CD4+/CD8+ ratio matters to age related health outcomes in HIV infected patients with comorbidities, frailty and disability.

Marianna Menozzi

Stefano Zona

Clinica delle Malattie Infettive, AUO Policlinico di Modena

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Prevenzione e gestione delle co-morbidità associate all'infezione da HIV

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

HIV EPIDEMICS IS CHANGING

Projected life expectancy of people with HIV according to timing of diagnosis

Fumiyo Nakagawa[a], Rebecca K. Lodwick[a], Colette J. Smith[a], Ruth Smith[b], Valentina Cambiano[a], Jens D. Lundgren[c,d], Valerie Delpech[b] and Andrew N. Phillips[a]

AIDS 2012, **26**:335–343

- Currently, about 50% of infected person in high-income countries are older than 50, with similar proportionate increases noted in non-industrialized countries.
- With this increase in life span, there is now a risk of developing chronic diseases associated with advanced age.

The AGING PROCESS is often accompanied by chronic comorbid conditions frequently associated in complex pictures so called multimorbidity; altered functional status and frailty.

[Nobili A.. J Comorbidity 2011; 1:28–44].

Frailty

"A state of vulnerability to poor resolution of homoeostasis after a stressor event" as a "consequence of cumulative decline in many physiological systems during a lifetime"

[Clegg et al, 2013]

Disability

"Successful aging" includes both disease burden and the ability to maintain functional status and independence

Frailty and HIV

A frailty index predicts survival and incident multimorbidity independent of markers of HIV disease severity

Giovanni Guaraldi[a], Thomas D. Brothers[b], Stefano Zona[a], Chiara Stentarelli[a], Federica Carli[a], Andrea Malagoli[a], Antonella Santoro[a], Marianna Menozzi[a], Chiara Mussi[c], Cristina Mussini[a], Susan Kirkland[d], Julian Falutz[e] and Kenneth Rockwood[f]

AIDS 2015, **29**:1633–1641

Frailty and HIV

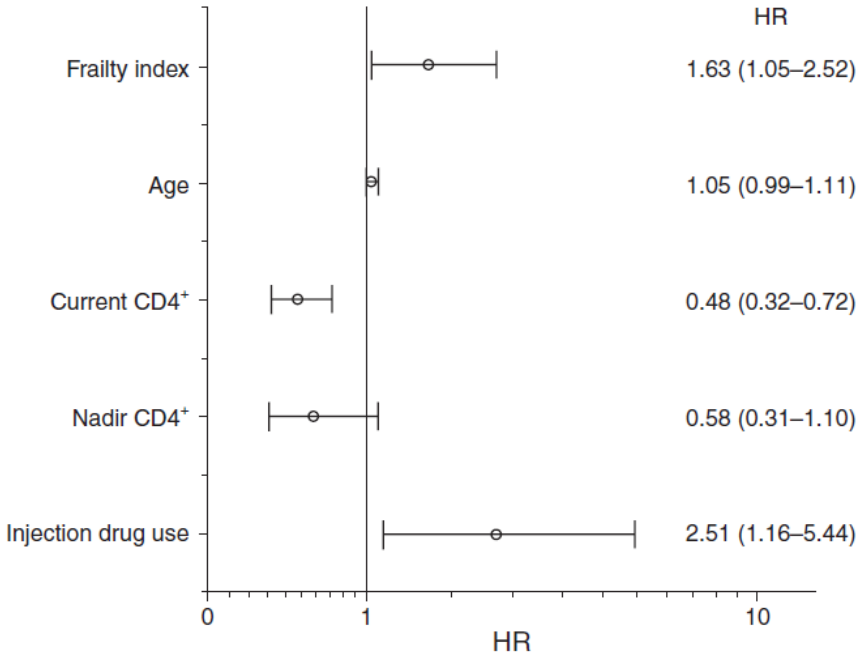


Fig. 1. Predictors of survival in multivariate analysis. Points represent adjusted HRs and whiskers 95% confidence intervals. HR, hazard ratio.

