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ORIGINAL ARTICLE

# Comparison between primary angioplasty and thrombolytic therapy on erectile dysfunction after acute ST elevation myocardial infarction

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**Acute ST elevation myocardial infarction has high mortality and morbidity rates. The majority of patients with this condition face erectile dysfunction in addition to other health problems. In this study, we aimed to investigate the effects of two different reperfusion strategies, primary angioplasty and thrombolytic therapy, on the prevalence of erectile dysfunction after acute myocardial infarction. Of the 71 patients matching the selection criteria, 45 were treated with primary coronary angioplasty with stenting, and 26 were treated with thrombolytic agents. Erectile function was evaluated using the International Index of Erectile Function in the hospital to characterize each patient's sexual function before the acute myocardial infarction and 6 months after the event. The time required to restore blood flow to the artery affected by the infarct was found to be associated with the occurrence of erectile dysfunction after acute myocardial infarction. The increase in the prevalence of erectile dysfunction after acute myocardial infarction was 44.4% in the angioplasty group and 76.9% in the thrombolytic therapy group ($P$=0.008). In conclusion, this study has shown that reducing the time of reperfusion decreases the erectile dysfunction prevalence, and primary angioplasty is superior to thrombolytic therapy for decreasing the prevalence of erectile dysfunction after acute myocardial infarction.**
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## INTRODUCTION

Erectile dysfunction (ED) is defined as the recurrent or persistent inability to achieve and/or maintain an erection for satisfactory intercourse.[1] The prevalence of ED in the general population is reported to be 19%–52%.[1,2] The risk factors for ED include diabetes mellitus, hypertension, hyperlipidemia, obesity and smoking, all of which are risk factors for coronary artery disease (CAD) as well.[1–6] Vascular disease of the penile arteries, including atherosclerosis, is the most common cause of ED, accounting for up to 80% of the cases.[4–6] It is presumed that ED is a marker of subclinical atherosclerosis.[4–6] Many patients experience ED approximately 2–3 years before the manifestation of CAD.[4–6] The prevalence of ED was demonstrated to be higher in CAD patients, and the ED score is correlated with the extent of CAD.[4–6] Myocardial infarction is a syndrome caused by total or subtotal occlusion of coronary arteries in which myocardial cell death eventually occurs. The amount of myocardial tissue loss is correlated with the time between the onset of chest pain and the initiation of treatment.[7] Myocardial infarction is classified as either ST elevation acute myocardial infarction or non-ST segment elevation acute myocardial infarction according to the electrocardiogram at the time of admission.[7] Acute ST elevation myocardial infarction (STEMI) involves the rupture of an atheromatous plaque resulting in occlusion of a coronary artery and is associated with high mortality and morbidity rates.[7] Two main treatment modalities for STEMI are primary percutaneous coronary intervention (PPCI) and thrombolytic treatment (TT).[7,8] In many ways, PPCI has been shown to be superior to TT in terms of mortality and re-infarction rates.[8] Additionally, the quality of life is affected by STEMI, and many patients face ED in addition to other health problems after STEMI.[8] The aim of the present study was to investigate the impact of the initial choice of reperfusion method on the preservation of erectile function in patients with STEMI.

## MATERIALS AND METHODS

### Patients and sample collection

This study was reviewed and approved by the Local Committee of Diskapi Yildirim Beyazit Research and Education Hospital, Ankara, on the ethics of clinical and animal studies and was conducted according to the committee's guidelines. Between May 2006 and October 2008, data for the patients were retrospectively evaluated. Information was gathered on patients who were admitted to the emergency department within the first 3 h after angina onset and who were hospitalized with a diagnosis of acute STEMI for the first time. The inclusion

