The pathway of NAFLD vs MAFLD toward significant fibrosis

Milic J[1], Renzetti S[2], Motta F[1], Gozzi L[3], Besutti G[4], Burastero G[3], Iadisernia V[3], Lebouche B[5], Al Hinai S[5], Deschenes M[5], Calza S[2], Raggi P[6], Mussini C[1,3], Sebastiani G[5], Guaraldi G[1,3]

[1]Modena HIV Metabolic Clinic, University of Modena and Reggio Emilia, Modena, Italy; [2]University of Brescia, Brescia, Italy; [3]Azienda Ospedaliera Universitaria Policlinico di Modena, Modena, Italy; [4]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [5]McGill University, Montreal, Canada; [6]University of Alberta, Edmonton, Canada

522

Background

The ongoing debate regarding non-alcoholic fatty liver disease (NAFLD)/metabolic-associated fatty liver disease (MAFLD) should consider risk of progression of fatty liver disease (FLD).

We aimed to describe transition of NAFLD and MAFLD states towards significant fibrosis in people with HIV (PWH).

Methods

This was a longitudinal study of two prospective cohorts (Modena HIV Metabolic Clinic and LIVEHIV Montreal) of PWH. FLD was assessed at least twice with controlled attenuation parameter (CAP ≥248 dB/m) by transient elastography. Significant liver fibrosis was defined as liver stiffness ≥7.1 kPa. NAFLD was defined as FLD in absence of significant alcohol intake or HBV or HCV co-infections. MAFLD was defined as the presence of FLD and at least one of the criteria shown in the Figure 1.

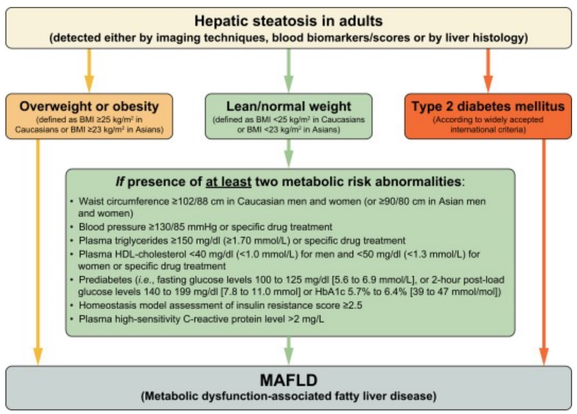


Figure 1. *MAFLD criteria according to Eslam M. JHepatol.2020;73(1):202-209].*

A continuous-time multi-state Markov model was used to describe the process in which a study patient moved through a series of states allowing joint analysis of care length, incidence of FLD or fibrosis progression or reversion. The probabilities to switch from one state to another were modelled according to an exponential distribution for time-to-event data, considering censored follow-up times.

The events were the transitions between the states. The analyses were performed separately for NAFLD and three MAFLD categories in which minimum two and maximum four assessments for FLD were considered.

The highest risk of MAFLD progression - **PWH with MAFLD with BMI >25 kg/m² (Figure 4).**

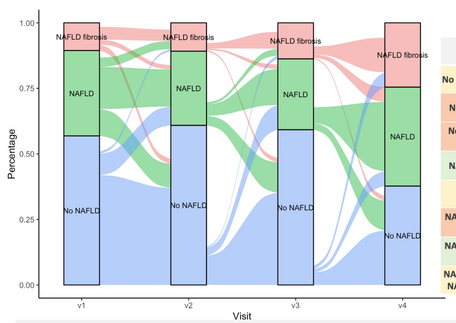
The highest risk of fibrosis progression - **PWH with MAFLD with BMI >25 kg/m² (Figure 4).**

The highest probability of MAFLD reversibility **– PWH with lean MAFLD (Figure 5).**

The highest probability of fibrosis reversibility – **PWH with diabetes (Figure 3).**

Results and discussion

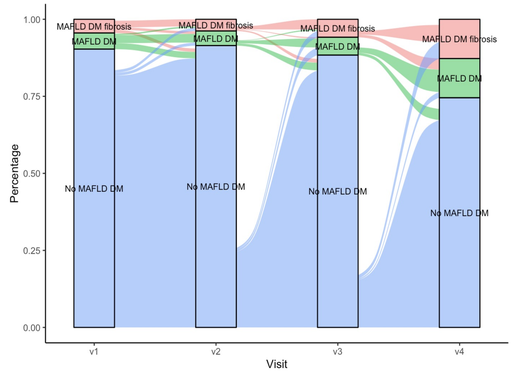
- A total of 888 PWH were screened for FLD, with a mean follow-up of 2 years, mean age 54.4 years, 77% males.
- At the first visit, after excluding PWH with alcohol intake and viral co-infections, prevalence of NAFLD was 42.9% (285/664).
- The overall prevalence of the MAFLD was 34.3% (305/888):
  - MAFLD with BMI≥25 kg/m² was present in 244 (27.5%),
  - MAFLD with diabetes in 86 (9.7%)
  - lean MAFLD in 33 (3.7%).



