Impact of Platelet Glycoprotein IIb/IIIa Receptor Inhibitors on Renal Function in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention

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Background: Worsening renal function in patients (pts) undergoing primary percutaneous coronary intervention (PPCI) for acute myocardial infarction (AMI) is associated with adverse clinical outcomes. Given platelet inhibition can modulate renal blood flow, we hypothesized that platelet glycoprotein IIb/IIIa inhibitors (GP IIb/IIIa) may decrease rate of renal function deterioration in pts undergoing PPCI. Methods and Results: Based on prospectively collected data, we analyzed rates of renal function deterioration in 603 consecutive pts (mean age 58±13 years, males 82%) with AMI treated with PPCI. Renal function deterioration was defined as an increase in serum creatinine (SCr) level of ≥25% or ≥0.5 mg/dl at 24 to 96 hours post-PCI compared with baseline value. Outcomes were stratified by treatment with GP IIb/IIIa. GP IIb/IIIa inhibition was associated with significantly lower rates of worsening renal function and lower 30-day mortality (Table). By multivariable analysis, adjusted for age, gender, diabetes mellitus, hypertension, baseline estimated glomerular filtration rate, anterior MI, Killip class on admission, and volume of contrast medium, treatment with GP IIb/IIIa was an independent predictor of preventing renal function deterioration after PPCI (odds ratio 0.35; 95% confidence interval 0.17 to 0.72; p=0.004). Conclusion: In this analysis, administration of GP IIb/IIIa to pts undergoing PPCI was associated with lower rates of worsening renal function and lower 30-day mortality.

Endpoints, %	GP IIb/IIIa inhibitors		P-value
	(+) N = 442 patients	(-) N = 161 patients	
SCr increase ≥25%, n (%)	101 (22.9)	51 (31.9)	0.02
SCr increase ≥0.5 mg/dl, n (%)	18 (4.1)	14 (8.8)	0.02
Maximum SCr change, mean±SD, mg/dl	0.14 ± 0.38	0.25 ± 0.45	0.005
30-day mortality, n (%)	10 (2.3)	12 (7.5)	0.005

Prognostic Value of Transient and Sustained Worsening Renal Function After Primary Angioplasty

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Background: Worsening renal function (WRF) is common in patients undergoing primary angioplasty and is associated with poor outcome. This study sought to determine the long-term prognostic implication of transient vs. persistent WRF after primary angioplasty for ST-elevation myocardial infarction (STEMI).

Methods: We used a prospective database consisting of all patients admitted with acute STEMI. A total of 572 patients were treated with primary angioplasty and survived the index hospitalization. Venous blood samples for creatinine were obtained on admission and at 24-h, 48-h, and 72-h thereafter. After the first 72-h from admission, creatinine measurements were checked only when clinically indicated. Patients were classified into 3 groups: 1) Patients without WRF during hospitalization (change in creatinine <25%); 2) Patients with an increase in creatinine of >25% that resolved by discharge (transient WRF); and 3) patients with an increase in creatinine >25% that did not resolve (persistent WRF). The primary end point was all-cause mortality after hospital discharge. The median follow-up was 15 months.

Results: During hospital course, transient and persistent WRF occurred in 62 (16.8%) and 76 (13.3%) patients, respectively. Mortality rates were higher in patient with transient or persistent WRF as compared with patients without WRF (16.1% and 11.8% vs. 4.4%, respectively; $P<0.0001$; **Figure**). In a Cox model, adjusting for multiple baseline characteristics (age, gender, baseline creatinine, hypertension, diabetes, smoking, anterior location of infarction, Killip class at admission), both transient (hazard ratio 3.0, 95% confidence interval 1.3 to 6.8; $P = 0.01$) and persistent WRF (hazard ratio 2.6, 95% confidence interval 1.1 to 6.2; $P = 0.02$) remained a significant independent predictor of post-discharge mortality.

