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ABSTRACTS

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338 Sudden coronary death, myocardial ischemia and postmortem high-sensitive cardiac troponin's levels

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Background: Ischemic heart disease (IHD) related to atherosclerotic coronary artery disease is one of the most prevalent causes of death in western countries. Postmortem diagnosis of IHD can be problematic in some autopsy cases, especially in early myocardial ischemia. High-sensitive troponin T (hs-TnT) is used in clinical practice as the gold standard to diagnose the myocardial ischemia, and might also be applied as an ancillary tool for postmortem evaluation. The goal of this study was to evaluate the diagnostic value of post-mortem serum hs-TnT assay in cases of sudden coronary death related to IHD. The influence of cardiopulmonary resuscitation (CPR) attempts on post-mortem hs-TnT levels was also evaluated.

Design: The hs-TnT values in serum were retrospectively analyzed on data retrieved from the database of autopsies performed during 3 years period. Study cases were selected on the basic of clinical history and/or morphological results suggesting the death from cardiac ischemia related to atherosclerotic coronary artery disease. Control cases included cases of violent death (hanging, gunshot, etc.) with no cardiovascular pathology at the morphological examination. Postmortem serum hs-TnT was measured with reagents by electrochemiluminescence immunoassay. The group's statistical comparison was performed using logistic regression model.

Results: 52 cases were included in the study group (mean age 53.5; age range 34-75) and 33 cases in the group of control (mean age 40.4; age range 15-69). A significant non-linear association between hs-TnT serum values and post-mortem diagnosis of sudden deaths related to IHD (*p*-value 0.005) was found with a different profile compared to the clinical field (peak around 90 ng/L, then slight decrease of the probability). No significant difference in the hs-TnT serum values was found between the CPR and the non-CPR cases (*p*-value 0.304).

Conclusions: The measurement of Hs-TnT serum values might be considered as an ancillary tool for the evaluation of death related to IHD, while taking necessary precautions in the interpretation of the results. It was however impossible to determine a cut-off value as for living patients, probably because of the non-specific and unpredictable rise of hs-TnT due to post-mortem alterations.

339 PRKAR1A Mutations in Syndromic and Non-Syndromic Cardiac Myxomas

Melanie Bois[1], *Elizabeth H Cheek*[2], *Benjamin Kipp*[1], *Rondell Graham*[1], *Joseph Maleszewski*[1]. [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, MN

Background: *PRKAR1A* mutations are associated with cardiac myxomas arising in the setting of Carney Complex (CNC). However, sporadic mutations of *PRKAR1A* in isolated (non-syndromic) cases have not been described. Herein, we report 8 patients with cardiac myxoma who underwent germline and somatic interrogation of *PRKAR1A* in tandem with PRKAR1A immunohistochemistry.

Design: Patients were prospectively identified at the time of surgical resection of cardiac myxoma (2015-2016). Genetic analysis of *PRKAR1A* was performed on both the resection specimen (somatic) and paired peripheral blood sample (germline). Variants were classified according to guidelines. PRKAR1A immunohistochemistry performed on formalin-fixed, paraffin embedded tissue sections. Salient clinical information was abstracted from the medical record.

Results: Eight individuals (5 women) were enrolled in the study. Median age was 71 (interquartile range 47- 83). Lesions occurred predominately in the left atrium (n=7, 88%), with one myxoma occurring in the right ventricle. Median lesional size was 3.4 cm (interquartile range 2.5-6.4). One patient with known CNC harbored a germline variant of unknown significance (c.891G>A(HET)) and an additional somatic pathogenic variant (c.720delG(HET)). Another, non-syndromic patient showed one pathogenic (c.838C>T) and one likely pathogenic (c.549+2_549+3insTT) variant in somatic tissue. Both of these individuals showed loss of PRKAR1A immunohistochemistry. A third patient with benign/likely benign somatic and germline variants showed loss of staining with immunohistochemistry.

Conclusions: Herein, we report the first case of biallelic somatic *PRKAR1A* mutations leading to cardiac myxoma in a non-syndromic patient, as documented by paired germline analysis. The reported data also support the notion that CNC patients are prone to development of cardiac myxoma due to underlying germline mutations in *PRKAR1A*. Moreover, we show that genomic variants translate to protein dysfunction by the loss of normal PRKAR1A expression in both CNC and non-syndromic patients. The single case of loss of PRKAR1A expression in the setting of normal *PRKAR1A* sequencing suggests the possibility of alternative mechanisms at play in a subset of cardiac myxomas, providing the framework for future studies.

