matched between non-dilated and dilated vessels. Differential expression of 12 proteins was observed between the groups and direct sequencing of digested peptides demonstrated that these proteins regulate the structural integrity of the vessel wall. Rapamycin blocked the expression of specific proteins, including lamin A, vimentin, alpha-1-antitrypsin, and alpha-actin. In addition, rapamycin significantly reduced the deposition of elastin, collagen III and fibronectin within the vascular wall. Neointimal formation was likewise decreased (from 13.1±3.2 to 6.2±1.4, p<0.05). Consistent with this finding, we also observed the suppressive effects of eplerenone on accumulation of extra cellular matrix in neointima in 2 weeks and in Group E (31.3±7.3%) than in Group C (40.4±9.4%, p=0.05). Anti-smooth muscle actin, anti-proliferative cell nuclear antigen (PCNA) and anti-macrophage antibodies were used for immunohistochemical examinations. Results: New formed neointima was observed in 2 weeks and was become thicker in 4 weeks. Part of endothelial cells was recovered in 4 weeks in both groups. In neointima, %fibrosis area was significantly smaller in Group E (33.7±15.8%) than in Group C (40.7±11.8%) (p<0.05) in 2 weeks and in Group E (31.3±3.7%) than in Group C (40.4±9.4%) (p<0.01) in 4 weeks. Therefore the %area of smooth muscle actin was larger in Group E than Group C. Positive staining for PCNA was seen in neointima, especially around stent strut and infiltrating cells including macrophages were mainly observed around stent strut in 2 weeks, but the number of positive cells was similar in both groups. Conclusions: Eplerenone suppresses accumulation of extra cellular matrix in neointima and will be useful to reduce restenosis after coronary stent implantation.

T158-55
Suppressive Effects of Eplerenone on Accumulation of Extra Cellular Matrix in Neointima After Coronary Stent Implantation Using Swine

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Background: Neointimal formation, mainly composed of smooth muscle cell proliferation, is principle cause of restenosis after coronary stent implantation. However increasing evidence suggests that accumulation of extra cellular matrix including collagen is also an important for neointimal formation. Importance of aldosterone on myocardial fibrosis in heart failure has been reported, but the effects of aldosterone on restenosis after stenting has not been elucidated. We examined the suppressive effects of eplerenone, a new type of strong aldosterone receptor antagonist, on the neointimal formation after coronary stenting using swine model. Methods: Palmaz-shatz stent (3.0 mm in diameter) were implanted on the anterior descending artery for 20 pigs aged 10 weeks weighing 2-2.5 kg. Those were divided into two groups (Group E; oral administration of eplerenone 200 mg/day from 1 week before to 4 weeks after stenting, Group C; oral administration of placebo). Pigs were sacrificed 2 weeks or 4 weeks after stenting. Samples were embedded in paraffin for histological examination. Masson’s trichrome staining was used for the assessment of collagen deposition and measurement of %fibrosis area. Anti α-smooth muscle actin, anti-proliferative cell nuclear antigen (PCNA) and anti-macrophage antibodies were used for immunohistochemical examinations. Results: New formed neointima was observed in 2 weeks and was become thicker in 4 weeks. Part of endothelial cells was recovered in 4 weeks in both groups. In neointima, %fibrosis area was significantly smaller in Group E (33.7±15.8%) than in Group C (40.7±11.8%) (p<0.05) in 2 weeks and in Group E (31.3±3.7%) than in Group C (40.4±9.4%) (p<0.01) in 4 weeks. Therefore the %area of α-smooth muscle actin was larger in Group E than Group C. Positive staining for PCNA was seen in neointima, especially around stent strut and infiltrating cells including macrophages were mainly observed around stent strut in 2 weeks, but the number of positive cells was similar in both groups. Conclusions: Eplerenone suppresses accumulation of extra cellular matrix in neointima and will be useful to reduce restenosis after coronary stent implantation.

T158-54
Knock-Out of P21 Escapes Radiation-Induced Cell Cycle Arrest and Apoptosis in Vascular Smooth Muscle Cell

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Background: Vascular smooth muscle cell (VSMC) proliferation is important in the pathogenesis of atherosclerosis and restenosis. In spite of delayed catch-up restenosis after intravascular radiation therapy, the biologic mechanism of radiation failure has not been well studied. We investigated the escaping mechanisms of radiation-induced cell cycle arrest and apoptosis.

Methods: Using different dosages of gamma radiation, the cell counts, cell cycle, apoptosis, expression and activity of cyclin dependent kinase (CDK), and expression of p16, p21, and p27 were examined with cultured rat and mouse smooth muscle cells.

