1145-104   Green Tea Inhibits Stat-1 Activation and Reduces Apoptosis in Cardiac Myocytes Exposed to Ischemia/ Reperfusion Injury

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Background. We have reported previously that the transcription factor STAT-1 is activated following I/R and is also a mediator of apoptotic cell death in cardiac myocytes. Recently green tea (GT) has been shown to have antioxidant properties and also to reduce the expression of STAT-1 in non-cardiac cells. In the present study, we have assessed the role of GT as a cardioprotective agent in cultured cardiac myocytes exposed to simulated I/R.
Methods. Primary rat neonatal cardiomyocytes were pre-treated with GT (50μg/ml) and either left under normoxic condition or exposed to simulated I/R by in an ischemic chamber for 4 hours followed by16 hrs or reoxygenation to simulate reperfusion. Western blotting and immunoflouresence studies were performed with specific phospho-antibodies against STAT1 Tyr701 and STAT1 Ser727. **Results.** Cardiac myocytes pre-treated with GT reduced the level of apoptotic cell death following simulated I/R injury from 37% (I/R) to 17 % (GT plus I/R). Western blot analysis demonstrated that GT also reduced the levels of phosphorylated STAT1-701 and STAT1-727 in cardiac myocytes exposed to simulated I/R. Immunoflouresence assessment confirmed that GT also abrogated nuclear translocation of activated STAT1-701 and STAT1-727 in cardiac myocytes exposed to simulated I/R. Finally treatment with GT also reduced the expression of FASL and FAS receptor in cardiac myocytes.
Conclusions. Our data demonstrates that GT is able to protect cardiac myocytes from apoptosis following simulated I/R injury, which may in part be acting by preventing the activation and nuclear translocation of STAT-1. Hence, GT may have a therapeutic role in modulating pro-apoptotic STAT-1 target genes.

1145-105   Bag-1 Relocates Within Cardiac Myocytes Following Ischemia/Reperfusion and Prevents Myocyte Apoptosis by Interaction With Hsc70

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Background. BAG-1 is a family of proteins, which promotes cell survival and modulates chaperone activity by interacting with a wide range of cellular targets. Here we examined the level of protein expression and the subcellular distribution of BAG-1 both in cultured myocytes and the isolated rat heart, as well as its potential cardioprotective role during ischaemia(I)/reperfusion(R) injury. **Methods and Results.** By immunocytochemistry, in tissue sections from control hearts, BAG-1 positive staining was seen in the nuclei of the majority of myocytes (57+/-6.3%). In only 2.4+/-0.5% of control myocytes cytoplasmic staining was observed. Conversely, in rat hearts exposed to 35 mins I and 120 mins R, nuclear staining for BAG-1 was reduced (10+/-2.3 %) with a corresponding increase in the number of myocytes exhibiting cytosolic localisation (28+/-4.7%; p<0.001 vs control). Since western blot analysis of rat hearts exposed to I/R did not detect any BAG-1 induction, the above finding suggest that BAG-1 can actively relocate from the nuclei to the cytoplasm upon I/R. Similar results were obtained by western blotting analysis of subcellular fractions from cultured myocytes and the intact heart. Overexpression of human BAG-1 in primary cultures of neonatal cardiac myocytes, exposed to 4 hours of simulated I followed by 16 hours of R, significantly reduced the percentage of TUNEL positive myocytes from 37+/-5.1% to 21+/-4.3% (p<0.001). Moreover, in both cultured myocytes and the intact heart following I/R, BAG-1 co-immunoprecipitated with HSC70. Finally, overexpression of a BAG-1 dominant negative, lacking the C-terminal BAG domain, which is critical for the interaction with the 70 kDa heat shock proteins HSC70 and HSP70, failed to ameliorate myocyte apoptosis induced by simulated I/R. **Conclusions.** We conclude, therefore, that BAG-1 is a cardioprotective protein and that I/R induces BAG-1 intracellular relocation. Furthermore, protection is dependent upon association with HSC70.

POSTER SESSION

1146   In-Hospital Complications of Acute Coronary Syndromes

Tuesday, April 01, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 9:00 a.m.-10:00 a.m.

