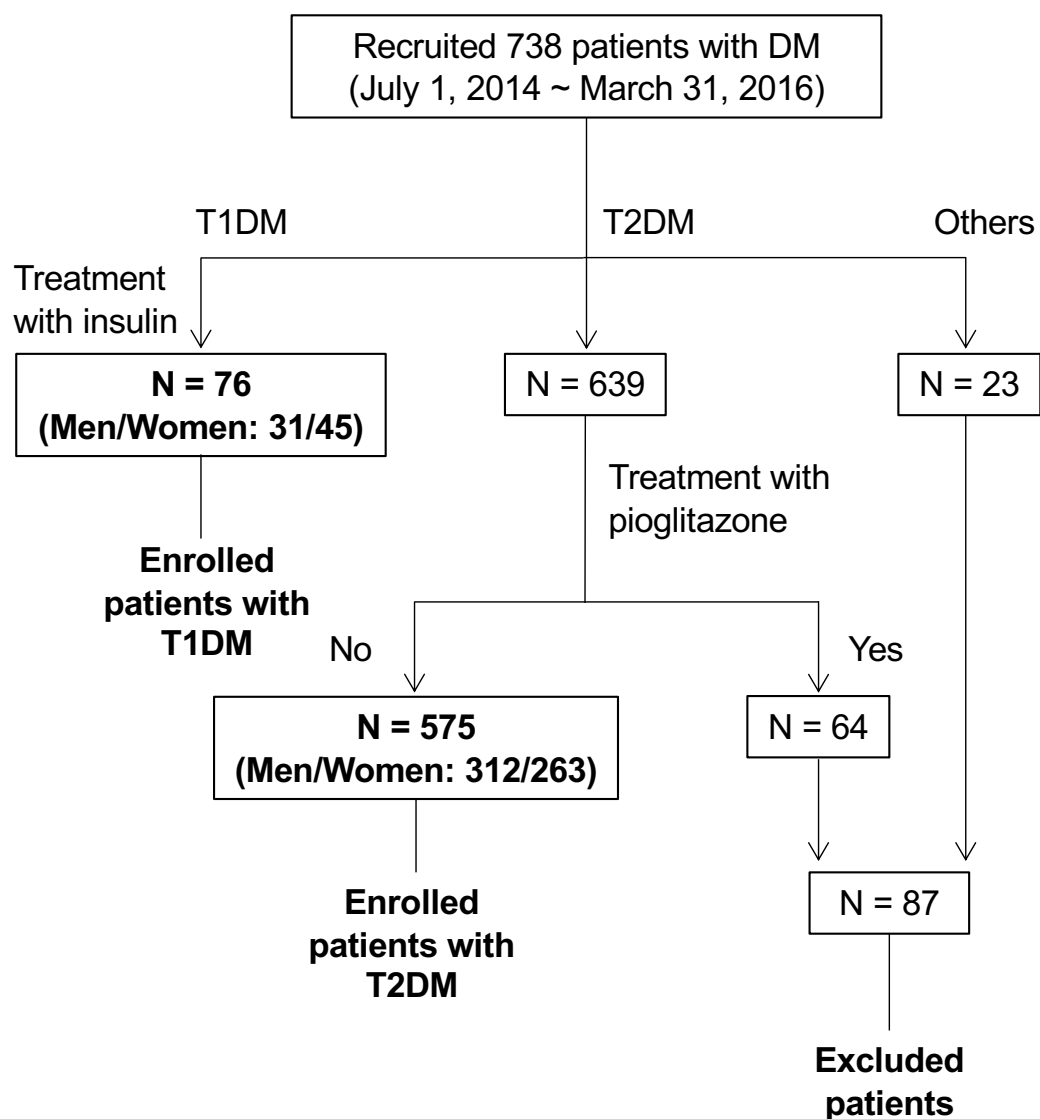


## Supplementary Figure S1



### Supplementary Figure S1. Selection of study participants.

Among 738 patients with diabetes mellitus (DM), a total of 76 patients with type 1 DM (T1DM, n = 76) and type 2 DM (T2DM, n = 575) were finally recruited for analyses in the present study.

