Survival of Defibrillators the "Real World"

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Background: Defibrillator (ICD) usage is expanding rapidly, especially the use of ICD's for primary prevention. The use of this advanced and costly technology is based on assumptions of cost versus survival benefit. Most of the analysis estimate 5-7 year battery life as a base for calculations of cost benefit. The purpose of this study was to evaluate the actual survival of implanted ICD's.

Methods: The study group included 298 patients who underwent ICD implantation between 1993 and November 2007 at our hospital. We evaluated all devices replaced and also looked at patients surviving for 5 years (60 month) after implant.

Results: There were 256 men (86 %) and 42 women, mean follow up 41±26 month (6 were excluded). 203 were implanted for secondary indications (68%). 69 Devices were replaced in 61 patients 1-3 devices replaced per patient. In patients who underwent replacement the average time to replacement was 53±13 month (13-97 month). Most of the devices were replaced due to battery depletion, need for upgrade or replacement at time of procedure due to lead failure. No device was replaced due to company alert (as the only indication). Altogether 81 patients had a follow-up of more than 60 months, 31 (38%) of them without replacement.

Conclusions: The longevity of ICD's may not be as expected. The rate of ICD replacement within 5 years is higher than assumed (in the cost-effective calculations) even with a very conservative policy regarding replacement due to company alerts. Cost benefit estimations should probably be based on actual clinical data. Evaluations relying mainly on expected device longevity estimations may be inaccurate.

Is There Really No Role for EPS Testing in Risk-Stratification of the ICD-Eligible Patient Population?

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The role of EPS testing in risk-stratification of CAD patients with decreased LVEF has been questioned based on poor predictability of a negative EPS in MUSTT and MADIT-II sub-studies. However "positive EPS" in these studies excluded ventricular flutter (Vfl) or polymorphic VT (PMVT) with 3 extra-stimuli, which may be inappropriate. The recently completed Alternans (MTWA) Before Cardioverter-Defibrillator (ABCD) study included mandatory EPS -- thus providing a unique opportunity to re-assess the appropriate definition of a "positive EPS" not only based on events but also as a marker of a MTWA+ (and thus high-risk) patient. We compared on a patient-to-patient basis EPS and MTWA in the 46 patients enrolled in the 2 Israeli centers of the ABCD study. Of the 17 MTWA+ patients, 7 patients had "only" inducible Vfl or PMVT with 3 extra-stimuli ("pseudo-negative" EPS); 9 had a traditionally-defined positive EPS; and only 1 EPS was completely negative; whereas 8 of the 25 MTWA- patients had completely negative EPS. All 10 EPS- patients were free of arrhythmic events during follow-up, whereas 4 of the 7 patients with "pseudo-negative" EPS and MTWA+ had arrhythmic events. In conclusion, the definition of a +EPS test for risk-stratification needs to be broadened to include inducible PMVT or Vfl with 3 extra-stimuli, the negative predictive value of a completely negative EPS warrants a second look as a marker of a low risk patient, and most importantly no patient should be denied an ICD based on a "pseudo-negative" EPS of Vfl or PMVT with 3 extra-stimuli!

Outcome after Implantation of ICD in Patients with Brugada Syndrome: a Multicenter Israeli Study (ISRABRU)

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Background: Many electrophysiologists recommend the implantation of a cardioverter-defibrillator (ICD) in patients with Brugada syndrome who are cardiac arrest survivors or presumed to be at high-risk of sudden death (patients with syncope, familial history of sudden cardiac death or inducible VF at EPS). This multicenter study analyzes the outcome of the patients implanted in Israel.

