

Impact of Revascularization on Outcomes in Patients with Non-ST-Elevation Acute Coronary Syndrome and Congestive Heart Failure. The Global Registry of Acute Coronary Events (GRACE)

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Background: Congestive heart failure (CHF) is a common and severe complication of Non-ST-Elevation (NSTEMI) acute coronary syndromes (ACS). It is associated with a major increase in short and long term mortality. Yet, patients with ACS and CHF are less likely to undergo coronary angiography or revascularization than ACS patients without CHF.

Aim: The aim of this study is to analyze the impact of early revascularization on outcomes.

Methods and Results: Of the 29 844 patients with NSTEMI-ACS enrolled in the Global Registry of Acute Coronary Events between April 1999 and June 2007, 4953 had CHF at presentation. One-fifth of the patients with CHF underwent in-hospital revascularization vs 35% in those without ($P < 0.001$). Revascularized patients with CHF were younger (72 vs 76 years) and more likely to be male (65% vs 55%) than nonrevascularized CHF patients. They also had lower heart rate (81 vs 88 beats/min), higher ejection fraction (49% vs 40%), and less frequent history of stroke (11% vs 16%) or CHF (24% vs 42%) (all $P < 0.001$). Patients who underwent revascularization were more likely to receive evidence-based cardiac medications during hospitalization (aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, thienopyridines, statins, and glycoprotein IIb/IIIa inhibitors) compared to patients who did not undergo revascularization. Patients with CHF had higher mortality rates in hospital (8.9% vs 0.9%) and from discharge to 6 months (9.6% vs 2.9%). After adjustment in a Cox model, patients who were revascularized had a lower risk of post-discharge to 6-month mortality (hazard ratio 0.64; 95% confidence interval 0.45–0.93).

Conclusions: Data from this large, multinational, contemporary observational study suggest that in patients with NSTEMI-ACS complicated by CHF, use of revascularization during the index hospitalization is associated with a significantly improved survival 6 months after discharge. These observations support current guidelines, which recommend early revascularization in high-risk NSTEMI-ACS patients and suggest substantial underuse of revascularization in this high-risk population.

The Obesity Paradox in Acute Coronary Syndrome Patients in Israel

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Background: While obesity is a coronary disease risk factor, its effect on acute coronary syndrome outcome (ACS) is inconsistent.

Methods: To explore the impact of body mass index (BMI) on short (30-day) and long (1-year) term clinical outcome, we retrospectively analyzed data of 5,751 patients [4,400 (77%) males, 2,754 (48%) with and 2,994 (52%) without ST-segment elevation ACS] from the Acute Coronary Syndrome Israel Survey (AC SIS), comprising data from ACS patients hospitalized in 2002, 2004 and 2006 during 2 months period in all coronary care units in Israel.

Results: Patients were divided into National Institutes of Health BMI-based 4 categories (Table). Mean BMI increased significantly during 2002, 2004 and 2006 (27.0 ± 4.0 , 27.2 ± 4.3 and 27.7 ± 4.5 kg/m², $p < 0.0001$; respectively). Time from chest pain onset to hospitalization and invasive procedure, Killip class on admission, left ventricular ejection fraction, creatinine clearance and in-hospital therapy were the same in all 4 groups.

	Underweight BMI<18.5 (n=43)	Normal 18.5-24.9 (n=1709)	Overweight 25.0-29.9 (n=2700)	Obese BMI≥30 (n=1299)
Age (yrs)	69.9±17.7	65.3±13.7	63.3±12.6*	61.4±12.4*
30-d mortality	9.3%	5.6%	3.3%	4.7%
OR [†] (95% C.I.)	0.91 (0.24-2.69)	1.0	0.50 (0.38-0.67)	0.88 (0.62-1.22)
1-year mortality	20.7%	12.3%	8.2%	9.4%
OR [†] (95% C.I.)	1.0 (0.34-2.96)	1.0	0.63 (0.49-0.80)	0.78 (0.57-1.06)

Values are expressed as mean±SD; * p for trend<0.0001; [†]OR=odds ratio adjusted for age, sex, hypertension, past angina, past myocardial infarction, smoking, hyperlipidemia, renal failure, stroke, peripheral vascular disease, > Killip 2, previous procedures (coronary artery bypass grafting operation, percutaneous coronary intervention), ST-segment elevation; BMI= kg/m².