340 KRAS Mutations in Papillary Fibroelastomas: Molecular Underpinnings Suggesting Neoplastic Etiology of an Enigmatic Lesion

Melanie Bois[1], *Dragana Milosevic*[2], *Benjamin Kipp*[1], *Joseph Maleszewski*[1]. [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic

Background: Papillary fibroelastoma (PFE) is an increasingly recognized cardiac tumor. Despite its prevalence, controversy exists as to the etiology of this lesion. Specifically, there is question as to whether it represents a reactive process or neoplasia. Understanding the molecular underpinnings, which may shed light on such a question, has been limited by the paucicellular nature of PFEs. Advances in sequencing techniques now permit targeted interrogation of lesions of low cellularity, such as these. Recently, *KRAS* mutations were reported in a small collection of PFEs, but the incidence of mutations and the clinical and pathological conditions that they arise in are yet unknown.

Design: Institutional archives were queried for cases of PFE (2001-2017). Cases were reviewed for confirmation of diagnosis and relevant clinical information was abstracted from the medical record. Formalin-fixed paraffin-embedded tissue was microdissected for tumor isolation. Extracted DNA underwent digital droplet polymerase chain reaction analysis of the most common *KRAS* mutations (codons 12, 13 and 61). Borderline cases were repeated. Fractional abundance of mutant DNA >1% and >14 copies detected was considered positive.

Results: 52 PFE were selected from 50 patients (32 women). Median age at the time of excision was 67 years (interquartile range 53.5-76). 13 (25%) PFEs harbored pathogenic variants (PV) in tested *KRAS* codons (8 in codons 12/13; 5 in codon 61). Mutations were mutually exclusive and discovered in an equal sex distribution (6 men). Median age of patients with KRAS mutation was 69 years (IQR 61.5-77.5); median size was 1.1 cm. No clinical or pathologic correlates differed significantly from cases without detectable PVs.

Conclusions: Hitherto, the molecular drivers of PFE formation have been unknown. Due to advances in molecular technique, we report on the largest series of PFE tested for *KRAS* mutations and present the largest cohort of *KRAS*-mutant PFEs to date, providing evidence in support of the notion that at least a subset of PFEs represents neoplasia. Lack of correlation with clinicopathologic data suggests that those cases without detectable PV in *KRAS* may harbor oncogenic mutations in untested genetic regions. Of paramount importance, identifiable PV in commonly mutated *KRAS* codons introduces potential targeted therapy options for ineligible surgical patients.

341 CD68/CD31 Immunohistochemistry Double Stain Demonstrates Increased Accuracy in Diagnosing Antibody-Mediated Rejection in Cardiac Transplant Patients

Carolyn Glass[1], *Yasmeen Butt*[2], *Tunc Gokaslan*[2], *Jose Torrealba*[2]. [1]UT Southwestern, [2]UT Southwestern Medical Center

Background: Antibody mediated rejection (AMR) occurs in 10%-20% of cardiac transplant patients and is associated with increased mortality. The endomyocardial biopsy, used to identify microvascular injury with intravascular macrophages, activated endothelial cells, immunohistochemical (IHC) evidence of complement deposition, and/or > 10% intravascular macrophages within capillaries, remains the primary diagnostic tool for AMR. However, as recently addressed at the XIIIth Banff Allograft Pathology Conference, identifying the intravascular location of macrophages by routine histology can present diagnostic challenges. This prompted us to perform a screen of cardiac transplant cases to determine if double labeling with an endothelial and histiocytic marker could improve diagnostic accuracy.

Design: Twenty-two cardiac transplant endomyocardial biopsies previously diagnosed at a high-volume transplant center as pAMR-2 based on histologic evidence of endothelial activation, endothelial deposition with C3d or C4d or >10% intravascular macrophages, were screened using a CD68/CD31 IHC double stain. To determine whether the diagnosis of pAMR-2 would be altered using the double stain, CD68 positive intravascular macrophage percentages were calculated and retrospectively compared in the same cases diagnosed using CD68 IHC alone.

Results: The CD68/CD31 double stain showed 13 of 22 (59%) cases which had been previously been diagnosed as >10% intravascular macrophages using a CD68 IHC stain alone, had <10% CD68 intravascular positivity. Use of the double stain altered the diagnosis of pAMR-2 in 33% of cases. The double stain showed a discrepancy of overcalling intravascular macrophages by >30%, >20% and >10% in

26%, 12% and 23% of cases, respectively. The mean C4d positivity by immunofluorescence was 75% (N=12), 37% for C3d by IHC (N=8), and 30% for >10% CD68 by IHC (N=22). The patients (mean age 51 years, 27% female) had 45 months post-transplant follow up, and one third of patients had pre-transplant left ventricular assist devices.

