

# Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting

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## ABSTRACT

**Background:** Delay in treatment and/or failure to provide reperfusion in ST-segment elevation myocardial infarction (STEMI) impacts on morbidity and mortality. This occurs more often outside metropolitan areas yet the reasons for this are unclear. This study aimed to describe factors associated with missed diagnosis of acute myocardial infarction (MAMI) in a rural and regional setting.

**Methods:** Using a retrospective cohort design, patients who presented with STEMI and failed to receive reperfusion therapy within four hours were identified as MAMI. Univariate analyses were undertaken to identify differences in clinical characteristics between the treated STEMI group and the MAMI group. Mortality, 30-day readmission rates and length of hospital stay are reported.

**Results:** Of 100 patients identified as MAMI (70 male, 30 female), 24 died in hospital. Demographics and time from symptom onset were similar in the treated STEMI and MAMI groups. Of the MAMI patients who died, rural hospitals recorded the highest inpatient mortality (69.6%  $p = 0.008$ ). MAMI patients compared to treated STEMI patients had higher 30 day readmission (31.6% vs 3.3%,  $p = 0.001$ ) and longer length of stay (5.5 vs 4.3 days  $p = 0.029$ ). Inaccurate identification of STEMI on electrocardiogram (72%) and diagnostic uncertainty (65%) were associated with MAMI. The Glasgow algorithm to identify STEMI was utilised on 57% of occasions, with 93% accuracy.

**Conclusion:** Mortality following MAMI is high particularly in smaller rural hospitals. MAMI results in increased length of stay and readmission rate. Electrocardiogram interpretation and diagnostic accuracy require improvement to determine if this improves patient outcomes.

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## 1. Introduction

The burden of heart disease is 20% greater in rural compared to metropolitan populations, with a higher rate of mortality and multiple hospital transfers often required to access specialised care [1]. Appropriate and timely clinical care of patients presenting with acute coronary syndromes (ACS), including acute myocardial infarction (AMI), is the subject of comprehensive guidelines nationally and internationally [2,3]. Timely access to evidence-based management of ST segment elevation myocardial infarction (STEMI) is imperative for optimal clinical outcomes [4].

For patients presenting with STEMI in non-metropolitan hospitals, reperfusion treatment is predominantly thrombolysis. If thrombolysis is delivered in a timely fashion, followed by transfer to a percutaneous coronary intervention (PCI) capable hospital, this provides outcomes similar to primary PCI, which is recommended where facilities are available [5]. The impact of delay in treatment and failure to provide reperfusion doubles mortality, and impacts on morbidity outcomes [6]. Differing clinical presentations and organisational factors can make the diagnosis of ACS challenging for clinicians, resulting in some patients not receiving appropriate care [7]. Internationally, the experience of failure to treat STEMI has been documented [8,9]. Australian data indicates more than one third of people presenting with STEMI and eligible for treatment did not receive recommended reperfusion therapy [10]. This rate is higher outside the metropolitan environment; reasons for this are unclear [6]. The purpose of this study was to outline the consequences of MAMI across a large health district. In addition, we sought to assess the demographic, clinical, ECG and organisational factors associated with patients presenting with STEMI and eligible for reperfusion therapy who did not receive timely treatment in a regional area.

## 2. Materials and methods

A retrospective medical record review of patients presenting to hospital with STEMI to identify those with a missed diagnosis of acute myocardial infarction (MAMI) was conducted from 2011 to 2016.

### 2.1. Setting

The health district services an area of 131,785 km<sup>2</sup>, covering major cities, inner regional, outer regional and remote populations [11]. The district comprises 37 hospitals, including general practitioner run hospitals ( $n = 27$ ), general physician on site/Fellow Australasian College of Emergency Medicine (FACEM) hospitals ( $n = 7$ ), nurse only hospitals ( $n = 2$ ), and a tertiary referral centre ( $n = 1$ ).