Conclusion: Overweight and obese BMI-based categories were associated with younger age and better survival than normal and underweight ACS patients. Our observation of a U-shaped relationship between increasing BMI and mortality in ACS patients warrants careful prospective evaluation.

Bypassing the Emergency Room to Reduce Door-to-Balloon Time in Primary PCI Improves Clinical Outcome – Experience from the Acute Coronary Syndrome Israeli Survey (AC SIS)

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Background – Primary PCI (PPCI) is the reperfusion strategy of choice for patients (pts) with ST Elevation Myocardial Infarction (STEMI). *Door-to-balloon time* is a strong predictor of myocardial salvage and clinical outcome. Only 35% of STEMI pts meet the recommended goal of the 2004 ACC/AHA Guidelines of ≤ 90 minutes. The objective of this work is to assess the strategy of direct referral of STEMI pts to the CCU for PPCI as observed from the national ACSIS 2004 and 2006.

Methods and Results – Data were collected from the ACSIS 2004&2006. We examined the effect of admission pattern [*Emergency room(ER), Direct to CCU (CCU)*]; on the time line and clinical outcome in the STEMI pts who underwent PPCI. Out of 4171 pts with ACS, a total of 1924 (46%) presented with STEMI, of them 793 (41%) underwent PPCI [583 pts (73.5%) arrived to ER, 193 pts (24.3%) arrived directly to CCU, (for 17 pts (2.1%) full data were missing)].

		ER	CCU	Pvalue
Door-to-balloon time (median, min)		79	45	0.018
Adherence to Guidelines (≤ 90 min)		59.2 %	88.8 %	<0.0001
Mortality (%)	30 days	5.3	6.2	NS
	1 year	7.3	6.1	NS
30-d MACE (%)		30	22.3	<0.038

Conclusions –

In the ACSIS; direct referral to the CCU for Primary PCI, by bypassing the ER, significantly reduces the Door-to-Balloon time, increases the rate of adherence to guidelines, and improves the clinical outcome. A national system for bypassing the ER in STEMI patients should be encouraged.

Optimal Timing of Percutaneous Coronary Intervention after Successful Thrombolysis – Analysis of Data from ACSIS 2002-2006

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Introduction: Clinical guidelines recommend routine angiography and percutaneous coronary intervention (PCI) after successful thrombolysis. However, the optimal timing of PCI has not been determined yet.

Methods: We analyzed data of the Acute Coronary Syndrome Israeli Survey (AC SIS) from 2002 to 2006. We excluded patients with failed thrombolysis. Patients with successful thrombolysis were divided to 3 groups: Group A - patients (age 61.6±13.6) who did not undergo PCI (n=150), of whom 30.7% did undergo angiography; Group B (age 57.8±12.4) – underwent PCI within 48 hours from admission (n=34); Group C (age 58.3±10.6) – underwent PCI >48 hours after admission. Major adverse cardiac events (MACE) were defined as death and re-infarction at 7 & 30 days.

Results: Patient in group A were significantly older (p=0.01). Most patients (86.5%) underwent PCI >48 hours after admission. MACE at 30 days occurred in 17.4% in group C, lower than groups B (35.3%) and A (26.7%) (p=0.019). Mortality at 7 days was higher in group A versus groups B & C, respectively (4.7%, 2.9%, 0.9%, p=0.006). Post infarction angina occurred more in group B than A & C, respectively (11.8%, 2%, 7.3%, p=0.027). Killip II on admission was highest in group A vs. groups B & C, respectively (12.7%, 8.8%, 6.0%, p=0.001).

Conclusions: Patients who did not undergo PCI after successful thrombolysis had worse outcome at 7 & 30 days. Patients who underwent PCI >48 hours after admission had the best outcome. Heart failure and post infarction angina were significantly more frequent in those who underwent early PCI.

