Ir Med J; July-August 2023; Vol 116; No. 7; P814
17th August, 2023

Management and outcomes of nonculprit coronary disease in STEMI patients

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Abstract

Aim

Recent large scale clinical trials have demonstrated the benefit of revascularisation of angiographically significant nonculprit coronary artery disease in patients presenting with ST elevation myocardial infarction (STEMI). Local practice may vary in terms of methods and timing of intervention. Our study aimed to retrospectively evaluate clinical practice at our centre in terms of management and outcomes of patients presenting with STEMI and angiographically significant nonculprit coronary disease.

Methods

A retrospective evaluation was undertaken of all patients presenting to our centre with STEMI from 2019-2021 with ≥1 angiographically significant nonculprit coronary artery stenosis.

Results

217 patients had angiographically significant nonculprit disease, mean age 63.5+/-11.3 years; 78.3% male. 123 patients (56.7%) underwent revascularisation (96 PCI, 27 CABG), 43 patients were managed with optimal medical therapy (OMT), 23 had negative functional testing, 18 patients died prior to assignment, and 10 patients lost to follow-up. OMT patients were significantly older at 69.8+/-9.4 years (p=0.006). 74 patients had outpatient PCI, median time was 36.5 days. No patients died awaiting outpatient PCI.

Conclusion

The majority of patients in our centre underwent revascularisation, or had invasive functional testing to determine OMT. Those assigned to primary OMT were older likely reflecting frailty. Revascularisation was primarily outpatient without adverse safety signals.

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Introduction

In recent years, several clinical trials have demonstrated the benefits of revascularisation of significant nonculprit coronary artery disease in patients presenting with STEMI without cardiogenic shock. The PRAMI trial in 2013 demonstrated the benefit of so-called "preventative" percutaneous coronary intervention (PCI) for nonculprit stenotic coronary disease versus optimal medical therapy in terms of reduction in anginal symptoms, nonfatal myocardial infarction (MI) and repeat revascularisation[1]. In the decade which followed, several studies have emerged to examine the optimal timing of revascularisation and methods of assessment of nonculprit coronary disease. However, many controversies still remain in the field, and significant variance exists within real-world clinical practice.

Given the existing controversies in this area, and the subsequent and incalculable impact of the COVID-19 pandemic on service delivery and patient care, we sought to assess the practices at our centre in terms of management strategies, timing of coronary revascularisation, and outcomes at one year in terms of inpatient mortality, 1-year mortality and readmission rates for primary cardiac issues (ischaemic chest pain, arrhythmia, heart failure) at one year.

Methods

For the purposes of this all-comers retrospective observational study, we reviewed the existing code STEMI database to identify all Code STEMI cath lab activations for the three-year period 2019-2021. To identify our target cohort, we reviewed the angiography reports of all such patients to distinguish those patients in whom the operating interventional cardiologist identified angiographically significant nonculprit coronary artery disease. No further exclusion criteria were included. Angiography reports, medical records, outpatient clinic letters, cardiothoracic conference meeting (heart team discussion) minutes, inpatient management databases and cardiac rehabilitation databases were reviewed as relevant to obtain further data regarding patient demographics, management strategies, hospital readmission and mortality at one year.

Obtained demographic and clinical data were collated and analysed in an anonymised manner with basic descriptive statistics using Microsoft Excel in a password-protected database in line with GDPR requirements. Normally distributed variables were expressed as mean ± SD and non-normally distributed variables as median and interquartile range (IQR), categorical variables were summarised using absolute values (percentage). Shapiro-Wilk testing was used for testing hypothesis of normal distribution of time to PCI data. Student's T-test was used to assess for difference in age in those patients in whom optimal medical therapy was chosen as a management strategy. Chi squared test was used to assess for differences in proportions between groups where appropriate.

Results

Patient Demographics and Management Strategy

A total of 575 patients with STEMI were referred for primary PCI to our centre from 2019-2021 (SPECIFY MONTHS). Of these, 217 (37.7%) were identified as having significant nonculprit coronary artery disease. Our population was predominantly male (n=170, 78.3%), with a mean age of 63.5 ± 11.13 years old. Table 1 outlines the breakdown of management strategies in our patient population. Of note, a total of 116 patients (53.5%) were discussed at the local cardiothoracic conference multidisciplinary meeting on review of the records of these meetings, with the remainder of strategies being determined by the primary cardiologist, with a small proportion of patients who died prior to strategy determination. Additionally, the cohort of patients in whom optimal medical therapy was selected upfront as their strategy were found to be significantly older with a mean age of 69.8 ±9.40 years (p=0.006). A total of 10 patients had an unknown revascularisation strategy due to repatriation to another centre or returned to their country of origin on discharge.

