Progression of liver disease, access to HCV treatment with direct acting antivirals and eradication rate according to sex in HIV/HCV coinfected patients in Italy

Barbara Rossetti[1,2], Patrizia Lorenzini[3], Antonella Cingolani[2], Alessandro Tavelli[4], Massimo Puoti[5], Ilaria Mastrorosa[3], Andrea Gori[6], Sergio Lo Caputo[7], Roberto Rossotti[5], Andrea Antinori[3], Antonella d'Arminio Monforte[8], Andrea De Luca[1,9] on behalf of ICONA Foundation study group

1 Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy; 2 Clinic of Infectious Diseases, Catholic University of Sacred Heart, Rome, Italy; 3 Infectious Diseases Department, INMI "Lazzaro Spallanzani", Rome, Italy; 4 ICONA Foundation, Milan, Italy; 5 Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; 6 Infectious Diseases Clinic, ASST di Monza, San Gerardo Hospital-University of Milano-Bicocca, Monza, Italy; 7 University of Bari, University Hospital Policlinico, Bari, Italy; 8 ASST Santi Paolo e Carlo, University of Milan, Clinic of Infectious and Tropical Diseases, Department of Health Sciences, Milan, Italy; 9 Department of Medical Biotechnologies, University of Siena, Italy

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BACKGROUND

Previous reports from ICONA cohort showed

- Declining prevalence of HCV infection in HIV+ pts entering care from 49% in 1997-2002 to 10% in 2009-2015
- HIV/HCV co-infection more frequent in females and in Italian natives
- Declining relative frequency of genotype 3 in co-infected patients, though less in females
- Increasing frequency of genotype 1a, mainly driven by younger patients and MSM

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OBJECTIVES

Aims of the study were:

- to describe concordance of liver fibrosis estimated by different non invasive methods
- to assess predictors of severe liver fibrosis as assessed by different non invasive methods
- to verify access to HCV treatment with direct acting antivirals (DAA) and virological response in HIV/HCV DAA-naïve patients enrolled in ICONA and HepaICONA cohorts, focusing on gender

METHODS

- HIV-1 infected, HCVRNA+, DAA-naïve patients were enrolled from Icona and HepaICONA cohorts from 1997 to 2017
- Liver fibrosis was assessed by FIB-4 index, APRI score and Transient Elastography (TE)
- DAA treatment failure was defined as an HCV RNA+ after 12 weeks of DAA-containing regimen completion
- Qualitative agreement between FIB-4 and TE, APRI and TE was assessed by kappa statistics
- Predictors of liver fibrosis, DAA treatment access and DAA failure were investigated by logistic regression

RESULTS

Table 1. Baseline characteristics (N=2,814)