Comparison of Recurrent to First Acute Myocardial Infarction Patients in Israel in 1998-2006

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Recurrent acute myocardial infarction (AMI) patients, who represent 14 to 30% of patients hospitalized for AMI, are at increased risk for complications and death following their acute coronary event

Objective: We compared the outcome of recurrent to first acute ST-elevation myocardial infarction (AMI) patients hospitalized in coronary care units in 1998-2006.

Methods: We performed biennial prospective nationwide AMI/ACS surveys, collecting data prospectively during January-February 1998, February-March 2000, February-March 2002, February-March 2004 and March-April 2006 from all patients hospitalized in all 25 operating CCUs in Israel

Results: Our cohort comprises of 4,511 STEMI patients, 3,651 First and 860 Recurrent MI. In-hospital complications occurred significantly less frequently in first AMI patients.

	1998	2000	2002	2004	2006	P trend
First MI	N=662	N=758	N=759	N=759	N=713	
Age (yrs)	63	62	62	62	61	0.04
Primary PCI	8	10	28	44	48	0.0001
Thrombolysis	54	50	35	22	15	0.0001
7-day mortality	5.1	7.7	4.4	4.3	3.2	0.005
30-day mortality	8.8	10.8	6.3	6.7	4.8	0.0001
Recurrent MI	N=148	N=190	N=188	N=173	N=161	
Age	66	66	65	65	64	0.58
Primary PCI	5	17	18	40	42	0.0001
Thrombolysis	49	44	30	19	14	0.0001
7-day mortality	8.8	7.4	8.0	5.8	7.5	0.53
30-day mortality	11.5	13.7	10.6	9.2	9.3	0.23

Conclusions: In spite of high rate of primary PCI in both first and recurrent STEMI patients, while mortality and hospital complication rates significantly declined in First MI patients, they remain high in Recurrent MI patients. Improved therapeutic approach is needed in these high risk cohort of patients.

Trends in Management and Outcome of Elderly Patients with STEMI in Israel: Data from ACSIS 2000-2006

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Background: The management and outcome of AMI pts have recently undergone major changes, reflecting the implementation of new treatment guidelines.

Aim: To evaluate trends in management and their impact on early mortality of elderly (≥ 75 yrs) pts with STEMI admitted to all 26 operating CCUs in Israel in 2000-2006.

Methods: The data were derived from biennial 2-monthly prospective nationwide ACS surveys (AC SIS 2000-2006).

Results: The age (81 ± 5 y), prevalence of women (41-49%), risk factors, and Killip-class \geq II on admission (33-38%), were comparable throughout the study period.

	2000	2002	2004	2006
	(N=224)	(N=208)	(N=208)	(N=162)
Rx in-hospital♥:	%	%	%	%
Aspirin	93	95	98	99
Clopidogrel	9	37	53	73
b-blockers	59	65	77	70
ACE-I/ARB	63	67	74	77
Statins	17	40	61	88
*SCORE(4)	8	21	43	53
Primary reperfusion	38	45	46	54
TLx/primary PCI	80/20	56/44	38/62	18/78
Angio	34	48	64	91
PCI in hospital	21	38	50	60
Stent	10	27	43	56
30-day mortality	26.8	18.3	17.3	16.0
Covariate adjusted OR (95% CI) [†]	1.0	0.45 (0.26-0.75)	0.42 (0.25-0.70)	0.37 (0.20-0.67)

♥ *p* for trend < 0.001 for all comparisons.

*SCORE(4)- management with 4 evidence-based medications (aspirin, b-blockers, ACE-I/ARB, statins).

[†] Adjusted for: age, sex, Killip (admission) \geq II, Anterior MI, heart-rate > 100 bpm, SBP < 100 mmHg, history of diabetes, hypertension, angina, renal failure, year performed.

Conclusion: In recent years the extent of both medical and interventional management of elderly STEMI pts changed substantially. The high degree of implementation and adherence to recommended guidelines was associated with a significant decline in early mortality.

Stent Thrombosis: A Poor Man's Disease?

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Objectives: Stent thrombosis (ST) is a rare but devastating complication of coronary stent implantation. ST incidence and potential predictors were assessed in a "real world" single center.

