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Abstracts

[42] EFFECT OF INTRAVENOUS NITROGLYCERIN THERAPY ON ERYTHROCYTE ANTIOXIDANT ENZYMES
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Intravenous nitroglycerin (glyceryl trinitrate, GTN) has been used as an anti-ischemic agent for the therapy of unstable angina, acute myocardial infarction and post-infarction angina. Nitric oxide (NO) and S-nitrosothiols (SNO) constitute the biologically active species formed via nitroglycerin bioactivation. The clearance rates of nitroglycerin greatly exceed hepatic blood flow with known extrahepatic metabolism being present in red blood cells (RBCs) and vascular wall. Increased levels of reactive oxygen species (ROS) formation can diminish the therapeutic action of organic nitrates by scavenging donated NO and oxidizing tissue thiols important in nitrate biotransformation. In vivo and in vitro studies reported herein show that red cell activity of antioxidant enzymes, catalase (CAT) and glutathione peroxidase (GPx), are significantly decreased after intravenous nitroglycerin treatment and incubation with GTN. Catalase activity (739.6 ± 92.3 k/grHb) decreased to 440.1 ± 111.9 and 459.8 ± 130.7 k/grHb after 1 and 24 hr GTN infusion, respectively. Similarly, selenium-GPx activity (5.8 ± 1.8 U/grHb) decreased to 3.2 ± 1.7 and 3.8 ± 1.1 U/grHb after 1 and 24 hr GTN infusion, respectively. The reported decrease in red cell antioxidant enzyme activities can generate an oxidant milieu which can lead to a rapid inactivation of nitroglycerin-donated NO and cause oxidation of tissue thiols important in nitrate biotransformation.

[43] CO-CULTURE OF SKELETAL MYOBLASTS AND MESENCHYMAL STEM CELLS TO AUTOLOGUE TRANSPLANT TREATMENT OF THE CARDIAC INSUFFICIENCY IN RATS.

Carvalho KAT, Rebellato CLK, Senegaglia AC, Souza-Guarita LC, Hansen P, Cury CC, Francisco JC, Scorsin M, Brofman PRS.

Introduction: Currently, two lines of research are being proposed in treatment of cardiac insufficiency in an attempt to address the main cause: skeletal myoblast transplant which increases contractile muscular mass and mesenchymal stem cells transplant which increases neoangiogenesis. Our objective is to develop a co-cultivation method of skeletal myoblasts and mesenchymal stem cells for an autologous co-injection.

Method: Skeletal myoblast and mesenchymal stem cells of 10 rats were isolated and co-cultivated. We used DMEM medium, with 10% Fetal Calf Serum (FCS), 1% ATB and growth factors. The cultures were maintained in incubator with 5% CO2 at 37°C. Assays were performed in culture flasks and the cells plated initially in variable proportions, skeletal myoblasts/mononuclear cells: 2:1; 1:1; 1:2, respectively and morphological observations were made regarding the cell survival, adhesion to substrate and confluence. The proportion 2:1 had a better cellular proliferation and the cells were co-cultivated in a concentration of 5 X 105/ ml, during 14 days. After 48 hours no adherent cells were aspirated from the flasks, just resting adherent cells: myoblasts and mesenchymal stem cells. The medium was exchanged 2-3 times a week during the culture period. The identification of the cells in culture were made using fast myosin and vimentine proteins by immunocytochemistry.

Results: Both cells types proliferated and expanded in the same conditions with yield of 5,5 x 107 (1,6 x 107-5, 4 x 108). The cells were positive for fast myosin and vimentine by proteins.

Conclusion: The co-culture of skeletal myoblasts and mesenchymal stem cells has shown to be an efficient method of co-cultivation, since the cells were able to proliferate together under the same conditions and with a good yield, creating the possibility of cellular interaction in vitro and perhaps in vivo.
Background In a valve bearing BMH model supplying failing goat hearts, two heart valves showed to be most effective for pumping. Furthermore linear muscle contractions are known to transfer much more power than concentric contractions in skeletal muscle ventricles (SMV). Because linear muscle contractions in SMVs are not possible, a tangential squeezing should become applied as a compromise between linear and eccentric contractions. An intra-operative stimulation setting with different intervals from R-waves should become evaluated for maximal stroke volumes.

Methods In 6 adult African Bore bocks, left latissimus dorsi muscle (LDM) was electrically pre-conditioned for two weeks and then wrapped around a pumping chamber of a Biomechanical Heart (BMH). LDM was fixed at the internal left thoracic wall and the muscle contracted concentrically as well as tangentially. The muscle’s origin was fixed externally to the thorax by an artificial tendon. Inlet and outlet of the chamber beard aortic and pulmonal valve-homografts. An ultrasonic flow probe was placed around the aorta caudal the BMH. Intra-operatively, a conductance catheter was placed within the pumping chamber for stroke volume evaluation and pumping function was additionally documented by X-ray examination.

