P487

Neurocognitive Screening Tests Are Associated with Cardiovascular Risk and VACS scores

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ABSTRACT

Background: HIV-associated neurocognitive disorders (HAND) are still highly prevalent despite effective antiretroviral treatment; several associated factors have been identified including cardio- e cerebrovascular risk factors. Despite the recommendation to perform screening neurocognitive (NC) tests in all HIV-positive patients there is still uncertainty regarding the optimal tools as well as the selection criteria.

Methods: In adult HIV-positive patients cardiovascular risk assessment [5-year D:A:D (DAD5) and 10-year Progetto Cuore (Cuore10) risk scores], mortality risk (VACS-index) as well as screening NC tests (IHDS, Clock Drawing Test, Frontal Assessment Battery) were performed. Patients with IHDS below 10 received a full NC testing by a trained neuropsychologist. Data are expressed as average (± standard deviation, SD) and parametric tests were used for all analysis (Pearson's test for continuous variables).

Results: 441 patients (78% male, 95.4% Caucasian) were enrolled. Age, BMI and eCRCL were 48 years (±11.5), 24.8 kg/m2 (±4.1) and 81.9 ml/min (±19.5) respectively. Average current and nadir CD4 were 538 cell/uL (±309) and 219 (±177); out of 407 patients on treatment (91.7%), 289 (71%) showed HIV RNA below 50 copies/mL.

Average DAD5 and Cuore10 were 3.2% (±3.8%) and 5.5% (±9%) and respectively 3.9% and 5.1% of patients fell in the high-risk strata (>10% and >20%, respectively). VACS index was 27.5 (±16.9). Average IHDS, Clock and FAB scores were 10.6 (±1.3), 1.28 (±1.25), 15.4 (±2); they were abnormal in 87/422 (20.6%), 88/354 (24.9%) and 13/101 patients (12.9%) respectively. IHDS scores were associated with clock (r=-0.15, p=0.007) and FAB scores (r=0.583, p<0.001); they were also significantly associated with VACS (r=-0.417, p<0.001), DAD5 (r=-0.333, p<0.001) and Cuore10 (r=-0.276, p<0.001) risk scores. With increasing DAD5 risk profiles patients presented higher prevalence of altered IHDS: 14.1% (low risk), 32.7% (intermediate risk) and 57.1% (high risk). Similar results were observed with Cuore10 risk strata (both for IHDS and FAB tests).

Conclusions: A significant proportion of HIV-positive efficaciously treated patients present altered neurocognitive screening tests (12.9% to 24.9%); this prevalence increases significantly in patients with high cardiovascular risk (28.6% to 57.1%). Beyond supporting the possible influence of cardio- and cerebrovascular abnormalities in HAND, these data suggest to screen for neurocognitive disorders patients with high cardiovascular risk profile.

INTRODUCTION

- HIV infects perivascular macrophages, microglial cells and astrocytes in the central nervous system: this may lead to neuronal damage through the production of several cytokines and mediators;
- Despite the neat reduction in cases of dementia after the introduction of HAART a significant proportion of patients may develop neurocognitive ("NC") disorders ("HAND");
- The Italian Guidelines suggest to screen HIV+ patients for cognitive and psychiatric disturbances;
- The exact prevalence and the exact pathogenesis of such disturbances are still debated: the latter may be multifactorial and beside virus-related factors (persistent viral replication, immune activation, CD4 cell count at nadir) age, comorbidities, co-infections (including HCV) and, potentially, neurotoxicity of ARVs must be considered;
- Neurocognitive disorders are more common in patients with diabetes and cardio/cerebro- vascular diseases; furthermore advanced MRI studies showed perfusion impairment in HIV-positive asymptomatic subjects.

AIM OF THE STUDY

To assess the prevalence of altered NC screening tests stratified by CVR scores in unselected HIV+ patients

MATERIAL & METHODS:

Prospective (baseline data), observational study;

Unselected adult HIV-positive patients undergoing a screening visit for neurocognitive and cardiovascular abnormalities.

Visits include:

