6th International Workshop on HIV & Aging

5 – 6 October 2015, Washington D.C., USA

Abstracts
Oral Presentations

Abstract: 1

Geriatrics and clinical care

Number of cardiometabolic disorders is associated with degree of frailty among people aging with HIV

T.D. Brothers[1], L.M.K. Wallace[2], A. Malagoli[3], R. Rossi[3], M. Manicardi[3], A. Santoro[3], O. Theou[4], S. Kirkland[5], K. Rockwood[4], G. Guaraldi[3]

[1]Dalhousie University, Faculty of Medicine, Halifax, Canada; [2]McGill University, Department of Neurology & Neurosurgery, Montreal, Canada; [3]University of Modena and Reggio Emilia, Department of Medical and Surgical Sciences for Adults and Children, Modena, Italy; [4]Dalhousie University, Department of Medicine, Halifax, Canada; [5]Dalhousie University, Department of Community Health & Epidemiology, Halifax, Canada

Introduction: Inflammatory cardiometabolic disorders become more common and can accumulate with age. Frailty also worsens with age and is associated with pro-inflammatory states. We sought to assess the burden of cardiometabolic disorders in a large ongoing HIV-positive cohort study, the relationship between cardiometabolic disorders and frailty, and whether they independently contribute to mortality.

Methods: This is an analysis of data from the Modena HIV Metabolic Clinic cohort study. All participants' first visits between 1/1/2005 to 31/12/2014 were included. The cardiometabolic disorders assessed were (1) cardiovascular disease (CVD); (2) hypertension; (3) diabetes mellitus type 2; (4) hyperlipidemia; (5) high waist circumference. Frailty was assessed using a 30-item frailty index based on deficit accumulation, and grouped into 0.1 increments for inclusion as a covariate. Variables included as items in the frailty index items not measures of cardiometabolic disorders. We used generalized linear models to assess relationships between these variables, and Cox regressions to assess survival.

Results: Data from 3,499 participants were included. The mean age was 45.0±7.5, 66% were men, 83% had undetectable viral load, and the median CD4 count was 543 (IQR 385-720). The mean number of cardiometabolic disorders was 1.1±0.9, and 26.8% of participants had two or more. The frequency of CVD was 2.5% (n=86), of hypertension was 19.7% (n=689), of diabetes was 7.2% (n=253), of hyperlipidemia was 66.3% (n=2320), and of high waist circumference was 15.2% (n=532). The mean frailty index score was 0.28±0.10. The number of cardiometabolic disorders increased with age (r^2=0.1, p<0.001) and with frailty index scores (r^2=0.04, p<0.001). With each additional cardiometabolic disorder, frailty index scores increased by 0.02 (95% CI 0.02-0.03, p<0.001), equivalent to around one additional deficit out of 30.
Participants with cardiometabolic disorders had higher mean frailty index values than participants without the disorder: CVD: 0.32±0.09 vs. 0.28±0.10, p=0.002; hypertension: 0.31±0.10 vs. 0.27±0.09, p<0.001; diabetes = 0.35±0.10 vs. 0.27±0.10, p<0.001; waist circumference = 0.30±0.10 vs. 0.28±0.11, p=0.001. This was not the case for hyperlipidemia: 0.28±0.10 vs. 0.28±0.11, p=1.0.
The mortality rate was 1.8% (n=64) over mean 3.9±3 years follow-up. Adjusting for the presence of each individual disorder in separate models, frailty index scores were significantly associated with survival. HRs for frailty index ranged from 2.23 (1.63-3.04) to 2.35 (1.73-3.20), all p<0.001.
Survival decreased with each additional cardiometabolic disorder (HR 1.30, 1.01-1.67, p=0.04), and in a separate model, survival decreased with each additional 0.1 increase in frailty index score (HR 2.35, 1.74-3.19, p<0.001). When included in the same model, frailty index was significantly associated with survival (p<0.001), but the number of cardiometabolic disorders was not (p=0.09).

Conclusions: Cardiometabolic disorders are common among people aging with HIV, even in this young cohort. Such disorders can accumulate in groups of two or more, and the number of disorders increases with the degree of frailty. Frailty and cardiometabolic disorders may share some pro-inflammatory pathophysiology, supporting the notion of a common 'inflammaging' process. Frailty increases risk of mortality even after adjusting for cardiometabolic diagnoses. HIV clinicians identifying multiple cardiometabolic

disorders in their patients might consider case-finding for frailty.

No conflict of interest

Abstract: 2

Geriatrics and clinical care

The effect of frailty-related phenotype on death is independent of three inflammatory markers among HIV-infected men receiving antiretroviral therapy

D.K. Ng[1], K.M. Erlandson[2], L.P. Jacobson[1], J. Margolick[3], A.S. Dods[4], F.J. Palella[5], J.E. Lake[6], L.A. Kingsley[7], T.T. Brown[4]

[1]Johns Hopkins University, Epidemiology, Baltimore, USA; [2]University of Colorado-Anschutz Medical Center, Medicine, Aurora, USA; [3]Johns Hopkins University, Molecular Microbiology and Immunology, Baltimore, USA; [4]Johns Hopkins University, Medicine, Baltimore, USA; [5]Northwestern University Medical Center, Medicine, Chicago, USA; [6]UCLA Medical Center, Medicine, Los Angeles, USA; [7]University of Pittsburgh, Epidemiology, Pittsburgh, USA

Introduction: A frailty-related phenotype (FRP) prior to the initiation of highly active antiretroviral therapy (HAART) predicts mortality after starting HAART and is also related to increased systemic inflammation. The purpose of this study was to describe the risk of death associated with FRP and the potential mediating effect upon death risk of systemic inflammation among ART-treated HIV-infected men in the Multicenter AIDS Cohort Study (MACS).

Materials and Methods: The first occurrence of FRP was identified among HIV-infected MACS participants receiving HAART who were 40 years of age or older after January 1, 2001. FRP was defined as the presence of 3 of 4 of the following self-reported conditions: unintentional weight loss of at least 10 lbs., physical health causing difficulty doing work/activities, problems walking several blocks and performing vigorous activities. Levels of three inflammatory markers, soluble tumor necrosis factor receptor type II (sTNF-r2), interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP), were treated as time varying covariates; multiple imputation was used to account for missing data. Inflammatory markers were categorized by the interquartile range (IQR) to describe low (reference; <25th percentile), medium (≥25th percentile and < 75th percentile), and high (≥75th percentile) levels. Cox proportional hazard models were used to describe risk of death, incorporating late entries with age as the time scale.

Results: Of 1063 HIV-infected men contributing 14419 person-visits, the median age at study entry (first visit seen from 2001 onwards) was 46 years [IQR: 41, 51] and the median follow-up was 9.4 years [IQR: 5.3, 11.8]. Among the 261 (25% of the total) men with FRP, 17% died (n= 44) during follow-up, whereas 10% died (n= 78) among men without FRP. When accounting for age as the time scale, the relative hazard (HR) of death related to FRP univariately was 3.6 (95%CI: 2.42, 5.25). The HR of death related to FRP was attenuated by 18% in a model that included sTNF-r2 (HR: 2.90, 95%CI: 1.95, 4.32), and by a more modest magnitude in models including IL-6 (-11%; HR: 3.2, 95%CI: 2.17, 4.76) or hs-CRP (-8%; HR: 3.3, 95%CI: 2.25, 4.92). In each of these models, a higher level of each inflammation biomarker was significantly associated with death, independent of FRP. Interaction between FRP and inflammatory marker levels was not observed.

Conclusions: Among HIV-infected men receiving ART, FRP is highly positive associated with mortality, an effect that appears to be mediated to a small extent by sTNF-r2, and a lesser extent by IL-6 and hs-CRP.

No conflict of interest

Abstract: 3

Geriatrics and clinical care

Two methods of measuring frailty among people aging with HIV

G. Guaraldi[1], R. Torelli[2], A. Malagoli[1], T. Brothers[3], L. Wallace[3], S. Garlassi[1], A. Santoro[1], C. Stentarelli[1], F. Carli[1], S. Sartini[2], O. Theou[3], S. Kirkland[3], S. Zona[1], K. Rockwood[3]

[1]University of Modena, HIV Metabolic Clinic Infectious Diseases Department, Modena, Italy; [2]University of Modena, Hand Rehabilitation Policlinico University Hospital, Modena, Italy; [3]Dalhousie University, Faculty of Medicine, Halifax, Canada

Background: The two most common methods of assessing frailty are via the frailty phenotype (FP) and the frailty index (FI). We assessed and compared their cross-sectional characteristics in the same sample of people aging with HIV in northern Italy.

Methods: Consecutive Modena HIV Metabolic Clinic participants were invited to participate in assessments to make up the frailty phenotype instrument, which are not included in the normal MHMC protocol. These were weight loss, exhaustion, low physical activity, slow walk speed, and weak grip strength. Participants with 3 deficits out of the 5 variables were identified as 'frail', and those with 1-2 deficits were identified as 'pre-frail'. A FI was constructed from 37 health variables collected at the same study visit. FI scores were calculated as the proportion of deficits out of the 37 variables.
We assessed the frequency of FP and the mean FI of the sample. We evaluated potential relationships between each frailty measure and (i) demographic factors, (ii) HIV-related factors, (iii) behavioral factors, (iV) HIV-Associated Non-AIDS (HANA) condition, (V) Multimorbidity (>3 HANA occurring in the same individual) and (Vi) Disability (assessed with a 17 item questionnaire).

Results: We included data from 312 participants. The mean age was 50.6± 7.4 and 74% were men. The median CD4+ T-cell count was 751 IQR (533-896). As classified by the FP scale, 10% of participants were frail, 30% were pre-frail, and 60% of participants were robust. The mean FI score was 0.30±10.
(i) According to both frailty instruments, frailty tended to increase with age and did not differ by gender.
(ii) Both instruments were also associated with nadir CD4 cell count, and a history of AIDS. FI but not FP was associated with duration of HIV infection duration of antiretroviral therapy and current CD4.
(iii) Frailty phenotype was not associated with any behavioural factors. Frailty index was significantly higher among people who reported more than 30 pack-years smoking history and people with a sedentary lifestyle.
(iV -V) Significantly higher FI scores were exhibited by participants with hypertension, diabetes, liver cirrhosis, osteoporosis / osteopenia, renal insufficiency, dyslipidemia, sarcopenia, and multimorbidity (all $p<0.05$). FP was not associated with any HANA condition.
(Vi) Both instruments were also associated with Disability ($p<0.001$ and $p=0.02$ for FP and index respectively). This association was higher for FP (AUC 0.66 and 0.63, respectively)

Conclusions: In this cross-sectional analysis, the FP and FI shared some common relationships with demographic and health factors, but had different relationships with chronic disease diagnoses and behavioral risk factors. The frequency of the FP was relatively low, but similar to other middle-aged samples. This may suggest the utility of the frailty index in HIV care settings.
Participants who were identified as frail via the FP were significantly more likely to report disability, but not higher rates of HANA or multimorbidity.
Further longitudinal work is needed to characterize the two frailty instruments' responsiveness over time, their predictive abilities, and their potential clinical roles in HIV care settings.

No conflict of interest

Abstract: 4

Geriatrics and clinical care

Ecological momentary assessment of daily functioning among older adults living with HIV

R.C. Moore[1], A.S. Rooney[1], C.A. Depp[1], L.T. Eyler[1], E. Granholm[1], R.K. Heaton[1], S.P. Woods[2], B. Gouaux[1], S.L. Letendre[3], M.M. Marquine[1], D.J. Moore[1]

[1]University of California San Diego, Psychiatry, San Diego, USA; [2]University of Houston, Psychiatry, Houston, USA; [3]University of California San Diego, Medicine, San Diego, USA

Introduction: Older HIV-infected adults experience substantial impairment in everyday functioning, and there is a significant public health need to better understand how best to assess and enhance functioning among those aging with HIV. The predominant approach to assess participation in functionally relevant behaviors is via global self-report measures, which are often subject to retrospective biases. As such, there is a need to identify novel assessment approaches for daily functioning among older HIV-infected adults. The goal of this pilot study was to test the feasibility and acceptability of ecological momentary assessment (EMA) delivered via smartphones. EMA is an ambulatory data collection technique that allows for real-time, in vivo assessment of time spent engaged in various daily life activities (e.g., self-care, cognitively stimulating activities, passive leisure activities), social interactions, and affective symptoms. A second goal of this study was to examine the relationship between EMA-measured daily functioning and neuropsychological performance.

Material & Methods: Twenty older (≥50 years) HIV-infected adults (mean age=59, range=51-67 years) completed a laboratory-based assessment of neuropsychological functioning: the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), as well as at-home EMA assessments five times per day for one week. EMA adherence was calculated by dividing number of surveys completed by total possible number of surveys, and rates and variability of participation in active and passive functional behaviors were aggregated within individuals.

Results: Results demonstrated feasibility and acceptability of EMA among older HIV+ adults, with an excellent adherence rate of 86% and low perceived burden. Aggregated across the week, participants spent 74% of their time at home, 63% of their time alone, and 31% of their time engaged in passive leisure activities (e.g., watching TV). Cognitive performance (RBANS score) was inversely related to time spent engaged in passive leisure activities ($r=-0.57$, $p=0.01$), but was unrelated to time spent engaged in self-care or cognitively stimulating activities. We also found that greater depressed mood was associated with greater variability in cognitively stimulating daily life activities (Wald $Chi^2=4.7$, $p=0.03$).

Conclusions: These findings suggest EMA is a feasible and acceptable tool to assess functional activities among older HIV-infected adults. The study revealed that participants spent a remarkable amount of time at home, alone, and engaged in passive activities. Findings additionally suggest that neurocognitive impairment is related to passivity, and depressed mood contributed to fluctuations in cognitively stimulating activity participation. It may be useful to leverage EMA technology to deliver interventions aimed at reducing social isolation and depressed mood and enhancing cognitive stimulation in an effort to diminish disability in this population.

No conflict of interest

Abstract: 5

HIV-infected aging patients: which relationship between precarity, frailty and comorbidity?

P. Enel[1], F. Retornaz[2], N. Petit[3], A. Darque[4], S. Bregigeon[5], I. Ravaux[6], K. Baumstark[7], . VISAGE Group[8]

[1]Assistance Publique - Hopitaux de Marseille, Public Health Department, Marseille, France; [2]Centre Gerontologique de Marseille, Geriatric Department, Marseille, France; [3]Assistance Publique - Hopitaux de Marseille, Geriatric Department, Marseille, France; [4]Assistance Publique - Hopitaux de Marseille, Pharmacy Department, Marseille, France; [5]Assistance Publique - Hopitaux de Marseille, Immuno-Hematology Department, Marseille, France; [6]Assistance Publique - Hopitaux de Marseille, Infectious Disease Department, Marseille, France; [7]Assistance Publique - Hopitaux de Marseille, Clinical Research Department, Marseille, France; [8]COREVIH PACA Ouest Corse, Coordination Department, Marseille, France

Background: Elderly HIV-infected patients (pHIV) may present particularities on both disease evolution and morbidity, as compared to younger patients. Moreover, pHIV experience more often precarioussituations and frailty seems to be more important and earlier in this population. Frailty phenotype is defined by Fried as a physiological vulnerability condition facing external disturbances, determined with 5 physical and physiological markers (weight loss, weakness, poor energy, slowness, low activity). Our study aimed to measure frailty and precarity prevalences in aging pHIV cared in hospital medical units and to study their relationship with HIV-infection characteristics and comorbidities.

