NAFLD in HIV

GIOVANNI MAZZOLA

Disclosures

I have received funding for membership of Advisory Boards, for the preparation of educational materials, for research and educational grants, for membership of speaker panels and for support for travel to conferences from the following companies:

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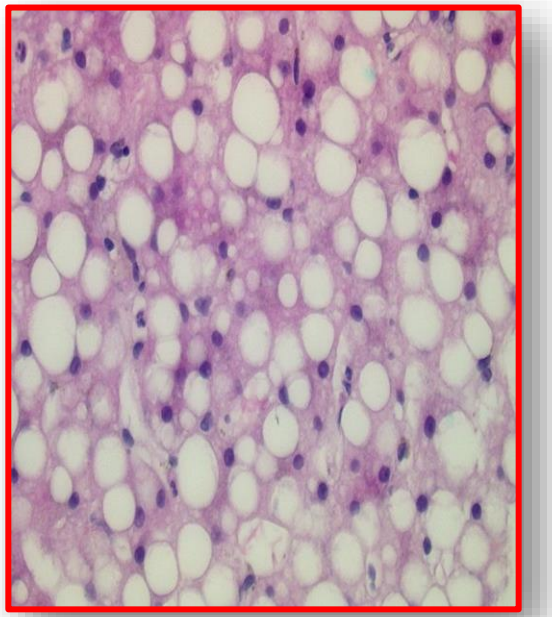
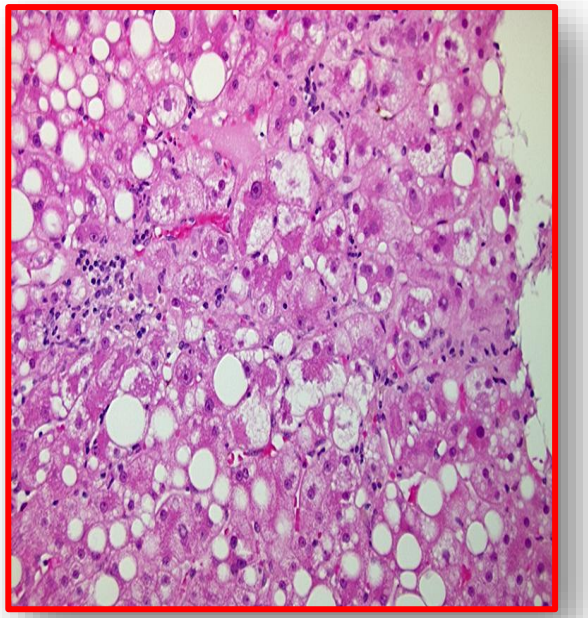
- Bristol-Myers Squibb
- Janssen-Cilag
- Viiv Healthcare
- Merck Sharp and Dohme
- Abbvie

NAFLD - Definition

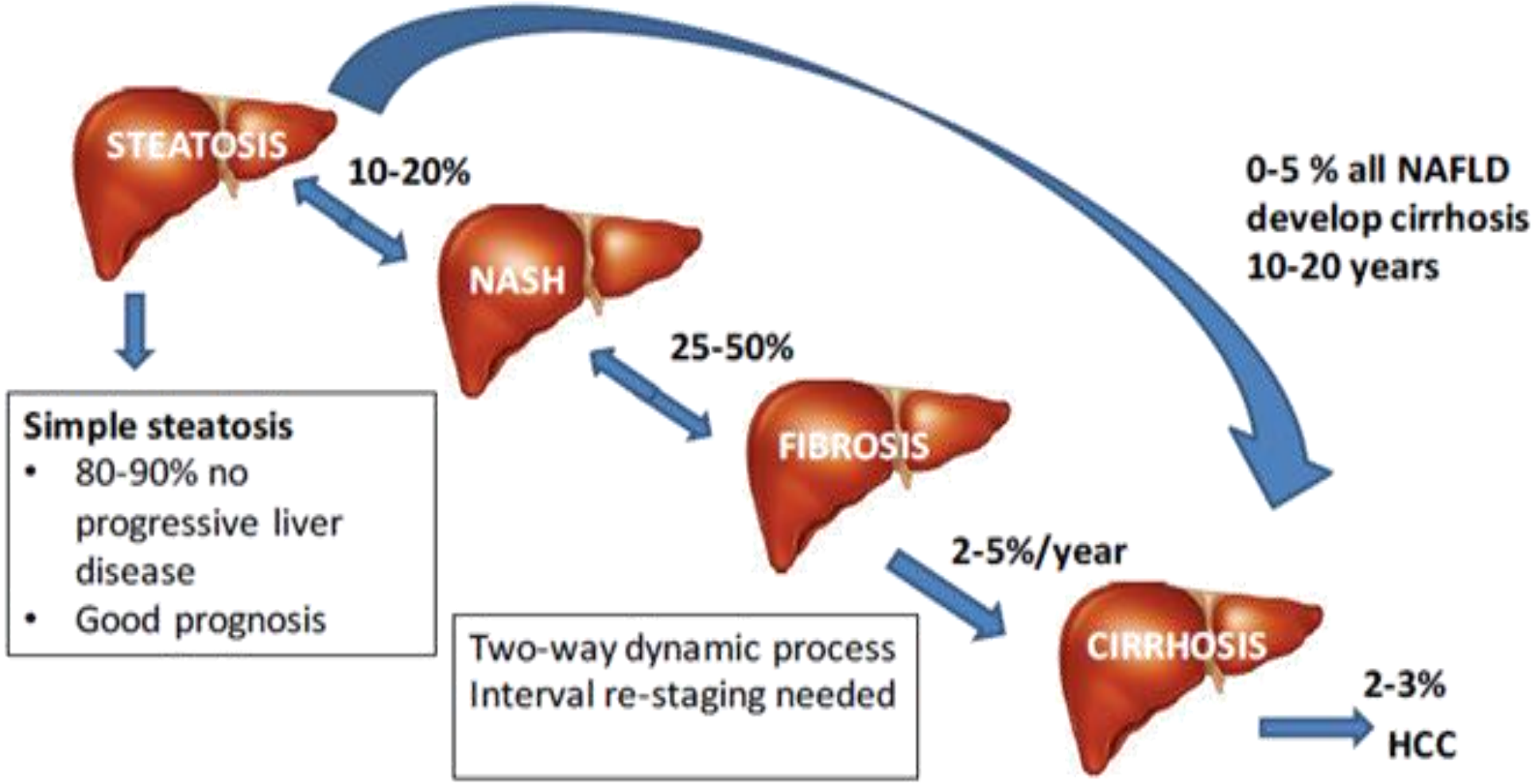
Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disorders characterized by macrovesicular hepatic steatosis occuring in the absence of significant alcohol consumption

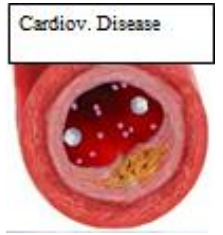
NAFLD is the hepatic expression of insulin resistance





NAFLD - Definition

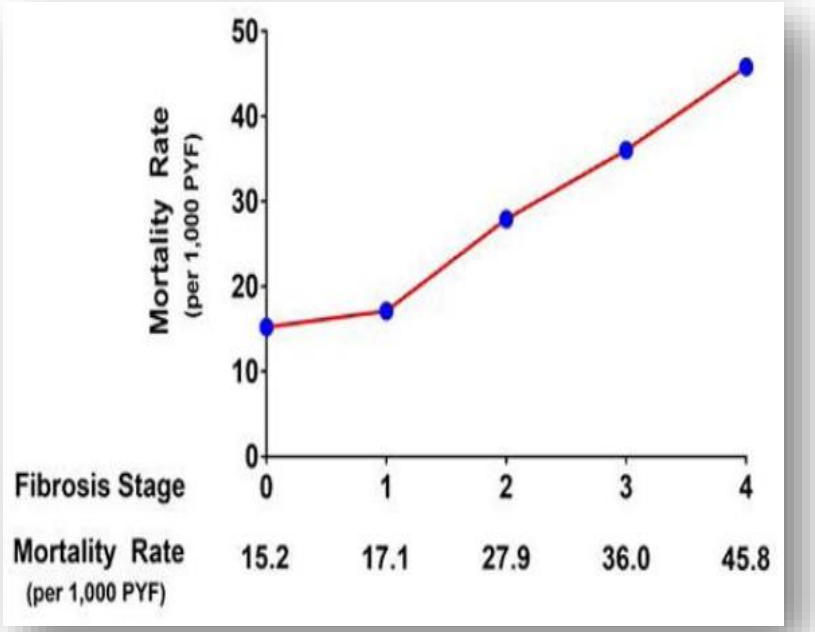




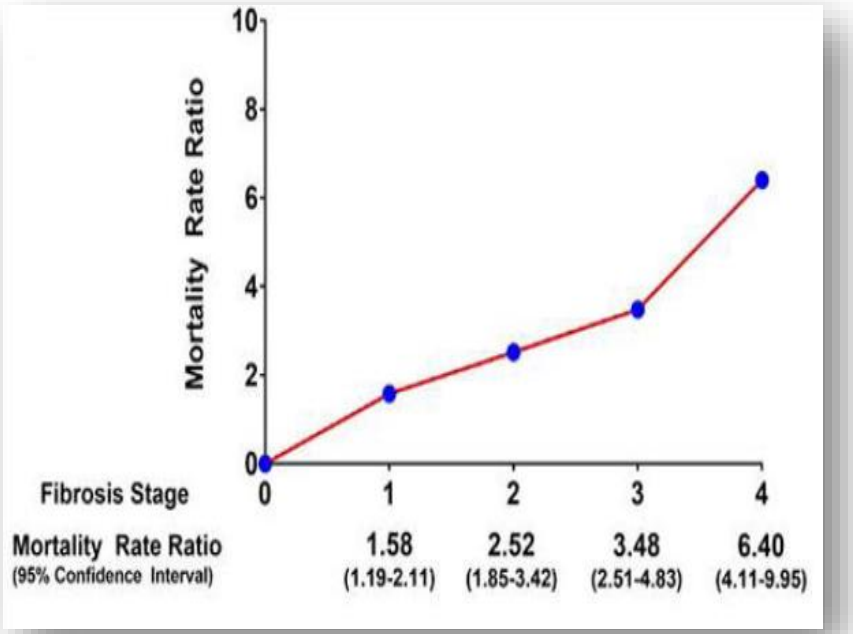
[1] Adams LA Hepatology. 2011 October ; 54(4): 1208–1216, [2] Schuppan D et al Journal of Gastroenterology and Hepatology 2013; 28 (Suppl. 1): 68–76 [3] Musso G et al. Annals of Medicine, 43:8, 617-649

Fibrosis and NAFLD outcomes

All Cause Mortality



Liver-related Mortality



Dulai et al, Hepatology 2017

Questions for Clinicians

1. *Whether the patient has NAFLD*
2. *Whether the patient is likely to have underlying NASH*
3. *Whether the patient has any fibrosis*
4. *Whether the patient has any advanced fibrosis?*

HIV MEDICINE BHIVA British HIV Association

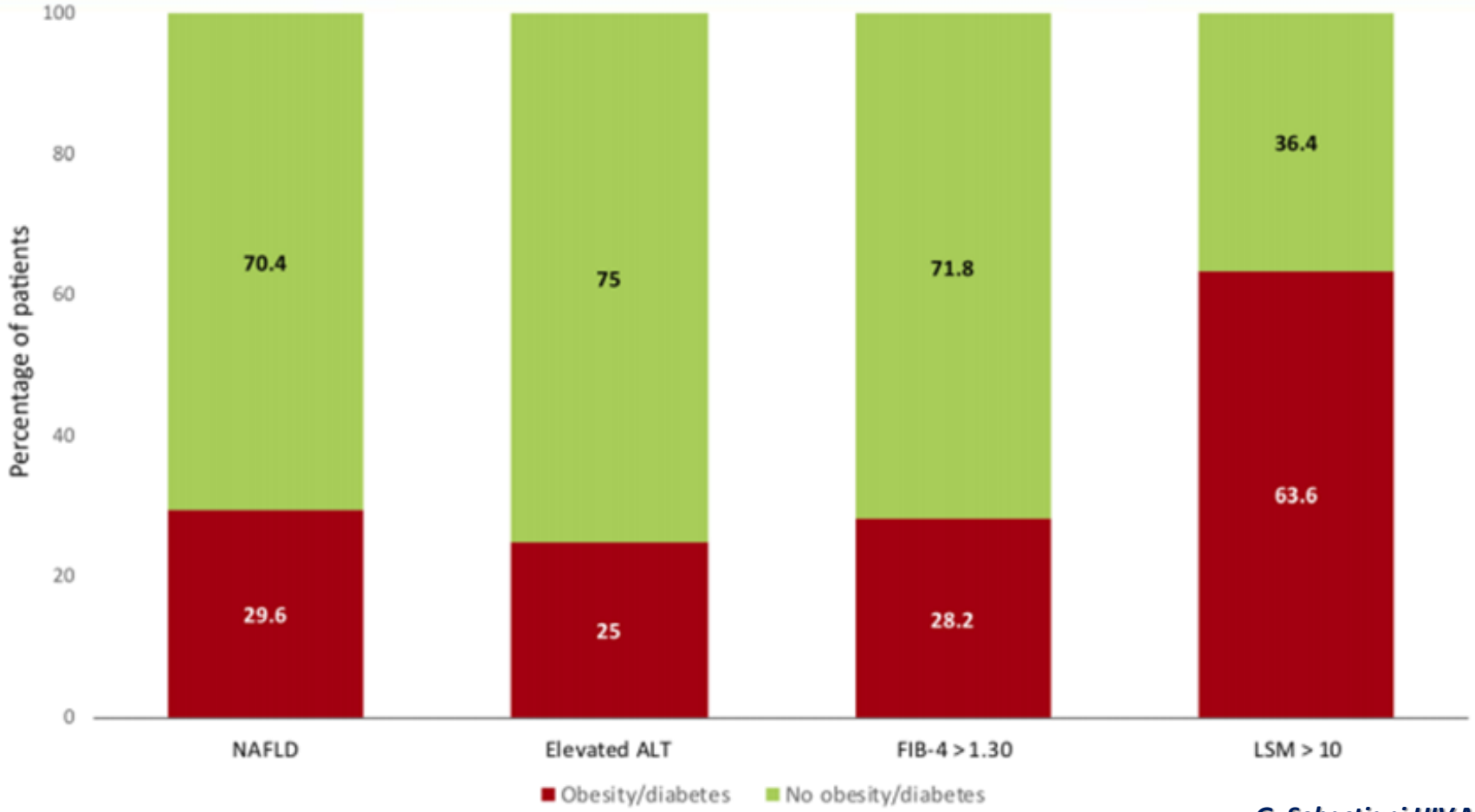
Original Research

Application of guidelines for the management of nonalcoholic fatty liver disease in three prospective cohorts of HIV-monoinfected patients*

G Sebastiani, S Cocciolillo, G Mazzola, A Malagoli, J Falutz, A Cervo, S Petta, T Pembroke, P Ghali, G Besutti, I Franconi, J Milic, A Cascio and G Guaraldi

