


Research Article

Does High Total Ischemic Time Have a Different Impact in Patients with st-elevation Myocardial Infarction Depending on Renal Function ?

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Abstract

Aim: The purpose of this study was to compare the influence of high total ischemic time (TIT) on in-hospital complications and prognosis in ST-segment elevation myocardial infarction (STEMI) patients with different renal functions.

Methods: A total of 224 STEMI patients with ≥ 6 hours TIT were selected for this study and divided into three groups according to GFR. Group 1 comprised 73 patients with < 60 ml/min/1.73 m² GFR. Group 2 consisted of 72 patients with ≥ 60 ml/min/1.73 m² and < 90 ml/min/1.73 m² and Group 3 comprised 79 patients with ≥ 90 ml/min/1.73 m². The groups' other characteristics were similar. The primary outcome was a 6-month death rate after admission for STEMI, and secondary outcomes were in-hospital death and complication of STEMI with lung edema (LE) or cardiogenic shock(CS).

Results: The incidence of LE and CS was significantly lower in Group 3 (1.3%) compared to Group 1 (15.1%) and Group 2 (6.9%) ($p = 0.006$). LE and CS rates did not differ significantly between Group 2 and Group 3 ($p = 0.103$). No significant between-group differences were found for in-hospital death in Group 1 (4.1%), Group 2 (1.4%), and Group 3 (0) ($p = 0.15$). Also, the authors found significant between-group differences for 6-month death. Group 1 (12.3%) showed a considerably higher 6-month death rate than Group 2 (2.8 %) and Group 3 (2.5%) ($p = 0.015$). No significant between-group differences were found for the 6-month death rate in Group 2 and Group 3 ($p = 0.999$).

Conclusion: STEMI patients with RD, a high level of TIT had a great impact on nosocomial complications and prognosis compared to STEMI patients with normal kidney function.

Key Points: Our study showed that in STEMI patients with RD, a high level of TIT had a great impact on nosocomial complications and prognosis compared to STEMI patients with normal kidney function. This was discovery of a clear relationship between RD and in-hospital complications and prognosis in the case of high TIT. Impaired renal function in patients with TIT, as an aggravating factor, doctors should pay due attention to avoid fatal complication. The result of the study gives us the opportunity to predict more likely complications in STEMI patient and be ready for them to choose the appropriate treatment.

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Abbreviations:

GFR: Glomerular Filtration Rate; **RF:** Renal Function; **ACS:** Acute Coronary Syndrome; **PCI:** percutaneous coronary intervention; **RD:** Renal Dysfunction; **STEMI:** ST-segment Elevation Myocardial Infarction; **TIT:** Total Ischemic Time; **LE:** Lung Edema; **CS:** Cardiogenic Shock

Introduction

A lot of adults suffer from chronic kidney disease, which they learn about when they get to the hospital for other reasons.[1] There is also an increased risk of cardiovascular diseases associated with decreased renal function (RF).[2-4] In patients with acute myocardial infarction, impaired renal function at the time of admission should indicate an increased risk of nosocomial complications.[5] Several studies have shown that even minor changes in glomerular filtration rate (GFR) increase the risk of developing de novo coronary heart disease or death after the first myocardial infarction.[6-8]

Patients with impaired RF had a worse outcome than patients with normal RF after acute coronary syndrome (ACS), which includes acute myocardial infarction, percutaneous coronary intervention (PCI) and coronary artery bypass grafting.[9] With the exception of caution regarding prescribed dosages and more liberal use of revascularization, current recommendations offer patients with renal insufficiency the same therapy as other patients with ACS.[10,11] Since clinicians may not be aware of impaired renal function, a special offer has been developed to help identify patients with cardiovascular diseases and impaired renal function.[12] Given this high risk, patients with renal dysfunction (RD) may benefit more directly from the intrusive technique than those without RD; however, the risk of adverse outcomes is also higher in patients with renal dysfunction.[13,14] Several laboratory tests were conducted to determine RF. GFR is the most reliable indicator of RF evaluation.[15] It is extremely important to understand what leads to poor outcomes in patients with renal insufficiency. Clinical manifestations of ACS in patients with RF differ markedly from those in patients without RF in the general population.[16-21] Firstly, the prevalence of chest discomfort in patients with ACS is inversely proportional to the stage of RD. As GFR decreases, the frequency of chest discomfort gradually decreases.[21] There is no doubt that myocardial reperfusion with primary PCI is the main therapy for acute ST-segment elevation myocardial infarction (STEMI), and it should be performed as soon as possible. In patients with RD, ischemia may last longer due to distortion of clinical symptoms. The total time of ischemia (TIT), measured from the onset of symptoms to reperfusion therapy, is crucial for the prognosis of patients with STEMI, and it should be carefully considered when determining the time to reperfusion.[22] It should also be noted that, TIT independently correlated with in-hospital mortality after PCI in patients with STEMI with an ejection fraction below 50%.[23] Also, according to the

