New-Onset Age of Nonalcoholic Fatty Liver Disease and Cancer Risk

C____ a L___, MD, P_D; T__ L__, MD, P_D; Q_____ Z___, MD, P_D; P____ J_a, MD, P_D; Me___ e S___, P_D; Q_a___, MD, P_D; G__a R_a, P_D; Y___ Ge, MD; S__ L__, MD; Z_e Wa__, P_D; Ha__ X_e, MD, P_D; J__ S___, MD, P_D; R___ Ha__, P_D; Y_e C_e__, MD; X_ Z_e__, MD; L__ S_e, MD; L_ De__, P_D; S___ W___, MD, P_D; Ha__ S___, MD, P_D

I_____ T__ ___e_a__e f___ __a__c_fa___ ___e_ d__ea_e (NAFLD) __ dec_ea____, a_d ___e ___e___ ea___-_a___ e___ f NAFLD __ __e a_ea__ a__ca_ed ___ __c_ea_ed ca_ce___ ___c _e____ __c_ea__.

__ __U___ T_e ___e __ _ea__ ca__ be___ee_ NAFLD _e_-___e_ a_e a_d ca_ce___.

____ _/___ _, ___ __ _, __ ___ ___ ___ _ T___ c____ __d __ a c__d c__ced a___ 179 328 _a__c__a___ c_ded __ __e Ka___a_ C____ S_d_ be__ee_ 2006 a_d 2021. I_ ___a_, 46 100 __c_de_ NAFLD ca_e_ _e_e _de___f_ed. F__ _ea__ ca_e_, a_a__ a__ca___ ___ac_ed ba_e__ (__ _de___ _e_e b_ 1 __ea__) a_d __e _a__a_ _e_ec_ed ___c_ea_a___ __ ___ac_ed__ __d c____. Da_a _e_e a_a__ed f___ Dece_be_ 2022 __ ___ A___ 2023.

_____ ___ ___ O___e__ f NAFLD.

__ _____ ____ ___ _____ ____ T_e ___a__ ca___ be___e__ ___e ___e___ ea___ f NAFLD a_d __e ___ _fd_ffe_e__ ca_ce__ _e_e a_a__a_ed ___ _e__ed C___e_____ _de__. P___a____ a____b__ab_e f_ac____ (PAF_) _e_e __ed __ __a___f___ea__ca_____ f NAFLD __ ca_ce___ a___ a d_ffe_e__ a_e_.

_____ A____ 63 696 _a__c__a___ (__ea_ [SD] a_e, 51.37 [12.43] _ea__; 10 932 fe_a_e [17.2%] a_d 52 764 _a_e [82.8%]), 31 848 __d__d_a___ _ad NAFLD a_d 31 848 __d__d_a__ _e_e __ __e c_____. D___a _ed_a_ (IQR) f____-__ _f 10.16 (7.89-11.67) _ea__, 2415 _a___ __ _e_e d_a_____ed ___ ca_ce__. C___a_ed __ __e __a_c_ed ____, _a_e_ _a_ed e__ __a_ 45 _ea__ a_ NAFLD ___e_ _e_b_ed a_ __c_ea_ed ___ f ca_ce__ (a___ __e_ a__a_d_a__ [AHR], 1.52; 95% CI, 1.09-2.12), a_d a_ __e ___e _a_e _f NAFLD __ __c_ea_ed, ___e ca_ce___ ____ dec_ea_ed (a_e 45-54 _ea__: AHR, 1.50; 95% CI, 1.15-1.97; a_e 55-64 _ea__: AHR, 1.13; 95% CI, 0.97-1.33; a_e >65 _ea__: AHR, 0.75; 95% CI, 0.45-1.27; P f__ ___e_ac____ < .001). A____ __ _a__ _a__d e__ __a_ 45 _ea__ a_ NAFLD ___e_, ca_ce__ ___e_a_ __ d__e___e a_d ___ ca_ce___, ____ AHR _a_e__ _f 2.00 (95% CI, 1.08-3.47) a_d 2.14 (95% CI, 1.05-4.36), _e_ec___e__. PAF_ a____e_ ed __a_ _a_e_ _a_ed e__ __a_ 45 _ea__ a_ NAFLD ___e_, 17.83% (95% CI, 4.92%-29.86%) __f ca_ce___ ___ __a_ a___b__ab_e __ NAFLD.

_____ ___ _____ _____U__ _ T___ d_ f___d __a_ NAFLD __ a__ca_ed ___ __c_ea_ed ca_ce___ ___ a_d ___e_ a_ ___ea____ __e_ __a_e, ___c___ a ___e__ ___e __ea_ __f NAFLD, __e _ea___ ___e ca_ce__.

