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Abstract # 631

Eradication of HCV: Effects on Cardiovascular Risk and Preclinical Atherosclerosis

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Background and Aim

- The association between HCV infection and cardiovascular events is a contentious issue. We previously showed that eradication of HCV in HIV/HCV-coinfected patients was associated with a reduction in the hazard of diabetes and renal failure and, unexpectedly, with a near-significant increase in the hazard of cardiovascular events [1].
- Our study aimed to assess changes in 10-year Framingham cardiovascular risk, aortic pulse wave velocity (**PWV**), and carotid intima-medial thickness (**cIMT**) in coinfected patients with and without SVR receiving anti-HCV therapy.
  - ***PWV,*** *considered the gold standard for the measurement of arterial stiffness, is an independent predictor of coronary heart disease and stroke in apparently healthy subjects* [2].
  - ***cIMT*** *is a predictor of myocardial infarction and stroke in adults without a history of cardiovascular disease* [3].

1. Berenguer J, et al. Hepatology 2017; 66:344
2. Mattace-Raso F, et al. Circulation 2006; 113: 657-663
3. O'Leary DH, et al. N Engl J Med 199; 340: 14-22

Methods

Study	Description
10-y CVR	• Framingham Cardiovascular Disease (10-year risk)* https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php
cIMT	• Scans were performed at each center by experienced technicians. • 12 segments of the R&L CA were studied in each patient (near and far wall segments of common CA, CA bifurcation, and internal CA) • Measurements obtained on digital images using manual calipers were performed by a single experienced vascular technician who was blinded to the participant's clinical characteristics. • The mean cIMT value (in mm) was calculated for each subject on the basis of the 12 measurements at the predefined segments
PWV	• Carotid-femoral PWV was assessed with SphygmoCor® CPV System – AtCor Medical Pty Ltd, West Ryde, New South Wales, Australia. • All measurements were performed by trained examiners, following well stablished recommendations (J Hypertens 2012;30:445-448).

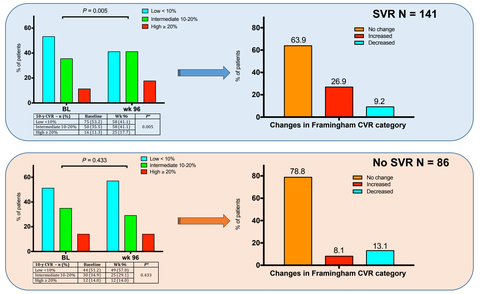
* We used age at baseline to calculate 10-y CVR at both time-periods (baseline and wk 96)

Patients characteristics

Characteristic	No SVR (n=90)	SVR (n=147)	Total (N=237)
Male sex, No. (%)	64 (71.1)	116 (78.9)	180 (75.9)
Age, y, median (IQR) (baseline)	49. 2 (46.4 - 52.6)	49.1 (45.6 - 52.5)	49.2 (46 - 52.6)
BMI (n=226), median (IQR)	24.2 (22 - 26.1)	24.6 (21.6 - 27.3)	24.4 (21.7 - 26.7)
Prior injection drug use, No. (%)	72 (80)	112 (76.2)	184 (77.6)
Methadone therapy, No. (%)	11 (12.2)	18 (12.2)	29 (12.2)
CDC disease category C, No. (%)*	29 (32.2)	35 (23.8)	64 (27)
CD4+, nadir, cells/mm^3, median (IQR)	191 (72 - 263)	166 (84 - 243)	171 (84 - 251)
cART during anti-HCV treatment, No. (%)	88 (97.8)	144 (98)	232 (97.9)
CD4+, baseline, cells/mm^3, median (IQR)	559 (410 - 842)	518 (377 - 762)	540 (377 - 802)
Undetectable HIV RNA load at baseline, No. (%)	76 (84.4)	131 (89.1)	207 (87.3)
Prior anti-HCV therapy, No. (%)	10 (11.1)	19 (12.9)	29 (12.2)
HCV genotype, No. (%)			
1	54 (60)	102 (69.4)	156 (65.8)
2	2 (2.2)	2 (1.4)	4 (1.7)
3	18 (20)	22 (15)	40 (16.9)
4	10 (11.1)	8 (5.4)	18 (7.6)
Other/mixed	5 (5.6)	12 (8.2)	17 (7.2)
Unknown	1 (1.1)	1 (0.7)	2 (0.8)
HCV-RNA, Log_{10} IU/mL, median (IQR)	6.5 (6 - 7)	6.2 (5.7 - 6.6) *	6.3 (5.9 - 6.7)
HBsAg positivity, No. (%)	2 (2.2)	4 (2.7)	6 (2.5)
Liver cirrhosis, No. (%) (METAVIR 4 or TE>12,5)	40 (44.4)	79 (53.7)	119 (50.2)
Current alcohol intake > 50 g/d, No. (%)	2 (2.2)	5 (3.4)	7 (3)
Diabetes mellitus	8 (8.9)	12 (8.2)	20 (8.4)
Current smoking	63 (70)	99 (67.3)	162 (68.4)
Arterial hypertension	12 (13.3)	15 (10.2)	27 (11.4)
Anti-HCV therapy			
Peg-IFN + RBV	30 (33.3)	50 (34.0)	80 (33.8)
Peg-IFN + RBV + HCV protease inhibitor	35 (38.9)	82 (55.8)	117 (49.3)
Peg-IFN + RBV + Daclatasvir	6 (6.7)	8 (5.4)	14 (5.9)
Sofosbuvir + RBV	19 (21.1)	7 (4.8)	26 (11.0)