Results Valve homografts and tangential mechanical squeezing of the pumping chamber are feasible in a chronic big animal model with good results in stroke volumes, which ranged from 2.3 ± 0.6 L/min to 3.1 ± 0.7 L/min with a BMH support in a 1:3 mode, measured by the conductance catheter method and visualized by ventriculo-graphy. A burst setting of 300 msec after the R-wave induced the highest stroke volumes, documented by ultrasonic flow measurements.

Conclusion Valve homografts, tangential mechanical squeezing and a defined stimulation intervals from the R-wave are a remarkable functional improvement in a preclinical big animal model of Biomechanical Hearts.
The current techniques such as Holter and Rtest are partially efficient to diagnose the cardiac arrhythmia because they are limited in time (24h for the Holter and one week for the Rtest). Furthermore, the telemetry cardiac arrhythmia system (for example Agilent) is expensive and limited in space because in general, it is only installed at hospital. So a new technique is proposed to remedy the previous drawbacks and to improve the accuracy and the efficiency of the diagnostic of ventricular tachycardia among the high risk patients to enable to propose the implantation of Implantable Cardioverter Defibrillator to prevent sudden death. A platform containing a local server connected to a Wireless ECG Sensor based on Bluetooth or IEEEE802.11b and a remote surveillance server dedicated to the remote continuous cardiac arrhythmias detection and monitoring over Internet is implemented and evaluated.

To realise a low cost, low energy consumption and compact wireless ECG sensor (WES) responding to the last AHA recommendation, the embedded basic technologies such as distributed real-time fault tolerant micro kernel, dedicated hardware and firmware and real-time TCP/IP protocol stack are implemented. The patient is equipped with a compact and portable (credit card format) wireless ECG sensor allowing the capture of 4 leads of ECG signals sampled at 500Hz and he may be filmed continuously by a low cost WEB camera: WEBCAM (indoors). The ECG signals are sent to a local server and will be processed to detect cardiac arrhythmias. The WES allows two operation modes: real-time and deferred.

In real-time mode, the WES may be configured to send continuously the ECG signals and the anomalies to the remote server; this configuration is adapted to the remote diagnostic but it is not adapted to monitor and to survey a large number of patients. For the remote monitoring, the WES may be configured to send the ECG signals only when a cardiac arrhythmia event is detected. The events to be sent are defined by the cardiologist. In this case, a message including a sequence of ECG signals (pre and post anomaly) and the images of the patient (indoors only) are sent immediately and automatically to the remote surveillance server. So according to the gravity of the symptom, cardiologist or physician can intervene in real-time or lately. To assure the processing of emergency message and real-time visualization of ECG signal, messages are classified into three levels: high (emergency message…), medium (ECG signal …) and low (image …). Thus with an adaptive algorithm tuning to the telecommunication traffic (especially low bandwidth medium), a classical MODEM (56Kbps) allows remote real-time visualization of 4 leads ECG signals. When the patient is at home, its images may be sent to the remote server but not in video rate, because the image is a low level message and bandwidth consuming, thus it is sent only when the network traffic is favourable.

Whereas in deferred mode, a report similar to a Holter report is sent periodically (for example once a day).

Furthermore, the patient may be contacted through Internet by the cardiologist anywhere and any time and the WES may be remotely reconfigured if necessary according to the patient state. When the network traffic is disturbed, ECG signals are temporally saved on the WES. The WES can save continuously 4 leads of ECG signals sampled at 500Hz during 24h. Our platform allows continuous remote cardiac arrhythmias monitoring and permits the patient to lead a normal life indoors and outdoors thus it is more efficient to diagnose cardiac arrhythmias. Currently the platform including a WES, a local server and the remote server, is evaluated at CHU of hospital of Gabriel Montpied at Clermont-Ferrand in FRANCE. The cardiac arrhythmias detection results are similar to the HP telemetry system ones evaluated on about ten patients. It is also evaluated by using MIT-BIH cardiac arrhythmias data base, the average cardiac arrhythmias detection is about 95%. We are working on the implementation of Intelligent Wireless ECG Sensor (IWES) by integrating the cardiac arrhythmia detection algorithm on a chip (ICAC). The ICAC is currently under evaluation and test on an FPGA. Thus the new platform contains a set of IWES and a remote server and it will be more reliable and friendly used.

[47] MECHANISMS UNDERLYING EFFECTS OF ENHANCED EXTERNAL COUNTERPULSATION THERAPY FOR ISCHEMIC HEART DISEASE.