results of Gao and colleagues's study, acute kidney injury is a significant risk factors for hospital death in patients with STEMI.[23] As mentioned earlier, TIT is a prognostic risk factor in patients with STEMI, and the purpose of this study was to compare the effect of high TIT on hospital-acquired complications and prognosis in patients with STEMI with different kidney functions.

Patients and Methods

Study design and population

This is a prospective, observational, single-center study, which was carried out at Erebuni Medical Center in Yerevan, Armenia in 2017-2022 years. A total of 224 STEMI patients with ≥ 6 hours TIT were selected for this study and all them categorised into three groups according to GFR. Total ischemic time was defined as the time from the onset of chest pain to the first balloon inflation during primary PCI.[10] Group 1 consisted of 73 patients whose GFR was < 60 ml/min/1.73 m². Group 2 consisted of 72 patients with GFR ≥ 60 ml/min/1.73 m² and < 90 ml/min/1.73 m² and Group 3 consisted of 79 patients with GFR ≥ 90 ml/min/1.73 m². GFR was estimated with the modification of diet in renal disease formula, which is calculated by using creatinine, age, gender, and race.[24] The patients were all white. All patients' demographic, angiographic, and clinical data, including age, gender, and cardiovascular risk factors like hypertension, diabetes, and STEMI localization, were gathered during the first few hours after admission. Iohexol was used as a contrast agent. Before and after PCI, RF was assessed for all patients. The European Society of Cardiology guidelines defined all variables and the criteria for the diagnosis of STEMI and acute heart failure,[11] and were guided by that.

All subjects participated voluntarily. Informed consent was obtained from all individual participants included in the study. Ethics committee of "Erebuni" Medical Center issued approval 01/483. All procedures performed in studies involving human participants or on human tissue were by the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards.

Treatment protocol

Patients with severe valvular heart disease, cancer, acute cerebrovascular disease, or other serious non-cardiac medical conditions with a life expectancy of less than one year were excluded from the study. Patients who declined to give written consent were also excluded. Following the ESC Guidelines on acute myocardial infarction in patients with ST-segment elevation, all enrolled STEMI patients in three groups underwent primary PCI using a standard technique through the radial artery route.[11] Every patient received as many stents as were deemed clinically necessary for the infarct-related artery. Aspirin, clopidogrel, statins, beta-blockers, heparin, angiotensin-converting enzyme inhibitors

or angiotensin II receptor blockers, diuretics, and other medications were given to all patients in the groups as part of standard pharmacological treatment for STEMI following current guidelines (Table I).

Table I: The groups were comparable in terms of received drugs

Received drugs	Group 1 n =73	Group 2 n = 72	Group 3 n=79	p Value
Aspirin No. (%)	73 (100)	72 (100)	79 (100)	–
Clopidogrel No. (%)	73 (100)	72 (100)	79 (100)	–
Heparin and LMWHs No. (%)	73 (100)	72 (100)	79 (100)	–
Statins No. (%)	73 (100)	72 (100)	79 (100)	–
B-blockers No. (%)	58 (79)	55 (76)	69 (87.3)	0.2
ACE inhibitors or ARBs No. (%)	59 (81)	62 (86)	70 (89)	0.39
Aldosterone antagonists No. (%)	23 (31)	26 (36)	24 (30)	0.73
Calcium antagonist No. (%)	15 (20)	19 (26)	17 (21)	0.67
Loop diuretics No. (%)	37 (51)	32 (44)	29 (37)	0.22

ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers, LMWHs, low molecular weight heparins. P<0.05 is considered significant.

