View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

dP/dtmax was recorded during Left Ventricular (LV) catheterization prior to and during Phenylephrine (PE) [5-50 micrograms/minute]. Infarct size was measured by tetrazolium and planimetry.
Results: Mean LV Ejection Fraction (EF) in the short axis in Group 1 was 88 ± 3% at baseline and decreased to 78 ± 4% at 4 months (p=0.03). In Group 2, EF decreased from baseline of 87 ± 4% to 51 ± 3% at 1 month (p=0.001) and did not change thereafter. Although EF in Group 3 decreased from 87 ± 4 % to 63 ± 3% at 1 month, EF progressively increased to 69±6% at 4 months, which was similar to controls but different than Group 2 (p=0.02). Septal wall thickening in Group 3 was 57.9 ± 11.6% at 4 months, which was nearly identical to the control septal thickening of 59.2 ± 8.9 %, and was significantly greater than Group 2 septal thickening which was only 27.8 ± 7% (p=0.02). dP/dtmax in Group 3 increased from 3568 ± 701 to 10062 ± 784 mmHg/s (p=0.001) with PE 50 micrograms/minute which was similar to maximum control, but only increased from 3955 ± 803 to a maximum value of 7534 ± 941 mmHg/s in Group 2. The infarct sizes averaged 2.98% ± 2.8% for Group 3 versus 22.1% ± 5.6 % for Group 2 at three months (p=0.02) and 9.2 % ± 2.0 for Group 3 versus 40.0 ± 9.2 for Group 2 (p=0.001) at four months. The HUCBC migrated from the periphery into the infarction and were aligned and in register with the host cardiomyocytes at 3 and 4 months.
Conclusion: HUCBC can significantly limit ischemic damage and improve LV function in the infarcted rat heart.

1078-93 Enhanced Angiogenesis With Autologous Bone Marrow Transplantation in a Porcine Nonreperfused Myocardial Infarction Model

Ron Waksman, Jana A. Fournadjiev, Richard Baffour, Laurent Leborgne, Rajbabu Pakala, David Hellinga, Hamid Yazdi, Edouard Cheneau, Roswitha Wolfram, Rufus Seabron, Keneth Horton, Frank Kolodgie, Renu Virmani, Elias Rivera, Washington Hospital Center, Washington, DC, Armed Forces Institute of Pathology, Washington, DC

Background: Cell transplantation is becoming a viable strategy to improve revascularization and left ventricular function after myocardial infarction (MI) injury. This study evaluated the effect of trans-epicardial bone marrow (BM) cell transplantation on infarct size, blood vessel formation and myocardial function in a porcine model of non-reperfused MI.
Methods: Coil implants were positioned in the coronary circulation of 13 domestic swine to produce MI. Twenty-eight days later, autologous BM was aspirated, labeled with bromdeoxyuridine (BrdU), and cultured for 48 hours. Animals underwent a left thoracotomy and 0.2 ml of BM (~ 1.5 million cells/ml) were injected at 8 sites (1 cm apart) within the infarcted and border regions of 8 swine; 5 animals injected with saline served as controls. Animals received systemic BrdU 24 hours prior to euthanasia at 28 days. Regional contractility was assessed by trans-epicardial echography performed at the time of BM injections and at the end of the study period.
Results: The infarct size (mm^2) was smaller in the BM transplanted group (81.83±10.65) than in the control group (147.72±23.25, p= 0.015). BrdU positive cells of BM treated and controls were 51.66% and 29.19%, respectively. Further, α-actin positive cells were significantly greater in the BM injected animals (BM= 314.8±37.4 vs. saline= 167.1±11.9/ $0.1mm^2$, p=0.02) as well as the number of factor VIII positive endothelial cells (BM= 363.3±28.2 vs. saline= 254.4±28.1 cells/$0.1mm^2$, p=0.03). The number of blood vessels >50μm was significantly increased in the BM group=317.9± 54.9 vs 149.12± 6.08(p<0.05). Wall motion score index was similar in the BM injected and saline groups at baseline (1.63±0.16 vs. 1.25±0.25, p=0.21) and at 28 days (1.83±0.22 vs. 1.63±0.38, respectively, p=0.62).
Conclusion: BM cell engraftment of infarcted tissue is feasible with cell viability maintained up to 28 days and is an effective strategy for infarct size reduction. Increased angiogenesis by BM transplantation in a model of non-reperfused MI was not sufficient to support an improvement in left ventricular function.