Conclusions: Based on our institution's experience at a high cardiac transplant volume center, over a third of patients were over-diagnosed as pAMR-2 using CD68 by IHC alone. We demonstrate here the value of using a CD68/CD31 double stain to accurately determine the percent of intravascular macrophages to diagnose the "I" component of pAMR-2.

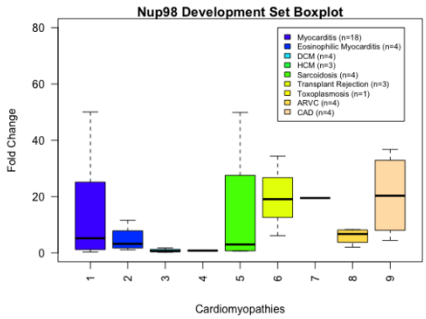
342 PSEN1 and Nup98 as Diagnostic Biomarkers for Myocarditis

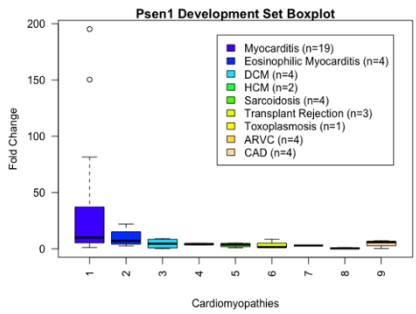
Paul J Hanson[1], *Li Cheng*[2], *Harpreet Rai*[2], *Erika L Jang*[3], *Bruce McManus*[4], *Michael Seidman*[5]. [1]University of British Columbia, Vancouver, BC, [2]University of British Columbia, [3]University of British Columbia, Vancouver, BC, [4]St. Paul's Hospital, Vancouver, BC, [5]Vancouver, BC

Background: Myocarditis, inflammation of the myocardium not associated with ischemia, is a spectrum of conditions causing considerable morbidity and mortality resulting from various etiologies, most commonly viral infection. Clinical symptoms are also variable, ranging from life threatening acute illness to chronic disease, while others never come to clinical attention. While variability among clinical presentations makes the frequency of myocarditis difficult to ascertain, it's estimated 9-20% of autopsies show myocarditis on histologic examination. Presently, the gold standard of diagnosis is inflammation shown on endomyocardial biopsy with or without myocyte damage. However, myocarditis diagnostic sensitivity is estimated as low as 30%. To improve upon this, we examined several markers implicated in the pathogenesis of viral myocarditis in animal models as possible diagnostic biomarkers. PSEN1 and Nup98 have emerged as promising candidates.

Design: Two groups were examined for PSEN1 and Nup98 immunohistochemical (IHC) staining: a development set of 50 cases (18 lymphocytic active or healing myocarditis, 4 eosinophilic myocarditis, 4 idiopathic dilated cardiomyopathy, 3 hypertrophic cardiomyopathy, 4 sarcoidosis, 3 transplant rejection, 1 toxoplasmosis, 4 arrhythmogenic right ventricular cardiomyopathy (ARVC), 4 coronary artery disease (CAD) and 5 normal controls) and a biopsy set of all (62) cardiac biopsies performed at SPH from January 2015-June 2016. Staining intensity was assessed by computer aided image analysis. Statistical analysis was performed using Mann Whitney *U* test and receiver operating characteristic (ROC) curves. All protocols were approved by the UBC/PHCRI Research Ethics Board.

Results: PSEN1 distinguished myocarditis from all other diagnoses in the development set (p=0.0001). Nup98 could distinguish inflammatory myocarditides from most other diagnoses in the development set (p=0.001). ROC values comparing myocarditis to all other cardiomyopathies was 0.85 for PSEN1 and 0.80 for Nup98. These findings appear hold true in preliminary analyses of the biopsy set.





Conclusions: PSEN1 and Nup98 appear to be valuable biomarkers, particularly in combination, for improving sensitivity of endomyocardial biopsy for diagnosing myocarditis, and may provide greater ability to deduce etiologic information from such biopsies. These insights will aid in personalization of treatment and significantly improve clinical outcomes.