First published: 23 October 2019 **https://doi.org/10.1111/hiv.12799**

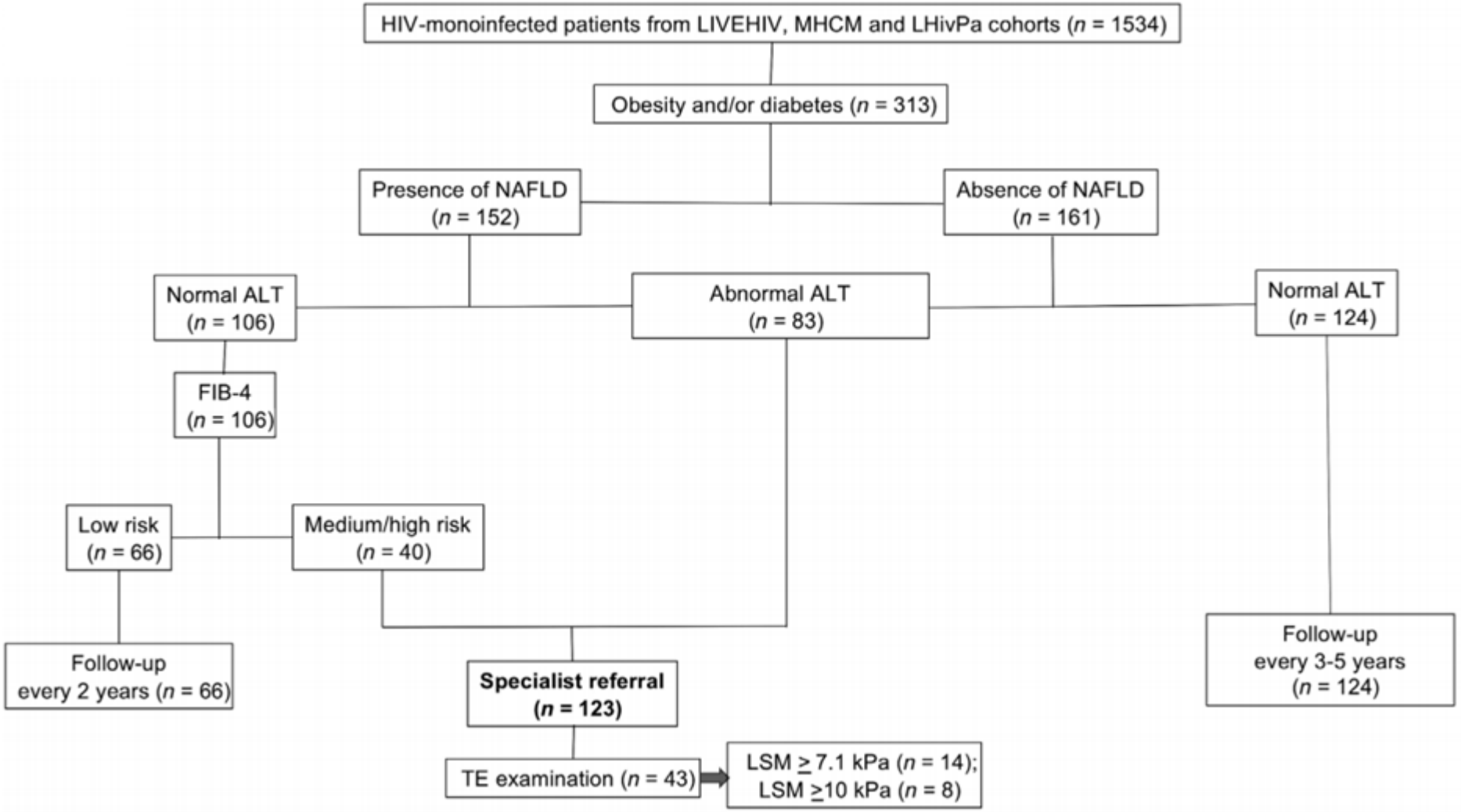
EASL/EACS
Application of Guidelines in HIV



G. Sebastiani HIV Medicine 2019

Proportion of patients with and without **obesity/diabetes** in those with nonalcoholic fatty liver disease (NAFLD), elevated alanine aminotransferase (ALT), fibrosis-4 (FIB-4) > 1.30 and liver stiffness measurement (LSM) > 10 kPa

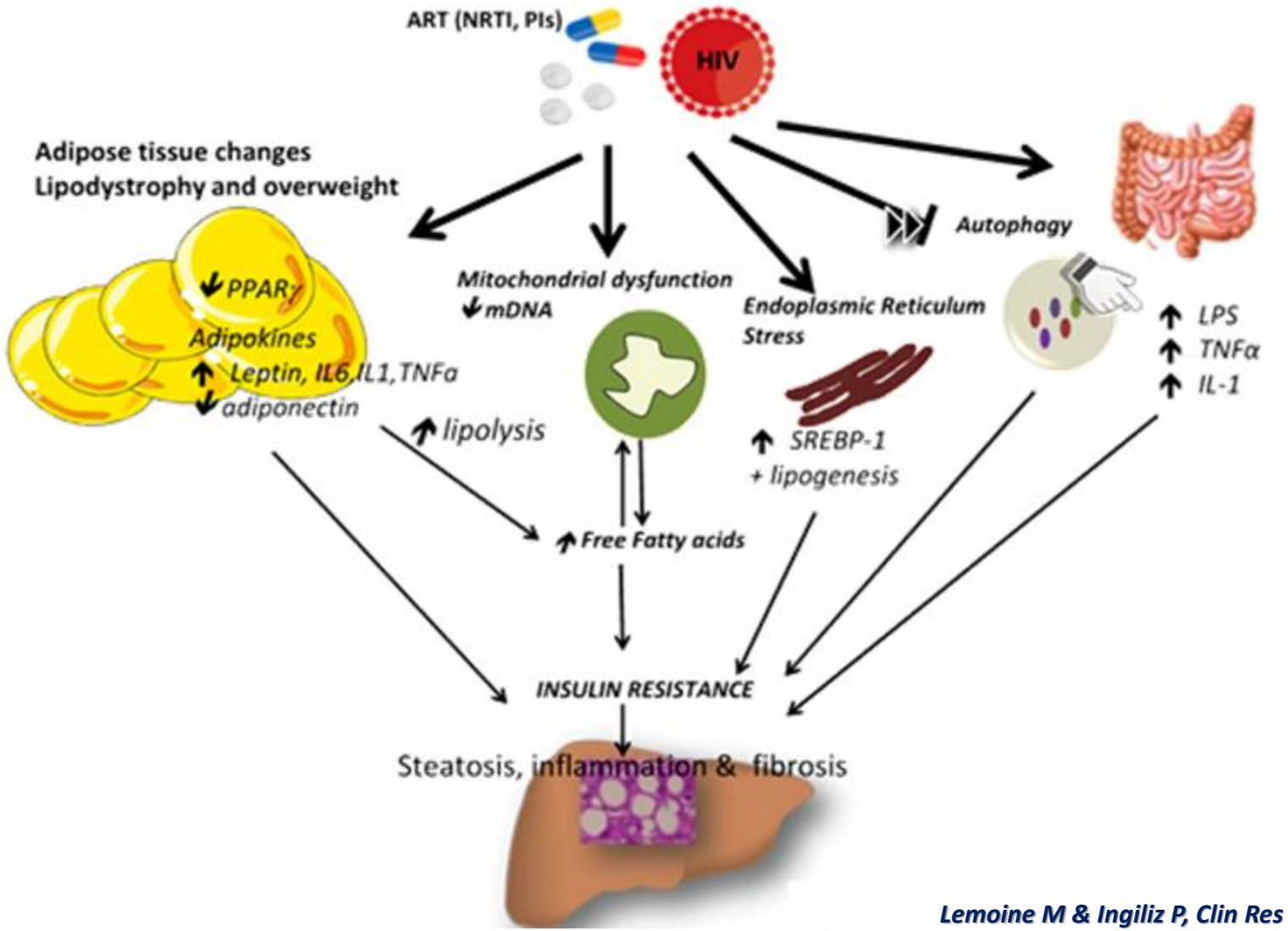
EASL/EACS diagnostic algorithm applied to 1534 HIVmonoinfected patients



G. Sebastiani HIV Medicine 2019

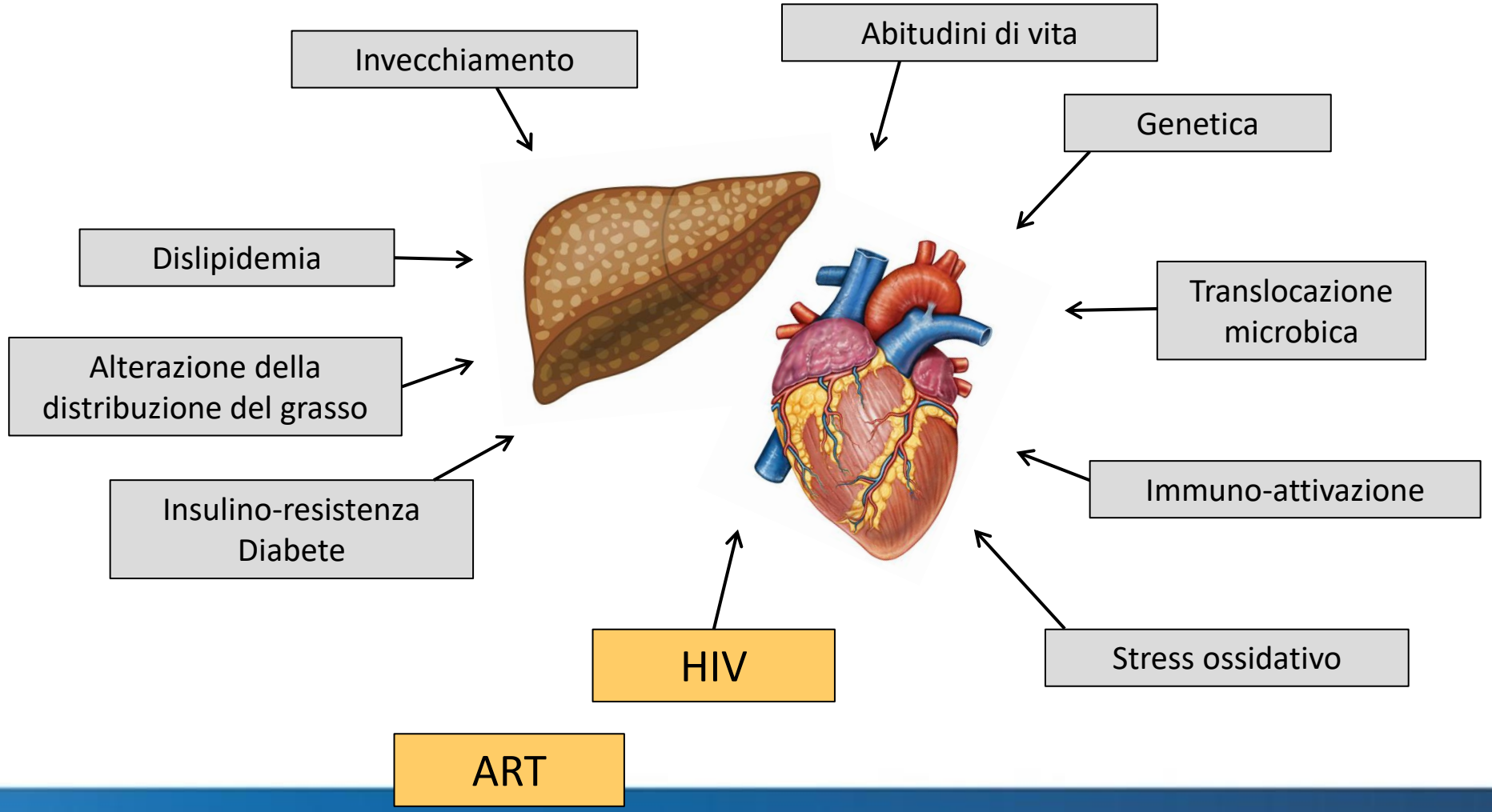
NAFLD pathogenesis in HIV infected patients

HIV and risk of NAFLD/NASH

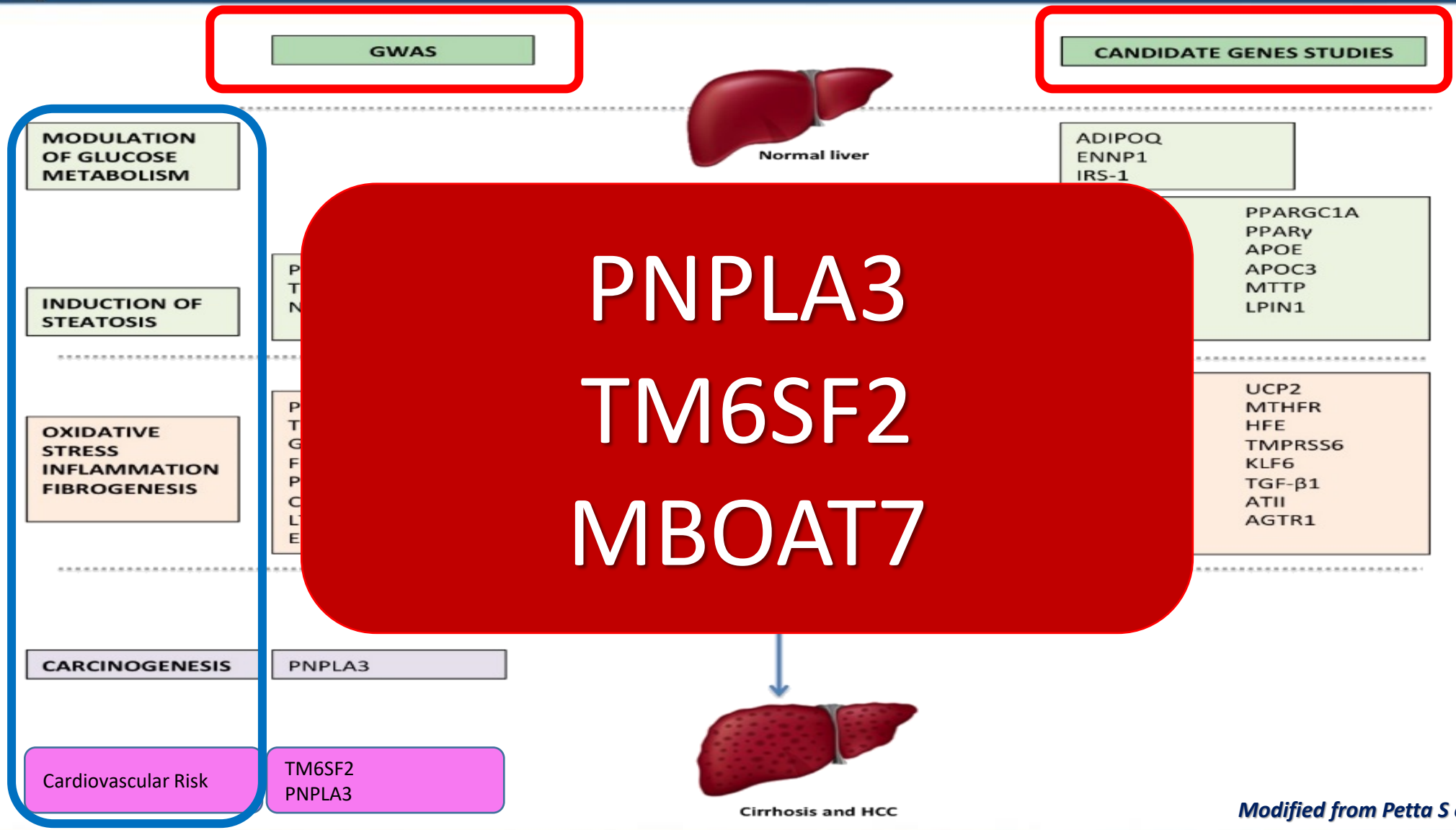


Lemoine M & Ingiliz P, Clin Res Hep Gastr 2012

NAFLD in HIV: Patogenesi



Genetic and NAFLD



Modified from Petta S et al, WJG 2016

Genetic and NAFLD in HIV

PLOS ONE

RESEARCH ARTICLE

Genetic polymorphisms associated with fatty liver disease and fibrosis in HIV positive patients receiving combined antiretroviral therapy (cART)