Conclusion: Worsening of renal function after primary angioplasty is an important risk factor for long-term mortality after hospital discharge. Furthermore, even a transient creatinine elevation is associated with increased risk.
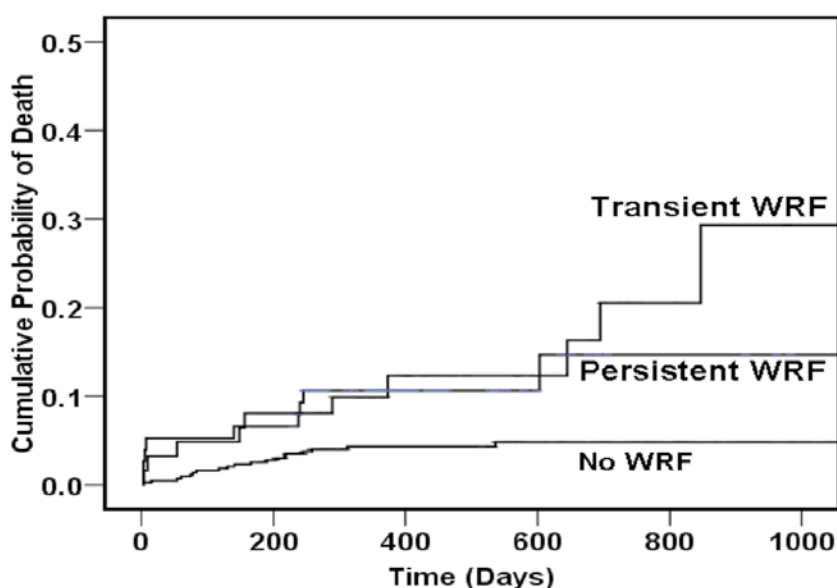
Figure: Kaplan-Meier curves of patients without WRF, patients with transient WRF, and patients with persistent WRF.

The Prevalence of Acute Myocardial Infarction Among Patients Presenting with Sustained Monomorphic Ventricular Tachycardia (SMVT)

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Sustained monomorphic ventricular tachycardia (SMVT) is a life threatening arrhythmia usually occurring in patients with structural heart disease. Since the symptoms and signs of SMVT can resemble an acute myocardial infarction (AMI), many patients presenting with SMVT on their first ECG are evaluated and treated for AMI. However, whether SMVT can be the presenting manifestation of AMI has received very little attention in the literature. Our goal was to determine the prevalence of AMI among patients presenting with SMVT.

Methods: 90 consecutive patients presenting with SMVT on their initial ECG were included in thus study. ECG tracings obtained immediately after restoration of sinus rhythm were read by "blinded" investigators. Coronary angiograms were read by a "blinded" investigator to assess for angiographic evidence of an acute coronary lesion. Among patients who satisfied the AMI criteria, we further defined a "primary" AMI as one associated with an acute coronary lesion, and a "secondary" AMI as one secondary to the arrhythmia.

Results: Patients' age was 65.2 ± 13 years and 83% were men. 72% had previous AMI. the most prevalent presenting symptoms were palpitations and chest pain (36% EACH) Heart rate during SMVT was 183 ± 43 and 40% were of RBBB configuration. Of the 90 patients, 54 (60%) underwent coronary angiography during the index hospitalization. Fourteen patients (15%) fulfilled the criteria of AMI, of whom only three (3%) fulfilled our definition of "primary" AMI.

During 916 ± 1269 days follow up of 70 patients who received an ICD, 51 (78%) had recurrent SMVT which required treatment by the device.

Conclusion: SMVT is a very rare initial presentation of AMI, , and acute coronary lesions are seldom identified during angiograpy. Thus, SMVT should be regarded as an arrhythmia secondary to a prior cardiac scar. The high rate of recurrent events among those patients strengthens this conclusion.

Primary PCI in Unconscious Patients with Acute Myocardial Infarction After Out-of-hospital Cardiac Arrest

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Background. The decision to perform primary percutaneous coronary intervention (PrPCI) in unconscious patients after out-of-hospital cardiac arrest (OHCA) is challenging due to uncertainty of prognosis of anoxic brain damage and difficulties of interpretation of ECG changes shortly after CA and CPR.

