Ninety-eight percent of events occurred on Days 0–3. All 3 pts with later events also had events on Day 0. In a multivariate model, only EF was a significant predictor of events, p<0.04. Of pts with EF<40%, 16% had events vs 8% with EF ≥40%, p<0.005. The 3 pts with events after Day 3 had EF 40–43%. Conclusion: It is safe to discharge AMI pts with EF >30% to home after hospital Day 3, if they have a low-risk primary PCI and have not experienced complications during Days 0–3. While EF predicts overall events, it is an imperfect tool for discharge planning.

7 INDICATIONS SPECTRUM FOR TEMPORARY CARDIAC PACEMAKER THERAPY IN A COMMUNITY HOSPITAL: S. Jan, U. Patel, A. Gupta, R. Alliani, S. Islam, S. Nirajan, A. Khanoe, A. Murphy-Timor, T. Wheeler, Departments of Biochemistry and Molecular Biology and Surgery, University of Louisville School of Medicine, Louisville, KY.

Purpose: A limitation of heart transplantation is the small time period during which a heart remains viable while it is being transported on ice. Some studies have shown that fructose-1,6-bisphosphate (FBP), a glycolytic intermediate, can help preserve heart tissue while it is in hypothermic storage. The purpose of this study was to understand the mechanism of this enhanced preservation and to explore other treatments that may extend heart viability during hypothermia. FBP’s protective effect may come from its change in calcium metabolism and from the phosphorylation of proteins. We evaluated whether FBP, through the phosphorylation of proteins, is useful in preserving heart tissue. Method: To assess mitochondrial membrane leakage, we measured the penetration of nitroblue tetrazolium and its reduction via succinate dehydrogenase. Using an experimental model in which cell morphology was observed as a measure of cell survival during hypothermic incubation, three possible preservatives were evaluated. Results: For freshly-prepared myocytes, Ca2+ was 33 ± 11% (n = 4) lower in FBP-treated than for control cells, after 24 h of hypothermic incubation it was 70 ± 11% (n = 4) lower in FBP-treated samples. LDLH release after 24 h was 25% lower for FBP-treated cells than for control cells. However, FBP had no effect on mitochondrial membrane leakage. The myosin ATPase inhibitor 2,3-butanedione monoxime (BDM) at 5 mM reduced the death rate by 70%, while the combination of BDM with FBP decreased it by 90%. Two potential treatments for increasing intracellular adenine nucleotide levels, 5 mM reduced the death rate by 70%, while the combination of BDM with FBP decreased it by 90%. Conclusion: Temporary support of conduction system prior to placement of permanent pacemaker was the commonest cause of temporary pacemaker in our study. Myocardial infarction associated temporary pacemaker among high risk group patient with a high mortality. Latrogenic cause of conduction disturbance is a frequent cause for need of temporary pacemaker.

8 EFFECTS OF FRUCTOSE-1,6-BISPHOSPHATE AND OTHER COMPOUNDS ON HYPOTERMIC PRESERVATION OF CARDIAC MYOCYTES: T. Kirillov, T. Mitrazapova, A. Adzhube, P. Usatyuk, V. Natarajan, A. Verin. Johns Hopkins School of Medicine, Division of Pulmonary and Critical Care Medicine, Baltimore, MD.

Purpose: Endothelial barrier dysfunction is often the underlying cause of vascular leakage and edema. It is important therefore to find ways to preserve barrier properties. Extracellular adenosine triphosphate (ATP) has been known to protect endothelial barrier in this regard. We have therefore investigated the mechanisms of endothelial barrier enhancement caused by extracellular ATP. Methods: Combination of pharmacological and molecular approaches is used in this study. Results: ATP and its non-hydrolyzed analogues enhanced barrier properties of cultured endothelial cell monolayers, caused remodeling of cell-cell junctions, and significantly attenuated thrombin-induced barrier disruption. Intracellular Ca2+ increase and Ekk activation caused by ATP were irrelevant to barrier enhancement. Inhibitory analysis and silencing RNA revealed the involvement of G proteins (specifically Gi, Go, and Gq) as well as protein kinase A and its substrate VASP in ATP-induced barrier enhancement. Contractile state of endothelial cells governed by myosin light chain (MLC) phosphorylation underlies barrier properties. ATP treatment decreased MLC phosphorylation and specifically activated myosin-associated phosphorylated substrate. Peptidation of Goq by protein kinase C (PKC) isoforms to the plasma membrane indicating their activation. PKC inhibitor Ro 31-8220 completely attenuated ATP-induced MLC phosphorylation. A 1973 study revealed an increased minimal effect on permeability induced by 100 ng/mL ATP. Collectively, these data suggest that low ATP concentration may protect endothelial monolayer integrity in increase in ATP production and activation of specific PKC isoforms.

9 MECHANISMS OF ENDOTHELIAL BARRIER ENHANCEMENT INDUCED BY ADENOSINE TRIPHOSPHATE: T. Kirillov, T. Mitrazapova, A. Adzhube, P. Usatyuk, V. Natarajan, A. Verin. Johns Hopkins University School of Medicine, Baltimore, MD.