Methods and results: All patients with Brugada syndrome who underwent ICD implantation in 11 Israeli centers between 1994 and 2007 were analyzed. There were 58 patients (52 males, 89.6%) with a mean age of 43.4 years. The indications for ICD implantation were a history of sudden cardiac arrest (10 patients, 17.2%), syncope [30 patients (51.7%) including 19 of 21 (90.4%) with inducible VF], inducible VF in asymptomatic patients (12 patients, 20.6%), history of familial sudden cardiac death (3 patients, 0.5%) and various reasons in 3 patients (0.5%). VF was induced in 4 of 5 (80%) patients who presented with cardiac arrest (n=10) and in 35 of 38 (92.1%) patients without documented cardiac arrest (n=48). During a follow up of 1-156 months (mean 42 + 35) months no patient died, 4 patients (7%) had an appropriate device therapy that was limited to those patients with a previous history of cardiac arrest. Indeed, the appropriate device therapy rate in these patients was 40%. Conversely, none of the other "high-risk" patients implanted with an ICD had an appropriate device therapy during a mean 36 + 30 months follow up period. The overall complication rate was 31.5% during follow-up, including an inappropriate shock in 16 (27.1%) patients caused by lead failure/ dislodgment (5 patients), T wave oversensing (2 patients), device failure (1 patient), sinus tachycardia (4 patients) and supraventricular tachycardia (4 patients). One patient suffered a pneumothorax and another brachial plexus injury during the implant procedure. One patient suffered a late (2 months) perforation of the right ventricle by the implanted lead that manifested with chest pain and hypotension without signs of cardiac tamponade. Eleven (18.9%) patients required a re-intervention either for infection (1 patient) or lead problems (10 patients). Eight patients (13.7%) required psychiatric assistance during follow-up due to complications related to the ICD (mostly inappropriate shocks in 7 patients).

Conclusions: In this Israeli patient population with the Brugada syndrome implanted with an ICD and followed during a mean 42-month period: 1) Appropriate device therapy was limited to cardiac arrest survivors while none of the other "high-risk" patients including those with a positive electrophysiologic study suffered an arrhythmic event; 2) The overall complication rate was particularly high, especially inappropriate device therapy, need for re-intervention and severe psychiatric disorders.

What Makes Patients with Implantable Cardioverter Defibrillator (ICD) Miserable? A Prospective Quality of Life Assessment

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The quality of life (QOL) in patients (pts) with Implantable Cardioverter Defibrillator (ICD) may be compromised by many facets of their illness and therapy

Aim of the study: To assess impact of socio-economical and clinical characteristics of ICD pts on their QOL and on their attitude toward arrhythmia symptoms and ICD therapy.

Methods: A prospective study on ICD pts, hospitalized in the Ha'Emek Cardiology Department. Demographic and clinical data was collected. A structured questioner on educational, social-economic background, experience with ICD therapy, attitude toward arrhythmia recurrences, death, and disability was administered by ICCU nurses to the pts. QOL was assessed by the Minnesota living with heart failure questioner (A high score signifies a low QOL).

Results: Thirty five pts, (5 female), mean age 68+/-10 (53-89). Time from the first ICD implantation was 2-12 years. Six pts were Israeli-Arab, 29 Israeli-Jews (5 new immigrant). Only 7 pts (21%) were employed. Seventeen pts (48%) received symptomatic ICD shocks. Eight pts (23%) had syncopal ventricular arrhythmia documented by the ICD. There was no significant difference in clinical baseline characteristics between pts who had ICD therapy or syncope and those who did not. Twenty one pts (60%) expressed fear of receiving ICD shock in public place and 14 pts (40%) expressed fear of dying from cardiac arrest. Nevertheless, 26 pts (74%) would recommend ICD to others. The mean QOL score was 21.2+/-16.7. The QOL in man was 19+/-16 versus 34+/-14 in women (p=0.063). QOL in pts who had ICD shock was 26+/-18 versus 16+/-14 (p=0.069). In pts with syncopal arrhythmia QOL was 33+/-19 versus 17+/-14 (p<0.015). No other clinical or socio-economical factor predicted QOL score.

Conclusion: In pts with ICD, the QOL is significantly lower following syncopal arrhythmia. Patient who had ICD shock and women tend to have a lower QOL.

Native Coronary Artery Plaque Composition of Intermediate Lesions as Assessed by Virtual Histology Intra-Vascular Ultrasound - Potential Implications for Interventional Strategy

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Background – One of the main morphologic characteristics of vulnerable plaque is a large necrotic core (NC). As most of acute rupture plaque events occur at lesion with mild stenosis we sought to investigate, using IVUS radiofrequency data analysis (virtual histology, VH), the NC distribution in coronary segments containing intermediate lesions

Methods - We have analyzed 42 native coronary segments with denovo lesions obtained from 26 non-ST elevation myocardial infraction patients (81% men, mean age 63±10.6 years, diabetes 50%, and unstable angina 50%). IVUS was performed using automatic pullback and ~2400 slices were analyzed for VH. Maximal necrotic core was defined by absolute NC area.