Aim. To evaluate outcome of unconscious patients with acute myocardial infarction resuscitated after OHCA who were treated with PrPCI and in whom this procedure was withheld.

Patients. Data sources: Rambam Intensive Cardiac Care (RICCa) and Primary Angioplasty Registry Rambam (PARR) databases - an ongoing registries of all consecutive patients admitted to ICCU and all consecutive patients treated according to PrPCI strategy, respectively. Study period: 01.2000-12.2006.

Results. Overall 45 patients were identified, 17(38%) were treated according to PrPCI strategy. Patient characteristics and outcomes presented in table (%).

	PCI (n=17)	No PCI (n=28)	P value
Age	59±11	68±12	0.023
Male	14 (82)	23 (82)	NS
Witnessed CA	16 (94)	26 (93)	NS
Bystander CPR	1 (6)	6 (21)	NS
Initial rhythm – asystole	2 (12)	11 (39)	0.048
Card. Shock	3 (18)	10 (36)	NS
STEMI	12 (71)	19 (68)	NS
Anterior location	7 (41)	7 (25)	NS
Severely reduced syst.LV function	4/15 (27)	10/16 (63)	0.045
Therapeutic hypothermia	2 (12)	4 (14)	NS
Survival	13 (76)	3 (11)	0.0001
Survival with good neurological outcome	9 (53)	1 (4)	0.0001

Conclusions. Patients after OHCA treated with PrPCI had better in-hospital survival and survival with good neurological outcome. These patients also had more favorable clinical characteristics which contributed to better outcome.

The Linear External-Work Pressure-Time Integral Relationship Ties the Frank and Starling Phenomena Together and Elucidates the Regulatory Roles of the Preload and Afterload

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Background: The mechanisms underlying the Frank Starling Law (FSL) of the heart are elusive and the prevalent concept suggests that the FSL is afterload independent. Isolated fiber studies suggest that the afterload determines cardiac function by modulating cross-bridge cycling and through established cross-bridge dependent cooperativity mechanisms. The study unveils the role of the afterload at the whole heart level. **Methods and Results:** The LV was exposed by left-thoracotomy in adult sheep (69.1±9.6Kg, n=8). Different afterloads were imposed by partial aortic occlusions. Transient inferior vena-cava occlusions (tIVCOs) were preformed at each steady afterload. External work (EW) and pressure time integral (PTI) were measured for each beat during the tIVCOs. A highly linear EW-PTI relationship (WPTiR) was found for each afterload (R^2=0.98±0.02) during the tIVCOs (n=54). Interestingly, the slope of the WPTiR was determined by the afterload. The slope was 34±2.8 mJ/mmHg/sec at baselines and decreased by 0.91±0.53 mJ/mmHg/sec per 1 mmHg·min/L increase in the peripheral resistance. The preload has a proportional effect on the EW and PTI. The afterload has opposing effects on the PTI and EW. Furthermore, a unique WPTiR was obtained during both occlusion and release phases of each tIVCO, while two distinct EW-preload relationships were observed, implying that the linear WPTiR is not a result of the FSL but relates directly to the underlying mechanism. **Conclusions:** A novel linear and afterload dependant WPTiR was described. This consistent WPTiR represents a basic feature of cardiac control of contraction that ties the Frank (pressure-preload) and Starling (EW-preload) phenomena together.

Sarcomere Lengthening Decreases the Rate of Cross-Bridge Cycling; Implications for the Ischemic Myocardium.