____ _____ I_ _eea_e___e ___e_a__e f___ __a__c_fa___ ___e_ d__ea_e (NAFLD) a___ca_ed ___ __c_ea_ed ___ _f ca_ce_?

_____ ___ I_ ___ c____ __d _f 63 696 a___c__a___ _____ d_ffe_e__ a_e_, NAFLD a____ca_ed ___ __c_ea_ed ca_ce__ ___ a_d __ ___e ___e_ a_e _f NAFLD a____ca_ed ___ __ea_e_ ___ _f ca_ce__.

_ ___ __ _ T_e f____ d __ a _ea___-___e NAFLD a__a___ca_ed ___ __c_ea_ed ___ _f ca_ce___, ___e__ a

Introduction

N..a.c..c fa..e...d..ea.e (NAFLD), a...a.c.a.ed ....f ca..e..d a.a.e, .cc...a..e.a.e 25% .f ..e ..ba. ..a... E...a.ed a.. NAFLD ..e.a.e.ce ..jec.ed ..eac. 33.5% b. 2030, ...a.e.....ba. b.c.ea...ea..[1,2] W......a.ca....e 2 d.abe.e. a.d ...e.ab..c .....d..e., NAFLD ..c.de.ce ..c.ea.e.a.....de.d.abe.e. a.d be..............e.a.e.ce.[3,4] T.e.a..ca..ed b. NAFLD a..d..ee.e...ad. a.............e..... NAFLD .a.d ...c....ca...c.d.....ac....c.ea.e.a.....de.d.abe.e. a.d be.. d..ea.e.[5,6] Se.e.a..e.c...de. a...f..d ..a NAFLD ...a.a...ca.ed ...ca.ce.....

Ma...a. a.d Ka..e.a...[6,7] f..d ..a..a...e...NAFLD .ad a 1.2-..15-f..d ....e...f ...e.. ca.ce...,a......e..a.ca.ce.. ,a.d.a..ca.ce....e. NAFLD-...d.c.ed NASH .a.e..e.ed a..a...ead......ca..e..f ..e.....ca.ce..d.ea........,.......a...e...B.a.d C....[8] T.e.e.ef.....e,...a...ed ...c.ea.e. .e. NAFLD ...c.de.ce .a...e....ed...e......c.ce....

I....a..y,...e..a...NAFLD .bec......e..A...a....e.....c...c ...ed...ea.e..e.ea.ed.d.ea...,..e-..de.......ce.ed NAFLD a....e....a.....a.e 30 .ea...[9] T.e.e ...c..e....e..a.a.e......be.ad.......ea..ca...f....e-....e NAFLD a..d.ffe.e. a.e......e...f d..e.....e...d..ea.e..,...c..a.ca.ce... He.e.e.,.....de..a....f ..c..ed ...ea........c...e.a..ca.ed......e..e.a.e NAFLD a..e.a....a. NAFLD ....e-....e a...e....

We .....e..e.d ..a.....e...e..e.a.e ..f NAFLD ....d be...a...ca.ed ......e..ca.ce..... T.e.ef....e,....de....ed .ea..ca....be.e.....ea.e..f .....e-....e NAFLD a..d ...e....f ...a...ca.ce.......e.....a.e.....ec..ec......

Methods

T.c.....d..a..a......ed b.....ee...c.c........e..f Ka..a. G..e..a. He.a..a.d Be.j... S.j.a. H....a.,a.d...e.d..f...ed ..e..d..e...f ...e He.....De.c..a.a...A.....a.c.a...........a...a.c.a..ed .....d a.f.e...ece....a.de..a.ed...d.c......e..e.ea.c..de.... a.d....ded ....e.f....ed c......e.....b..........e.....e.a.e.ee.a.e.....T......d..e....ed f......e S..e....e.Re......f Ob.e..a....a. S..d.e.. E..d.e....... (STROBE) ..e......... .de....e.