Results – Investigated segment location included LM 2, LAD/Diagonal 22, LCX/OM 15, Ramus 1 and RCA 2. The mean segment and lesion length were 31±20mm 12±7mm, respectively. Maximal NC area was present at MLD site in 35%, proximal to MLD site in 51% and distal to it in 14% of segments. The mean distance between MLD site and non-MLD Max NC site was 8.5±7 mm. Maximal NC area had less plaque burden, ~50% larger NC area and calcification and significantly less fibrous and fibrofatty tissues, compared to MLD site (Table). Max NC area was inversely related to plaque burden (r= -0.1147, p=0.0001) and to %FF (r= -0.684, p=0.0001), was proportional to %Ca (r=0.68, p=0.001).

IVUS/VH	MLD site	Non-MLD Max NC site
CSA	4.44±1.62	7.76+3.95
Plaque burden (%)	67±11	57.68±9.18
NC area (mm^2)	0.97±0.77	1.46±0.87
NC (%)	16.44±10	22.4±10.14
Calcium (%)	8.14±8.18	13.4±9.56
Fibrous (%)	73.63±43.94	53.28±14.73
Fibrofatty (%)	17.88±13.55	10.88±7.42

* P<0.0001 for all comparisons

Conclusions – In segments containing intermediate lesion, plaque containing maximal NC area is often located in angiographycally segments adjacent to the MLD site. This preliminary observation may carry implications for designing optimal interventional strategies and should be evaluated in larger patient's population.

Computerized Gradual Angioplasty Improves Outcome of Coronary Stenting – Final Results of a Randomized Controlled Trial

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Background: Mechanical trauma caused by PCI is a major reason for restenosis and subsequent target lesion revascularization (TLR). Drug-eluting stents (DES) reduce this problem as compared to bare-metal stents (BMS) with an increased risk of late thrombosis. To minimize this trauma we developed an automated computerized device with slow and gradual inflation (CAPSID). In a previous study in patients undergoing POBA or stenting we demonstrated improved outcomes particularly in the stented patients. The objective of this prospective study was to examine whether use of CAPSID reduced MACE and TLR in patients undergoing stenting.

Methods: Patients undergoing stenting were eligible for the study and randomized to CAPSID or standard manual inflation. Exclusion criteria were acute MI, total occlusions, bifurcation lesions, or vein grafts. Clinical follow-up for MACE was performed up to 12 months, with repeat coronary angiography performed for clinical symptoms or positive stress testing with TLR as needed.

Results: 310 patients have been randomized and have completed 12 month follow-up. Baseline clinical characteristics were similar, including age, sex, risk factors, the number of patients with unstable coronary syndromes, QCA data in both the CAPSID and control groups. 90% of the patients in each group received BMS. There was a significant reduction in MACE (death, MI, TLR) in the CAPSID group - 8% vs. 18% in the control group based on significant reductions in MI (1% vs. 7%) and TLR (5% vs. 12%) in the CAPSID group, $p<0.05$.

Conclusions: Gradual computerized balloon inflation using the CAPSID device results in a reduction in MACE and TLR in patients undergoing stenting. This method may be a valuable adjunct to BMS implantation which may provide results comparable to DES without the risk of late thrombosis.

# Coronary Optical Coherence Tomography (OCT) – A Single Center Experience

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Background: OCT is a new high-resolution light-base infrared imaging modality for visualization of intra-coronary microstructures during the course of PCI.

Objective: To evaluate the use of intra-coronary OCT among patients undergoing coronary angiography and angioplasty for feasibility, safety and imaged findings.

Methods and Results: OCT was employed in 6 patients. Two patients with occlusive balloon technique while in four patients imaging was obtained with non occlusive technique. The mean age was 63±7 yrs, the majority had unstable angina at presentation (67%), four patients had pre and post stent deployment imaging for optimal stent deployment. In every case imaged, an unexpected finding has been revealed. For example (Figure): case #1 (left panel) showed severe DES mal-apposition of 360° that was well corrected with post dilatation; case #2 (middle panel) demonstrated thrombus containing lesion with tissue prolapse following angioplasty of a totally occluded graft; Case #3 (right panel) showed intimal proliferation @4 months after DES implantation. All OCT procedures went uneventfully.
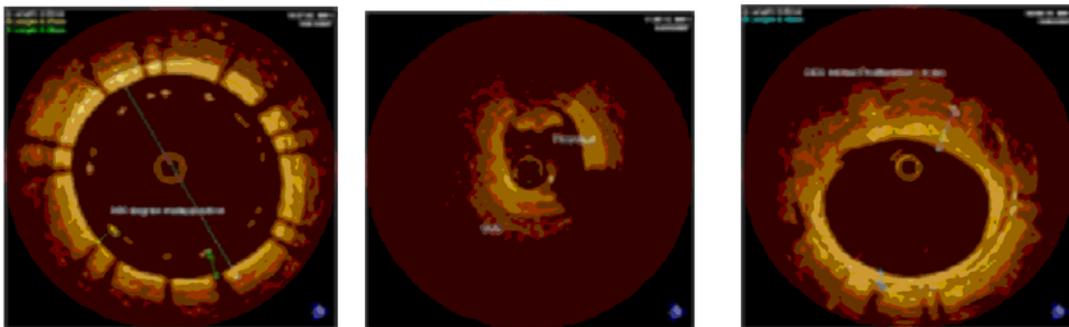
Conclusions- Intra-coronary OCT imaging is feasible and seems to be safe. It provides high resolution imaged insights into intimal tissue, fibrous cap, stent apposition, tissue prolapse and the presence of thrombus in atherosclerotic lesions.