Material & Methods: This 18-months prospective multicenter study carried in 2013-2014 had involved pHIV ≥50 years, cared in 18 HIV-dedicated hospital medical units, in PACA area, South-East of France. Patients were to fill an anonymous self-questionnaire to auto-report two Fried criteria (weight loss and activity level), precarity (French social validated EPICES score with eleven social life items) and treatments. Physicians were to report HIV-infection and comorbidities history, and to measure tree Fried criteria: grip strength, energy Visual Analogue Scale and walking time. The five Fried criteria rank population in: frail (≥3 criteria), pre-frail (1 or 2 criteria) and no-frail (0 criteria). We used T test, Chi square test and Anova statistical analysis on SPSS.

Results: We included 509 pHIV: 72.7% (n=370) were men, median age was 56.6[52.4-62.6] years and 36.6% (n=186) were ≥60 years. Median HIV-infection lifetime was 20[13-25] years, 22.2% (n=113) were at aids stage. A majority of pHIV (87.4% (n=445) had undetectable viral load, nadir median CD4 was 207[100-331] copies/ml and last median CD4 was 596[425-813]. Body mass index was normal (59.5%, n=303), underweight (3.7%, n=19), overweight (26.5%, n=135) and obesity (8.3%, n=42). The six more frequent comorbidities were: dyslipidemia (36.4%), lipodystrophy (30.5%), hepatitis B or C (26.0%), psychiatric disorders (25.7%), arthrosis and osteo-pathologies (22.5%) and hypertension (22.2%). A majority of pHIV (59.6%) had ≥2 comorbidities and 37.3% ≥3. Frailty prevalence was 6.4% (n=32), 58.0% (n=291) pVIH were pre-frail and 35.7% (n=179) were no-frail. The distribution of the 5 Fried criteria was: weight loss (13.1%, n=66), weakness (20.2%, n=100), poor energy (7.3%, n=36), slowness (5.2%, n=26) and low activity (50.9%, n=248). Precarity prevalence was 49.3% (n=242). Precarity was related to: sexe (57.8% female vs 45.4% male, p=.014), number of HIV-lifetime years (19±8 vs 17±7, p=.011), last CD4<350 (61.9% vs 47.0%, p=.027), comorbidities ≥3 (56.6% vs 44.7%, p=.011). Frail pHIV were more precarious (68.8%, n=22/32) than non-frail (47.6%, n=218/458) (p=.010). In multivariate analysis, precarity remained related to female sex (p=.021), last CD4 <350 copies/ml (p=.049), frailty (p=.048) and comorbidity ≥3 (p=.001).

Conclusions: Our study shows the interest to measure frailty and precarity in HIV-infected aging patients. About 2/3 of our pHIV were frail or pre-frail, only 1/3 were no-frail and about 1/2 were precarious. HIV-infected aging patients need preventive actions to avoid risk of evolution because Fried phenotype is associated with increased morbi-mortality and loss of autonomy. Preventive actions must be related with the type of decreased criteria, for example nutrition

program or appropriate physical activity, and to the social status to improve welfare.

No conflict of interest

Abstract: 6

Geriatrics and clinical care

Longitudinal association between depressive phenotype and cognitive impairment in men with and without HIV

N.M. Armstrong[1], P. Surkan[2], A.L. Gross[1], G.J. Treisman[3], N.C. Sacktor[4], M. Irwin[5], S. Wolinsky[6], R. Stall[7], L.P. Jacobson[8], A.G. Abraham[8]

[1]Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology, Baltimore, USA; [2]Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, USA; [3]Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, Baltimore, USA; [4]Johns Hopkins University School of Medicine, Department of Neurology, Baltimore, USA; [5]UCLA David Geffen School of Medicine, Department of Psychiatry and Biobehavioral Sciences, Los Angeles, USA; [6]Feinberg School of Medicine, Department of Medicine-Infectious Diseases, Chicago, USA; [7]University of Pittsburgh Medical Center, Department of Behavioral and Community Health, Pittsburgh, USA
[8]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, USA

Background: More than half of those living with HIV/AIDS today are over the age of 50. Since HIV is likely to cross the blood-brain barrier after infection, clinical manifestations of Central Nervous System disorders relating to HIV infection include depression and cognitive impairment. We hypothesize that individuals with a depressive phenotype have a risk of cognitive impairment than those with a non-depressive phenotype. Specifically, individuals with HIV/AIDS may be more at risk for cognitive impairment, especially if they have depression than those without HIV/AIDS.

Materials and Methods: This study included 543 HIV-infected and 417 HIV-uninfected men from the Multicenter AIDS Cohort Study (MACS) with 5 or more years of follow-up from year 2000 onward. Depressive symptoms were assessed semi-annually using the Center for Epidemiologic Studies-Depression Scale (CES-D); a CES-D of 16 or greater across three consecutive visits was used to establish a depressive phenotype. Indicators of executive function/psychomotor speed (Trail-making Tests A (TMT-A) and B (TMT-B) and Symbol Digit Modalities Test (SDMT)) also were collected at semi-annual visits. Reaction times of Trail-making Tests A and B were log-transformed. We examined the association of executive function/psychomotor speed decline over time with a depressive phenotype using linear random effects models, adjusting for age, HIV status, race, and education. Then, we stratified the analysis by HIV status to evaluate the effects of depression on cognitive function.

Results: There were 349 individuals with a depressive phenotype and 611 individuals with a non-depressive phenotype. Those with a depressive phenotype were more likely to be non-white (P=0.001), HIV positive (P=0.001), not college graduates (P=0.002) and have more comorbidities (P<0.001), compared to those with a non-depressive phenotype. After covariate adjustment, those with a depressive phenotype, on average, reproduced 2.70 fewer symbol-digit pairs on the SDMT than those with a non-depressive phenotype (95% confidence interval, CI: -4.19, -1.38), and also took 1.05 seconds longer to perform TMT-A (95% CI: 1.01,1.09) and 1.09 seconds longer to perform TMT-B (95% CI: 1.04 , 1.15) than those with a non-depressive phenotype across visits. Among HIV-positive individuals, those with a depressive phenotype, on average, took 1.07 seconds longer to perform TMT-A (95% CI: 1.01,1.13) and 1.11 seconds longer to perform TMT-B (95% CI: 1.04,1.18) as well as had 3.44 fewer pairs on the SDMT(95% CI: -5.27,-1.59) than those without after adjusting for covariates. Among HIV-negative individuals, those with a depressive phenotype took 1.10 seconds longer on TMT-B (95% CI: 1.02,1.19) and had 2.48 fewer pairs on the SDMT (95% CI: -5.07,-0.02) than those without a depressive phenotype, yet there were no statistically significant differences in performance on TMT-A between the depressed and non-depressed phenotypes after adjusting for covariates (estimate=1.07; 95% CI: 1.00,1.14).

Conclusions: Participants with a depressive phenotype were at elevated risk for cognitive impairment than those with a non-depressive phenotype, and the effect of depression was stronger among HIV-positive individuals for processing speed. Performance of these participants on the Trail Making and Symbol Digit Modalities tests suggests greater psychomotor slowing and worse executive functioning among depressed.

No conflict of interest

Abstract: 7

Aging amplifies HIV neurocognitive impairment

R.K. Heaton[1], D.R. Franklin[1], S.L. Letendre[2], R.J. Ellis[3], C. Fennema-Notestine[1], F. Vaida[4], D. Smith[2], A.C. Collier[5], C.M. Marra[6], D.B. Clifford[7], B.B. Gelman[8], N. Sacktor[9], S. Morgello[10], D.M. Simpson[11], J.A. McCutchan[2], I. Grant[1], for the CHARTER Group

[1]UCSD HIV Neurobehavioral Research Program, Psychiatry, San Diego, USA; [2]UCSD HIV Neurobehavioral Research Program, Medicine, San Diego, USA; [3]UCSD HIV Neurobehavioral Research Program, Neuroscience, San Diego, USA; [4]UCSD HIV Neurobehavioral Research Program, Family Medicine & Public Health, San Diego, USA; [5]University of Washington, Medicine, Seattle, USA; [6]University of Washington, Neurology, Seattle, USA; [7]Washington University in St. Louis, Neurology, St. Louis, USA; [8]University of Texas Medical Branch, Pathology, Galveston, USA; [9]Johns Hopkins University, Neurology, Baltimore, USA; [10]Icahn School of Medicine at Mount Sinai, Pathology, New York, USA; [11]Icahn School of Medicine at Mount Sinai, Neurology, New York, USA

Introduction: Modern antiretroviral therapy (ART) has substantially extended the survival of HIV infected persons into their later years, raising the possibility that age-related organ changes, including neurodegenerative and cerebrovascular changes, might amplify HIV effects on the brain. This study investigated the effects of age, HIV, and vascular and metabolic markers on neurocognitive (NC) function.

Materials & Methods: 843 HIV+ participants from the CHARTER study along with 677 HIV+ and 377 HIV- participants from the HNRP were selected for analysis. Subjects received comprehensive neuromedical, neurocognitive, and laboratory assessments. Logistic regression was used to examine the effects of age and HIV disease variables on global and domain specific cognitive function. Interactions between age and HIV disease and vascular markers were also modeled in analyses of HIV+ participants.

Results: Using scaled scores, HIV+ cases performed worse than HIV- in all domains and globally (all $p<.01$). There were significant age x HIV interactions with older HIV+ performing incrementally worse in the executive, speed of information processing, working memory, learning and memory domains as well as globally (all $p<.01$). Exploratory analyses of HIV disease markers showed age interactions with AIDS diagnosis and a main effect for nadir CD4 on global deficit score. Current CD4, ART status, and plasma viral load were not related to NC performance.

Conclusions: Our results show disproportionate reduction in neurocognitive performance in HIV+ persons as they age, and that both AIDS diagnosis and nadir CD4 may play a role in amplifying these effects.

No conflict of interest

Abstract: 8

Metabolic / cardiovascular complications

The association between comorbidities and neurocognitive impairment in aging Veterans with HIV

A. Perra[1], M. Dux[2], T. Lee-Wilk[2]

[1]VA Maryland Health Care System, Neurology, Baltimore, USA; [2]VA Maryland Health Care System, Neuropsychology, Baltimore, USA

Introduction: The VA is the largest healthcare provider of HIV and hepatitis C (HCV) care in the country, and with better treatments for both conditions, Veterans are living longer. One complication of HIV and HCV is neurocognitive impairment (NCI), with mild deficits observed in approximately 50% of patients with HIV and 30% of patients with HCV. Among Veterans, 30% are co-infected with HIV and HCV, and there is data to suggest that NCI is more pronounced among these patients. However, studies have not consistently identified a link between infectious disease related factors (e.g., viral load) and NCI. Therefore, increased attention has been directed towards the potential contributory role of chronic, age-associated non-infectious medical comorbidities (e.g., cardiovascular & metabolic dysfunction) to NCI. In the current study, we examined the relative associations of infectious disease related factors and non-infectious medical comorbidities on NCI in Veterans mono-infected with HIV or co-infected with HIV/HCV. We predicted that non-infectious medical comorbidities would account for significant variance in NCI, above and beyond that associated with infectious disease related markers. Further, given increased rates of diabetes in patients with HIV and HCV, we conducted exploratory analyses to examine the association between markers of metabolic function (e.g., HgbA1c and blood glucose levels) and NCI.

Material & Methods: Participants included 68 Veterans with HIV (99% male; 84% African American/16% Caucasian; 55.9 ±9.8 years of age; 12.1±2.2 years of education). Approximately 50% of the sample was co-infected with HCV. All participants were referred for neuropsychological assessment in the context of cognitive concerns. Participants were administered a comprehensive neuropsychological battery assessing a range of domains (e.g., learning/memory, processing speed, attention/working memory, language, executive function). Data from medical records were extracted to compute infectious disease (e.g., viral load, CD4 count, HCV status, etc.) and non-infectious disease (e.g., cardiovascular risk factors, diabetes, vitamin deficiencies, etc.) composite scores for each participant.

Results: Hierarchical multiple regression analyses were conducted to assess the relative contribution of infectious disease (ID) and non-infectious disease (non-ID) markers to NCI. After controlling for the ID composite, the non-ID composite accounted for significant variance in learning/memory (R^2change=0.17, $p<0.05$), attention/working memory (R^2change=0.22, $p<0.05$), and processing speed (R^2change=0.21, $p<0.05$). The reverse relationship was not supported (i.e., controlling for non-ID composite, ID composite did *not* account for significant variance in neurocognitive function). Follow-up analyses demonstrated that among the non-ID composite, cardiovascular/metabolic risk factors were most strongly associated with neurocognitive function. Exploratory zero-order correlations were conducted between neurocognitive scores and markers of metabolic function (e.g., HgbA1c, blood glucose levels). Elevated dispersion in A1c values was associated with worse performance on measures of memory ($r=-.34$, $p<0.05$) and attention/working memory ($r=-.38$, $p<0.05$).

Conclusions: As predicted, non-ID comorbidities, primarily cardiovascular and metabolic risk factors, accounted for deficits in memory, attention/working memory, and processing speed, above and beyond that associated with ID related markers. Further, inconsistency in HgbA1c levels was associated with worse performance on measures of memory and attention/working memory. These results highlight the importance of addressing age-associated medical comorbidities in the management and treatment of Veterans with HIV.

No conflict of interest

Abstract: 9

Neurology

Global Gray Matter Atrophy Associated with Neurocognitive Impairment in HIV

P. De Alwis[1], A. Summers[2], T. Shirazi[2], P. Siyahhan Julnes[1], S. Steinbach[1], J. Snow[2], B. Smith[1], A. Nath[1], D.S. Reich[1], G. Nair[1]

[1]National Institutes of Health, National Institute of Neurological Disorders and Stroke, Bethesda MD, USA; [2]National Institutes of Health, National Institute of Mental Health, Bethesda MD, USA

Background: HIV Associated Neurocognitive Disorder (HAND) manifests in 20-65% of all HIV patients as a decline in learning, mood, memory, and/or motor function. MRI offers a unique opportunity to understand anatomical changes in the brain associated with manifestations of HAND in HIV patients. Here we evaluate virologically-treated HIV subjects and well-matched controls for any associations between brain volume and cognitive function.

Material & Methods: HIV patients without the clinical diagnosis of HAND (HIV cohort, n=56, 70% male, mean age 52 ± 6 years, 52% African American), HIV patients with clinical diagnosis of HAND (HAND cohort, n=13, 54% male, mean age 52 ± 9 years, 77% AA), and control subjects recruited from the same socio-economic background but without HIV infection (Control cohort, n=25, 40% male, mean age 46 ± 11 years, 60% AA), were imaged on a 3T Philips scanner using 8-channel head coil. FreeSurfer was used on the FLAIR and MPRAGE images to segment the brain structures, and their volumes tabulated after carefully checking the quality of segmentation. Volumes of total white matter (WM), total grey matter (GM), total intracranial volume (ICV), and total cerebrospinal fluid volume (CSF) were compared across the three groups. One-way ANOVAs, and two-tailed t-tests were conducted across all groups to test for significant differences, and group data is expressed as mean ± standard error of the mean.

