The Yield of BNP in Prediction of Ischemia During Dobutamine Stress Echocardiography

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Objectives: Dobutamine stress echocardiography (DSE) is a valuable tool for the noninvasive evaluation of myocardial ischemia. Recently, B type natriuretic peptide (BNP) has emerged as a biomarker with the potential of risk stratification & ischemia prediction. This study was performed to assess the correlation between BNP levels before and after DSE and myocardial ischemia as demonstrated by DSE.

Patients and methods: 26 patients referred for DSE were recruited for the study after signing informed consent. Before DSE, baseline echocardiography determined LV size, ejection fraction, and pulmonary artery systolic pressure. First NT pro-BNP sample was obtained after venous catheter insertion before dobutamine infusion. IV dobutamine was infused up to 50 mcg/kg/min to reach the target heart rate, IV atropine was used up to 1 mg if needed. Second NT pro-BNP sample was obtained immediately after the end of the exam. SPSS-13 software was used for statistical calculations.

Results: Mean age was 69 (47-83) years, 58% were females, 13 had established CAD, 9 had previous MI. Average LVEF was 58 (30-70)%, 80% of patients had EF $\geq$ 50%;: 5 patients had chest pain during DSE, 7 had ECG changes. 6 had wall motion abnormalities at baseline study. LV function did not improve or deteriorated in 3,
6 had evidence of inducible ischemia. Mean NT pro-BNP first sample value was 408 (17-2381) pg/ml, second sample was 401 (16-2292) pg/ ml, mean difference between the 2 samples was -7.67 (-89 to 82) pg/ml. There was a significant statistical correlation between 2 NT pro-BNP samples and baseline EF (p=0.031 & 0.027), when EF was divided into normal (>50%) and abnormal group, the correlation was even higher (p=0.001). There was no correlation between any of 2 NT pro-BNP value, their average, their relative change (and ratio between the change and the average) and the presence of inducible ischemia.

Conclusion: In this pilot study, NT pro-BNP levels before and after DSE and the difference between them did not correlate with the presence of inducible myocardial ischemia on DSE. Our study did not show any added value of NT pro-BNP levels during dobutamine stress echocardiography.

Nitrous Oxide Inhalation for Transoesophageal Echocardiography- An Alternative to Benzodiazepine Sedation?

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Background: Transoesophageal echocardiography (TEE) is usually performed using benzodiazepine sedation, which is a limiting factor for elderly patients or those with respiratory insufficiency. Kalinox®, an equimolar mixture of nitrous oxide and oxygen, with no depressive respiratory action and fast reversible effects, seems ideally suited for performing TEE but has never been evaluated. The aim of the present study was to evaluate TEE feasibility and efficiency using Kalinox compared to standard care using benzodiazepine.

Methods: We prospectively enrolled 80 consecutive patients referred for TEE. In the 35 first patients, TEE was performed using intravenous benzodiazepine (Midazolam) and in the 45 last patients using Kalinox (nasal delivery). Pain and tolerance induced by the examination were evaluated on a 0-10 scale. Remembrance of the examination by the patient and quality of the TEE by the operator were also evaluated.

Results: All TEEs were performed by the same experienced operator. TEE duration was not different (6±3 vs. 7±4 min respectively, p=0.57). Patients in the Kalinox group felt TEE to be more difficult (p=0.005) and remembered the procedure more clearly (p<0.0001) but pain experience was not different (7% vs. 9% had a pain score ≥5 respectively, p=0.75). Percentage of patients who agreed to have a second TEE if necessary was slightly lower (77% vs. 94% respectively, p=0.04). The operator judged TEE quality satisfactory in similar proportions (76% vs. 68% respectively, p=0.44).

Conclusion: These preliminary results show that TEE using Kalinox is feasible, provides similar pain relief despite more discomfort for the patient, and acceptable conditions for the operator. Thus, Kalinox use could be considered as an alternative to benzodiazepine sedation for patients intolerant to benzodiazepines such as elderly or respiratory-insufficient patients.

Accuracy and Reproducibility of Left Ventricular Outflow Tract Diameter Measurement Using Transthoracic as Compared to Transesophageal Echocardiography

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Background: Accurate measurement of left ventricular outflow tract diameter (LVOTd) is essential for reliable estimation of aortic valve area (AVA) using the continuity equation. Transesophageal echocardiography (TEE) can accurately delineate the LVOT. The purpose of this study was to assess the accuracy and reproducibility of LVOTd measurement using transthoracic echocardiography (TTE) with harmonic imaging as compared to TEE.

