

The natural history of NASH-induced advanced fibrosis in a large cohort of patients with type-2 diabetes

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1 INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) is a progressive disease that can lead to advanced fibrosis (AF) especially in patients with type-2 diabetes (T2D)
- Relatively small studies based on liver histology have shown that liver fibrosis has a bidirectional nature in NAFLD patients
- However, large-scale data on AF progression and regression in diabetics are lacking

2 AIM

- To assess the transition of AF in a large cohort of diabetics and define factors associated with worsening or improvement in fibrosis

3 METHOD

- Using ICD-9 codes, all T2D with the diagnosis of NAFLD at a large tertiary center were identified
- Patients with secondary causes of hepatic steatosis (excessive alcohol consumption, hepatitis C etc.) were excluded
- Non-invasive scores to assess AF were calculated at baseline (BL) and then recalculated using last follow up (LF) laboratory values to assess for the transition using the following cutoffs (AST/ALT > 1.4, APRI > 1.5, FIB-4 > 2.67, NFS > 0.676)
- Patients were divided into 4 groups as follows: No AF either times (BL and LF), AF both times, transition from no AF at BL to AF at LF, transition from AF to no AF.
- Clinical factors are associated with transition in AF status were assessed

4 RESULTS

- A total of 50,695 subjects are included in the analysis with a mean age of 51.2±11.6 at BL and 59.6±11.6 years at LF
- Median duration between 1st and last available labs was 84.4 (24 -199) months
- The prevalence of obesity, hypertension, chronic kidney disease (CKD), hyperlipidemia and coronary artery disease (CAD) increased during this period (p<0.001)

- During this period, 25.8% of subjects transitioned from no evidence of AF to AF (progression), 6.4% transition from AF to no AF (regression) and, the rest stayed stable (**Figure1**)

- Clinical factors associated with transition from no AF to AF were female gender, African-American race, and the presence of baseline obesity, CKD or CAD

- In terms of T2D medications, the use of insulin was associated with progression to AF (OR (95%CI) =1.36(1.29, 1.43), p<0.001), whereas the use of oral hypoglycemic agents was protective (OR (95% CI) = 0.92 (0.87, 0.97), p=0.002) (**Table 1**)

- The use of statins was associated with increased odds of AF regression (OR (95% CI) = 1.12 (1.00, 1.25) (p =0.045) (**Table 2**)

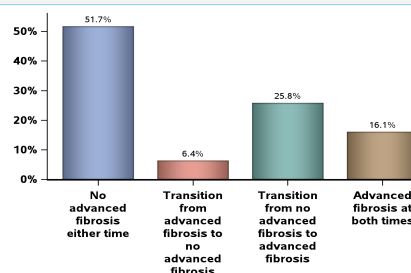


Figure 1. Transition in advanced fibrosis based on noninvasive fibrosis scores

Table 1. Analysis of factors associated with transition from no AF to AF in subjects without suspected AF at baseline

Factor	OR (95% CI)	p-value
Female vs. Male	1.22 (1.16, 1.28)	<0.001
Ethnicity		
African-American vs. Caucasian	1.10 (1.04, 1.16)	<0.001
Other vs. Caucasian	0.88 (0.79, 0.97)	0.01
Age at 1st lab (5 year increment)	1.23 (1.21, 1.24)	<0.001
Family history of Diabetes	0.93 (0.89, 0.98)	0.004
Family history of HTN	0.91 (0.86, 0.95)	<0.001
1st PLT (25 unit increment)	0.91 (0.90, 0.92)	<0.001
1st ALT (25 unit increment)	0.76 (0.73, 0.80)	<0.001
1st AST (25 unit increment)	1.38 (1.29, 1.48)	<0.001
1st ALP (25 unit increment)	1.05 (1.03, 1.06)	<0.001
1st Albumin (1 unit increment)	0.81 (0.78, 0.84)	<0.001
Months between labs (24 month increment)	1.14 (1.13, 1.16)	<0.001
CAD	1.11 (1.05, 1.18)	<0.001
CKD	1.67 (1.55, 1.79)	<0.001
Obesity	1.46 (1.39, 1.53)	<0.001
Hyperlipidemia	0.74 (0.70, 0.78)	<0.001
DVT	1.32 (1.18, 1.48)	<0.001
Malnutrition	1.21 (1.03, 1.42)	0.019
Diuretics	1.31 (1.24, 1.38)	<0.001
Oral Hypoglycemics	0.92 (0.87, 0.97)	0.002
Insulin	1.36 (1.29, 1.43)	<0.001
ARB	0.94 (0.89, 0.99)	0.027
Beta_Blockers	1.20 (1.14, 1.27)	<0.001
Fibrates	0.90 (0.84, 0.97)	0.005
PPI	1.06 (1.01, 1.11)	0.012
PTX	1.43 (1.03, 1.99)	0.034

Table 2. Analysis of factors associated with transition from AF to no AF in subjects with suspected AF at baseline

Factor	OR (95% CI)	p-value
Age at 1st lab (5 year increment)	0.83 (0.81, 0.85)	<0.001
Family history of HTN	1.19 (1.08, 1.31)	<0.001
Family history of Obesity	0.39 (0.22, 0.70)	0.002
1st PLT (25 unit increment)	1.13 (1.11, 1.14)	<0.001
1st AST (25 unit increment)	1.04 (1.03, 1.06)	<0.001
1st ALP (25 unit increment)	0.97 (0.94, 0.99)	0.004
1st Albumin (1 unit increment)	0.86 (0.82, 0.90)	<0.001
Months between labs (24 month increment)	0.94 (0.92, 0.97)	<0.001
CKD	0.61 (0.54, 0.70)	<0.001
Obesity	0.53 (0.48, 0.59)	<0.001
Hyperlipidemia	1.45 (1.31, 1.62)	<0.001
Diuretics	0.62 (0.56, 0.68)	<0.001
Insulin	0.88 (0.80, 0.97)	0.007
Statins	1.12 (1.00, 1.25)	0.045
Fibrates	1.23 (1.06, 1.42)	0.006

5 CONCLUSIONS

- We provide data on the natural history of AF transition in a large cohort of patients with T2D based on noninvasive scores
- AF regressed in 6% of the patients without any NAFLD-specific interventions despite increase in the prevalence of risk factors
- The effects of commonly used medications in diabetics on AF progression need further analysis

7 REFERENCES

Singh A, Le P, Peerzada MM, Lopez R, Alkhouri N. The Utility of Noninvasive Scores in Assessing the Prevalence of Nonalcoholic Fatty Liver Disease and Advanced Fibrosis in Type 2 Diabetic Patients. J Clin Gastroenterol. 2018 Mar; 52(3):268-272.

8 CONTACT

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