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Enhanced external counterpulsation (EECP) has been shown to reduce angina and ischemia in patients with coronary artery disease. EECP involves sequential inflation and deflation of compressive cuffs wrapped around the lower extremities. These sequential events may increase diastolic aortic pressure and cardiac output and decrease cardiac afterload. This therapy may represent a valuable alternative for symptomatic patients despite an optimal medical treatment who cannot benefit for a conventional revascularisation by angioplasty or coronary artery by pass. Mechanisms who underlying these improvements include mechanical support as like intra aortic balloon with an increase in coronary blood flow, and other beneficial effects on endothelial function, opening or expansion of collateral vessels and a possible peripheral conditioning. However these mechanisms are poorly understood. We conduct a study including two populations of patients: asymptomatic high cardiovascular risk and confirmed
stable coronary patients. High risk patients underwent only one session, coronary artery disease patients underwent 35 sessions of EECP therapy according to the classical treatment protocol. Patients were randomized in two groups: sham-control EECP and active treatment. We proposed preliminary results concerning the acute effects of EECP. This study investigates the effect of a single session of EECP in left ventricular filling evaluated by Doppler echocardiography and cGMP levels measured by radio immunoassay in whole blood, platelet-rich plasma and isolated platelets. For this purpose we performed a Doppler echocardiography and a blood sampling before and just after the (first) EECP session. Twenty patients were included in the echocardiographic study: 6 underwent a “low” (inactive) external pressure session and 14 a “high” (active) pressure treatment. After EECP session, in patients treated by EECP, peak of E wave decreased significantly, deceleration time is prolonged but this trend is not statistically significant. None of these effects was observed in patients of inactive group.

Eighteen patients had blood samplings in order to assess cGMP and evaluate their endothelial function. Whole blood and platelets contents of cGMP increase significantly one hour after EECP treatment. Inhibition of NO synthesis by L-NMMA reduce cGMP after EECP whereas superoxide dismutase catalase increase the cGMP platelet contents after EECP. These results indicate that EECP activates NO pathway.

Our preliminary results suggest that the mechanisms underlying the beneficial effects of EECP may result from several potential effects. Among these effects, hemodynamical improvement of diastolic function and activation of NO pathway by acute shear stress stimuli may participate in the improvement in symptoms and exercise tolerance described in chronic treatment by EECP. Further investigations need to be performed for determine the complex interrelationship of cardiac and peripheral effects of this therapy.

[48] EXERCISE TRAINING AFTER CARDIAC RESYNCHRONIZATION IN CHRONIC HEART FAILURE. RESULTS OF A PILOT STUDY.
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Background: Exercise training improves exercise tolerance in chronic heart failure (CHF) patients. Recently, cardiac resynchronization has been shown also to increase functional capacity in CHF patients with intraventricular conduction delay. The aim of this pilot study was to assess complementary effects of these two non-pharmacological approaches to optimize both hemodynamic and symptomatic improvements.

Methods: We studied 8 CHF pts (mean age: 67 ± 7 years, 7 men, mean LVEF: 0.18 ± 0.08 ) who underwent 18 ± 8 sessions of exercise training after bi-ventricular pacing implantation. Exercise tolerance were evaluated before and after pacemaker implantation, and at the end of the rehabilitation.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Before PM</th>
<th>After PM</th>
<th>After Ex training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex duration (sec)</td>
<td>112 ± 37</td>
<td>218 ± 22</td>
<td>243 ± 45 *</td>
</tr>
<tr>
<td>Workload (watts)</td>
<td>44 ± 5</td>
<td>58 ± 0</td>
<td>61 ± 8 *</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/mn)</td>
<td>9.5 ± 1.0</td>
<td>13.2 ± 1.2 §</td>
<td>14.6 ± 2.8 *</td>
</tr>
<tr>
<td>% theor VO2</td>
<td>0.39 ± 0.09</td>
<td>0.53 ± 0.07 §</td>
<td>0.62 ± 0.2 * #</td>
</tr>
</tbody>
</table>

§ = p<0.05 before-after PM, * = p<0.05 before PM-after training, # = p<0.05 after PM-after training

Conclusion: Exercise training after cardiac resynchronization provides additional improvement in effort tolerance in CHF patients. These preliminary results encourage to perform a randomized study to evaluate benefits of combined strategy (resynchronization and exercise training) compared to resynchronization therapy alone in CHF patients.

[49] LONG TERM RESULTS AFTER CARDIOMYOPLASTY.
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Cardiomyoplasty (CMP) was proposed as a palliative treatment in congestive heart failure. Long term survival and functional outcome after CMP were analysed in a series of 21 consecutive patients. Between December 1989 and February 1997, a CMP procedure was performed in 21 male patients with a mean age of 56 years. All patients were in NYHA class III; 10 patients had ischemic cardiomyopathy and 11 had primary dilated cardiomyopathy. Reinforcement CMP was isolated in 12 patients and associated with a cardiac procedure in 9. There was no perioperative death and all patients were discharged from hospital. Four patients had heart transplantation: 8, 9, 11 and 26 months after CMP. In July 2003 the mean follow-up was 6±1 years. There were 16 deaths: heart failure 8, sudden death 5, death after transplantation 3. The actuarial survival was 52±22
% at 5 years and 23±20 % at 10 years; it was better in primary than in ischemic cardiomyopathy: 64±29 % vs 40±31 % at 5 years and 41±33 % vs 10±19 % at 10 years (p<0.001). The probability to be free of CMP failure (death or transplantation) was 43±21 % at 5 years and 22±19 % at 10 years. The probability to be free of acute congestive heart failure after CMP procedure was 71±20 % at 3 years, 59±23 % at 5 years and 31±26 % at 10 years; it was better in primary than in ischemic cardiomyopathy: 70±29 % vs 52±31 % at 5 years. Five patients were still alive: 4 patients 10, 10.5, 12.5 and 13 years after isolated CMP were in NYHA class II, II, III, III respectively; and 1 patient 6.5 years after CMP and then transplantation was in class 2.