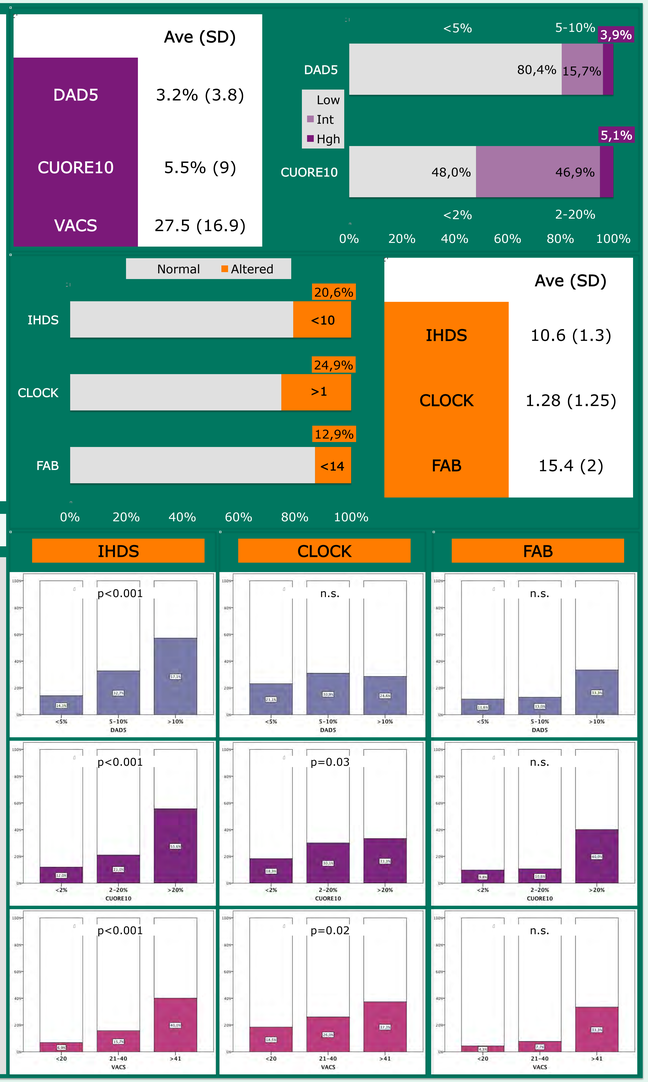
- Detailed history and physical examination
- anthropometric measures (height, weight, abdominal circumference)
- blood pressure
- 12 lead ECG
- IMT (carotid ultrasound)
- IHDS: motor speed, psychomotor speed, memory-recall
- Clock drawing test (CLOCK): global function, visuo-spatial and executive functions
- Frontal assesment battery (FAB): global function, fronto-temporal functions
- Calculation of 10 year Progetto cuore (Cuore10) and 5 year D:A:D: (DAD5) rand VACS scores. Calculation of FIB-4 (non invasive hepatic fibrosis).

Patients are then referred to a multidisciplinary team including cardiologists and nutritionists (if in the high risk strata) and/or to neuropsychologist for complete NC tests (NPZ-8, if IHDS<10 and/or clock>1 and/or FAB<14); longitudinal data will be recorded as for CV and NC events.

Data are expressed as average (± standard deviation, SD) and parametric tests were used for all analysis (Pearson's test for continuous variables).

RESULTS (n=441)

gender (male: n, %)	344	78%	estimated CrCl ml/min (ave, SD)	81.9	19.5
ethnicity (Caucasian: n, %)	421	95.5%	HCV-positive n (%)	110	24.8%
age years (ave, SD)	48	11.5	HIV RNA <50 cps/mL n (%)	140	60.9%
BMI Kg/m² (ave, SD)	24.8	4.1	CD4+ T Lymphocytes n/uL (ave, SD)	538	309
Diabetes n (%)	22	6.1%	CD4+TLs at nadir mg/dL (ave, SD)	219	177
Smoking n (%)	244	55%	On HAART n (%)	407	91.7%
Total Chol >190 mg/dL n (%)	194	54%	Third drugs PI	175	43.5%
HDL Chol <39 mg/dL n (%)	137	38.2%	Third drugs NNRTI	157	39.1%
Antihypertensive drugs n (%)	94	26%	Third drugs RAL	78	19.4%
Statins n (%)	56	15.5%	Third drugs MVC	14	3.5%
			Low dose aspirin n (%)	26	7.2%



PREDICTORS OF ALTERED SCREENING TESTS

	Univariate	*Multivariate*
IHDS	Age, BMI, abdominal circumference, smoking habit, diabetes, previous CV events, anxiety, high FIB-4 and nadir CD4 below 200 cells/mm³	**Age** **Smoking** **Diabetes**
CLOCK	Age, female gender, hyper total cholesterol, high FIB-4, HCV Ab+, alcohol abuse, arterial hypertension	**Age** Female gender
FAB	Age, BMI, smoking, hypo HDL cholesterol, alcohol abuse, anxiety, previous siphilis, plasma HIV RNA >50 copies/mL	**Smoking** **BMI** Alcohol abuse

CONCLUSIONS and DISCUSSION

- We reported the results of neurocognitive performance screening test in a large cohort of HIV-positive patients; **20-24%** had abnormal results and full NC testing was planned (still ongoing).
- In this cohort or relatively young patients (with highly prevalent risk factors) a high CV risk was observed in **3.9%** (>10% at 5 years, D:A:D) and **5.1%** (>20% at 10 years, Progetto Cuore).
- Patients with high CV risk had a higher chance of having abnormal IHDS and CLOCK tests but not FAB:
  - The different explored areas (excluding psychomotor speed, shared by IHDS and FAB) may explain this observed difference;
  - This observation is in agreement with several other data showing a higher prevalence of HAND in patients with diabetes and cardio/cerebrovascular disease;
- CV risk factors (Age, BMI, smoking habit, diabetes) and others (female gender, alcohol abuse) are associated with these abnormalities.
- Neurocognitive screening evaluations may be prioritized in patients with high cardiovascular risk.
  - The effect of optimal management of CV risk factors (blood pressure, total cholesterol, etc.) on neurocognitive performance in HIV-positive patients need to be evaluated in prospective studies.

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