017 ^[19]	Abu Dhabi, UEA. 4 RS pemerintah dan swasta di Abu Dhabi dalam <i>Abu Dhabi Health Services Company.</i>	Pasien terdiagnosis STEMI yang mendapat tindakan PCI di 4 RS pemerintah, n=455	Patients with DTB time of more than 90 minutes, n = 104	Patients with DTB time of 90 minutes or less, n = 334	5