Probability of state transition for NAFLD

Path	Estimates
No NAFLD - No NAFLD	80.3%
No NAFLD - NAFLD	17%
No NAFLD – NAFLD with fibrosis	2.6%
NAFLD – no NAFLD	36.4%
NAFLD - NAFLD	53.4%
NAFLD – NAFLD with fibrosis	10.2%
NAFLD with fibrosis - NAFLD	21.3%
NAFLD with fibrosis – NAFLD with fibrosis	58.5%

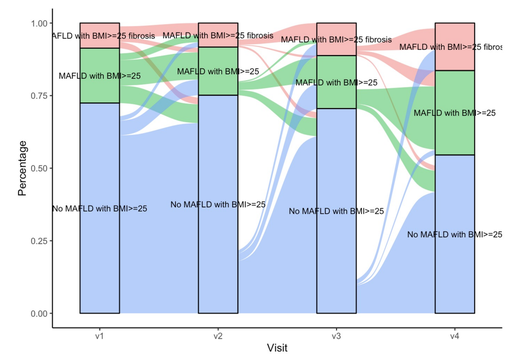
Figures 2-5 *show alluvial plots of state transitions in NAFLD (Figure 2) and in MAFLD with BMI≥25 kg/m2 (Figure 3), with diabetes (Figure 4) and lean MAFLD (Figure 5). Each panel is accompanied by table with probabilities to move from one state to another.*



Probability of state transition of MAFLD with diabetes

Path	Estimates
No MAFLD - No MAFLD	96.9%
No MAFLD - MAFLD	1.5%
No MAFLD – MAFLD with fibrosis	1.6%
MAFLD – no MAFLD	40%
MAFLD - MAFLD	52.3%
MAFLD – MAFLD with fibrosis	7.7%
MAFLD with fibrosis - MAFLD	18.9%
MAFLD with fibrosis – MAFLD with fibrosis	58.5%

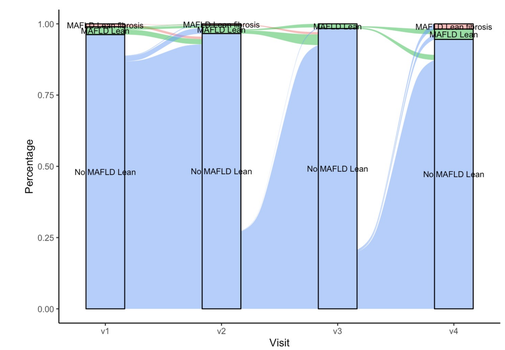
Figure 3



Probability of state transition of MAFLD with BMI ≥ 25

Path	Estimates
No MAFLD - No MAFLD	88.3%
No MAFLD - MAFLD	8.2%
No MAFLD – MAFLD with fibrosis	3.5%
MAFLD – no MAFLD	35.7%
MAFLD - MAFLD	53.1%
MAFLD – MAFLD with fibrosis	10.5%
MAFLD with fibrosis - MAFLD	18.8%
MAFLD with fibrosis – MAFLD with fibrosis	55.2%

Figure 4



Probability of state transition of MAFLD with BMI <25 (lean)

Path	Estimates
No MAFLD - No MAFLD	98%
No MAFLD - MAFLD	1.7%
No MAFLD – MAFLD with fibrosis	0.3%
MAFLD – no MAFLD	65.8%
MAFLD - MAFLD	28.9%
MAFLD – MAFLD with fibrosis	5.3%
MAFLD with fibrosis - MAFLD	10%
MAFLD with fibrosis – MAFLD with fibrosis	0%

Figure 5

Conclusion

- Use of Markov models depicts dynamic changes of FLD with or without fibrosis over time.
- The highest risk of liver fibrosis progression was observed in PWH with MAFLD with BMI >25.
- MAFLD categories offer the possibility to stratify PWH at highest risk of hepatic and extra-hepatic adverse outcomes.

Corresponding author:
Jovana Milic, MD, PhD; jovana.milic@gmail.com