1078-94 Acute Myocardial Infarction Is a Stimulus for Stem Cell Mobilisation and Elevated Erythropoietin Serum Levels

Korff Krause, K. Jaquet, K. Kyriazis, B. Fehse, C. Lange, A. Zander, K. H. Kuck, St. Georg Hospital, Hamburg, Germany, University of Hamburg, Hamburg, Germany

Introduction: Bone marrow derived stem cells have the capacity to home infarcted heart tissue, and promote cardiac repair as shown in experimental data in animal models. So we addressed the question wether progenitor cells that have been shown to differentiate into endothelial cells and cardiomyocytes in vitro and in vivo are mobilized in peripheral blood (PB) in patients with coronary heart disease (CHD) and determined growth factor serum levels.
Methods: PB was taken from 16 pts. with acute myocardial infarction (AMI), 8 pts. with angina pectoris (AP) an 10 pts. without CHD who underwent cornary angiogram (control) and analysed with FACS analysis (percent/1 million cells). Growth factor and Epo serum levels were determined with ELISA technique (mU/ml). Samples were drawn at time point (TP) 1 (day 1-3 after ischemic event) and time point (TP) 2 (day 4-8).
Results: The mean values of CD34+, CD117+ and CD133+ cells were all elevated in pts. with either AMI or AP compared to the control group. Pts. with AMI had doubled cell counts of CD117+ and CD34+ progenitor cells in PB compared to pts. with AP. Epo was significantly elevated in pts. with AP and AMI:

	Time point 1 (mean)	Time point 2 (mean)
CD34: AMI/AP/control (%)	0.21/0.19/0.10	0.31/0.27/0.12
CD117: AMI/AP/control (%)	0.09/0.05/0.06	0.30/0.05/0.06
CD133: AMI/AP/control (%)	0.20/0.21/0.11	0.19/0.11/0.10
Epo: AMI/AP/control, (mU/ml)	34.0/24.0/9.0	30.0/27.5/8.2

Conclusion: Pts. with AMI have increased CD34+, CD117+ and CD133+ precursor cell mobilisation after ischemic events. Acute myocardial infarction is a stimulus for CD117+ and CD34+ progenitor cell mobilisation and Epo may play a role in its regulation.

1078-95 Intracellular Calcium Regulates Tumor Necrosis Factor-Alpha-Induced Embryonic Stem Cell Migration

Emel Kaplan, Yu Chen, Jiang-Yong Min, Jamal S. Rana, Qinen Ke, James P. Morgan, Beth Israel Deaconess Medical Center, Boston, MA

Background: Previously we have shown that after systemic injection of murine embryonic stem cells (ESCs), these cells home to the hearts of mice suffering from myocarditis. The purpose of this study was to visualize the migratory pattern of ESCs during TNF-alpha induced chemotaxis and to test the association between intracellular calcium concentration ([Ca2+]i) and ESC motility.
Methods: We used high speed optical sectioning microscopy to observe and record the behavior of ESCs. A direct viewing chemotaxis chamber with two concentric wells (Dunn chamber) allowed us to establish a linear concentration gradient of TNF-alpha. ESCs were suspended in a physiological buffer and maintained at 37 °C. Cell movement was monitored every two minutes over a three hour period, using concentrations of TNF-alpha of 2.0-10.0 ng/l (n=45). Changes in [Ca2+]i were measured with the fluorescent dye fura-2/AM.
Results: At these concentrations of TNF-alpha we found that ESCs migrated towards TNF-alpha in a dose-related manner with mean rates of 1.3-3.6 μm/min. The total movement of the ESCs also varied with different concentrations of TNF-alpha. Furthermore, TNF-alpha induced the formation of proteopodia, which in turn play an important role in migration and homing of stem cells.
During migration ESCs showed an increase in intracellular Ca2+. To further investigate the role of Ca2+ in the migration of ESCs, we monitored cells in the presence and absence of extracellular Ca2+ and found that presence of extracellular Ca2+ had a positive effect on migration (n=20).
Conclusion: These results demonstrate that ESCs are highly motile and respond to different concentrations of TNF-alpha in a dose-related manner. Also, an increased [Ca2+]i has a positive effect on such a migration of ESCs. These mechanisms may play a critical role in heart-specific homing of ESCs, after systemic injection.