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The effects of stretch, encountered in ischemic myocardium, on force development and energy consumption, are not well understood. Prevalent theories suggest that stretch increases the force per cross-bridge (XB) but decreases the number of strong XBs (N_{XB}). We hypothesize that XB kinetics is determined by the filament sliding velocity. XB transition-rate from strong to weak state increases during shortening and decreases during stretch. Consequently, the stretch increases the force by increasing N_{XB}. The study investigates these opposing predictions under stretch conditions. **Methods:** Trabeculae were isolated from rat right ventricles. Sarcomere length was measured by laser diffraction and controlled by a fast servomotor. The number of strong XB (N_{XB}) was evaluated by fast and small oscillations. Stretches at different velocities (0-2.4μm/s) and instants were imposed on isometric twitches. **Results:** Faster stretches yielded larger forces. A tight linear correlation between force and N_{XB} was obtained, implying that the force increased due to the increase in N_{XB}. The phenomenon can not be attributed to the Force-length relationship since fast stretches (>1.6μm/sec) increased N_{XB} by >100% with only small (7.8%) sarcomere lengthening. Identical increase in force and N_{XB} was observed when similar stretches were imposed at different instants, suggesting that the phenomenon is activation level independent. **Conclusions:** stretch increases the number of strong XBs but decrease XB cycling rate and energy consumption. This yields a protective effect in the stretch ischemic myocardium by reducing energy consumption. The post-systolic shortening may results from the energy stored in the XBs that were recruited during the stretch.

Routine Upstream Use of GP IIb/IIIa Inhibitor (Eptifibatide) Preceding Primary PCI in STEMI

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Background: TIMI-3 flow rates pre primary-PCI (PPCI) for STEMI preceded by conventional therapy (aspirin and heparin) are reported in only 10-15% of patients. Adjunctive therapy with IIb/IIIa inhibitors before PPCI might increase these rates.

Methods: 144 patients (age 59 ± 13 yrs) with STEMI <12 h who underwent successful PPCI were pre-treated by protocol, with eptifibatide (in the CCU or ER) before emergency catheterization over the last 4 years (2004-2007). The primary end-point was TIMI-3 flow in the infarct-related artery on the first diagnostic angiogram pre PPCI.

Results:

Pain to Balloon (hr)	N	TIMI -0	TIMI -3	Eptifibatide to balloon (min)
<3	65	25 (38%)	25 (38%)	56 ± 22
3-6	51	17 (33%)	16 (31%)	85 ± 43
>6	28	16 (57%)	6 (13%)	100 ± 92
All	144	58 (40%)	47 (33%)	70 ± 56

The average time from pain onset to eptifibatide therapy was 100 min in pts with TIMI-3 flow, and 150 min in all other pts. TIMI 2-3 flow was more frequently observed in pts who received eptifibatide <180 min from pain onset than in those who received it >180 min from pain onset (53% vs. 30%, respectively, $p < 0.01$). The average duration of eptifibatide therapy before PPCI was 70 min (range 10-270 min).

Conclusions: Routine adjunctive upstream use of eptifibatide in the ER or CCU in patients with STEMI before PPCI is associated with a 33% TIMI-3 flow in the infarct-related artery prior to intervention. This rate seems to be inversely correlated with the time from pain onset to eptifibatide therapy.

Stent Thrombosis Clinical Manifestation: Drug Eluting vs. Bare Metal Stents

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Background: Stent thrombosis has been the focus of intense interest because of high associated morbidity and mortality.

Objectives- We investigated the differences in angiographic definite stent thrombosis (ST), according to ARC definition, in patients with drug eluting stents (DES) vs. bare metal stents (BMS) implanted at out institution.

Methods: We evaluated all consecutive ST events during the period from 8/2000 and 7/2007, and recorded in details their clinical characteristics, median time to the ST event and outcomed in term of mortality at 30 days and 6 month.

Results: During the last seven years we identify 52 patients (55 vessels) who developed ST in the BMS group and 17 patients (19 vessels) that had ST in DES. Patients' demographics are described in the following **Table**.

Stent Thrombosis	BMS	DES	P value
Patients No	**N=52**	**N=17**	
Age (yr)	63±12	61±11	
Male	81%	71%	0.4
HTN	55%	53%	0.7
Dyslipidemia	55%	71%	0.4
Smoker	35%	18%	0.04
NIDDM	33%	29%	0.8
Previous CABG	2%	29%	0.04
renal failure	12%	24%	0.3
2/3 VD	54%	82%	0.08

The median time to stent thrombosis was 6 days (range 3 to 60d) in the BMS versus 100 days (range 14 to 450) in the DES group (p=0.03). ST in BMS was associated with mortality at 30 days of 7.7% as compare to 5.9% in the DES group (p=0.8). Following 6 month, the mortality rate in the BMS group was 19% vs. 12% in the DES group (p=NS). Recurrent ST were encountered in 4 patients in each group, with one (25%) mortality event in the BMS group, no mortality in the DES group and the need for revascularization (PCI, CABG) was 50% in both groups.