Study outcomes

The primary outcome was a 6-month death rate after admission for STEMI, and secondary outcomes were in-hospital death and complication of STEMI with lung edema (LE) or cardiogenic shock(CS). At the end of 6 months after admission, the rates of complications were compared between groups.

Statistical analysis

Software called SPSS 26.0 (SPSS Inc., USA) was used to digitize and collect survey data. Standard statistical techniques were applied. Each calculated p-value had a two-tailed significance level of 0.05 to be considered statistically significant. While categorical variables are summarized based on the frequency and group percentage, continuous variables were summarized as mean and standard deviation.

The analysis of patients' data included in the study was performed using the following statistical tests:

- The ANOVA test was used to compare continuous variables between the three groups in the study.
- Student's t-test was used to compare continuous variables between two subgroups of patients.

- Pearson's chi-squared test was used to compare the frequencies of the indicators were compared in the study.
- Categorical variables between groups were analyzed using Fisher's z-transformation test as necessary.

Results

A total of 224 patients with STEMI were included. The mean GFR in Group 1 was 48.4±10.4 ml/min/1.73 m², in Group 2 73.7±8.4 ml/ min/1.73 m², and in Group 3 105.9±16.0 ml/ min/1.73 m² (p < 0.001). The mean TIT in Group 1 was 8.5±1.9 hours, while in Group 2 it was 8.4±1.8 hours and in Group 3 it was 8.9±1.9 hours (p=0.29). The average age of patients in Group 1 was 67.5±9.6 years old, 67.8±7.9 years old in Group 2, and 65.1±8.0 years old in Group 3 (p = 0.079). The percentage of males was 63.0% in Group 1, 63.9% in Group 2, and 72.2% in Group 3 (p = 0.42). There was a high prevalence of cardiac risk factors and/or comorbid conditions in the groups: 23.3% in Group 1, 25.0% in Group 2, and 22.8% in Group 3 had a history of diabetes (p = 0.95), while 72.6% in Group 1, 70.8% in Group 2, and 64.6% in Group 3 had a history of hypertension (p = 0.53). Prior MI was reported by 11.0 % in Group 1,

Table II: Baseline demography and clinical characteristics stratified according glomerular filtration rate

Characteristics	Group 1 GFR < 60 n=73	Group 2 GFR = 60-90 n = 72	Group 3 GFR > 90 n=79	p Value
TIT, hours (SD)	8.5 ± 1.9	8.4 ± 1.8	8.9 ± 1.9	0.288
GFR (ml/min/1.73 m ²) (SD)	48.4 ± 0.4	73.7 ± 8.4	105.9 ± 16.0	< 0.001
Age, years (SD)	67.5 ± 9.6	67.8 ± 7.9	65.1 ± 7.0	0.079
Male No. (%)	46 (63)	46 (63.9)	57 (72.2)	0.42
Prior MI No. (%)	8 (11)	7 (9.7)	2 (2.5)	0.1
Hypertension No. (%)	53 (72.6)	51 (70.8)	51 (64.6)	0.53
Diabetes No. (%)	17 (23.3)	18 (25)	18 (22.8)	0.95
Anterior STEMI No. (%)	38 (52.1)	30 (41.7)	32 (40.5)	0.3
EF(%) (SD)	37.8 + 8.7	41.1 ± 8.7	42.1 ± 6.7	0.004
Killip I class at the time of admission No. (%)	30 (41)	32 (44)	36 (46)	0.85
Killip II class at the time of admission No. (%)	43 (59)	40 (56)	43 (54)	0.85

EF, ejection fraction GFR; glomerular filtration rate; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; SD, standard deviation; TIT, total ischemic time.
P < 0.05 is considered significant.