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criteria were defined as the presence of acute STEMI within 6 h of angina onset and the achievement of successful reperfusion. Acute STEMI was defined according to the World Health Organization criteria.[7] A total of 71 male (mean age of 54.3±10.1 years) patients who met the inclusion criteria were included in the study. Exclusion criteria were defined as follows: patients with an atrial fibrillation or flutter, patients with a bundle branch block or any other intraventricular conduction delay evident on the admission electrocardiogram, patients who could not be reperfused with TT and required emergency percutaneous coronary intervention (causing crossover between the groups), patients with renal failure, previous myocardial infarction or a previous coronary artery bypass graft operation, congenital disease, pericardial disease, systolic left ventricular dysfunction on echocarfdiographic evaluation at 24 h after admission, severe valvular heart disease, liver cirrhosis, thyroid disease, or previous pelvic, penile, urethral or prostate surgery. The patients were treated by either PPCI or TT. The choice of the treatment method was based upon the hospital's facilities at the time of treatment and the recommendations of the 2004 ACC/ESC ST-elevation MI guidelines.[9] The 71 patients matching the selection criteria were grouped according to the initial revascularisation method; 45 patients were treated with primary percutaneous transluminal coronary angioplasty and stenting, and 26 patients were treated with thrombolytic agents (streptokinase). Low-flow nasal oxygen, oral acetylsalicylic acid (325 mg), clopidogrel (600 mg loading dose and 75 mg $day^{-1}$ maintenance dose), a beta blocker (metoprolol succinate 25, 50, 100 or 200 mg $day^{-1}$ according to the patient's blood pressure, heart rate and clinical status), an angiotensin converting enzyme inhibitor (according to the blood pressure), unfractionated heparin and atorvastatin (80 mg) were administered to all patients.

### Primary angioplasty procedure

Before the procedure, 600 mg of oral clopidogrel was given to each patient in the cardiac catheterisation room. The procedure was performed using a standard angioplasty technique using a 6-French (Fr) guiding catheter via the femoral artery approach. A bolus of 100 IU $kg^{-1}$ of heparin was administered intra-arterially after insertion of the vascular catheter. The target lesions were initially treated with appropriate balloon predilatation as necessary, followed by intracoronary stenting. Bare metal stents (Ephesos, Nemed Company, Istanbul, Turkey) were implanted during PPCI whenever technically feasible in group 1. After stent implantation, heparin was routinely administered. The sheaths were removed the same day.

### TT

Oral clopidogrel (75 mg) was given to each patient. Streptokinase was given intravenously at 1.5 million units over approximately 60 min. Reperfusion after TT was assessed according to clinical criteria, defined as complete relief of chest pain, resolution of ST elevation by at least 50%, development of reperfusion arrhythmias, early creatine kinase (CK) and creatine kinase-MB fraction (CK-MB) peaks.

### Echocardiographic evaluation

Each patient underwent a complete two-dimensional transthoracic echocardiographic evaluation in the left lateral decubitus position from multiple windows. Echocardiographic evaluations were performed after 48–72 h of acute myocardial infarction and 6 months after the STEMI. A GE Vivid 3 (General Electric, Haifa, Israel) echocardiograph with a 2.5-MHz transducer was used. Echocardiography measurements were performed according to the recommendations of the American Society of Echocardiography, and the studies were recorded and stored on compact disks. The left ventricle volume and ejection fraction were obtained by the modified biplane Simpson's method. The left atrium and left ventricle end-diastolic and end-systolic dimensions were measured from the parasternal long-axis view.

Erectile function was evaluated by urology specialists using the International Index of Erectile Function (IIEF) during the hospitalisation period to identify sexual function just before the MI and 6 months after STEMI by the same urology specialists.[10] The answers to questions through 5 and 15 were used to determine the score for erectile function, and the cases were classified as without ED (score greater than 25 points) or mild (score 17 to 25), moderate (score 11 to 16) and severe ED (score 10 points or less). No treatment for ED was applied within the 6-month period prior to the second IIEF evaluation for each patient.