Conclusions: ST remains a severe complication for both BMS and DES although the average time interval from implantation to event is different (i.e. longer for DES vs. BMS). There was no difference in terms of mortality in both groups after six month but we noticed a worse prognosis among patients with ecurrent episodes of ST.

Prevalence and Prognostic Significance of Persistent Anemia after Acute Myocardial Infarction

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Background: Recent studies have shown that anemia occurring during an acute myocardial infarction (AMI) is an independent indicator of mortality. Anemia may be viewed as a transient phenomenon, secondary to antithrombotic agents and invasive procedures. However, anaemia might worsen or fail to improve after hospital discharge .

Methods: We studied 1110 pts with AMI who survived the acute event. Hemoglobin (Hb) levels were obtained at hospital discharge and >3 weeks after discharge (median 5.2 months). The relationship between post-discharge Hb and the primary endpoints of all-cause mortality were evaluated using Cox models, adjusting for age, gender, creatinine, previous infarction, diabetes, hypertension, smoking, anterior infarction, coronary revascularization during hospital stay, Killip class at admission, presence of known malignancy, pre-discharge Hb and pre-discharge ejection fraction .

Results: Using the WHO definition (Hb < 13 g/dL in men and < 12 g/dL in women), anemia was present in 392 pts at hospital discharge (35.3%). At follow up, anemia was present in 218 (55.6%) and 64 (8.9%) pts with and without anemia at hospital discharge, respectively. During a median follow up of 13 months after the post-discharge Hb measurements, 89 patients died (8.0%). The Kaplan-Meier curves of pts with and without anemia after hospital discharge are shown in the Figure. In a multivariable Cox regression model, the adjusted HR was 1.3 for each 1 gr/dL decrease in post discharge Hb (95% CI 1.1-1.4, P = 0.0004). In a similar model, the HR for mortality in pts with anemia after hospital discharge was 2.0 (95% CI 1.2-3.4, P = 0.008) compared with pts with increasing Hb level.

Conclusion: Pts after AMI who are discharged with anemia frequently fail to increase their Hb levels, and some Pts develop anemia after hospital discharge. Persistent or worsening anemia after AMI is associated with markedly increased risk for mortality .

Figure: Mortality of patients with and without post-discharge anemia
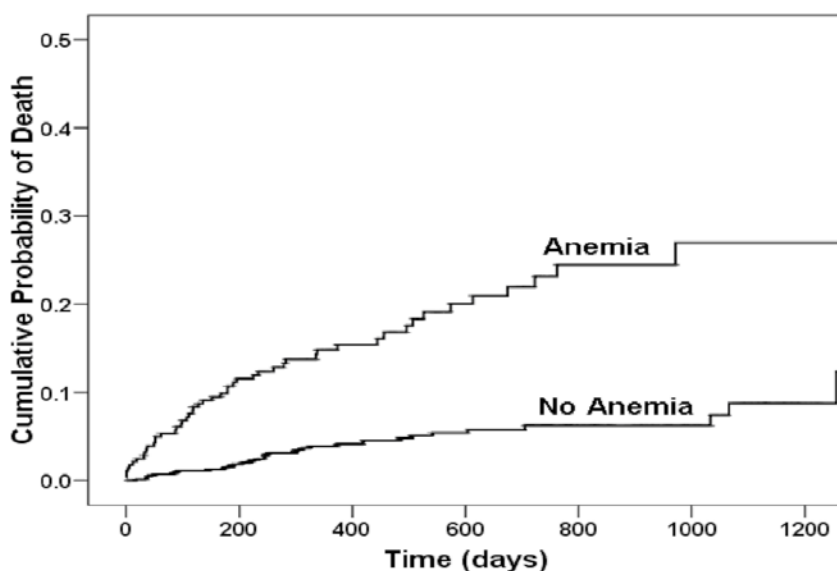
Relationship between Activated Clotting Time (ACT) and Ischemic and/or Hemorrhagic Complications Following Primary PCI in STEMI pts Treated with Heparin Combined with Eptifibatide