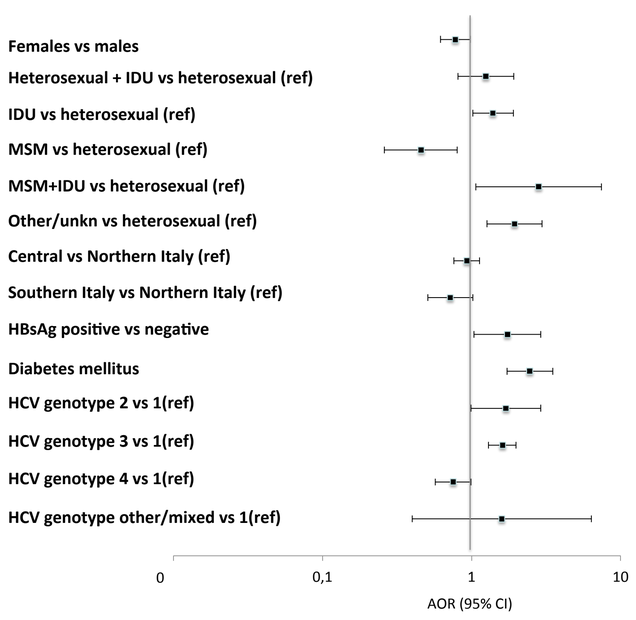
		Overall	Males (n=2071, 73.6%)	Females (n=743, 26.4%)	p
Age, years, median (IQR)		52 (48-55)	53 (49-56)	51 (47-54)	<0.001
Mode of HIV transmission, n(%)					
	Heterosexual contacts	350 (12.4%)	164 (7.9%)	186 (25.0%)	<0.001
	Hetero +IDU	250 (8.9%)	138 (6.7%)	112 (15.1%)	
	IDU	1,769 (62.9%)	1389 (67.1%)	380 (51.1%)	
	MSM	222 (7.9%)	222 (10.7%)	0	
	MSM+IDU	20 (0.7%)	20 (1.0%)	0	
Natives, n(%)		2.660 (94.5%)	1984 (95.8%)	676 (91.0%)	<0.001
Area of residence, n(%)					
	Northern Italy	934 (33.2%)	685 (33.1%)	249 (33.5%)	<0.001
	Central Italy	1,601 (56.9%)	1209 (58.4%)	392 (52.8%)	
	Southern Italy	279 (9.9%)	177 (8.5%)	102 (13.7%)	
HBsAg positive, n(%)		83 (3%)	70 (3.4%)	13 (1.8%)	0.039
Alcohol use, n(%)		820 (29.1%)	653 (31.5%)	167 (22.5%)	<0.001
Diabetes mellitus, n(%)		150 (5.3%)	135 (6.5%)	15 (2.0%)	<0.001
AIDS diagnosis, n(%)		416 (14.8%)	315 (15.2%)	101 (13.6%)	0.287
CD4, cells/mL median (IQR)		585 (379-828)	579 (378-820)	594 (382-836)	0.390
HIV-RNA >200 cp/mL, n(%)		246 (8.7%)	165 (8.0%)	81 (10.9%)	0.043
On ART, n(%)		2,443 (86.8%)	1795 (86.7%)	648 (87.2%)	0.709
Previously treated for HCV, n(%)		751 (26.7%)	591 (28.5%)	160 (21.5%)	<0.001
HCVRNA, log_{10} IU/mL, median (IQR)		6.0 (5.4-6.5)	6.1 (5.5-6.5)	5.9 (5.3-6.4)	<0.001
HCV genotype					
	1	95 (3.4%)	75 (3.6%)	20 (2.7%)	0.002
	1a	1,060 (37.7%)	810 (39.1%)	250 (33.7%)	
	1b	319 (11.3%)	235 (11.3%)	84 (11.3%)	
	2	80 (2.8%)	59 (2.8%)	21 (2.8%)	
	3	657 (23.3%)	440 (21.2%)	217 (29.2%)	
	4	445 (15.8%)	331 (16.0%)	114 (15.3%)	
	other	10 (0.4%)	9 (0.4%)	1 (0.1%)	
FIB-4 (in 2,708 pts), median (IQR)		1.8 (1.2-3.1)	1.85 (1.21-3.21)	1.68 (1.13-2.78)	<0.001
FIB-4 >3.25, n (%)		630 (23.3%)	487 (24.4%)	143 (20.0%)	0.012
APRI (in 2,713 pts) median (IQR)		0.66 (0.38-1.32)	0.68 (0.40-1.42)	0.55 (0.34-1.08)	<0.001
APRI >1.5, n (%)		592 (21.8%)	467 (23.4%)	125 (17.5%)	<0.001
Liver Stiffness (in 1,844 pts), kPa median (IQR)		9.2 (6.1-15.4)	9.9 (6.3-16.6)	8.4 (5.6-13.2)	<0.001
Fibrosis stage by TE, n(%)					
	F0-F1	622 (33.7%)	448 (32.2%)	174 (38.5%)	0.006
	F2	343 (18.6%)	251 (18.0%)	92 (20.3%)	
	F3	295 (16%)	224 (16.1%)	71 (15.7%)	
	F4	584 (31.7%)	469 (33.7%)	115 (25.4%)	