Methods: We searched our database for cases of "definite" stent thrombosis (according to the ARC Dublin definitions). Each case was matched by procedure date, age and gender, with 3 cases of stenting that did not result in ST. Demographic and clinical parameters were compared and socio-economic status was determined according to "Geocartography" polling and market survey database.

Results: 3401 patients underwent stent implantation at our hospital during 2004-2006. 29 cases (0.85%) of "definite" subacute / late stent thrombosis were recorded. No mortality was recorded during 30 days, which may imply a low rate of ST detection that is based on the strict angiographic criteria. Thrombosis occurred 2 days-3 years after stent implantation. Eighty percent of the patients were males and the mean age was 63 ± 11 . All presented with acute myocardial infarction (AMI). Premature clopidogrel administration was reported in 60%. Patients with ST had significantly higher rates of AMI at the time of initial procedure (76 vs. 32%, $p<0.001$), cigarette smoking (60 vs. 28%, $p<0.001$) and use of long stents ($>15\text{mm}$, 72 vs. 60%, $p=0.01$). Bare metal and drug eluting stents use were similar between the groups. Socioeconomic status was significantly lower at the ST group, 4 ± 0.6 vs. 5.4 ± 0.3 (mean \pm SE, scale 1-10, $p<0.05$).

Conclusions: Stent thrombosis incidence in our population is at least 0.85%. ST appears in patients of significantly lower socio-economic status in addition to certain clinical predictors. These results warrant stricter follow-up and support policy by healthcare providers on patients at risk for stent thrombosis.

Chronic Pre-treatment with Statins and the Outcomes of Patients with ST-Segment Elevation Myocardial Infarction Treated with Primary PCI

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Background: Beyond lipid-lowering effects, statins have favorable effects on platelet adhesion, thrombosis, endothelial function, plaque stability, and inflammation. These pleiotropic effects could contribute to the preservation of microvascular function during ischemia and reperfusion. There is limited data about the impact of chronic pre-treatment with statins on the outcome of patients with ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI). Accordingly, our aim was to evaluate the effect of previous treatment with statins on clinical outcomes of such patients.

Methods: We studied 950 consecutive patients with STEMI treated with primary PCI, who were included in our primary PCI registry between 01/2001 – 07/2007. Excluded were patients with cardiogenic shock. Patients were allocated into two groups: those who received chronic pretreatment with statins (n=327) and those who did not (n=623).

Results: As shown in the Table below, despite significantly worse baseline clinical characteristics and similar procedural characteristics, patients who received previous treatment with statins had a lower 30 day mortality rate. At 6 months mortality differences were no longer significant. Multivariate analysis adjusted for factors such as diabetes and the CADILLAC score, showed that previous statin therapy was associated with an odds ratio of 0.4 (0.13-0.96, P=0.04) for 30 day mortality.

Conclusions: The present study suggests that chronic pretreatment with statins before primary PCI for STEMI may be associated with lower short-term mortality, possibly through preservation of the microvascular integrity. Large prospective trials should be performed to verify these findings.

Variable	Previous Treatment with Statins (n=327)	No Previous Treatment with Statins (n=623)	P value
Mean Age (yrs)	62±12	60±13	0.006
Women	22%	16%	0.03
Diabetes	34%	20%	0.0001
Hypertension	58%	38%	0.0001
Hyperlipidemia	79%	27%	0.0001
Smoker	40%	48%	0.01
Previous MI	18%	8%	0.0001
Previous CABG	5.8%	1.1%	0.0001
LVEF<40%	41%	43%	0.5
CADILLAC score	4.5±3.5	4.1±3.6	0.1
Post TIMI 3 flow	96%	95%	0.8
No Reflow	5.3%	6.2%	0.6
GP IIb/IIIa use	75%	78%	0.2
Procedural Success	96%	95%	0.8
Clinical Outcomes			
30 day death	1.5%	3.7%	0.05
30 day re-MI	3.4%	2.6%	0.5
6 months death	4.1%	5.8%	0.3
6 months re-MI	5.8%	4.4%	0.3

Comparative Analysis between Real World Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting for Unprotected Left Main

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Background – Revascularization procedure for unprotected left main (LM) disease, in a real world scenario in our institute, is mostly dictated by assessment of the predicted operative mortality risk. In order to investigate the impact of patients' assessed operative risk and procedural type on early mortality we evaluated, in prospective manner, the outcome of consecutive patients who underwent percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG).