Leona Dold, Carolin Luda, Carolynne Schwarze-Zander, Christoph Boesecke, Cordula Hansel, Hans-Dieter Nischalke, Philipp Lutz, Raphael Mohr, Jan-Christian Wasmuth, Christian P. Strassburg, Jonel Trebicka, Jürgen Kurt Rockstroh, Ulrich Spengler

Published: June 8, 2017 • https://doi.org/10.1371/journal.pone.0178685

117 HIV-positive patients on cART, with Steatosis evaluated by CAP

No genetic parameters risk factors for hepatic steatosis

NAFLD prevalence in HIV infected persons

Two-fold higher chance of liver steatosis with HIV

Presence of steatosis in HIV and non-HIV individuals paired by the nearest neighbor propensity score with a caliper of 0.05

	OR (95% CI)	p value
HIV infection	2.1 (1.49-2.95)	< 0.001

Logistic regression-based scores were used for matching and balance between groups was checked with usual procedures

Pacheco A. et al, IAC 2018

The Epidemic of NAFLD in HIV

	Patient population	Number of patients with HIV mono-infection	NAFLD diagnostic assay	NAFLD prevalence in patients with HIV mono-infection	Predictors of NAFLD in patients with HIV mono-infection
Hadigan et al (2007)[19]	Consecutive patients with HIV who did not abuse alcohol	33	MRS	42·0%	High HOMA-IR, visceral adiposity, high BMI, and high plasma ALT and triglyceride concentrations
Guaraldi et al (2008)[20]	Patients with HIV who did not abuse alcohol or have viral hepatitis	225	Liver-to-spleen attenuation on CT	36·9%	Male sex and large waist circumference
Ingiliz et al (2009)[21]	Patients with chronic elevation in liver test results that had no genetic cause and had no HCV, HBV, or autoimmune disease	30	Liver biopsy	Of the total patient cohort, 60·0% had steatosis and 53·0% had NASH	High fasting plasma glucose concentration
Crum-Cianflone et al (2009)[22]	Patients with HIV who did not have HCV or HBV	267	Ultrasound and 55 liver biopsies	31·0% of patients assessed by ultrasound had NAFLD; 36·0% of patients assessed by biopsy had NAFLD and 20·0% had NASH	Large waist circumference, and high plasma triglyceride and LDL concentrations
Li Vecchi et al (2012)[23]	Patients with HIV mono-infection or HIV–HCV co-infection	57	Ultrasound and transient elastography	54·0%	Lipodystrophy, high plasma triglyceride concentration, metabolic syndrome, high plasma cholesterol concentration, and ART use for more than 1 year
Li Vecchi et al (2013)[24]	Patients with HIV mono-infection or HIV–HCV co-infection	69	Ultrasound and transient elastography	46·3%	High plasma triglyceride concentrations and diabetes
Sterling et al (2013)[25]	Patients with HIV who did not have HCV or HBV, did not abuse alcohol, and did not have diabetes mellitus or elevated liver test results	14	Liver biopsy	Of the total patient cohort, 65·0% had steatosis and 26·0% had NASH	High HOMA-IR and serum GGT concentrations, which predict steatosis
Nishijima et al (2014)[26]	Patients with HIV who did not have HBV or HCV, and did not abuse alcohol	435	Ultrasound	31·0%	High BMI and dyslipidaemia
Price et al (2014)[16]	Multicenter AIDS Cohort Study: patients with HIV who did not abuse alcohol	465	Liver-to-spleen attenuation on CT	13·0%	*PNPLA3* genotype and cumulative dideoxynucleoside exposure
Macias et al (2014)[27]	Patients with HIV in a walk-in clinic	505	Transient elastography with CAP	40·0%	High BMI, and high fasting plasma glucose and plasma triglyceride concentrations
Sulyok et al (2015)[28]	Outpatients with HIV mono-infection or HIV–HCV co-infection	136	Transient elastography with CAP	49·5%	High BMI, diabetes, and hypertension
Morse et al (2015)[29]	Patients with HIV who had elevated serum ALT concentrations for 6 months, were on ART, and did not have chronic liver disease	62	Liver biopsy	Of the total patient cohort, 55·0% had NASH and 18·0% had bridging fibrosis	Diabetes, obesity, and *PNPLA3* genotype
Lui et al (2016)[30]	Patients with HIV who did not have HBV or HCV	80	Transient elastography and MRS	28·7%	High BMI, metabolic syndrome, high fasting glucose and serum triglyceride concentrations

Verna et al, Lancet Gastr Hep 2017

The burden of liver steatosis in HIV

Authors	Country	N	Gold standard	Prevalence	Factors
Morse *et al* *CID 2015*	USA	62	Liver biopsy	73%	-
Mohr *et al* *Medicine 2015*	Germany	341	-	-	-
Lombardi *et al* *Dig Liver Dis 2016*	UK	125	US	55%	Male sex, age, HOMA-IR, GGT
Liu *et al* *AP&T 2016*	China	80	MRI	29%	Triglycerides
Macias *et al* *HIV Med 2016*	Spain	326	CAP	37%	-
Sebastiani *et al* *J Hepatol 2017*	Canada	538	CAP	36%	BMI, triglycerides
Lemoine *et al* *AIDS 2017*	France	405	-	-	-
Perazzo et al *IAS 2017*	Brazil	395	CAP	35%	MS, cumulative use of D-drugs

Prevalence of NAFLD/NASH in HIV+: a meta-analysis

Ovid®

Prevalence and risk factors of nonalcoholic fatty liver disease in HIV-monoinfection

James Maurice;Amee Patel;Alasdair Scott;Krish Patel;Mark Thursz;Maud Lemoine;

AIDS. 31(11):1621–1632, JULY 17TH, 2017

OBJECTIVE: To identify the prevalence and risk factors of nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) and fibrosis in HIV-monoinfected patients.

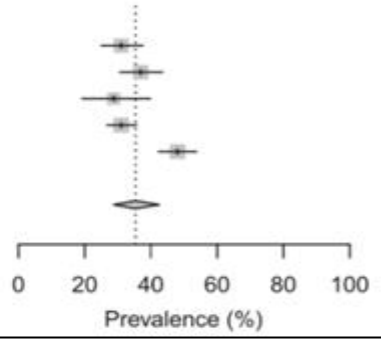
DESIGN : **Systematic review and meta-analysis.**

Prevalence of NAFLD/NASH in HIV+: a meta-analysis

NAFLD Prevalence

Study	Events	Total	Prevalence (%)	95% CI	Weight
Crum−Cianflone	67	216	31.02	[24.92; 37.65]	20.2%
Guaraldi	83	225	36.89	[30.57; 43.56]	20.7%
Lui	23	80	28.75	[19.18; 39.95]	15.1%
Nishijima	135	435	31.03	[26.71; 35.62]	22.3%
Vuille−Lessard	144	300	48.00	[42.22; 53.82]	21.8%
Random effects model		**1256**	**35.32**	**[28.80; 42.45]**	**100%**

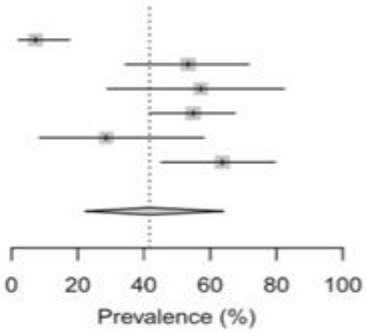
Heterogeneity: I2=85.3%, tau2=0.0947, P<0.0001



NASH Prevalence

Study	Events	Total	Prevalence (%)	95% CI	Weight
Crum−Cianflone	4	55	7.27	[2.02; 17.59]	15.8%
Ingiliz	16	30	53.33	[34.33; 71.66]	17.5%
Lemoine	8	14	57.14	[28.86; 82.34]	15.6%
Morse	34	62	54.84	[41.68; 67.52]	18.6%
Sterling	4	14	28.57	[8.39; 58.10]	14.9%
Vodkin	21	33	63.64	[45.12; 79.60]	17.6%
Random effects model		**208**	**41.67**	**[22.30; 64.00]**	**100%**

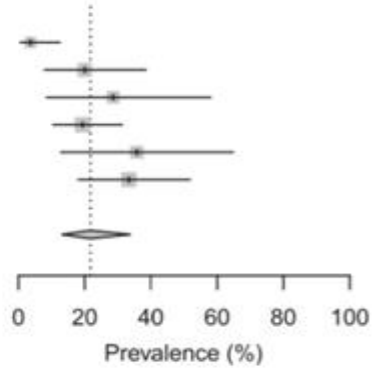
Heterogeneity: I2=83.1%, tau2=1.1, P<0.0001



Fibrosis Prevalence

Study	Events	Total	Prevalence (%)	95% CI	Weight
Crum−Cianflone	2	55	3.64	[0.44; 12.53]	11.2%
Ingiliz	6	30	20.00	[7.71; 38.57]	17.7%
Lemoine	4	14	28.57	[8.39; 58.10]	14.0%
Morse	12	62	19.35	[10.42; 31.37]	21.9%
Sterling	5	14	35.71	[12.76; 64.86]	14.9%
Vodkin	11	33	33.33	[17.96; 51.83]	20.4%
Random effects model		**208**	**21.72**	**[13.13; 33.74]**	**100%**

Heterogeneity: I2=59.3%, tau2=0.3358, P=0.0311



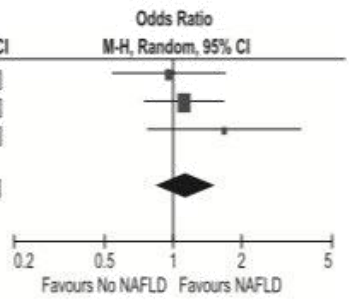
Maurice, AIDS 2017

NAFLD IN HIV

(m) Supressed Viral Load

Study or Subgroup	NAFLD Events	NAFLD Total	No NAFLD Events	No NAFLD Total	Weight	Odds Ratio M-H, Random, 95% CI
Crum-Cianflone	33	67	75	149	28.2%	0.96 [0.54, 1.70]
Nishijima	73	135	154	300	56.5%	1.12 [0.74, 1.68]
Vuille-Lessard	133	144	137	156	15.4%	1.68 [0.77, 3.66]
Total (95% CI)		**346**		**605**	**100.0%**	**1.14 [0.84, 1.55]**
Total events	239		366			

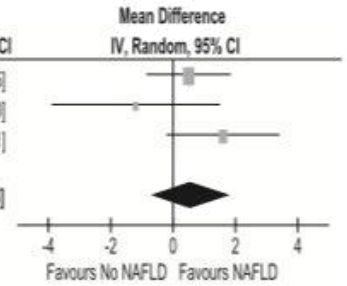
Heterogeneity: Tau² = 0.00; Chi² = 1.30, df = 2 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)



(n) Duration of HIV

Study or Subgroup	NAFLD Mean	NAFLD SD	NAFLD Total	No NAFLD Mean	No NAFLD SD	No NAFLD Total	Weight	Mean Difference IV, Random, 95% CI
Guaraldi	13.4	5	83	12.9	5	142	48.0%	0.50 [-0.85, 1.85]
Lui	8.2	4.9	23	9.4	7	57	18.4%	-1.20 [-3.90, 1.50]
Vuille-Lessard	14.5	8.1	144	12.9	7.9	156	33.6%	1.60 [-0.21, 3.41]
Total (95% CI)			**250**			**355**	**100.0%**	**0.56 [-0.72, 1.83]**

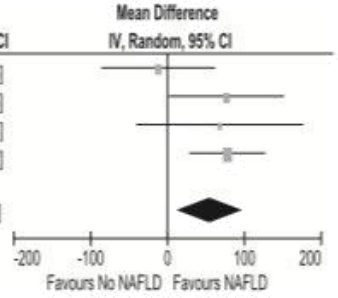
Heterogeneity: Tau² = 0.41; Chi² = 2.89, df = 2 (P = 0.24); I² = 31%
Test for overall effect: Z = 0.86 (P = 0.39)



(o) CD4 Count

Study or Subgroup	NAFLD Mean	NAFLD SD	NAFLD Total	No NAFLD Mean	No NAFLD SD	No NAFLD Total	Weight	Mean Difference IV, Random, 95% CI
Crum-Cianflone	526.8	263.5	67	538.9	242.7	149	23.9%	-12.10 [-86.26, 62.06]
Guaraldi	585.9	271.3	83	509.1	284.9	142	23.6%	76.80 [1.95, 151.65]
Lui	551	207	23	483	263	57	13.2%	68.00 [-40.71, 176.71]
Nishijima	421	253	135	343	222	300	39.2%	78.00 [28.48, 127.52]
Total (95% CI)			**308**			**648**	**100.0%**	**54.83 [11.55, 98.11]**

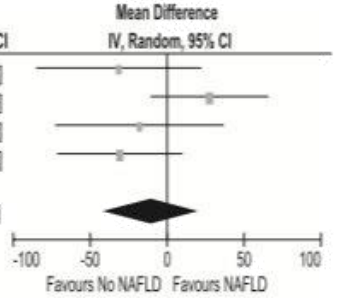
Heterogeneity: Tau² = 605.49; Chi² = 4.33, df = 3 (P = 0.23); I² = 31%
Test for overall effect: Z = 2.48 (P = 0.01)



(p) CD4 Nadir

Study or Subgroup	NAFLD Mean	NAFLD SD	NAFLD Total	No NAFLD Mean	No NAFLD SD	No NAFLD Total	Weight	Mean Difference IV, Random, 95% CI
Crum-Cianflone	273.4	172.1	67	304.9	214.9	149	20.8%	-31.50 [-85.25, 22.25]
Guaraldi	199.7	146.1	83	172.2	133.1	142	30.3%	27.50 [-10.80, 65.80]
Lui	107	101	23	125	139	57	20.3%	-18.00 [-72.83, 36.83]
Vuille-Lessard	217.2	173.1	144	248	186.6	156	28.6%	-30.80 [-71.50, 9.90]
Total (95% CI)			**317**			**504**	**100.0%**	**-10.68 [-41.46, 20.10]**

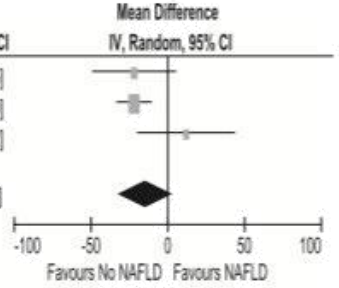
Heterogeneity: Tau² = 432.17; Chi² = 5.37, df = 3 (P = 0.15); I² = 44%
Test for overall effect: Z = 0.68 (P = 0.50)



(q) Duration of HAART

Study or Subgroup	NAFLD Mean	NAFLD SD	NAFLD Total	No NAFLD Mean	No NAFLD SD	No NAFLD Total	Weight	Mean Difference IV, Random, 95% CI
Lui	76	47	23	98	75	57	26.4%	-22.00 [-49.35, 5.35]
Nishijima	76	47	135	98	75	300	51.9%	-22.00 [-33.61, -10.39]
Vuille-Lessard	153.1	132.9	144	141.2	149.1	156	21.7%	11.90 [-20.02, 43.82]
Total (95% CI)			**302**			**513**	**100.0%**	**-14.65 [-32.79, 3.49]**

Heterogeneity: Tau² = 129.87; Chi² = 3.90, df = 2 (P = 0.14); I² = 49%
Test for overall effect: Z = 1.58 (P = 0.11)



Maurice, AIDS 2017

NAFLD IN HIV

Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-019-05861-7

REVIEW

Check for updates

Nonalcoholic Fatty Liver Disease Among Individuals with HIV Mono-infection: A Growing Concern?