Bifurcation Lesions in the Coronary Arteries: Association between Geometric Changes after Intervention and Clinical Results

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Background: Recent studies show that after bifurcation percutaneous coronary interventions (PCIs) severe morphological changes might occur. These changes appear especially at the angle between the distal main-branch and the side-branch (DMB-SB), with clinical impact that is not known yet.

Objectives: To evaluate clinical outcome of bifurcation PCIs according to the severity of angulation changes between bifurcation branches after the procedure

Methods: We used the CardiOp (Paieon Medical) system for 3-dimensional reconstruction of the coronary vessels. We conducted evaluation of 118 images from 23 patients (78% men, age 60±14 years) with bifurcation lesions in the coronary arteries undergoing angioplasty procedures. We included only interventions performed in both the main vessel and the side-branch (non-provisional) and only cases where no drug-eluting stents were used. Angles between bifurcation branches were measured, before and after stenting. For each patient a follow-up clinical evaluation was performed for up to 1 year with documentation of adverse-events such as death, myocardial infarction or need for repeat revascularization.

Results: Of the 23 patients studied, 10 patients (43%) needed target-vessel revascularization in 1-year follow-up (the TVR group). In the TVR group a non-significant trend towards a decrease in DMB-SB angle appeared (67±20 degrees vs. 54±18, p=0.13) whereas in the non-TVR group there was almost no change in the mean angle after PCI (60±14 vs. 63±18), this difference between the TVR group and the non-TVR group is statistically significant (p<0.05). Significant decrease in DMB-SB angle (more than 15 degrees) appeared in 40% of cases in the TVR group whereas in no patients of the non-TVR group (p<0.05).

Conclusion: Interventions at coronary bifurcations could result in significant geometrical changes. After intervention, a severe decrease in the angle between the distal-main branch and the side-branch could be associated with increased restenosis.
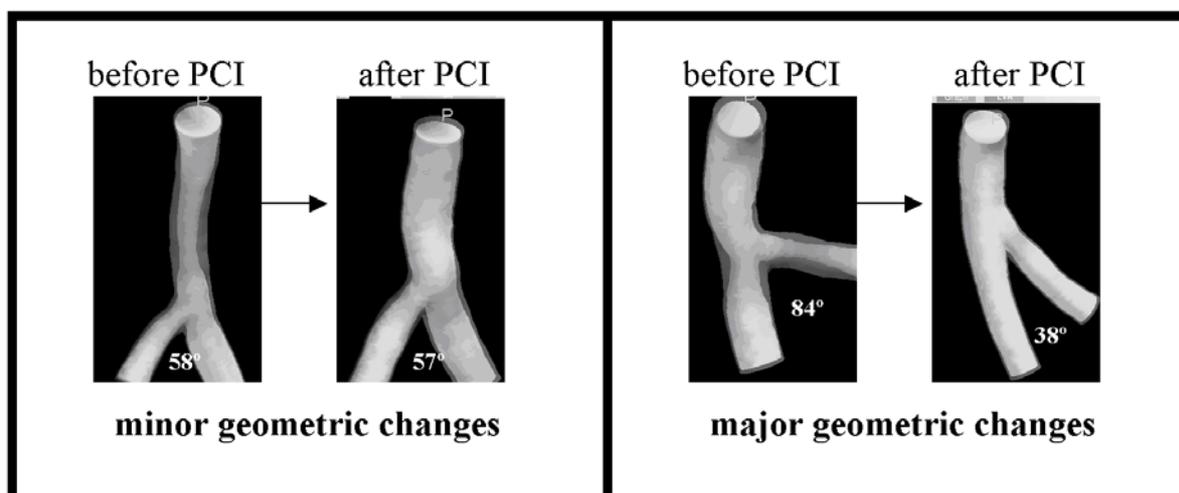
Atherosclerotic Coronary Plaque Characteristics in Diabetic Compared to Non-Diabetic Patients - Insights from Comprehensive Virtual Histology Analysis

