and (4) normal without heart instrumentation plus Carvedilol(n=6). In groups 2 and 3, after baseline measurements had been obtained, rapid left ventricular (LV) pacing was initiated at 210 bpm for 3 weeks, followed by an additional week of pacing at 240 bpm with an external pacemaker. Carvedilol, was begun 2 weeks after initiation of pacing and continued for 2 weeks. Carvedilol was begun 2 weeks after baseline measurement for the control dogs with heart instrumentation. SR membranes were prepared from canine ventricular tissue, Protein concentration was measured by Bradford assay.
Results: Here, we show that systemic oral administration of Carvedilol reverses protein kinase A hyperphosphorylation of RyR2, restores the stoichiometry of the RyR2 macromolecular complex, and normalizes single-channel function in a canine model of heart failure.
Conclusions: These results may, in part, explain the improved cardiac function observed in heart failure patients treated with Carvedilol.

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Bradykinin limits cardiomyocytic apoptosis via restoration of nitric oxide after cardioplegic arrest

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Aims: Our previous studies revealed that cardioplegia-induced cardiac arrest (CCA) under cardiopulmonary bypass (CPB) could decrease cardiomyocytic nitric oxide (NO) and increase apoptosis. We hypothesized that pre-treatment with bradykinin would improve the profile of antiapoptotic proteins and inhibit cardiomyocytic apoptosis.
Methods: New Zealand white rabbits (10 in each group, each 2.5-3.5 kg) received total CPB. Rabbits were weaned from CPB and reperfused for 4 hours before the hearts were harvested. Blood was sampled at various time points. Bradykinin and/or NO agonists or inhibitor was infused systemically 30 minutes before beginning of the extracorporeal circulation and continued through the whole procedure. The ascending aorta was cross-clamped for 60 minutes while cold crystalloid cardioplegic solution was intermittently infused into the aortic root every 20 minutes. The myocardia of the reperfused hearts and control hearts were harvested and studied for evidence of apoptosis, ischemia/reperfusion-induced proinflammatory gene expression and inflammatory cytokine production by cardiomyocytes.
Results: Pretreatment of the cardiomyocytes with bradykinin could prevent the ischemia/reperfusion-induced inflammatory and apoptotic effects, which could be reversed with NO synthase inhibitor. Bradykinin antagonist could worsen the inflammatory and apoptotic responses of cardiomyocytes, which could be reversed with exogenous NO donor. Restoring NO concentration after CCA under CPB with bradykinin could modulate the (1) nuclear translocation of NF-κB, (2) iNOS mRNA expression, (3) cytochrome c production, and (4) occurrence of apoptosis.
Conclusions: CCA under CPB can decrease endogenous NO production, which can be restored with bradykinin supplementation via NO-mediated pathway. Exogenous bradykinin can ameliorate the myocardial inflammatory response by inhibition of NF-κB translocation, inflammatory gene expression, iNOS expression, and cytochrome c production.

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Effect of myocardial revascularization on left ventricular systolic function in patients with heart failure

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Background: The aim of the study was to assess early and long-term results of myocardial revascularization in patients with low left ejection fraction (LVEF) below 35% who underwent either elective coronary artery bypass grafting (CABG) or elective percutaneus transluminal coronary angioplasty (PTCA).
Material and methods: The study group comprised 176 patients (103 after standard CABG and 73 following PTCA) hospitalized in the Department of Cardiac Surgery, Medical University of Lodz, Poland between 1999 and 2004. All patients had preoperative coronary angiography and echocardiography at rest. A postoperative control echocardiography was done twice: between 5th and 7th day and 6th and 12th month after the procedure. The following parameters were then assessed: general LVEF, regional systolic abnormalities, left ventricular and left atrial dimension, left ventricular diastolic function and secondary mitral regurgitation (if present).
Results: The patients from both groups did not differ in the respect of sex and age, however diabetes was more frequent in the surgical group. A complete revascularization was achieved in 91 patients treated with CABG (88%) and in 33 patients treated with PTCA (45%). Significantly more early in-hospital deaths were observed in surgical group compared with PTCA group (15 patients [14.5%] vs. 3 patients [0.41%], respectively). In postoperative echocardiography, slightly bigger improvement in LVEF, higher reduction in a quantity of myocardial segment with systolic abnormalities and decrease in left ventricular dimension were observed in the surgical group, but the results were not statistically significant. Also restrictive abnormalities of left ventricular diastolic function were predictors of worse early outcome in both groups. During follow-up both groups did not differ significantly when incidence of strokes and myocardial infarctions was analyzed.
Conclusions: (1). Complete surgical revascularization of myocardial in patients with heart failure yields with better results than PTCA as far as left ventricular systolic function was concerned. (2). Percutaneus methods of revascularization patients with low LVEF yield with lower in-hospital mortality but involve more frequent need for repeat revascularization. (3). Restrictive left ventricular diastolic abnormalities were connected with worse prognosis in both groups. (4). Progress in surgical and percutaneus methods of revascularization gives a better chance for survival in patients with significant lesion of left ventricle - a population of the highest risk.

