To Assess the Use of Ancillary Studies in the Determination of Cause of Death

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Background: Our institution has a busy adult autopsy practice, situated in West Dublin, with a catchment area of almost one quarter of a million people. Approximately 270 autopsies are performed annually. Histology is taken routinely in all autopsies, with additional studies (toxicology, neuropathology, microbiology) being undertaken in specific cases, as per the guidelines of the Royal College of Pathologists. Due to the paucity of literature regarding the use of microbiology sampling in adult autopsy practice, a particular emphasis was placed on investigating the contribution of microbiology in the determination of cause of death.

Results: This case series includes all adult autopsies performed in our institution over a 2-year period. Basic demographics and clinical details including location of death (in-hospital, out of hospital) were recorded. The use of additional studies was recorded. Final reports were then compared with provisional and interim reports to evaluate the contribution of each additional study.

Results: 500 autopsies were carried out (35% female; 65% male). 21% of deaths occurred in the emergency department, 45% in hospital and 34% out of hospital. Microbiology testing, including blood cultures and tissue swabs, was carried out in 15% and toxicology was carried out in 52% of cases. Provisional reports were issued in 73% of cases, with determination of cause of death deferred pending additional studies in 27%.

Conclusion: This large case series highlights the importance of SADS as the major cause of SCD particularly in the young, followed by cardiomyopathy; SCD organ retention and referral to specialist cardiac pathologists must be regarded as the ‘gold standard’. When the autopsy identifies SADS or cardiomyopathy, the families of victims should be referred for cardiac screening since a significant proportion of these conditions are inherited.

Well’s Scores Accurately Predict Presence of Massive Pulmonary Thromboembolism at Autopsy

RA Girard, V Galli, M Colaco, B Fyfe. UMDNJ Robert Wood Johnson University Hospital, New Brunswick, NJ.

Background: Well’s scores are utilized clinically to predict risk for pulmonary thromboembolism (PTE). Radiographic correlate studies have confirmed a high negative predictive value (NPV). This is the first autopsy study correlating Well’s scores with PTE.

Methods: An retrospective analysis of 85 adult autopsies from 2009 to 2011 was performed. Three cases were excluded due to inability to calculate Well’s score due to death on arrival to hospital. Well’s criteria were derived from chart review [clinical signs and symptoms of deep vein thrombosis (DVT), PTE first on differential diagnosis, heart rate > 100 bpm, immobilization ≥ 3 days or surgery in the previous four weeks, previous DVT or PTE, hemoptysis, and malignancy within 6 months]. Final autopsy reports were evaluated for presence or absence of PTE. Cases were classified by Well’s score using the Clinical Decision Rule (CDR) [≥ 4, PTE unlikely; > 4, PTE likely]. Final autopsy reports were reviewed to classify cases as massive PTE (mPTE) with large saddle thromboembolism as cause of death, other PTE (oPTE) with small acute or chronic PTE that played a contributory role but were not sole cause of death, and negative PTE (nPTE) with no autopsy evidence of massive or other PTE.

Results: 85 autopsies with 11 PTE were studied, 3 were mPTE and 8 were oPTE. CDR accurately identified mPTE cases as likely for PTE. The oPTE all were classified as unlikely for PTE (false negative). For mPTE the CDR has a high NPV (100%) and a positive predictive value (PPV) of 23%. Detailed analysis of the ten falsely positive CDR revealed underlying malignancy (4), clinical signs of DVT (5), and positive DVT in the past (6) as the most prevalent criteria for the elevated score. The oPTE group (false negatives) contained 8 patients with CDR 1.5-4. Applying CDR to all PTE (oPTE plus mPTE) yielded a NPV of 89% and PPV of 23%.