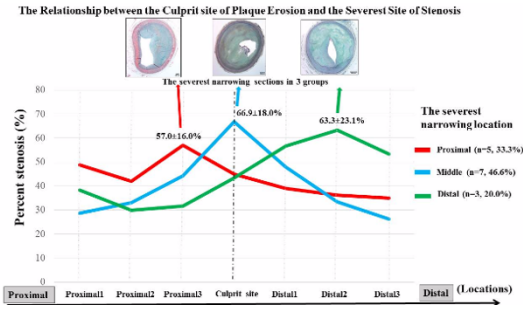
343 Does endothelial disturbed blood flow play a role in the etiology of plaque erosion?

Hiroyuki Jinnouchi[1], *Renu Virmani*[2], *Aloke V Finn*[3], *Maria E Romero*[4]. [1]CVPath, Inc., [2]CV Path, Gaithersburg, MD, [3]CVPath Institute, [4]CVPath, Inc., Gaithersburg, MD

Background: Plaque erosion is the second most prevalent cause of coronary thrombosis following rupture, and is characterized by absence of the endothelial layer and less advanced underlying atherosclerotic lesions as compared to ruptures. However, the mechanisms leading to thrombosis in erosions remain unclear, especially the relationship of severe luminal narrowing and the site of thrombus formation. It is commonly believed that vessel constriction proximal to the culprit site causes endothelial damage and thrombosis. Therefore, we evaluated relationship between the site of severest narrowing and the location of thrombus.

Design: We obtained 15 erosion lesions from hearts of 4 men and 11 women who had died suddenly. Three major epicardial coronary arteries (i.e. left anterior descending, left circumflex, and right coronary artery) were removed from the heart, embedded in paraffin, sectioned at 3-4 mm intervals from proximal to distal end, and stained with H&E and Movat pentachrome stains. The luminal stenosis at the site of culprit lesion, and 3 proximal and 3 distal sections were evaluated for the extent of luminal narrowing and expressed as % cross-sectional area luminal narrowing.

Results: The 15 lesions occurred in 8 left anterior descending (LAD), 4 right (RCA), 3 left circumflex (LCX) coronary arteries. In 5 (33.3%) cases the severest narrowing was located proximal to the culprit site of thrombus, in 7 (46.6%) the severest site of narrowing occurred at the culprit site, and in 3 (20.0%) cases the severest site of narrowing was distal to the culprit site of thrombus. In the group in which the severest narrowing was at the culprit site, the maximum percent stenosis 66.9±18.0%, whereas in the group in which the severest stenosis was proximal to the culprit site the maximum stenosis was 57.0±16.0%. In the group in which the severest narrowing was distal to the culprit site the maximum stenosis was 63.3±23.1%.



Conclusions: In erosion lesion, the most severe narrowing is located in the proximal position in 33.3% of cases. This location is likely to lead to turbulent blood flow distally which is responsible for de-endothelialization and thrombosis. In 2/3 of cases the mechanism of erosion remains unknown.

344 Which One is the Prognostic Factor: A Cohort Study on 15 Pulmonary Artery Sarcoma Cases

Li Li, Beijing, China

Background: Pulmonaryartery sarcoma (PAS) is a rare mesenchymal tumor arising from the pulmonary artery intima and exhibiting primarily intraluminal growth especially in early stages. To date, the understanding of the histogenesis of PAS remains fragmentary and only few case series correlated the histologic classification, grade, stage with the clinical data. In the present study, to identify the potential novel diagnostic markers and molecular therapeutic targets of PAS, we performed a cohort study with integrated clinical presentation, prognosis, histopathologic grade, stage and immunohistochemistry analysis on 15 PAS.

Design: The tumor tissues were analyzed by histopathology and immunohistochemistry. All tumors were classified and graded according to the Armed Forces Institute of Pathology classification and FNCLCC grading system. The stage of PAS was classified according to 8th edition WHO TNM system. The immunohistochemical stainings

used the following antibodies: platelet-derived growth factor receptor α (PGDFRA), epidermal growth factor receptor (EGFR) and MDM2. Follow-up data was obtained by contacting the patient or patient's family.