Endothelial barrier dysfunction is often the underlying cause of vascular leakage and edema. It is important therefore to find ways to preserve barrier properties. Extracellular adenosine triphosphate (ATP) has been known to protect endothelial barrier in this regard. We have therefore investigated the mechanisms of endothelial barrier enhancement caused by extracellular ATP. Methods: Combination of pharmacological and molecular approaches is used in this study. Results: ATP and its non-hydrolyzed analogues enhanced barrier properties of cultured endothelial cell monolayers, caused remodeling of cell-cell junctions, and significantly attenuated thrombin-induced barrier disruption. Intracellular Ca2+ increase and Ekk activation caused by ATP were irrelevant to barrier enhancement. Inhibitory analysis and silencing RNA revealed the involvement of G proteins (specifically Gi, Go, and Gq) as well as protein kinase A and its substrate VASP in ATP-induced barrier enhancement. Contractile state of endothelial cells governed by myosin light chain (MLC) phosphorylation underlies barrier properties. ATP treatment decreased MLC phosphorylation and specifically activated myosin-associated phosphorylated substrate. Peptidation of Goq by protein kinase C (PKC) isoforms to the plasma membrane indicating their activation. PKC inhibitor Ro 31-8220 completely attenuated ATP-induced MLC phosphorylation. A 1973 study revealed an increased minimal effect on permeability induced by 100 ng/mL ATP. Collectively, these data suggest that low ATP concentration may protect endothelial monolayer integrity in increase in ATP production and activation of specific PKC isoforms.

10 AN ANALYSIS OF PATIENTS’ INTEREST IN RESEARCH FROM A MEMORY SPECIALTY CLINIC: N. Lane, T. Oll, S.A. Meade, A.M. Slater, C.E. Gleason, S. Asthana, University of Minnesota Department of Medicine, Gonda Memory and Aging Center, and Gerontology, Wm. S. Middleton Memorial Veterans Hospital, GREEC, Madison, WI.

Purpose: Assessing and prospectively identifying successful recruitments of patients at a geriatric specialty memory clinic is the most difficult tasks facing research centers. As the prevalence of many diseases continues to increase, the need for research into effective treatments and potential cures for these diseases gains critical importance. When an individual has reached a critical level, it has become necessary to re-evaluate the potential resources for recruitment. One such resource for subject recruitment is specialty clinics whose primary focus is patient care. While there is a need for investigation into the potential number of subjects to be enrolled, however, a realistic examination of the population that presents to specialty clinics of this nature is required. Methods: We performed an analysis of patient interest in research from a course of one year in a geriatric specialty memory clinic in Madison, Wisconsin. Results: Data revealed that the majority of patients (67%) who presented to this clinic were poor clinical research candidates. Reasons for consideration as a “poor candidate” include an age evidence for a dementia diagnosis, transportation constraints, caregivers’ guilt, fear of memory loss, fear of gaining weight, and a desire to keep patients out of a hospital setting. Conclusion: The majority of patients coming to a specialty clinic are not the best candidates for recruitment to clinical research trials.

11 THE RISK OF NEPHROLITHIASIS IN SPONDYLOARTHITIS: S.A. Leonard, J.A. Singh, H. Stapleton, University of Minnesota, University of Minnesota School of Medicine, Minneapolis, MN.

Purpose: Inflammatory arthritis is not generally considered a risk factor for nephrolithiasis; however previous studies have found a higher point prevalence of nephrolithiasis in rheumatoid arthritis (RA) patients. We investigated the incidence of renal stones in patients with spondyloarthropathy (SPA) as compared with rheumatoid arthritis (RA) controls. Methods: This study was designed as a VA retrospective cohort study. The study group was obtained from patients followed in the geriatric arthritis clinic, with the diagnosis of SPA. Controls were rheumatoid arthritis (RA) patients. Results: The sample size was calculated using an alpha of 0.05, a power of 0.80, an estimated prevalence of nephrolithiasis in the RA group of 5% and 16% in the RA group. Patients were recruited through chart review at the VA Medical Center in Minneapolis. Patients were followed from the date of diagnosis until the occurrence of an event (nephrolithiasis) or censoring at the end of the study (30 March 2005). The primary endpoints were the incidence of nephrolithiasis in RA and SPA patients. Conclusion: These results show an increase in the prevalence of kidney stones in SPA compared to RA. This is similar to the findings of Mladenovic et al. These results suggest that other studies should be done to ascertain the cause of increased nephrolithiasis in SPA.

12 CONCENTRATION-DEPENDENT EFFECTS OF VASCULAR ENDOTHELIAL GROWTH FACTOR ON ENDOThelial PERMEABILITY: T. Mitrazapova, I. Kolosova, P. Usatyuk, V. Natarajan, A.D. Verin, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.

Increased endothelial permeability is involved in the pathogenesis of many cardiovascular and pulmonary diseases. Vascular endothelial growth factor (VEGF) is considered to be a major permeability increasing cytokine. On the other hand, VEGF is known to have beneficial effect on endothelial cells (EC), increasing their survival. In most cases barrier-disruptive properties of VEGF were observed at rather high concentrations, while lower concentrations induce cell migration and proliferation. We found that 10 ng/mL VEGF significantly improved barrier properties of cultured human pulmonary artery EC (HPAEC), as indicated by a transendothelial resistance measurement (20 ± 2.6% increase, p < 0.01), while 100 ng/mL VEGF had barrier-disruptive effect (40 ± 3.2% decrease, p < 0.01). Consistent with these data, EC-treatment with 10 ng/mL VEGF enhanced VE-cadherin staining at the cell periphery, suggesting stabilization of cell-cell contacts. Level of myosin light chain phosphorylation (an index of EC contraction and barrier disruption) was dramatically increased after treatment with 100 ng/mL, but not with 10 ng/mL VEGF. In contrast, HP AEC, but not HPAEC, increased expression of intercellular adhesion molecule 1 (ICAM-1) (known barrier-protective stimulus) compared with non-stimulated cells (61% ± 86% and 109% ± 157% fold/μg protein, respectively, p < 0.024). Stimulation with 10 ng/mL, but not with 100 ng/mL VEGF, caused transcriptional up-regulation of intercellular adhesion molecule 1 (ICAM-1). These results suggest that other studies should be done to ascertain the cause of increased permeability in SPA.