Conclusions: Well’s CDR is an effective tool used clinically for excluding acute PTE. This study confirms a high NPV for mPTE (100%) that decreases to 89% when including all PTE. Common causes for falsely elevated CDR include underlying malignancy, prior DVT, and clinical suspicion for DVT. This first autopsy study confirms the utility of Well’s CDR to assess PTE risk. It is particularly useful for screening for massive PTE and less useful for smaller/chronic PTE. This study also shows that new clinical tools may help guide post-mortem investigations, potentially facilitating less invasive exams (viroscopy). This is a first post-mortem analysis of such a clinical tool, the Well’s Criteria for pulmonary thromboembolism.
identified. DNA was extracted from available specimens. Portions of CYP2C9 and VKORC1 genes containing relevant polymorphisms were ampliﬁed by PCR. Amplitons were analyzed by high resolution melting, and genotypes were determined by comparing subject melting curves to known controls. Frequencies of alleles were compared to those of the general population, matched for race, as published in medical literature.

Results: 82 subjects were genotyped, including 59 non-Hispanic white and 19 Hispanic white decedents. The frequency of CYP2C9 *2 was signiﬁcantly higher in both groups than in the general population (non-Hispanic, 0.45 versus 0.16, p = 3.3 x 10^-10; Hispanic, 0.48 versus 0.08, p = 0.03). The frequency of CYP2C9 *3 was not different.

Conclusions: A variant allele conferring enhanced sensitivity to warfarin was overrepresented in the sample population compared to the general population. There were no signiﬁcant diﬀerences in VKORC1 genotypes between Hispanic and non-Hispanic white decedents. Whether genotyping would have prevented deaths cannot be determined by the present study, and warrants further investigation.

5 Histopathologic Evaluation of In-Sent Stent Restenosis at Autopsy in Patients with Coronary Stents

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Background: Pathologic evaluation of stented coronary arteries at autopsy is labor-intensive. There is no standardized technique for evaluation of stented coronary arteries, and plastic processing requires specialized techniques. The objectives of this study were to assess the impact of in-sent ﬁndings on the ﬁnal cause of death using parafﬁn based histologic methods.

Design: A retrospective study of 87 inantra coronary stents from 45 autopsy cases (35 medical examiner and 10 hospital cases). Stents were removed using microdissection with tungsten carbide scissors or clamped sections were embedded and processed in parafﬁn. Restenosis was deﬁned as >75% vessel narrowing as determined morphometrically. Thrombosis and ﬁbrosis deposition were documented in each case.

Results: There were 23 Taxus, 21 Endeavor, 10 Cypher, 9 RX Achieve, 6 Xience, 5 MultiLink Vision, 4 MultiLink Rx, 3 NIR, 3 PalmaSchatz, 2 AVE GFX, 1 and 1 underdetermined stent type. 85 were in native arteries, and 2 in vein grafts. 54 stents were successfully dissolved, 2 were microdissected after unsuccessful electrolysis, and 31 were not evaluable. Of 5 patients with recent placement, causes of death were acute thrombosis of non-stented artery (2), in-stent thrombosis (1), complications of myocardial infarction (MI, 1) and iatrogenic right ventricular puncture (1). Of the 40 patients with only chronic stents, causes of death were noncoronary (24; 16 unnatural), and coronary (21; 13 sudden cardiac death). Of 32 stents in the coronary death group (CDG) after chronic stent placement, 8 had in-stent restenosis (25%) vs. 5 of 45 in the non-coronary death group (NCDG) (11%, p=0.01); mean percent stenosis was 45% vs. 35%, respectively (p<0.01). Two thombi were found, one organizing in a vein graft in the NCDG, and one organized occlusive thrombus in the CDG. There were 2 intramural total occlusions in the CDG and 1 in the NCDG. The rate of arthromyogenic substrates (healed MI, cardiomyoid) was similar in the CDG and NCDG.

Conclusions: In this study, 1 of 5 deaths in the acute group was related to the stent, and nearly half of stent thromboses were found. There is a mild non-signiﬁcant increase in restenosis and neo-intima in coronary deaths vs. non-coronary deaths. The cause of death is rarely impacted by in-sent ﬁndings at autopsy.

6 Rapid Autopsy Program for Pancreatic Carcinoma: Correlation of Histologic Subtypes and Pattern of Spread with Mucin Phenotype and Molecular Markers

EM Linde, NA Rammers, DJ DeMaio, JM Anderson, MA Hollingsworth, AJ Lazenby. University of Nebraska Medical Center, Omaha, NE; University of Nebraska Medical Center, Omaha, NE.