The health district's reperfusion strategy for patients with ACS, implemented in 2010, utilises the computerised Glasgow algorithm for identification of STEMI on electrocardiograph (ECG). This algorithm has acceptable diagnostic accuracy in interpretation of STEMI [4,12]. Integrated within this system is the ability to electronically transmit ECGs for review by a cardiologist when STEMI is detected using the algorithm. Under this reperfusion strategy >500 acute STEMI patients are identified and treated per annum across the district.

### 2.2. Sample

Medical records of patients who presented with STEMI to any hospital in the district and failed to receive timely reperfusion therapy, when not contraindicated, were reviewed from 2011 to 2016. For this analysis STEMI diagnosis was based directly on European Society of Cardiology guidelines, and includes patients who exhibited a clinical presentation, ECG changes, and pathology consistent with STEMI [12]. Patients were required to meet criteria for standard reperfusion therapy [2]. Patients who presented with a STEMI and who were not identified, had treatment commenced, or it was clear on review that STEMI was not considered within a four-hour period were defined as MAMI. All clinical case

histories, medical records, ECG, and pathology were reviewed independently by two senior cardiologists to confirm MAMI, in the absence of any clinical contraindications to either reperfusion therapy. To take account for time and resource challenges a four hour arrival to treatment time was set, this took into consideration guideline directives to commence reperfusion therapy within 120 min of arrival in combination with the above parameters [12]. Five patients were excluded from the analysis due to end-stage disease processes, including cancer and dementia.

### 2.3. Data sources

A database of patients identified as MAMI was developed and populated using information from medical records and online clinical databases. Ethical approval was obtained from the institutional human research ethics committee (AU201711-02). This study was conducted in accordance with the declaration of Helsinki. Patients were identified as MAMI through retrospective examination of clinical databases (ECG, ACS and STEMI) and audit of transfer to other hospitals reports.

### 2.4. Factors of interest

- Patient factors; including age, gender, aboriginality and cardiovascular disease risk factors
- Hospitalisation-related factors; including inpatient mortality, length of hospital stay and 30-day-readmission, type of myocardial infarction and time of presentation to hospital,
- ECG factors and STEMI characteristics; Timing of ECG, usage of Glasgow ECG interpretation algorithm, appropriate recognition of STEMI using the algorithm, delays in diagnosis and accuracy of interpretation of ECG. Inaccurate ECG interpretation was defined as failure to make a STEMI diagnosis despite ECG criteria indicating STEMI, regardless of whether the Glasgow algorithm was used. Diagnostic uncertainty was defined as delay in access to expert clinical support and confusion around the correct treatment and referral processes. Treatment indecision is defined as where STEMI was diagnosed yet reperfusion therapy was not given despite an absence of contraindication.
- Organisational factors; Hospitals were classified as tertiary (bed capacity >500), metropolitan (>200 and  $\leq 500$  beds), rural referral (>100 and  $\leq 200$  beds) and small rural ( $\leq 100$  beds).

### 2.5. Statistical methods

Data analysis was conducted using IBM SPSS Statistics (version 22, Chicago, IL, USA). Descriptive statistics are presented by counts and percentages for categorical variables and means and standard deviation (SD) for continuous variables. Patient demographic data from the MAMI group were contrasted against data for treated STEMI at the local referral hospital. The two groups are heterogeneous and should be viewed for presentation demographics only. Univariate analyses to identify differences in clinical characteristics were performed on data comparing two groups. The sample size was insufficient to undertake multivariate analysis. Categorical variables were analysed using a chi-square test, while continuous variables such as age were analysed via analysis of variance (ANOVA). Comparisons were performed using Bonferroni corrections and statistical significance level was set to  $p < 0.05$ .

## 3. Results

Over the five-year period approximately 1392 patients presented with a STEMI to the hospitals in the region. Of these, 100 patients were identified as missed acute myocardial infarctions (MAMI); 24 of these MAMI patients died in hospital.

