

A Comparative Analysis of Mortality/Myocardial Infarction Outcomes Using Drug-Eluting Stents vs. Bare Metal Stents in a Large Single Center Israeli Clinical Setting

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Background: The placement of drug-eluting stents (DES) decreases the frequency of repeat revascularization procedures in patients undergoing percutaneous coronary intervention (PCI) in randomized clinical trials. However, concerns have been raised about their long-term safety in 'all commerce' routine clinical practice among large population cohorts.

Methods: From our hospital and HMO Network Database we conducted a clinical registry of all patients undergoing PCI at our institution. We identified a cohort of 4750 patients who received at least one DES (n=2273) during PCI and compared the mortality and myocardial infarction (MI) risk-adjusted outcomes to patients treated using bare metal stents alone (BMS; n=2477) during an index PCI procedure between April 1, 2004, and July 1, 2007.

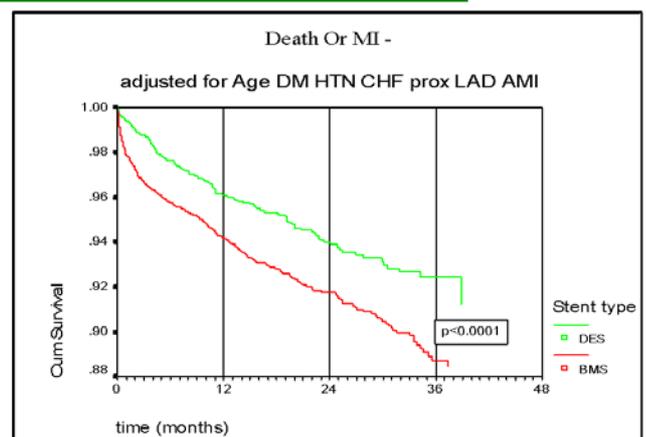
Results: Patients receiving DES were somewhat younger, had more diabetes, hypertension, sustained less heart failure, had less acute or recent MI, and had more proximal LAD culprit lesions (Table).

| | All Pts | BMS | DES | P value |
|---------------------------|-------------|-------------|-------------|---------|
| n | 4750 | 2477 | 2273 | |
| Male | 75.3% | 75.6% | 75.1% | NS |
| Age | 65.8 | 66.4 | 65.2 | <0.0001 |
| DM | 38.7% | 35.7% | 42.0% | <0.0001 |
| HTN | 70.7% | 69.0% | 72.5% | 0.01 |
| Prior CABG | 15.8% | 15.4% | 16.2% | NS |
| CHF | 16.8% | 18.7% | 14.8% | <0.0001 |
| Smoking Hx | 35.5% | 36.0% | 34.5% | NS |
| Prior MI | 24.0% | 29.9% | 18.3% | <0.0001 |
| Prox LAD (culprit) | 16.6% | 8.8% | 25.1% | <0.0001 |

The 3-year mortality rate was significantly higher in the BMS group than in the DES group (9.7% vs. 4.7%, $P<0.0001$), whereas the 3-year rate of any MI was similar in the two groups (3.3% and 2.9%, respectively; $P=NS$). The risk-adjusted (for age, DM, HTN, CHF, MI, PCI in Prox. LAD) composite endpoint of Death/MI was significantly higher among BMS treated patients (12.1% vs. 7.5%, $P<0.0001$). Patients who were treated using DES alone had the lowest composite endpoint (7%).

Conclusions: According to our long-term

experiences, DESs do not jeopardize the 3 year clinical outcomes (i.e. death/MI) among 'all commerce' group of patients in a wide variety of clinical scenarios. On the contrary, our risk-adjusted data would indicate a *prognostic benefit* for DES utilization which commences early and sustains for at least 3 years following index PCI.



Predictors and Prevalence of Early Stent Thrombosis in Patients with Acute Coronary Syndrome

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Background: While early stent thrombosis (EST) is an uncommon phenomenon, it has devastating consequences. Activation of platelets and coagulation system play a major role in the pathogenesis of acute coronary syndrome (ACS) and might impact on EST. The prevalence and predictors of EST in ACS patients have not been specifically examined.