Fig. 1 Factors associated with liver fibrosis

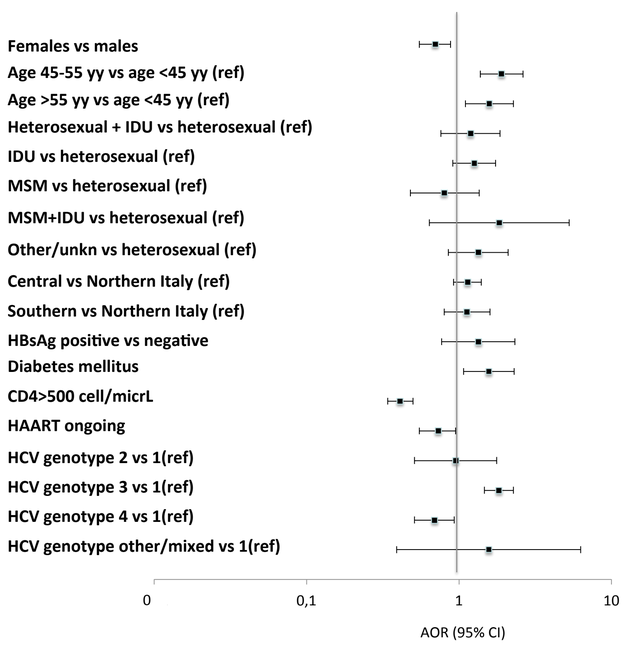
Multivariable models*

*mutually adjusting for listed factors and for nationality

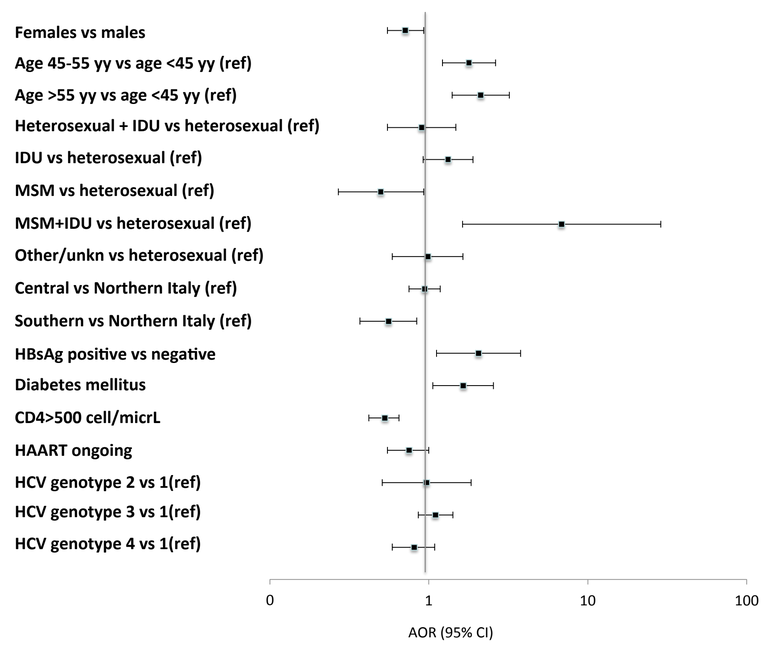
a. Predictors of FIB-4>3.25



b. Predictors of APRI>1.5



c. Predictors of stiffness ≥13 kpa (TE)



✓ Females are consistently associated to less fibrosis, diabetes and older age# to more fibrosis by all methods

✓ MSM+IDU risk group, HBsAg+ status, HCV G3 vs 1 and CD4<500 cell/micrL are associated to more fibrosis by 2 methods

age not assessed for FIB-4 as it is included in the index

✓ Qualitative agreement of severe fibrosis assessment by different non-invasive was fairly good