1078-96 The Role of Collateral Circulation in the Acute Phase of ST-Segment Elevation Myocardial Infarction Treated With Primary Coronary Intervention

Peter Elsman, Arnoud W. J. van t' Hof, Kor Miedema, Stoffer Reiffers, Felix Zijlstra, Isala Klinieken, location Weezenlanden, Zwolle, The Netherlands

Background: The role of collateral flow in the first hours of infarction remains unclear. Our aim was to determine whether angiographic evidence of coronary collateral flow has a beneficial effect on infarct size and left ventricular function in acute myocardial infarction (MI) treated with early primary coronary intervention (PCI).
Methods: Between 1994 and 2001 1074 patients with acute MI treated with early PCI, TIMI 0 or 1 flow at first contrast injection and technical adequate angiograms for collateral flow detection were analysed.
Results: Comparing collateral flow grade 0, 1 and 2/3, increased collateral flow is associated with lower incidence of Killip class ≥ 2 at presentation (12.% versus 9.8% versus 4%, p for trend 0.01), decreased use of intra aortic balloon pumping (IABP) post-PCI (17.2% versus 12.8% versus 4.7%, p for trend 0.0005), better myocardial blush grade (MBG)(MBG3: 21.2% versus 25.4% versus 29.2%, p for trend 0.04) and smaller enzymatic infarct size ($LDHQ_{36}$) (1947±1553 U/l and 1893±1549 U/l versus 1221±767 U/l, p=0.001). These beneficial effects are particular present in LAD related infarcts.
Conclusion: Presence of angiographically detectable collaterals have a protective effect on enzymatic infarct size and pre- and post-intervention hemodynamic conditions in patients with acute MI treated with early PCI, in particular when Rentrop grade 2/3 is present and in LAD related infarcts.

1078-97 The Protective Effect of Edaravone on Myocardial Damage During Ischemia-Reperfusion in Rabbit Heart

Yujirou Tanabe, Shinji Okubo, Yachiyo Hoshiba, Kenji Takeda, Sumiyo Kudoh, Michihiko Kitayama, Seiyu Kanemitsu, Hiroichi Tsugawa, Noboru Takekoshi, Kanazawa Medical University, Uchinada, Japan

[Background]A free radical scavenger, edaravone has the ability to stimulate prostacycline release and to inhibit the lipoxygenase pathway in the arachidonic acid cascade. We demonstrated whether edaravone attenuates the myocardial damage in the ischemia-reperfusion rabbit heart.
[Methods]All rabbits underwent sustained coronary artery occlusion(CAO) for 30 min followed by 180 min of reperfusion. 1)Control(n=8), 2)Edaravone-early(n=8, 3mg/kg i.v):10 min before reperfusion, 3) Edaravone-immediately(n=8, 3mg/kg i.v):immediately after reperfusion, and Edaravone-late(n=8, 3mg/kg i.v):5 min after reperfusion were studied. Infarct size was determined by TTC staining. The percentage of apoptosis cells (nuclear DNA fragmentation detection via fluorescence microscopy) was calculated and DNA ladder assay was prepared from the ischemic region.
[Results] 1)Infarct size as a percent of the area at risk in control was 42.8±5.2%. Edaravone-early (23.5±3.3%) and Edaravone-immediately (24.5±5.3%) were significantly reduced infarct size (p<0.01) compared with control group. However, when edaravone was present 5 min after reperfusion, protection was completely abolished (39.6±4.5%). 2) The findings of DNA fragmentation were significantly(p<0.01) decreased in Edaravone-early (2.5±1.8%) and Edaravone-immediately (3.2±1.8%) group compared with control (15±3.9%) and Edaravone-late (13.5±3.3%).DNA laddering were attenuated in Edaravone-early and Edaravone-immediately group. [Conclusions] Single bolus adminis-

tration of edaravone at 10 min before reperfusion and immediately after reperfusion had a cardioprotective effect against ischemia-reperfusion injury, but the treatment with edaravone at 5 min after reperfusion did not show this protective effect.

1078-98 Transplantation of Autologous Bone Marrow Mononuclear Cells Does Not Alter Arrhythmia Threshold in Adult Swine With Chronic Myocardial Ischemia

Fernando Tondato, Aysegul Yegin, Jianhua Cui, Mio Ebato, Bunken Ebato, Steve Frohwein, Jesse Rios, Keith Robinson, Nicholas Peters, James Sanzo, Traci Goodchild, Mark Ungs, Nicolas Chronos, American Cardiovascular Research Institute, Atlanta, GA