* P<.05 compared with the No SVR group

Changes in 10-y Framingham CVR (N=227)

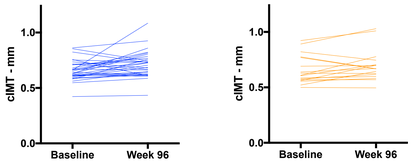


10-y CVR – n (%)	Baseline	Wk 96	P*
Low <10%	53 (57.1)	58 (61.1)	0.005
Intermediate 10-20%	19 (20.5)	18 (18.9)	
High >20%	21 (22.6)	19 (20.0)	

10-y CVR – n (%)	Baseline	Wk 96	P*
Low <10%	44 (51.2)	44 (51.2)	0.433
Intermediate 10-20%	19 (22.1)	23 (26.7)	
High >20%	23 (26.8)	19 (22.1)	

Changes in carotid intima-medial thickness (N=49)

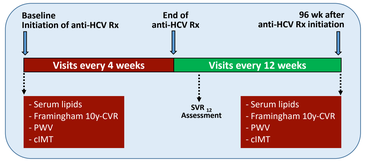
No significant differences were found in baseline characteristics between patients with (N=49) and without (N=188) cIMT determinations



Variable – median (IQR)	SVR N=31	Non-SVR N=18	P
cIMT – mm			
Baseline	0.64 (0.61 - 0.71)	0.62 (0.57 - 0.78)	0.079
Week 96	0.71 (0.62 - 0.77)	0.67 (0.62 - 0.75)	0.642
Median change	0.03 (-0.02 - 0.11)	0.02 (-0.02 - 0.1)	0.198
P (repeated measures)	0.011	0.223	

Study Design

- Multicenter prospective study of naïve and anti-HCV therapy experienced HIV/HCV-coinfected patients initiating anti-HCV therapy between Feb 2012 and Feb 2016 in 14 centers in Spain
- Clinical data were recorded at each institution using a common database via an online form. This database included all demographic, clinical, virological, and laboratory data.
- All the centers were monitored to verify that all the information in the database was consistent with the patient's medical records.



10y-CVR: 10 year cardiovascular risk; **PWV:** carotid-femoral pulse wave velocity; **cIMT:** carotid intima-medial thickness

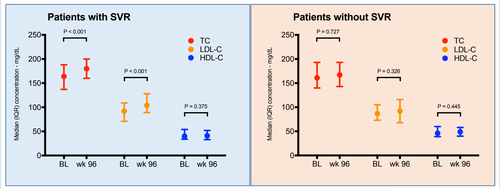
Flow chart

262 Patients recruited in the participating centers

25 initiating statins during the study period were excluded

237 patients evaluable for this study
- 227 with paired 10y-CVR evaluation
- 128 with paired PWV
- 49 with with paired cIMT

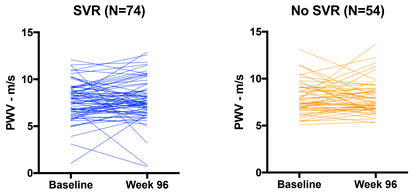
Changes in serum lipids (N=227)



Variable – median (IQR)	SVR N=141	Non-SVR N=86	P
Total cholesterol (TC)			
Baseline	164 (137 - 188)	161 (140 - 193)	0.520
Week 96	180 (160 - 200)	167 (143 - 193)	0.004
Median change	15 (-3 - 39)	1 (-25 - 20)	0.001
P (repeated measures)	<0.001	0.727	
LDL cholesterol			
Baseline	92 (71 - 109)	87 (73 - 105)	0.484
Week 96	104 (89 - 128)	92 (68 - 116)	0.004
Median change	14 (-3 - 32)	0 (-12 - 25)	0.032
P (repeated measures)	<0.001	0.326	
HDL cholesterol			
Baseline	40 (34 - 54)	46 (39 - 60)	0.570
Week 96	41 (33 - 52)	49 (40 - 58)	0.015
Median change	-1 (-6 - 5)	2 (-5 - 8)	0.303
P (repeated measures)	0.375	0.445	

Changes in pulse wave velocity (N=128)

No significant differences were found in baseline characteristics between patients with (N=128) and without (N=109) PWV determinations



Variable – median (IQR)	SVR N=74	Non-SVR N=54	P
PWV – m/s			
Baseline	7.8 (6.5 - 8.9)	7.4 (6.8 - 9.1)	0.279
Week 96	7.6 (6.7 - 8.8)	7.4 (6.8 - 8.8)	0.971
Median change	0.3 (-0.8 - 1.3)	0.1 (-0.9 - 1.1)	0.635
P (repeated measures)	0.551	0.853	

Conclusions

- We found that SVR was followed by a statistically significant increase in Framingham 10 year cardiovascular risk in patients with SVR but not in patients without SVR.
- The increase in cardiovascular risk was driven by the rise in serum LDL-C in patients with SVR.
- We found small increases in PWV and cIMT in patients with and without SVR.
- Our findings do not support a mid-term beneficial effect of HCV eradication on cardiovascular risk or preclinical atherosclerosis in coinfected patients

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