### Statistical analysis

Non-normally distributed continuous variables are presented as the median, interquartile range (IQR) and the minimum and maximum values, and the categorical variables are presented as the number and percentage. The comparisons between non-normal continuous variables regarding the treatment groups were performed with the Mann–Whitney U test, and chi-squared or Fisher's exact tests were used for categorical comparisons. Covariance analysis was used to compare the post-STEMI IIEF scores. The significance level was set as $P<0.05$.

## RESULTS

A total of 71 male patients were enrolled in this study (mean age: 54.3±10.1 years). Of these, 28 patients (39.4%) had an anterior MI, and 43 patients (60.6%) had a non-anterior STEMI. Fourteen patients (19.7%) had hypertension, 15 patients (21.1%) had diabetes mellitus, 55 patients (77.5%) had a smoking history and 21 patients (29.6%) had a family history of coronary heart disease. In terms of treatment, 45 patients (63.4%) were treated with PPCI, and 26 patients (36.6%) were treated with TT.

No significant differences were found between the two groups with respect to age, hypertension, smoking, dyslipidemia, reperfusion time, body mass index, peak troponin levels, left ventricular ejection fraction, left ventricular end-systolic and end-diastolic volumes, the type of reperfusion method used (PPCI or TT) or the STEMI localisation in both groups. Diabetes was more common in the TT group compared with the PPCI group (11% *vs.* 38%; $P=0.007$). Systolic blood pressure was higher in the TT group than the PPCI group (120±35 mmHg *vs.* 110±30 mmHg; $P=0.039$). Plasma fasting glucose levels were also higher in the TT group compared with the PPCI group (137±88 mg $dl^{-1}$ *vs.* 120±45 mg $dl^{-1}$; $P=0.009$) (**Table 1**). There was no statistically significant correlation between the localisation of the infarct, the heart rate on admission, the blood pressure on admission, the echocardiographic parameters or the ED parameters. The median post-STEMI IIEF score was higher in the PPCI group (26(12) *vs.* 19(7); $P=0.020$), and the decrease in IIEF score was lower in the PPCI group (2(8) *vs.* 6(7); $P=0.048$) (**Table 2**). The demographic and baseline characteristics of the study population revealed several differences; hence, the pre-STEMI IIEF score, the baseline systolic blood pressure, the baseline plasma glucose and the DM status were set as covariant variables, and the post-STEMI IIEF scores were compared without confounding the effects of these covariants. The estimated marginal mean±s.e.m. of the PPCI and TT groups were 21.4±0.7 and 21.0±0.9, respectively, and the difference in the

**Table 1 Patient demographic and baseline characteristics**

| | *PPCI* (N=*45*) | | *TT* (N=*26*) | | P |
|---|---|---|---|---|---|
| | *Median (IQR)* | *Min.–Max.* | *Median (IQR)* | *Min.–Max.* | |
| Age (year) | 53 (14) | 36–73 | 52 (20) | 42–77 | 0.396 |
| BMI (kg $m^{-2}$) | 26.8 (4.4) | 23.5–34.0 | 29.6 (5.1) | 21–36.5 | 0.141 |
| Reperfusion time (h) | 2.8 (2.4) | 0.5–12.0 | 3.0 (1.4) | 2.0–6.0 | 0.796 |
| Pulse ($min^{-1}$) | 75 (25) | 35–140 | 84 (22) | 51–110 | 0.166 |
| Systolic BP (mmHg) | 110 (30) | 50–180 | 120 (35) | 70–180 | 0.039* |
| Peak troponin (ng $dl^{-1}$) | 1.1 (3.1) | 0.0–14.0 | 2.2 (23.4) | 0.0–50.0 | 0.493 |
| Left ventricular ejection fraction (%) | 60 (14) | 40–70 | 57 (13) | 41–74 | 0.738 |
| Left ventricular end-systolic diameter (cm) | 3.4 (0.8) | 2.3–4.3 | 3.6 (0.7) | 1.9–4.5 | 0.473 |
| Left ventricular end-diastolyc diameter (cm) | 5.2 (0.7) | 3.1–6.6 | 5.3 (0.7) | 4.2–6.2 | 0.747 |
| Plasma glucose (mg $dl^{-1}$) | 120 (45) | 77–380 | 137 (88) | 99–360 | 0.009* |
| Anterior myocardial infarction, *n* (%) | 18 (40%) | | 10 (38%) | | 0.898 |
| Hypertensive, *n* (%) | 7 (16%) | | 7 (27%) | | 0.246 |
| Dyslipidemia, *n* (%) | 4 (9%) | | 0 (0%) | | 0.289 |
| Smoker, *n* (%) | 35 (78%) | | 20 (77%) | | 0.934 |
| Diabetic, *n* (%) | 5 (11%) | | 10 (38%) | | 0.007* |
| Family history positivity for coronary artery disease, *n* (%) | 14 (31%) | | 7 (27%) | | 0.710 |
| Pre-infarction angina, *n* (%) | 13 (29%) | | 9 (35%) | | 0.654 |