- FIB-4>3.25 and stage F4 at TE kappa=0.48
- APRI>1.5 and stage F4 at TE kappa= 0.40

✓ Age >45 years was the only independent predictor of discordant severe fibrosis

- By APRI and TE
- By FIB-4 and TE

Fig.2 Predictors of DAA treatment access

(n=1,093 treated of 2,814)

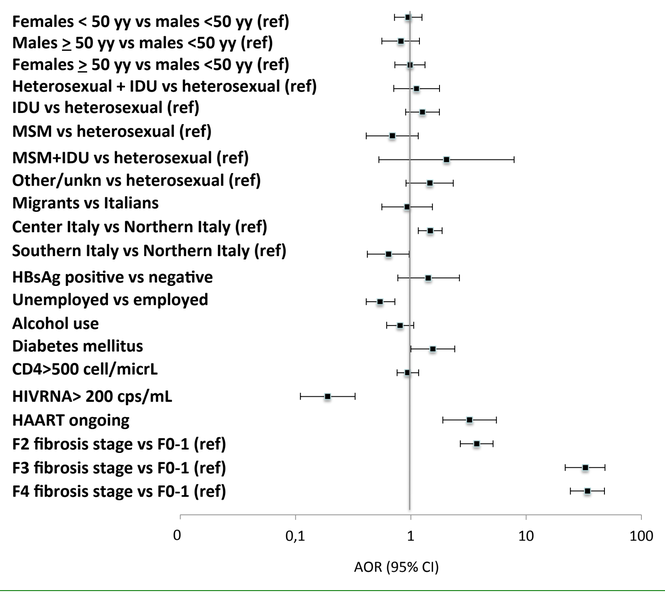
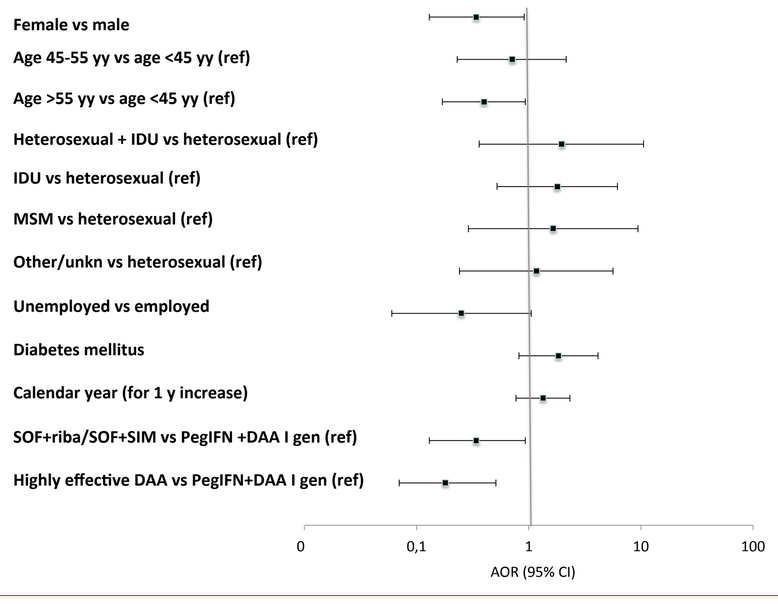


Fig. 3 Predictors of DAA failure

(n=55 of 775 evaluable)



CONCLUSIONS

- Fairly good concordance of FIB-4/APRI/TE in predicting severe fibrosis in HIV/HCV patients except in older patients
- Males, older patients with those with diabetes show a higher risk of severe fibrosis by any non-invasive assessment method
- Different DAA access based on country region of residence and delayed access in unemployed individuals highlight the importance of removing barriers to treatment access in HIV/HCV co-infected patients also in countries as Italy with universal treatment access
- Lower risk of DAA treatment failure in females warrants specific investigations

Contact information:

Barbara Rossetti, MD E-mail: brossetti1982@gmail.com

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ICONA Foundation Study Group

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