Methods: We prospectively studied 50 pts (mean age 69±14y, 20 with aortic stenosis (AS) and 30 without AS). LVOTd was measured offline in a blinded fashion in both systole and diastole by 2 experienced observers using TTE in the parasternal long axis view and TEE in the midesophageal aortic view (~130°).

Results: There was good correlation between TTE and TEE (r=0.91). LVOTd was significantly smaller by TTE as compared to TEE (2.11±0.21 cm vs. 2.16±0.22 cm, mean difference -0.05±0.09 cm, p=0.0003). Bland-Altman analysis showed 95% confidence interval of +0.14 and -0.24 cm for LVOTd measurement by TTE vs. TEE. Inter and intra-observer variability for LVOTd was 4.8±4.1% and 2.8±1.9% for TTE and 4.2±3.1% and 2.5±1.6% for TEE (p=NS). In patients with AS, estimated AVA was 0.93±0.22 cm^2 using TTE and 0.96±0.24 cm^2 using TEE, p=0.08. Diastolic LVOTd by TTE was smaller compared to systolic LVOTd by TEE (-0.07±0.08 cm, p<0.0001), especially when LVOTd was large, but there was excellent correlation between the two (r=0.95).

Conclusions: LVOTd is slightly underestimated by TTE as compared to TEE, but using harmonic imaging is accurate and reproducible. LVOTd measurements at end diastole can be used to predict systolic LVOTd when systolic images are suboptimal.

Comparison of Conventional and High-Frequency ECG Analysis in Detecting Ischemic Heart Disease During Dobutamine Echocardiography

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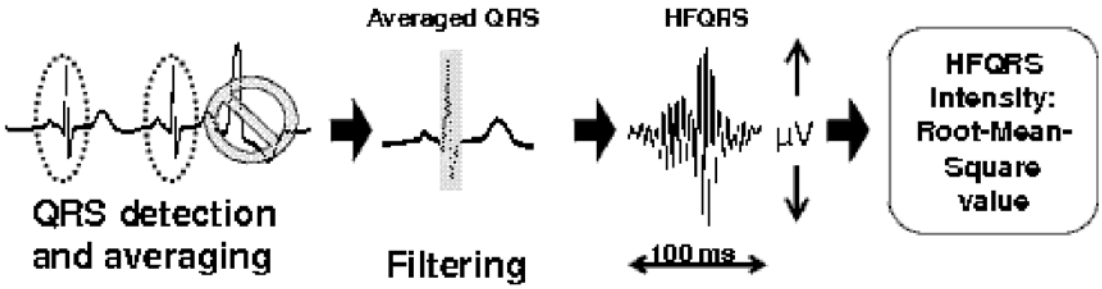
A novel technique for electrophysiological detection of stress induced ischemia, based on analysis of the high frequency mid-QRS potentials (HFQRS), has recently been reported to outperform conventional exercise ECG interpretation. Our aim was to test the performance of this technique in patients undergoing dobutamine echocardiographic imaging.

Methods: The study included 71 pts (67±14 y, 39 men) referred to clinical dobutamine echocardiography, which served as the comparative diagnostic test for ischemia. Conventional ECG was combined with high resolution ECG acquisition that was digitized and analyzed offline using the HyperQ™ System (BSP, Tel Aviv, Israel). HFQRS signals were extracted and time-intensity curves calculated (figure). Relative intensity change in HFQRS during the test was used as an index of ischemia.

Results: The dobutamine echocardiographic test was positive in ten patients, negative in 55 patients, while six patients had inconclusive results. HFQRS analysis was possible in 45 patients and conventional ECG interpretation was available in 33 patients. HFQRS analysis showed better specificity than conventional ECG interpretation (85% vs 55%, $p<0.01$), and overall accuracy was significantly improved (82% vs. 55%, $p<0.01$) when HFQRS was employed.

Conclusions: HFQRS analysis presents a significant improvement over conventional ECG interpretation in detecting ischemia during dobutamine stress and may thus aid in enhancing the non-invasive diagnosis of ischemic heart disease. Further testing in a larger patient population is required to accurately assess the diagnostic performance of this technique.



Correlates of Echocardiographic Left Atrium and Ventricular Parameters and GFR in Hospitalized Patients

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Introduction: Chronic kidney disease is associated with increased cardiovascular (CV) risk. Left ventricular hypertrophy (LVH) together with coronary artery disease has been considered the main target of intervention in these patients. LVH is highly prevalent in CKD even in early stages. The aim of the study was to investigate the relationship between Glomerular filtration rate (GFR) and LV, left atria (LA) echocardiographic parameters in hospitalized patients.

Methods: Retrospective chort analyses of all patients hospitalized in Internal Medicine A during the study period was performed. GFR was estimated by means of the serum creatinine level using the MDRD Equation formula. LVH, LA volume, area and diameter were determined according to echocardiographic criteria.

