

Supplemental Online Content

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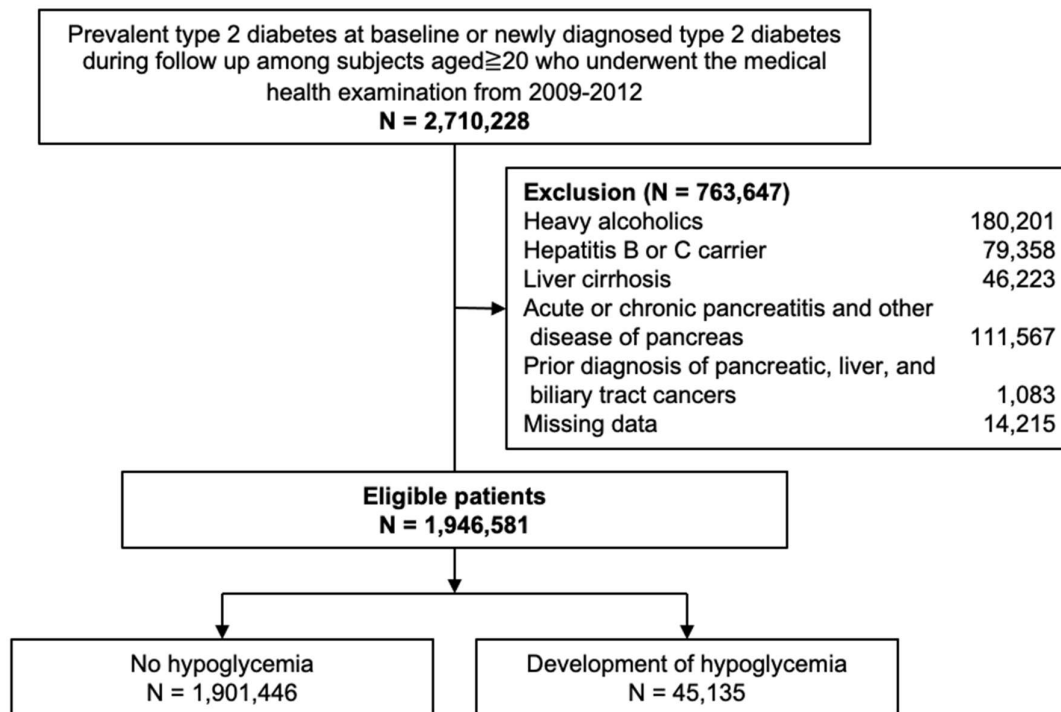
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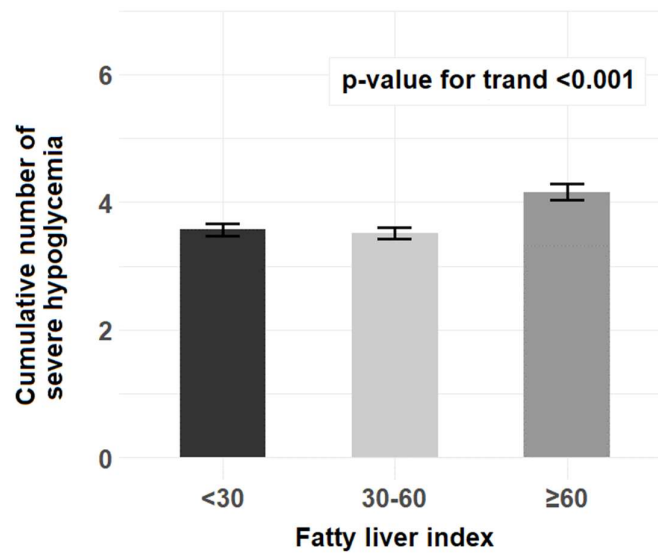
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This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Study Flowchart With Data From the Database of National Health Insurance Service



eFigure 2. Number (Multiplied by 100) of Cases of Severe Hypoglycemia per Person During the Follow-up Period According To Fatty Liver Index



Least-square means and standard errors were adjusted for age, sex, smoking and alcohol habits, exercise, body mass index, severe hypoglycemia in previous 3 years, insulin, sulfonylurea or glinides use, history of hypertension, chronic kidney disease, cardiovascular disease, and follow-up duration. Analyses were conducted in a repeatedly extracted database based on the same inclusion/exclusion criteria during the revision.

eTable 1. Association Between Traditional Risk Factors and Severe Hypoglycemia Events