Results and Discussion: The GM volume was significantly lower in HAND (518.5 ± 19.7 cm^3) in comparison to the Control (585.6 ± 12.6 cm^3) and HIV (579.6 ± 9.5 cm^3, ANOVA p=0.012) groups. Both cortical and sub-cortical GM volumes were significantly lower in HAND than other groups. The WM volume trended to be lower in HAND (410.6 ± 17.1 cm^3) in comparison to the Control (430.9 ± 8.6 cm^3) and HIVs (444.3 ± 7.4 cm^3, ANOVA p=0.075). In conjunction with the reduction of GM and WM, CSF volume showed a significant increase in HAND (p=0.038).
When corrected for intracranial volume (ICV), neither the WM nor GM volume fractions reached significance (p=0.12 and 0.13 respectively with ANOVA). However, the CSF volume fraction was significantly larger in the HAND compared to the Control and HIV cohorts (by 17% and 13%, respectively, p=0.038), and subcortical GM volume fraction significantly smaller in the HAND compared to the HIV cohort (by 8.5%, p=0.033). Further analysis such as correlations of observed brain volumes with cognitive and psychological scores, as well as adjusting for age and co-morbidities among the groups is being done.

Conclusions: Significant reduction was seen in the global GM volume in patients diagnosed with HAND. Association of atrophy within various cortical regions with neurocognitive scores may help better diagnose and characterize HAND. Recruiting control subjects from the same socio-economic background as the HIV group enables adjustment for co-morbidities and better understanding of neurodegeneration and inflammation due to HIV.

No conflict of interest

Abstract: 10

Geriatrics and clinical care

Perceived Stress influences prefrontal cortex function in midlife women with HIV infection

L.H. Rubin[1], M. Wu[1], V.J. Meyer[1], E.E. Sundermann[1,2], R.J. Conant[1,3], R. Smith[1], S. D'Sa[1], K.M. Weber[4], M.H. Cohen[4,5], D.M. Little[6,7], P.M. Maki[1,8]

[1]University of Illinois at Chicago, Psychiatry, Chicago, USA; [2]Albert Einstein College of Medicine, Einstein Aging Study and the Department of Neurology, Bronx, USA; [3]University of Oklahoma Health Science Center, OB/GYN, Oklahoma City, USA; [4]Core Center, Cook County Health and Hospital System and Hektoen Institute of Medicine, Chicago, USA; [5]Departments of Medicine Stroger Hospital and Rush University, Chicago, IL, USA; [6]Baylor Scott & White Health, Temple, TX, USA; [7]Texas A&M University, Health Science Center, Temple, USA; [8]Department of Psychology, University of Illinois at Chicago, Chicago, IL

Background: Deficits in verbal learning and memory are a prominent feature of neurocognitive function in HIV-infected midlife women, and are associated with high levels of perceived stress. Specifically, high perceived stress is associated with prefrontal-based aspects of verbal memory performance, namely memory retrieval and semantic clustering. Our structural imaging findings link these stress-related memory impairments in HIV-infected midlife women to prefrontal cortical atrophy. To understand the neural basis of this stress-related memory impairment, we examined the effects of stress on activation of the prefrontal cortex and strategic encoding during a verbal memory task in a sample of HIV-infected midlife women.

Materials and Methods: Participants included 36 HIV-infected women (Mean age=43.7 years; range 27-59) from the Chicago Consortium of the Women's Interagency HIV Study (WIHS). Participants underwent functional magnetic resonance imaging (MRI) during a verbal memory task and completed a standardized measure of verbal learning and memory (Hopkins Verbal Learning Test-HVLT) and stress (Perceived Stress Scale-10; PSS-10).

Results: Compared to HIV-infected women with lower stress (PSS-10 scores in lower two tertiles), HIV-infected women with higher stress (scores in the top tertile) performed worse on HVLT outcomes assessing verbal memory and strategic encoding (p's<0.05). A similar pattern was observed on the in-scanner verbal memory task (p's<0.05). During encoding, there were no differences between patterns of brain activation between the two groups of women. However, during recognition, women with higher perceived stress demonstrated greater medial prefrontal cortex and posterior cingulate cortex deactivation compared to women with lower perceived stress (p's<0.05). In the overall group, there was a trend for greater deactivation in the medial prefrontal cortex to be associated with less efficient strategic encoding (r=-0.31, p=0.06).

Conclusions: The stress-related verbal memory deficits, particularly with less efficient strategic encoding in midlife HIV-infected women, may be partially accounted for by alterations in prefrontal cortex functioning. Understanding the role of the prefrontal cortex in stress-related memory impairments will be particularly important for women aging in the context of HIV as the prefrontal cortex is also particularly vulnerable to aging.

No conflict of interest

Abstract: 11

Effect of aging on organ systems (renal, musculoskeletal, hepatic and endocrine)

HIV Patients Exhibit Similar Rates of Emphysema Progression Observed in Older HIV-Uninfected Patients with Higher Cumulative Smoke Exposure

J. Leung[1], A. Malagoli[2], A. Santoro[2], G. Besutti[2], G. Ligabue[2], D. Dai[3], J. Mayo[4], S. Lam[5], D. Sin[6], S. Man[6], G. Guaraldi[2]

[1]Centre for Heart Lung Innovation, Medicine, Vancouver BC, Canada; [2]University of Modena and Reggio Emilia, Modena HIV Metabolic Clinic, Modena, Italy; [3]University of British Columbia, PROOF Centre for Excellence, Vancouver, Canada; [4]University of British Columbia, Department of Radiology, Vancouver, Canada; [5]University of British Columbia, BC Cancer Research Centre, Vancouver, Canada; [6]Centre for Heart Lung Innovation, Medicine, Vancouver, Canada

Background: HIV patients face the burden of chronic obstructive pulmonary disease (COPD). How quickly COPD phenotypes such as emphysema progress, what risk factors are associated with COPD progression in an HIV-infected population, and whether this risk of progression is in excess compared to HIV-uninfected patients are unknown.

Materials & Methods: Full serial computed tomography (CT) images of the chest were obtained in 405 HIV-infected patients who attended an outpatient HIV metabolic clinic at the University of Modena and Reggio Emilia. These images were blindly assessed for emphysema by 2 radiologists with a score assigned to each of the 5 lobes and the lingula using the following algorithm: 0=0%, 1=1-25%, 2=26-50%, 3=51-75%, 4=76-100% emphysema. A total score was calculated from the sum of the scores with emphysema progression defined as any positive change in total score. A multivariable logistic regression model was used to determine which clinical factors were associated with emphysema progression. The HIV cohort was then compared to a similarly characterized non-HIV population enrolled in the Pan-Canadian Early Detection of Lung Cancer Study.

Results: In the HIV-infected cohort, the median time interval between the first and last CT scans was 3.36 years (range 0.08 to 7.81 years). The median number of CT scans per individual was 2 (range 2 to 7). 224 (55%) of individuals had emphysema at baseline, with 60 (15%) demonstrating progression of emphysema by their last available CT scan. In the univariate model, individuals who demonstrated emphysema at baseline were most likely to show progression of emphysema on subsequent CT scans (p=7.18e-14). Those with both centrilobular and paraseptal emphysema distribution (as opposed to having only centrilobular or paraseptal emphysema) were also at the highest risk of progression (p=1.13e-13). Other risk factors for emphysema progression included current smoking (p=8.89e-06) and low baseline DLCO (p=0.0004). In the multivariable logistic regression model, having both centrilobular and paraseptal emphysema on baseline CT scan (p=0.013) and low baseline DLCO (p=0.005) was significantly associated with emphysema progression. The combination of baseline emphysema score, baseline emphysema distribution, and baseline DLCO had an AUC of 0.85 for predicting emphysema progression compared to an AUC of only 0.65 using baseline FEV1/FVC and 0.54 using baseline FEV1 %Predicted. A subset of the HIV cohort (n=301) was then matched to an HIV-uninfected lung cancer screening cohort (n=301) by sex and by time interval between first and last CT scans. HIV patients were significantly younger (median age 49 years vs. 63 years, p=2.2e-16) and had a greater proportion of never smokers (21% vs. 0%, p=2.2e-15) and fewer smoking pack-years (median 17 pack-years vs. 50 pack-years, p=2.2e-16). Despite these differences, HIV patients exhibited similar rates of emphysema progression (n=46, 15%) compared to HIV-uninfected patients (n=52, 17%) (p=0.581).

Conclusions: Rates of emphysema progression in HIV are similar to those found in an older HIV-uninfected cohort with greater cumulative smoke exposure. In this HIV cohort, spirometry had a limited role in identifying individuals at high risk of emphysema progression, while baseline

emphysema, emphysema distribution, and DLCO, showed greater predictive value.

No conflict of interest

Abstract: 12

Malignancy

Incidence of non-AIDS-defining cancers (NADCs) between 1984 and 2014 in the Multicenter AIDS Cohort Study (MACS) by HIV status and viral infection etiology

E.C. Seaberg[1], E. Breen[2], G. D'Souza[1], D. Wiley[3], C.R. Rinaldo[4], J. Margolick[5], J.P. Phair[6], L.P. Jacobson[1]

[1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, USA; [2]Univeristy of California Los Angeles, David Geffen School of Medicine, Los Angeles, USA; [3]Univeristy of California Los Angeles, School of Nursing, Los Angeles, USA; [4]University of Pittsburgh Graduate School of Public Health, Infectious Diseases and Microbiology, Pittsburgh, USA; [5]Johns Hopkins Bloomberg School of Public Health, Molecular Microbiology & Immunology, Baltimore, USA; [6]Northwestern University, Feinberg School of Medicine, Chicago, USA

Background: With improved survival and aging, HIV-infected (HIV+) persons are at risk for non-AIDS morbidity, including non-AIDS-defining cancers (NADCs). It remains unclear whether the increasing risk of some cancers with age that is observed in the general population might be accelerated in HIV+ individuals. Factors that may contribute to an increased risk in this population compared to uninfected (HIV-) persons include coinfection with oncogenic viruses, HIV itself, chronic inflammation and immunosuppression. Our goal was to compare the incidence of NADCs in HIV+ men to that among at-risk HIV- men, determine whether the effect of HIV differs by age, and examine the HIV and age effects separately for NADCs with and without a viral etiology.

Material & Methods: We determined the incidence of NADCs among the 7317 MSM enrolled in the MACS between 1984 and 2014. Incident cancers were confirmed through medical records abstraction, autopsy reports, cancer registry matching, and death certificate verification. All NADCs were classified as being virus-related (HPV: anal and oral cancers, HBV/HCV: liver cancer, and EBV: Hodgkins lymphoma) or virus-unrelated (all other NADCs excluding squamous and basal cell skin cancers). Cancer incidence rates were computed using person-years analysis and compared using Poisson Regression.

Results: We observed 327 NADCs during 96,150 person-years of follow-up (incidence rate [IR]=34.0/10,000 p-years), 74 were virus-related (IR=7.7/10,000 p-years) and 253 were virus-unrelated (IR=26.3/10,000 p-years). During the 30-year study period, HIV infection was associated with a higher incidence of virus-related NADCs among men <55 years old (IR ratio [IRR]=7.2, 95% CI 3.4-15.2) and among men 55 and older (IRR=2.7, 95% CI 1.1-6.6). The same was true for virus-unrelated NADCs, though the IRRs were smaller; IRR=1.8, 95% CI 1.3-2.6 and IRR=1.3, 95% CI 0.9-1.9 among younger and older men, respectively. The effect of HIV did not differ significantly by age for either virus-related or –unrelated cancers (interaction p>0.1). During the current HAART era (2005-2014), the results for virus-related NADCs were essentially unchanged with the IRRs being 7.4 (95% CI 1.7-32.2) and 3.9 (95% CI 1.2-12.6) among younger and older men, respectively. For virus-unrelated NADCs, however, there was no difference by HIV with the IRRs being 0.9 (95% CI 0.4-1.8) and 1.1 (95% CI 0.7-1.7) among the younger and older men, respectively.

Conclusions: During the past 30 years, the incidence of NADCs was significantly higher among HIV+ vs. HIV- MSM regardless of their age. In the current era of effective HIV treatment, however, the excess incidence of NADCs among HIV-infected MSM exists solely for cancers with a viral etiology. Although our data indicate that the risk of NADCs due to HIV-infection does not increase with age, it remains possible that virus-related NADCs occur at an earlier age among HIV+ vs HIV- men. However, an alternate explanation is that HIV+ men are more likely than

HIV- men to be infected with the corresponding oncogenic viruses. Further research is required to determine the relative contributions of these two factors in generating the increased incidence of virus-related NADCs that we observed among HIV-infected men in the MACS since 2005.

No conflict of interest

Abstract: 13

Effect of aging on organ systems (renal, musculoskeletal, hepatic and endocrine)

Trends of non-HIV chronic comorbidities among HIV-positive individuals on highly active antiretroviral therapy in British Columbia from 2000-2009

B. Gali[1], S. Jabbari[2], W. Zhang[2], W. Chau[2], E. Eyawo[2], V. Lima[2], H. Samji[2], K. McGrail[1], R. Hogg[2], D. Moore[2]

[1]University of British Columbia, School of Population and Public Health, Vancouver, Canada; [2]BC Centre for Excellence in HIV/AIDS, Epidemiology and Population Health, Vancouver, Canada

Background: Highly active antiretroviral therapy (HAART) has transformed HIV from a uniformly fatal condition into a largely treatable chronic disease. Reduced HIV-related morbidity and mortality has allowed other chronic diseases to assume greater importance among HIV-positive individuals. We designed a study to characterize how HAART expansion in British Columbia (BC), Canada has affected the incidence of chronic non-HIV related comorbidities.

Methods: Our analysis was performed using an administrative population-based dataset of HIV-positive individuals (≥19 years) in BC. Using ICD-9/10 codes for case identification, we assessed the following chronic diseases among HIV-positive individuals who had accessed HAART during the study period from 2000 to 2009: cardiovascular disease (CVD), diabetes mellitus (DM), hypertension (HTN), asthma/chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and chronic liver disease (CLD). Prevalent cases of these diseases were identified pre-baseline (4-year washout period) and excluded from the analyses. Disease incidence was determined by the number of new cases per year over a ten-year period. We used Poisson's log-linear regression analysis to measure trends in incidence rates.