Results: The cell counts after irradiation with 0, 2, 8, 16 Gray (Gy) (n=9, each) were 3.2±8, 2.34±3.94, and 1.3±0.01/ml at 24h, and 5.1±2.0, 1.8±0.2, and 1.2±0.01/ml at 48h, respectively. However, the proportion of apoptosis was minimal, at approximately 10 in 1×10^6 cells. The proportions of cells in the G0/G1, S and G2/M phases were 61, 9 and 30% at 12 hours after 16Gy radiation (control in log phase 61, 34 and 5%), and 67, 7 and 26% (control in confluent phase, 79, 12 and 9%) at 48 hours. By immunoblot analysis and kinase assay, gamma-irradiation with 8 or 16 Gy increased the expression of p21, negative regulator of cell cycle progression, and decreased the expression and activity of CDK2, an important kinase during the later stages of G1/S progression, as well as the expression and activity of CDK1, which is important in the G2/M phase transition. In contrast, radiation did not affect the expression or activity of either CDK4 or CDK6. The cell cycle inhibitors, p27 and p16 were not involved in the radiation-induced cell cycle arrest of VSMCs. When p21 knocked out, VSMC proliferation was enhanced, and radiation induced cell cycle arrest and apoptosis were not observed.

Conclusions: Gamma radiation could effectively inhibit VSMC proliferation via cell cycle arrest rather than apoptosis induction, by enhancing p21 expression and suppressing CDK1 and 2. But, the knock-out of p21 escaped antiproliferative effect of radiation. So these findings 3p expression be the important mechanism of radiation failure and delayed catch-up restenosis.

T158-56
Effects of Wine, Beer, and Whisky on Vascular Endothelium and Thrombosis Fibrinolysis System

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Introduction: Evidence suggests that red wine is associated with decrease cardiovascular risk in general population. It is still unknown whether alcohol or other substances such as bioflavonoids affect endothelial function and thrombosis/fibrinolysis system. We compared the effects of red wine, white wine, beer and whisky on endothelial function and thrombosis/fibrinolysis system.

Methods: The population of the study consisted of 80 healthy young individuals (24±1.6 years old). They were randomised into five equally sized groups and received 264 ml red wine (8 males, 8 females), 264 ml white wine (7 males 9 females), 633 ml of beer (7 males females), 79 ml whisky (9 males 7 females), and 8 ml whisky (8 males 8 females). Forearm blood flow was determined by gauge-strain plethysmography, at baseline, at 1 hour and 4 hours after intake. Endothelium-dependent dilation (EDD) and endothelium-independent dilation (EID) were calculated as the %change of flow from baseline to the maximum flow during reactive hyperemia or after sublingual nitroglycerin administration respectively. Plasma levels of vonWillebrand factor (vWF) and tissue plasminogen activator (tPA) were determined at baseline at 4 hours after alcohol consumption.

Results: EDD was significantly increased after 1 hour red wine or beer consumption (from 96.6±9.7% and 73.5±8.4% to 125±13.6% and 93.4% respectively; p<0.05 for both), while it returned at baseline at 4 hours (100.9±18.8 and 83.7±20.8 respectively; p=NS compared to baseline). EDD remained unchanged in the other groups (p=NS). vWF was decreased in the beer and red wine groups (from 65±4.9 and 68±4.9 to 54±5.6 and 56±3.9% respectively; p<0.05 for both), but not in the other groups. EID and tPA remained unchanged in all groups.

Conclusions: Acute consumption of red wine or beer and not of white wine and whisky increases endothelium-dependent dilation, and decreases vWF levels. These findings indicate that only red wine and beer are associated with improvement of endothelial function and reduced thrombogenicity.

T158-57
Vascular Access Site Complications Post Percutaneous Coronary Intervention

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Background: Vascular access site complications can occur after percutaneous coronary interventions (PCI). Potential contributing factors include anti-thrombotic regimes, sheath size, and patient comorbidities. These have evolved significantly over the past decade.

Method: Vascular complications in 16,201 consecutive PCI patients from 1979 to 2002 were recorded using the Mayo Clinic Interventional Registry. The patients were divided into four groups based on PCI procedure date. Group I (1979-1989), N= 3085, balloon angioplasty alone was used in the majority. Group II (1990-1995), N=4753, stent era with vigorous anticoagulation pre and post PCI. Group III (1996-1999), N=4827, antiplatelet agents replaced oral anticoagulation and glycoprotein IIb/IIIa inhibitor use was initiated. Group IV (2000-2002), N=3636, use of clopidogrel along with continued use of Glycoprotein IIb/IIIa inhibitors.

Results: The patients in Group IV were significantly older, had a larger body mass index (BMI), a higher percentage of females, diabetes, hypercholesterolemia, and hypertension compared to the other three groups. Sheath size used in Group IV was significantly smaller (French size) compared to Groups II & III (6.4±0.8 vs 8.2±0.7 & 7.8±0.9 respectively; P<0.01). The use of glycoprotein IIb/IIIa inhibitors was significantly greater in Group IV compared to Groups II & III (87% vs 5% & 42% respectively; P<0.01). Even