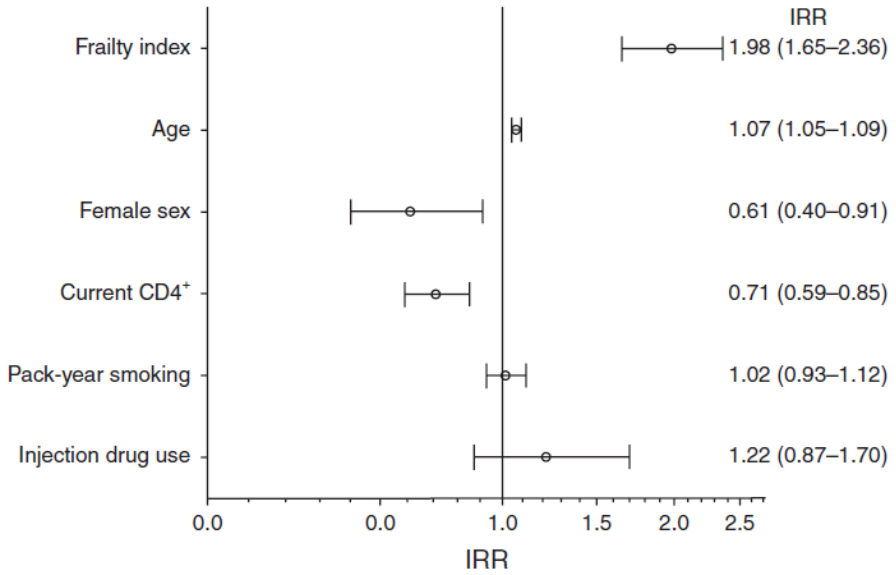


Fig. 2. Predictors of incident multimorbidity in multivariate analysis. Points represent adjusted IRRs and whiskers 95% confidence intervals. IRR, incident rate ratio.

AGING, IMMUNE SYSTEM & FRAILTY

THE ROLE OF IMMUNOSENESCENCE IN THE DEVELOPMENT OF AGE-RELATED DISEASES

ıs FÜLÖP[1*], GILLES DUPUIS[2], JACEK M. WITKOWSKI[3] AND ANIS LARBI[4]

Rev Inves Clin. 2016;68:84-91

Inversion of the CD4:CD8 ratio (<1) has been identified as a hallmark of immunosenescence and an independent predictor of mortality in the general population.

In HIV-uninfected adults, CD4+/CD8+ ratio increases over the lifespan, and inversion of the CD4+/CD8+ ratio in the elderly has been associated with risk of frailty and chronic viral infections, such as cytomegalovirus

[Castilho et al]

Aim

- The aim of this study was to describe associations between a clinical markers of immune activation (CD4/CD8 ratio) and meaningful clinical endpoints of ageing (Multimorbidity, Frailty and Disability) in HIV patients attending the Modena HIV Metabolic Clinic.

Methods

- Cross sectional study
- Modena HIV Metabolic Clinic
- Inclusion criteria
  - Age >18 years
  - Documented HIV infection
  - Being on ARV treatment from at least 6 months
  - Access in MHMC within 2008 and 2016
  - HIV viral load <40 copies/ml
- Data Collection
  - Anthropometric and Epidemiologic characteristics
  - Bioumoral examination: CD4/CD8 ratio
  - Comorbidities assessment (charts and anamnestic)
  - Frailty assessment (Frailty Index)
  - Disabilty assessment (IADL and/or SPPB and/or FALLS) (if available)

Methods

- CD4CD8 ratio cut-off: 0.8 (median value and literature data)
- Multimorbidity (MM) defined as presence of at least 3 comorbidities among: cardiovascular events, chronic kidney disease, hypertension, chronic obstructive pulmunary disease, cancer and diabetes mellitus.
- Frailty (FI) defined as Frailty Index value above 0.31 (median value and literature data)
- Disability (D) defined as:
  - Presence of at least 1 deficit at IADL questionnaire
  - SPPB score <9
  - Falls assessment within the last year