Results: The study sample (n=8620) was predominantly white (70%, based on known ethnicity) male (83%) with a median CD4 cell count of 240 cells/µL and viral load of 80,000 copies/ml at HAART initiation. Between 2000-2009, incidence rates per 1000 person-years (95% confidence interval) of DM, HTN, and CKD significantly increased each year after adjusting for age, sex, baseline weighted Charlson Comorbidity Index (CCI), CD4 cell count and viral load ($p<0.001$ for each analyses); incidence rates of CLD showed a significant decrease over time ($p<0.001$). Incidence rates increased from 2000 to 2008: 4-fold for DM (2.60 (1.16, 5.85) to 10.19 (7.13, 14.56)); increased 3-fold for HTN (5.21 (3.03, 8.97) to 17.63 (13.32, 23.33)); and increased 2-fold for CKD (5.60 (3.10, 10.11) to 9.57 (6.45, 14.19)). Incidence rates for CLD were much greater than all other chronic diseases and decreased from 2001 to 2008 for CLD (95.15 (80.81, 11.20) to 32.46 (24.91, 42.30)). Incidence rate patterns for CVD and COPD/asthma did not significantly change over the study period ($p=.055$ and $p=0.315$ respectively).

Conclusions: We observed marked population-level increases in incidence rates for both DM, HTN and CKD; even greater population level decreases in incidence rates for CLD; and no trends for CVD and COPD/asthma among HIV-positive individuals on HAART over a ten-year period. Understanding how these chronic conditions affects future disability and death among the aging HIV-positive population is an important area of further research.

Abbreviations: *HAART: highly active antiretroviral therapy; BC: British Columbia; ICD-9/10: International Classification of Diseases 9th and 10th edition; CVD: cardiovascular diseases; DM: diabetes mellitus; HTN: hypertension; COPD: chronic obstructive pulmonary diseases and asthma; CKD: chronic kidney disease; CLD: chronic liver disease; CCI: Charlson Comorbidity Index; 95% CI: 95% confidence interval*

No conflict of interest

Abstract: 14

Metabolic / cardiovascular complications

Impact of maraviroc, dolutegravir and darunavir/ritonavir on human coronary endothelial cells functions according to age

M. Auclair[1], P. Afonso[1], M. Caron-Debarle[1], J. Capeau[1]

[1]Inserm UMRS938 Université Pierre et Marie Curie Site Saint-Antoin, Faculty of Medicine, Paris cedex 12, France

Background: HIV-infected patients are aging and, even well controlled by antiretroviral treatment (ART), present an increased incidence of cardiovascular diseases associated with atherosclerosis. Endothelial dysfunction is an early alteration leading to atherosclerosis. While protease inhibitors have been previously shown to participate to the increased cardiovascular risk, CCR5 or integrase inhibitors were not. Whether these ART could exert beneficial endothelial effects has not been evaluated.

Material & Methods: Human coronary artery endothelial cells (HCAEC) from young and old non-HIV infected individuals were treated during 15 days with maraviroc (MVC), dolutegravir (DTG), MVC+DTG and ritonavir-boosted darunavir (DRV/r) at Cmax concentrations reported in pharmacokinetic studies. We evaluated endothelial function by the level of endothelial nitric oxide (NO) synthase (eNOS) and by NO production. We measured the secretion of adhesion molecules sICAM and sVCAM and of inflammatory cytokines of IL-6 and IL-8. Inflammation was also assessed by the level of activated NF-kappaB, oxidative stress by reactive oxygen species production and senescence by the level of SA-associated beta-galactosidase. Cell-cycle arrest/senescence proteins p53 and phospho-p53, p16, p21 and prelamin-A were evaluated by western blot. All experiments were repeated three times.

Results: When using HCAEC from a young adult, with a low basal level of senescence, DRV/r exerted a limited deleterious impact on all the endothelial functions. Moreover, DRV/r induced accumulation of prelamin-A resulting in enhanced senescence. MVC had minimal effects while DTG decreased inflammation and senescence by specifically repressing the p53/p21 pathway.
HCAEC from an aged adult presented constitutively a high level of replicative senescence with accumulation of prelamin-A, endothelial dysfunction, inflammation and oxidative stress. The p53/p21, p16 and prelamin-A senescence pathways were involved. MVC and DTG were each able to decrease oxidative stress, inflammation and senescence and to improve endothelial dysfunction by acting on the p53/p21 and p16 but not the prelamin-A pathway. Their effects were not additive suggesting that DTG and MVC improved the same pathways.

Conclusion: We report here that MVC and DTG exerted beneficial effects on cultured human endothelial cells from non HIV-infected individuals while DRV/r exerted mild deleterious effects. DTG improved both stress-induced and replicative senescence. MVC improved only replicative senescence. The intensity of the long-term effects of the drugs were dependent upon individual's age suggesting that the beneficial *vs* deleterious long-term effects of different ART classes could vary according to patient's age. This needs to be clinically assessed.

Conflict of interest
financial relationship(s): This study was supported by a research grant of ViiV-Healthcare

Abstract: 15

Immunology

Loss of CD96 Expression as a New Biomarker for T-cell Senescence in HIV-1 Infection

M. El-Far[1], P. Ancuta[1], J.P. Routy[2], J.P. Goulet[1], M. Durand[1], N. Bernard[3], C. Tremblay[1]

[1]CHUM Resarch Center (CRCHUM), Tissue Injury Infection Immunity and Inflammation, Montréal, Canada; [2]McGill University Health Centre: Glen Site, Division of Hematology and Chronic Viral Illness Service, Montréal, Canada; [3]Research Institute of the McGill University Health Centre, Division of Experimental Medicine, Montréal, Canada

Background: Persistent inflammation in HIV infection is associated with disease progression by impacting different aspects of cellular functions, differentiation and survival. This inflammation also induces a premature aging of immune cell (immunosenescence), reflected by a limited replicative lifespan of immune cells, that predicts morbidity and mortality in HIV-1 infected subjects. Therefore, identification of new biomarkers of immunosenescence in HIV infection and dissection of the underlying mechanisms is urgently needed to advance both diagnostic and treatment tools. The aim of the current study was to identify novel biomarkers associated with HIV disease progression, inflammation and immunosenescence.

Materials and Methods: We had access to the Canadian Cohort of HIV-infected slow progressors, SP (Study # CTN 247; subjects maintaining CD4 counts over 500/microliter for over 7 years, in the absence of treatment). We identified several SP subjects who experienced a sudden loss of viral control and significant decline in their absolute CD4 counts (average increase of viral load: 5 to 79 fold and average loss of CD4 counts: 211 cells/microliter). We performed a genome-wide transcriptional profiling on peripheral blood mononucleated cells isolated from n=5 SP subjects before and after the loss of virological control. Flow cytometry analysis was used to validate top differentially-expressed gene expression. Mitogenic stimulation was used to measure lymphocyte proliferation in T-cells expressing high *versus* low levels of select genes.

Results: Loss of the virological control within the slow progressor group was associated with significant changes in gene expression of 1,286 genes including different candidates involved in both innate and adaptive immune responses. Among these transcripts, we observed a significant down-regulation of CD96 (T cell-activated increased late expression (TACTILE)), a member of the immunoglobulin superfamily (IgSF) expressed on NK and T-cells and involved in the regulation of cell activation and cytokine production. Of note, CD96 is known to be down-regulated in response to inflammation and LPS stimulation. We hypothesized that high levels of CD96 expression on $CD8^+$ T-cells are associated with a robust control of HIV replication. To validate this hypothesis, we studied the expression of CD96 at protein level on $CD8^+$ T-cells from SP *versus* HIV-infected subjects with a typical disease course (typical progressors). We observed that $CD8^+$ T-cells from typical progressors expressed significantly lower levels of CD96 compared to SP. Furthermore, in both groups of subjects, $CD96^{high}$ *versus* $CD96^{low}$ cells expressed significantly higher levels of CD28, CD27 and CD127 and low expression of the senescence marker CD57. At the opposite, $CD96^{low}$ $CD8^+$ T-cells exhibited a $CD28^-CD27^-CD127^-CD57^+$ phenotype, indicative of advanced stage of differentiation, likely senescent. Of note, the expression levels of CD96 (MFI) on memory $CD8^+$ T-cells negatively correlated with the expression of the activation marker CD38 and the exhaustion marker PD-1. Finally, $CD96^{high}$ *versus* $CD96^{neg}$ cells exhibited a superior ability to proliferate in response to mitogenic stimulation.

Conclusions: Our results identify CD96 as a marker of competent $CD8^+$ T-cells and suggest that down-regulation of CD96 is likely to promote uncontrolled cell activation leading to both $CD8^+$ T-cell exhaustion and senescence. Experiments are currently in progress to dissect signalling pathways downstream of CD96 that control anti-HIV properties of $CD8^+$ T-cells.

No conflict of interest

Abstract: 16

Immunology

Differences in associations of CD4/CD8 ratio, sex, and age on risk of mortality in HIV-infected adults on ART

J.L. Castilho[1], B.E. Shepherd[2], J. Koethe[1], M. Turner[1], S. Bebawy[1], J. Logan[1], W.B. Rogers[1], S. Raffanti[1], T.R. Sterling[1]

[1]Vanderbilt University School of Medicine, Department of Medicine Division of Infectious Diseases, Nashville, USA; [2]Vanderbilt University School of Medicine, Department of Biostatistics, Nashville, USA

Introduction: In the setting of antiretroviral therapy (ART), CD4/CD8 ratio is a marker of immunosenescence and is associated with non-communicable diseases in HIV-infected adults. Expansion of CD8 cell populations occurs with natural aging, and in elderly HIV-uninfected adults, lower CD4/CD8 ratio predicts mortality independent of age. Sex differences in CD4 and CD8 cell counts have been observed in both HIV-infected and uninfected adults. Whether sex differences in CD4/CD8 ratio are associated with varying risk of mortality in aging HIV-infected adults has not been defined.

Materials & Methods: We conducted an observational study of HIV-infected adults after their first year of virologic suppression on ART (baseline) at the Vanderbilt Comprehensive Care Clinic between 1998-2012. Baseline CD4/CD8 ratio, CD4, and CD8 cell counts were compared for women and men of young (<40 years), middle (40-49 years), and older (50+ years) ages. Effects of age and sex on the association of CD4/CD8 ratio and mortality were analyzed with Cox proportional hazard models using interaction terms and stratification by age.

Results: Analyses included 2,006 HIV-infected adults on ART with one year of virologic suppression. Patients were followed for a median of 3.6 years, contributing 8,762 person-years and 129 deaths. For all age groups, median CD4/CD8 ratio was significantly higher among women vs. men: <40 years (n=880): 0.71 vs. 0.62 (p<0.001); 40-49 years (n=763): 0.65 vs. 0.51 (p<0.001); and 50+ years (n=363): 0.61 vs. 0.44 (p<0.001). Among those <40 years, women had significantly higher absolute CD4 cell counts than men (555 vs. 475 cells/mm^3, p<0.001) but had no difference in CD8 cell counts. Conversely, women aged 50+ years had significantly lower CD8 cell counts compared to similarly aged men (722 vs. 912 cells/mm^3, p<0.001) but had similar CD4 cell counts. In survival analyses, there was no statistically significant sex difference or interaction between sex and CD4/CD8 ratio on mortality risk. In adjusted analyses, there was a significant interaction between age and CD4/CD8 ratio on mortality risk (interaction term p value 0.048). In stratified analysis, low CD4/CD8 ratio was significantly associated with risk of mortality only among patients aged <40 years, a relationship that persisted after adjusting for age and CD4 cell count (adjusted hazard ratio per 0.1 decrease in CD4/CD8 ratio = 1.16 [95% CI 0.99-1.35], p=0.077). CD4/CD8 ratio was not associated with mortality in unadjusted or adjusted models of older patients.

Conclusions: In HIV-infected adults on ART, CD4/CD8 ratio was consistently higher among women than men. In older adults, the sex disparity was driven by differences in CD8 cell counts, but in younger adults by differences in CD4 cell counts, reflecting aging-related immunosenescence similar to uninfected populations. Women had improved CD4/CD8 ratio but did not have improved survival compared to men among any age group in adjusted analysis. CD4/CD8 ratio was not associated with mortality risk in adults 50+ years of age but was inversely associated with mortality risk the youngest population. This finding suggests that immunosenescence may be more associated with mortality risk in younger rather than older HIV-infected adults on ART.

No conflict of interest

6th International Workshop on HIV & Aging

5 – 6 October 2015, Washington D.C., USA

Abstracts
Poster Presentations

Abstract: 17

Geriatrics and clinical care

HIV-related characteristics, attitudes and behaviors of older people in Botswana

K. Matlho[1], M. Randell[2], J. Kefas[3], R. Lebelonyane[4], T. Driscoll[2], J. Negin[2]

[1]University of Sydney, Sydney Medical School / Public health, Sydney, Australia; [2]University of Sydney, Public Health School of Public Health, Sydney, Australia; [3]National AIDS Coordinating Agency Botswana, HIV Prevention, Gaborone, Botswana; [4]Ministry of Health Botswana, HIV Prevention and Care, Gaborone, Botswana

Background: Botswana has the second-highest prevalence of HIV in the world recorded. The focus of HIV interventions in Botswana remains targeted at those aged 15-49 despite the fact that the successful roll out of antiretroviral therapy since 2002 has yielded an increasing population aging with the disease. We set out to examine the HIV-related characteristics, attitudes and behaviors of this often ignored older cohort (50-64 years) in Botswana, relative to the 'younger' (25-49 years) more documented cohort.

Methods: We utilised the Botswana AIDS Impact Survey 2013 (BAIS IV), a national two-stage sample survey design that focused on the HIV-related behavioural patterns of the population aged 10-64 years and the HIV prevalence and incidence rates among those aged 6 weeks through age 64 at national, district and sub-district level.The study was funded by the Botswana Government and conducted by the National AIDS Coordinating Agency, Ministry of Health and Central Statistical Office. Analyses were conducted using SAS, to estimate past trends and current levels of HIV in the adult (25-64) population in Botswana.

Results: Overall, HIV prevalence among older adults (50-64 years old) was 24.6%, compared to 35.1% among the younger (25-49 years) (p<0.0001) cohort; prevalence was slightly higher among older males (28.1%) than females (22.1%) (p=0.02). Among older adults, 58.9% reported sexual activity in the past year; HIV prevalence among that group was 22.9%. Condom use among older adults was low: 59.0% of older adults reported inconsistent or no condom during sexual intercourse with their main partner. Older men (6.0%) were unaware of their HIV-positive status than older women (3.0%) (p=0.002) and 85% of older people living with HIV reported to be on antiretroviral therapy. Co-morbidities were higher among older adults who reported higher prevalence rates of diabetes (8.2%), tuberculosis (8.6%) and hypertension (31.4%) compared to 2.7%, 4.9% and 10.4 % for the younger (25-49 years) old cohort respectively.

Conclusions: The primary focus for HIV interventions in Botswana has been on younger adults. It is however apparent that more need more focus needs to be given to the aging population as evidenced by the High HIV prevalence in older adults, most probably due to aging of people living with HIV. It is important however to note that older adults remains sexually active and therefore likely to contract HIV in later-life. While more effort is needed on the clinical, social, cultural, economic, and behavioral factors that explain the high infection rates, concerted and focused interventions aimed at addressing HIV among older adults in Botswana is of paramount agency.