Abbreviations: BMI, body mass index; PPCI, primary percutaneous coronary intervention; TT, thrombolytic treatment; IQR, interquartile range.
*$P<0.05$, PPCI *vs.* TT.

estimated mean±s.e.m. between the groups was 0.4±1.2 ($P=0.730$). Multilinear regression analysis of ED after STEMI showed that only the reperfusion time (h) (beta coefficient=0.28; $P=0.01$) and the reperfusion method (beta coefficient= 0.34; $P=0.003$) were significantly different between the PPCI and TT groups, favouring PPCI for preserving erectile function after STEMI (**Table 3**).

**Table 3 Multilinear regression analysis of erectile dysfunction after acute ST elevation myocardial infarction**

| | *Beta coefficient* | P *value* |
|---|---|---|
| Age | −0.11 | 0.93 |
| Reperfusion time (h) | 0.28 | 0.01* |
| Reperfusion method | 0.34 | 0.003* |

*$P<0.05$, primary percutaneous coronary intervention *vs.* thrombolytic treatment.

## DISCUSSION

Previous randomized trials indicate that primary angioplasty in STEMI reduces the rates of death, stroke, recurrent ischemia and re-infarction compared with TT.[8] To the best of our knowledge, our study is the first study investigating the choice of reperfusion method on the incidence of ED after STEMI. As has been observed in many other areas, PPCI is superior to TT for preserving erectile function, independent of other risk factors. In other words, PPCI seems to be better than TT for preserving the patient's quality of life in terms of erectile function. The presence of diabetes mellitus or hyperglycemia as well as higher systolic blood pressure at the time of admission might be related to worse outcomes in the TT group. Hyperglycemia increases the levels of reactive oxygen species, such as superoxide anion, which inactivates nitric oxide to form peroxynitrite and increases oxygen-derived free radicals through activation of protein kinase C and other cellular elements.[11] Hyperglycemia and diabetes at the time of admission are both known to be negative prognostic factors in STEMI patients.[9] Diabetes mellitus, hyperglycemia and higher systolic blood pressure cause endothelial dysfunction, leading to a decrease in vascular nitric oxide levels and resulting in impaired vasodilation; the increase in the free radical concentration also leads to ED as well as to atherosclerotic damage.[9,11] Comparison of the covariant variables, the post-MI IIEF scores and the regression analysis revealed the superiority of PPCI over TT as a reperfusion strategy.