Study Population and Data Source

S..d.....a..c..a..e..e.e...ec.ed f.....e Ka..a. C...S...d.,a..........e...ec..ec....d....a.be.a..J..e 2006 (eMe...d... S...e...e.1).[10] F....d....d.d.a.......ad. .de..... .e...c.a..e..a...a..a.ea...c.e.be..ee. 2006 a.d 2017 a..d c.....e.ed f..........-.e.a.a............e..a...e.ec.ded. A....a..f 179 328 a....c.a........e..e...c..ded. T..e.....a. .ee....d.a................f NAFLD, ca..ce..,.ea....a....c............ (...ac....a.e ≥30 ..../d...f ..a..e...a.d ≥20 ..../d...f....fe..a.e.),...e.a...B......f.ec...,.....e..e.d..ea.e.....e..e...ec..ded. T.e f.......a.ca.e........c.....ded .f 46 100 ..a....e....de...e..ed ...e-....e NAFLD be..ee.. 2006 a.d 2017. Af.e..e.c....d...........a.e......................c..a..ed a.d a..a......e....f d.a.........,35 860 ....a....e.....e..a....ed.

T.e. ..a..c...ed....a..f....ed b......ad......e....ec...ea...d d.a...a.d a....c....a..ed ......e...ca....ea..a.............e.a...e...ea.-a.............ec.a....e.a.d a.......ed a.d ....e..a.c...ed 1:1 ba..ed ....a..e (..de........e..b.. 1..ea..) a.d...e.f.a...e.........e..ca.e.... T.e f...-..f-....e..e ca..e.a.....d......e....e-....e NAFLD ...a..de...f..ed. F......a...e,......de..f.e.d a...a...ea.e a...a.... 2010.......e-....e NAFLD a...a...e 45..ea.... A....e..a....e.,........ac......d.d.d....a......e...a.d ...e...ec..ed f..........e......f.d.d a...e.....NAFLD ....a.d a..a...ca.ed...e..........ca. ...ea..a...a.....2010 a.. a...e.. 44..46..ea...;.b...................e.f....ed ....a..........2010. Af.e.a............ed.a. (IQR) f......-..f ..6.85 (5.58-7.24)..ea...,31 848 ....a........f..a...ca..e......c..ded....e......d (.....e..1) a.d ...e...e......ed acc...d.......a.e....

Figure 1. Study Flowchart

179 328 Individuals participated in the Kailuan health examinations from 2006-2017

59 571 Excluded
940 Participants diagnosed with cancer at baseline (first) examination
53 248 Participants diagnosed with NAFLD at baseline (first) examination
5383 Participants with excessive drinking or chronic liver disease at baseline (first) examination

46 100 Participants were diagnosed with new-onset NAFLD during the resurvey among 119 757 participants; median (IQR) follow-up, 6.85 (5.58-7.24) y

10 240 Participants without data of covariates

35 860 Participants with new-onset NAFLD

Participants without NAFLD were 1:1 matched on age (1 y older or younger) and sex and examination year to individuals with new-onset NAFLD

63 693 Patients in final analyses
31 848 Patients with new-onset NAFLD
31 848 Patients in control group

Diagnosed age <45 y	Diagnosed age 45-54 y	Diagnosed age 55-64 y	Diagnosed age ≥65 y
8984 Case	10 271 Case	8585 Case	4008 Case
8952 Control	10 273 Control	8572 Control	4051 Control

NAFLD indicates nonalcoholic fatty liver disease.

Continuous variables were presented as mean (SD) for... and ... distributed data... were c...ared

... *t* test... ...a...... of ...a...ce. S...e...ed c...... ...a...ab...e were ...e...e...ed a...... ...ed...a... (IQR)
a...d c...a...ed ... ...e K...a...-Wa... ... ...e...... Ca...e...ca... ...a...ab...e were ...e...e...ed as ...e...ce... and
c...a...ed ... ...e χ² ...e...... C...e...... ... ...a...ed ...a...a...e ....f ca...ce...... c...de...ce. Beca...e

...... de...d.d...... ...ee...... e...a...... ...f ....a...a...a...d...a..., ...e ...ed a...e......ed C...
...e...e...... ...de... ...ca...c...a...e ...ea...a...e ...a...a...d...a... (AHR) a...d 95% CI f... ...ca...ce...... c...de...ce. T...
f...... e...a...... ...e...a...ca...... f NAFLD e...... ...e...... ...ca...ce...... c...de...ce ac...... ...a...e... ....,

...... a...... a...b...ab...e f...ac...... (PAF...) ...e...e...ca...c...a...ed[12,13] (eMe...d... S...... ...e...e 1).