Results:

Data analysis was performed on 1000 consecutive patient's laboratory and echo files during 16 months (1/ 2006 -4/ 2007). In 397 pts (M/F 147/250) all data existed and thus were included. Mean Age was 76.5±8 (38-94y).The Correlation of GFR with LVH (posterior wall and septum) and LA Volume was good (r^2=0.68 and 0.62 respectively $p<0.05$). The Correlation of GFR with LA Area was Borderline (r^2 = 0.45, p=0.058) and no correlation was found with LA diameter (r^2=0.35, p=0.64).Creatinine clearance was inversely related to LVH (r=-0.132, $P<0.0001$).

Conclusions: GFR is associated with altered LV dimensions. These data may help explain the high cardiovascular mortality observed in patients with renal dysfunction. The incidence of LV diseases progressively increases as GFR deteriorates. This observation is more accurate when volumes are used and less when area and diameter are used.

Classification of Left Heart Functional Dimensions by Clustering Cardiac Echo-Doppler Measurements. A Mathematical Data Mining Technique Can be Used to Find Pathological Patterns

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Introduction: Cardiac Echo-Doppler (Echo) data may contain hidden information that cannot be revealed and identified by an experienced cardiologist. Thus, important relations between Cardiac dimensions (CD) may be misinterpreted. Clustering is commonly used in Data Mining (DM) and aimed to partition data into clusters.

Aim and methods: The aim was to find if mathematical tool such as clustering algorithms can find possible correlations between CD in order to upgrade and improve echo diagnostic abilities. Therefore clustering algorithms including K-means (KM), Kohonen (Koh) and TwoStep (TS) were applied on 24,400 data objects of Cardiac Echo measurements.

Results: The commercial DM tool Clementine (Clem) was used. Each algorithm generated different clusters. Despite this, between left atrial Area (LAad) and ascending aortic Diameter (AsAod), pathological positive correlations were identified and both negatively correlated with EF (table 1).

Conclusions: This work is an example from a series of works which shows that mathematical Data Mining technique can be apply on Echo measurements, find correlations between CD and thus may be used to look for hidden pathological patterns.

Cardiac Dimension vs. clustering algorithm	K-means	Kohonen	TwoStep
AsAod (mm)	29.2±4.8	*31.9±3.5	*33.8±4.2
Lad (mm)	*32.3±4.1	*36.6±5.2	*44.7±8.8
LAa (cm2)	*15.5±3.2	*19.4±3.8	*28.1±7.0
LVEDD (mm)	*46.5±4.1	*50.7±4.7	*55.7±8.5
LVESD (mm)	*28.9±3.2	*38.3±5.5	*42.4±10.8
EF %	*63.2±3.7	*41.4±11.1	*44.8±14.8
STH (mm)	*8.7±1.3	*10.2±1.4	*11.2±2.4
PWT (mm)	8.5±1.2	9.7±1.2	10.5±1.8

Table 1: LAd and left atrial area (LAa), LV end diastolic and systolic diameter (LVEDD)-LVESD), Ejection fraction (EF), Septal&Posterior wall thickness (STH-PWT).*= $P<0.01$ (in column only).

Routine Coronary Angiography pre Valve Surgery is it Time to Change the Paradigma ?

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Aim: To assess the usefulness for routine coronary angiography in patients referred for valve surgery.

Methods: Patients diagnosed with valve disease on clinical and echocardiographic findings and who underwent routine coronary angiography in the absence of clinical ischemia, were analyzed as to the presence and severity of coronary artery disease. Data was collected from the catheterization reports.

Results: 99 patients from private and public hospitals were catheterized . 40% were females. Average female age was 69years and males 63years. 67% of the patients had normal or non obstructive disease and 13% only 1 vessel disease. However in the patients under 60 years 88% were normal and 8% had only one vessel disease. In this subgroup no female had coronary artery disease. Only 13% underwent concomitant cabg.

Conclusions.High rate of normal and non obstructive disease especially in females under the age of sixty.

Recommendations..No need for routine coronary angiography prior to valve surgery in patients under 60. coronary CT scan can serve as an alternative.

Characteristics and Management of Hospitalized Old Patients with Severe Aortic Stenosis

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Introduction: Severe aortic stenosis (sev-AS) is common in old patients but there are no guidelines for its management at this age. We studied characteristics and management of these patients compared to younger sev-AS patients and to old patients without sev-AS.

Methods: Patients with sev-AS over age 70 (group 1 = 37 patients, age 84.6±4.2) were retrospectively compared to old patients with mild AS (group 2 = 20 patients, age 84.8±2.5) and to younger patients with sev-AS (group 3 = 17 patients, age 68±7.9, $p<0.001$ vs. other groups).