Margaret Morrison[1] · Heather Y. Hughes[2,3] · Susanna Naggie[4,5] · Wing-Kin Syn[6,7,8]

Received: 21 May 2019 / Accepted: 24 September 2019

Abstract

Purpose of Review Liver disease is a leading cause of non-AIDS-related death in the HIV population since the introduction of highly active antiretroviral treatment (HAART). Recent studies suggest that patients with HIV are at high risk for nonalcoholic fatty liver disease (NAFLD) and progressive liver fibrosis. Evidence for the prevalence, risk factors, and diagnostic methodologies of NAFLD in patients with HIV mono-infection is summarized here.

Recent Findings Although limited, published studies suggest that the prevalence of NAFLD is higher (30–50%) and progresses at an increased rate in patients with HIV compared to the general population. Identifying those at risk for significant liver fibrosis is critical, preferably with non-invasive screening tests. While there is a paucity of evidence in this population, transient elastography (TE) appears to provide a sensitive, non-invasive screening modality.

Summary Identifying NAFLD early will allow for dietary and lifestyle interventions, as well as future drug therapies to decrease the risk of progressive liver fibrosis and cirrhosis in the high-risk HIV population. Clinicians should be aware of this risk and consider using TE for NAFLD diagnosis and surveillance.

Prevalenza di NAFLD in una coorte di pazienti con infezione da HIV: fattori di rischio ed inaspettato ruolo protettivo di Atazanavir e Darunavir sulla progressione della fibrosi epatica

Mazzola G., Cervo A., Gioè C., Colletti P., Quartararo P., Trizzino M., Mililli D., De Luca A., Mazzola S., Petta S., Cascio A.

Studio osservazionale di coorte prospettico
Gennaio – Giugno 2018
U.O.C. Malattie infettive Policlinico Palermo

OBIETTIVI DELLO STUDIO

- *Valutare la prevalenza di NAFLD e di fibrosi epatica nei pazienti con infezione da HIV seguiti presso il nostro ambulatorio*

- *Valutare i fattori di rischio ad esse correlati*

Metodo dello studio

- Arruolamento previo consenso informato
- Esecuzione di FibroScan
- Prelievo di sangue per test genetico
- Raccolta dati clinici
- Analisi statistica

Steatosi : CAP ≥ 248db/m

Steatosi Severa : CAP ≥ 285db/m

Fibrosi : TE ≥ 7.1 kPa

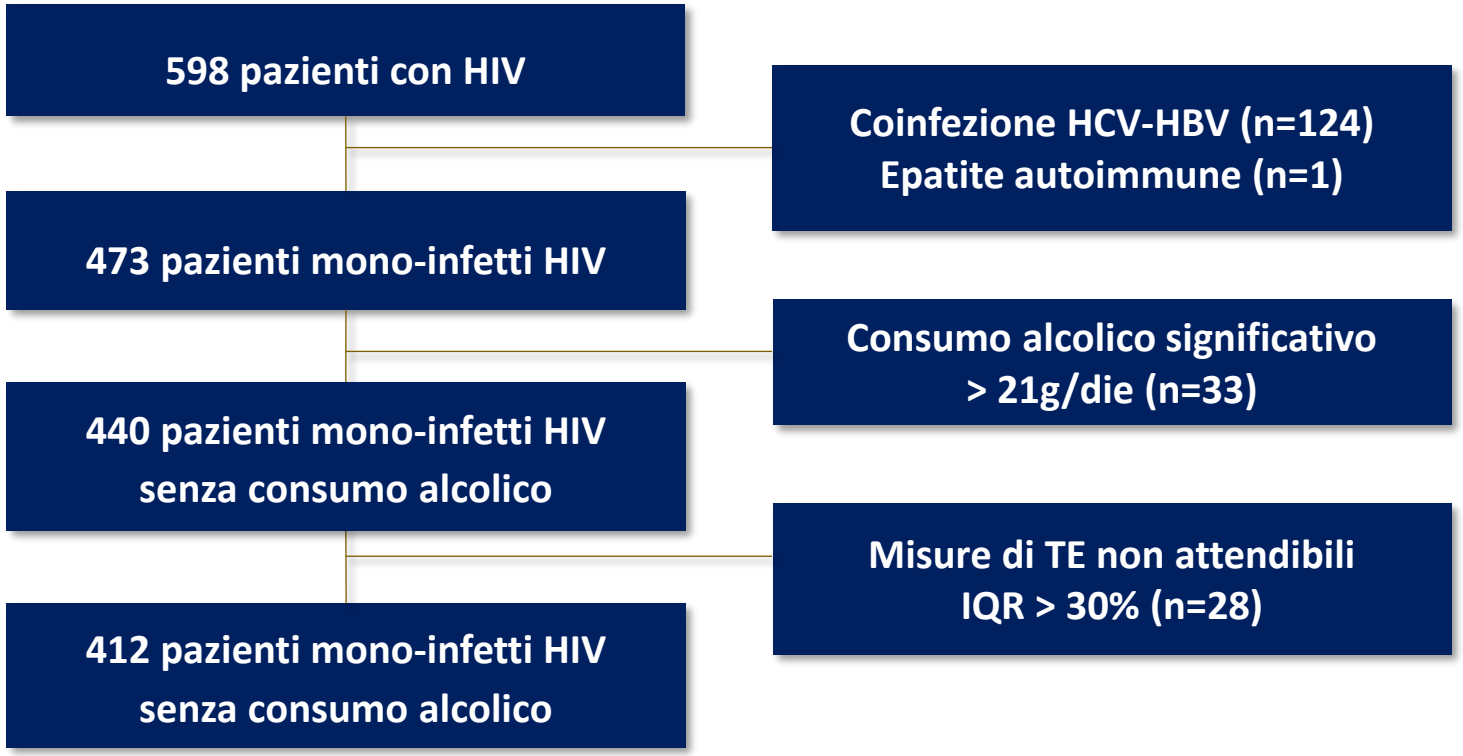
Cirrosi : TE ≥ 13 kPa

Polimorfismi PNPLA3

Analisi univariata e multivariata tramite regressione logistica

Mazzola G. et al.

Flow-chart: selezione dei partecipanti allo studio

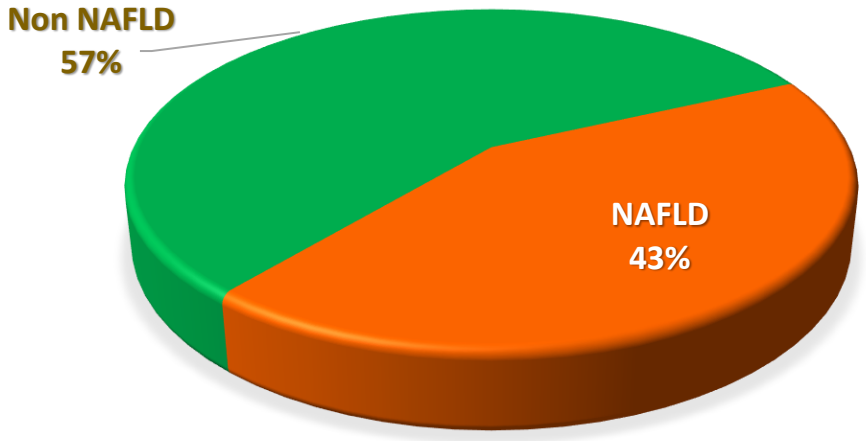


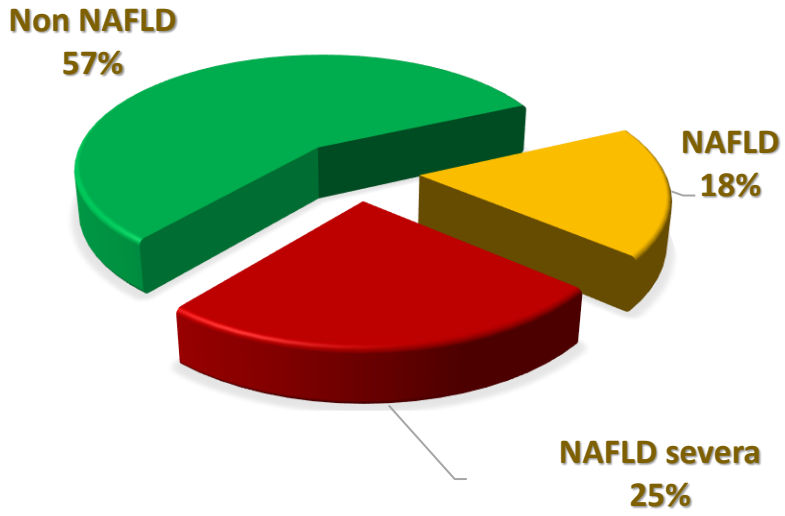
Mazzola G. et al.

Risultati

La prevalenza di NAFLD nella nostra popolazione è del **43%** (176/412 pz);

la prevalenza di NAFLD severa è del **25%** (102/412 pz).



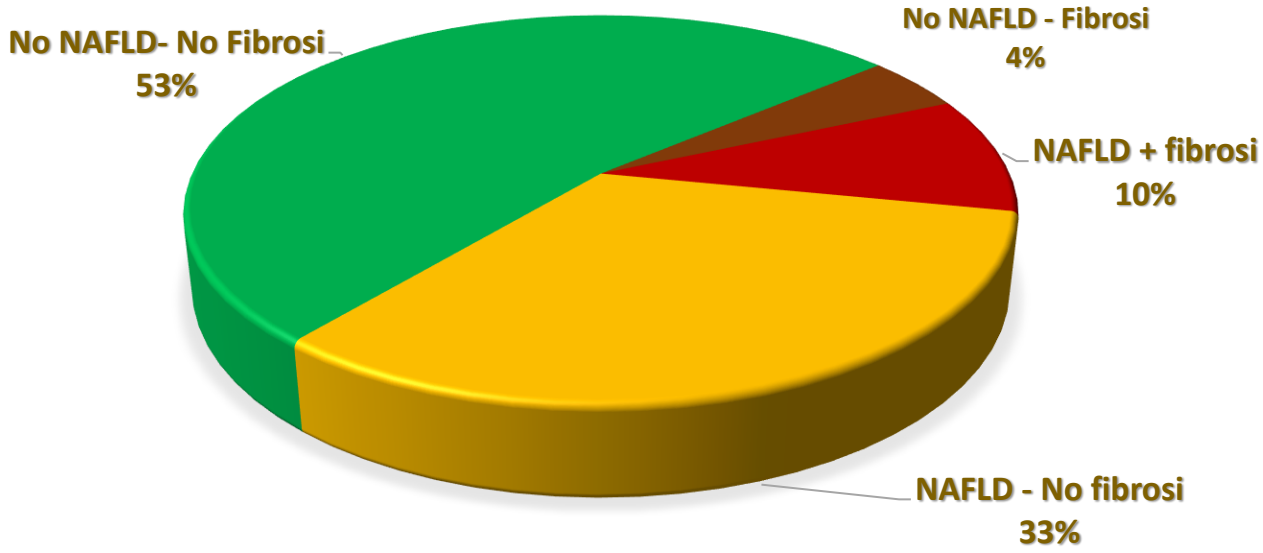


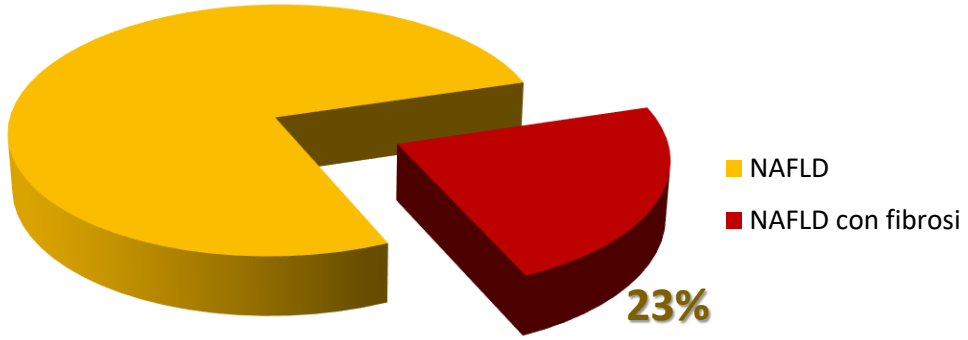
Mazzola G. et al.

Risultati

La prevalenza di fibrosi epatica nella nostra coorte è del 14% (59/412 pz)

La prevalenza di fibrosi epatica nei pazienti HIV con steatosi è del 23% (40/176 pz)





La prevalenza di cirrosi epatica è del 2% (8 pz, di cui 6 con NAFLD)

Mazzola G. et al.