CMP seems to have been useful for patients in comparison with medical treatment but less than heart transplantation. The occurrence of sudden death often in patients with good functional results hid the benefit of the procedure. CMP was more liable to stabilize primary than ischemic cardiomyopathy. Good functional outcome observed more than 10 years after the surgery point to a possible renewal of this surgical concept.

[50] GENE THERAPY OF CORONARY ARTERY DISEASE WITH PHVEGF165.

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Background: We initiated clinical study to determine safety and activity of gene encoding vascular endothelial growth factor (VEGF) 165 administered directly into the myocardium as the only treatment and during coronary artery by pass grafting operation (CABG). Our trials with the plasmid encoding VEGF165 shows that intramyocardial application is safe and patients have benefited with the therapy.

Methods: VEGF gene transfer was performed in 31 patients (29 male, 2 female, ages from 48 to 73 years old). 200µg of the plasmid encoding VEGF165 was injected into the ischaemic, viable myocardium that could not be surgically revascularized in patients undergoing CABG and 400µg in patients without CABG. Patients with ejection fraction (%EF) < 30%, fertile females, acute myocardial infarction (MI), retinopathy and neoplasms were excluded from the study. 15 patients had performed CABG, in 16 cases there was no possibility of CABG because of surgical limitations and the application of genes encoding VEGF165 was the only solution. %EF, myocardial perfusion, ECHO, angiogram, ventriculography, quality of life and nitroglycerin consumption were evaluated pre- and postoperatively.

Results: The most of patients tolerated surgery uneventfully, in both groups of patients 2 deaths occurred. In three cases the evidence of myocardial infarction was noted. %EF improvement haven’t been noticed so far. Most of patients were angina free at 6 months after surgery. Patients reported much better quality of life and reduction of nitroglycerin use. A reduction in ischaemic defects on SPECT scans were observed, particularly on rest SPECT scans. In some of patients angiography revealed improved collateral filling. Conclusions: Direct myocardial administration of genes encoding VEGF165 can be an effective method of treatment patients with chronic and advanced coronary artery disease either as a supplementary or as a sole therapy.

[51] A MECHANICAL VALVE FOR LVAD DESTINATION THERAPY?

By Sidney Levitsky, M.D.

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One of the troubling aspects of LVAD development has been the valvular components of the devices. Tissue valves have had durability problems that limit longer-term usage associated with destination therapy. Mechanical valves have problems with hemolysis and thromboembolism, may require higher levels of anticoagulation, and suffer from potential cavitation damage. A mechanical valve appropriate for destination therapy must have exceptional flow dynamics, be minimaly damaging to the blood, be resistant to cavitation damage and allow reduced levels of anticoagulation. The On-X valve, developed for standard valve replacement therapy in the late 1990’s, has properties that make it a promising candidate for trial in LVAD destination therapy. Bench studies have demonstrated a higher threshold for cavitation. Clinical studies of the valve have shown it to have superior hemodynamics with a 19mm valve mean gradient of 9 mmHg and an effective orifice area of 1.5 cm2. Combined with this flow advantage is a low propensity for blood damage with postoperative LDH values in the normal range even in double valve replacement and low rates of thromboembolism especially in the face of erratic anticoagulation control. A clinical study in a poorly-anticoagulated South African population of over 200 mainly mitral or double valve replacement patients, with up to 3 years of follow-up and approximately 20% of the population not anticoagulated at all, has produced no thrombosed valves and only one thromboembolic event to date. Clinical results indicate a real opportunity for reduced anticoagulation and have prompted the start of a study of the valve using aspirin only for anticoagulation. This background has also led to the initiation of tests of the On-X valve in several LVAD platforms for destination therapy.
A TECHNIQUE OF MITRAL VALVE REPAIR SPECIFICALLY CONCEIVED FOR ISCHEMIC REGURGITATION
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IRCCS Ospedale Maggiore ed Università degli Studi di Milano
Milan, Italy

Objective
Chronic ischemic mitral regurgitation (MR) carries a poor outcome and remains a challenging management problem. Traditional approaches (valve replacement) or recently proposed techniques (reductive annuloplasty, edge-to-edge, chordal cutting) don’t give satisfying results.

We propose a new technique of valve repair addressed to the main pathophysiologic mechanisms. The procedure and immediate results are analysed.

Methods
Post-infarction ventricular remodelling causes chronic ischemic MR by asymmetric apical displacement of papillary muscles. Posterior papillary muscle is usually affected resulting in restricted motion of posterior mitral leaflet (PML) and anterior leaflet “pseudo-prolapse”; a variable degree of annular dilation is generally present.

Type I and III regurgitation, according to Carpentier’s classification, coexist and make the treatment difficult. A new technique was conceived to address these specific alterations.