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BACKGROUND: Unfractionated heparin (UFH) is the most widely used anti-thrombin medication during percutaneous coronary intervention (PCI). Uncertainty remains about the optimal activated clotting time (ACT) for prevention of ischemic or hemorrhagic complications especially when combined with GP-IIb/IIIa receptor inhibitors.

AIM: We tested the relationship between ACT and cardiac or bleeding complications in STEMI pts undergoing primary PCI and treated using UFH in conjunction with GP-IIb/IIIa receptor inhibitors (eptifibatide [Ept] as a bolus plus infusion for 8-18 h).

METHODS: We evaluated the outcome at 30 days of 527 consecutive patients who underwent primary PCI. Patients were divided into 25-s intervals of ACTs.

RESULTS: The main results are shown in the **Table** as follow:

	<216 sec N=128	216-244 sec N=134	245-280 sec N=133	>280 sec N=132	P-value
Age (year)	58±12	59±11	58±12	60±12	0.5
Male	90%	87%	85%	78%	0.05
DM	22%	31%	16%	19%	0.02
Ant MI	48%	47%	43%	48%	0.9
2/3 VD	56%	65%	51%	57%	0.1
BMI (Kg/m^2)	27.5±4.2	26.9±4.3	27.3±3.6	27.6±4.2	0.6
Hemoglobin drop{mg%}	0.6±1.0	0.7±1.0	0.9±1.3	1.0±1.2	0.02
30 d Death	2.3%	2.2%	0%	0%	0.1
30 d ST	2.3%	3%	1.5%	0%	0.1
30 d Re-MI	3.1%	2.2%	1.5%	0.8%	0.5
Groin Hematoma	3.9%	1.5%	5.3%	4.6%	0.4
MACE	6.3%	7.5%	3.8%	3.8%	0.4
Hemorrhagic CVA	0%	0%	0%	0%	1.0

CONCLUSIONS: In STEMI patients undergoing primary PCI and treated using UFH+Ept, an ACT higher than >245s tended to be associated with better suppression of ischemic events but at hazards of higher hemoglobin drop due to hemorrhagic complications during the course of hospitalization.

The Significance of ST Elevation in Right Precordial Leads in Acute Anterior Myocardial Infarction

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Background: The clinical implications of ST-segment elevation in the right precordial leads in the circumstances of anterior acute myocardial infarction (AMI) are unknown.

Objectives: To asses the clinical utility of ST-segment elevation in leads V_3R and V_4R in anterior AMI.

Methods: This study comprised 120 consecutive patients admitted within 12 hours of symptom onset of anterior ST elevation AMI. All had 18-lead electrocardiograms with right precordial leads. Patients were stratified into two groups based on whether they had ST elevation ≥ 1 mV in V_3R and V_4R (group A) or not (group B).

Results: Group A included 39 patients (age mean±SD 59±11 years, males 82%) and group B included 81 patients (age 58±14 years, males 84%). Group A patients were more likely to experience primary ventricular fibrillation (VF) and comprised more patients who suffered from heart failure (HF) during hospitalization, compared with group B [for VF 8/39 (20%) vs. 2/81(2%), p=.0019, for HF 15/39 (38%) vs. 14/81(17%), p=.021]. Patients in group A compared with group B had a trend towards less spontaneous reperfusion (14% vs. 32%, p=.063), and had a higher incidence of multivessel coronary artery disease [median (interquartile range) of 2 (1-3) vs. 1 (1-2), p=.097 respectively]. There was no significant difference in the size of the infarct analyzed by peak CPK, or sum of ST-segment elevations.

Conclusions: In anterior ST-segment elevation AMI, right precordial leads could predict primary VF and HF during hospitalization, and if confirmed in large cohorts should be a routine part of the initial electrocardiogram.