NAFLD IN HIV - Comparison Study

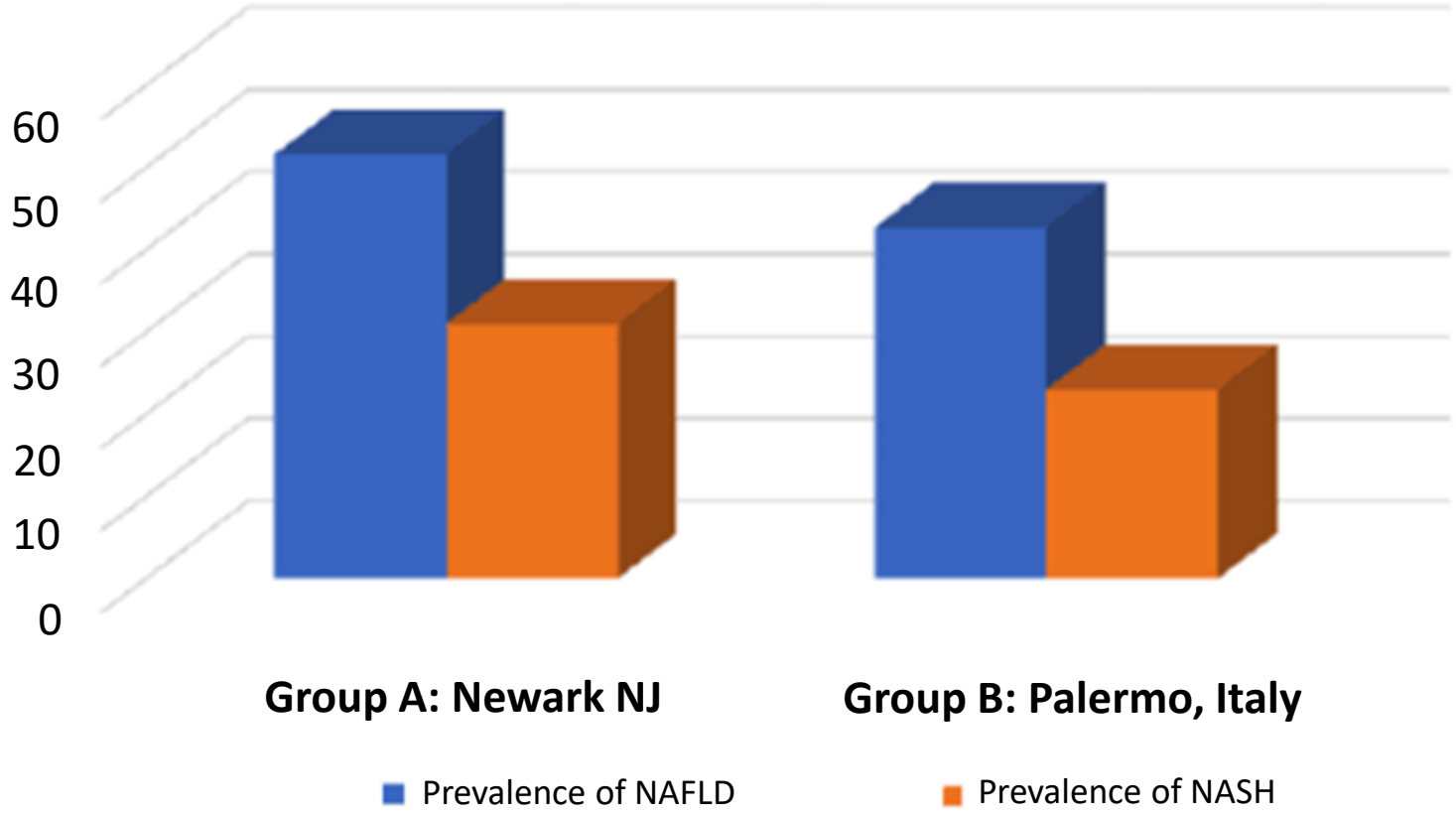
A Comparison Study of Prevalence and Risk Factors for Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH) by Transient Elastography (TE) in HIV Infected Patients

ID Week 2019 Oct 2-6 Wash DC

HendAl-Saleh, MD•, Sunny Choe, PhD•, James P Fallon, MS•, PrerakP. Shukla, MD•'•, Herbert Galang, MD,•, Justin Mathew, MD•, Saraswathi Lakkasani, MD•, PegahMalekazari, MD4, Jihad Slim, MD•

NAFLD IN HIV - Comparison Study

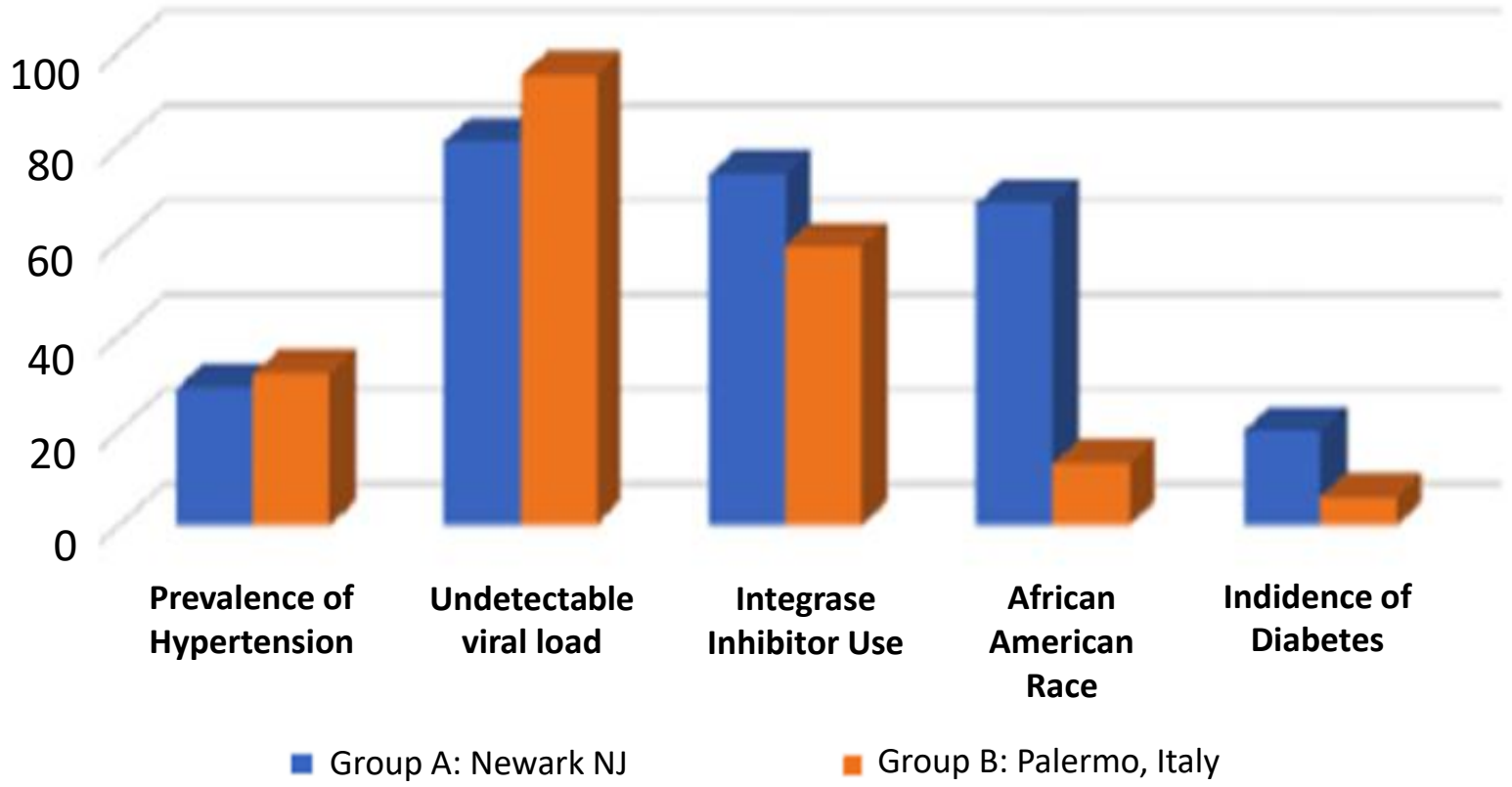
Comparison of the two cohort studies



HendAl-Saleh, ID WEEK 2019 Oct 2-6 Wash DC

NAFLD IN HIV - Comparison Study

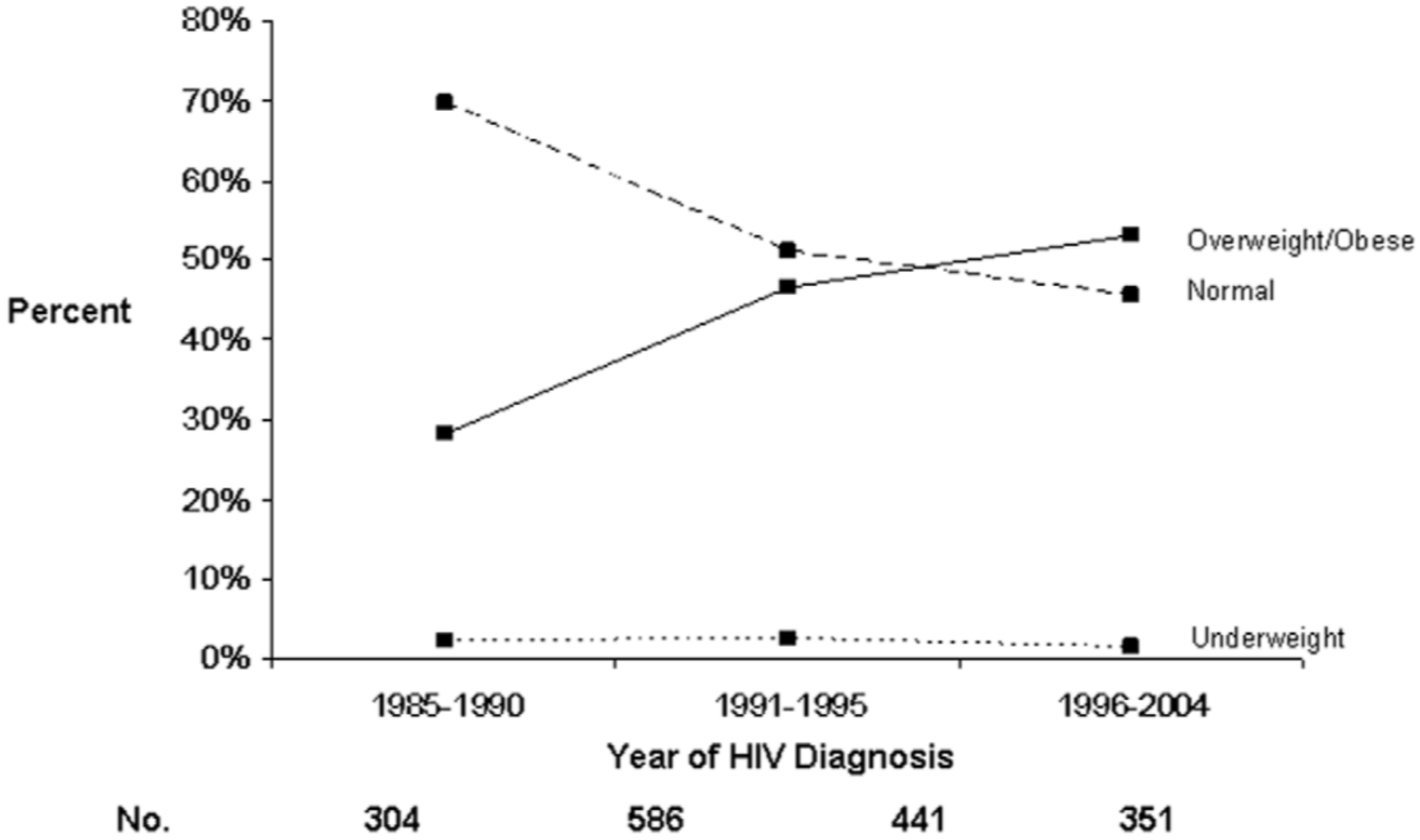
Main differences between the two cohort studies



HendAl-Saleh, ID WEEK 2019 Oct 2-6 Wash DC

NAFLD and increased rate of obesity in HIV infected persons

Increased rate of obesity in HIV infected persons



Crum-Cianflone, PLoSONE 2010

Increased rate of obesity in HIV infected persons

HIV MEDICINE BHIVA British HIV Association

Abstract

EACS 2019 – Abstract Book

First published: 06 November 2019 | https://doi.org/10.1111/hiv.12814

PS12/6

Hepatic steatosis in HIV monoinfected individuals: which impact has baseline BMI and treatment with integrase inhibitors?

J Bischoff, C Schwarze-Zander, C Boesecke, J-C Wasmuth, R Mohr, K van Bremen, L Dold, M Praktiknjo, C Jansen, JK Rockstroh, J Trebicka

Studio longitudinale osservazionale con 412 pazienti arruolati tra il 2013 e il 2017:

significativi valori di CAP più elevati e maggiore aumento di peso nei pazienti in trattamento con **INI** rispetto ai pazienti trattati con PI o NNRTI

Fatty liver in lipodystrophy

ELSEVIER

Metabolism

Volume 96, July 2019, Pages 66-82

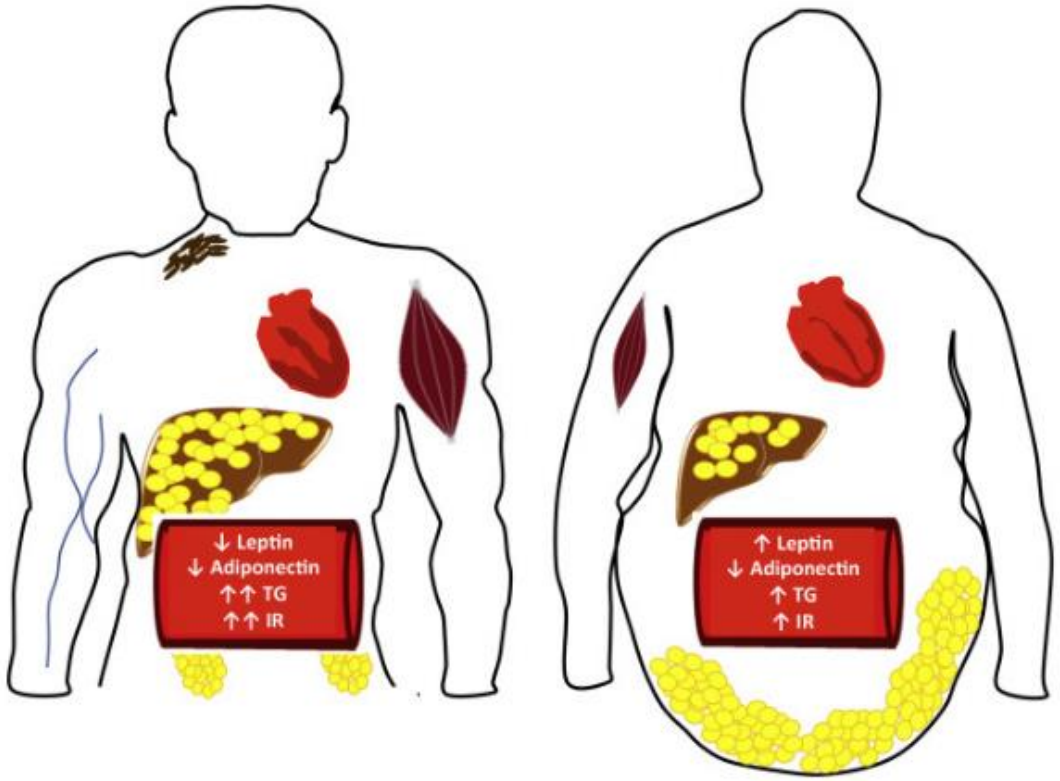
Review

Fatty liver in lipodystrophy: A review with a focus on therapeutic perspectives of adiponectin and/or leptin replacement