Objective: To determine the incidence and predictors of EST in ACS patients from the ACSIS 2006.

Methods: Patients were followed for 30 days. Definite EST was diagnosed in patients with angiographic or autopsy evidence of thrombus. Probable EST was diagnosed if unexplained deaths occurred within 30 days after the procedure or in patients with acute myocardial infarction (MI) involving the target-vessel territory.

Results: Of 1202 ACS patients who underwent percutaneous coronary intervention (PCI) with stenting, 30 (2.5%) sustained EST (19 definite, 11 probable). ST-elevation MI (STEMI) versus NSTEMI/unstable angina patients were more than 4 times likely to sustain ST (3.9% vs. 0.9% p=0.001). The incidence of EST was even higher in STEMI patients who underwent primary PCI (5.6%). Other predictors of EST included: Killip class ≥ 2 (6.4% vs. 1.9%, p<0.01), multi-vessel coronary artery disease (3.6% vs. 0.7%, p=0.02). Drug eluting stent use was not associated with higher risk for EST (3.1% vs. 2.2%, p=0.4). On multivariate analysis only STEMI [OR=6.7, 95% CI (2.5-23)], prior MI [OR=2.8, 95%CI (1.2-6.3)], and Killip class ≥ 2 [OR=3, 95% CI (1.3-6.6)], remained independent predictors of EST.

Conclusion: Among ACS patients, those with STEMI, prior MI and those hemodynamically unstable on admission, are at higher risk for EST.

The Impact of Calculated Patient Prosthetic Mismatch on Morbidity, Mortality and Quality of Life After Aortic Valve Replacement

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Objective: a midterm assessment of patient prosthetic mismatch (PPM) impact on morbidity, mortality and quality of life after aortic valve replacement (AVR).

Methods: Between August 1996 and August 2006, 459 patients (227 female, mean age 74.5 ± 9.3 years, 41-93) underwent primary AVR with or without coronary artery bypass graft (CABG) due to aortic stenosis. Severe PPM was defined as Effective Orifice Area Index (EOAI) < 0.65 and moderate as $0.65 > \text{EOAI} > 0.85$. Clinical assessment, quality of life evaluation (the MOS questionnaire scores) and echocardiographic measurements were performed during follow-up (mean 35 months).

Results: Overall hospital mortality was 4.3%. Severe and moderate mismatch were observed in 7.7% (35/459) and 33.2% (152/459) of patients, respectively. In patients ≥ 75 years, moderate or severe PPM was observed in 49.4% (126/255). Post operative mean gradients for patients with severe or moderate PPM were 19.0 ± 7.5 mmHg and 15.2 ± 6.9 mmHg for patients with no PPM ($p < 0.001$). Multivariate analysis revealed that early mortality was associated with female gender (O.R. =3.3, $p=0.027$), age over 80 (O.R. =3.5, $p=0.003$), congestive heart failure (O.R. =3.0, $p=0.012$), IDDM (O.R. =10.7, $p < 0.001$), and smoking (O.R. =3.7, $p=0.015$) but not with any degree of PPM. Late mortality was associated only with NIDDM (O.R. =2.25, $p=0.031$). In addition, poor quality of life assessment was not associated with any degree of mismatch.

Conclusions: PPM is common after AVR, particularly in the elderly population. Patients with PPM have higher postoperative gradients. However, PPM is not associated with reduced survival, functional capacity or poor quality of life, even if severe.

Incidence and Significance of Tricuspid Valve Insufficiency in Patients after Coronary Artery Bypass Surgery

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Introduction: Tricuspid regurgitation (TR) is usually functional and secondary to mitral valve disease. There is minimal data on new TR after CABG. We sought to determine the incidence and predictors, as well as late outcome of TR after CABG.