No conflict of interest

Abstract: 18

Geriatrics and clinical care

The attitude of Botswana health policy-makers and service providers toward a population aging with HIV

K. Matlho[1], R. Lebelonyane[2], T. Driscoll[3], J. Negin[3]

[1]University of Sydney, Sydney Medical School / Public health, Sydney, Australia; [2]Ministry Of Health Botswana, HIV Prevention and Care, Gaborone, Botswana; [3]University of

Sydney, Public Health School of Public health, Sydney, Australia

Background: The advances and roll out of antiretroviral therapy in Botswana, as it is in many countries that have universal access to ARV's, has transformed HIV into a manageable chronic condition leading to the emergence of a significant population aging with this disease. The impact of the HIV epidemic on older people is shaped by the social, political, demographic, and economic circumstances in which they live. Although there has been some realisation of this development at international level, no clear defined intervention strategy has been established in most highly affected countries. It is believed that >20 % of approximately 350 000 People Living with HIV (PLWH) in Botswana are above the age of 50 years, which implies that approximately 1 in 4 people above the age of 50 years, in Botswana, are living with HIV. We explored attitudes of policymakers and service providers towards HIV among older adults (>=50 years old) in Botswana.

Methods: We conducted qualitative face-to-face interviews with 15 consenting personnel from the Ministry of Health, medical practitioners and non-governmental organizations involved in the administration of medical care, services, planning, strategies and policies that govern social, physical and medical interventions aimed at people living with HIV and health in general. The Shiffman and Smith's four category based framework of how health issues become a priority was used as a guide for our analysis.

Results: Amidst an HIV prevalence of 24.6% among those aged 50-64 years, the respondents passively recognised the predicament posed by a population aging with HIV but exhibited a lack of comprehension and acknowledgement of the extent of the issue. The issue of HIV and aging is seldom discussed and when it does it's blended within the context gerontology and the holistic lack of geriatric care. An underlying persistent ageist stigma regarding sexual behaviour existed among a number of interviewees. Respondents also noted the lack of defined geriatric care within the provision of the national health care system. There seemed, however, to be a debate among the policy strategists and care providers as to whether the response should be specifically aimed towards older adults living with HIV or rather to improve health services for older adults more generally. Health systems in Botswana are still configured for individual diseases rather than coexisting chronic diseases even though it has become increasingly common for patients, particularly the aged, to have two or more medical conditions at the same time.

Conclusions: HIV among older adults remains a low priority among policymakers in Botswana but is at least now on the agenda. The major focus for the government remains treatment and prevention aimed at the younger more 'viable ' population rather than the aftermath and broader challenges that come about as a consequence of the success of treatment based intervention. Action will require more concerted efforts that not only recognize HIV as a lifelong infection but also recognise HIV managements as an important component of the provision of effective and progressive geriatric care. A reorientation of services around multimorbidity might be needed to address future health complexity.

No conflict of interest

Abstract: 19

Geriatrics and clinical care

The Association of Mid-Life Smoking Status on Cognitive Processing Speed Performance Among HIV-Seropositive and Seronegative Older Men: The Multicenter AIDS Cohort Study

W. Akhtar-Khaleel[1], R.L. Cook[1], R.J. Beyth[2], T. Manini[3], C.C. Price[4], S. Shoptaw[5], P.J. Surkan[6], L.A. Teplin[7], R. Stall[8], M. Plankey[9]

[1]University of Florida, Department of Epidemiology, Gainesville, USA; [2]Malcolm Randall VA Medical Center, Department of Gerontology, Gainesville, USA; [3]Institute on Aging, Department of Aging & Geriatric Research, Gainesville, USA; [4]University of Florida, Department of

Clinical Psychology, Gainesville, USA; [5]David Geffen School of Medicine, Department of Family Medicine and Psychiatry, Los Angeles, USA; [6]Johns Hopkins University, Department of International Health, Baltimore, USA; [7]Northwestern University, Department of Psychiatry and Behavioral Sciences, Chicago, USA; [8]University of Pittsburgh, Department of Behavioral and Community Health Sciences, Pittsburgh, USA; [9]Georgetown University, Department of Medicine, Washington, USA

Introduction: Smoking is a possible risk factor for age related cognitive decline. It is unclear if the association differs among people living with HIV. We examined whether smoking severity at midlife is associated with cognitive processing speed among older HIV-seropositive and seronegative men who have sex with men (MSM).

Material and Methods: Data from 191 older HIV-seropositive and seronegative MSM from the Multicenter AIDS Cohort Study were examined. All participants had information on smoking history collected before the age of 50, and at least 10 years of follow up after the age of 50. Smoking history was categorized as never smoker (n=91); former smoker, <20 pack-years (n=21); former smoker, ≥ 20 pack-years (n=30); current smoker, <20 pack-years (n=15); current smoker ≥ 20 pack-years (n=34). The raw score of three neuropsychological tests (Trail Making A, Trail Making B, and Symbol Digit Modalities Test) were log transformed (Trail Making A and B) and used in linear mixed models to assess associations between smoking history and subsequent ten-year decline in cognitive processing speed.

Results: Our preliminary findings demonstrated that compared to never smokers, former smokers who smoked 20 pack-years or more had a greater rate of decline in Trail Making A (β(10^Est): 0.0026 (95% CI: 0.0005, 0.0048)) and Trail Making B (β(10^Est): 0.0049 (95% CI: 0.0025, 0.0073)). Compared to never smokers, current smokers who smoked less than 20 pack-years at age 50 had a greater rate of decline in Symbol Digit Modalities (β: -0.117 (95% CI: -0.219, -0.015)). Among HIV-seropositive participants, former smokers who smoked less than 20 pack years had a greater decline in Trail Making A, while former smokers who smoked 20 pack years or more had a greater decline in Trail Making B compared to HIV-seropositive never smokers.

Conclusions: Current and past smoking were each associated with more rapid decline in cognitive processing speed in older HIV seropositive and seronegative men, however the effect sizes were small. Smoking cessation tailored to MSM should be encouraged to optimize health with aging in this subpopulation.

No conflict of interest

Abstract: 20

Geriatrics and clinical care

A study on the effects of aging, nutrition, and exercise during HIV infection

R. Rayapu[1], R. Monica Rachana[1], R. Rohith teja[1], S. Ramola[1], S. Sudharani[1], R. Sarath Babu[1], R. Sabari girish[1]

[1]BOSS&CIPCA (A CBO), HIV/AIDS, Tirupati, India

Introduction: Aging, nutrition, and physical activity can influence outcomes in many chronic conditions. In HIV-infected patients, aging may result in an increased susceptibility from secondary infections and a delayed immune response. Optimal nutrition is an important adjunct in the clinical care of patients with HIV. Nutritional interventions can improve the quality and span of life. It can also support the effectiveness of medications and improve the patient's resistance to infections. Moderate physical activity can improve many immune parameters. In HIV- infected people, with age, alternative therapies such as nutrition and physical activity can complement medical management.

Method: The 'Blood donors Organization for Social Service' (BOSS) and its AIDS branch 'Centre for Information; Prevention and counseling on AIDS' (CIPCA)' is a registered first charitable non-govt. voluntary community based organization in India. It has started working on HIV/AIDS and blood donations in the year 1987.

It has conducted several randomized studies and here we are presenting the outcome of the study on HIV replication, aging, diet, exercise and immunity.

Results (Outcomes): We observed in people living with HIV/AIDS, with aging, the body has a decreased ability to respond to stress, therefore, making a person prone to illness. With advanced age, many diseases mimic HIV, therefore, making the diagnosis delayed at times. The majority of older patients are diagnosed with HIV only when they become symptomatic, and by then the disease would have progressed considerably. There is evidence of accelerated immunosenescence in HIV-infected individuals as they age.

Dietary therapy is an important adjunct in the clinical care of patients infected with HIV. We observed that in many conditions, achieving and maintaining optimal nutrition can improve an individual's immune function, reduce the incidence of complications associated with HIV infection. Hence we adopted multiple strategies to improve nutritional outcomes, including ARVs, treatment of confections, nutritional counseling, nutritional supplements and providing pharmacologic agents to stimulate appetite. We observed that adequate intake of micronutrients and macronutrients is essential for the restoration and maintenance of body cell mass and normal function, including immunity.

We observed the physical activity has assisted in weight management, lean muscle development, and body fat reduction. Physical activity on HIV-infected individuals showed improvements in body composition with decreased waist circumference and waist-to-hip ratio, increased lean body mass, and cardio metabolic fitness.

Conclusion: Age-related immunosenescence can increase the challenges of controlling viral loads and optimizing CD4+ T-lymphocyte cell counts. Because immunosenescence is an inherent phenomenon that may be accelerated by HIV, strategies that can potentially modify this process should be used. Nutrition therapy may support the effectiveness of the medical treatments by improving cellular function through the supplementation of both macronutrients and micronutrients. Physical activity can exert positive effects on metabolic and cardiovascular functions while not imposing deleterious effects on the immune system. Recommendations for regular exercise should become an integral part of their care across all ages.

No conflict of interest

Abstract: 21

Geriatrics and clinical care

Pain, Health Service Utilization and Mortality among Persons Aging with HIV Infection and Substance Use

S.R. Isenberg[1], D. Pigott[2], S.H. Mehta[3], S.M. Dy[3], G.D. Kirk[2]

[1]Johns Hopkins Bloomberg School of Public Health, Health Behavior and Society, Baltimore, USA; [2]Johns Hopkins University School of Medicine, Infectious Disease, Baltimore, USA; [3]Johns Hopkins University School of Public Health, Epidemiology, Baltimore, USA

Introduction: Since the advent of effective antiretroviral therapy, HIV-infected persons are living longer. Yet, persistent disparities in survival and health care utilization remain, particularly for those co-impacted by substance use. Pain symptoms pose a significant burden for both HIV-infected and substance use populations. However, limited data exists on the relationship of pain symptoms to adverse clinical outcomes in the aging HIV-infected population. In this study, we sought to evaluate the association of pain symptomatology with emergency department (ED) utilization, hospitalization, and mortality among persons aging with HIV infection and substance use.

Materials and Methods: This study was performed in the AIDS Linked to the Intravenous Experience (ALIVE) cohort of persons with prior or current injection drug use. Pain symptoms were assessed semi-annually by self-report using the MOS-HIV Health Survey pain scale (graded from none to severe pain on Likert scale). Hospitalization events and emergency department use were assessed at consecutive study visits from 2005 to 2012. Mortality events

were assessed through linkage to the National Death Index. Logistic regression models with generalized estimating equations were used to estimate the odds (odds ratios [OR] with 95% confidence intervals [CI]) of pain symptoms associated with ED use and hospitalization. Cox proportional hazards models with time varying covariates were used to estimate the risk (hazard ratios [HR] with 95% confidence intervals [CI]) for mortality.

Results: Of 1939 ALIVE participants at baseline, the median age was 47 years and 31% were HIV-infected; 38% had mild pain, 21% had moderate pain, and 11% had severe pain. In multivariable models adjusting for socio-demographics, comorbidity, substance use, and HIV status, the presence of pain symptoms was significantly associated with increased risk of emergency department use: mild pain (OR 1.21; 95% CI, 1.08, 1.36), moderate pain (OR 1.41; 95% CI, 1.23, 1.61), severe pain (OR 1.71; 95% CI, 1.45, 2.02); increased hospitalization risk: mild pain (OR 1.22; 95% CI, 1.05, 1.42), moderate pain (OR 1.56; 95% CI, 1.32, 1.85), severe pain (OR 1.89; 95% CI, 1.54, 2.32); and increased mortality: moderate pain (HR 1.48; 95% CI, 1.03, 2.14), severe pain (HR 2.14; 95% CI, 1.45, 3.16).

Conclusions: A majority of aging HIV-infected and at-risk injection drug users reported pain; one-third had moderate to severe pain that interfered with daily activities. Self-reported pain was significantly associated with mortality and health care utilization in a dose-response manner, independent of HIV status, comorbidity or substance use. Further elucidation of pain pathways in the aging HIV-infected population may facilitate targeted interventions to reduce health care utilization and improve survival for aging HIV-infected persons and their high risk counterparts.

No conflict of interest

Abstract: 22

Geriatrics and clinical care

Aging-Related Strength Decline is Accelerated in HIV-Infected Men

J.A. Schrack[1], K.N. Althoff[1], L.P. Jacobson[1], K.M. Erlandson[2], B.D. Jamieson[3], S.L. Koletar[4], J. Phair[5], L. Ferrucci[6], T.T. Brown[7], J.B. Margolick[8]

[1]Johns Hopkins Bloomberg School of Public Health, Epidemiology, Baltimore, USA; [2]University of Colorado, Infectious Diseases, Denver, USA; [3]UCLA, School of Medicine, Los Angeles, USA; [4]Ohio State, School of Medicine, Columbus, USA; [5]Northwestern University, Feinberg School of Medicine, Chicago, USA; [6]National Institute on Aging, Translational Gerontology Branch, Baltimore, USA; [7]Johns Hopkins School of Medicine, Endocrinology, Baltimore, USA; [8]Johns Hopkins School of Public Health, Molecular Microbiology & Immunology, Baltimore, USA

Introduction: Grip strength, a component of frailty, predicts functional decline, disability, and death, and has been proposed as a biomarker of biological aging. Although an increased risk of frailty has been well documented in those aging with HIV, differences in the trajectory of grip strength decline by HIV-serostatus have not been defined. Thus, assessment of the longitudinal changes in grip strength in persons aging with HIV may provide an important method of gauging health and longevity in this population. The objective of this study was to identify factors associated with grip strength decline in HIV-infected (HIV+) and similar uninfected (HIV-) men.

Materials & Methods: The study was performed between 2007 and 2014 in the Multicenter AIDS Cohort Study (MACS). Grip strength was assessed in 1,886 (897 HIV+ and 989 HIV-) men $\geq$ 40 years (mean baseline age 50.2 $\pm$7.6 years) at each semi-annual clinic visit. During the 7-year study period, the mean number of assessments was 11.5 per participant (range 2-19). The primary outcome was grip strength in kilograms of force (kg); clinically weak grip strength was defined as grip strength < 26 kg, as outlined by the Foundation for the NIH Sarcopenia Project.

The association between age and grip strength was modeled using linear regression models with generalized estimating equations for repeated measures, adjusted for HIV serostatus, age, height, weight, race, education, smoking, drug and alcohol use, diabetes, hypertension, arthritis, depression, hepatitis B, and hepatitis C infection. In a HIV-specific model, coefficients were included for nadir CD4, the presence of undetectable HIV RNA, and history of AIDS-defining illness.

Results: Grip strength at age 50 averaged 41.7 kg and 40.3 kg for HIV- and HIV+ men, respectively (p <0.001). In fully adjusted models, there was a 0.47 kg decline in grip strength with each one-year increase in age after age 50 (p <0.001) and a negative association between grip strength and HIV status (β= -0.81 kg, p = 0.018). In stratified analyses, the magnitude of decline with increasing age was greater in HIV+(β= -0.47 kg, p = < .001) compared to HIV- (β= -0.43 kg, p = < .001) men. In HIV-specific models, a history of AIDS was strongly associated with lower grip strength (β= -1.74 kg, p <0.001). In fully adjusted time-to-event Cox proportional hazard models, there was a 42% greater risk of developing clinically weak grip strength in HIV+ compared with HIV- men (aHR 1.42; 95% CI, 1.05 – 1.91).