Background: Pancreatic ductal adenocarcinoma (PDAC) is the 4th leading cause of cancer-related death with 1 and 5 year survival rates of 20-40% and 5%, respectively. Only 20% of patients are surgical candidates and 70% have metastatic disease at presentation. Histology alone does not adequately predict biologic behavior or response to therapy. Novel molecular markers may aid in early diagnostic and therapeutic options.

Results: 84 patients were autopsied (2002-2011, mean postmortem interval 2.1 hrs). Degree of diﬀerentiation (1: poorly, 13: diﬀerentiated, and undiﬀerentiated (4); no clear association of diﬀerentiation with mucin types was seen. Signet ring cell features (7) was associated with decreased Lewis expression. Clear cell change (8) was not correlated with a particular mucin pattern. Two major patterns of intra-abdominal spread were noted: senescent studding (unmeasurable, minute foci of minimally invasive tumor) and carcinomatosis (diﬀuse large invasive tumor foci). Cases with senescent studding (10) had increased expression of MUC17, 6, 5AC, 7, and 4 (mild) when compared to carcinomatosis (6), in which the expression of MUC17, 7, and 6 was lost.

Conclusions: 1. Two distinct patterns of intra-abdominal spread of tumor were noted: senescent studding and carcinomatosis. These correlated with distinct mucin phenotypes.

7 C4d: A Marker for Cardiac Allograft Vasculopathy

MK Mirza, S Fedson, Y Chi, SR Marino, AN Hussein. University of Chicago Medical Center, Chicago, IL; Munster Community Hospital, Munster, IN.

Background: In the past decade C4d has emerged as a potential marker for antibody-mediated rejection (AMR); however, evidence on its use as a prognostic tool has been controversial. To date, there is no consensus of the value of C4d in the pathologic assessment of AMR. Here, we present a correlation of our prospective study of C4d immunoreactivity in endomyocardial biopsies with clinical cardiac dysfunction, cellular rejection, HLA status, death, and cardiac allograft vasculopathy (CAV) at autopsy.

Design: 3758 endomyocardial surveillance biopsies from 200 heart transplant recipients (0004-9/2010) were stained prospectively for C4d. Immunohistochemical stains were performed on parfaﬁn-embedded tissue using an anti-human C4d polyclonal antibody. Speciﬁc diffuse endothelial staining was considered positive. All patients had at least 1 year of follow-up. Cardiac dysfunction at the time of positive biopsy was evaluated by standard echocardiography. Cellular rejection was graded per ISHLT 1990.

Results: Positive C4d staining was present in 43 biopsies from 25 patients (12%); 9/25 patients (36%) had clinically signiﬁcant cardiac dysfunction at the time of positive biopsy. In C4d positive patients, the mean PRA was 33%. At ﬁrst C4d positivity, concurrent cellular rejection was grade 1 (0/25); grade 2 (2/25) (29%) and 3 (2/25) (21%). Cellular rejection was present in 10/10 C4d positive patients, while histologic evidence of cardiac allograft vasculopathy (CAV). Six of 8 C4d negative patients (75%) had no CAV, while 2/8 had CAV. Six C4d positive deaths did not have autopsy. Nine of 25 (36%) C4d positive patients are alive 1-3 years post-transplant.

Conclusions: C4d positive patients contributed to 67% of the overall mortality. All 10 autopsies (100%) on C4d positive patients revealed CAV as the cause of death. In the C4d negative group, 75% of all deaths were due to non-cardiac causes. These ﬁndings show a positive association of C4d with CAV and death. Our results indicate a prognostic role for C4d in heart transplantation warranting routine detection of this marker in the pathologic evaluation of cardiac AMR.

8 Do Patients Presenting with Atherosclerotic Heart Disease and Sudden Cardiac Death Have a Higher Body Mass Index? Nair V, S Guglani, GM Nair, M Pickup, C Rao, J Fernandes. Hamilton Health Sciences, McMaster University, Hamilton, Canada.