Methods: All patients undergoing pure CABG between 1999-2005 and having pre and post-operative echocardiogram in our institution were included. New TR was defined as moderate or greater after surgery, in patients having mild or less TR before surgery. Clinical, surgical and echocardiographic data was entered into our database. Univariate and multivariate analysis was performed in order to identify risk factors for development of new TR. All patients developing new TR underwent late follow-up, including echocardiography.

Results: There were 448 patients, 48 (11%) developed new TR. Predictors for TR were: pulmonary hypertension ($p=0.02$), disease in the RCA ($p=0.004$), elevated CPK levels ($p=0.003$), post-operative decrease in LV ($p=0.02$) or RV function ($p=0.03$), and deterioration of mitral regurgitation after surgery ($p<0.0001$). Four patients died in the follow-up period. Late echocardiogram was available in 32 patients at mean period of 26 months (range 3-84), and showed resolution of TR in 22 patients (69%).

Conclusions: Around 11% of patients will develop new significant TR after CABG. This was mainly correlated with peri-operative myocardial damage. In the majority of patients the TR will resolve spontaneously.

Routine Use of Bilateral Skeletonized Internal Thoracic Artery Grafting – Long Term Results

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Background: Skeletonized harvesting of the internal thoracic artery (ITA) decreases severity of sternal devascularization, thus reducing the risk of postoperative sternal complications in patients undergoing bilateral ITA grafting (BITA).

Methods: Between 1996 and 2001, 1515 consecutive patients underwent skeletonized BITA grafting. Of the 1179 male and 336 female patients, 641 (42.3%) were older than 70 years and 519 (34.3%) had diabetes.

Results: Operative mortality was 2.9%. Early postoperative morbidity included sternal infection (1.6%), cerebrovascular accident (3%) and perioperative myocardial infarction (1%). Multiple regression analysis showed chronic obstructive pulmonary disease (COPD) (OR 11.7, 95% CI 4.5-30.13), repeat operation (OR 13.6; 95% CI 3.4-5.4) and Diabetes Mellitus (NIDDM and IDDM: OR 4.26 95% CI 1.7-10.8 and OR 6.9 95% CI 1.4-35.6, respectively) to be associated with increased risk of sternal infection. Follow-up (between 6 and 12 years) revealed 305 late deaths. Kaplan-Meier 10 year survival for patients younger than 65, between 65-74, and older than 75 was 87%, 75% and 52%, respectively. Cox regression analysis revealed increased overall mortality (early and late) in patients with peripheral vascular disease (HR 1.8, 95% CI 1.39-2.33), patients older than 75 years (HR 7.23, 95% CI, 4.16-12.55), repeat operations (HR 2.19, 95% CI 1.19-4.03), patients with preoperative congestive heart failure (HR 1.56; 95% CI 1.22-1.99), and chronic renal failure (HR 1.49, 95% CI 1.07-2.07). Operations performed without CPB were associated with better postoperative survival (HR 0.69 95% CI 0.51-0.93).

Conclusions: BITA grafting is associated with low morbidity and good long term results. Use of skeletonized BITA is an appropriate technique for the elderly and most of the diabetics; however, it is not recommended for repeat operations or for patients with COPD.

Timing of Cardiac Catheterization and Acute Renal Failure after Cardiac Surgery

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Background: The incidence of acute renal failure (ARF) after cardiac surgery and the risk of mortality associated with it continues to be high. The aim of this study was to evaluate if timing of cardiac catheterization influences the incidence of postoperative ARF.

Patients and methods: Four hundred and eight patients undergoing cardiac surgery were prospectively evaluated. Mean age was 66+/-10 years, 22% were female, 38% diabetic, 69% had hypertension and 15% had peripheral vascular disease. Preoperative creatinine level and calculated creatinine clearance (CrCl) were 1.05+/-0.6 mg/dl and 82+/- 27 ml/min, respectively. Of the study population 39% underwent surgery within 24h of cardiac catheterization, 30% underwent surgery between the first and fifth day of catheterization, and 31% underwent surgery more than 5 days after cardiac catheterization. Endpoints were ARF, defined as a decrease in the calculated CrCl of 25% or more by the third postoperative day, and hospital mortality.