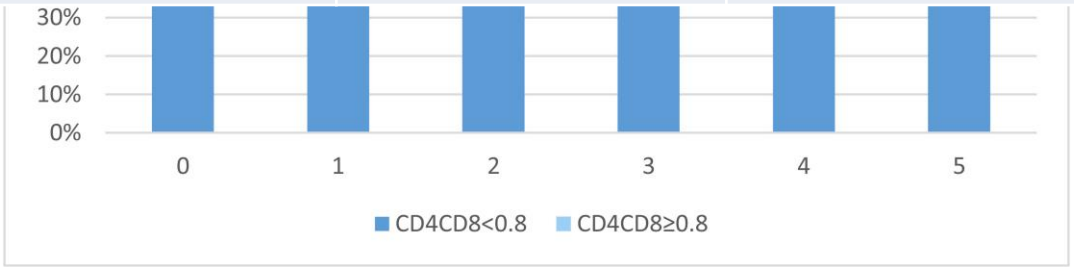
Results

Variable	CD4/CD8 ratio <0.8	CD4/CD8 ratio ≥0.8	P value
	N(%) or median(IQR)	N(%) or median(IQR)	
Total number of patients	1470 (49)	1475 (51)	
Anagraphic and anthropometric characteristics			
Female Sex	391 (26.6)	550 (37)	<0.001
Age	49 (45-54)	50 (45-54)	0.9
Smokers	775 (53)	854 (58)	0.004
Packyear (if smoker)	20.8 (10-32)	17.9 (9.3-30)	0.004
Physical activity			0.162
No activity	717 (49)	665 (45)	
1-3 times/week	549 (37)	606 (41)	
>3 times/week	132 (9)	126 (8.5)	
Alcohol intake			0.923
No alcohol	841 (57)	830 (56)	
Mild	538 (37)	546 (37)	
Intense	14 (0.9)	16 (1.1)	
BMI	23.8 (21-26)	23.3 (21-25.7)	0.001
Biohumoral characteristics			
LDL cholesterol	113 (91-137)	112 (92-136)	0.791
HDL cholesterol	45 (37-57)	51 (41-62)	<0.001
Total cholesterol	188 (161-26)	189 (165-217)	0.352
Glucose	94 (86-103)	93 (87-102)	0.451
25OH-Vitamin D	25.2 (18-32)	27 (20-32)	0.223
GOT	24 (20-34)	23 (19-31)	<0.001
HOMA index	2 (1.2-3)	1.7 (1.1-2.8)	<0.001
C Reactive Protein	0.2 (0.13-0.3)	0.2 (0.18-0.22)	0.262

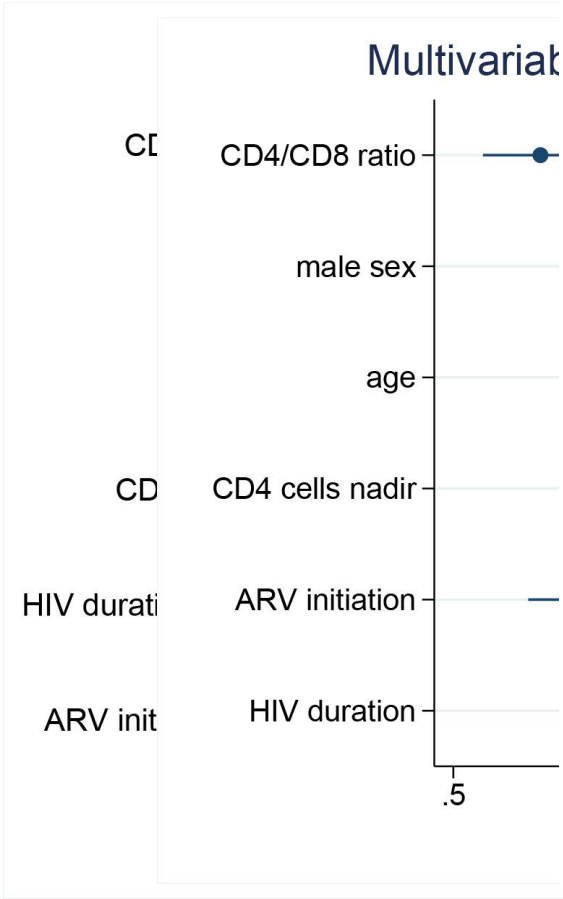
Variable	CD4/CD8 ratio <0.8	CD4/CD8 ratio ≥0.8	P value
	N(%) or median(IQR)	N(%) or median(IQR)	
HIV characteristics			
HIV duration (months)	241 (158-299)	239 (156-299)	0.427
Risk Factor			<0.001
IDU	409 (28)	357 (24)	
MSM	453 (31)	407 (27.5)	
Heterosexual	431 (29)	557 (37.8)	
Other	177 (12)	154 (10)	
CDC C	375 (25.5)	305 (20.7)	0.005
Age at ARV initiation	36 (31-43)	36 (31-42)	0.0052
ARV initiation period			0.106
Pre HAART	437 (30.4)	397 (27.4)	
Early HAART	637 (44)	696 (48)	
Late HAART	363 (25)	358 (24.7)	
CD4 cells nadir	163 (60-260)	221 (109-330)	<0.001
CD4 cells count	530 (392-708)	760 (601-951)	<0.001
CD8 cells count	1024 (775-1336)	662 (505-853)	<0.001
CD8CD38 cells count	84 (51-152)	58.5 (38-94)	<0.001
HCV coinfection	443 (36%)	400 (32)	0.027