Table 1. Management Strategy for patients with significant nonculprit coronary artery disease

Management Strategy	Number (%)
PCI	96 (44.2%)
CABG	27 (12.4%)
Total for complete revascularisation	123 (56.6%)
Optimal medical therapy – FFR negative	23 (10.6%)
Optimal medical therapy – upfront	43 (19.8%)
Total for medical therapy	66 (30.4%)
Unknown	10 (4.6%)
Death prior to management decision	18 (8.3%)

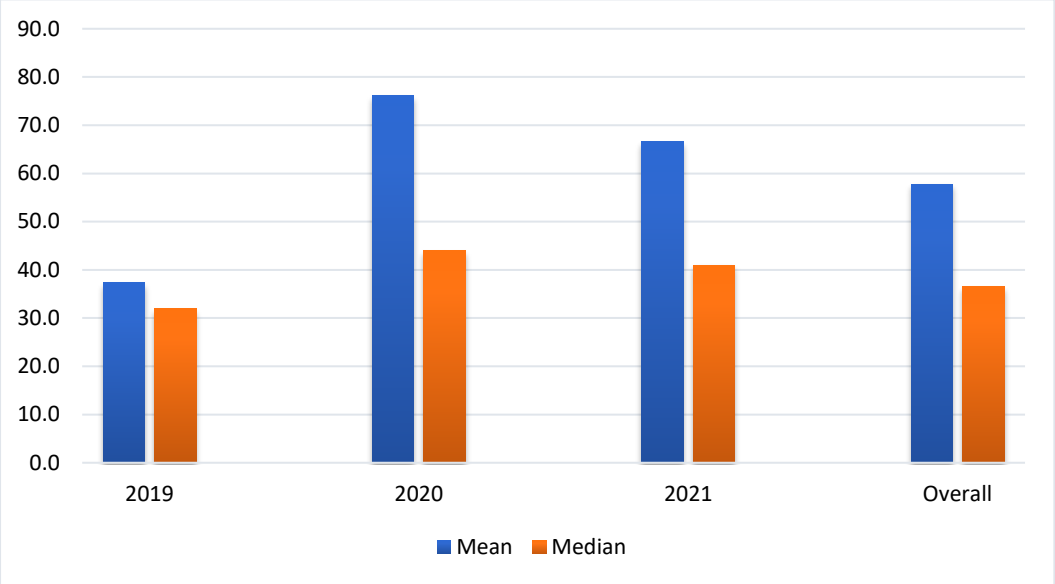
CABG = coronary artery bypass grafting, FFR = fractional flow reserve, PCI = percutaneous coronary intervention

Timing of Nonculprit PCI and the Impact of COVID-19

Of the 96 patients in whom further PCI was offered for management of their nonculprit coronary disease, 74 of these patients (77.1%) were undertaken as elective outpatient procedures. with the remaining 21 patients having PCI at the time of their index procedure or prior to their discharge from hospital. Of the patient who underwent inpatient PCI of nonculprit disease, 10 patients (10.4% of total cohort and 47.7% of inpatient revascularisation group) had complete revascularisation performed during their index procedure.

The data for outpatient PCI is summarised in Figure 1. The combined data was not normally distributed ($p=9.1x10^{-12}$) with significant positive skew of the data. The overall median time to outpatient PCI was 36.5 days (IQR 28.5); the positive skew was reflected in a mean of 57.8 ± 58.8 days. On analysis of each year individually, this phenomenon was more pronounced in 2020 and persisted into 2021; in 2019 a mean of 37.3 ± 25.2 days and median of 32 (IQR 11.0) was observed. This was felt to reflect the significant delay in some outlier cases secondary to the impact of the COVID-19 pandemic on the timely delivery of outpatient cardiology services. With regard to adverse events prior to outpatient revascularisation, no deaths were recorded and only one patient presented to hospital prior to their planned date with a need for urgent revascularisation.

Figure 1. Mean and median time to outpatient PCI from date of index presentation (days)



Mortality and Readmission Outcomes

A total of 18 patients died during their index inpatient presentation, representing 8.3% of our total cohort. The primary contributors to the cause of death are summarised in Table 2. No further patients died within the initial 30 days post STEMI, with a total mortality figure of 26 patients (12.0%) at one year follow-up. In terms of hospital readmissions, while 67 patients (30.9%) had at least one recorded hospital readmission in the one year following their STEMI, only 23 patients (10.6%) had an admission with a primary cardiac issue. Notably, while inpatient mortality and readmission rates under cardiology were similar between patients receiving PCI and OMT, there was significantly higher mortality (9.1% vs 1.0%, p = 0.013) at one year in the OMT group than the PCI group. Overall admission rates were numerically higher in the OMT group but not significantly so (39.4% vs 27.1%, p = 0.099). This may further

reflect the complexity and comorbidity burden of patients with multivessel coronary disease encountered in contemporary clinical practice.