Results: 47% of patients who underwent surgery within 24h from cardiac catheterization have shown a decrease in calculated CrCl of 25% or more, as apposed to 29% in patients who underwent surgery between the 1st and 5th day after catheterization, and 23% in those who underwent surgery more than 5 days after catheterization (p=0.05). Mortality rate among patients who underwent surgery within 24h from catheterization was independently associated with acute renal failure ([OR]1.9, p=0.02). Preoperative calculated CrCl of less than 60ml/min and cardiac surgery within 24h from catheterization were independently related to hospital mortality ([OR]8, p=0.005).

Conclusion: Cardiac surgery performed within 24h from cardiac catheterization is a significant risk factor for acute renal failure, especially among patients with preoperative reduced renal function. Proper timing and patient selection is highly recommended.

Comparison between Surgical Arterial Revascularization and Drug Eluting Stents in Multivessel Patients with Diabetes Mellitus

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Background: Reduction of re-stenosis and re-intervention was recently reported with the introduction of drug-eluting stents (DES). This study compares mid-term outcome of surgical arterial revascularization in patients with diabetes mellitus to that of percutaneous interventions (PCI) incorporating DES (Cypher).

Methods: Two hundred and two diabetic patients with multi-vessel disease who underwent left-sided arterial revascularization between May 2002 and December 2005 were compared with 187 diabetics who underwent Cypher stenting. Multi-vessel patients in the surgical group were treated with two ITAs. After performing propensity score with patients' characteristics, COX regression was used in order to evaluate predictors of outcome events.

Results: Follow-up ranged between 6-52 months. Four-year survival (Kaplan-Meier) of the two groups was similar (91.3% and 87% for the surgical and Cypher groups, respectively, $p=0.87$). However, angina-free survival (72% vs 47%, respectively, Log Rank $p<0.001$) and re-intervention-free survival (91% vs 76%, $p=0.000$) were better in the surgical group. After adjustment to propensity score, assignment to the Cypher group was associated with increased risk of angina return (OR 4.0, 95% CI 2.6-6.21, $p=0.000$), re-interventions (OR 3.36, 95% CI 1.7-6.62, $p=0.000$) and MACE (OR 3.47, 95% CI 1.85-6.49, $p=0.000$).

Conclusions: Outcome of diabetic patients who underwent surgical arterial revascularization is better than that of PCI patients treated with DES.

Quality of Mitral Valve Repair: Median Sternotomy Versus Port-Access Approach

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Objectives

The feasibility and safety of minimally invasive mitral valve (MV) repair using Port-Access was previously demonstrated. However long term quality of the repair, is not well investigated.

Methods

We studied 101 consecutive patients that underwent MV repair for isolated posterior leaflet prolapse. 50 patients underwent port-access approach, and 51 median sternotomy (MS) approach. In port-access approach we used EndoClamp® balloon (32) or Chitwood clamp (18). Patients in port-access group were younger; mean age of 55±11 versus 61±13 (p<0.05). Other patient's characteristics including MV pathology and mitral repair technique were comparable.

Results

Operative, bypass and aortic clamp times were significantly longer in the port-access group. There was no early death. There were more early postoperative pulmonary complications in port-access group. Early post operative echocardiography showed none of patients in both groups, had more than grade 2 mitral regurgitation. Mean hospital stay was 6.2±5.0 days in port-access group versus 7.6±4.2 in sternotomy group (NS). At mean follow-up of 31±30 months, NYHA improved from 1.9±0.9 to 1.5±0.6 in port-access group (p<0.01), versus 2.4±0.9 to 1.7±0.6 in sternotomy group (p<0.01). There were four (8%) late deaths in sternotomy group, versus none in port-access group (p=0.04). Freedom from reoperation was 98% and 100%, in port-access and MS groups, respectively. Echocardiography follow-up revealed 84% (42/50) and 86% (44/51) of patients (Port-access and MS groups, respectively) were free from moderate or severe mitral regurgitation (NS).