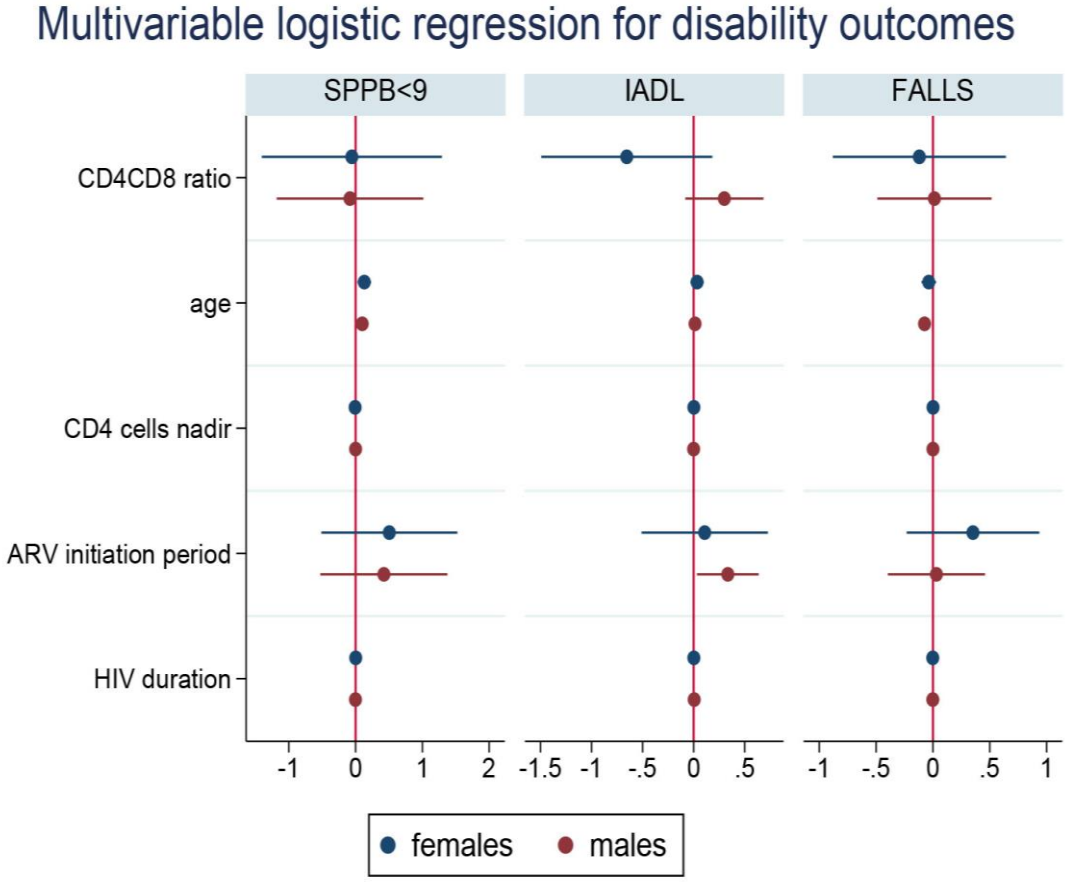
Results

Variable	CD4/CD8 ratio <0.8	CD4/CD8 ratio ≥0.8	P value
	N(%) or median(IQR)	N(%) or median(IQR)	
Age Related Health Outcomes			
Multimorbidity (2945 pts)	90 (6.1)	55 (3.7)	0.003
Multimorbidity & Frailty (1299 pts)	66 (9.1)	35 (6.1)	0.040
Frailty (2643 pts)	722 (54.8)	577 (43.5)	<0.001
IADL (830 pts)	94 (25.3)	118 (25.7)	0.903
SPPB<9 (459 pts)	13 (6.28)	15 (5.95)	0.884
FALLS_yn (665 pts)	57 (19.6)	76 (20.3)	0.815



Logistic regression models: Age Health Related Outcomes





Discussion

- We demonstrated an independent association between routinely performed markers of immune reconstitution and the most important clinical features of patients aging with HIV (lower CD4/CD8 ratio is associated to comorbidities alone or aggregated in multimorbidity and frailty).

Discussion

- Longitudinal studies are needed to assess changes in multimorbidity and frailty according to pathological or physiological CD4/CD8 movements during life.
- Interventional studies may be useful to monitor immunological to clinical relations, trying to lower immune activation (ARV strategies? Co-medication effect?).

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