Results: Of 15 patients, 13 received tumor resection and had follow-up data. PAS were classified as intimal sarcoma (IS, n=10), undifferentiated pleomorphic sarcoma(UPS, n=2), myxofibrosarcoma (n=1), osteosarcoma (n=1) and chondrosarcoma (n=1). The intimal sarcoma lesions were grade 2 or 3 by FNCLCC grading system. Of which, 6 were stage II, 2 stage III and 2 stage IV. EGFR and MDM2 were expressed in 90% of IS respectively or simultaneously. PDGFRA was expressed in 50% of IS. Follow-up revealed that 7 of 8 patients with IS died (n=4) or recurred (n=3) within 6 months, one patient was alive to end of follow-up for 3 months. The median survival time for IS patients was shorter than other tumor subtypes (2.38±2.20vs15.6±9.81, p=0.003). There was no statistic difference in survival time by histologic grade, stage and immunological features. The rest tumor subtypes showed no immunostainings of PDGFRA, EGFR and MDM2, except that one UPS expressed EGFR.

Conclusions: Intimal sarcoma is the most common type of pulmonary artery sarcoma and the median survival time of IS patients was short. The prognosis of IS has limited relationship with histological grade and stage. MDM2 is the most sensitive and specific biomarker for IS. Our findings provide a novel biomarker for diagnosis of IS and a rationale for therapies that target MDM2, PDGFRA and EGFR in IS.

345 PREVIOUSLY PUBLISHED

346 Enhanced Detection of Myocardial Ischemia Utilizing C4d Antibody

Stanley Radio[1], *Mariam A Molani*[1], *Luo Zhou*[2]. [1]Univ. of Nebraska Med. Ctr., Omaha, NE, [2]The Insitute of Forensic Science, Fujian Provincial Dept. of Public Security

Background: Detection of early myocardial ischemia remains a challenge. Immunoperoxidase staining with C4d has been described as a valuable adjunct in autopsy specimens. We sought to further characterize staining with this antibody and Masson trichrome stain in both adult and pediatric patients in both autopsy and surgical pathology specimens.

Design: The department files from Jan. 2012 through Sept. 2017 were retrospectively analyzed to identify autopsy hearts, explanted native hearts, apical left ventricular cores removed at the time of left ventricular assist device (LVAD) placement, and posttransplant biopsies (BX) to identify patients with myocardial ischemia of less than 3 weeks duration. A representative section from each specimen was evaluated for histologic features (myocyte hypereosinophilia, waviness, contraction band necrosis, dropout, inflammation, granulation tissue, collagen) and positive dark staining with C4d or Masson trichrome.

Results: Seventeen autopsy hearts (12 adult, 5 pediatric) were examined along with eleven apical core specimens. Positive C4d staining was present in 11/12 adult (1+n=7, 2+n=4) and 4/5 (1+n=1, 2+n=3) pediatric autopsy hearts. Masson trichrome staining was positive in 8/12 adults and 5/5 pediatric autopsy hearts. Positive C4d staining was present in 10/11(1+n=2, 2+n=8) apical core specimens while Masson trichrome was positive in 6/11.In addition, C4d highlighted preservation/ischemic injury in 85 BX. Staining was negative in areas of individual myocyte injury due to rejection.

Conclusions: Our study confirms the utility of C4d staining in detecting ischemia including specimens not previously described including apical cores and BX.

347 PREVIOUSLY PUBLISHED

348 Isomerism of Atrial Appendages and its Relationship with Splenic Abnormalities and with Other Asymmetric Organ Systems

Nathaniel Robinson[1], *William D Edwards*[1], *Joseph Maleszewski*[1]. [1]Mayo Clinic, Rochester, MN

Background: Isomerism implies bilateral right- or left-sidedness and affects asymmetric organ systems (cardiovascular, respiratory, and digestive). Right isomerism is often associated with asplenia, and left isomerism with polysplenia. The goal of this study was to examine the interrelationships between isomerism of the cardiac atrial appendages and splenic abnormalities, and the frequency of concordant and discordant sidedness among the three asymmetric systems.

Design: Institutional autopsy archives were queried for cases of isomerism (1960-2015). Evaluation included review of gross specimens as well as autopsy and clinical records. Cases were categorized by isomerism (of atrial appendages) and by syndrome (asplenia or polysplenia).

Results: 55 cases were found in the specified time period. For atrial appendage isomerism: 37 were right, 11 left, 5 normal sidedness, and 2 indeterminate. For the spleen, 35 had asplenia, 16 polysplenia, 2 single spleens, and 2 unknown. Of the 37 with right isomerism, 34 (92%) had asplenia, 2 (5%) polysplenia, and 1 (3%) unknown splenic status. For the 11 with left isomerism, 9 (82%) had polysplenia and 2 (18%) had a single spleen. Of the 35 with asplenia, 34 (97%) had right isomerism and 1 (3%) was indeterminate. For the 16 with polysplenia, 9 (56%) had left isomerism, 5 (31%) a single spleen, and 2 (13%) right isomerism. Concordant right isomerism of the atrial appendages, lungs and abdominal viscera occurred in 56%. All cases with left isomerism of atrial appendages had discordant sidedness of abdominal viscera and/or lungs. Discordant sidedness involved the abdominal viscera in 55% of cases with isomeric right atrial appendages and in 100% of those with isomeric left atrial appendages.