We performed a valve repair in 12 patients with the following procedure: after standard left atriotomy, an incision was made to detach from the annulus the tethered segment of the PML (generally at P2-P3 level). Secondary chordae were transacted to increase leaflet mobility. The involved portion of the annulus was plicated with interrupted sutures. The residual defect of the leaflet surface was closed suturing the margins not to the annulus but between them in order to increase the area of the PML. Finally the plicated annulus was reinforced with a Gore-Tex strip.

Coronary revascularization and left ventricular reshaping (Dor procedure) were added when clinically required.

Results
One hospital death was recorded (8%) and 1 patient (8%) underwent early mitral valve replacement. In all patients immediate postoperative echocardiography showed good results (MR less than grade 1) and no systolic anterior motion was detected.

At the mean follow-up of 17 ± 6,5 months (range 3-31) no valve related events were registered and 9/11 patients (82%) were in NYHA I-II. At early post-discharge echocardiographic control 8/11 patients (73%) showed trivial or no MR.

Conclusions
The procedure restores mitral geometry toward a correct annular diameters ratio, it repositions the tethering leaflet acting on P2-P3 annulus and PML area is extended to achieve a better coaptation. Moreover a posterior reinforcing band preserves the dynamic motion of the annulus ideally allowing better ventricular function.

Immediate results are encouraging but further study will be required to assess repair durability and patients’ outcome.

CARDIAC RESYNCHRONIZATION THERAPY AFTER CABG IN PATIENTS WITHOUT LEFT BRANCH BLOCK
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Cardiac Resynchronization Therapy (CRT) has proved to be good treatment for patients suffering from myocardial insufficiency and left branch block. Recent studies show that this therapeutic option should not be limited to patients with this ECG abnormality. Our aim was to show that patients, especially the ones with a poor ejection fraction, profit from this therapeutic option after CABG.

Three groups (20 patients each), all without left branch blocks, underwent elective CABG. The first two groups had poor ejection fractions (< 35%). But only one of both groups received permanent biventricular stimulation for seven days after surgery. The third group consisted of patients with good ejection fractions. They also received continuous biventricular stimulation. Before and on the first, third, seventh and tenth day after the surgical treatment the following parameters were established: left ventricular function obtained through transthoracic echocardiography, myocardium-specific enzymes (Creatininkinase and Isoenzyme), Brain Natriuretic Peptide (BNP) and ECG.

No patient had a preoperative left branch block or developed one after CABG. Our first results (n = 36) indicate a significant improvement (p<0.002) in left ventricular function for patients with poor ejection fractions during biventricular pacing. Due to these better ejection fractions the patients only stayed in ICU up to 2 days. Only one patient in this group did not benefit from...
biventricular pacing. Without biventricular pacing after CABG the left ventricular functions of patients with poor ejection fractions were reduced even more \( (p=0.05) \) in the early postoperative days. Patients with a good left ventricular function did not benefit from biventricular pacing. With them, there even was a decrease in left ventricular function during biventricular pacing. The evaluation of BNP after CABG was similar to these results of left ventricular function. Patients with a poor ejection fraction, who received biventricular stimulation, reached near-preoperative BNP-levels on day 10. In contrast to this, patients who did not receive biventricular stimulation did not show any decrease in BNP-levels until postoperative day 10.

We conclude that patients with a poor left ventricular function benefit most from biventricular pacing in the early postoperative days. To us there is indication for this therapy in patients who suffer from an ischemic myocardial dilatation. A left branch block is not necessary. But echocardiographic analysis showed an improvement of the left ventricular contraction similar to the one observed in patients who received cardiac resynchronisation therapy due to a left branch block. We explain our results in the following way: Our patients do not suffer from a block in Tawara branch but from one further downstream in the dilated ventricular myocardium.

We recommend that these patients should receive a permanent CRT. In our opinion there are the following criteria for the implantation of a biventricular pacing device: poor ejection fraction (< 35 %), ischemic myocardial dilatation, postoperative benefit from non-permanent biventricular pacing and decrease of BNP-level during biventricular pacing before day 10. These patients should receive a permanent epicardial lead implanted on the left ventricle during CABG procedure. About ten days after CABG a permanent CRT device should be implanted. Therefore we implant a rightatrial and rightventricular lead transvenously and we use the leftventricular epicardial lead for leftventricular stimulation.

[54] REDUCTION OF NUCLEAR FACTOR KAPPA B ACTIVITY POST MYOCARDIAL INFARCTION IMPROVES VENTRICULAR REMODELING BY ATTENUATING THE INFLAMMATORY RESPONSE

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Ludwig Boltzmann Institute for Cardiosurgical Research, Institute of Biomedical Research, AKH Wien, Universität Wien, Vienna, Austria

Objective: The transcription factor nuclear factor kappa B (NF-kB) plays an important role in the inflammatory response following myocardial infarction (MI). We hypothesized that NF-kB+ blockade by gene-therapeutic overexpression of its inhibitor Inhibitor KappaB alpha (IkB) in an animal model of acute ischemia reduces the inflammatory response and therefore reduces ventricular remodeling.