DEVICES / ARTIFICIAL HEART

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Multicenter clinical evaluation of the HeartMate II axial flow left ventricular assist device in patients with severe heart failure: hemodynamic effects, pump performance and quality of life

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Background: Advances in the field of mechanical circulatory support have focused on the development of smaller, quieter left ventricular assist devices (LVAD) that have improved durability and the potential for improved quality of life while maintaining the hemodynamic benefits of the first generation pulsatile pumps. We report the results of the HeartMate II® (HMII) pilot study in which a 400 gm axial flow LVAD was used to support patients (pts) with NYHA Class IV heart failure (HF) as a bridge to cardiac transplantation.
Methods: The HMII was implanted in 46 pts (36% female) with a me-

dian age of 40 yrs (range:14-69) and a median BSA in women of 1.65 (range: 1.40-2.20) and in men 2.01 (range: 1.61-2.28). Most pts had either ischemic (35%) or idiopathic (40%) cardiomyopathy. Pre-operatively pts were systemically hypotensive (mean systolic BP=97±12 mmHg) with elevated filling pressures (rt atrial pressure=12±7 mmHg; pulmonary capillary wedge pressure=24±7 mmHg) despite treatment with positive inotropic agents (97%) or an intraaortic balloon pump (22%). The HMII was implanted via an inflow cannula placed in the left ventricular (LV) apex and an outflow graft attached to the ascending aorta. Echocardiography was used to determine the appropriate pump speed using reduction in LV size, displacement of the septum toward the LV free wall and opening of the aortic valve.

Results: The cardiac index improved from 2.0±0.5 to an estimated pump flow index 2.9±0.5 L/min/m^2 at one week at an average pump speed of 9216±368 rpm. The median duration of mechanical support was 118 days (longest= 2 yrs; 9 pts>1 yr), representing 21 pt-years on the device. There were no pump failures and one pump was replaced following accidental trauma. Common adverse events included perioperative bleeding (38%) and driveline infection (11%). Two pts had a stroke and there was 1 TIA. Of the 46 pts, 32 (70%) survived (19 transplanted, 1 recovered, 12 ongoing) and 30% died on the device, most within 30 days of multisystem organ failure. Three months following implant, improvements were seen in submaximal exercise performance (52% of pts had > 200 meter increase in 6 minute walk distance), 71% of pts had NYHA Class I-II symptoms, and 76% reported their health as good, very good or excellent. 154 pts have subsequently been enrolled in the phase II trial for transplant and non-transplant candidates.

Conclusions: The HMII axial flow LVAD is reliable and restores hemodynamics with minimal adverse events in pts with advanced HF while improving functional status, exercise performance, and quality of life.

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TandemHeart percutaneous ventricular assist device in cardiac surgery of patients with advanced and acute heart failure

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Background: Temporary ventricular assist devices (VADs) are used in 0.2%-1.2% of all cardiac surgical cases. The hospital discharge rate with temporary VADs as "bridge to recovery" in the post-cardiotomy setting remains low. This study evaluates a recently developed VAD (TandemHeart pVAD, Cardiac Assist,Pittsburg) in this setting.