...S...b...... ...a...a...e ...e...e ba...ed ....f...a...... a...d ...e...f...c... (eMe...d... S...... ...e...e 1).
Se...... ...a...a...e ...e...e...e...f...ed ...a...e ...e...b...e...... f...e ...... Pa...c...a... ....e...e
...da...... ...ed ...ca...ce...... ...ef...... ...ea...ff... - ...e...e...e c...ded ...a...d ca...a...... ...e......,
a...... ....a...ec...e...d. P...e...... ...c...e ac...... ...a...e...f...ed ....e ...a...e...e
....e ...a...... ca...... f...... ...e...fac... ....c...e. F...a...., ...ee...c...ded ...a...c...a...... ...ed
...ed...ca...... a...d ...e...f...ed...e ...a..., ...ca...ac...... . D...... ...ef...... ...-...e...d, ...dea...... ...a...ac...a...
...c...... ...e...e...e. C...e...... ...de...... (F...ea...d G...a... ...de...) ...e...a...ed f...ed c......b...a...,
...c...d... ...e...ca...e-...ec...f...c a...a...d f...c...... a...d ...b...d...b...... ...a...a...d f...c......... S...a...ca...
a...a...e ...e...e...f...ed ...... SAS ...a...ca...f...a...e......... 9.4 (SAS I...... ...e) a...d R ...a...ca...
...f...a...e......... 4.2.0 (R P......ject f...... S...a...ca...C...... ....). A 2-...ded *P* < .05 ...a...c...... ...de...ed
...a...a...ca...... f...ca...... Da...a ...a...e...a...a...ed f...... Dece...be... 2022 .... A......... 2023.

...e...e......

...a......... ...h......c......c...

A...... 63 696 ...a...c...a...... (...ea... [SD] a...e, 51.37 [12.43] ...ea......; 10 932 fe...a...e [17.2%] a...d
52 764 ...a...e [82.8%]), ...e...e a...da...e...f ...a...c...ed (31 848 ...d...d...a...) a...d ca...e (31 848
...d...d...a...) ....e...e ...a...c...ed (...... ...). I... ...e...ca...e...... ..., ...e...e ...e...e 8984 ...a...e... ...a...ed ...e...
...e... 45 ...ea......, 10 271 ...a...e... ...a...ed 45 ...... 54 ...ea......, 8585 ...a...e... ...a...ed 55 ...... 64 ...ea......, a...d 4008
...a...e... ...a...ed 65 ...ea...... ....de...... C...a...ed ....e...... a...c...ed ...., ...a...e...... ...e... -...e NAFLD
...... f...e ...ac...ed...e...... a...... ...ca...ac......; ...a...d a...... ...e...... ...ea...ce... f... ...e...e... ...; ...ef...e...e ....ad
...e...e ...a...d...be...; a...d ...e...... ...ea... (SD) ...a...c...c... fe...... ...ce...a...d...e...e...... f...... ...ce...de..., ...a
...c......e...e..., ...e...e...... C-...eac...... ...e...... ..., a...d ...a...a...ea...... ...a...fe...a...e (ALT) a...d ....e...... ...ea...
(SD) ...e...e...... f... ...-...de...... ....e...c...e...e...... a...d ...a...b...b......... W...... ...a...... ...ce...a...e... NAFLD
...e... -...e...e a...e, ...e...... .... f ...e...e ...... a...d dabe...e...... ...e...e ...e...a... ....e...a... (SD) ...b...d...
....a...... ...de (ca...c...a...ed...a...e...... ...a...... ...a...d...ded...b...... ....e...... ...a...ed) ...e...e...ed...ced.
M...... e...e..., ...ea... (SD) ...a...c...c... fe...... ...ce...a...d...e...e...... f...... ...a...c...e...e...... ..., ...e...e...... ...e...e C-...eac...e
....e...., a...d ...a...b...b...... ...ca...ed ....e...e...e... f...... ...ce...de... a...d ALT dec...ea...ed a...... ...e NAFLD
...e... -...e a...e ...c...ea...ed. I... add...... , ...ec...... ...a...ed ba...e...... c...a...ac...e...... c...b...e...e... e...c...ded
...a...c...a... a...d ....e...... ...ed ....e...d (eTab...e 2 S...... ...e...e 1). T...e...e ...e...e ....f ca...
d...ffe...e...ce... be... ...ee... .... fac...... ...c...a...a...e, ..., ...e...e......, a...d dabe...e......

D...... ....e...d a...... (IQR) f...... ...... -...... ...f 10.16 (7.89-11.67) ...ea......, 2415 ...a...e... ....e...ed a...... ...ed ...
...ca...ce...... B... a...e...... ..., ...e ...ed...a... (IQR) f......... -......... a... 10.10 (7.02-11.03) ...ea...... f... ...a...c...a... ...a...ed
...e... ...a... 45 ...ea......, 10.11 (8.63-11.66) ...ea...... f...... ...a...c...a... ...a...ed 45 ...... 54 ...ea......, 10.13 (7.84-12.25)

aged ... than 45 years (AHR, 1.52; 95% CI, 1.09-2.12). ... 45 ... 54 years (AHR, 1.50; 95% CI, 1.15-1.97) a... e of NAFLD. C...de... ... e... ca... be ... een NAFLD a... d d... e... e... ... ... ca... ce... f d... ... ... de...,[14] ef ... e... cac... a... ed AHR f d... e... ... e... ca... ce... Re...