Background: Bone marrow-derived mononuclear cells (BM-MNCs) can give rise to endothelial progenitor cells and localized transplantation of BM-MNCs in ischemic myocardium may augment neovascularization. However, not much is known of the arrhythmogenic potential of BM-MNCs after intramyocardial transplantation. Objective: Evaluate the threshold for ventricular arrhythmia induction with conventional electrophysiologic study (EPS) with programmed stimulation in swine with chronic myocardial ischemia treated with autologous BM-MNCs. Methods: Adult Yucatan swine underwent left circumflex (LCX) ameroid implantation. At 4 weeks, animals were randomized to receive either BM-MNCs (n=8) or DMEM culture medium as control (n=8). Bone marrow (30-50ml) was aspirated from sternum and if necessary, iliac crest. Mononuclear cells were isolated using density gradient centrifugation. Catheter-based (Boston Scientific Stiletto^{TM}) intramyocardial injections were performed with combined fluoroscopic and intracardiac echocardiography (ICE) guidance. The treatment group received total of 1 x 10^8 BM-MNCs at 10 sites, 5 in ischemic (LCX), and 5 in non-ischemic (LAD) region. Four weeks after cell treatment, global wall motion score index (GWMSI) was evaluated by dobutamine stress echocardiography. Subsequently, electrophysiologic study was performed with right ventricle stimulation at apex and outflow tract, using a basic cycle length of 500 and 400msec and 1-3 extrastimuli. Results: No difference was found in total number of cases with inducible arrhythmias in BM-MNC and control groups: 3 out of 8 animals (38%) in BM-MNC group (2 polymorphic VT and 1 VF) and 3 out of 8 animals (38%) in control group (1 monomorphic VT and 2 VF). There was also no difference in global wall motion (GWMSI=1.03 in BM-MNCs; 1.17 in sham, p=0.38) and there was no correlation between GWMSI and ventricular arrhythmia induction (1.29 for induced pigs; 1.01 for non-induced, p=0.09). Conclusion: Transplantation of autologous BM-MNCs into ischemic myocardium did not alter the threshold for ventricular arrhythmia. Left ventricular dysfunction was not related to arrhythmia inducibility.

1078-99 Monocyte Chemoattractant Protein-1 Induced Monocyte Infiltration and Angiogenesis Does Not Result in Arteriogenesis or Improved Cardiac Function in Chronically Infarcted Myocardium

Ernst R. Schwarz, Dennis A. Meven, Philipp H. Kersting, Tanja Tussing, Erik C. Skobel, Peter Hanrath, The University of Texas Medical Branch, Galveston, TX, Rheinisch Westfaelische-Technische Hochschule, Aachen, Germany

Monocyte chemoattractant protein 1 (MCP-1) stimulates invasion of monocytes into ischemic tissue with concomitant adhesion to endothelial cells. This process has been shown to be involved in the induction of arteriogenesis, i.e., the development of functional arterioles resulting in improvement of perfusion in contrast to angiogenesis without changes in blood flow. The effects of MCP-1 on angiogenesis and arteriogenesis and changes of left ventricular function were tested in infarcted rat hearts. Anesthesized rats were subjected to open-chest ligation of the left coronary artery with subsequent myocardial infarction. After six weeks, animals were randomized to receive either MCP-1 (3µl in 0.15ml NaCl, group1, n=9) or saline (0.15ml, group 2, n=9), which was injected after thoracotomy into the myocardium at the infarct border zones. Transthoracic echocardiography was performed for assessment of left ventricular dimensions and cardiac function (ejection fraction, EF) at baseline, six weeks after myocardial infarction, and four weeks after MCP-1 or saline injection, by use of a 12 MHz pediatric transducer. For microscopic analysis, myocardial tissue was stained by Elastica-van-Giesson and von-Willebrand factor for blood vessels and endothelial cells, respectively. In a subset of animals, hearts were excised 24 hours after MCP-1 (n=4) or saline (n=4) administration for assessment of monocyte infiltration by staining of the CD 31 antigen. EF decreased from 60±3% to 25±5% in group 1 (p<0.005) and from 58±2% to 26±4% in group 2 (p<0.005) after coronary occlusion, without further changes four weeks after treatment (EF 26±3% in group1, EF 25±5% in group 2). At the injection site, 391±10 endothelial cells were found in group 1 versus 285±14 in group 2 (p<0.005). Monocyte infiltration was shown in MCP-1 treated animals but not in saline treated animals. There were 19±2 arteriolar structures in group 1 versus 16±1 in group 2, p>0.05. A single intramyocardial injection of MCP-1 into the infarct border zone induced neo-angiogenesis and monocyte infiltration. MCP-1 injection did not result in arteriogenesis or functional improvement of chronically infarcted myocardium in this experimental rat model.