Stergios A. Polyzos, Nikolaos Perakakis, Christos S. Mantzoros

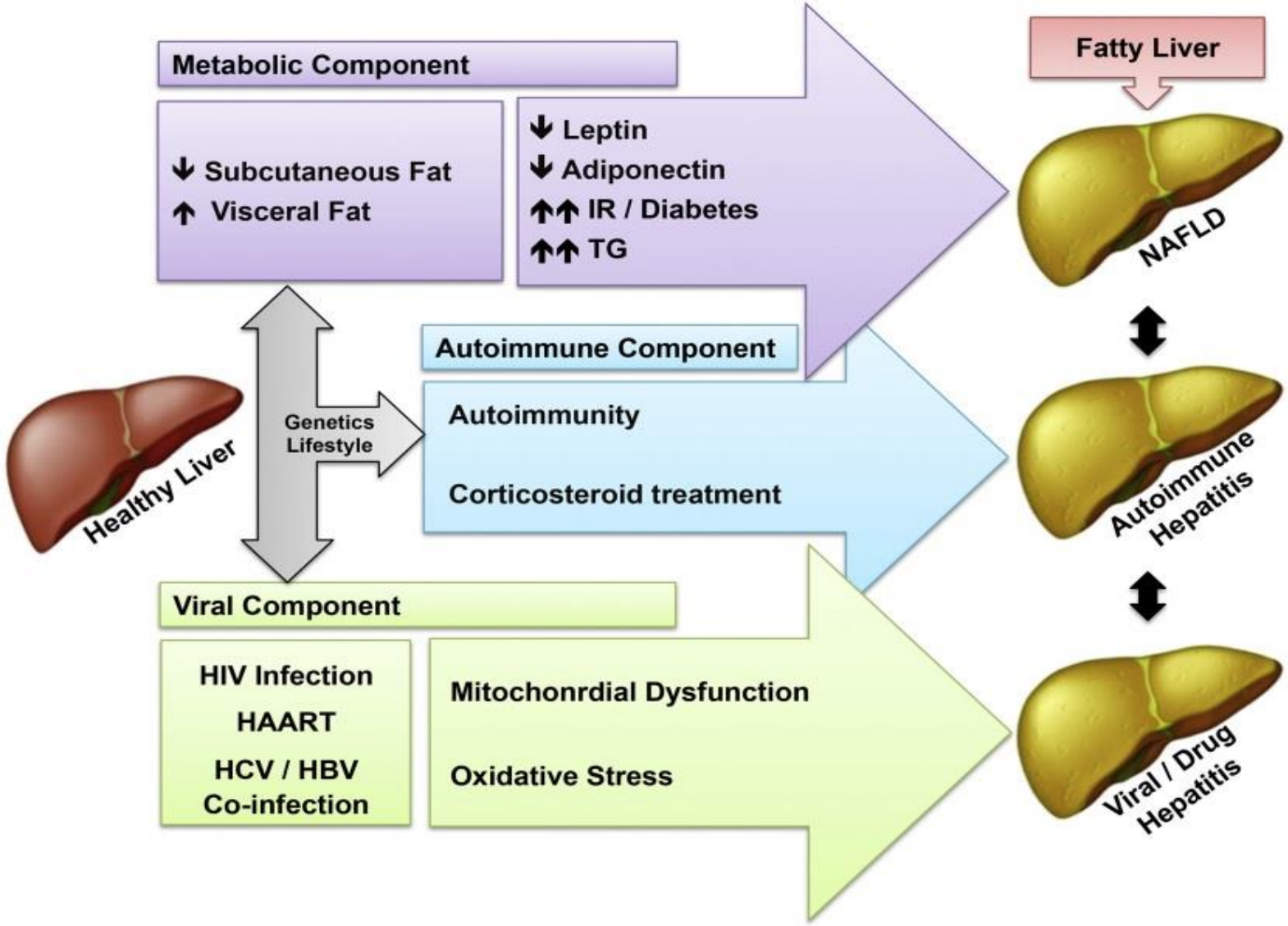
https://doi.org/10.1016/j.metabol.2019.05.001

Fatty liver in lipodystrophy



Metabolic abnormalities in CGL vs. obesity. Individuals with CGL have a muscular appearance with prominent veins, hepatomegaly and occasional heart muscle hypertrophy. The complete lack of adipose tissue results in low leptin and adiponectin levels, high triglycerides and severe insulin resistance. They initially develop hepatic steatosis that progresses rapidly to NASH and liver fibrosis.

Fatty liver in lipodystrophy



Clinical Infectious Diseases

MAJOR ARTICLE

Prevalence, Predictors, and Severity of Lean Nonalcoholic Fatty Liver Disease in Patients Living With Human Immunodeficiency Virus

Adriana Cervo,[1,2] Jovana Milic,[3,4] Giovanni Mazzola,[2] Filippo Schepis,[5] Salvatore Petta,[6] Thomas Krahn,[1] Bertrand Lebouche,[1,7] Marc Deschenes,[8] Antonio Cascio,[2] Giovanni Guaraldi,[3] and Giada Sebastiani[1,8,]

CONCLUSIONS

NAFLD affects 1 in 4 lean patients living with HIV mono-infection. Investigations for NAFLD should be proposed in older patients with dyslipidemia and elevated ALT, even if normoweight.

CID 13 Aprile 2020

Clinical Infectious Diseases

MAJOR ARTICLE

Changes in Liver Steatosis After Switching From Efavirenz to Raltegravir Among Human Immunodeficiency Virus–Infected Patients With Nonalcoholic Fatty Liver Disease

Juan Macías,[1] María Mancebo,[1] Dolores Merino,[2] Francisco Téllez,[3] M. Luisa Montes-Ramírez,[4] Federico Pulido,[5] Antonio Rivero-Juárez,[6] Miguel Raffo,[7] Montserrat Pérez-Pérez,[7] Nicolás Merchante,[1] Manuel Cotarelo,[8] and Juan A. Pineda[1]; for the Spanish AIDS Research Network-HEP09 Study Group

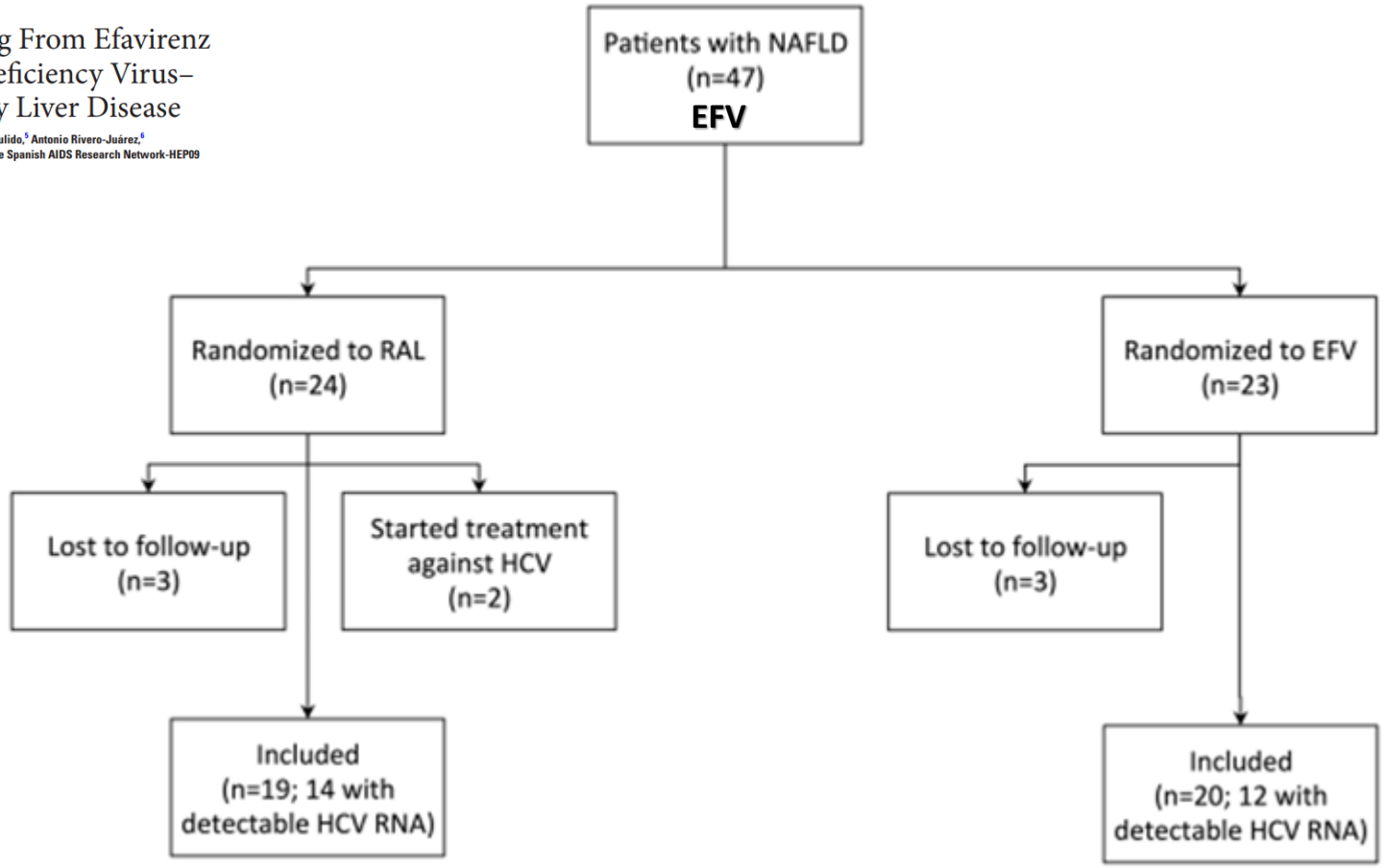
CID 2017 set 15

Disposition of the study patients

Clinical Infectious Diseases
MAJOR ARTICLE

Changes in Liver Steatosis After Switching From Efavirenz to Raltegravir Among Human Immunodeficiency Virus–Infected Patients With Nonalcoholic Fatty Liver Disease

Juan Macías,[1] María Mancebo,[1] Dolores Merino,[2] Francisco Téllez,[3] M. Luisa Montes-Ramírez,[4] Federico Pulido,[5] Antonio Rivero-Juárez,[6] Miguel Raffo,[7] Montserrat Pérez-Pérez,[7] Nicolás Merchante,[1] Manuel Cotarelo,[8] and Juan A. Pineda[1]; for the Spanish AIDS Research Network-HEP09 Study Group



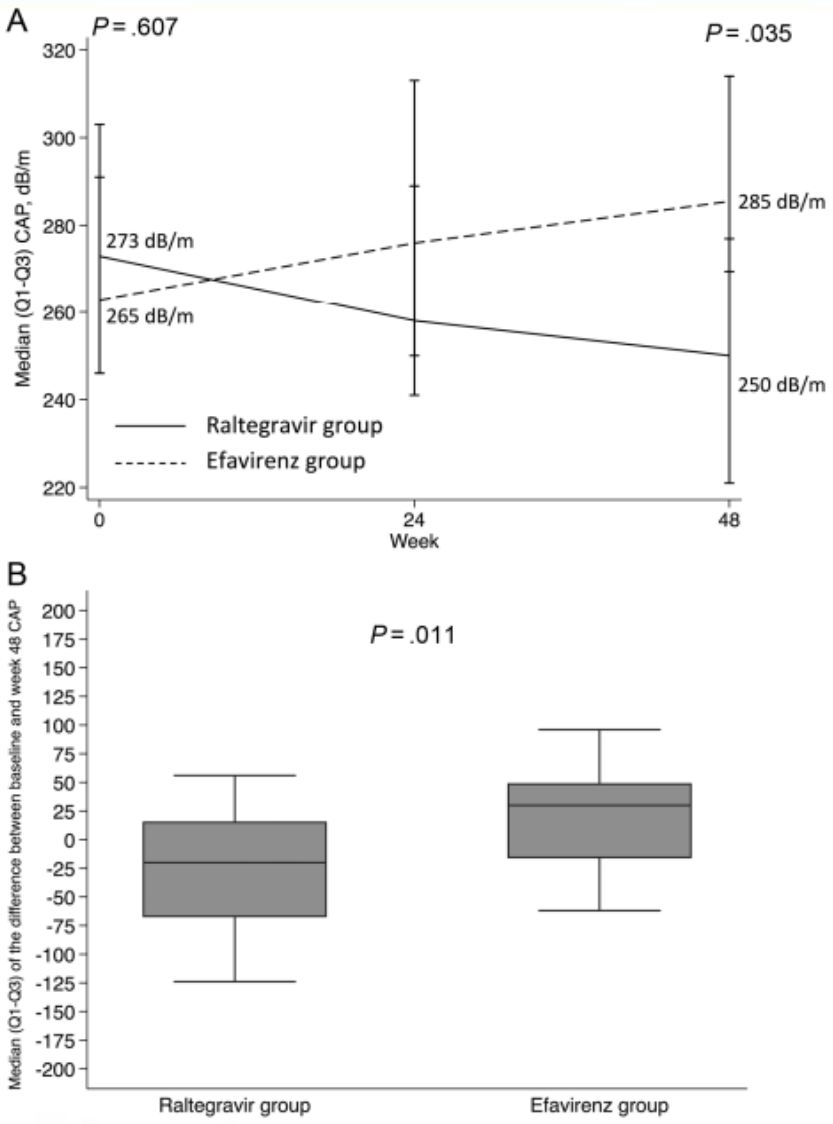
Abbreviations: EFV, efavirenz; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease; RAL, raltegravir.

Changes in CAP values

Clinical Infectious Diseases
MAJOR ARTICLE

Changes in Liver Steatosis After Switching From Efavirenz to Raltegravir Among Human Immunodeficiency Virus–Infected Patients With Nonalcoholic Fatty Liver Disease

Juan Macías,[1] María Mancebo,[1] Dolores Merino,[2] Francisco Téllez,[3] M. Luisa Montes-Ramírez,[4] Federico Pulido,[5] Antonio Rivero-Juárez,[6] Miguel Raffo,[7] Montserrat Pérez-Pérez,[7] Nicolás Merchante,[1] Manuel Cotarelo,[8] and Juan A. Pineda[1]; for the Spanish AIDS Research Network-HEP09 Study Group



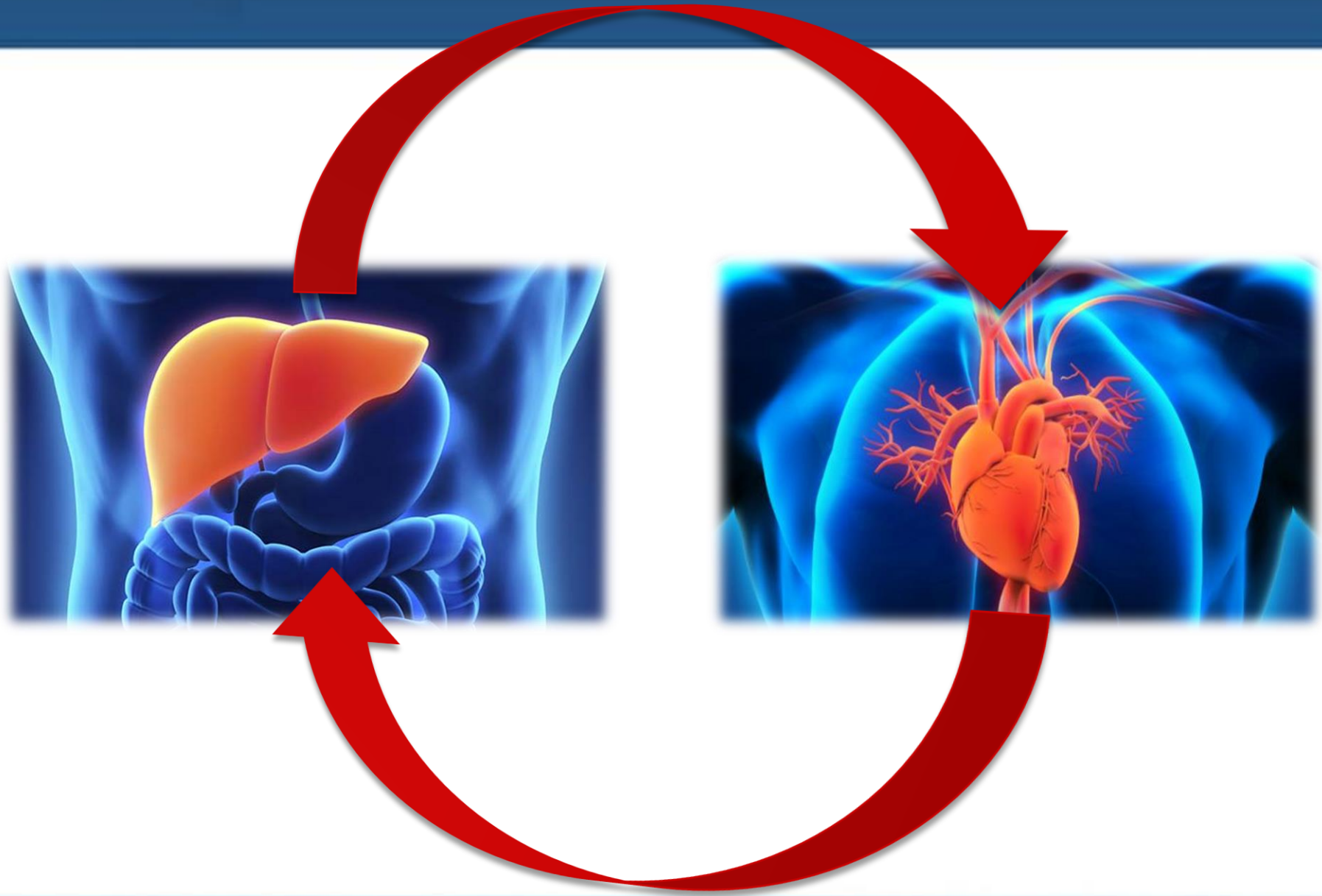
A, Median (Q1–Q3) controlled attenuation parameter (CAP) values by treatment group during follow-up (solid lines, raltegravir group; dashed lines, efavirenz group). P values show comparisons between treatment groups.