Background: A raised body mass index (BMI) has been associated with an increased risk of morbidity and mortality in atherosclerotic coronary heart disease (CHD) patients. We sought to identify an association between sudden cardiac death (SCD) in patients with atherosclerotic CHD and an increased BMI.

Design: A review of all SCD at the Hamilton General Hospital Forensics Unit, for the calendar year 2010, was performed. Clinical details including age, height, weight, symptoms prior to demise and histopathological details from the autopsy were collected. The body mass index was calculated in all cases. Standard statistical methods were used to determine if BMI was higher in patients with atherosclerotic CHD presenting with SCD. The control group for comparison included SCD patients without evidence of atherosclerotic CHD. Sub group analysis included comparison of BMI based on the sex of SCD patients.

Results: One hundred and ten (16%) of 666 autopsies conducted in 2010 were classiﬁed as SCD. Seventy-one (64.5%) cases of SCD were attributed to atherosclerotic CHD. Sudden cardiac death in the remaining patients was attributed to other causes. The results are summarized in Table 1 and Table 2.

Table 1

| Age in Years | Male SCD Patients with | Male SCD Patients without | p-value | Paired t-test |
|-------------|-----------------------|--------------------------|--------|--------------|
| 59.78 ± 11.17 | 0.08 ± 12.91 | 0.003 (NS) | 0.23 ± 13.74 | 0.45 (NS) |

Table 2

| Age in Years | Male SCD Patients with | Male SCD Patients without | p-value | Paired t-test |
|-------------|-----------------------|--------------------------|--------|--------------|
| 59.78 ± 11.17 | 0.08 ± 12.91 | 0.003 (NS) | 0.23 ± 13.74 | 0.45 (NS) |

Conclusions: A significant diﬀerence was not noted in the BMI of SCD patients with and without atherosclerotic CHD. Analysis of BMI based on the sex of the patients also did not demonstrate a signiﬁcant diﬀerence. Men presenting with SCD due to atherosclerotic CHD tended to be signiﬁcantly older than those presenting with SCD due to other causes.
9 Acute Hepatic Hemorrhage in Hospital-Based Autopsy Series: A 21-Year Review
SI Odronic, ER Rodriguez, CD Tan. Cleveland Clinic, Cleveland, OH.
Background: Acute hepatic hemorrhage can have a variety of causes. In this study, we reviewed the etiology and associated findings in hospital-based autopsy cases of liver hemorrhage.
Results: Nineteen cases of acute liver hemorrhage were found. There were 3 children and 10 adults with age ranging from 3 to 75 years. There was a female predominance (M:F ratio of 3:10). Nine cases were iatrogenic (64%), 3 cases were spontaneous (23%), and 1 case was traumatic (8%). Of the 9 iatrogenic cases, 5 were due to cardiopulmonary resuscitation (CPR) and 4 cases occurred after procedures related to the hepatobiliary system. Eight cases involved the right lobe, 4 cases involved the left lobe, and 1 case involved both lobes. Three cases showed subcapsular hematoma that did not rupture. Ten cases were associated with hemoperitoneum which was the immediate cause of death in 5 patients. The clinical team was not aware of the hepatic hemorrhage prior to autopsy in 2 of the 5 cases with massive hemoperitoneum. Most cases of liver injury in the hospital setting were iatrogenic in nature.

10 Isolated Right Ventricular Myocardial Infarction
SI Odronic, ER Rodriguez, CD Tan. Cleveland Clinic, Cleveland, OH.
Background: Isolated acute right ventricular myocardial infarctions (RVMI) are not well characterized. The right ventricle is less susceptible to ischemia, but several factors can increase oxygen demand or decrease oxygen supply, and predispose the right ventricle to ischemic damage. The incidence of isolated acute RVMI may be underestimated due to lack of detection. Tetracycline staining is useful in the detection of early myocardial ischemia.
Results: Based on 40 cases of right ventricular myocardial infarction reviewed, 10 cases were associated with RVMI. The utility of tetrazolium staining to detect myocardial ischemia in this setting is a useful and sensitive method to look for evidence of early acute ischemic changes.