Conclusions: Aging-related decline in grip strength is accelerated in HIV-infected men, which may contribute to decreased active life expectancy and lower quality of life with advancing age.

No conflict of interest

Abstract: 23

Geriatrics and clinical care

Changes with menopause in the distribution of a frailty index (FI) in HIV infected women

S. Zona[1], T. Brothers[2], A. Malagoli[1], M. Menozzi[1], F. Carli[1], C. Stentarelli[1], L. Wallace[2], O. Theou[2], S. Kirkland[2], C. Mussini[1], K. Rockwood[2], G. Guaraldi[1]

[1]University of Modena, HIV Metabolic Clinic Infectious Diseases Department, Modena, Italy; [2]Dalhousie University, Faculty of Medicine, Halifax, Canada

Background: Menopause is a physiological aging transition associated with rapid metabolic and physical changes.
The aim of this study was to describe changes with menopause in the longitudinal distributions of a frailty index (FI) in HIV infected women.

Methods: Observational retrospective study including consecutive HIV+ women aged >40 yrs, including at least 2 FI assessments at the Modena HIV Metabolic Clinic. Women were stratified according to menopause status (as assessed by hormone levels, i.e. FSH or LH >35 ng/mL and estradiol<30 ng/mL) in 3 groups: pre-menopausal only (350 women), post-menopausal only (148 women), and women with observations both in pre- and post-menopause (182 women). Frailty was assessed using a 30-item frailty index (FI) based on deficit accumulation. The association between FI and STRAW groups was assessed using age-adjusted GEE linear regression model. In the subset of the transition-period group (in which at least the 1st FI was assessed in the pre-menopause state and a 2nd FI in the post-menopause state), we described the distribution of FI and time from menopause (transitional, early and late menopause) according to Stages of Reproductive Aging Workshop (STRAW) criteria. GEE linear regression model was used to evaluate association between time from menopause and FI.

Results: A total of 680 HIV+ women were included accounting for 1725 FI evaluations (985 in pre-menopausal women and 740 after menopause). A total of 3068 person-year follow-up were included. All women were on HAART, 85% had undetectable viral load, and the median CD4 count was 537 (IQR 381–719).
Baseline mean age in the pre-menopause, post-menopause and in transition-period groups was 42±2, 52±6, and 46±4 years, respectively; mean follow-up period was 3.5±2.3, 3.8±2.6, and 6.7±2.7 years, respectively. Baseline FI in the pre, post, and transition menopause groups were 0.30±0.09, 0.40±0.09, and 0.31±0.08, respectively.

GEE regression analysis showed that menopause was associated with FI (ß=0.04, 95% CI 0.03; 0.05, p<0.001) independently by age. Lowess curves demonstrate that across all ages, women in menopause have higher FI values than pre-menopause women.
We included data from 131 women who were evaluated in the pre-menopausal, transition, early, and late menopausal period, accounting for a total of 579 FI evaluations. A total of 1577 person-year follow-up was included. FI values significantly increased in the early-menopause period (early vs. pre-menopause ß=0.01, 95% CI 0.001; 0.02, p=0.038); and tended to stabilize after 3 years from menopause (Late menopause vs. pre-menopause ß=0.01, 95% CI -0.0001; 0.02, p=0.05).

Discussion: A frailty index was used to describe deficit accumulation across stages of reproductive aging in HIV-infected women on HAART. We observed dynamic changes in FI values, with rapid increases in the first 3 years after onset of menopause and subsequent stabilization.

No conflict of interest

Abstract: 24

Metabolic / cardiovascular complications

Characteristics and outcome of patients diagnosed with HIV at older age

I. Asher[1], K. Mahlab Guri[1], D. Elbirt[1], S. Rosenberg Bezalel[1], F. Maldarelli[2], O. Mor[3], Z. Grossman[4], Z. Sthoeger[1]

[1]Kaplan Medical Center, Neve or Allergy clinical immunology and AIDS Center, Rehovot, Israel; [2]National Cancer Institute, Clinical Retrovirology Section, Bethesda, USA; [3]Ministry of Health, Central Virology Laboratory, Ramat Gan, Israel; [4]Tel-Aviv University, School of Public Health, tel Aviv, Israel

Objectives: To characterize the clinical, virological and immunological status at presentation and the outcome of patients diagnosed with HIV above the age of 50 compared to HIV patients diagnosed at younger age.

Design: A retrospective cohort study of 418 patients diagnosed with HIV between the years 2004-13 in an Israeli HIV/AIDS center.

Methods: Patients with new HIV diagnosis ≥50 years of age defined as 'older'; and <50 defined as 'younger'. The mean follow-up period was 53±33 months. Patients with <2 CD4/VL measurements or with <1 year of follow-up were excluded. Time of HIV infection was estimated by HIV sequence ambiguity assay. Ambiguity index≤0.43 indicated recent (≤1 year) HIV infection
.
Results: 89 (21%) patients were diagnosed with HIV at older age. Those older patients presented with more comorbitites (34% vs 8%; *p*<0.001), lower CD4 cell counts (197±181 vs 283±200 cells/µl; *p*<0.001) and higher VL (710798 ± 1165515 vs 415574 ± 1085787 copies/ml; *p*=0.02) compared to the younger patients. The rate of AIDS defining illness was similar in both groups (24% vs 16%; *p*=NS). At the end of the study, the older patients had a higher mortality rate (21% vs 3.5%; *p*<0.001), lower CD4 cell counts (381 ± 228 vs 483 ± 261 cells/µl; *p*<0.001) and higher VL (515517 ± 1197000 vs 191447 ± 745000 copies/ml; *p*=0.03) compared to the younger patients. The later differences in outcome weren't due to delayed HIV diagnosis of older patients and were also observed between older and younger patients who presented with similar CD4 cell counts and VL and among older and younger patients with a recent (<1year) HIV infection.

Conclusions: One fifth of HIV patients are diagnosed at older age (≥50). Those older patients have a less favorable outcome compared to the younger patients. This point to the mandatory need of educational and screening programs within older populations and for a closer follow-up of older HIV patients.

No conflict of interest

Abstract: 25

Metabolic / cardiovascular complications

Changes in Weight and Body Composition Across the Lifespan Among HIV+ and HIV- Men and Women

K.M. Erlandson[1], L. Zhang[2], J.A. Schrack[2], J.E. Lake[3], K.N. Althoff[2], J. Margolick[4], F. Palella[5], S.L. Koletar[6], L.P. Jacobson[2], T.T. Brown[7]

[1]University of Colorado Denver, Infectious Diseases, Aurora, USA; [2]Johns Hopkins University, Epidemiology, Baltimore, USA; [3]University of California-Los Angeles, Infectious Diseases, Los Angeles, USA; [4]Johns Hopkins University, Molecular Microbiology and Immunology Epidemiology, Baltimore, USA; [5]Northwestern University Feinberg School of Medicine, Infectious Diseases, Chicago, USA; [6]Ohio State University Medical Center, Infectious Diseases, Columbus, USA; [7]Johns Hopkins University, Endocrinology Diabetes and Metabolism, Baltimore, USA

Background: An increasing prevalence of overweight/obesity among HIV+ persons in cross-sectional studies or following antiretroviral therapy (ART) initiation may contribute to the higher rates of obesity-related diseases seen among HIV+ older adults. The objective of this study was to compare weight changes by HIV serostatus, and explore changes across the lifespan. Such data could inform obesity prevention efforts to decrease the impact of obesity-associated diseases with aging.

Methods: HIV+ (HIV-1 RNA <400 copies/mL on ≥ 2 ART agents) and HIV- participants 17-75 years old (yo) under observation from 1999-2014 in the Multicenter AIDS Cohort Study (MACS) and Women's Interagency HIV Study (WIHS) were included. Outcomes included body mass index (BMI), waist circumference (WC), and hip circumference (HC) measurements; separate models were created for men and women. Age was investigated as continuous and categorical variables for early (<40), middle (40-60), and older (>60 years) ages. Covariates considered in the models included race/ethnicity, substance use, depression, viral hepatitis B (HBV) and C (HCV) infection, CD4+ lymphocyte (CD4) count, and ART duration. Univariate models included age group, demographic and HIV-related variables. Mixed linear regression models were used to estimate univariate and multivariate (including age and covariates with p>0.10 in univariate models) associations with BMI, WC, and HC.

Results: At baseline, among 758 women (53% HIV+) and 694 men (40% HIV+), the median ages were 40 and 46 years, respectively. The majority of women were black (53%) and/or Hispanic (27%); the majority of men were white (86%). More than 90% of HIV+ participants had a CD4 ≥200 cells/mm^3, and had received ART for <5 years. Up to age 60, each year of increased age was associated with a significant BMI increases irrespective of HIV serostatus, but HIV- women and men gained significantly more BMI/year than HIV+ persons (p<0.0001). After age 60, BMI decreased among all participants, with the greatest declines among women (HIV-: -0.15 kg/m^2/year, HIV+: -0.12 kg/m^2/year). Significant increases in WC were observed across all age strata regardless of HIV serostatus. WC had significantly greater increases/year after 60 years of age in HIV+ compared to HIV- men, and significantly less WC increase/year up to age 60 in HIV+ compared to HIV- women. HC increased until age 60 (p<0.0001); HIV+ women had less HC increase/year until age 60 while HC in HIV+ men was not significantly different from HIV-men. Black race (p<0.0001) and Hispanic ethnicity (p<0.05) were associated with greater BMI; marijuana or stimulant use (p<0.0001), depression (p<0.01), and HCV (p<0.0001) were associated with lower BMI. Compared to non-smokers, female smokers had significantly lower BMI (-0.50 kg/m^2, p<0.0001); male smokers did not (p=0.28). Among HIV+ women and men, lower CD4 and shorter ART duration were associated with lower BMI (p<0.001).

Conclusions: HIV+ men and women had lower BMI, WC, and HC than HIV- counterparts; minorities and persons <60 years had the greatest risk for age-related weight gain. The BMI reduction after age 60 could represent either weight loss (potentially associated with a poor prognosis) or a survival effect of thinner individuals living longer.

No conflict of interest

Abstract: 26

Metabolic / cardiovascular complications

Autonomic Function Tests and Pulse Wave Velocity in HIV Disease: correlation to vascular ageing

M. Manicardi[1], P. Guaraldi[2], A. Santoro[3], A. Lattanzi[1], A. Malagoli[3], P. Salvi[4], A. Grillo[5], R. Rossi[1], C. Mussini[3], P. Raggi[6], P. Cortelli[2], G. Guaraldi[3]

[1]University of Modena, Cardiology, Modena, Italy; [2]University of Bologna, Neurology, Bologna, Italy; [3]University of Modena, Infectious Disease, Modena, Italy; [4]University of Milano, Cardiovascular Neural and Metabolic Science, Milano, Italy; [5]University of Trieste, Cardiology, Trieste, Italy; [6]Mazankowski Alberta Heart Institute, Cardiology, Alberta, Canada

Background: Autonomic dysfunction is related to increased cardiovascular disease and mortality, being responsible of both subclinical coronary artery disease and cardiac arrhythmias. In addition augmented sympathetic activity arises vascular constriction contributing to parietal arterial stiffness.
Arterial stiffness can be assessed by measuring the velocity of the initial pulse wave propagation between two sites (PWV) measured with a PulsePen® tonometer.
We assessed whether subclinical autonomic dysfunction, as evaluated by a complete battery of autonomic function tests (AFTs), correlates with PWV change over 10 year follow up.

Methods: We retrospectively analyzed 14 HIV-infected men on stable antiretroviral therapy who, underwent in 2006 extensive ANS investigations including the head-up tilt test (HUTT), Valsalva maneuver, deep-breathing test, handgrip test (HG) and cold face test and baseline endothelial dysfunction test using PWV. PWV change was subsequently assed in 2015 to measure vascular ageing.

Results: Fourteen HIV+ patients were included in the study. At baseline the mean age was 41.0±5.9, all had undetectable viral load, and the median CD4 count was 543 (IQR 385-720).
Among participants, 1 (7%) had altered Tilt test, 2 (14%) had a pathological deep breathing test, while 4 (28%) showed low pressure response on cold face test. PWV at time of enrollment was 7.10±0,96 m/sec and 6.64 ±1.18 m/sec. At baseline we did not find any correlation between PWV and any AFT results. At 10 years follow up change in PWV correlated significantly with the change in heart rate during deep breathing test r=0.016.

Discussion: This study has addressed the correlation between AFTs and PWV progression in the context of ageing. Deep breathing HR variability is a simple clinical bedside tests can assess autonomic dysbalance giving insights into vascular function/ageing. This preliminary data are hypothesis generating suggesting patho-physiological role of Autonomic Nervous System and vascular ageing in HIV infected patients.

No conflict of interest

Abstract: 27

Neurology

Subjective Memory Impairment is associated with Cognitive Status and Mood in Middle Aged HIV-Positive Adults

A. Kamkwalala[1], T. Hulgan[2], P. Newhouse[1]

[1]Vanderbilt University School of Medicine, Psychiatry, Nashville, USA; [2]Vanderbilt University School of Medicine, Infectious Diseases, Nashville, USA

Background: With the successful status of anti-retroviral treatment in the United States, adults living with chronic HIV-1 infection now routinely survive into their 50's 60's, and beyond, in many cases exceeding 15 years since infection. However, increased life expectancy in the HIV-positive population introduces the added

complication of age-related cognitive decline. Aging with HIV has been associated with higher risk of mood disorders and poorer cognitive outcomes compared to HIV-negative adults. As HIV-clinics around the country and the world continue to treat a steadily aging HIV-positive population, the addition of routine cognitive screening to their medical care may be beneficial to identify the early signs of cognitive impairment, such as symptoms of HIV-Associated Neurocognitive Disorders (HAND). The aim of this study was to evaluate the usefulness of a brief mood and cognitive test battery to assess a sample of patients seeking medical care at the Vanderbilt University Comprehensive Care Clinic in Nashville, Tennessee.

Methods: Patients were approached individually by study staff (AK) during their regular visits to the VCCC, and invited to participate in a 45-minute mood and memory screening. Participants completed the Memory Functioning Questionnaire (MFQ), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), a 16-word Buschke Selective Reminding Task (BSRT), and four measures from the COGState Computerized Testing Battery: The Groton Maze (GML), Detection Task (DET), Identification Task (IDN), and One-Card Learning (OCL).

Results: Subjective memory complaints, as measured by the MFQ were associated with poorer mood symptoms, and impaired performance on the OCL task of the COGState Battery, and the Buschke Selective Reminding Task (BSRT).

Conclusions: Periodic brief memory and cognitive screening, especially with subjective reporting of symptoms, may be useful to clinicians to identify patients in their HIV clinics at higher risk for the onset of age-related cognitive impairments, allowing for assessment and intervention.