... e... e... a... ... ef... a... ca... ce... ... e; ... e... f d... e... ... e... ca... ce... a... ... e... a... e aged ... than 45 years (AHR, 2.00; 95% CI, 1.08-3.47) a... d 45 ... 54 years (AHR, 1.94; 95% CI, 1.46-2.74) a... e-... e... NAFLD. T... e... ... f ca... ce... ... ... c... de... ... ce dec... ea... ed ... ... a... ... c... ea... e... ... e... ea... e ... f NAFLD; ... e... ... ea... e f... e-... ... e... of NAFLD a... 65 years ... ... de... ... c... a... ed ... ... e... a... c... ed ... ... , ... e... ... f... a... ca... ce... ... e (AHR, 0.75; 95% CI, 0.45-1.27; P f... ... e... ac... ... < .001) a... d ... d... e... ... e... ... e... ca... ce... (AHR, 0.71; 95% CI, 0.50-1.02; P f... ... e... ac... ... < .001) ... ... e ca... e... ...

We f... ... e... ca... fed ... ea... ... ca... ... be ... ... ee... ... e... -... ... e NAFLD a... d d ffe... e... a... ... e... ... a... d ... e... ... f d ffe... e... ... ca... ce... ... e... (eF... ... e1 ... S... ... e ... e... 1). A... ... ... a... ed a... ... be... ed f... ... e... ca... ce... , c... ... ... ec... a... ca... ce... (CRC), a... d ... ... ca... ce... Y... ... e... a... f NAFLD ... ... e ... ... a... ... ca... ed ... ... ea... e... ... ... f e... a... d ... ... ca... ce... A... ... ... a... e... ... a... ed ... ... a... 45 years a... ... e-... ... ... e NAFLD, ... e AHR... ... f ... e... a... d ... ... ca... ce... ... a... ... 2.66 (95% CI, 1.16-6.11) a... d 2.14 (95% CI, 1.05-4.36), ... e... ... ec... ... e... ... . N... ... ... f ca... d ffe... e... ... e... ... e be... ... ed ... ... e... ... of CRC a... ... ... a... e... ... ... e... ... e... a... ... NAFLD ... ... e (a... e <45 years: AHR, 2.05; 95% CI, 0.68-8.87; a... e 45-54 years: AHR, 2.89; 95% CI, 1.43-5.51). S... ... a... ... ... a... ... ... e... ca... ce... a... d a... b a... dde... a... de... ... ... a... e... a... c... b... ed ... ... c... ca... ce... , ...