POSTER SESSION

1079

New Horizons in Surgical Revascularization

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1079-77 Late Angiographic Patency of the Magnetic Vascular Port (MVP®) System for Coronary Artery Anastomosis

Uwe Klima, Sven Martens, Gerhard Wimmer-Greinecker, Jan Gummert, Randall Wolf, Volkmar Falk, Ricardo A. Costa, Alexandra J. Lansky, Ecaterina Cristea, Roxana Mehran, Filip Casselman, Frank van Praet, Hugo Vanermen, Cardiovascular Research Foundation, New York, NY

The MVP® System is a magnetic anastomotic coupling system that allows quick and reliable connections between a coronary artery and an autologous bypass graft. One magnetic clip set (3 miniature magnets) forms a port in the target vessel while a matching magnetic clip set forms an identical port of opposite polarity in the terminal portion of the graft vessel. When brought together, the two ports form the anastomosis. This multi-center European registry represents the first MVP® clinical experience for anastomosis between the left anterior descending artery (LAD) and the left internal mammary artery (LIMA). We report the 6-month angiographic follow-up (FU). **Methods:** 48 consecutive patients underwent coronary bypass surgery, including LIMA to the LAD using the MVP® device. Angiographic FU was performed and the results compared to the graft occlusion rate for the control arm of the GABI trial (German Angioplasty vs. Bypass Surgery Investigation), which was 13% at six months of FU. **Results:** Angiographic results at FU are shown in the Table. **Conclusions:** In this European multi-center registry, the MVP® anastomosis device and target vessel patency was 93.8% and 91.7% respectively for anastomosis between the LIMA and LAD at 6 months of FU. The device and target vessel occlusion rates of 6.2% and 8.3%, were equivalent to the historic control obtained in the GABI trial (13% occlusion). In addition, there was no evidence of thrombus, ectasia, aneurysmal dilatation, intimal flap or ulceration in any of the cases at FU.

Angiographic Results at 6-month FU

Variable	N=48
Device Patency, % (TIMI 3)	**45/48 (93.8%)**
Target Vessel Patency, % (TIMI 3)	**44/48 (91.7%)**
Graft Diameter, mm	2.04±0.30
Target Vessel Diameter (Interpolated Normal), mm	1.96±0.32
Bend, degrees	7.08+/-7.43
Tortuosity, %	2/48 (4.2%)
Thrombus/Calcium/Ulceration/Intimal Flap, %	0/48 (0%)

1079-78 Preoperative QRS Widening and Ventricular Dysrhythmia Predict Adverse Outcomes Following Left Ventricular Reconstruction for Ischemic Cardiomyopathy

Katherine J. Hoercher, Richard Lee, Patrick M. McCarthy, Jingyuan Feng, James B. Young, Randall C. Starling, Eugene H. Blackstone, Cleveland Clinic, Cleveland, OH

Objective: Interventions that target the cardiac conduction system such as AICD placement and biventricular pacing improve symptoms and survival in patients with congestive heart failure.However, the role of the conduction system in outcome after surgical ventricular reconstruction, the excision of dyskinetic and akinetic segments of myocardium, remains undefined. We reviewed our experience with left ventricular reconstruction (LVR) in patients with ischemic cardiomyopathy to determine the effect of preoperative conduction abnormalities on outcome after surgery.
Methods: LVR was performed in 223 pts (80% male, mean age 62± 10 yrs, 66% NYHA Class III/IV) between 1/97 and 8/02. Mean pre-operative EF was 26 ± 9%. QRS duration was 122 ± 32msec and an AICD was present in 15%. Time related outcomes considered were 1) survival, 2) freedom from composite event (transplant, return of NYHA class IV, and LVAD), and 3) readmission for heart failure. Mean follow-up is 1.5 ± 1.1 yrs.
Results: Survival at 30 days, 1yr, and 3 yrs was 98%, 92%, and 86% respectively. Patients who had an AICD preoperatively had a higher early mortality (<2 years) (95% vs 77% 2 yrs, p=0.0001). Freedom from composite event was 97%, 89%, and 83%. Patients who had a prolonged preoperative QRS were more likely to suffer a composite event (p=0.0002). Freedom from readmission for heart failure was 99%, 80%, and 61% at 30 days, 1 yr, and 3 yrs. Patients with a prolonged preoperative QRS had more frequent rehospitalizations (p=0.006).
Conclusion: Surgical left ventricular reconstruction in heart failure patients with ischemic cardiomyopathy yields an encouraging medium term survival and freedom from hospitalization for heart failure. Preoperative predisposition to lethal ventricular arrhythmia requiring an AICD was a strong predictor of mortality. This deserves closer examination. Left ventricular dysynchrony (prolonged QRS) was a strong predictor of residual or recurrent heart failure and further underscores the importance of ongoing investigations of cardiac resynchronization therapy as an adjunctive treatment to surgery for heart failure in this group of at risk patients.