11 Pulmonary Hypertension in Adult Sickle Cell Patients at Autopsy
JE Pogoriler, AN Husain. University of Chicago, Chicago, IL.
Background: Pulmonary hypertension (PH) in patients with sickle cell disease (SCD) has a poor prognosis. Previous autopsy studies have reported up to 100% of SCD patients with muscular hypertrophy and intimal fibrosis, 60% with pleomorphic lesions, and 50-75% with chronic thromboembolic disease. However, clinically less than a third of SCD patients have PH, and half of these have pulmonary venous hypertension (PHV) due to left ventricular diastolic dysfunction. Given the discrepancy in the severity of histological and clinical findings, we examined a larger series of SCD autopsies.
Results: This was a retrospective analysis of adult SCD patients autopsied at our institution since 1993. Patients were included if hemoglobin electrophoresis confirmed SCD or if there was a history of complications from SCD. Autopsy reports, all lung slides and elastic, trichrome, reticulin and iron stains on one section were examined from each case.
Results: Pleuroparenchymal lesions were entirely absent in all 19 patients. Five patients had no vascular changes and 4 had only rare calcified small arteries. Of the remaining 10 patients, 6 had recanalization of large (>1mm) vessels and 6 had frequent recanalization of smaller arteries. Variable degrees of intimal fibrosis and/or muscular hypertrophy were present in only 7 cases (37%). In addition, 3 patients (16%), all with evidence of chronic stromboembolic disease, had extensive thickening of the alveolar walls due to increased capillary vessels (Fig 1A). Reticulin stain (Fig 1B) confirmed increased capillaries in individual alveolar septa rather than congestion and atelectasis. Unlike pulmonary capillary hemangiomatosis (PCH), however, no capillary invasion of bronchi such as a multidisciplinary program. Trichrome stain (Fig 1C) confirmed that wall thickening was not due to fibrosis.

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Background: Acute hepatic hemorrhage can have a variety of causes. In this study, we reviewed the etiology and associated findings in hospital-based autopsy cases of liver hemorrhage. Design: Retrospective search of subcapsular hematoma and liver laceration from a single medical center between 1990 and 2011 was performed. Fetuses and patients with liver transplantation or remote history of liver laceration were excluded. Results: Thirteen cases of acute liver hemorrhage were found. There were 3 children and 10 adults with age ranging from 3 to 75 years. There was a female predominance (M:F ratio of 3:10). Nine cases were iatrogenic (64%), 3 cases were spontaneous (23%), and 1 case was traumatic (8%). Of the 9 iatrogenic cases, 5 were due to cardiopulmonary resuscitation (CPR) and 4 cases occurred after procedures related to the hepatobiliary system. Eight cases involved the right lobe, 4 cases involved the left lobe and 1 case involved both lobes. Three cases showed subcapsular hematoma that did not rupture. Ten cases were associated with hemoperitoneum which was the immediate cause of death in 5 patients. The clinical team was not aware of the hepatic hemorrhage prior to autopsy in 2 of the 5 cases with massive hemoperitoneum. Most cases of liver injury in the hospital setting were iatrogenic in nature.

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ANNUAL MEETING ABSTRACTS

Design: Postmortem organ specific morphologic studies including electron microscopy (EM) and immunofluorescence (IF) were performed in 10 cases of progressive GBM treated with TMZ and BEV containing regimens. 9 male and 1 female subjects were included, ranging from 50 to 77 years of age (median 57 years old). All subjects were treated at the Johns Hopkins Medical Center, Baltimore and received palliative care prior to their death. All patients initially received standard treatment for GBM with subsequent monthly TMZ. After GBM progression they received BEV every other week at 10 mg/kg with TMZ or irinotecan (5-49 treatments, median 17 treatments). Medical records of all 10 subjects were reviewed. Clinical toxicities and laboratory abnormalities were documented. Institutional review board (IRB) clearance and autopsy consents form the next of kin were obtained.