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Background – Diabetic patients known to have more diffuse coronary artery disease. Preliminary IVUS radiofrequency data analysis (virtual histology, VH) also suggest larger necrotic core (NC) in culprit lesions of patient with diabetes. However, the relation between diabetics and NC distribution in non-severe coronary obstruction was not fully elucidated. Accordingly, we sought to investigate plaque characteristics of whole coronary segments containing intermediate lesions in patients with and without diabetes.

Methods - We have analyzed 39 native coronary segments with denovo lesions obtained from 23 non-ST elevation myocardial infraction patients (83% men, mean age 64±11, unstable angina 56%, hypercholesterolemia 82%). IVUS was performed using automatic pullback and ~2100 slices were analyzed for VH. Comparison between groups was performed for most severe obstruction [minimal luminal diameter, (MLD)] and for maximal necrotic core sites.

Results – In diabetic patients, plaque composition at MLD site contained less fibrous tissue but other wise was similar to non-diabetic patients. Maximal NC area sites also differed between groups (Table). Strong correlation was noted between NC% and calcium deposition (r=0.79 and 0.61 for diabetics and non diabetics, respectively, p<0.0001 for both), whereas inverse correlation was noted between NC% and fibrous tissue in both groups (r= -0.58 and -0.68, respectively, p<0.001).

IVUS/VH	Diabetes		Non-Diabetes	
	MLD site	Non-MLD Max NC	MLD site	Non-MLD Max NC
CSA	4.5±1.8	6.2±2.1	4.8±1.6	7.1±3.1
Plaque burden (%)	69±12	63±8	66±1	59±11
NC area (mm2)	1.08±0.97	1.68±1	0.88±0.58	1.35±0.81
NC (%)	16.5±11.48	24.5±10.3	16.1±9.2	22.4±9.4
Calcium (%)	9.9±10.6	15.5±10.7*	5.7±5.0	9.8±5.7*
Fibrous (%)	53.0±12.05¶	49.9±14.7**	63.5±9.1¶	58.0±12.0**
Fibrofatty (%)	20.5±15.2	10.1±7.6	14.6±8.4	9.8±5.8

*, **, ¶: p value <0.05 between compared parameters.

Conclusions – Plaque composition of atherosclerotic coronary segments containing intermediate lesions in diabetics and non-diabetics differ in the amount of fibrous and calcified tissues. Similar relations between NC and other plaque components may suggest similar pathophysiological process. Further studies are needed to explore these early observations.

"Normal Coronary Artery" with Slow Flow Improved by Adenosine Injection, Not so Normal for the Myocytes

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Background: Some patients with chest pain and ischemia by objective criteria, undergoing coronary angiography, show no significant coronary narrowing (CN) but slow flow. For these cases we challenge the entity "normal coronary arteries".

Methods: 35 patients with chest pain and evidence of ischemia (dynamic ECG changes, ischemia at exercise test, radioisotope scan or stress echo), underwent coronary angiography. No significant CN (>50% minimal lumen diameter stenosis) was found but there was a slow coronary flow phenomena defined by angiography frames count (FC) for each coronary artery. Intra coronary (IC) adenosine was given (40-80 micrograms) followed by repeat dye injection with FC (at the same projections) and LV pressure recording.

Results:

	LAD FC	LCX FC	RCA FC
Pre Adenosine IC injection	45±12	26±8	26±7
Post Adenosine IC injection	18±3	14±4	15±6
Post/Pre	0.40	0.53	0.57

Mean LV diastolic pressure and trans-myocardial gradient where 11.5±4 and 82±12 mmHg respectively.

Conclusions: Slow coronary flow with no epicardial artery narrowing, indicates failure to deliver sufficient blood to meet the myocytes metabolic demand due to small intramyocardial blood vessel malfunction. The good but short term response to adenosine injection calls for specific oral medication (Dipyridamole? Calcium channel blocker?) to get a similar long term effect in addition to the general recommendation of risk factors modifications.