Results: Majority of patients were female (73, 50 and 67% in groups 1-3, respectively). Severity of AS was similar in groups 1 and 3 (mean gradient 56±24 vs. 54±17mmHg; valve area 0.61±0.18 vs. 0.69±0.14cm^2). Surprisingly, other echo parameters were similar in all groups as was the prevalence of hypertension (72-79%), atrial fibrillation (21-54%), diabetes (25-50%) and IHD (27-54%). Hyperlipidemia and smoking were more common in group 3 (67 and 22% vs. 29-35% and 0-4%, respectively). Common reasons for admission were heart failure (54-57%) and vertigo/syncope (19-33%). Blood pressures, heart rates, laboratory results on admission were similar but creatinine was higher in groups 1-2 vs. group 3. A cardiological consult was requested in 22% of group 1 but in 94% of group 3 patients. Accordingly, valve replacement was recommended in only 11% of group 1 vs. 72% of group 3 patients.

Conclusions: Old patients with sev-AS patients have similar characteristics to younger patients with sev-AS but are treated like old patients with mild AS.

Combined Surgical and Percutaneous Approach in the Cath Lab toTreat AF

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Background: Isolation of the major part of the left atrial posterior wall, including the four pulmonary veins, could become the treatment of choice in patients with paroxysmal and persistent AF, if a continuous transmural lesion could be made. Available epicardial monopolar ablation devices used in the minimally invasive surgical treatment of AF yield inconsistent results with this box-lesion. We therefore combined a mono-lateral right thoracoscopic approach with a standard percutaneous transseptal EP procedure to limit the shortcomings of both procedures.

Methods and results: Patients with paroxysmal or with persistent AF were operated on in the EP cath lab. In one case, endocardial evaluation of the lesion line in a patient with PAF showed a gap at the roof of the LA, which could be closed with another epicardial application. In another patient with persistent AF, the monopolar ablation device failed to create a continuous lesion in the connecting lines between right and left pulmonary veins, so endocardial RF ablation was necessary to close the gaps. Since the surgical device acts as an anatomical landmark for the box-lesion while serving as a protective wall between the atrium, the phrenic nerves, and the oesophagus, endocardial RF energy could be accurately and safely delivered.

Conclusion: A combined minimally invasive surgical and percutaneous EP approach in the cath lab appears feasible and safe. This procedure has the potential to overcome the shortcomings of each procedure, reduce complications, and increase success rate.

Implication of Exercise Training on Cardiomyopathy and Catecholamine-dependent Polymorphic Ventricular Tachycardia CPVT in Calsequestrin Deficient Mice

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Catecholamine-dependent polymorphic ventricular tachycardia (CPVT) is a lethal ventricular arrhythmia evoked by physical or emotional stress. Recessively inherited CPVT is caused by either missense or null-allele mutations in the cardiac calsequestrin (CASQ2) gene. It was suggested that defects in CASQ2 causing protein deficiency, impair Ca^{2+} uptake to the sarcoplasmic reticulum and Ca^{2+}-dependent inhibition of ryanodine channels, leading to diastolic Ca^{2+} leak, after-depolarizations and arrhythmia.

To examine the effect of exercise training on left ventricular remodeling and arrhythmia, CASQ2 knockout ($CASQ^{\square E9}$) mice and wild-type controls underwent echocardiography and heart rhythm telemetry before and after a 6-week training protocol using treadmill exercise. RT-PCR was used to measure the expression of A and B-type natriuretic peptide genes (ANP and BNP).

Left ventricular fractional shortening was impaired in $CASQ^{\square E9}$ (35±3% vs. 41±8% in controls, $p<0.05$) but improved after training (44±5% and 51±3 in $CASQ^{\square E9}$ and control mice, respectively, p=NS). The exercise tolerance was 16±1 min in $CASQ^{\square E9}$ mice vs. 29±2 in controls, $p<0.01$, but improved in trained animals (26±2 vs. 30±3 min, respectively, p=NS). The hearts of $CASQ^{\square E9}$ mice had higher basal expression of the BNP gene, but ANP was not significantly different from controls. After training, the expression of both natriuretic peptide genes was markedly decreased in $CASQ^{\square E9}$ and controls. Exercise training was not associated with a change in CPVT severity, but appeared to decrease the prevalence of ventricular arrhythmia during stress.

We conclude that in $CASQ^{\square E9}$ mice, recapitulating the phenotype of human CPVT, exercise training is beneficial and could offer a strategy for prophylactic and therapeutic interventions.