Table 2. Primary contributors to inpatient mortality in STEMI patients with multivessel disease

Cause of Death	Number (%)
Cardiogenic shock	10 (55.6%)
Ventricular arrhythmia	5 (27.8%)
Mechanical complications	3 (16.7%)

Discussion

Following the publication of the PRAMI study, many further studies soon followed to address gaps in the data regarding revascularisaiton of nonculprit coronary artery disease. The CvLPRIT trial demonstrated superiority of complete revascularisation at index presentation in terms of reduction in ischaemia driven revascularisation, and DANAMI-3 PRIMULTI showing that staged revascularisation of nonculprit disease on the basis of fractional flow reserve (FFR) assessment for demonstration of flow limitation was superior to culprit-only PCI in terms of reduction of repeat revascularisation[2,3.] Importantly, the COMPLETE trial was the first randomised trial which was adequately powered to show a clear benefit in terms of robust clinical outcomes; a 26% relative risk reduction in the composite endpoint of MI or cardiovascular death was observed, largely driven by a 32% reduction in myocardial infarction at a median follow-up of 3 years[4]. Of note, the benefit was observed irrespective of timing of complete revascularisation, with approximately one-third of patients undergoing PCI as an elective outpatient with a target time of less than 45 days; a median of 23 days was achieved in the study. A recent systematic review and meta-analysis of complete revascularisation in acute coronary syndromes demonstrated similar outcomes irrespective of timing of revascularisation as seen in COMPLETE, but further study in this area is required[5]. Notably the recently published BIOVASC trial suggested an increased risk of urgent revascularisation and MI in staged revascularisation compared with immediate PCI, however the trial was powered to look at noninferiority rather than superiority in terms of timing of revascularisation[6]. The MULTISTARS-AMI trial, also designed to demonstrate noninferiority of immediate versus staged complete revascularisation, is ongoing and will provide further data in this area[7].

In the context of existing knowledge gaps in this area, real-world clinical practice remains variable between individual centres, both in terms of management strategies (infarct-related PCI only versus culprit and nonculprit PCI) as well as timing of same. Rathod et al. conducted a retrospective observational study which showed similar outcomes in outpatient versus inpatient complete revascularisation; potentially justifying early discharge to reduce length of

stay[8]. Interestingly, a Swiss study on outpatient staged PCI did not demonstrate significant differences in major adverse cardiovascular events (MACE) at 1 year when dichotomised to early (<4 weeks) versus late (≥4 weeks) at their centre(9). Clearly however, confounders inherent to the structure and organisation of healthcare systems and pathways will impact on such studies.

Within out centre, 56.6% of patients presenting with STEMI and angiographically significant nonculprit coronary disease were referred for complete revascularisation either by PCI or CABG. A further 10.6% underwent invasive functional testing with fractional flow reserve and were deemed non-significant necessitating optimal medical therapy only. A significant proportion of our cohort had nonculprit disease managed conservatively in the first instance. Notably this subgroup was generally older than the overall mean age of our patient cohort. While a formal assessment of frailty was not captured within our data, this finding may suggest a group in which more invasive measures may not have been seen as appropriate. It should be noted that there are emerging data suggesting that the observed benefit of revascularisation in nonculprit disease may be attenuated in older patients, particularly above 75 years old; as such aggressive optimal medical therapy may be a reasonable strategy in such patients, but given the under-representation of this population in existing large-scale trials further study is required[10]. Given the paucity of data in such groups, shared clinical decision making between patient and physician may be a reasonable approach to tailor care on a case-by-case basis.

The observed inpatient mortality in our cohort is comparable to the experience internationally in the pre-pandemic era[11]. Notably a large US registry study with similar mortality findings noted a trend towards increased mortality after the onset of the COVID-19 pandemic, with delays in medical contact and changes in health system performance associated with poorer outcomes[12]. Hospital admission rates were high within this cohort of patients, however this observation is in keeping with existing studies in this area, with rates as high as 61.7% in one Canadian study in patients with an acute coronary syndrome admission[13]. Notably, the majority of the patients requiring hospital admission within one year presented with issues unrelated to their index presentation, again reflecting the complexity and multimorbidity of this cohort. A recent systematic review identified comorbidities such as hypertension, renal disease and diabetes as risk factors for readmission, which are common in STEMI patients; indeed the factors that predispose to a risk of presentation with STEMI also portend predictive value of hospital admission with other diagnoses[14].

The majority of patients in whom PCI was recommended for complete revascularisation were managed in the outpatient setting, with low event rates for adverse events. This provides an interesting contrast to the recent BIOVASC trial in which a significant and early trend was seen with regard to MIs and unplanned revascularisations in the staged PCI group; however the retrospective, observational nature of our data dictates our findings to be interpreted with

caution. In addition, the effect of the COVID-19 pandemic on patient reluctance to attend hospital with potential ischaemic symptoms cannot be quantified. The ongoing MULTISTARS-AMI will provide further insights into optimal revascularisation timing.

Declarations of Conflicts of Interest:

None declared.

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