Group	Incident cases, n	Person-years, n	Incident rate per 1000 p-y	aHR (95% CI)
Age, y				
20-39	501	761,866	0.7	0.75 (0.68-0.82)
40-59	7259	4,522,871	1.6	Ref.
60-69	13,544	2,666,211	5.1	2.01 (1.95-2.07)
70-79	19,612	1,603,974	12.2	3.76 (3.65-6.88)
≥80	4132	206,911	20.0	5.43 (5.20-5.67)
Sex				
Male	19,887	5,557,185	3.6	Ref.
Female	25,161	4,204,647	6.0	1.04 (1.01-1.06)
Insulin use				
No	32,390	9,072,352	3.6	Ref.
Yes	12,658	689,480	18.4	3.07 (3.00-3.14)
Sulfonylurea/glinides use				
No	10,260	5,551,866	1.8	Ref.
Yes	34,788	4,209,966	8.3	1.87 (1.74-2.01)
Severe hypoglycemia within previous 3 years				
No	41,535	9,703,353	4.3	Ref.
Yes	3513	58,479	60.1	4.02 (3.87-4.17)
Hypertension				
No	10,588	4,327,682	2.4	Ref.
Yes	34,460	5,434,150	6.3	1.30 (1.27-1.33)
Chronic kidney disease				
No	29,494	8,630,239	3.4	Ref.
Yes	15,450	1,123,179	13.8	1.89 (1.85-1.93)
Cardiovascular disease				
No	34,295	7,123,257	4.8	Ref.
Yes	6294	636,874	9.9	1.12 (1.09-1.15)

Adjusted hazard ratios (aHRs) and 95% CIs were adjusted for age, sex, smoking and alcohol habits, exercise, body mass index, severe hypoglycemia within previous 3 years, insulin, sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease

eTable 2. Cutoff Values of Fatty Liver Index Deciles

Deciles of FLI	Male	Female
D1	<12.3	<7.1
D2	12.3-20.4	7.1-12.1
D3	20.4-28.5	12.1-17.4
D4	28.5-36.7	17.4-23.1
D5	36.7-45.2	23.1-29.5
D6	45.2-54.0	29.5-36.8
D7	54.0-63.2	36.8-45.6
D8	63.2-73.0	45.6-56.2
D9	73.0-83.5	56.2-70.4
D10	≥83.5	≥70.4

FLI, fatty liver index.

eTable 3. Association Between Fatty Liver Index and Incident Severe Hypoglycemia Events in Patients With Newly Diagnosed Type 2 Diabetes

Group (Fatty liver index)	Incident cases, n	Person-years, n	Incident rate per 1000 p-y	Model 1	Model 2	Model 3
Overall						
<30	1713	1,473,352	1.2	Ref.	Ref.	Ref.
30-59	1335	1,316,490	1.0	0.87 (0.81-0.94)	1.34 (1.24-1.46)	1.18 (1.07-1.30)
≥60	1185	1,240,595	1.0	0.82 (0.76-0.89)	2.27 (2.05-2.51)	1.88 (1.67, 2.11)

Model 1 was unadjusted. Model 2 was adjusted for age, sex, smoking and alcohol habits, exercise, and body mass index. Model 3 further adjusted for severe hypoglycemia within previous 3 years, insulin, sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease. Values with statistical significance are printed in bold. Analyses were conducted in a repeatedly extracted database based on the same inclusion/exclusion criteria during the revision.

eTable 4. Fine-Gray Competing Risk Model for Estimating the Subdistribution Hazard Ratio

Group (Fatty liver index)	Model 1	Model 2	Model 3
Overall			
<30	Ref.	Ref.	Ref.
30-59	0.77 (0.75-0.79)	1.02 (1.00-1.05)	0.97 (0.95-1.00)
≥60	0.58 (0.57-0.60)	1.22 (1.18-1.27)	1.16 (1.12-1.20)
<p>Model 1 was unadjusted. Model 2 was adjusted for age, sex, smoking and alcohol habits, exercise and BMI. Model 3 further adjusted for severe hypoglycemia within previous 3 years, insulin, sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease. Values with statistical significance are printed in bold. Analyses were conducted in a repeatedly extracted database based on the same inclusion/exclusion criteria during the revision.</p>			