**Table 1**  
Characteristics of MAMI patients compared to treated STEMI from 2011 to 2016.

| Variable                                          | Treated STEMI<br>(n = 1292) | MAMI Patients<br>(n = 100) | P<br>value   |
|---------------------------------------------------|-----------------------------|----------------------------|--------------|
| Male gender n (%)                                 | 950 (73.5)                  | 70 (70)                    | 0.465        |
| Age (years) m (SD)                                | 63.9 (12.9)                 | 66.3 (12.4)                | 0.302        |
| Indigenous n (%)                                  | 47 (3.6)                    | 4 (4)                      | 0.776        |
| Hypertension n (%)                                | 796 (61.6)                  | 42 (42)                    | 0.076        |
| Dyslipidaemia n (%)                               | 496 (38.4)                  | 38 (38)                    | 1.000        |
| Diabetes n (%)                                    | 314 (24.3)                  | 33 (34)                    | 0.081        |
| Prior smoking n (%)                               | 693 (53.6)                  | 42 (42)                    | 0.039        |
| Prior myocardial infarction n (%)                 | 231 (17.9)                  | 26 (26)                    | 0.072        |
| Prior CABG n (%)                                  | 37 (2.9)                    | 9 (9)                      | <b>0.008</b> |
| Prior PCI n (%)                                   | 130 (10.1)                  | 14 (14)                    | 0.291        |
| Presentation to hospital m (SD)                   |                             |                            |              |
| 7 am–3 pm                                         | 707 (54.7)                  | 62 (62)                    | 0.190        |
| 3 pm–11 pm                                        | 377 (29.2)                  | 21 (21)                    | 0.115        |
| 11 pm–7 am                                        | 204 (15.8)                  | 17 (17)                    | 0.767        |
| Symptom onset to presentation<br>(minutes) m (SD) | 150.5 (144.4)               | 155.6 (131.4)              | 0.903        |
| Anterior infarction n (%)                         | 528 (41)                    | 67 (67)                    | <b>0.000</b> |
| Length of stay; m (SD)                            | 4.3 (3.7)                   | 5.5 (4.5)                  | <b>0.029</b> |
| 30-day readmission n (%)                          | 43 (3.3)                    | 24 (24)                    | <b>0.001</b> |

**CABG:** Coronary Artery Bypass Graft; **M:** Mean; **PCI** Percutaneous Coronary Intervention; **SD:** standard deviation; **STEMI:** ST segment Myocardial Infarction.

Characteristics of the treated STEMI and MAMI groups are presented in Table 1. Compared with the treated STEMI group, demographics of the MAMI group were similar in terms of age, comorbidities and time from symptom onset to presentation. MAMI patients were more likely to have previous CABG (9% vs 2.9%;  $p = 0.008$ ) and present with anterior infarction (67% vs 41%;  $p < 0.001$ ).

Patients who survived MAMI had a significantly higher thirty-day readmission rate compared with treated STEMI (24% vs 3.3%,  $p = 0.001$ ). The MAMI cohort showed a longer length of stay when compared with the treated STEMI group (5.5 days versus 4.3 days,  $p = 0.029$ ). The MAMI patients who died in hospital ( $n = 24$ ) had a higher proportion of women compared with the MAMI group that survived to discharge (46% versus 25%).

MAMI patients most commonly presented to small rural hospitals (Fig. 1). Of the patients with MAMI who died, smaller rural hospitals recorded the highest inpatient mortality (69.6%  $p = 0.008$ ) compared to no mortality for MAMI in the large tertiary referral hospital (Fig. 1).

The most common factors associated with MAMI were failure to identify STEMI on ECG (72%) and diagnostic uncertainty (65%) respectively. Of the MAMI patients, 57% had an ECG performed on a machine

equipped with the Glasgow algorithm. Where the Glasgow algorithm was utilised, it correctly identified STEMI in 93% of occasions. Despite correct machine identification of STEMI in these cases, reperfusion therapy was not given in a timely manner.