No conflict of interest

Abstract: 28

Neurology

Novel Approach to Measuring Intracranial Vascular Caliber: Applications in HIV Infected Individuals

C. Artrip[1], W. Liu[1], P.M. De Alwis[1], D. Reich[1], G. Nair[1]

[1]National Institutes for Health, National Institute of Neurological Disorders and Stroke, Bethesda MD, USA

Background: Several post-mortem MRI studies have shown an increase in blood-vessel wall-thickness in HIV infected individuals, indicating possible arterial remodeling. Measurements in cerebrovascular structure could offer insight into neurocognitive deficits of an HIV infected individual. In this study, cerebrovascular caliber measurements in HIV and control cohorts were studied using high-resolution susceptibility weighted imaging (SWI) sequences.

Methods: SWI were acquired at 0.55 mm isotropic resolution in 29 HIV subjects (50.8± 8.1 y/o, 69% male, 100% on ART) and 20 without HIV (47.0± 11.5 y/o, 70% male) on a Philips 3T scanner with 8-channel head coil. Cross-sectional areas of the A1 segment of the anterior cerebral arteries, M1 branch of the middle cerebral arteries, and the septal veins (SV) along the anterior wall of the lateral ventricles were measured using MATLAB in a blinded fashion. Clinical evaluation included 15 HIV with HIV-associated neurocognitive disorders (HAND), 14 HIV positive, 16 HIV negative (socio-economically matched control subjects), and 4 healthy volunteers (HV). ANOVA tests were used to compare samples between cohorts, paired t-tests to compare differences between left and right segments, and a power analysis performed to determine optimal sample size for future studies.

Results: M1 and A1 caliber was measured from 15 HAND, 14 HIV, 16 control, and 4 HVs. Average M1 area was 8.28±1.60 mm^2 for HAND, 8.39±1.77 mm^2 for HIV, 8.45±1.64 mm^2 for Control, and 8.79±1.56 mm^2 for HV. Average A1

area was 5.36±2.13 mm^2 for HAND, 5.76±2.83 mm^2 for HIV, 5.49±2.55 mm^2 for Control, and 6.41±2.6mm^2 for HV. No significant differences were detected in the M1 or A1 across cohorts (ANOVA p=.737 and p=.711, respectively). Comparisons between left and right segments were consistent (p=0.9) and no age association was detected. There was a significant 49% difference between the cross-sectional area of M1 and A1 (8.41± 1.61mm^2 and 5.60± 2.46mm^2 respectively, p<<.01). SV caliber measured from 9 HIV and 10 Control subjects were 2.48±0.47 and 2.75± 0.56 mm^2, respectively. There was no significant differences between HIV positive and control subjects (p=.28). Power analysis of individual vessels suggested a sample size of 29, 130, and 33 subjects for a 10% change in M1, A1, and SV caliber respectively (a=0.05, b=0.8, 2-tailed).

Discussion and Conclusions: While no differences were seen in intracranial vessel caliber in HIV and control groups, there were significant differences between the M1 and A1 branches substantiating the usefulness of the method in detecting vascular changes. Possibly, vessel wall changes do not significantly affect the total vascular cross-sectional area since the wall is typically 0.5-1.4 mm thick, and a change of only 10% has been reported in extra-cranial vessels. Consistency between the left and right vessel branches highlights the reliability and reproducibility of the method. Power analysis suggests that increasing the sample size to ~35 in each group could potentially detect up to a 10% change in M1 and SV caliber. Future analysis of other neurological diseases and comorbidities may characterize significant influences on vasculature. This novel methodology using high-resolution SWI segmentation reliably quantifies intracranial vascular caliber and anatomical structures.

No conflict of interest

Abstract: 29

Neurology

Yoga for Persons with HIV-related Neuropathy: A Case Series

D. Kietrys[1], M. Galantino[2], K. Logan[3], S. Gould-Fogerite[4], K. O'Brien[5], E. Cohen[6], R. Jermyn[7], J.S. Parrott[8]

[1]Rutgers, School of Health Related Professions - DPT Program-South, Stratford, USA; [2]Stockton University, Physical Therapy, Galloway, USA; [3]NovaCare Rehabilitaion, Physical Therapy, Southampton, USA; [4]Rutgers, Primary Care, Newark, USA; [5]University of Toronto, Physcial Therapy, Toronto, Canada; [6]Rutgers, School of Health Related Professions, Stratford, USA; [7]Rowan University, Physical Medicine and Rehabilitation, Stratford, USA; [8]Rutgers, Interdisciplinary Care, Newark, USA

Background: Distal sensory polyneuropathy (DSP) is a common complication of HIV disease. DSP-related pain has been associated with disability, reduced quality of life (QOL) and impaired function. Yoga has been shown to improve mental and physical status in people with a number of chronic diseases. Our purpose was to assess feasibility and measure the impact of 4 weeks of yoga in persons with HIV-related DSP in the feet.

Materials and Methods: Of 55 patients scheduled at a HIV pain clinic over 6 months, 22 had DSP. Four completed the study. Inclusion criteria were diagnosis of HIV disease and DSP in the feet, controlled HIV disease status, average foot pain of at least 4/10, sensory symptoms in the feet, and an established regime of pharmacologic management. The age range was 33-64 years (mean 52.3 years). Time since HIV diagnosis ranged from 7 months-30 years (mean 18.4 years). Time since diagnosis of DSP ranged from 7 months-15 years (mean 8.1 years). Baseline mean rating of average foot pain was 5.3/10. At baseline, one participant had been hospitalized 7 months prior due to meningitis, used a walker for ambulation, and had lower extremity (LE) impairments that were not related to DSP. Participants engaged in twice weekly yoga classes for 4 weeks.

Results: Five-time sit-to-stand test improved in all participants at W5, with sustained improvement at W9 in 3. Six-minute walk test distances showed clinically meaningful improvement in 3 participants at W5, and the gains were sustained at W9 in 2. Multi-directional reach test performance to the side (left or right) and forward improved in most cases at W5 with carryover to W9 in some instances. One participant improved in the backward direction at W5 and W9. Great toe vibratory sensation threshold (tested with a biothesiometer) improved (bilaterally) in the participant that had a history of meningitis at W5 and W9. For one participant, Pain Severity and Pain Interference improved at W5 and W9, and Average Pain improved by W9. The other 3 participants had similar pain scores over time, as measured with the Brief Pain Inventory. However, pain-related quality of life (QOL) (from pain subscales of the MOS-HIV) improved by >20% for all participants at W5, and gains were sustained for 2 at W9. Mental Health Summary QOL and Physical Health Summary QOL scores improved for all participants at W5, with sustained improvement at W9 in 3. Self-reported LE function (as measured with the LEFS and LLFI) improved (on both instruments) in 1 participant at W5 and W9. Disability scores (assessed via WHO-DAS and HDQ) were in general unchanged, although one participant had an improved HDQ score at W5.

Conclusions: Recruitment was challenging. The intervention was feasible and safe. No adverse events occurred. There were inconsistent outcomes between individuals, but there were several instances of improvement in impairments, function, and QOL. A limitation was that the intervention was conducted for only 4 weeks. Further research is needed to determine if yoga is an effective intervention for individuals with HIV-related DSP.

No conflict of interest

Abstract: 30

Pharmacology

The Effect of Gender and Age on the Relative Bioavailability of Doravirine: Results of a Phase I Study in Healthy Subjects

M. Behm[1], K.L. Yee[1], L. Fan[1], P. Fackler[1]

[1]Merck & Co. Inc., Kenilworth NJ, USA

Background: Doravirine (MK-1439) is a novel, well tolerated, once-daily, non-nucleoside reverse transcriptase inhibitor in development for the treatment of human immunodeficiency virus-1 infection in combination with other antiretroviral therapy. Here, we report data from a Phase I study designed to evaluate the effect of gender and age on the pharmacokinetics (PK) of doravirine.

Materials & Methods: This was an open-label, parallel-group study of 36 healthy subjects: 12 elderly males, 12 elderly females, and 12 young females. PK data for young male subjects were obtained from a separate study (Protocol number 001, Anderson et al. *Antivir Ther*. 2015;20(4):397-405; n=6). Elderly subjects were 65-80 years of age, and young subjects between 18-50 years of age. Each subject received a single 100-mg dose of doravirine under fasting conditions, and blood samples were taken at pre-specified timepoints up to Day 4. Key PK parameters were area under the concentration-time curve ($AUC_{0-\infty}$), peak plasma concentration (C_{max}), and plasma concentration at 24 hours ($C_{24\ hr}$). For the evaluation of gender on the PK of doravirine, data from young and elderly subjects could be pooled if the 90% confidence intervals (CIs) of the geometric mean ratio (GMR) for elderly/young subjects were contained within pre-specified bounds (0.5, 2.0) and if $p>0.05$ for the between-group comparison. Likewise, for the evaluation of age on the PK of doravirine, data from male and female subjects could be pooled if both criteria were met.

Results: Data from elderly male and young male subjects were poolable, as were data from elderly female and young female subjects. The

evaluation of gender was, therefore, based on pooled data from elderly and young subjects. Doravirine $AUC_{0-\infty}$ and $C_{24\ hr}$ were similar in male and female subjects. The GMRs (female vs male) and 90% CIs for $AUC_{0-\infty}$, C_{max}, and $C_{24\ hr}$ were 119.95% (102.86, 139.88), 141.84% (122.76%, 163.87%), and 101.72% (83.63%, 123.72%), respectively, suggesting that there is no clinically-meaningful difference in the relative bioavailability of doravirine with respect to gender. Data from elderly male and elderly female subjects were not poolable; for this reason, the effect of age on the PK of doravirine was evaluated separately for each gender. For elderly male versus young male subjects, the GMRs and 90% CIs for $AUC_{0-\infty}$, C_{max}, and $C_{24\ hr}$ were 85.35% (66.51%, 109.53%), 91.83% (72.95%, 115.59%), and 81.20% (59.15%, 111.47%), respectively. For elderly female versus young female subjects, the GMRs and 90% CIs for $AUC_{0-\infty}$, C_{max}, and $C_{24\ hr}$ were 96.98% (79.35%, 118.52%), 118.05% (97.82%, 142.45%), and 93.79% (72.41%, 121.47%), respectively. Thus, the relative bioavailability of doravirine was similar in young and elderly subjects for both genders. Overall, 8 subjects (22%) had at least one adverse event (AE) following treatment with a single dose of doravirine. Almost all were of mild intensity; one was of moderate intensity. No AEs were serious, and none led to premature discontinuation from the study.

Conclusions: Neither age nor gender affected the relative bioavailability of a single dose of doravirine in healthy subjects. Doravirine was generally well tolerated, irrespective of age and gender.

Conflict of interest
financial relationship(s): Employee of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA

Abstract: 31

Effect of aging on organ systems (renal, musculoskeletal, hepatic and endocrine)

Long-term Impact of HIV Wasting on Physical Function in the Multicenter AIDS Cohort Study

T. Brown[1], X. Li[2], J.B. Margolick[3], A. Abraham[2], J.E. Lake[4], F.J. Palella[5], S.L. Koletar[6], K.M. Erlandson[7]

[1]Johns Hopkins University, Endocrinology and Metabolism, Baltimore, USA; [2]Johns Hopkins University, Epidemiology, Baltimore, USA; [3]Johns Hopkins University, Molecular Microbiology and Immunology, Baltimore, USA; [4]Johns Hopkins University, Infectious Diseases, Los Angeles, USA; [5]Johns Hopkins University, Infectious Diseases, Chicago, USA; [6]Ohio State University, Infectious Diseases, Columbus, USA; [7]University of Colorado, Infectious Diseases, Denver, USA

Introduction: The long-term consequences of wasting among HIV-infected persons are not known but may be a risk for physical function decline with aging.

Material & Methods: Survival after wasting was examined among Multicenter AIDS Cohort participants using Kaplan-Meier analysis.HIV-infected participants surviving ≥2 years after a clinical diagnosis or weight trajectory consistent with wasting and with available physical function assessment data (grip strength, gait speed, and quality of life [QoL]) were matched to HIV-infected and -uninfected men without wasting. Matching criteria included age, calendar year, and CD4 cell count and plasma HIV-1 RNA (HIV-infected only). Multivariable linear regressionanalyses adjusted for age, cohort, race, hepatitis C status, and number of comorbid illnesses were used to assess the impact of wasting on subsequent physical function.

Results: Overall (unadjusted) median survival was lower among HIV-infected men with any wasting (9.1 years) compared to HIV-infected men without wasting (11.6 years). Among 85 HIV-infected men surviving ≥2 years after wasting,

we evaluated physical function outcomes compared to 249 HIV-infected and 338 HIV-uninfected men without wasting. In multivariable regression models, HIV-infected men with prior wasting had lower grip strength and poorer physical QoL than HIV-infected men with no wasting (p≤0.03), and poorer physical QoL but higher mental QoL than HIV-uninfected men (p≤0.05).

Conclusions: A history of wasting among HIV-infected persons portends poorer survival compared to persons without a wasting history. Furthermore, HIV-infected survivors of wasting may represent a population of adults atincreased risk for complications associated with aging, including weakness and impaired physical QoL.

Conflict of interest
financial relationship(s): EMD-Serono

Abstract: 32

Immunology

CD4/8 ratio in individuals with perinatally acquired HIV-1 infection: a potential indicator of premature immune ageing.

K.M. Pollock[1], C. Foster[2], S. Fidler[1]

[1]Imperial College London, Medicine, London, United Kingdom; [2]Imperial College Healthcare NHS Trust London, Paediatrics and Genitourinary Medicine, London, United Kingdom

Introduction: Individuals with perinatally acquired HIV-1 infection are surviving into adulthood with improved combination antiretroviral therapy (cART). HIV-1 infection is associated with immunosenescence, although the impact of cART and the long-term clinical effects of such ageing are not yet understood. Reduced CD4/8 ratio was identified as part of an immune risk profile (IRP) associated with mortality in aged individuals, especially men, in large cohorts untested for HIV-1 (Wikby et al 2008). We hypothesized that an indicator of detrimental immune ageing; CD4/8 ratio <1 would be observed in young adults with perinatally acquired HIV-1 infection, even in those on effective combined antiretroviral therapy (cART) with suppressed viral load (VL<50 copies RNA/ml).

Material & Methods: Data were accessed from the electronic records of the Imperial College Healthcare NHS Trust '900 clinic'. This clinic provides clinical care for young adults aged 18ys+ with perinatally acquired HIV infection. The data were coded and anonymised prior to analysis in accordance with National Research Ethics guidance on accessing and researching data collected for clinical purposes. CD4/8 ratios were calculated using absolute CD4 and CD8 cell values reported by the local accredited Clinical Pathology laboratory. Data were analysed using IBM SPSS version 22 for Windows. Appropriate statistical testing was used following tests for normality.

Results: N=124 were included in the final analysis. There were 64 (51.6%) females and 60 (48.4%) males and the majority, 78 (62.9%) were of Black African origin. 97 (78.9%) were on cART of whom 80 had HIV-1 VL <50 RNA copies/ml. Mean age for women was 23.3ys (22.6-24.1) and for men was 22.6ys (21.9-23.3), p=0.155. Mean CD4/8 ratio for all women was 0.77 (0.64-0.89) and for men was 0.74 (0.61-0.86), p=0.753 and for those on cART was 0.85 (0.70-1.00) and 0.77 (0.62-0.92), respectively, p=0.877. Of the 97 individuals taking cART, 67 (69.1%) had a CD4/8 ratio <1. In those on cART no sex- or regimen-(protease inhibitor vs. non protease-inhibitor) related differences in the proportion of individuals with a CD4/8 ratio<1 were found on univariate analysis (p=ns). The greatest proportion of females on treatment had VL<50 and CD4/8 ratio <1 (25/48), although this was not statistically significant (p=0.469). No males on treatment had a VL≥50 and CD4/8 ratio ≥1.0 (p=0.009).

