TCT-215
Effect Of Renal Denervation Therapy On Blood Pressure And Pulse Pressure In Young Compared To Old Patients
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Background: Renal sympathetic denervation (RDN) via a percutaneous radiofrequency catheter significantly decreases blood pressure in patients with resistant hypertension. High pulse pressure (PP), the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP), is related to increased artery stiffness. Trials have suggested that PP may have predictive value in terms of cardiovascular complications, especially in older patients. It may be important to evaluate changes in PP as well as SBP and DBP when assessing the efficacy of antihypertensive therapy. The long-term effects of RDN on SBP, DBP and PP in young vs. elderly patients have not studied.

Methods: We retrospectively analyzed patients from the Symplicity HTN-1 and HTN-2 trials who received RDN. Inclusion criteria were a baseline SBP ≥160 mmHg, treated with ≥3 antihypertensive drugs, an estimated glomerular filtration rate ≥45 mL/min/1.73m² and suitable renovascular anatomy. Patients were divided into two groups based on age (< 65 and ≥ 65 years).

Results: The mean age of the 2 groups was 52±9 years (n=167) and 70±4 (n=72) respectively. Both groups had similar SBP at baseline. The older group displayed significantly lower DBP and significantly higher PP. The relative effect of RDN on SBP and DBP was comparable in the two groups. More importantly, the PP decreased significantly in both groups and the drop in SBP was greater than the drop in DBP.

Drops in PP were primarily due to decreases in SBP rather than DBP. This may help preserve myocardial perfusion pressure, of special importance in the elderly with occult coronary disease. Results: Young vs. elderly patients have not studied.

Conclusions: This assessment provides insight into the similarities in size and anatomic distribution of renal nerves and ganglia, and their spatial distribution relative to the renal artery in human and porcine model. We conclude that the anatomicity of both these models are similar and the porcine model is relevant for translation of understanding renal ablation prior to human use.

TCT-217
Pathologic Insight Into Nerve Injury in Swine Treated with Ultrasound Renal Artery Denervation System.
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Background: Selective renal nerve denervation (RND) constitutes a minimally invasive approach for treatment of refractory hypertension. Ultrasound energy consisting of high-frequency sound waves emitted circumferentially [PARADISE ReCor Medical] was used to ablate renal nerve activity. Post-treatment histopathologic changes in renal nerves include loss of select neuronal markers in sub-acute and chronic post-treatment periods were assessed.

Methods: Swine (n=12) underwent unilateral RND [10 or 20 watts] and were terminated at 3-, 28- and 180-days post-treatment period. A non-powered catheter was delivered to each renal arterial artery (n=12) serving as a control. Right and left renal arteries with intact aorta and kidney were perfusion fixed and processed for routine light microscopy. Histology sections were stained with HE and Movat Pentachrome. Select histologic sections were immunostained against neuromullation protein (NFP) and tyrosine hydroxylase (TH).

Results: Acute phase animals showed nerve fascicles with necrosis accompanied by peri-neural and surrounding soft tissue inflammation. In the sub-acute and chronic phases, nerve injury was characterized by epl/perineural inflammation and fibrosis with soft tissue chronic inflammation. Smaller nerve fascicles were also seen in the soft tissue around injured nerves in the chronic phase. In the acute phase, the reaction to NFP and TH was equivalently strong whereas TH was negative in 28- and 180d animals while NFP expression was variable, as strong staining was observed in the smaller fascicles.

Conclusions: RND using ultrasound produced varying degrees of injury to nerve fascicles associated with renal arteries where the expression of selective neuronal markers correlated with the extent of injury. A lack or weak expression NFP suggests structural damage while the absence of TH, an enzyme utilized in the synthesis of norepinephrine represents functional loss. In the sub-acute and chronic phases, the absence of TH in select nerves strongly positive for NFP indicates a persistent treatment effect. Moreover, recognized smaller nerves around injured fascicles in the chronic phase that are positive for NFP may represent evidence of nerve regeneration.

Physiologic Assessment

Hall D

Tuesday, October 23, 2012, 8:00 AM–10:00 AM

TCT-216
A Preclinical Comparative Histological Evaluation of the Renal Artery and Nerves in the Human Cadaver and Swine model
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Background: Renal nerve ablation has been proposed as a novel treatment for patients with refractory hypertension. Evaluation and comparison of the cadaveric human renal artery and nerves with the normotensive swine model currently used for preclinical renal artery ablation studies is valuable for interpretation of preclinical model data.

Methods: Ten human cadaver and thirty swine renal arteries with an equal representation of both genders and sides (left/right) were collected, and pressure fix in 10% NBF. The tissue was paraffin embedded, stained with Hematoxylin and Eosin and prepared at 3 mm intervals for evaluation.

Results: In the human model, 230±87 nerves per renal artery were identified and the number of nerves close to the renal artery ostia was similar to the distal sections (near the kidney). 97% of the human renal nerves were less than 0.4 mm in diameter. 85% of the nerves were within 2 mm of the arterial adventitia. Ganglia were present in 30% of cadaver sections and tended to be in the proximal sections. In swine, 95±35 nerves were identified per renal artery. Nerve size was predominantly < 0.5

mm in diameter (99%). Nerves were found at a distance less than 1 mm from the arterial luminal surface (48%), and decreased in frequency as a function of distance (20% at 1–2 mm to 17% at distances >4 mm). Swine renal ganglia were seen in 2.3% of the sections and 2.4 mm from the arterial lumen. A recognizable pattern to the spatial distribution of renal nerves and ganglia along the renal artery was not noted in either model.