Methods: MI was induced in male Sprague-Dawley-rats by ligation of the LAD and followed by adenovirus-mediated intramyocardial delivery of IkB-gene \( (n=12) \) respectively of a LacZ-reporter-gene \( (n=12) \). Sham-operated animals \( (n=12) \) received neither ligation nor gene transfer. 5 days after MI IkB-expression and tissue levels of TNF-alpha and IL-1beta were determined by westernblotting. Seven weeks after MI cardiac function was evaluated by transthoracic echocardiography and pump function curves on an isolated working heart.

Results: In the treatment group IkB-Lvels were 5,95fold higher whereas TNF-alpha and IL-1beta protein levels were significantly reduced by 72,6% and 73,2%, respectively, in the remote area compared to LacZ-transfected hearts \( (n=6; p=0.05) \). Concerning in vivo hemodynamics Ikb-treated hearts showed reduced systolic and diastolic left ventricular dimensions with consequently preserved ejection fraction compared to the LacZ-MI-group (Table 1). Ex vivo both infarct groups were shifted left-and-downward significantly compared to the sham-operated hearts \( (p<0.01) \), however this shift was less pronounced in the Ikb-group \( (p<0.05) \) compared to the LacZ-MI-group. Data are given as mean +/- SD.

Conclusion: Overexpression of IkB alpha after MI attenuates the inflammatory response involved in cardiac remodeling, reduces left ventricular dilatation and therefore enhances cardiac function.

Table 1: In vivo hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>Infarct + IkB (I) ( n=6; \text{mean} \pm \text{SD} )</th>
<th>Infarct + LacZ (II) ( n=6; \text{mean} \pm \text{SD} )</th>
<th>Sham – operated (III) ( n=6; \text{mean} \pm \text{SD} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end diastolic dimension, cm</td>
<td>(0.69 \pm 0.07)</td>
<td>(0.84 \pm 0.05) (p&lt;0.05) vs. I</td>
<td>(0.52 \pm 0.09) (p&lt;0.01) vs. I,II</td>
</tr>
<tr>
<td>LV end systolic dimension, cm</td>
<td>(0.53 \pm 0.09)</td>
<td>(0.66 \pm 0.03) (p&lt;0.05) vs. I</td>
<td>(0.31 \pm 0.08) (p&lt;0.01) vs. I,II</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>(62% \pm 3%)</td>
<td>(45% \pm 8%) (p&lt;0.05) vs. I</td>
<td>(79% \pm 5%) (p&lt;0.01) vs. I,II</td>
</tr>
</tbody>
</table>

[55] AUTOLOGOUS PERIPHERAL BLOOD STEM CELLS TRANSPLANTATION FOR MYOCARDIAL REGENERATION: A NOVEL STRATEGY FOR CELL COLLECTION AND SURGICAL INJECTION.

Giulio Pompilio, Aldo Cannata, Fedro Peccatori, Francesco Bertolini, Angelo Nascimbene, Maurizio C Capogrossi and Paolo Biglioli.
Background. We describe an original technique for intramyocardial injection of peripheral blood-derived stem cells (PBSC) collected by apheresis in order to induce and positively select with anti CD-133 antibody.

Materials and methods. We designed a pilot clinical phase-1 trial to assess the feasibility and safety of PBSC transplantation for myocardial regeneration and angiogenesis. We enrolled so far 2 patients with evidence of a large ischemic area in the left ventricle with target coronary artery not suitable for traditional revascularization; and 2 others patients candidates to surgical revascularization with a distinct large recent inferior infarction. 10 mg/Kg/die of Lenograstim were subcutaneously administered for 4 consecutive days in order to mobilize stem cells from the bone marrow to the peripheral blood. Stem cells mobilized were collected by means of apheresis and processed in order to purify the CD133+ cells fractions. All patients received PBSC intramyocardial injection and concomitant off-pump coronary artery bypass grafting, but patient 4, which was treated by PBSC implant alone through a minimally-invasive trans diaphragmatic approach. Patients are followed up for 6 months after surgery.

Results. In mean we collect 1-5x106 CD133+ cells/Kg in a final volume of 15 mL. Both the procedures and postoperative course were uneventful and no complications related to PBSC mobilization, collection and injection were noted. White blood cell count normalized in all cases before hospital discharge. Patients are recovering well at a mean of 4 months from the intervention. Patients 1 and 2 completed the 6-months follow-up. SPECT and echocardiographic reinvestigation showed in patient 1 significant improvement in perfusion of the anterolateral wall, and in patient 2 restoration of viability of the inferior wall.

Conclusions. This novel method of peripheral bone marrow stem cells collection and intramyocardial injection is safe, feasible and reproducible. However, further evidences are needed in order to definitely assess safety issues and clinical results.
The results of these studies indicate extensive development of myocardial neovascularisation after the transplantation of a free skeletal muscle flap onto the heart. The good results in patients stress the importance of a further ongoing of this promising technique in myocardial revascularisation.