eTable 5. Risk of Severe Hypoglycemia by Fatty Liver Index Components

Group	Incident cases, n	Person-years, n	Incident rate per 1000p-y	aHR (95% CI)
Gamma GT Quartile				
1	15,472	2,533,735	6.1	Ref.
2	10,950	2,366,361	4.6	0.91 (0.89-0.93)
3	9736	2,448,823	4.0	0.91 (0.88-0.93)
4	8977	2,413,505	3.7	1.05 (1.02-1.08)
Waist circumference Quartile				
1	11,347	2,368,339	4.8	Ref.
2	10,872	2,515,384	4.3	0.89 (0.86-0.92)
3	10,671	2,381,082	4.5	0.92 (0.89-0.95)
4	12,245	2,497,619	4.9	1.10 (1.05-1.14)
Body mass index, kg/m²				
<18.5	1646	139,950	11.8	1.71 (1.62-1.80)
18.5-22.9	15,291	2,453,462	6.2	Ref.
23-24.9	11,120	2,486,748	4.5	0.75 (0.73-0.77)
25-29.9	14,624	3,960,684	3.7	0.65 (0.64-0.67)
≥30	2454	721,580	3.4	0.68 (0.65-0.71)
Triglyceride, mg/dL				
<150	25,704	5,177,760	5.0	Ref.
≥150	19,431	4,584,664	4.2	1.00 (0.98-1.02)

Adjusted hazard ratios (aHRs) and 95% CIs were adjusted for age, sex, smoking and alcohol habits, exercise, body mass index, prior history of severe hypoglycemia within the 3 years, insulin or sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease.

eTable 6. Adjusted Hazard Ratios for Severe Hypoglycemia in Groups With FLI 60 or Greater and Between 30 and 60 vs Group With FLI Less Than 30, in Detailed Subgroups

Group	FLI <30 (ref.)	30 ≤ FLI <60	FLI ≥60	p-value for interaction
Age, y				
<60	Ref.	0.90 (0.84-0.96)	1.17 (1.08-1.28)	<0.001
≥60	Ref.	1.02 (0.99-1.04)	1.22 (1.17-1.27)	
Body mass index, kg/m²				
<18.5	Ref.	1.17 (0.87-1.55)	1.71 (1.02-2.88)	<0.001
18.5-23	Ref.	1.07 (1.02-1.12)	1.31 (1.18-1.45)	
23-25	Ref.	1.02 (0.98-1.07)	1.20 (1.12-1.29)	
≥25	Ref.	0.94 (0.90-0.99)	1.06 (1.01-1.12)	
Chronic kidney disease				
No	Ref.	1.01 (0.98-1.04)	1.28 (1.22-1.33)	0.076
Yes	Ref.	0.97 (0.92-1.01)	1.07 (1.01-1.13)	
Cardiovascular disease				
No	Ref.	1.00 (0.97-1.02)	1.20 (1.15-1.24)	<0.001
Yes	Ref.	0.97 (0.91-1.03)	1.17 (1.07-1.28)	
Insulin				
No	Ref.	0.99 (0.96-1.01)	1.30 (1.25-1.36)	0.006
Yes	Ref.	1.01 (0.95-1.06)	1.13 (1.05-1.21)	
Sulfonylurea/Glinides				
No	Ref.	1.04 (1.01-1.07)	1.19 (1.11-1.29)	<0.001
Yes	Ref.	0.94 (0.90-0.99)	1.25 (1.21-1.30)	

Fully adjusted for age, sex, smoking and alcohol habits, exercise, body mass index, prior history of severe hypoglycemia within the 3 years, insulin or sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease. Values with statistical significance are printed in bold.

eTable 7. Association Between Fatty Liver Index, AST/ALT Ratio, and Incident Severe Hypoglycemia Events

AST/ALT ratio	Group (Fatty liver index)	Incident cases, n	Person-years, n	Incident rate per 1000 p-y	Model 1	Model 2	Model 3
< 0.8	< 30	2529	550000	4.6	Ref.	Ref.	Ref.
	30 - 59	2554	947503	2.7	0.59 (0.56-0.62)	0.81 (0.77-0.86)	0.86 (0.81-0.91)
	≥ 60	1955	1082272	1.8	0.40 (0.37-0.42)	0.91 (0.86-0.97)	0.99 (0.92-1.06)
≥ 0.8	< 30	19839	3309185	6.0	1.31 (1.25-1.36)	0.93 (0.89-0.97)	1.05 (1.01-1.10)
	30 - 59	11857	2312437	5.1	1.12 (1.07-1.17)	1.01 (0.97-1.05)	1.07 (1.02-1.12)
	≥ 60	6194	1366780	4.5	0.99 (0.94-1.04)	1.32 (1.25-1.39)	1.38 (1.31-1.45)

Model 1 was unadjusted. Model 2 was adjusted for age, sex, smoking and alcohol habits, exercise and BMI Model 3 further adjusted for severe hypoglycemia within previous 3 years, insulin, sulfonylurea or glinides use, history of hypertension, chronic kidney disease, and cardiovascular disease. Values with statistical significance are printed in bold. Analyses were conducted in a repeatedly extracted database based on the same inclusion/exclusion criteria during the revision.