

Original Article

Impact of timing to coronary angiography in acute coronary syndrome on contemporary clinical practice

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Abstract: Recent studies appear to suggest a correlation between timing to coronary angiography and clinical outcome among patients with acute coronary syndrome (ACS). We aim to study 12-month outcomes of ACS patients who are stratified according to early (≤ 24 hours), intermediate (>24 to <48 hours) and delayed (≥ 48 hours) coronary angiography. This is a prospective observational study of patients with ACS defined as either unstable angina pectoris or non-ST elevation myocardial infarction (MI) admitted between October 2008 and July 2009. Baseline clinical characteristics of age, gender, cardiovascular risk factors (diabetes mellitus, hypertension, dyslipidemia) and TIMI score were analyzed and adjusted for outcomes. The primary outcome was combined major adverse cardiovascular events (MACE) of death or non-fatal MI, as well as target vessel revascularization (TVR) up to 12 months. This study consisted of 642 patients (75% males, mean age 60 ± 13) with median follow-up of 7 months and median TIMI score of 4. Over half (50.2%) were categorized as high-risk (TIMI score ≥ 4). 281 patients (43.5%) had early angiography, 170 (26.5%) had angiography between >24 to <48 hours and 191 (30%) patients had delayed angiography ≥ 48 hours. In high-risk patients, the primary outcome occurred in 10.9% of patients in the early group, as compared with 13.2% in intermediate group and 23.9% in delayed group ($p=0.015$) at six months. However, in low-risk patients (TIMI scores <4), there was no significant difference between the groups (7.1% vs. 3.4% vs. 5.9%, $p=0.316$) at six months. Compared to the intermediate and delayed groups, patients in the early group had lower overall MACE at 12 months (21% vs. 14% vs. 10%, $p=0.006$) that was largely related to a lower frequency of death at 12 months (11% vs. 7% vs. 4.6%, $p=0.03$). There were no differences in rates of TVR between the groups (4% vs. 7% vs. 3.5%, $p=0.14$). In this observational analysis, an early strategy to coronary angiography was associated with improved survival at one year while an early to intermediate strategy benefitted the subgroup of high-risk patients with significant reductions in cardiovascular events at six months.

Keywords: Myocardial infarction, acute coronary syndrome, coronary angiography

Introduction

Recent studies have demonstrated a correlation between timing to coronary angiography and clinical outcome among patients with acute coronary syndrome (ACS) [1]. An early invasive strategy has been shown to reduce ischemic endpoints by reducing revascularization as well as hard endpoints by reducing mortality and myocardial infarction [2, 3].

In the management of patients with acute coronary syndrome, the findings of these studies have led to the adoption of an early invasive strategy where coronary angiography is performed within 48 to 72 hours of hospital presentation [4, 5].

In this study, we aim to investigate the role of early invasive strategy in a contemporary cohort of patients with acute coronary syndrome on clinical outcomes over a one year period.

Materials and methods

Design and study population

A total of 642 patients with acute coronary syndrome defined as either unstable angina or non-ST elevation myocardial infarction were admitted between October 2008 and July 2009.

Baseline clinical characteristics of age, gender, cardiovascular risk factors (diabetes mellitus, hypertension, dyslipidemia) and TIMI score were

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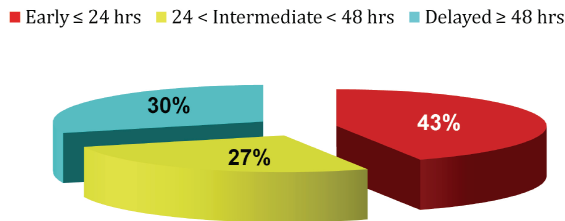


Figure 1. Timing to angiography.

analyzed and adjusted for outcomes. Follow-up data was obtained from medical records or telephone follow-up. All patients completed follow-up. Ethical approval for the study came from our local institutional review board.

Clinical endpoints

The primary outcome was combined major adverse cardiovascular events (MACE) of death or non-fatal MI, as well as target vessel revascularization (TVR) up to 12 months. Nonfatal myocardial infarction included peri-procedural myocardial infarction as well as nonfatal myocardial infarction that occurred during follow-up. Death included all-cause death at index hospital admission and on follow-up. TVR was defined as PCI within a vessel treated during the index procedure or any CABG after the index procedure that is driven by clinical indications. If a patient underwent more than one PCI during this time frame, the initial one was taken as the index procedure.

Data and statistical analysis

ACS patients who are stratified according to early (≤ 24 hours), intermediate (>24 to <48 hours) and delayed (≥ 48 hours) coronary angiography from time of hospital presentation to coronary angiography. The TIMI risk score for ACS [6] was determined for each patient; TIMI score ≥ 5 was defined as high-risk in our study.

Categorical variables were presented as percentages and compared using chi-square/Fisher's exact test. Continuous variables are presented as the mean $\pm$ standard deviation and comparisons were made by means of analysis of variance. Clinical event rates were determined and compared between the three groups with the log-rank test after adjusting for significant covariates at baseline. All statistical tests

were two-sided and a value of $p < 0.05$ was considered statistically significant. Data management and analysis were performed using the Statistical Package for Social Sciences (SPSS) Windows version 17.

Results

Patients and procedures

During the study period, 642 patients were followed up for a median duration of 7 months. 75% were males and mean age of the patients was 60 ± 13 years. Over half (50.2%) were categorized as high-risk (TIMI score ≥ 5). 281 patients (43.5%) had early angiography, 170 (26.5%) had angiography between >24 to <48 hours and 191 (30%) patients had delayed angiography (**Figure 1**).