HAEMODYNAMIC AND ULTRASOUND ASSESSMENT OF THE SKELETAL MUSCLE VENTRICLE AND THE INTRA-AORTIC BALLOON PUMP IN NORMAL CIRCULATION AND IN ACUTE HEART FAILURE

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Aim:
The intra-aortic balloon pump (IABP) is the most common clinical cardiac assist device. It inflates in diastole, augmenting aortic pressure and coronary artery flow, and it deflates during systole unloading the heart (counterpulsation).

We used a porcine model to assess:
1. The effect on aortic pressure and left anterior descending coronary artery (LAD) blood flow of a skeletal muscle ventricle (SMV) and an IABP in the same animal.
2. The haemodynamic influence of the SMV in acute heart failure brought about by LAD occlusion.
3. The potential use of ultrasound in monitoring SMV function.

Methods:
SMVs were connected to the thoracic aorta in seven anaesthetized pigs. IABPs were simultaneously placed into the descending thoracic aorta. The devices were activated during diastole in every third cardiac cycle. Pressure in the aortic root and LAD flow were recorded during periods in which either the SMV or the IABP was active. In two pigs the LAD was snared, resulting in acute heart failure. The haemodynamic effect of the SMV was then assessed on the compromised system. To minimize inter-animal variation, the difference between haemodynamic variables during the assisted and unassisted cycles was expressed as a percentage of the unassisted value.

Echocardiography was used to visualize the heart and the SMV. Blood flow and volume changes during different phases of the cardiac cycle were assessed.

Results:
Table: Haemodynamic comparison of the SMV with the IABP and under conditions of acute heart failure. (EVR-endocardial viability ratio)

<table>
<thead>
<tr>
<th></th>
<th>% increase in mean diastolic aortic pressure</th>
<th>% increase in peak diastolic aortic pressure</th>
<th>% increase in EVR</th>
<th>% increase in mean diastolic LAD flow</th>
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<tr>
<td>Normal Circulation</td>
<td>(mean ± standard error of mean, n=7)</td>
<td>(mean ± standard error of mean, n=7)</td>
<td>(mean ± standard error of mean, n=7)</td>
<td>(mean ± standard error of mean, n=7)</td>
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<tr>
<td>SMV</td>
<td>22.4 ± 4.0</td>
<td>35.6 ± 3.7</td>
<td>32.1 ± 5.2</td>
<td>42.6 ± 9.5</td>
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<tr>
<td>IABP</td>
<td>19.8 ± 2.3</td>
<td>27.8 ± 8.8</td>
<td>23.5 ± 4.5</td>
<td>35.5 ± 4.7</td>
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<tr>
<td>Acute Heart Failure</td>
<td>(mean ± standard deviation, n=2)</td>
<td>(mean ± standard deviation, n=2)</td>
<td>(mean ± standard deviation, n=2)</td>
<td>(mean ± standard deviation, n=2)</td>
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<tr>
<td>SMV</td>
<td>9.2 ± 1.7</td>
<td>25.4 ± 14.5</td>
<td>8.9 ± 0.6</td>
<td>20.6 ± 8.2</td>
</tr>
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</table>

The IABP and the SMV both acted as effective counterpulsators and significantly increased the EVR and mean diastolic LAD flow during the assisted beat. The SMV also increased the EVR and the mean diastolic LAD flow in the acute heart failure model.

Limited information is available in the literature about echocardiography in pigs. The narrow rib spaces make visualization of the porcine heart difficult. Echocardiographic assessment was performed both transthoracically and with the transducer positioned directly on the heart and SMV. With the SMV activated, echocardiography provided good visualisation of the structure of and blood flow within the heart, the proximal coronary arteries, the SMV and the descending aorta.

Conclusion:
1. In all cases the SMV acted as an effective counterpulsator, with effects that were as good as or better than an IABP.
2. The SMV seems to be effective in acute heart failure.
3. The SMV therefore offers the potential for providing the known benefits of the IABP in an ambulant patient.
4. The use echocardiography for non-invasive haemodynamic monitoring and for detection of thrombus formation within the SMV appears to be feasible in the porcine recovery model.
Objectives: Cellular cardiomyoplasty using autologous skeletal muscle cells in a patient.

Material and methods: To obtainment of muscle through biopsy (10grs). Separation of fatty tissue, minced, and digestion with collagenase type I (1.5mgr/ml/2gr by weight) and trypsin 1x. Filtration of the cellular suspension, centrifugation and sowing of this suspension in culture medium, with 20% of human serum. Culture for three weeks until obtainment of between 250 million cells. Flow cytometry for the identification of the myoblasts was carried out.

Results: Through flow cytometry, using CD56 as an indicator of the presence of myoblasts, between 70-80% of this type of cells after three weeks of culture were obtained. Different studies showed a significant improvement in ventricular function in the treated patient.

Conclusions: The culture of autologous myoblasts is a rapid and simple technique where after three weeks of culture a great number of cells for implantation are obtained. Satellite cells implanted in a myocardial lesion were associated with a functional improvement of global contraction.

Objectives: Cellular cardiomyoplasty using myoblasts obtained from satellite cells of muscle are used to repair the non-functional myocardium tissue and to be a complement to revascularization surgery allowing a major recovery cardiac function.