1146-106   Management and Outcomes of Patients With Acute Coronary Syndromes and Gastrointestinal Bleeding

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Background: Potent antiplatelet/ antithrombin agents along with early revascularization are increasingly used in patients hospitalized with acute coronary syndromes (ACS). An important adverse event associated with these therapies is gastrointestinal bleeding (GIB); yet, the optimal management and outcomes related to GIB in ACS patients are poorly studied.
Purpose/ Methods: We retrospectively analyzed the diagnostic studies, pathological/ clinical findings and survival associated with GIB in patients hospitalized with ACS at a tertiary center between 1996-2001.
Results: Three percent (80/3045) of patients with ACS developed or had concurrent clinically significant GIB. In-hosptial mortality was significantly higher in patients with versus without GIB (36% vs. 5%, p<0.001). Thirty-patients underwent endoscopy during the index hospitalization with no associated complications of death, arrhythmia, urgent ischemia, or hemodynamic deterioration. Definitive GI diagnosis from endoscopy are shown in the table below.

Endoscopy N (%)	30 (38.5%)
Gastritis N(%)	7 (9%)
Peptic ulcer disease N(%)	7 (9%)
Polyps N%)	6 (7.7%)
Neoplasm N(%)	6 (7.7%)
Diverticulosis N(%)	4 (5.1%)
AVM N(%)	1 (1.3%)
Mallory Weiss Tear N(%)	1(1.3%)
Esophagitis N(%)	1 (1.3%)

Conclusion: GIB is a rare complication following ACS associated with eightfold higher in-hosptial mortality. Endoscopy may be safely performed during the ACS hospitalization and confirms diagnosis of GI malignancy in 7.7% of patients.

1146-107   Major Bleeding Incidence After Coronary Artery Bypass Grafting in Patients With Unstable Angina/Non-ST Elevation Myocardial Infarction Based on Coronary Artery Bypass Graft Timing in TACTICS-TIMI-18

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Background: Observational studies report an association between major bleeding rates after coronary artery bypass grafting (CABG) and timing of antithrombotic therapy peri-CABG. In 1 non-randomized study, pts having CABG <5d of the last dose of clopidogrel had a 2-10 fold higher major bleeding rate compared to pts not receiving it. In contrast, a comparison of similar pts in the CURE trial found higher transfusion rate and no difference in TIMI major bleeding post CABG. We **hypothesized** that the difference in bleeding seen in observational studies (and attributed to only 1 factor, clopidogrel) might be explained by other factors such as pt characteristics, CABG timing, and other treatments. **Methods:** In TACTICS-TIMI 18, 2220 pts with unstable angina/non-ST MI (UA/NSTEMI) were treated with aspirin, heparin and tirofiban for 48 hours (clopidogrel reserved for post-stent in all but 5 patients). We evaluated associations of major bleeding and stroke in relation to CABG timing. **Results:** Factors related to increased bleeding in addition to those below, were: history of diabetes, MI, aspirin, PCI, CABG, stable angina, PVD, and current troponin T, ST deviation, and 3VD.

Characterstics	CABG≤5d N=222	CABG≥5D DURING HOSP N=128	CABG after hosp N=59	P
Age	64.1± 10.5	62.2± 9.5	62.0± 10.9	0.15
Male	74%	73%	64%	0.33
3 vessel disease	65%	59%	43%	0.01
Left main	29%	16%	0	<0.001
ASA stopped ≤5 days pre-op	0%	32%	N/A	<0.001
IABP	7.7%	2.3%	1.7%	0.04
Death	3.6%	3.1%	3.4%	0.97
Stroke	2.3%	0.8%	0%	0.3
MI	5.4%	6.25%	10.2%	0.410
Major Bleed	21%	5.5%	0%	<0.001

30-day post-CABG death, MI, or stroke rates did not differ among groups, but there was a significantly higher rate of major bleeding in pts sent for CABG<5d (P<0.001). By multivariate analysis, major bleed risk in CABG<5d remained higher after "correcting" for baselinedifferences(OR=4.4, 95% ci-1.6-12.1,P=0.004).

Conclusion: 1)In UA/NSTEMI, CABG performed <5d has 4 fold major bleeding rate compared to CABG performed >5d 2)Major bleeding is also dependent on disease severity, antithrombotic therapy, other procedures 3)Caution is required in interpreting observational studies that attribute associations (eg higher bleeding) to any 1 factor.