The baseline clinical characteristics of the three groups are shown on **Table 1**. Patients who underwent early coronary angiography were younger, had less diabetes, lower creatinine levels and higher haemoglobin levels at baseline, higher ejection fractions and lower TIMI risk scores.

The extent of anatomical coronary disease did not differ between the three groups. Treatment of coronary disease after coronary angiography also did not differ between the groups.

Clinical outcomes

The primary outcome up to one year follow-up was 10% in the early group, 21% in the intermediate group and 14% in the delayed group ($p = 0.006$) (**Table 2**).

In high-risk patients, the primary outcome occurred in 10.9% of patients in the early group, as compared with 13.2% in intermediate group and 23.9% in delayed group ($p = 0.015$) at six months (**Figure 2**). However, in low-to-intermediate risk patients (TIMI scores < 5), there was no significant difference between the groups (7.1% vs. 3.4% vs. 5.9%, $p = 0.316$) at six months (**Figure 2**).

During the index hospital admission, there was a non-significant trend towards higher survival rates among patients who received early coronary angiography (97% vs 93% vs. 95%, $p = 0.11$) (**Table 2**).

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Table 1. Baseline Clinical Characteristics, Angiography findings and Interventions.

	Early	Intermediate	Delayed	p value
Age (yr, SD)	59.4 (10.7)	60.4 (12.8)	61.9 (14.8)	0.03
Male (%)	79.6	73.8	67.4	0.011
Diabetes (%)	31	35.9	45	0.008
Hypertension (%)	60.1	62.4	56.5	0.52
Hyperlipidemia (%)	66.2	62.9	59.2	0.3
Mean Ejection Fraction (%)	52.1	51.7	46.9	0.0002
Mean Creatinine	104.1	115.6	149.6	0.0007
Mean Hb	13.8	13.6	13.1	0.0001
TIMI score 5-7 (%)	18.9	22.9	38.7	<0.0001
Extent of coronary disease				0.23
Normal coronaries	2.49	1.2	1.1	
Single vessel	22.4	19.4	22	
Two-vessel	25.3	26.5	21.5	
Three-vessel	42.4	39.4	48.7	
Minor disease	7.5	13.5	6.8	
Interventions				0.22
Medical	17.8	23.5	22.5	
PCI	59.4	51.2	59.2	
CABG	22.8	25.3	18.3	

Table 2. Clinical Outcomes at One Year.

	Early	Intermediate	Delayed	p value
Hospital survival	97.15	92.94	95.33	0.11
Deaths	4.63	10.99	7.06	0.031
MI	4.63	5.29	8.9	0.14
TVR	3.56	4.126.81	6.81	0.24
Any MACE	10.32	20.94	14.12	0.0056

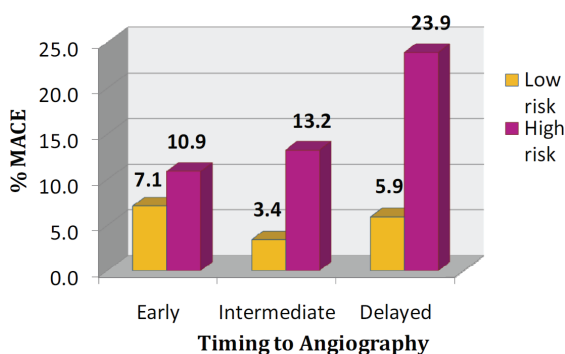


Figure 2. Six months MACE stratified by TIMI Risk Scores.

At one year, compared to the intermediate and delayed groups, patients in the early group had lower overall MACE (21% vs. 14% vs. 10%, $p=0.006$) that was largely related to a lower

frequency of death at 12 months (11% vs. 7% vs. 4.6%, $p=0.03$). There was a non-significant trend towards higher rates of non-fatal MI within one year among the delayed group (9% vs. 5% vs. 4.6%, $p=0.14$).

There were no differences in rates of TVR between the groups (4% vs. 7% vs. 3.5%, $p=0.14$).

Discussion

In this observational study involving patients with acute coronary syndrome who underwent coronary angiography, there were significant differences at baseline between patients who underwent early versus intermediate to delayed timing to coronary angiography.

Given the heterogeneity of patients who present with ACS, risk stratification of patients becomes

important so that the benefits outweigh the risks associated with early invasive strategy. We have found that an early to intermediate timing within 48 hours to hospital presentation for ACS benefitted the subgroup of high-risk patients with significant reductions in cardiovascular events at six months. This finding is similar to studies performed that demonstrated substantial benefit among high-risk patients as defined by various risk indicators such as age, renal impairment, diabetes, troponin elevation and ST segment deviation [2, 3, 6, 7].

As a whole, while severity of anatomical coronary disease did not differ between the groups, a substantial proportion within the early group and delayed group had two- or three- vessel coronary disease in aggregate. These two groups at both ends of the spectrum in terms of timing to coronary angiography had similar rates of percutaneous coronary intervention or CABG. At one year, event-free survival was highest in patients who received coronary angiography within 24 hours. This finding was largely driven by the hard endpoint of all-cause death at one year.

We acknowledge limitations of the present study. Like all observational studies, our findings should be interpreted in the context of the inherent flaws of any observational study, which include study selection bias and inability to adjust for confounding by unmeasured factors. However, this study represents a highly representative sample of patients who underwent PCI in routine clinical practice. Our design is based on a computerized registry with complete institutional coverage, enabling study of a well-defined large population with complete follow-up reviewed carefully from medical records and telephone follow-up over time.

Conclusion

This study confirms the short-term and mid-term benefit of early invasive strategy in patients with acute coronary syndrome particularly in patients at high-risk based on clinical risk indices and knowledge of coronary anatomy.

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