Material and methods: To obtainment of muscle through biopsy of 10 human multiorgan donors. Separation of fatty tissue, minced, and digestion with collagenase type I (1.5mgr/ml/2gr by weight) and trypsin 1x. Filtration of the cellular suspension, centrifugation and sowing of this suspension in culture medium, with 20% of human serum. Culture for three weeks until obtainment of between 100-200 million cells. Immunohistochemistry and flow cytometry for the identification of the myoblasts was carried out.

Results: Through flow cytometry, using CD56 and desmin as indicators of the presence of myoblasts %CD56: 63 and %desmina: 41% of this type of cells after three weeks of culture were obtained. Different studies showed a significant improvement in ventricular function in the treated patient.

Conclusions: The culture of autologous myoblasts is a rapid and simple technique where after three weeks of culture a great number of cells for implantation are obtained.
Introduction: The use of metallic cardiac valves produces some problems. However, the use of valvular homografts, although these are less durable, has several advantages. However, in the last few years, the viability of valvular homografts has been observed and this viability affects the clinical durability.

Objectives: To analyze the influence of cold ischemic time (2-24 hours) and of cryopreservation (liquid phase) on the viability of the valvular fibroblasts and in the level of apoptosis.

Material and methods: Obtained cardiac valves of 10 pigs. 3 work groups were established; group 1: 2 hours of ischemia, group 2: 24 hours of ischemia, both in fresh and group 3: programme cryopreservation (–1ºC/min) after 2 hours of ischemia, storage in liquid nitrogen during a week and thawing. All the samples were evaluated by anatomo-pathological study of the wall, muscle and veil. At the same time, the presence of cellular death due to apoptosis was evaluated directly in the tissue by Apodetec (BD) system and in a suspension of cells by flow citometry with double dye using Anexina V and propidium iodure.

Results: The study through flow citometry showed viabilities of 51.34% in group 1, 53.85% in group 2 and 42.84% in group 3. The analyses of observed mortality indicated that a 3.96%, 2.78%, 5.28% of the cells, respectively in each group, died through apoptosis, while a 48.66%, 46.15% and 57.16% died due to necrosis. The study of apoptosis in the tissue confirmed the presence of a small number of cells distributed throughout all the tissue in the samples of group 2 and of group 3, together with an increased number of picnosis in the cells.

Conclusions:
1. The viability of the valves differ slightly due to the ischemic time and/or the cryopreservation,
2. The ischemia for 24 hours produces, slightly a greater cellular damage according to the level of necrosis and apoptosis.

[61] MUSCULAR COUNTERPULSATION: A LOW INVASIVE AND LOW COST APPROACH TO FAILING HEART

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OBJECTIVE: Muscular CounterPulsation (MCP) is a new left ventricular assist device that consists in stimulating some skeletal muscles with an electric signal during diastole. We designed an animal study to evaluate a device based on muscular counterpulsation that should reproduce the same hemodynamic effects as IABP in a completely non-invasive way.

METHODS: three calves, 56±6 kg in weight, in general anaesthesia, equipped with EKG, Swan-Ganz, pressure probe in the carotid artery and flow probe in the left femoral artery, received muscle counterpulsation (MCP). MCP consists of electrically induced skeletal muscle contraction during early diastole, triggered by EKG and microprocessor-controlled by a portable device. The stimulation signals consists of rectangular bi-phase fully balanced constant voltage impulses with a width (plus/minus) of 1 ms at a frequency of 200 Hz during a train duration of 75 ms set at 15-20Volts amplitude. For each animal the following parameters were considered: mean aortic pressure (mAoP), CO, CI, LVSWI (left ventricular stroke work index), SVR (systemic vascular resistance) mean femoral artery flow (Faf). We did 3 sets of measurements: baseline (BL), after 20 (M20) and 40 (M40) min of cardiac assistance. Those measurements have been repeated after 40 min of rest for 3 times. Results are expressed as mean±S.D.

RESULTS:

<table>
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<tr>
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<th>mAoP</th>
<th>mCVP</th>
<th>CO</th>
<th>LVSWI</th>
<th>SVR</th>
<th>Faf</th>
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<tr>
<td>Baseline</td>
<td>76.5±12</td>
<td>11.5±3</td>
<td>5±1</td>
<td>0.77±0.1</td>
<td>1040±15</td>
<td>75.5±10</td>
</tr>
<tr>
<td>MCP</td>
<td>60.1±7</td>
<td>23.6±2</td>
<td>4.8±0.4</td>
<td>0.69±0.2</td>
<td>608±25</td>
<td>92.3±12</td>
</tr>
<tr>
<td>MCP vs Baseline</td>
<td>n.s.</td>
<td>P&lt;0.001</td>
<td>n.s.</td>
<td>n.s.</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
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</table>

CONCLUSIONS: MCP showed an efficient cardiac unloading. Moreover, MCP reduced SVR and increased the peripheral circulation without requiring any vascular access nor anticoagulation therapy. Even if muscular mass and painful muscular contraction could be limiting factors, we believe this device has great potential in the treatment of heart failure.