Methods: Between August 2001 and August 2004, 14 patients (0,6% of all cardiac surgical cases) were supported by VADs. Eleven of them underwent insertion of the TandemHeart. They were all male, with a mean age of 65.6 years (range 48-87), a mean LVEF of 26.8%±13.6 (range 10-55), a median Euroscore of 9 (range 6-17). In 7 of 11 patients acute heart failure occurred as perioperative decompensation of preexisting end stage chronic heart failure. The mean LVEF in this group was 18.6%±5.5 (range 10-25). Five of them underwent CABG and endoventriculoplasty procedures, one AVR and undersized mitral annuloplasty, and one Redo MVR of a thrombosed prosthetic valve. Four of the 11 patients with acute heart failure due to acute coronary syndromes, underwent CABG as salvage (n=2) or as emergency (n=2) procedures. In all patients with acute ischemia and in one patient with preexisting heart failure TandemHeart insertion was preceded by IABP insertion. The major indication for VAD insertion was failure to wean from CPB (9 patients, intraoperative insertion by "open percutaneous technique", or by direct cannulation). Other indications were preoperative decompensation of chronic heart failure (1 patient, preoperative percutaneous insertion) and postcardiotomy sudden cardiac arrest (1 patient, postoperative direct insertion).

Results: The mean duration of support was 88±98.4 hours (range 0.5-264 hrs). The mean pump flow was 3.09±1L/min (range 2.1-6). Eight of 11 patients were successfully weaned (72.72%) from the device and 6 of 11 patients were discharged from hospital (54.54%). The major complication was bleeding, noted mainly in patients receiving anticoagulation preoperatively. No device malfunctioning was noted. Survival in 1 and 4 years was 45.45% and 36.36% respectively. All survivors are in functional class I or II.

Conclusion: Safety of the TandemHeart in cardiac surgery was demonstrated by this study. Support led to successful weaning from CPB, in patients that would have probably died without assistance, resuscitation from refractory postoperative cardiac arrest, and preoperative hemodynamic stabilization in decompensated chronic heart failure. Device application was effective, with high weaning rate and satisfactory early and mid-term survival.

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Can we use continuous monitoring of right ventricular pressures to predict hospitalisations in patients with severe chronic heart failure?

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In patients (pts) with advanced chronic heart failure (CHF) frequent hospitalisations (HOSP) occur. Changes in volume (overload/depletion) are often misdiagnosed by clinical assessment. It has been hypothesized that continuous haemodynamic monitoring by implantable devices (IHM) detects increases in filling pressures before the onset of symptoms and/or changes of physical signs, allowing earlier treatment and reducing morbidity.

Aim: To verify how right heart (RH) hemodynamics changes in pts hospitalised because of worsening CHF.

Methods: 10 pts with advanced CHF and frequent cardiovascular HOSP were implanted with a device (Chronicle IHM – Medtronic Inc, Minesota) designed to record beat-to-beat right ventricular systolic (RVSP) and diastolic pressure (RVDP), pts activity and estimate of pulmonary artery diastolic pressure (ePAD). Pts during events activated high-resolution storage for 2 minutes by applying a magnet over the device; an external reference box recorder accounted for ambient barometric pressure; an external programmer read stored RV pressures. Hemodynamic changes were considered sustained when lasting >6 days. HOSP were characterized by presence/absence of inotropic infusion for treatment of low cardiac output state (LCO).

Results: IHM data were available in 7 pts (soon after implantation 1 pt died and 2 pts had a spoiled catheter). Among pts (males, mean age 56.8 years) 6 were in the heart transplant list; aetiology of CHF was ischemic heart disease; NYHA class IIIb-IV; echo left ventricular ejection fraction (LVEF) was 21±2%. RH catheterisation findings were: systolic pulmonary artery pressure 59±8 mmHg, cardiac output 3±1.3 L/min, right atrial pressure 5±2 mmHg. During follow-up (15±7 months) 1 pt died, 2 were transplanted and 1 was implanted with a defibrillator. The total number of HOSP during follow-up was 22 (in 68% inotropic support was required). In the week before HOSP, the following hemodynamic changes were observed: RVSP was increased in 9 pts (41%), unchanged in 11 (50%) and decreased in 2 (9%); RVDP was increased in 18 pts (81%), unchanged in 3 (14%) and decreased in 1 (5%); ePAD was increased in 10 pts (45.5%), unchanged in 10 (45.5%) and decreased in 2 (9%).

Conclusions: In this small sample of pts with advanced CHF, an increase of RVSP and ePAD occurred only in about 40% of episodes of worsening CHF; noticeably, RVDP increased in 82% of cases. Information on RVSP cannot correctly be matched with clinical status in advanced CHF pts, as worsening of symptoms and HOSP are frequently related to LCO conditions.