Increased prevalence of Chronic Kidney Disease in Non-Alcoholic Fatty Liver Disease does not contribute to overall mortality risk

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Introduction:

Previous studies support a link between non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD).

Our aim was to investigate the prevalence and long-term future risk of CKD, and its effect on mortality, in patients with biopsy-proven NAFLD, with repeated assessment of renal function.

Material and methods:

Patients with NAFLD were selected from a liver biopsy register in Malmö, Sweden.

Malmö Preventive Project (MPP), a population-based prospective cohort, was used as a control group.

Estimated glomerular filtration rate (eGFR) at baseline and follow-up was calculated using the CKD-EPI equation. CKD 3-5 (<60 mL/min/1.73m^2) was classified as CKD.

Patients´ hospital medical records were scrutinized for diagnoses, anthropometrics and laboratory tests. Mortality data was acquired from a national register of causes of death.

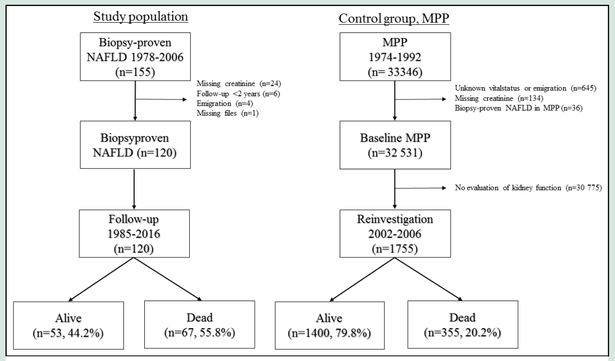

Figure 1. Flowchart for participant inclusion.

Results:

In all,120 patients with NAFLD (mean follow-up time 19.50±8.95 years) and 1755 controls (32.85±3.83 years) were identified (figure 1).

There was a higher prevalence of CKD in NAFLD (12.5% compared to 2.1%, p<0.001) at baseline, but not at follow-up (table 1).

	NAFLD (n=120)		Control group (n=1755)		
	Mean±SD, N (%)	Median (IQR)	Mean±SD, N (%)	Median (IQR)	p-value
Sex F/M	47 (39.2)/ 73 (60.8)	n/a	511 (29.1)/ 1244 (70.9)	n/a	0.016
Age at baseline (years)	52.46±13.14	54.11 (42.62-62.45)	43.25±7.71	44.28 (36.17-48.24)	<0.001
Age at CKD follow-up (years)	69.53±11.99	70.08 (62.57-78.55)	67.34±5.96	67.65 (62.13-71.06)	0.005
Age at endpoint (years)	71.96±11.71	71.69 (65.58-81.60)	76.10±6.42	76.89 (70.63-81.61)	<0.001
Follow-up time (years)	19.50±8.95	18.80 (13.41-26.63)	32.85±3.83	33.79 (30.46-35.36)	<0.001
Creatinine (µmol/L) baseline	86.78±18.57	89.00 (75.00-98.75)	88.06±14.47	88.00 (78.00-97.00)	0.458
eGFR (mL/min/1.73m^2) baseline	81.63±18.65	79.90 (69.38-97.08)	86.70±14.22	86.59 (76.18-96.81)	0.004
CKD stage baseline 1	43 (35.8)	n/a	726 (41.4)	n/a	<0.001
2	62 (51.7)		993 (56.6)		
3	15 (12.5)		35 (2.0)		
4	0 (0.0)		1 (0.1)		
5	0 (0.0)		0 (0.0)		
Creatinine (µmol/L) follow-up	106.74 ±87.53	86.00 (71.00-113.00)	n/a	n/a	
Cystatin C (mg/L) follow-up	n/a	n/a	1.11±0.31	1.06 (0.95-1.20)	
eGFR (mL/min/1.73m^2) follow-up	67.82±24.41	68.15 (51.85-87.20)	68.56±17.19	69.09 (57.18-79.78)	0.742
CKD stage follow-up 1	25 (20.8)	n/a	185 (10.5)	n/a	0.124
2	50 (41.7)		1030 (58.7)		
3	36 (30.0)		517 (29.5)		
4	6 (5.0)		20 (1.1)		
5	3 (2.5)		3 (0.2)		

Table 1. Clinical and biochemical characteristics at baseline and follow-up.