Table. Baseline Clinical Characteristics of Participants

Characteristic[a]	Total patients, No. (%) (N = 63 696)			Patients by NAFLD onset age, No. (%)				
	Control group (n = 31 848)	New-onset NAFLD (n = 31 848)	P value	<45 y (n = 8984)	45-54 y (n = 10 271)	55-64 y (n = 8585)	≥65 y (n = 4008)	P value
Age, y, mean (SD)	51.37 (12.43)	51.37 (12.43)	.96	36.04 (6.57)	50.32 (2.28)	59.30 (2.76)	71.42 (5.16)	<.001
Sex								
Female	5466 (17.2)	5466 (17.2)	>.99	1242 (13.8)	2211 (21.5)	1498 (17.4)	515 (12.8)	<.001
Male	26 382 (82.8)	26 382 (82.8)		7742 (86.2)	8060 (78.5)	7087 (82.6)	3493 (87.2)	
Regular physical activity	5176 (16.3)	4874 (15.3)	.001	1087 (12.1)	1261 (12.3)	1668 (19.4)	858 (21.4)	<.001
Current smoker	6864 (21.6)	6787 (21.3)	.46	2406 (26.8)	1800 (17.5)	1681 (19.6)	899 (22.4)	<.001
GSD	672 (2.1)	726 (2.3)	.15	85 (0.9)	204 (2.0)	265 (3.1)	172 (4.3)	<.001
Gallbladder polyps	560 (1.8)	548 (1.7)	.74	160 (1.8)	176 (1.7)	154 (1.8)	58 (1.4)	.52
Diabetes	3164 (9.9)	3152 (9.9)	.88	363 (4.0)	1086 (10.6)	1116 (13.0)	587 (14.6)	<.001
Hypertension	12 442 (39.1)	14 518 (45.6)	<.001	2434 (27.1)	4657 (45.3)	4875 (56.8)	2552 (63.7)	<.001
BMI								
<24.00	13 545 (42.5)	8511 (26.7)	<.001	2074 (23.1)	2843 (27.7)	2348 (27.4)	1246 (31.1)	<.001
24.00-27.99	13 036 (40.9)	16 867 (53.0)		4835 (53.8)	5479 (53.3)	4549 (53.0)	2004 (50.0)	
28.00	5267 (16.5)	6470 (20.3)		2075 (23.1)	1949 (19.0)	1688 (19.7)	758 (18.9)	
Mean (SD)	24.84 (3.44)	25.78 (2.97)	<.001	26.06 (3.02)	25.67 (2.97)	25.75 (2.92)	25.53 (2.99)	<.001
Waist circumference, mean (SD), cm	86.88 (9.87)	89.22 (9.11)	<.001	88.86 (8.47)	88.99 (8.84)	89.62 (9.68)	89.74 (9.82)	<.001
Triglyceride, median (IQR), mg/dL	109.86 (77.97-161.25)	129.36 (90.37-194.03)	<.001	139.10 (96.57-215.30)	136.44 (93.12-208.21)	122.27 (87.71-177.20)	112.52 (80.63-158.59)	<.001
Total cholesterol, median (IQR, mg/dL)	189.05 (165.85-213.40)	196.39 (173.58-222.30)	<.001	189.82 (167.40-213.02)	197.94 (175.52-196.39)	200.65 (156.96-227.71)	196.78 (173.20-223.07)	<.001
HDL-c, median (IQR), mg/dL	53.35 (45.42-63.40)	52.58 (44.07-63.02)	<.001	51.42 (43.30-61.08)	54.12 (45.23-64.95)	51.80 (44.07-63.02)	52.19 (44.07-62.24)	<.001
hs-CRP, median (IQR), mg/dL	0.11 (0.05-0.25)	0.14 (0.07-0.29)	<.001	0.13 (0.06-0.26)	0.14 (0.00-0.28)	0.14 (0.07-0.3)	0.16 (0.07-0.36)	<.001
Total bilirubin, median (IQR), mg/dL	0.77 (0.60-0.97)	0.76 (0.60-0.96)	<.001	0.73 (0.57-0.93)	0.75 (0.59-0.95)	0.79 (0.62-0.99)	0.81 (0.63-1.01)	<.001
ALT, median (IQR), U/L	19.0 (14.0-26.0)	20.0 (15.0-28.0)	<.001	23.00 (16.0-34.0)	20.00 (15.0-28.0)	19.00 (14.4-25.2)	17.00 (13.0-22.3)	<.001

Abbre... a... ... : ALT, a... a... ... ea... ... a... ... fe... a... e; BMI, b... d... ... a... ... de... (ca... ... aded a... ... ... a... ... ... d ded b... ... ... e... ... e... ... a... ed); GSD, ... a... ... ... ed... ... ea... e; HDL-c, ... -de... ... ... e... ... ... c... e... e... ; ... -CRP, ... e... ... ... C-... ea... ... e ... ... e... ; NAFLD, ... a... c... ... f... a... ... e... ... d ... ea... e.

SI c... ... e... ... fac... ... : T... c... ... ... a... ... ... ea... ... ... a... fe... a... ... e... ... ... c... ... a... a... ... e... , ... b... 0.0167; HDL-c a... d ... ... a... c... e... e... ... a... d ... ... e... ... e... ... , ... b... 0.0259; ... -CRP ... ... a... ... e... ... , ... b... 10; ... a... ... b... ... b... ... ... c... ... e... e... , ... b... 17.104; ... ... ce... de... ... ... e... ... e... ... , ... b... 0.0113.

[a] C... a... ce... ... c... ... e... ea... e... ed ... ... e... e... a... ... a... ... c... ce... ... e... ... e-... ... e NAFLD a... f... ... da... ... ... ed.

a ca d ffe e ce e e b e ed AHR, c c d be ed b e a e e. We c d c ed b a a e e a ea ca be ee e - e NAFLD a d e

No...aja...e a.[29,30] A ea..e....e a e.f NAFLD a a...ca ed... a..ea.e...e...d.f ..c..ea ed ALT...e e.. C...a..ed... a.e... ..c..ea ed ALT e e.., a.e.... NAFLD a..d... .a.ed... a ALT e.e.e. b.ed a. .e..... f...e..c....a d...e..ca..ce..

