BLOOD BASED BIOMARKERS AS NON INVASIVE SCREENING TOOLS FOR HEPATIC FIBROSIS IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS (#0006)

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ABSTRACT

BACKGROUND: NAFLD is dramatically increasing in parallel with the pandemic of Type 2 Diabetes Mellitus (T2DM).

OBJECTIVES: We aimed to assess the performance of the most commonly used non-invasive blood biomarkers for liver fibrosis in subjects with T2DM .

METHODS: We investigated 120 consecutive people with T2DM attending the Diabetic Outpatient Clinic at an Academic Hospital in Athens, Greece. All had demographic, clinical and biochemical data recorded. Hepatic Steatosis (HS) was estimated by Magnetic Resonance Imaging determined by Proton Density Fat Fraction Software (MRI-PDFF) and defined as the percentage of total liver fat divided by the liver volume. HS of >5% was considered abnormal. Liver Stiffness Measurement (LSM) was estimated by Two Dimensional Shear Wave Elastography (2D SWE) (Supersonic Image, Aix-en-Provence, France).The PNPLA3(I148M) variant was evaluated by standard molecular techniques. FIBROMAX™, APRI Index, NAFLD Fibrosis score, BARD score, FIB-4 Index were calculated.

RESULTS: 97 subjects (80.8%) had HS of >5%. Only 16 subjects (14%) had LSM >8.0kPa. Among APRI score (p=0.001), NAFLD Fibrosis score (p=0.408), FIB-4 Index (p=0.658), BARD score (p=0.701),FibroTest (p=0.921),FibroTest was diagnostically closer to LSM (SWE). LSM (SWE) was directly correlated with both ActiTest (r 0.405, p< 0.001) and NashTest2 (r 0.299, p=0.002). ActiTest predict subjects need to perform LSM (SWE)by 5.632 times (p<0.001, C.I. 3.213-8.051) and NashTest2 by 3.981 times (p<0.001,C.I. 2.398-5.563).

CONCLUSION: Subjects with T2DM may require predictive models for hepatic fibrosis specifically developed for them. Extrapolation of results from non-diabetic population may result in misclassification.

INTRODUCTION

Non alcoholic fatty liver disease (NAFLD) has been of particular interest over the last two decades, as it affects almost a quarter of the world's population. Type 2 Diabetes seems to be an independent risk factor for the development of NAFLD. Almost 70% of people with Type 2 Diabetes are estimated to have NAFLD and 20-30% to have non-alcoholic steatohepatitis (NASH).Thus it is important to recognize high-risk people with NASH and advanced fibrosis in order to provide them with optimal management.

In this study we aimed to assess the performance of the most commonly used blood non-invasive biomarkers for the prognostication of fibrosis as measured by 2D SWE in a population exclusively of adults with established T2DM . Furthermore, we tried to investigate the prognostic value of ActiTest and NashTest 2 in the development of fibrosis

RESULTS / TABLES

16 subjects (14%) had LSM > 8kPa. FibroTest was the only proprietary score diagnostically closer to LSM estimated by SWE (p=0.921). LSM (SWE) was directly correlated with both ActiTest (r 0.405, p< 0.001) and NashTest2 (r 0.299, p=0.002). ActiTest predict subjects need to perform LSM (SWE) by 5.632 times (p<0.001, C.I. 3.213-8.051) and NashTest2 by 3.981 times (p<0.001,C.I. 2.398-5.563).

DISCUSSION

Several reasons could explain the low performance of the assessed non-proprietary clinical models. First of all, parameters used such as ALT, lipid profile and fasting glucose can be affected by glycemic control variability based on diet and hypoglycemic agents as long as lipid lowering and blood pressure medication. Moreover, NAFLD Fibrosis score and BARD score use the presence of diabetes or hyperglycemia to identify high risk subjects for liver fibrosis in a mixed population. FibroTest has the advantage not to include glycemic related parameters and this might explain its superiority towards the other non-invasive panels and models.

We also showed a direct correlation between LSM (SWE) with both ActiTest and NashTest2. A combination of both biomarkers on top of FibroTest might be an option to improve diagnostic accuracy based on the complex pathogenetic factors leading to NASH.

2D SWE vs Proprietary Scores in Diagnosis Of Liver Fibrosis

		LSM (2D SWE)				P value
		F0-F1	F2	F3	F4	
APRI Index						
<0.5 no fibrosis	N	96	5	7	1	0.001
	%	88.1%	4.6%	6.4%	0.9%	
0.5-0.7 some liver damage	N	1	1	0	0	
	%	50.0%	50.0%	0.0%	0.0%	
0.7-1 significant fibrosis	N	0	1	0	1	
	%	0.0%	50.0%	0.0%	50.0%	
NAFLD Fibrosis Score						
F0-F2 < (-)1.455	N	23	3	2	0	0.408
	%	82.1%	10.7%	7.1%	0.0%	
F2-F3 (-) 1.455- (+) 0.675	N	63	4	5	1	
	%	86.3%	5.5%	6.8%	1.4%	
F3-F4 > (+) 0.675	N	11	0	0	1	
	%	91.7%	0.0%	0.0%	8.3%	
FIB-4 Index						
Normal <0.68	N	20	2	1	0	0.658
	%	87.0%	8.7%	4.3%	0.0%	
F0-F2 0.97 (0.69-1.37)	N	55	2	5	1	
	%	87.3%	3.2%	7.9%	1.6%	
F3-F4 1.95 (1.38-3.08)	N	21	3	1	1	
	%	80.8%	11.5%	3.8%	3.8%	
BARD Score						
Low risk	N	8	0	0	0	0.701
	%	100%	0.0%	0.0%	0.0%	
High risk	N	89	7	7	2	
	%	84.7%	6.7%	6.7%	1.9%	
FibroTest						
F0-F1/F2	N	78	6	5	2	0.921
	%	85.7%	6.6%	5.5%	2.2%	
F2-F4	N	17	1	1	0	
	%	89.5%	5.3%	5.3%	0.0%	

SUMMARY

Although well-validated biomarker panels for the diagnosis of NASH are quite promising, people with Type 2 Diabetes may require predictive models that have been specifically developed for them, as extrapolation of results from population with no diabetes may result in significant misclassification. Based on the complex pathogenetic factors and dynamic activity of NASH, a combination of different non-invasive biomarkers might be an option to improve diagnostic accuracy in detecting liver fibrosis in this particular population and minimise the need for liver biopsy.

CONCLUSION

Subjects with T2DM may require predictive models for hepatic fibrosis specifically developed for them. Extrapolation of results from non-diabetic population may result in misclassification.