

NASH-related increases in plasma bile acid levels depend on insulin resistance

Guillaume Grzych, Oscar Chávez-Talavera, Amandine Descat, Dorothée Thuillier,
An Verrijken, Mostafa Kouach, Vanessa Legry, Hélène Verkindt, Violeta Raverdy,
Benjamin Legendre, Robert Caiazzo, Luc Van Gaal, Jean-Francois Goossens,
Réjane Paumelle, Sven Francque, François Pattou, Joel T. Haas, Anne Tailleux, Bart
Staels

Table of contents

Fig. S1.....	2
Fig. S2.....	3
Fig. S3.....	4

Selection Criteria:

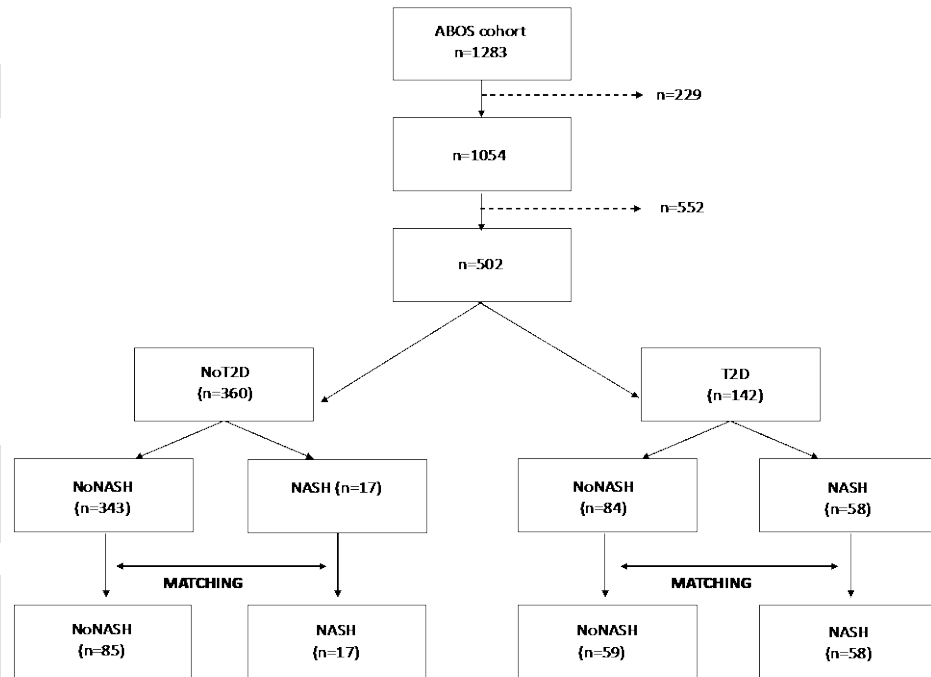
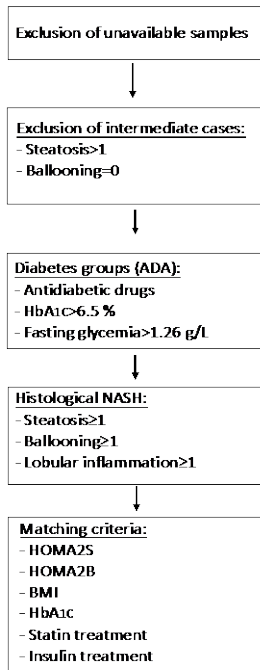


Fig. S1. Patient selection flowchart

In the whole cohort (n=1283), 1054 patients had sufficient blood and liver sample to perform assays. To determine the specific influence of NASH, excluding isolated steatosis, on plasma BAs, we excluded patients with isolated steatosis >1 (NAFL) and/or some degree of ballooning or lobular inflammation but insufficient to qualify for the diagnosis of NASH. Then, the 502 remaining patients were separated in T2D and No-T2D groups. Within these 2 groups (No-T2D and T2D), patients were classified in No-NASH and NASH groups according to liver biopsy scoring. Finally, we matched each subgroup of patients by HOMA2S, HOMA2B, BMI, HbA_{1c} and insulin/statin treatment to obtain homogeneous groups on these parameters.

