EFFECT OF HEART RATE ON DOPPLER INDICES OF LEFT VENTRICULAR DIASTOLIC FILLING IN MAN

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Although a number of factors including age, myocardial compliance, and LV preload and afterload have been shown to influence Doppler measurements of transmitral flow, few data exist regarding the effect of heart rate on Doppler indices of left ventricular diastolic filling. Therefore we studied 10 normals (mean age 29 yrs) using pulsed-wave Doppler from the apex. We used a 2.5 MHz transducer with the sample volume placed at the mitral annulus. Transmitral flow measurements included maximal early (E) and late (A) filling velocity, integrated velocity (FVI), time to peak filling velocity, and mean deceleration. Measurements were recorded during spontaneous heart rate (BASE) and transesophageal atrial pacing (PACE) at 90/min.

Results (mean±SD): (*=p≤.05)

	Heart Rate	E m/s	A m/s	E/A	%A of FVI
BASE	72±12	.55±.1	.37±.05	1.55±.44	.27±.06
PACE	88±4*	.58±.11	.49±.1*	1.21±.28*	.38±.17*

No change in mean values for deceleration rate (4.4 m/s^2) or time to peak filling velocity (60 msec) was observed between the two recordings. At increased rates, E velocity remains unchanged, %A of FVI increases, and A velocity increases approximately 2% for each 1 beat increment of heart rate. Thus, the atrial transport component of diastolic filling becomes greater at higher heart rates, perhaps as a compensatory response to the decreased diastolic flow period. This finding must be accounted for when evaluating Doppler transmitral flow velocities before and after interventions.

THE SUCCESSFUL APPLICATION OF A LOCAL INFUSION ANGIOPLASTY CATHETER IN A RABBIT MODEL OF FOCAL FEMORAL ATHEROSCLEROSIS.

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The local infusion of the vessel wall (VW) with biologically active substances at the time of balloon angioplasty (BA) may be important in reducing complications. The ability of a Local Infusion Angioplasty Catheter (LIAC) to simultaneously perform a successful BA and to infuse the VW with a biologically active substance was evaluated. Bilateral focal femoral atherosclerosis was produced in New Zealand White rabbits by air dessication injury followed by a 28 day 2% cholesterol, 6% peanut oil diet. BA, was performed in 5 vessels, with a single 1 min inflation, using a LIAC (2.25mm balloon to 5Atm (n=1), or a 2.0mm balloon, to 7.5 Atm (n=3) or 10 Atm (n=1)). The VW was infused with r-tPA during the 5 and 10Atm inflations (n=2) and with saline during the 7.5Atm inflations (n=3). Angiograms were obtained before, during and immediately after BA. Histologic sections were prepared and immunohistochemistry performed with a monoclonal antibody to r-tPA. The 10 Atm and 2 of the 7.5 Atm inflations achieved successful BA, defined as a > 20% increase in angiographic lumen diameter. An immunoperoxidase reaction identified r-tPA in the vessel wall of those rabbits that received r-tPA but not in those that received saline. Thus, this preliminary study indicates that the LIAC performs successful BA and probably achieves local infusion of the VW.

Wednesday, March 21, 1990
10:30AM–12:00NOON, Room 41
Factors in Restenosis: Experimental Observations

LOCAL DRUG DELIVERY TO INHIBIT RESTENOSIS: INITIAL IN VIVO RESULTS WITH AN INFUSION BALLOON

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Restenosis following coronary angioplasty is, in large part, the result of local smooth muscle proliferation. Delivery of agents with antiproliferative actions at the site of angioplasty may therefore inhibit restenosis. We performed initial studies in dogs using a new infusion balloon (IB) which delivers soluble agents directly into the vessel wall through multiple small holes (USCI). In 10 animals, IB inflation to 4 atmospheres was performed in the anterior descending coronary artery and 3-7 cc. of infusate was delivered over 1 min. Control inflation was performed in the circumflex using a balloon without infusion side holes. Number of animals, agents used and time of sacrifice were: (2) buffered saline, 72 hr. and 2 hr.; (2) aurin tricarboxylic acid (TCA) 400 μM, 72 hr. and 2 hr.; (1) TCA 200 μM, 2 hr.; (1) TCA 1 mg/kg/cc, 72 hr.; (2) Heparin 5,000 U/cc, 14 d; (2) Heparin 40,000 U/cc and Omnipaque 50%, 14 d. Perfusion fixed histologic samples demonstrated no perivascular inflammation or injury in any of the IB treated arteries. There were no differences between the IB artery and control artery. There was no evidence of acute hemorrhage into the wall or excessive intraluminal thrombus formation in animals sacrificed at 2 hr. Despite potent antiplatelet activity, TCA did not alter systemic platelet or clotting function when delivered locally through the IB.

We conclude that direct infusion of active agents into the vascular wall is feasible without local injury or systemic effect and may be an effective method for delivering agents designed to inhibit restenosis following angioplasty.

EVIDENCE FOR NEUTROPHIL AND COMPLEMENT ACTIVATION EARLY AFTER PTCA.

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It has been suggested that activation of neutrophils and the complement system (C) play a role in post-ischemic myocardial dysfunction and in restenosis. The aim of this study was to test whether PTCA activates neutrophils and C. Neutrophil activation was assessed ex vivo by 1.measurement of plasma lactoferrin (LF) and plasma myeloperoxidase, to study release of specific and azurophilic granules respectively. 2.chemiluminescence and 3.plasma fluorescent thiobarbituric acid reactive substances (TBARS). These measurements were performed in blood drawn from the coronary sinus, before and immediately after PTCA (7 Pts) or coronary angiography (A) (4 Pts).

After PTCA, LF increased 2 fold ($p<0,02$, paired t-test) whereas after A a non significant increase of +12 % was observed. Plasma myeloperoxidase and TBARS did not change significantly in both groups. Whole blood chemoluminescence stimulated in vitro by phorbol-myristate acetate and zymosan increased after PTCA, while the increase was non significant after A. Neutrophil count and adherence properties were not modified by PTCA or A.

Total hemolytic complement (CH 50), C_3, C_4 and factor B decreased slightly (7 to 16 %) after PTCA and after A.

Conclusion : Early after PTCA, the neutrophil oxidative response is increased (chemiluminescence), suggesting priming of the neutrophils, possibly by complement activation. Furthermore, the presence of LF in the plasma suggests neutrophil activation. The role of angiographic dye in the priming process, as well as the consequences of neutrophil activation deserve further study.