B, Comparison of median changes in CAP values. Boxplots represent the median of the difference in CAP value between baseline and week 48.

NAFLD and cardiovascular risk in HIV infected persons

Non Alcoholic Fatty Liver Disease and Significant Liver Fibrosis Increase cardiovascular risk in HIV mono-infected patients

Mazzola G, *Cervo A, Gioé G, Quartararo P, Milic J, De Luca A, Trizzino M, Mazzola S, Colletti P, Petta S, Sebastiani G, Guaraldi G, Cascio A*



Aim

The aim of this study was
to assess the impact of NAFLD and liver fibrosis
on cardiovascular risk in PLWH

Study Design

- Retrospective study of three prospectively maintained cohorts of HIV-infected patients:
  - "Liver Pathologies and HIV in Palermo" (LHIVPa) cohort
  - "Modena HIV Metabolic Clinic" (MHMC) cohort
  - "Liver Diseases in HIV" (LIVEHIV) cohort in Montreal

- All patients underwent Transient Elastography.

- Data on demographic, clinical, biochemical and HIV-related characteristics were collected within at least 3 months from the TE measurement.

Methods

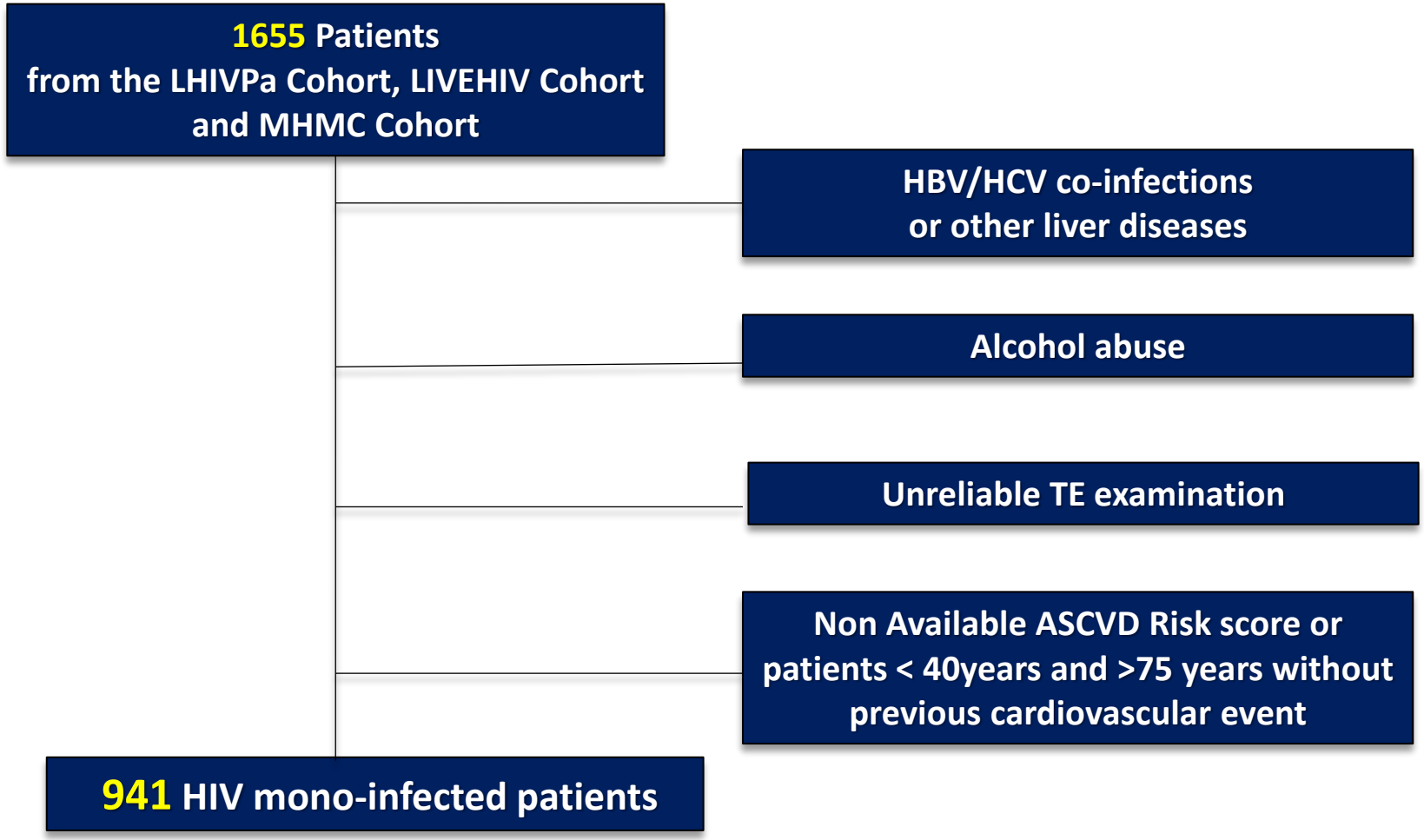
- NAFLD and significant liver fibrosis were defined as controlled attenuation parameter **(CAP) ≥ 288 dB/m** and as liver stiffness measurement **(LSM) > 7 kPa**, respectively.
- Cardiovascular risk was assessed with Atherosclerotic Cardiovascular Disease (**ASCVD**) Risk Estimator, according to the American College of Cardiology/AHA in patients **aged 40 – 75 years**, and categorized as:
  - low < 5%,
  - borderline 5 – 7.4%,
  - intermediate 7.5 – 19.9%
  - high ≥ 20%
- Patients with **previous cardiovascular events** were considered as high risk, regardless of age and ASCVD Risk score.

Statistical Analysis

- Univariable analysis by outcome status (cardiovascular risk classes) **using t-test and Fisher's exact test** for continuous and categorical variables, respectively

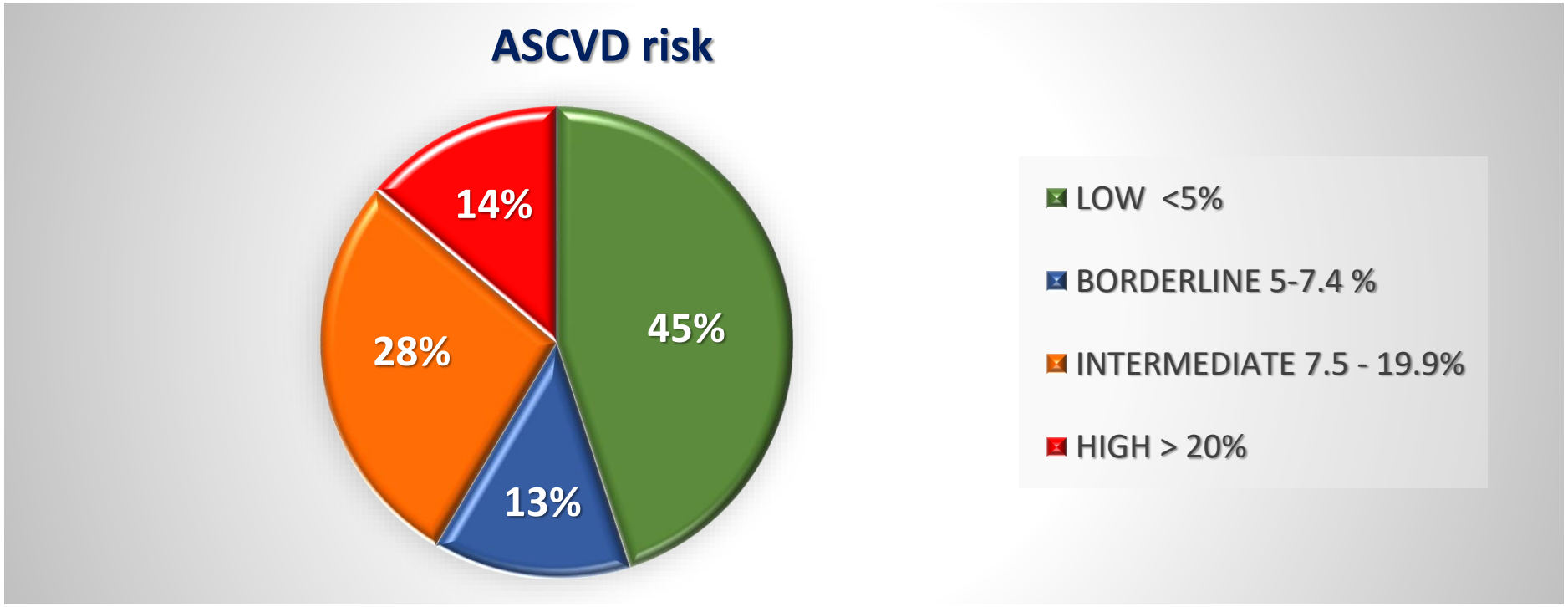
- Multivariable analysis using **adjusted logistic regression**

Flow-chart


1655 Patients
from the LHIVPa Cohort, LIVEHIV Cohort
and MHMC Cohort
HBV/HCV co-infections
or other liver diseases
Alcohol abuse
Unreliable TE examination
Non Available ASCVD Risk score or
patients < 40years and >75 years without
previous cardiovascular event
941 HIV mono-infected patients

Results

941 HIV mono-infected patients (mean age 53 years, 74% males, 98% on ART) were included



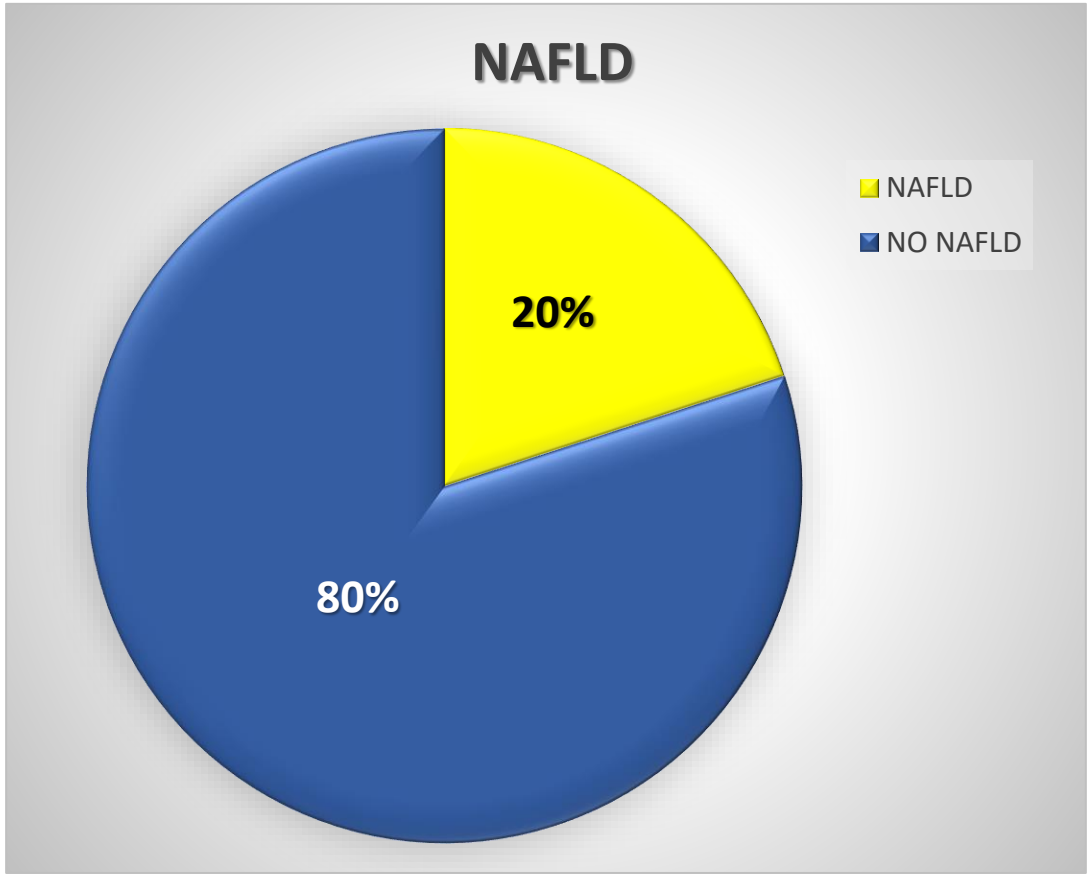
Results

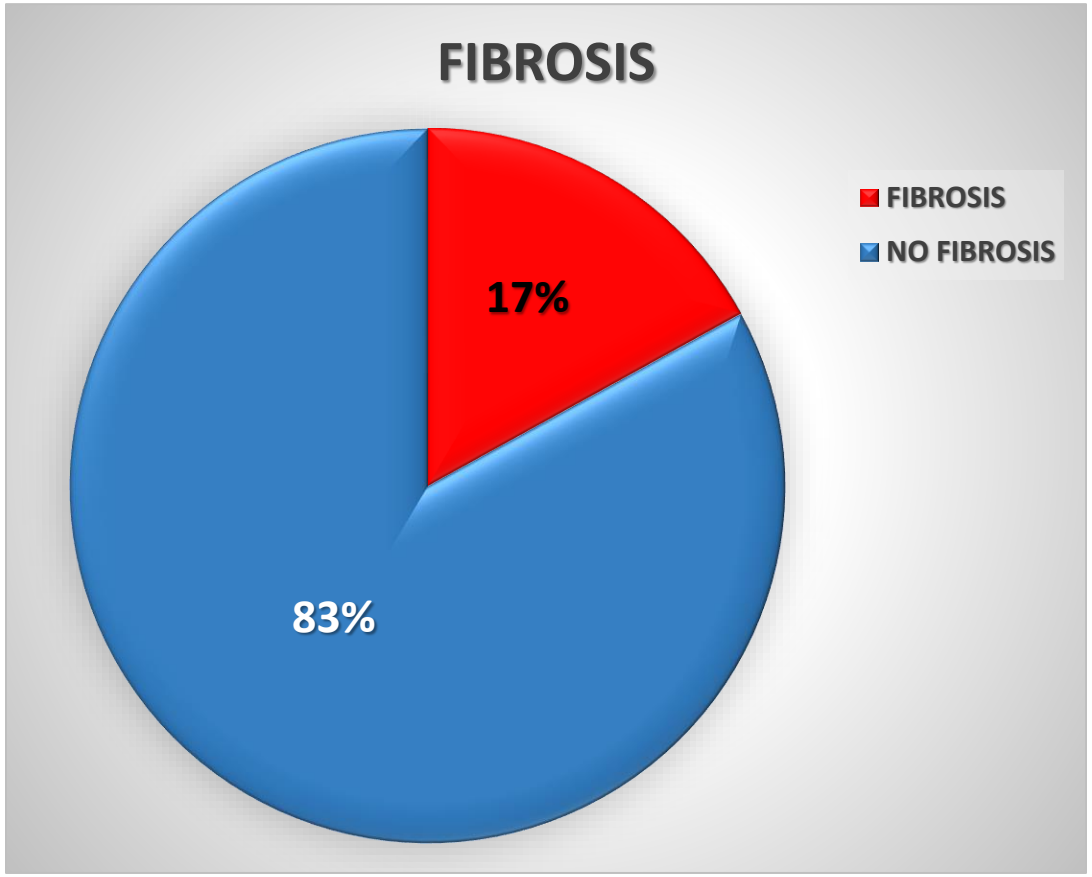
Characteristics of the whole study population by ASCVD risk classes