Methods – All patients who were referred for revascularization procedure were assessed for predicted operative mortality using the EuroScore system, which integrated patient-related, cardiac-related and operative-related parameters.

Results – 270 patients underwent revascularization procedure for unprotected LM disease (PCI, n=71; CABG, n=199). Of note, 14 (5.2%) patients were presented with cardiogenic shock (PCI, n=12 (17%) vs. CABG, n=2 (1%), p=0.0001). Patients who underwent PCI were more often women (37% vs 26%, p=0.06), older (75±12 years vs. 67±10, p=0.0001), had a lower ejection fraction (48±13% vs. 54±10%, p=0.007), had higher rates of chronic renal failure (27% vs. 11%, p=0.01), history of previous CABG (10% vs. 1.5%, p=0.001) and previous stroke (20% vs. 10%, p=0.03). Presence of additional two or three-vessel disease was similar (86% vs. 88%, p=0.8). EuroScore was significantly higher among those who were referred to PCI (8±3.7 vs. 5.6±3, p=0.0001) with predictive mortality of 10.2% and 6.5%, respectively. Unadjusted mortality rate was higher, although not statistically significant, among those who underwent PCI (11% vs. 6.6%, p=0.2). Adjusted mortality increased in concordance with EuroScore (OR =1.4, 95% CI 1.2-1.7, p=0.01) per 1 score with no impact for the revascularization performed. Importantly, mortality rate among non-cardiogenic shock patients was identical (5.1% vs. 5.2%, p=1.0).

Conclusions – In a current real world scenario, patients who are referred for unprotected LM PCI compared to those who undergo CABG, have substantially higher risk profile and hemodynamic instability. Adjusted mortality rates are comparable between the two strategies. This observation suggests the need for studies aim to evaluate paradigm for unprotected LM revascularization.

Natural History of Saphenous Venous Grafts after Drug Eluting Stenting: Continuous Progression of Disease

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BACKGROUND: Percutaneous coronary intervention (PCI) of saphenous vein graft (SVG) lesions is associated with worse outcomes and high incidence of in-stent restenosis compared with PCI of native coronary arteries. Long-term prognosis is limited by the continuous progression of the disease even after successful drug-eluting stent [DES] implantation

OBJECTIVES: The purpose of the present report was to evaluate the long-term clinical and angiographic outcomes of DES implantation in SVG lesions.

METHODS: Data from consecutive patients who underwent PCI of SVG were imputed into a clinical Database. We evaluated the clinical outcomes up to three years after DES stenting. Included 88 patients [95-grafts] [87% male]. Major adverse cardiac events (MACE) including death, myocardial infarction, target lesion revascularization (TLR), and target vessel revascularization (TVR) were recorded.

RESULTS: The patients mean age was 69±9yrs and the mean age of SVG was 10.5±5.2yrs. The presenting diagnosis was ACS in 72% of patients. And 59% had DM and 15.7% of lesions were 'in-stent' restenotic. Distal protection device was used in 37% of cases and procedural success was achieved in all patients.

	Six months [n=88]	One year [n=84]	Two years [n=56]	Three years [n=38]
Death	1.1%	1.2%	7.7%	7.9%
MI	2.3%	3.6%	7.7%	13%
Stent thrombosis	0%	2.4%	5.9%	7.9%
TVR/graft	7.4%	12.1%	33%	56%
TLR/graft	6.3%	9.9%	28%	49%
CABG	1.1%	3.6%	9.8%	13%
MACE	11.4%	17.9%	41%	66%

CONCLUSIONS: DES implantation in SVG lesions appears safe with favorable and improved short-term outcomes. Nonetheless, long-term results are limited by disease progression in degenerated SVGs and prolonged need for repeat target lesions/vessel revascularization procedures.