The duration of ischemia, estimated as the time from the onset of chest pain to time of re-opening of the occluded coronary artery, is the most important factor for myocardial functional recovery and mortality after myocardial infarction. The initiation of reperfusion therapy as early as possible has substantially decreased in-hospital mortality rates and has improved the outcome in survivors of the acute phase of MI.[9] There is a critical time period in the beginning of STEMI.[9] During first hour after the onset of angina, both reperfusion methods are equal with respect to the rates of death, stroke, recurrent ischemia and re-infarction. This study showed that early reperfusion therapy preserves

**Table 2 International Index of Erectile Function (IIEF) scores**

| | *PPCI* (N=*45*) | | *TT* (N=26) | | P |
|---|---|---|---|---|---|
| | *Median (IQR)* | *Min.–Max.* | *Median (IQR)* | *Min.–Max.* | |
| Pre-MI IIEF | 28 (4) | 19–30 | 25 (5) | 19–30 | 0.160 |
| Post-MI IIEF | 26 (12) | 10–30 | 19 (7) | 13–26 | 0.020* |
| IIEF difference (pre–post) | 2 (8) | (−1)–15 | 6 (7) | 0–15 | 0.048* |
| Pre-MI ED incidence, *n* (%) | 9 (20%) | | 9 (35%) | | 0.173 |
| Post-MI ED incidence, *n* (%) | 25 (56%) | | 21 (81%) | | 0.032* |

Abbreviations: ED, erectile dysfunction; IQR, interquartile range; MI, myocardial infarction; PPCI, primary percutaneous coronary intervention; TT, thrombolytic treatment.
*$P<0.05$, PPCI *vs.* TT.

the erectile function, regardless of the type of reperfusion strategy used. ED is a common health problem in patients with CAD, and the prevalence varies between 42% and 70%. There is an association between the severity of CAD and ED.[12–16] Many researchers have reported that ED manifests approximately 24–36 months before the manifestation of CAD.[12] Previous studies reported that the existence ED is associated with a twofold increase in the risk of STEMI among men.[14–16] Ortiz *et al.*[15] reported that the incidence of sexual dysfunction after STEMI ranges from 50% to 75% of all patients and is often present before the cardiac event. In the presence of many risk factors, atherosclerosis affects the endothelium of the arteries. Because the coronary arteries are larger than the penile arteries, they are better able to tolerate the stenosis, which delays the onset of symptoms.[15] Silent ischemia and ED are also known to occur in patients with uncomplicated diabetes.[16] These findings support the idea that ED and CAD share similar pathophysiological mechanisms and form a dangerous cycle.

Some of the data from our study were similar to data that have been previously reported in the literature. For example, 20% of the patients treated with PPCI and 35% of the patients treated with TT had ED before the STEMI. It was also surprising that the post-STEMI ED prevalences of both groups were higher than the expected levels, indicating the importance of the problem despite optimal treatment of the underlying cardiac problem. We did not apply any treatment for ED during follow-up after STEMI. However, those patients required more attention regarding the application of therapies such as beta blockers, and those patients were considered candidates for ED treatment.

According to the results of present study, we found that PPCI was favourable over TT to reduce the prevalence of ED after STEMI, and PPCI should be the preferred treatment when taking into account the patient's quality of life after STEMI. It is possible that the better microcirculatory perfusion provided by PPCI results in decreased vasoactive substance release from the myocardium and better protection of the microcirculatory function in other highly fragile organs. Further studies are needed to explain this link and determine the mechanism.

The absence of testosterone levels is a major limitation of this study. Other limitations are the small sample size and the absence of long-term follow-up.

## CONCLUSIONS

This study has two important findings: first, early reperfusion of STEMI can preserve erectile function; second, PPCI is superior to TT for reducing the prevalence of ED after STEMI.

## AUTHOR CONTRIBUTIONS

RA communicated the intellectual idea, designed the study and gave final approval of the version to be published. ÖK carried out the data analysis and wrote the manuscript. SO involved in drafting the manuscript, critically revising and important intellectual content. NK, LS, HE evaluated erectile function using the International Index of Erectile Function. MMB contributed to the interpretation of the patients' follow-up and data. MBV provided primary data interpretation, contributed to the writing of the manuscript, conducted the final review and edited the language. HK participated in the treatment of patients during hospital follow-up. EY supervised the primary percutaneous interventions and evaluated the echocardiography data.

## COMPETING FINANCIAL INTERESTS

The authors declare no conflict of interest.

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