Conclusions: Not all patients (8%) with right isomerism have the asplenia syndrome, and not all patients (18%) with left isomerism have the polysplenia syndrome. Similarly, not all patients (3%) with asplenia have right isomerism, and not all patients (44%) with polysplenia syndrome left isomerism. Only 27% of cases in this study had concordant sidedness of their atrial appendages, lungs, and abdominal viscera, but all that did had right isomerism. Thus, discordant sidedness was more often associated with left isomerism (100%) or the polysplenia syndrome (100%) than with right isomerism (55%) or the asplenia syndrome (43%). Abdominal sidedness is more variable in left isomerism or the polysplenia syndrome than in right isomerism or the asplenia syndrome.

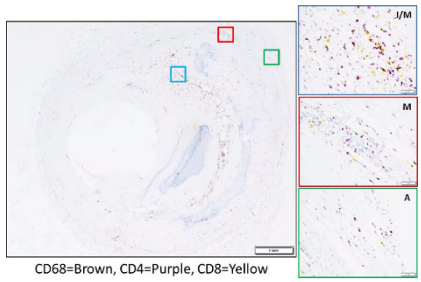
349 Plaque Vulnerability: The Role of Inflammation in the Pathophysiology of Ruptures

Maria E Romero[1], *Sho Torii*[2], *Hiroyuki Jinnouchi*[3], *Frank Kolodgie*[3], *Aloke V Finn*[4], *Renu Virmani*[5]. [1]CVPath, Inc., Gaithersburg, MD, [2]CVPath, [3]CVPath, Inc., [4]CVPath Institute, [5]CV Path, Gaithersburg, MD

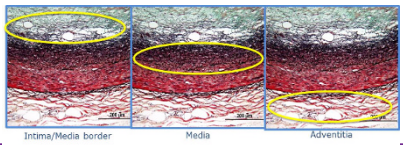
Background: Acute coronary syndromes are predominantly caused by plaque rupture (PR), a lesion morphologically characterized by a large necrotic core and thin (<65 micron) fibrous caps infiltrated by macrophages and lymphocytes. Current theories implicate blood flow disturbances and micro-calcification of the fibrous cap, as the root cause of rupture. We hypothesize that adaptive immune responses specifically at the intimal/medial border may also play a critical role however, differences in severity of inflammation and composition between ruptured plaques their precursor lesions, the thin cap fibroatheroma (TCFA) have not been established.

Design: Morphologic features and cellular components, distribution and severity of the adaptive immune response were evaluated in equal number of 120 coronary sections with confirmed PR or TCFA. Plaque inflammation was regionally assessed within the adventitia, intimal/medial (I/M) border, and media using a scoring system accounting for both the severity of inflammation and relative location based on quadrants, Inflammatory Score: 0-20 = 1, 21-100= 2, 101-200 = 3, 201-400 = 4, >400 cells = 5. In addition, single and multiplex immunohistochemistry was performed in select cases to further classify the predominant inflammatory cells types.

Results: The severity and distribution of inflammation was statistically greater for PRs relative to TCFAs (P< 0.001) for the I/M border, while no differences were noted for the media or adventitia. Inflammation was generally accompanied by medial degeneration where the severity of injury was also greater for PRs compared to TCFAs (P= 0.02) with a complete absence of medial noted in 46.7% of ruptures vs. 21.7% of TCFAs. PRs exhibited an association between neovascularization and CD163$^+$ macrophage also expressed at the I/M borders with co-localized CD68-positive macrophages while CD45RO and CD4-postive T cells along with plasma cells were greatest at I/M borders. B-lymphocytes were mainly confined to the adventitia. Finally, HLA-DR was also highly expressed at the I/M border as an indicator of inflammatory cell activation.



CD68=Brown, CD4=Purple, CD8=Yellow



Conclusions: Inflammation and medial degeneration localized to the intimal-media border may represent key factors whereby TCFAs eventually commit to rupture. These findings may be important for the underlying mechanism of rupture and may help identify these lesion destined prior to rupture by development of new innovative imaging tools.