MAFLD, e..ece...... ..ed..e.., .c..e...a..ca.ed.... e ab..cd...de..a d a bee..a...ca...ed... a.. .ca..ce..[31] O..... d a..f...da a..ca...be..ee..MAFLD a..d ca..ce.. a d.f..ef...e, ...ed...e..de c..bed a...ca... be..ee a.e. f MAFLD ...e.a..d ca..ce.....

I...e f e.d..f..b..c..ea..,Z...e a[32] f...da.c..ce...e.d.f....e..NAFLD...e.,..c.de ce a......d..d a....e...a..a..e 45..ea.....a.....a.f..de..a..e.......C...a ...e...e a...decade. We f....d a.a..e.....ea....e NAFLD a..d a....e..ca..ce....., a..c..f...ed b.PAF...T..e..ef..d.....e....a..ea...c.ee....a d..e..e.....f NAFLD...a..be c..ca...ed..ce..b..e..e..ca..ce..cc...e..ce. I..c..ea..ed a..a..e..a..d...e..ac...a..e..eeded .....c......e NAFLD..e..de...c....C...a.

T....d...a..e..e..a......a.......F...,..e Ka..a..c....c.........a...f..a..e.......e.., e..ad.. .....e...a..e..b..a. Add...a...a...,NAFLD d..a.........e..ed...........a...d...ead..f...e..b....,

...: D. W and H.S. had f acce. a f eda a. e d ad a e e . b f . e. e. f eda a a d e acc ac f eda a a . D. C. L , T. L , Q . Z a , a d J a c b ede a .

Concept and design: C. L , T. L , J a, Q Z a , R a , X e, Ha , De , W , H.S .

Acquisition, analysis, or interpretation of data: C. L , Q . Z a , S , Q Z a , Ge, L , Wa , J.S , C e , Z e , S e .

Drafting of the manuscript: C. L , T. L , S , Ge, J.S , C e , Z e , W .

Critical review of the manuscript for important intellectual content: C. L , Q . Z a , J a, Q Z a , R a , L , Wa , X e, Ha , S e , De , H. S .

Statistical analysis: C. L , Q Z a , R a , Ge, Wa , X e, C e , W .

Administrative, technical, or material support: C. L , Q . Z a , J a, Ge, J.S , De .

Supervision: Q . Z a , S , De , H. S .

1. La a JV, Ma HE, A ee QM, e a ; NAFLD C e C . Ad a c e ba b c ea a e da f NAFLD: a c e a e e . *Nat Rev Gastroenterol Hepatol*. 2022;19(1):60-78. d :10.1038/ 41575-021-00523-4

2. E e C, Ra a H, L ba R, Y Z, Sa a AJ. M de ee de c f ac c fa e d ea e de a e a e e a c ea e b de f d ea e. *Hepatology*. 2018;67(1):123-133. d :10.1002/ e .29466

3. T H, M c e AR, R de M. NAFLD a d d abe e e . *Nat Rev Gastroenterol Hepatol*. 2017;14(1):32-42. d :10.1038/ a .2016.147

4. Y e H. N a c c fa e d ea e a a ca ea d ac e e c e f e ab c d e. *Lancet Diabetes Endocrinol*. 2014;2(11):901-910. d :10.1016/S2213-8587(14)70032-4

5. B e CD, Ta e G. NAFLD: a e d ea e. *J Hepatol*. 2015;62(1)( ):S47-S64. d :10.1016/j.j e . 2014.12.012

6. Bj K, W d a L, Ha H. R f e a c a de a e a c c a ce NAFLD: a a -ba ed c d . *Liver Int*. 2022;42(4):820-828. d :10.1111/ .15195

7. Ma a A, Sc e E, M ca A, A A, B e CD, Ta e G. C ca , bd a d a f a c c fa e d ea e. *Metabolism*. 2020;111S:154170. d :10.1016/j. e ab .2020.154170

8. ...