Conclusions: We found a high proportion of individuals with treated HIV-1 infection with CD4/8 ratio <1, even in those on cART. Previously published work in aged HIV-1 uninfected cohorts suggested the IRP, including the reduced CD4/8 ratio, to pertain particularly to men. Although we did not find any sex-related differences in our cohort, a significant proportion of both young men

and women had suppressed CD4/8 ratios despite effective cART. Resolving the complex effects of chronic HIV-1 infection and social and demographic factors on immune ageing was beyond the scope of this work. Our findings however indicate the potential that premature immune ageing is occurring in this cohort and warrant further more detailed immunological analysis.

No conflict of interest

Abstract: 33

Older HIV-infected Hispanics are at Increased Risk for Neurocognitive Impairment

M. Marquine[1], D.J. Moore[1], D. Byrd[2], M. Rivera-Mindt[3], M. Cherner[1], D.J. Jeste[1], R. Ellis[4], S. Letendre[5], R.K. Heaton[1]

[1]University of California San Diego, Psychiatry, San Diego, USA; [2]Mount Sinai Hospital, Neurology and Psychiatry, New York, USA; [3]Fordham University, Psychology, Bronx, USA; [4]University of California San Diego, Neurosciences, San Diego, USA; [5]University of California San Diego, Medicine, San Diego, USA

Background: Hispanics are disproportionally affected by HIV/AIDS, especially in the older age ranges. Despite availability of more effective antiretroviral therapy (ART), HIV-associated neurocognitive (NC) impairment remains common. The limited data available indicate that HIV-infected (HIV+) Hispanics are at increased risk for NC impairment compared to HIV+ non-Hispanic Whites, particularly among older cohorts. Yet, Hispanics are a very heterogeneous group, and prior work has focused on HIV+ older Hispanics living in the northeastern United States (U.S.), who were primarily of Caribbean descent. The purpose of the present study was to investigate ethnic differences in NC function between older HIV+ non-Hispanic Whites and Hispanics of primarily Mexican descent.

Materials & Methods: HIV+ English-speaking adults aged 50 or older, who participated in cohort studies at the UC San Diego HIV Neurobehavioral Research Program were included in the present study (years of age: *M*=57.7, *SD*=6.2; years of education: *M*=13.1, *SD*=2.3; 95% male; 83% AIDS; 94% on ART; current CD4: *Median*=489, *IQR*=325-682; 17% with detectable plasma HIV RNA). Participants included 20 individuals who self-identified as Hispanic, and 40 non-Hispanic Whites, who were matched two-to-one to Hispanics on age, gender and years of education. NC function was assessed via the NIH-Toolbox Cognition Battery (NIH-TB CB), which has extensive normative data for Hispanics and non-Hispanic Whites. Possible covariates that were considered included estimates of quality of education/premorbid functioning (NIH-TB CB Oral Reading), HIV disease characteristics (estimated duration of infection, AIDS status, nadir and current CD4, ART status, and detectable HIV RNA in plasma and CSF), and psychiatric comorbidities (current mood, and current and lifetime history of major depressive and substance use disorders). To investigate ethnic group differences in NC performance, we conducted two types of analyses on the NIH-TB CB Fluid composite T-scores and the individual test scores comprising this composite. Initially, we contrasted ethnic groups via a series of separate independent sample t-tests. We then conducted linear regression models adjusting for covariates that differed between the groups (p<.10).

Results: Results from independent sample t-tests showed that Hispanics performed significantly worse on the Fluid composite (*Mean T*=40.2, *SD*=10.0) than non-Hispanic Whites (*Mean T*=49.2, *SD*=10.1, p<.01). Analyses on individual tests indicated Hispanics scored significantly lower on the Flanker Inhibitory Control and Attention test (Hispanics: *Mean T*=38.3, *SD*=14.8; non-Hispanic Whites: *Mean T*=50.7, *SD*=10.6, p<.01), Pattern Comparison (Hispanics: *Mean T* =43.06, *SD*=10.8; non-Hispanic Whites: *Mean T*=50.9, *SD*=12.5, p=.02), and Picture Sequence Memory test (Hispanics: *Mean T*=41.4, *SD*=5.4; non-Hispanic Whites: *Mean T*=46.1, *SD*=9.2, p=.02). Results from multivariable models adjusting for significant covariates (i.e. oral reading and lifetime substance use disorder) yielded similar findings.

Conclusions: Older HIV-infected Hispanics may be particularly vulnerable to NC impairment compared to their non-Hispanic White

counterparts. These ethnic differences do not appear to be driven by lower quality of education or premorbid functioning, worse HIV disease characteristics, or psychiatric comorbidities. Future studies aimed at identifying biomedical and psychosocial factors driving these ethnic differences are key for the development of targeted, culturally-relevant interventions to prevent and/or ameliorate NC dysfunction in this vulnerable segment of the HIV+ U.S. population.

No conflict of interest

Abstract: 34

Recognition of cognitive impairment by community health care professionals to identify at risk patients for referral and assessment?

D. Cummins[1], D. Waters[1], C. Aggar[1], C. O'Connor[2]

[1]University of Sydney, Sydney Nursing School, Sydney, Australia; [2]Community Health Sydney Local Health District, Sexual Health Service, Sydney, Australia

Introduction: HIV associated Neurocognitive Disorder (HAND) can cause disability and affect a person's quality of life. HAND is difficult to identify as signs and symptoms (S&S) are nonspecific. Early cognitive impairment is often displayed by changes in behaviour and is generally detected in the early stages by informal caregivers. People living with HIV (PLHIV) may not have an informal caregiver who may notice subtle cognitive changes. Two unique specialist HIV community teams based in Sydney, Australia provide case management, clinical care and support to PLHIV. In the absence of an informal caregiver, team members may be an alternate caregiver and are well placed to notice cognitive changes during home visits and initiate early referral for assessment.
Aim: to ascertain which patient characteristics and risk factors are collected to assist with identifying PLHIV at risk of HAND.

Method: A questionnaire and file audit collected data from community multidisciplinary HIV specialist programs based in Sydney to ascertain patient characteristics, identify patients who may be at increased risk of cognitive changes and to inform gaps in data collection.

Results: Combined data from both teams had a total of 262 patients. Ninety one per cent (n=238) were male, 8% (n=21) female and 1% (n=3) transgender. The average age was 51 years (sd 11.09). Seventy one per cent (n=186) identified as gay, 61% (n=160) lived alone, and 33% (n=86) did not have an informal caregiver. Forty six per cent (n=120) were referred for case management. The average duration of HIV infection was 15 (sd 8.965). There was a large amount of data not captured by the specialist HIV community teams, particularly T cell nadir (91%, n=238), a key predictor of cognitive impairment. Viral load 38% (n=99), T cell count 33% (n=86), year of diagnosis 23% (n=60), prescribed antiretrovirals 15% (n=39), hyperlipidaemia 44% (n=115), diabetes 43% (n=113), hypertension 42% (n=110), high cholesterol 41% (n=107), HCV 22% (n=58), informal caregiver 19% (n=50) and those living alone 14% (n=37) were also substantial missing data. In addition, 76% (n=199) of patients were prescribed antiretroviral drugs but only 53% (n=105) had medication documented. Much of the documented data was provided by the patient rather than a clinician or HIV specialist, impacting on validity of information. A total of 20% (n=52) of PLHIV audited were at risk of HAND; that is they were aged 45 years or older, gay, lived alone and had no identified informal caregiver.

Conclusion: Community HIV teams are well placed to recognise cognitive changes in their patients. Collection of information regarding PLHIV is important to assist clinicians to identify people at increased risk of HAND. Improved documentation processes are required. A tool needs to be developed to allow systematic identification of those at risk. This could lead to early referral and recognition of HAND and improved health outcomes and well being for PLHIV.

No conflict of interest

Abstract: 35

Changes in renal biomarkers following tenofovir discontinuation in aging HIV-infected viral-suppressed patients, Montreal, Canada

A. Talbot[1], C. Laprise[1], L.P. Vezina[1], S. Dufresne[1], P. Côté[1], B. Lessard[1], F. Laplante[1], R. Pilarski[1], D. Tessier[1], M.E. Turgeon[1], E. Sasseville[1], J.G. Baril[1]

[1]Clinique du Quartier Latin, Family Medicine, Montreal QC, Canada

Introduction: Despite the fact that many studies have evaluated risk factors for chronic kidney disease (CKD), few studies have investigated the role of different renal biomarkers in the development of CKD in HIV-infected patients, and their use in the prevention of progressive CKD. As studies have shown that tenofovir disoproxil fumarate (TDF) is associated with CKD, clinicians from the Clinique médicale du Quartier Latin in Montreal, Canada, developed an investigational kidney algorithm to help physicians standardize the monitoring of kidney biomarkers for HIV-infected patients using TDF as part of their highly active antiretroviral theray (HAART). Our objective was to compare the changes in the algorithm renal biomarkers before and after TDF discontinuation, in an aging and virologically-supressed population.

Methods: This is a retrospective chart review of patients from the HIV-positive cohort of the Clinique Médicale du Quartier Latin, Montreal, Canada, under active care between May 1, 2012 and November 30, 2014. To be selected, patients had to be exposed to TDF and to discontinue it during the study period, have a suppressed viral load <200 copies/ml in the last 12 months before TDF discontinuation, and have a complete panel of algorithm renal biomarkers before and after TDF discontinuation The algorithm renal biomarkers included: serum phosphates (PO_4); urine PO_4 level; calculation of the fraction of excretion of PO_4 ($FePO_4$); proteinuria, glycosuria on urianalysis; and protein/creatinine ratios on urine spot . Wilcoxon signed-rank test and McNemar test were used to compare changes in the algorithm renal biomarkers before and after TDF discontinuation.

Results: Of the 1,442 patients followed at the clinic during the study period, 875 received TDF and 123 patients discontinued TDF. Finally, 28 patients met our inclusion criteria. Twenty-seven of the 28 patients were male with a mean age of 55 years old (standard deviation: 7.6), a median time of HIV infection of 14.6 years (Interquartile range (IQR): 11.4-20.5) and received a median of 48 months (IQR: 20.8-70.5) of TDF prior to TDF discontinuation.
In the background regimens prior to TDF discontinuation, 18 patients received ritonavir-boosted protease inhibitors, 10 non-nucleoside reverse-transcriptase inhibitors and 5 integrase inhibitors. Before TDF discontinuation, the median CD_4 cell count was 555 cells/µL (IQR: 385-835).
All 28 patients had abnormalities in 1 renal biomarker, and 26 had at least 2 abnormal biomarkers. Median estimated glomerular filtration rate was 65 ml/min/1.73m^2 (IQR: 54-84) prior to TDF discontinuation and 69 ml/min/1.73m^2 (IQR: 54-84) after TDF discontinuation (p=0.2689).
A statistically significant change was observed only for the protein/creatinine ratio, with 0.045 g/mmol before and 0.014 g/mmol after TDF discontinuation (p<0.001). The protein/creatinine ratio measurements were taken at a median time of 5 months after TDF discontinuation.

Conclusion: According to an analysis confined to these 28 patients, the protein/creatinine ratio seems the most reversible biomarker of tubulopathy in the short term for aging, TDF-exposed patients. Further studies are necessary to evaluate the protein/creatinine ratio as a potential screening tool for sub-clinical tubulopathy in HIV-infected patients exposed to tenofovir.

Conflict of interest
financial relationship(s): I received research grant from ViiV and speaker grant from Merck, BMS and AbbVie . My husband is working as a Global Medical Director at ViiV.

Abstract: 36

Retrospective analysis of concomitant diseases in HIV patients

S. Toropov[1], S.A. Buzunova[1], A.A. Sizov[1], S.A. Bykov[1], S.S. Valikhova[1], V.V. Rassokhin[1]

[1]AIDS CENTER, Clinical Pharmacy and Pharmacology, St. Petersburg, Russia

Introduction: With account of the potency of currently used highly active antiretroviral therapy HAART regimens, the conditions of HIV patients must increasingly depend on concomitant diseases and the conventional risk factors of their development. In Russia, HIV patients who are older than 40 years show manifestations of premature aging associated with increased risks of metabolic disorders and deadly heart diseases, altered mineralization of bones, and compromised glomerular filtration. Therefore, the objective of the present study was to assess concomitant diseases and metabolic alterations in HIV patients aged above 40.

Materials and methods: A retrospective analysis of medical records of 589 HIV-infected patients from different regions (St. Petersburg, Rostov, Novosibirsk) was performed. Inclusion criteria: age over 40 years, receiving HAART. We estimated metabolic parameters, 10-year risk of fatal cardiovascular disease (with use of SCORE scale), glomerular filtration rate, 10-year risk of fracture (FRAX).

Results: Average duration of receiving HAART was 4.9 years. By the beginning of a period under evaluation, each patient received HAART for 4.9 years on average. A Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) was given to 43%, protease inhibitors (PI) to 43%, Raltegravir to 9%, Enfuvitride to 2%, and Maraviroc to 0.1% of the patients. Reduced viral loads were detected in 458 patients (81%). In 107 patients (19%) HIV replication continued. In 212 patients (36%), CD4 cell counts were $< 350 \acute{} 10^6$ L^{-1}. Prevalence of arterial hypertension was 45%, ischemic heart disease 9%, myocardial infarction 9%, stroke 3%, familial predisposition to heart disease 17%. Prevalence of excessive body mass 49%, normal 42%, decreased 9%; disorders of lipid metabolism 34%, diabetes mellitus 34%, obesity and metabolic syndrome 23%. Prevalence of smoking was 55%, daily alcohol intake 11%, abstinence of alcohol - 15%. Prevalence of high or very high 10-years risk of deadly cardiovascular diseases was 28%. Prevalence of proteinuria and increased glomerular filtration rate were 12% and 98%, respectively, suggesting the presence of risk factors of renal disorders. Because other drugs, besides ARV, were taken by 37% of the patients to treat concomitant diseases, the problem of drug metabolism and adverse drug interactions is relevant. Prevalence of patients with high risk of fracture within 10 years (osteoporosis) was 24% and moderate risk (osteopenia) - 48% makes osteoporosis.

Conclusion: The high risk of cardiovascular diseases and the low mineral density of bones in HIV patients warrant an optimization of HAART by using modern safe drugs and additional therapeutic and preventive measures. The high levels of smoking and alcohol drinking are additional modifiable risk factors, which must motivate health care providers to encourage patients to turn to healthier lifestyles. A high level of involvement of HIV patients in HAART does not necessarily mean that immunosuppression and HIV replication are controlled. In assessing HAART, it is not enough to take HIV RNA and CD4 cells into account. It is necessary to assess patient conditions with regard to risk factors of concomitant pathologies.

No conflict of interest