350 Pathology of Human Peripheral Artery Atherosclerosis and Calcification

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Background: Lower extremity peripheral arterial disease (PAD) is a common manifestation of atherosclerosis, and heralds a poor prognosis due to its association with coronary and cerebrovascular atherosclerosis. Many patients with PAD may be asymptomatic or have atypical presentations. Understanding PAD requires appreciating atherosclerosis progression and calcification in the intima and media of these arteries

Design: Twelve lower extremities were obtained from 8 cadavers from asymptomatic individuals 70 years of age or older (median age=82) with known risk factors for atherosclerosis. Cases with previous vascular or orthopedic surgery were excluded. The femoral, popliteal, tibio-peroneal trunk, anterior and posterior tibial, peroneal, and dorsalis pedis vascular tree was removed, radiographed, and fixed. 6 leg arteries were decalcified and cut at 3- 4-mm intervals, and embedded in paraffin. Sections were stained with H&E and Movat. Another 6 leg vessels were cut without decalcifying and segments heavily calcified on X-rays were embedded in spurr resin, sawed at 3- 4 mm intervals and slides prepared using EXAKT grinding and stained with H&E. The rest of the segments were embedded in paraffin and stained with H&E, Movat, and von Kossa. All sections were classified according to modified American Heart Association (AHA) classification of atherosclerosis. Calcification in the intima and media was quantitated as microcalcification, punctate, fragmented, sheet and nodular calcification

Results: A total of 2987 atherosclerotic peripheral artery sections were evaluated. Plaque type distribution was significantly different between above the knee (AK) lesions and below the knee (BK) lesions. Atherosclerotic lesions were more common in AK than BK (AK vs. BK; 92.9% vs. 56.5%) and acute thrombotic lesions were exclusively observed in AK (8 lesions from 6 vessels), and 5 in 8 (62.5%) the acute thrombotic lesions occurred from calcified nodule and the rest were plaque ruptures. Chronic total occlusion (CTO) lesions were more frequent in BK. In the non-decalcified lower extremities (1578 sections), intimal and medial calcification were common (intimal, 75.3%; medial, 86.2%). Intimal calcification was more severe AK than BK [AK vs. BK; 15.1 (9.6-17.5) % vs. 1.6 (0.2-10.6) %, respectively, p=0.01]. Diabetic had greater calcification than non-diabetics

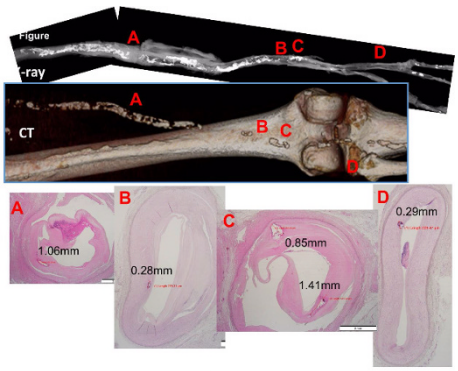

Figure 1: X-ray, CT scan and histologic correlation of SFA

Conclusions: Atherosclerosis and intimal/medial calcification are highly prevalent in asymptomatic high risk patients with significant difference in AK and BK lesions

351 MicroCT Evaluation of Coronary Artery Disease and Correlation with Histopathology

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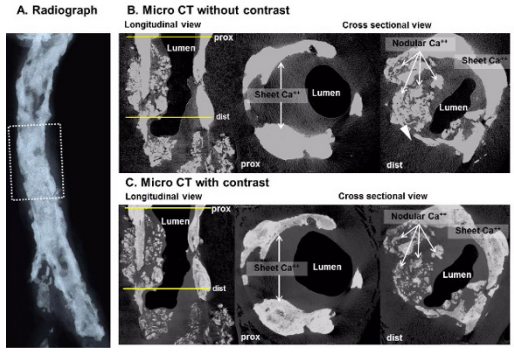
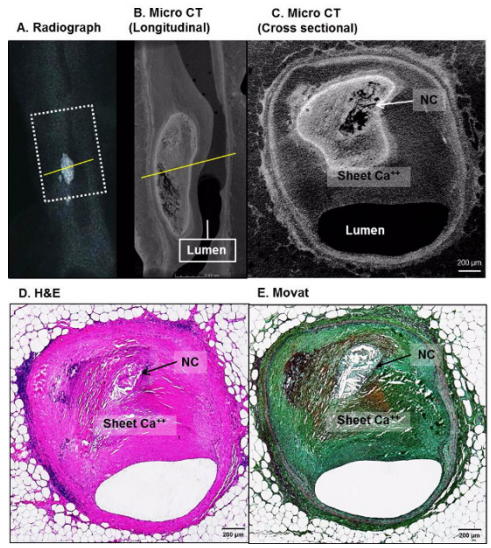
Background: There is a direct correlation between coronary artery calcification (CAC), presence of coronary artery disease (CAD) and development of advanced atherosclerosis. The extent and pattern of calcification have clinical prognostic implication, and imaging studies have been used to determine the presence and extent of CAC. The gold standard imaging modality for the visualization of the coronary arteries remains the invasive technique of coronary angiography via coronary catheterization. The purpose of this study is to assess the detection of type of calcification, necrotic core size, cholesterol clefts and length of coronary lesions by MicroCT imaging of the coronary artery tree and correlation with routine histology sections