13. L JH, Ta AS, L SH. P a a b ab e f ac ba ed a a ff ce c e ca e de f ed a e . *Ann Epidemiol*. 2022;75:57-66. d :10.1016/j.a e de .2022.08.050

14. P e EE, W VW, R e a M. N -ac c fa e d ea e. *Lancet*. 2021;397(10290):2212-2224. d :10.1016/S0140-6736(20)32511-3

15. Ka a F, Ka e JR, Ma a Se a R f e a ce a-a ce a e a c fa e d ea e. *Gastroenterology*. 2018;155(6):1828-1837.e2. d :10.1053/j. a .2018.08.024

16. C a ab D, Wa J. N ac c fa e d ea e a d c ec a ca ce : c ea a d . *Life Sci*. 2020;262:118507. d :10.1016/j. f .2020.118507

17. W K, Z a MZ, We e EK, e a. N -ac c fa e d ea e a d c ec a ca ce a. *Cancer Causes Control*. 2019;30(2):165-168. d :10.1007/ 10552-018-1095-

18. Ma a A, Pe acca G, Bea ce G, e a. N -ac c fa e d ea e a d c ea ed f cde e a e a cca ce : a ea a a f b e a a c de . *Gut*. 2022;71(4):778-788. d :10.1136/ j -2021-324191

19. L ba R, F ed a SL, S a GI. Mec a a d d ea ec e ce f ac c fa e d ea e. *Cell*. 2021;184(10):2537-2564. d :10.1016/j.ce .2021.04.015

20. S TG, R e ae B, Ha je K, e a. N -ac c fa e d ea e c d ea d a d a ca ed c ea ed - e a . *J Hepatol*. 2021;75(5):1034-1041. d :10.1016/j.j e .2021.06.034

21. L H, Y TC, Z a X, e a. A e a d e ea e a ce f e -e a ed dea ac c fa e d ea e. *Hepatology*. 2023;77(2):573-584. d :10.1002/ e .32633

22. Wa e RW, Be b GM, S EP, e a. A c a a PNPLA3 a ca ed a ea da f NAFLD a e f a -e c b ba . *J Hepatol*. 2020;72(6):1070-1081. d :10.1016/j.j e .2020.01.029

23. Z a M, S L, S L, e a. A ca f e 2 dabe e ea e ca d a c a d ea a d a : T e Ka a S d . *Diabetes Care*. 2021;44(6):1426-1432. d :10.2337/dc20-2375

24. L Y, Fe X, Ca X, e a. A e a e f ac c fa e d ea e c de ce: e e e e a ca e ab cc a e. *Diabetol Metab Syndr*. 2022;14(1):181. d :10.1186/ 13098-022-00930-

25. Ya H, C e SH, Ya LY, Ma LG, Ca LY, W SL. [C ea f ac c fa e d ea e a d ffe e a e f e e- e d abe e e]. *Zhonghua Gan Zang Bing Za Zhi*. 2022;30(6):631-636. d :10.3760/c a.j.c 501113-20200804-00434

26. Sc d V, Wa e R, Sa e C, e a. N -ac c fa e d ea e a d a ed c e a e de f ed c f e -e -e e a fe e e f d abe e e : e f e TULIP d. *Diabetologia*. 2017;60(12):2341-2351. d :10.1007/ 00125-017-4407-

27. W CL, J D, F a d N, e a. NF B1 a e f e -d e a ce a ca a. *Nat Commun*. 2015;6:6818. d :10.1038/ c 7818

28. O d M, M a S, Tc a T, e a. Ce a e e ce ced e a e-de e de e a ea a . *Nat Commun*. 2017;8:15691. d :10.1038/ c 15691

29. Na a aja Y, Ka e JR, Y X, e a. R f c a d e a ce a ca ce a e NAFLD a d a e e. *Hepatology*. 2020;72(4):1242-1252. d :10.1002/ e .31157

30. R CE, E e a JE. E e a ed e a a ea a fe a e a d a- a a fe a e d a e U ed S a e a . *Gastroenterology*. 2009;136(2):477-85.e11. d :10.1053/j. a .2008.10.052

31. L Z, L C, S C, e a. Me ab c d f c -a ca ed fa e d ea e a d e f 24 e c f ca ce . *Metabolism*. 2022;127:154955. d :10.1016/j. e ab .2021.154955

32. Z F, Z J, Wa W, e a. U e ec ed a d c ea e e b de f NAFLD C a f 2008 2018: a e a c e e a d ea-a a . *Hepatology*. 2019;70(4):1119-1133. d :10.1002/ e .30702

1.

1. De e a f Ne -O e N ac c Fa L e D ea e

2. C a f Ba e C a ce c Be ee I c ded a d E c ded Pa c a

3. N be f O e Ca e 4 G

4. R f Ca ce b H e e C-Reac e P e Le e

5. R f Ca ce b A a e A a fe a e Le e

6. A ca f Ne -O e N ac c Fa L e D ea e W R f Ca ce C e R A a

7. R f O e a Ca ce E c d 63 176 Pa c a W <1 F -U

8. R f O e a Ca ce E c d 56 651 Pa c a W Re a P ca Ac , 52 536 Pa c a