Results: The cause of death in most patients was bronchopneumonia (8/10). Clinically, apart from symptoms related to tumor progression in relevant cases, 8 subjects receiving BEV treatment developed proteinuria (trace to 3+) and 4 subjects developed hypertension. In 9/10 of unlimited autopsies (one was brain and kidney only). There was a significant morphologic evidence of TMZ/BEV-related injury in heart, liver, adrenal glands, thyroid, pancreas, spleen, or bone marrow. In all subjects the glomeruli revealed diffuse variable degree of glomerular basement membrane thickening with segmental to double contours and without proliferative lesions. EM examination of the kidneys showed homogenized substructure and subendothelial rarefactions with some wrinkling of the glomerular basement membrane. The vasculature showed variable mural thickening as observed in hypertensive IF. Exam formation showed no immune complex depositions.

Conclusions: With the exception of the kidneys, there appears to be no significant end-organ damage associated with treatment with TMZ and BEV of variable durations. Renal toxicity manifests as mild-to-moderate endothelial damage which was clinically associated with variable proteinuria and hypertension.

14 Utility of Rapid Cytologic Techniques in the Autopsy Setting

P A VanderLaan, JF Krane, GL Winters. Brigham and Women’s Hospital, Boston, MA.

Background: In the autopsy the may be augmented by providing families and clinicians with more timely results. Rapid cytologic techniques employed during the processing of organ cores provide quick and accurate pathologic diagnoses as well as maximizing the educational experience in an academic hospital setting. Few publications have addressed the utility of cytologic techniques as an immediate diagnostic tool in the autopsy setting.

Design: Over a 2 month period of time at a tertiary care academic hospital, rapid cytologic diagnostic techniques were applied to 41 consecutive autopsy cases when focal lesions were present (24 male, 17 female, age range = 31-100 years). Air-dried touch preparation, smear, and fine needle aspiration slides were stained with a Hemacolor rapid stain, and evaluated during the processing by a cytologist fellow with cytology attending consultation. Results were included in preliminary autopsy diagnoses and correlated with final histologic outcomes.

Results: Focal lesions amenable to cytologic sampling were present in 49% (20/41) of all autopsy cases over this time period. Of these, 15% (3/20) represented the primary tissue diagnosis of previously unknown malignancy, 50% (10/20) correlated with the utility of cytologic techniques as an immediate diagnostic tool in the autopsy setting.

Conclusions: This study provided good overall cytomorphology, and in a number of cases directed first pathologic diagnoses of ARVC.

15 Transthyretin Amyloidosis: The Heart and beyond

Q. Li, X. Zhang, J. Libien. SUNY Downstate Medical Center, Brooklyn, NY; The Mount Sinai Medical Center, New York, NY.

Background: The most common mutation leading to cardiac amyloidosis in the US is the V122I mutation, present in 34% of African-Americans. We studied the distribution of TTR amyloid deposition in autopsy material from our population and African-American patient population in order to better characterize the pathology associated with the V122I mutation. Since an association of wild-type TTR deposition in systemic senile amyloidosis (SSA) and myocardial infarction has been reported in a Finnish population, we also assessed whether any myocardial infarcts were present.

Design: Cases of TTR cardiac amyloidosis and age-matched controls were identified from 2007-2010 autopsy records. The presence of amyloid deposition in tissues was examined by H&E, Congo Red, and TTR immunohistochemistry. Amyloid was measured by TUNEL staining.

Results: Four cases of TTR cardiac amyloidosis (average age 82.8 years; range 80 to 87 years) were identified. TTR gene sequencing identified mutant TTR (V122I) in three cases and wild-type (WT) TTR in one case. Nine myocardial infarcts were identified in cases or controls, however, there was an increase in apoptosis in the myocardium in the TTR cases compared to controls. Cardiac amyloidosis was in a patchy and diffuse distribution with no significant differences in endocardium, epicardium, and myocardium in all the cases and in particular there was no difference between the two V122I cases. Amyloid was not present in the major coronary arteries but was found in smaller epicardial vessels in all of

16 The Histopathology of the Liver in HIV+ and Acquired Immunodeficiency Deficiency Syndrome (AIDS) Individuals in the HAART Era

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Background: Many publications have addressed the changes in the liver of AIDS patients but have not been well documented in the HAART era. With longer survival, patients are now developing more advanced and varied liver disease without the opportunistic infections that they once had. Recently, an association between didanosine and non-cirrhotic portal hypertension (NCPH) due to HAART has been described.