Table III: Effect of high total ischemic time on in-hospital complications and prognosis

Outcome variable	Group 1 n=73	Group 2 n=72	Group 3 n=79	P Value
6-month death No. (%)	9 (12.3)	2 (2.8)	2 (2.5)	0.015
In-hospital death No. (%)	3 (4.1)	1 (1.4)	0	0.15
Lung edema and cardiogenic shock No. (%)	11 (15.1)	5 (6.9)	1 (1.3)	0.006

P < 0.05 is considered significant.

9.7% in Group 2, and 2.5% in Group 3 (p = 0.1). Anterior STEMI was present in 52.1% of Group 1, 41.7% of Group 2, and 40.5% of Group 3 (p = 0.3). (Table II). The incidence of LE and CS was significantly lower in Group 3 (1.3%) compared to Group 1 (15.1%) and Group 2 (6.9%) (p = 0.006). LE and CS rates did not differ significantly between Group 2 and Group 3 (p = 0.103). No significant between-group differences were found for in-hospital death in Group 1 (4.1%), Group 2 (1.4%), and Group 3 (0) (p = 0.15). In the first group, 4 patients needed dialysis, in the second group 2 patient and in the third group also 2 patients. There was no statistical difference between the groups (P = 0.56). Also, the authors found significant between-group differences for 6-month death. Group 1 (12.3%) showed a considerably higher 6-month death rate than Group 2 (2.8 %) and Group 3 (2.5%) (p=0.015. No significant between-group differences were found for the 6-month death rate in Group 2 and Group 3 (p = 0.999). (Table III).

Discussion

The relationship between TIT and the prognosis following PCI in patients with STEMI has been shown in numerous studies.[23,25] The main finding of this study was the discovery of a clear relationship between RD and in-hospital complications and prognosis in the case of high TIT. The TIT values between groups in the current study did not differ significantly but were higher than optimal in the three groups: the mean TIT in Group 1 was 8.5±1.9, while in Group 2 it was 8.4±1.8 and in Group 3 it was 8.9±1.9 (p=0.29). Our groups differed slightly regarding prior myocardial infarction and ejection fraction. The incidence of prior MI was low in Group 3 (2) compared to Group 1 (8) and Group 2 (7) (P = 0.1). EF was lower in Group 1 (37.8 + 8.7 %) compared to Group 2 (41.1 + 8.7 %) and Group 3 (42.1 + 6.7 %) (P = 0.004) (Table II). The authors reasoned that high TIT must have a more significant impact on patients with RD. Patients with low TIT did not participate in this study. There is no doubt about statistically significant variations in intra-hospital complications and prognosis across patients with various RF if all other data were comparable. In-hospital complications and prognosis varied between STEMI patients who had high TIT and various RF, according to the results of the current study. This means that a rise in the TIT, in the presence of RD,

affects more obviously the course of the disease and results in in-hospital complications and prognosis. Our study found that patients with RD and high TIT were more likely to develop complications such as PE or CS. Also, our study proved that revascularization delay has a higher impact on prognosis in STEMI patients with RD. Noteworthy is the fact that there is insufficient data in the literature that would indicate the importance of TIT, especially in patients with RD. This study suggests that TIT value deserves more attention in STEMI patients with RD to make the prognosis more predictable.

Study limitations

There are some limitations to this study. The study's main limitations are its single-center design and small sample size. The second limitation is that RD was diagnosed solely based on GFR calculations at the time of admission, with no prior documentation.

Conclusion

TIT with assessment of renal function are independent predictors of nosocomial complications. This fact is especially important in patients with concomitant pathologies, such as RD. Our study showed that in STEMI patients with RD, a high level of TIT had a great impact on nosocomial complications and prognosis compared to STEMI patients with normal kidney function. In STEMI patients with high TIT, assessing RF may help predict in-hospital complication.

Declarations:

Conflict of Interest Disclosure: None

Author Contributions:

1. Harutyun Petrosyan - Have treated patients
2. Hamlet Hayrapetyan - Have controlled and coordinated treatment (Head of the Department.)
3. Anastasiia Veprintseva - Worked with the database
4. Shagen Torozyan - Operated patients
5. Norik Ghazaryan - Worked with the database

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