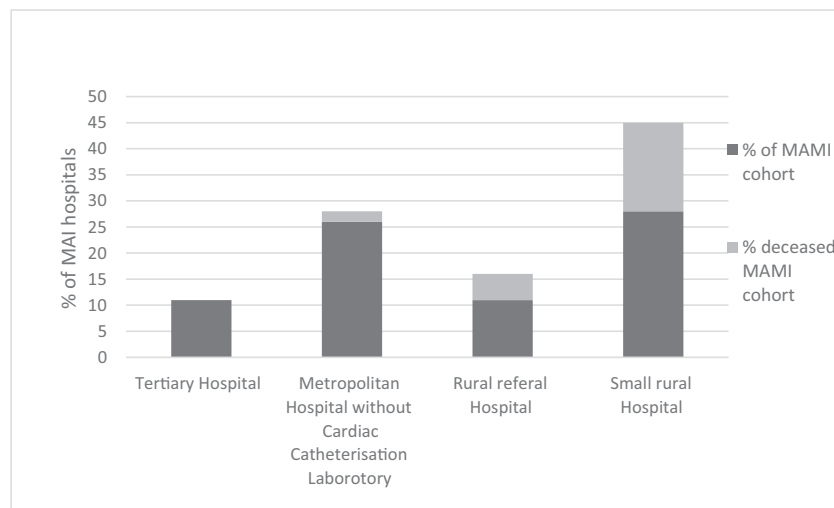
#### 4. Discussion

This paper describes the patient characteristics and clinical factors associated with the missed diagnosis of acute myocardial infarction in a rural and regional setting. Patients who had MAMI had a three-fold higher mortality when compared to the region's published mortality rate [5]. There was a 20% increased LOS, and eight times the readmission rate for MAMI patients compared to treated STEMI patients. Alarmingly anterior infarction was the most represented infarct type among patients with MAMI. Understanding the problem more specifically will assist in informing clinicians and policy makers.

The high proportion of STEMI patients not receiving reperfusion therapy is widely described in the literature and has been examined over a long period of time [13–15]. Previous reasons for not receiving reperfusion when indicated included late presentation, atypical symptomatology, gender and co-morbidity factors, plus clinician performance and system issues [9,15–17]. The preponderance of MAMI in rural compared to metropolitan hospitals reflects the difficulty of practice away from a tertiary centre in the treatment of STEMI [18]. Previous contributing reasons reported for this include the complex clinical presentation of ACS [7]. Difficulties maintaining a viable clinical roster with scarce resources and potentially long distances remain a challenge in the rural and regional setting [18]. Interpretation of complex ECGs when this is not the core clinician's role or expertise remains challenging, although the availability of effective ECG algorithms should minimise this [4]. The impact that a centralised ECG reading service to assist with accurate ECG interpretation and to help reduce diagnostic uncertainty would have on rural and regional health districts would be important to investigate and needs to be tested in a prospective research trial.

#### 5. Strengths and limitations

This retrospective analysis allows the evaluation of health outcomes in a real-world rural setting, however there are several important limitations. Data were collected from various sources where the denominator of missed MI cannot be accurately ascertained and direct causation of MAMI cannot be determined due to the limitations of current data systems. We compared the differences of two relatively small groups and the sample size limited statistical comparisons. In particular,



**Fig. 1.** Initial presentation hospital and outcomes for patients presenting with MAMI The majority of patients presented to rural hospitals, with no particular hospital overrepresented. Higher mortality was seen with MAMI in these locations. MAMI: missed acute myocardial infarction.

important determinants of MAMI may have been missed due to a type II error. A variety of data sources were utilised to minimise missing relevant patients. Medical record review data is reliant on the accuracy and interpretation of documentation of care. Two cardiologists confirming MAMI enabled reliability of diagnosis and admission parameters based on the application of an evidence based guideline definition of STEMI. This paper identifies the consequences of missed diagnosis of myocardial infarction, identifies modifiable factors associated with the development of MAMI, and may inform potential barriers to the successful treatment of STEMI.

## 6. Conclusion

MAMI occurs more often in smaller rural hospitals, results in increased mortality, longer LOS, and higher rate of hospital readmission. Common factors associated with MAMI are failure to correctly interpret the ECG and diagnostic difficulty. Better identification of MI may reduce MAMI and should be the focus of future research to improve patient outcomes in rural settings.

## Declarations

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