Design: Since 1999, our institution has accrued over 250 HIV+/AIDS autopsy cases via an NIH-funded Manhattan Brain Bank database. These individuals volunteer to donate their organs at post-mortem. From this cohort, we selected 77 archival liver autopsy specimens that performed a detailed necropsy report and analysis. Stage and grade for chronic hepatitis was based on Knodell's classification. Histologic examination was performed on 77 cases.

Results: There were 40 males and 37 females; average age was 49 years (range = 20-84). Mean HIV infection duration was 11.7 years (range = 2 months-20 years). Six patients had recent (<1 year) of HAART treatment. C4D counts were documented for 39 patients: 14 with 0-100, 19 with 100-399, and 6 more than 400 C4D+ cells. Twenty-seven of seventy (35%) were (+) for viral hepatitis (19 HCV; 7 HCV+HBV; 1 HBV). Cirrhosis was seen in 15/27 (55%); 8 (30%) had NCPH (3NRH, 5 HPS); 4 (15%) had steatohepatitis. Only 1 of 8 patients with NCPH and positive viral hepatitis was taking HAART at the time of death. Of the 50 cases with negative viral hepatitis, 15/50 (30%) had cirrhosis; 19/50 (38%) had cryptogenic chronic hepatitis with fibrosis ranging from mild to advanced fibrosis; 11/20 (55%) had NCPH; 5/50 (10%) had steatohepatitis.

Conclusions: This study documents that significant liver disease occurs in HIV/AIDS. Our series shows that the incidence of noncirrhotic portal hypertension is high in this patient population and that chronic idiopathic hepatitis in the absence of HCV or HBV infection, and alcohol use is common. The etiology of this hepatitis remains to be elucidated. Patient involved in this study may have taken pre-HAART era medications such as didanosine, but was not documented.

17 DSG2 Mutations in ARVC: A Molecular Autopsy Study

J Young, M Zhang, F Tavera, J Oliveira, A Travers. University of Maryland Medical School, Baltimore, MD; Shanghai Medical College, Fudan University, Shanghai, China; National Institutes of Health, Bethesda, MD; Messejana Heart and Lung Hospital, Fortaleza, Brazil.

Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a disease of the cardiac muscle that causes severe arrhythmias and sudden death. It has been linked to mutations in several desmosomal related proteins including plakophilin-2 (most prevalent), desmoglein-2, (DSG2), desmocollin-2, desmoplakin, and plakoglobin. Clinical series of ARVC patients report mutations of any type in approximately 50% of patients, and DSG2 mutations in approximately 10% of patients. However, the diagnosis of ARVC is clinically variable and can be challenging in living patients. In this study, to determine the role of DSG2 mutations in ARVC, we sequenced DSG2 in autopsy cases with definitive histologic diagnoses of ARVC.

Design: DNA was extracted from the post-mortem tissues of 25 patients dying suddenly with ARVC, and the 15 exons of DSG2 were sequenced. The primers were designed using Primer Express 3.0 software. Direct sequencing for both sense and antisense strands was performed with a BigDye Terminator DNA sequencing kit on a 3130 Genetic Analyzer with SeqScape software.

Results: DSG2 mutations were identified in 2 of 25 ARVC patients, both of which were novel. One of the mutations (3075_3076 ins C) is an insertion in exon 15 and is considered to be damaging, while the other (2092G>A), a missense change in exon 14, was determined to be ‘possibly damaging’ by PolyPhen and ‘benign’ by Mutation Taster and Sift software.

Conclusions: There have been few molecular autopsy series of ARVC patients that have included DSG2 for mutations in desmosomal related proteins. Here we report two novel DSG2 mutations in patients dying suddenly with histologically diagnosed ARVC. In this small autopsy series, we observed a DSG2 mutation prevalence of 8% in ARVC patients, which corresponds to the approximately 10% seen in clinical ARVC series. This study establishes the usefulness of molecular autopsy studies in patients with sudden death.