Conclusions

In mid term follow-up, quality of simple posterior mitral valve repair via port-access approach compares well with conventional MS approach.

A Novel Mutation in the HCN4 Gene Causes Familial Sinus Bradycardia in Two Unrelated Moroccan Families

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Background: HCN4 channel plays a major role in the diastolic depolarization of sinoatrial node cells. We and others have previously shown that mutant HCN4 channels are associated with familial sinus bradycardia (SB).

Methods and Results: Two 20 years old men of North African Jewish decent were admitted. One survived an out of hospital cardiac arrest during extreme exercise. The other presented with weakness and pre-syncopal events. Both had significant SB (minimum 35, mean 53), which was also found in several other first degree family members. Holter and exercise testing showed SB at rest with normal response to exercise. Echo demonstrated normal heart structure. Sequencing of the HCN4 gene in both patients revealed a C to T transversion at nucleotide position 1454, which results in an alanine to valine change in the protein (A485V). Multiple alignments of different species show a conserved alanine at this position. The mutation was also found in the bradycardic relatives of the second patient and was not found in the non bradycardic relatives as well as in 50 healthy controls. The mutation is located in a conserved locus in the ion channel pore. A mutation in the pore was found in expression systems to decrease the funny current.

Conclusions: We describe a new mutation in the HCN4 gene in two unrelated patients with symptomatic familial SB. The existence of this mutation in two unrelated SB individuals from the same ethnic backgrounds suggests that it may be a relatively common cause for unexplained congenital SB in this ethnic group.

Outcome of Patients with Drug-induced High-degree Atrioventricular Block

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Background: Since information is scarce regarding the natural history of patients with drug-induced (DI) AV-block (AVB), indications for permanent pacing are inconsistent. We sought to determine the outcome of patients with drug-associated AVB.

Methods: 165 consecutive patients with high-degree AVB receiving drugs that affect conduction (presumably DIAVB), were studied retrospectively. The culprit drug was discontinued and decision on permanent pacing was taken by the attending physician. Patients were followed up to pacemaker implantation or, in non-implanted cases, till death or last follow-up, and were divided into 3 groups. Group A: pacemaker implantation (PMI) during index hospitalization; Group B: Discharged without PMI, but re-hospitalized and underwent PMI later during follow up; Group C: no need for PMI till end of follow-up.

Results:

| | Group A N=107 | Group B N=23 | Group C N=35 | <i>P</i> value | <i>P</i> value (B vs. C) |
|-----------------------------|------------------|-----------------|--------------------|-------------------|-----------------------------|
| Age (years±SD) | 76±9 | 76±8 | 73±12 | NS | NS |
| Males | 41(38%) | 8(33%) | 16(47%) | 0.53 | 0.29 |
| Ischemic heart disease | 59(55%) | 6(25%) | 14(41%) | 0.02 | 0.20 |
| Syncope | 67(63%) | 6(25%) | 8(24%) | 0.0001 | 0.89 |
| Mobitz type II | 19(18%) | 3(13%) | 9(27%) | 0.36 | 0.19 |
| CAVB | 55(51%) | 4(17%) | 4(12%) | 0.0001 | 0.59 |
| Wide QRS | 32(30%) | 4(17%) | 1(2.9%) | 0.003 | 0.07 |
| Chronic atrial fibrillation | 27(25%) | 11(46%) | 6(18%) | 0.05 | 0.02 |

Conclusion: Of patients discharged without PMI, 40% will need PMI at a later stage. The presence of atrial fibrillation predicted future need for PMI among those patients, while wide QRS was a borderline predictor.

Larger prospective studies are required to better characterize this group of patients in order to avoid unnecessary PMI