	ASCVD Risk Classes			
N = 914	Low N = 423	Borderline N= 128	Intermediate N= 260	High N=130
DEMOGRAPHIC CHARACTERISTICS				
Age (years)	49 (5.6) (40-65)	54 (5) (41-67)	57 (5.6) (40-72)	61 (7.5) (41-78)
Male gender (%)	242 (57)	99 (77)	239 (92)	113 (87)
Ethnicity (%)				
White/Caucasian	390 (92)	114 (98)	238 (91)	124 (95)
Black non-Hispanic	27 (7)	13 (10)	17 (6)	4 (3)
Other	6 (1)	1 (1)	5 (2)	2 (2)

Results

Prevalence of NAFLD and significant liver fibrosis was 20% and 17%, respectively





Results

Univariable and multivariable analysis by outcome, i.e. 10 years CVD risk, in the overall study population

	Univariable			Multivariable		
	OR	95% CIs	P value	aOR	95% CIs	P value
NAFLD (CAP ≥ 288 dB/m)	1.86	1.34-2.60	< 0.01	1.77	1.16-2.69	< 0.001
Liver Fibrosis LSM ≥ 7.1 kPa	1.66	1.69-2.37	< 0.01	1.54	0.97-2.44	0.06
BMI > 25 Kg/m²	1.79	1.36-2.35	< 0.01	1.79	1.34-2.41	< 0.001
Nadir CD4 < 200/mmc	1.40	1.07-1.84	0.01295	1.21	0.9-1.60	0.19
Active IVDU	1.55	1.06-2.27	0.01925	0.82	0.64-1.50	0.93
Duration HIV (years)	-	-	< 0.001	1.04	1.03-1.06	< 0.001
NAFLD: LiverFibrosis				0.49	0.23-1.07	0.07

12° CONGRESSO NAZIONALE
Italian Conference on AIDS and Antiviral Research
12-16 ottobre 2020 DIGITAL EDITION

NAFLD PHENOTYPE AND PREVALENCE ACROSS THE MENOPAUSE SPECTRUM IN WOMEN WITH HIV

J. Milic[1], A. Cervo[2], A. Malagoli[1], V. Menozzi[1], D. Morini[1], F. Carli[1], A. Raimondi[1], M. Menozzi[1], I. Franconi[1], C. Mussini[1], G. Sebastiani[3], G. Guaraldi[1]

[1]University of Modena and Reggio Emilia, [2]Infectious Diseases Unit, PROMISE, University of Palermo, Palermo, Italy, [3]Chronic Viral Illness Service, McGill University Health Centre, Montreal, Canada

Background and Aims: Both menopause and non-alcoholic fatty liver disease (NAFLD) are major metabolic events with potential systemic effects. The objective of the study was to describe natural history of NAFLD during menopause transition and the interplay between these two conditions in women living with HIV (WLWH).

Method: This was a cross-sectional study of consecutive WLWH attending Modena HIV Metabolic Clinic in 2018-2019. Women with hazardous alcohol intake and hepatitis B or hepatitis C virus co-infection were excluded. NAFLD and significant liver fibrosis were assessed with transient elastography and defined as controlled attenuation parameter (CAP) >248 dB/m and as liver stiffness measurement >= 7.1 kPa respectively. Menopause was determined according to STRAW criteria including 4 periods: reproductive, transitional, early and late menopause. Due to low absolute number of NAFLD cases, these criteria were further simplified dividing WLWH as "pre-menopause" if being in the first two periods and "post-menopause" if being in the last two periods. Two logistic regression models were built to explore predictors associated with NAFLD in pre-menopause and post-menopause periods, using as covariates metabolic and anthropometric variables.

Results: We analyzed 296 WLWH with mean age=54.3 (+-7.9) years, current median CD4=710 µL (IQR=543-896) and HIV RNA undetectability in 98.3% of cases. Overall, NAFLD and significant fibrosis prevalence in WLWH were 33.8% and 11.8% respectively. NAFLD and significant fibrosis were observed in 33.3% and 7.4% in reproductive, 29.4% and 11.8% in menopause transition, 32.6% and 12.9% in early menopause and 56.3% and 12.5% in late menopause respectively (p=0.07 and p=0.66). Table shows characteristics between WLWH with NAFLD in reproductive and menopause period. In two multivariate logistic models, HIV duration, lipoatrophy, CD4/CD8 ratio and obesity were not associated with an increased risk of NAFLD in pre-menopause and post-menopause, while the HOMA was the only co-variate to predict NAFLD in post-menopausal WLWH (OR=0.38, 0.15-0.8; p=0.03).

Conclusion: Prevalence and phenotype of NAFLD and liver fibrosis did not differ across the menopause in WLWH, suggesting that more complex immune-metabolic pathways, not captured by STRAW criteria, are involved in NAFLD natural history in aging WLWH.

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NAFLD PHENOTYPE AND PREVALENCE ACROSS THE MENOPAUSE SPECTRUM IN WOMEN WITH HIV

J. Milic[1], A. Cervo[2], A. Malagoli[1], V. Menozzi[1], D. Morini[1], F. Carli[1], A. Raimondi[1], M. Menozzi[1], I. Franconi[1], C. Mussini[1], G. Sebastiani[3], G. Guaraldi[1]

[1]University of Modena and Reggio Emilia, [2]Infectious Diseases Unit, PROMISE, University of Palermo, Palermo, Italy, [3]Chronic Viral Illness Service, McGill University Health Centre, Montreal, Canada

Variable	Pre-menopause NAFLD	Post-menopause NAFLD	p
	32 (34.4%)	61 (65.6%)	
Age, years, mean (±SD)	49.5 (±6.6)	57.8 (±6.6)	
BMI, kg/m², mean (±SD)	26.9 (±5.9)	26.3 (±7.1)	0.56
Waist circumference, cm, mean (±SD)	94.1 (±13.6)	91.3 (±10.3)	0.44
Obesity (%)	8 (25%)	11 (18.3%)	0.63
HIV duration, years, median (IQR)	23.8 (14.8-27.6)	26.3 (23.9-30.3)	0.03
Nadir CD4, median, c/µL, median (IQR)	251 (145-385)	199 (100-277)	0.11
Current CD4, median, c/µL, (IQR)	727 (533-931)	716 (575-923)	0.75
CD4/CD8 ratio, mean (±SD)	1.1 (±0.5)	1.2 (±0.6)	0.67
Type 2 diabetes (%)	4 (12.5%)	16 (16.2%)	0.21
Multimorbidity (%)	5 (15.6%)	46 (75.4)	<0.001
FIB 4, mean (±SD)	1.2 (±0.9)	1.5 (±0.7)	0.09
LDL cholesterol, mg/dl, mean (±SD)	129 (±41.5)	125 (±41.2)	0.67
HDL cholesterol, mg/dl, mean (±SD)	62.6 (±16.3)	57.7 (±13.7)	0.21
Triglycerides, mg/dl, mean (±SD)	103.7 (±40.7)	143.1 (±77)	0.01
HOMA, mean	2.4 (±1.2)	3 (±1.9)	0.54

© 2015. Published by The Company of Biologists Ltd | Disease Models & Mechanisms (2015) 8, 1037-1046 doi:10.1242/dmm.019950

RESEARCH ARTICLE

Ovarian senescence increases liver fibrosis in humans and zebrafish with steatosis

Elena Turola[1,*], Salvatore Petta[2,*], Ester Vanni[3], Fabiola Milosa[1], Luca Valenti[4], Rosina Critelli[1], Luca Miele[5], Livia Maccio[6], Vincenza Calvaruso[2], Anna L. Fracanzani[4], Marcello Bianchini[1], Nazarena Raos[1], Elisabetta Bugianesi[3], Serena Mercorella[1], Marisa Di Giovanni[6], Antonio Craxì[2], Silvia Fargion[4], Antonio Grieco[5], Calogero Cammà[2], Franco Cotelli[7] and Erica Villa[1,‡]

Conclusions

In conclusion, this study on a large cohort of women and age-matched men with histological diagnosis of NAFLD shows that **menopausal status increases the risk of fibrosis severity**. These data were supported and reinforced by our findings in overfed zebrafish with experimental steatosis. These results, which need validation in other NAFLD settings, suggest that a more intensive management should be planned for females with NAFLD in pre- and early menopause.

EASL

THE INTERNATIONAL LIVER CONGRESS

15-19 April 2020
London, UK

POSTERS
THU-001 – THU-519

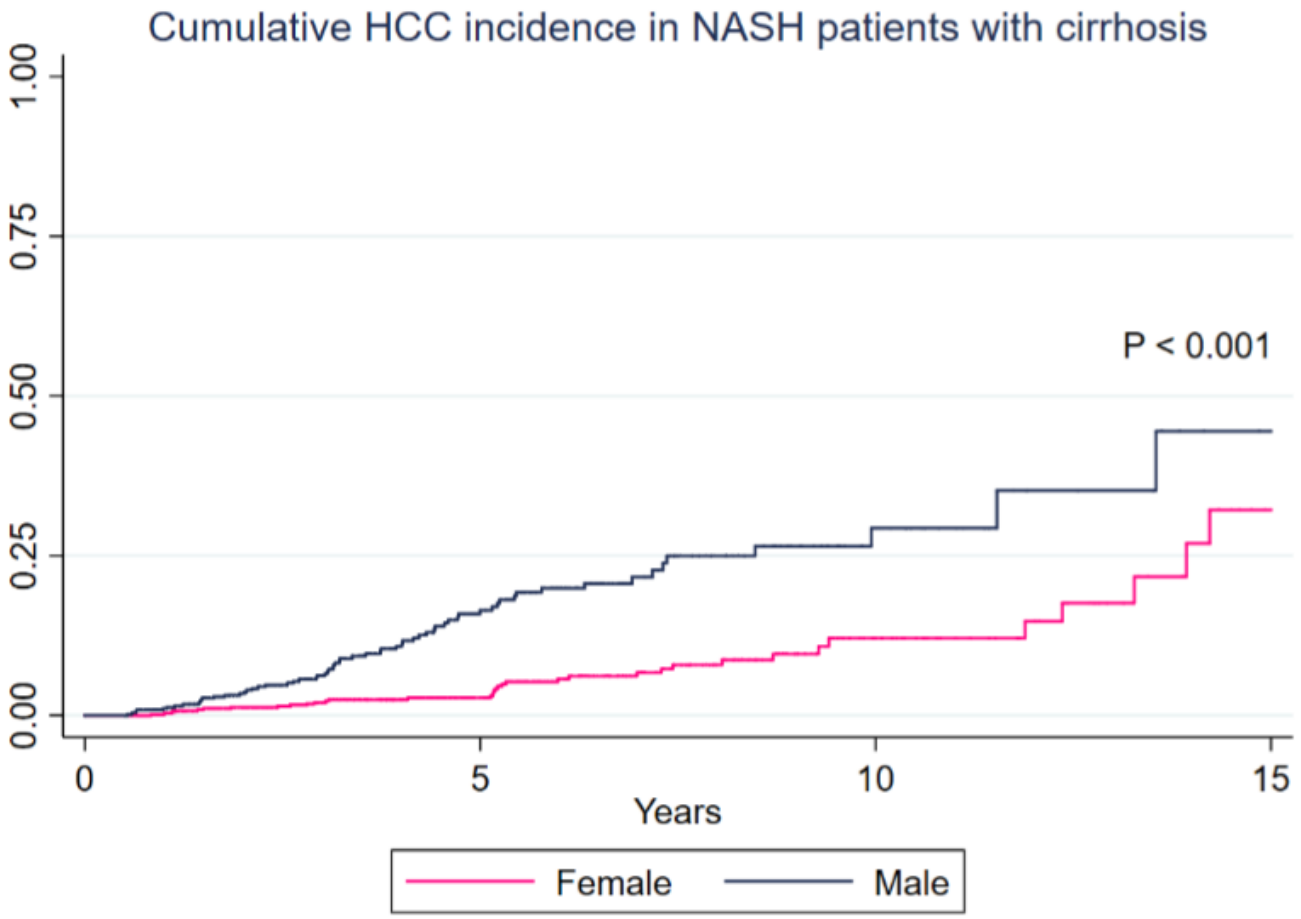
Poster programme version as of 10.04.2020

THU029

Gender difference and hepatocellular carcinoma incidence in non-alcoholic steatohepatitis patients with advanced liver fibrosis

Kanokwan Pinyopornpanish[1,2], Arthur McCullough[1], Carlos Romero-Marrero[1]

[1]*Cleveland Clinic Foundation, Digestive Disease and Surgery Institute, Cleveland, United States,*
[2]*Chiang Mai University, Internal Medicine, Chiang Mai, Thailand*



Conclusions

- Current guidelines recommend **early initiation of cART** that is less likely to induce insulin resistance, mitochondrial dysfunction and dyslipidemia.

- In contrast, as a result of **increasing life expectancy** in good health, this population will adopt the more traditional risk factors for NAFLD/NASH (lifestyles).

- HIV-treating physicians should be aware of the etiology, pathogenesis and treatment of NAFLD/ NASH in order to identify and treat the patients at risk (screening)

Thanks for your attention!