When stratifying CKD prevalence in age groups there was only a significant difference in the highest age group (> 55 years) at baseline (figure 2).

There was a significant correlation between NAFLD and CKD at baseline after adjusting for associated co-variates (age and metabolic risk factors, p=0.001).

Patients with NAFLD who developed CKD at follow-up had significantly higher prevalence of metabolic risk factors, including diabetes mellitus, compared to NAFLD patients without CKD (data not shown).

Crude mortality was higher in NAFLD patients with CKD at baseline (figure 3). Diabetes mellitus contributed to the increased risk of mortality, not CKD *per se* (table 2).

	Model 1 NAFLD and controls (n=1875)			Model 2 NAFLD (n=120)		
	HR	95% CI	p-value	HR	95% CI	p-value
Sex (male)	1.05	0.80-1.39	0.705	1.04	0.58-1.87	0.900
Age	1.17	1.15-1.20	0.020	1.12	1.08-1.16	<0.001
CKD 3-5	0.77	0.46-1.29	0.325	0.75	0.35-1.16	0.462
Diabetes mellitus	3.10	1.99-4.82	<0.001	1.99	1.11-3.58	0.021
Hypertension (>140/90)	1.00	0.77-1.31	0.976	1.16	0.65-2.06	0.628
Cardiovascular disease	1.00	0.62-1.61	0.999	0.66	0.29-1.48	0.310
Obesity (BMI >25)	1.28	1.03-1.59	0.023	1.56	0.79-3.08	0.206
NAFLD	2.48	1.67-3.68	<0.001	n/a	n/a	n/a

Table 2. Hazard ratios for overall mortality. Model 1: Entire study population. Model 2: NAFLD patients.

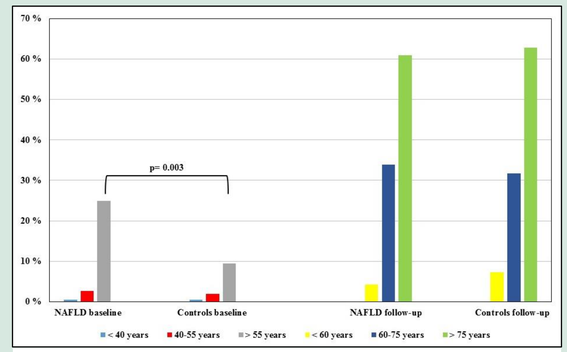

Figure 2. CKD prevalence at baseline and follow-up according to age groups.

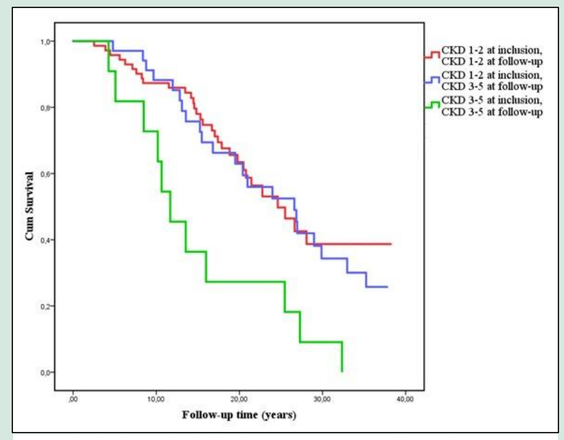

Figure 3. Crude survival of NAFLD patients according to CKD-development. Log-rank test p<0.001 between CKD 1-2/1-2 and 3-5/3-5. Log-rank test p<0.003 between CKD 1-2/3-5 and CKD 3-5/3-5.

Conclusion:

NAFLD is independently associated with CKD. Mortality is increased in NAFLD patients with long-term CKD due to diabetes mellitus, not influenced by CKD *per se*.

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