Conclusions: This assessment provides insight into the similarities in size and anatomic distribution of renal nerves and ganglia, and their spatial distribution relative to the renal artery in human and porcine model. We conclude that the anatomicity of both these models are similar and the porcine model is relevant for translation of understanding renal ablation prior to human use.

TCT-218
Evaluating Ischemia In The Myocardium Of A Chronic Total Occlusion To Determine The Value Of Percutaneous Recanlization
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Background: It remains controversial as to whether recanalizing a chronic total occlusion (CTO) in a patient with stable coronary artery disease (CAD) is of value, particularly for occlusions with extensive collateralization or impaired left ventricular function in the region supplied by the CTO. We evaluated the presence of ischemia using fractional flow reserve (FFR) of the myocardium supplied by the vessel with CTO in patients referred for cardiac catheterization and long-term outcomes after recanalization compared with a non-CTO control group.

Methods: Patients who underwent FFR and successful percutaneous coronary intervention (PCI) of a CTO were retrospectively evaluated. FFR of the CTO vessel was determined after the CTO was minimally recanalized with balloon angioplasty (usually 5mm in diameter).
Conclusions: In patients with a CTO and an intermediate stenosis of the donor artery, the ischemic fractional flow reserve (FFR) which returns to the normal range with CTO recanalization. This reversion to normal is likely related to the pooling of both small and large supply area together in the same study. Thus, the FFR value together with the number of corresponding left ventricular ischemic index (LVIi) measurement predicts more precisely the severity of the ischemia on the scintigraphy than the fractional flow reserve alone.

Characteristic (ROC) curve was significantly higher for LVIi than FFR (0.92 vs. 0.78; p < 0.001). Analyzing all the FFR values independently of the localization of the lesions, they also correlated significantly with the rDSc, but the relation was less strong (rDSc vs. FFR: 0.696 vs. 0.637, p = 0.029). The sensitivity, specificity, PPV and NPV of TAG cut-off < -0.654 (HU/mm) for FFR <0.80 were 47.5%, 91.2%, 79.2%, 71.2%, and those of CCO cut-off >0.063 were 65.0%, 61.4%, 54.2%, 71.4% on a per-vessel basis. Both TAG and CCO did not show significant incremental value when added to diameter stenosis >50% by QCA (p = NS). In left anterior descending artery (LAD) and non-LAD subgroup analyses, no significant reclassification was found by TAG, but reclassification was significantly negative by CCO in LAD subgroup (net reclassification index = -12.7%, p = 0.027).

Conclusions: Intracoronary attenuation-based CCTA analyses, TAG and CCO, showed moderate correlation with physiological coronary artery stenosis and no incremental value to the QCA. The value of CCO seemed to be limited for the evaluation of stenosis in LAD.

TCT-222
Combining parameters of coronary angiography and intracoronary pressure measurement predicts more precisely the severity of the ischemia on the myocardial perfusion scintigraphy than the fractional flow reserve alone.

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Background: Current concept regards the fractional flow reserve (FFR) as an indicator of the ischemic consequence of a coronary lesion independently of the localization on the coronary tree.

Methods: The coronary angiograms of 28 patients were analyzed by a computer program called Holistic Coronary Care. The software registered 23 epicardial coronary segments using the modified Syntax segmentation system and rendered the supplied left ventricular segments on the standard 17-segment polar map to each coronary branch. FFR measurements of 36 vessels were compared with the myocardial perfusion SPECT studies performed before the invasive procedure. We introduced a new ischemic index by combining the FFR with the number of the corresponding myocardial segments (Ni: left ventricular ischemic index (LVIi) = N x (1 - FFR)). This index was correlated with the regional myocardial perfusion defects identified on the scintigrams. Perfusion reversibility score of 2 or above was considered as indicative of active ischemia (regional Difference Score: rDSi).

Results: Close linear relationship was found between the LVIi and the rDSi (P < 0.001) (y = -2.20 + 3.75x, r = 0.88, p < 0.001). Analyzing all the FFR values independently of the localization of the lesions, they also correlated significantly with the rDSi, but the relation was less strong (rDSi vs. FFR: 0.60 vs. 0.637, p = 0.04). LVIi > 0.5 on myocardial scintigraphy with 77.8% sensitivity and 94.4% specificity when the cut off value was set to 0.96. FFR alone predicted the ischemia on the scintigraphy with 77.8% sensitivity and 94.4% specificity at the best 0.8 cut off value. The area under the Receiver Operating Characteristic (ROC) curve was significantly higher for LVIi than FFR (0.92 vs. 0.78; P < 0.001).

Conclusions: Our results shows that the LVIi > 0.96 indicates clinically relevant stenotic lesion. In this concept the FFR value together with the number of corresponding left ventricular segments rather than alone predicts the severity of myocardial ischemia.