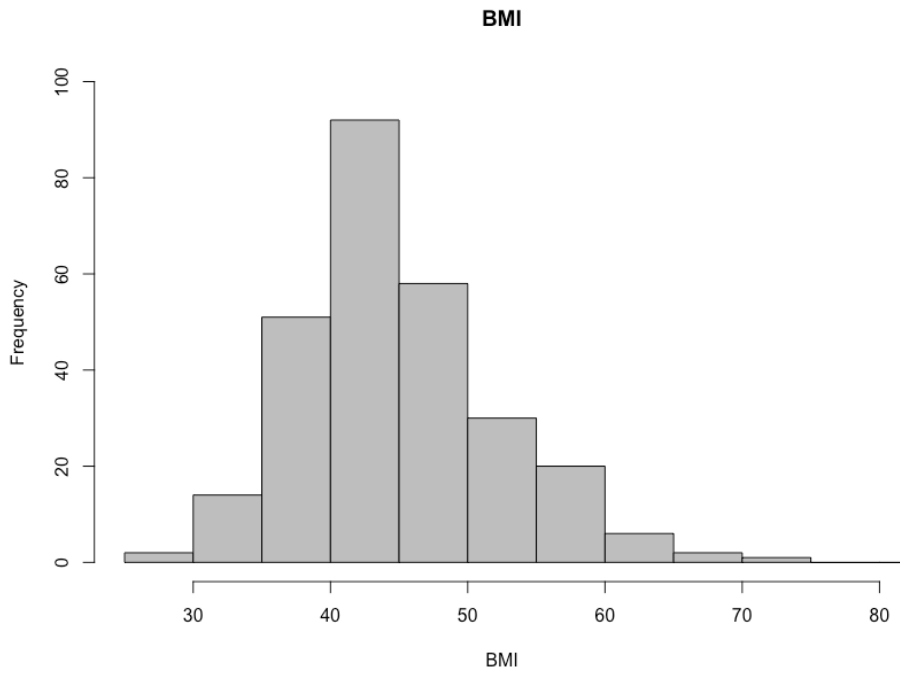


Fig. S2. BMI distribution in the combined cohort (n=239).

Bile acid cluster	Acronym and definition
Free cholic acid	CA (I)
Free chenodeoxycholic acid	CDCA (I)
Free hyocholic acid	HCA (I)
Free deoxycholic acid	DCA (II)
Free lithocholic acid	LCA (II)
Free ursodeoxycholic acid	UDCA (II)
Free hyodeoxycholic acid	HDCA (II)
Glyco-cholic acid	GCA (I)
Glyco-chenodeoxycholic acid	GCDCA (I)
Glyco-deoxycholic acid	GDCA (II)
Glyco-lithocholic acid	GLCA (II)
Glyco-ursodeoxycholic acid	GUDCA (II)
Glyco-hyocholic acid	GHCA (I)
Glyco-hyodeoxycholic acid	GHDCA (II)
Tauro-cholic acid	TCA (I)
Tauro-chenodeoxycholic acid	TCDCA (I)
Tauro-deoxycholic acid	TDCA (II)
Tauro-lithocholic acid	TLCA (II)
Tauro-ursodeoxycholic acid	TUDCA (II)
Tauro-hyocholic acid	THCA (I)
Tauro-hyodeoxycholic acid	THDCA (II)
Total CA	CA + GCA + TCA
Total CDCA	CDCA + GCDCA + TCDCA
Total DCA	DCA + GDCA + THCA
Total LCA	LCA + GLCA + TLCA
Total UDCA	UDCA + GUDCA + TUDCA
Total HCA	HCA + GHCA + THCA
Total HDCA	HDCA + GHDCA + THDCA
Total primary BAs	Total CA + Total CDCA + Total HCA
Total secondary BAs	Total DCA + Total LCA + Total UDCA + Total HDCA
Total free BAs	CA + CDCA + DCA + LCA + UDCA + HCA + HDCA
Total conjugated	GCA + GCDCA + GDCA + GLCA + GUDCA + GHCA + GHDCA + TCA + TCDCA + TDCA + TLCA + TUDCA + THCA + THDCA
Total BAs	Total Free BAs + Total Conjugated BAs
Total 12aOH BAs	Total CA + Total DCA
Total non12aOH BAs	Total CDCA + Total LCA + Total UDCA + Total HCA + Total HDCA
Ratio 12aOH	Total 12aOH BAs / Total non12aOH BAs
Total 6aOH BAs	Total HCA + Total HDCA
Total non6aOH BAs	Total CA + Total CDCA + Total DCA + Total LCA + Total UDCA
Ratio 6aOH	Total 6aOH BAs / Total non6aOH BAs

Table S1. Definition of the bile acid clusters and ratios. BAs = Bile acids. I : Primary BA, II: Secondary BA