Design: A CT scan of six whole hearts and evaluation of a total of 18 vessels was performed using the (Nikon, Model XT H 225ST) to capture the coronary tree. Coronary segments were immersed in diluted MD76R contrast medium for 1 hour at 37 degrees Celsius, patted dry, and mounted to the manipulator. Geometric magnification for segments yielded a voxel size of approximately 6 microns, with a minimum effective detectable particle size of approximately 10 microns. Images of the vessels were captured in various planes and reconstructed using the Nikon Metrology CTPRO3D and rendered using the VGStudio 3.0 MAX software with all Hounsfield values below the tissue layer (<50HU) removed. All coronary arteries were sectioned, decalcified and cut at 3- to 4-mm intervals, dehydrated, and embedded in paraffin. Sections were stained with H&E and Movat Pentachrome for light microscopy analysis.

Results: Out of 18 vessels examined, MicroCT analysis was able to detect calcifications, necrotic core size, and presence of cholesterol clefts in cross-sections of the vessels with detail similar to routine histology sections stain with H&E or Movat Pentachrome. Longitudinal sections by MicroCT were also obtained, allowing measurement of the length of coronary lesions, which is not always possible on routine histologic evaluation. However microcalcifications were not detected by MicroCT





Conclusions: MicroCT imaging as a method of coronary disease evaluation is introduced correlating relevant coronary lesions as compared with light microscopy analysis. Detection of type of calcification, necrotic core size, cholesterol clefts and length of coronary lesions is possible using MicroCT imaging analysis.

352 Giant Cell Arteritis is not Associated with Varicella Zoster Virus in Temporal Artery Biopsies

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Background: Giant cell arteritis (GCA) is an inflammatory disorder of medium and large-sized arteries that can lead to blindness if untreated. Temporal artery biopsy is the gold standard for diagnosis, and treatment includes urgent initiation of high-dose corticosteroids. Symptoms are caused by progressive occlusion of the arterial lumen due to immune cell mediated destruction and remodeling of vessel walls. The precise cause of GCA is unknown, and a variety of infectious agents have been hypothesized to play a role, including Varicella Zoster Virus (VZV). While VZV reactivation has a similar predilection for older adults and females as does GCA, the detectability of the virus and its proposed role in GCA pathogenesis is highly controversial.

Design: All temporal artery biopsies positive for GCA at a large academic medical center over a ten-year period were identified. Five-micron slides were prepared for each positive case and negative controls. Slides were treated with enzyme digestion for 10 minutes, stained with VZV antibody cocktail (SG1-1, SG1-SG4, NCP-1, and IE-62) (Cell Marque, Rocklin, CA) at 1:100 dilution, and detected with alkaline phosphatase (red chromogen). Slides were reviewed independently by two study pathologists blinded to clinical history and original biopsy diagnosis.

Results: Over a ten-year period, 41 temporal artery biopsies were identified with active arteritis and the presence of giant cells. The average age (73.8 +/- 8.0 years) and sex distribution (68% female) were similar to negative controls where there was an absence of vascular inflammation (n=10; 72.9 +/-11.3 years, p=0.8; 80% female, p=0.5). VZV immunohistochemistry was positive in 0/41 (0%) GCA positive and 0/10 (0%) negative cases, with 100% concordance between pathologists.

Conclusions: The role of VZV in GCA pathogenesis remains controversial, with some studies reporting detectable virus in the majority of positive cases and some negative controls, and others reporting no detectable virus in any cases. Twelve biopsies included in the present study were previously analyzed by unbiased next generation sequencing and were negative for VZV nucleic acid. Combined with the lack of detectable VZV antigen, these results argue against a clinically relevant association with GCA, and support neither routine testing for VZV nor treatment with antiviral drugs, at least in our patient population.