## Supplementary Table S1

Supplementary Table S1. Characteristics of the enrolled and excluded patients

	Enrolled n = 651	Excluded n = 87	P
Age, years	65 ± 13	64 ± 13	0.573
Sex, Men	343 (52.7)	55 (63.2)	0.068
BMI	24.7 ± 4.4	25.5 ± 5.4	0.101
Systolic BP, mmHg	139 ± 18	136 ± 19	0.115
Diastolic BP, mmHg	78 ± 12	76 ± 12	0.253
Heart rate, per minute	81 ± 14	80 ± 13	0.491
Current smoking habit	109 (17.0)	14 (16.3)	0.998
Alcohol drinking habit	162 (25.3)	16 (18.6)	0.229
Duration of DM, years	14 [6-22]	15 [9-20]	0.776
Family history			
DM	375 (57.6)	50 (57.5)	0.999
Comorbidity			
Hypertension	375 (57.6)	50 (57.5)	0.702
Cardiovascular disease	224 (34.5)	30 (34.5)	1.000
Medication			
Anti-diabetic drugs			
Insulin	288 (44.2)	26 (29.9)	0.011
GLP-1 analogs	32 (4.9)	2 (2.3)	0.414
Sulfonylureas	166 (25.5)	41 (47.1)	< 0.001
Biguanides	320 (49.2)	46 (52.9)	0.569
α-glucosidase inhibitors	100 (15.4)	23 (26.4)	0.014
DPP-4 inhibitors	432 (66.4)	59 (67.8)	0.904
Glinides	49 (7.5)	5 (5.7)	0.665
SGLT2 inhibitors	10 (1.5)	1 (1.1)	0.998
Anti-dyslipidemic drugs			
Statin	331 (50.8)	57 (65.5)	0.012
Biochemical data			
Total protein, g/dL	7.3 ± 0.5	7.3 ± 0.5	0.690
AST, IU/L	21 [17-27]	19 [16-26]	0.114
ALT, IU/L	19 [14-28]	17 [13-26]	0.473
γGTP, IU/L	25 [17-46]	27 [19-40]	0.925
BUN, mg/dL	17 ± 8	16 ± 4	0.418
Creatinine, mg/dL	0.80 [0.64-1.00]	0.80 [0.60-1.00]	0.760
eGFR, mL/min/1.73m <sup>2</sup>	67 ± 23	71 ± 24	0.154
Uric acid, mg/dL	5.3 ± 1.4	5.3 ± 1.5	0.804
TC, mg/dL	183 ± 35	181 ± 36	0.629
LDL-C, mg/dL	106 ± 28	104 ± 23	0.423
HDL-C, mg/dL	53 ± 15	55 ± 13	0.248
Non-HDL-C, mg/dL	130 ± 33	126 ± 29	0.301
Triglycerides, mg/dL	104 [74-158]	94 [76-155]	0.675
CRP, mg/dL	0.10 [0.06-0.20]	0.08 [0.06-0.15]	0.170
Glucose, mg/dL	141 [118-175]	142 [121-167]	0.939
Hemoglobin A1c, %	7.2 [6.6-7.9]	7.2 [6.6-7.8]	0.822
C-peptide, ng/mL	1.52 [0.94-2.46]	1.49 [0.96-2.58]	0.746
TNFR1, ng/mL	1.58 [1.25-2.16]	1.52 [1.29-2.01]	0.545
TNFR2, ng/mL	3.38 [2.70-4.52]	3.40 [2.75-4.23]	0.747
FABP4, ng/mL	16.5 [11.5-23.8]	24.2 [16.3-33.5]	< 0.001

Variables are expressed as number (%), means ± standard deviation or medians [interquartile ranges].

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; CRP, C-reactive protein; DM, diabetes mellitus; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; FABP4, fatty acid-binding protein 4; GLP-1, glucagon-like peptide-1; γGTP, γ-glutamyl transpeptidase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SGLT2, sodium-glucose co-transporter-2; TC, total cholesterol; TNFR, tumor necrosis factor receptor; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

## Supplementary Table S2

Supplementary Table S2. Characteristics of the enrolled patients with DM divided by sex

	T1DM		T2DM	
	Men (n = 31)	Women (n =45)	Men (n = 312)	Women (n = 263)
Age, years	60 ± 13	59 ± 15	66 ± 12	65 ± 14
BMI	23 ± 3	23 ± 4	24 ± 4	25 ± 5
Systolic BP, mmHg	135 ± 15	134 ± 18	139 ± 18	140 ± 18
Diastolic BP, mmHg	81 ± 9	74 ± 12	79 ± 12	77 ± 11
Heart rate, per minute	81 ± 14	81 ± 13	80 ± 14	83 ± 14
Current smoking habit	8 (25.8)	2 (4.7)	80 (25.8)	19 (7.4)
Alcohol drinking habit	16 (51.6)	1 (2.3)	125 (40.3)	20 (7.8)
Duration of DM, years	12 [6-20]	15 [6-27]	15 [7-22]	13 [7-22]
Family history				
DM	13 (41.9)	23 (51.1)	169 (54.2)	170 (64.6)
Comorbidity				
Hypertension	20 (64.5)	27 (60.0)	229 (73.4)	193 (73.4)
Cardiovascular disease	6 (19.4)	9 (20.0)	132 (42.3)	77 (29.4)
Medication				
Anti-diabetic drugs				
Insulin	31 (100)	45 (100)	122 (39.1)	90 (34.2)
GLP-1 analogs	1 (3.1)	0 (0)	14 (4.5)	17 (66.5)
Sulfonylureas	0 (0)	0 (0)	82 (26.3)	84 (31.9)
Biguanides	5 (16.1)	6 (13.3)	155 (49.7)	154 (58.6)
α-glucosidase inhibitors	2 (6.5)	3 (6.7)	54 (17.3)	41 (15.6)
DPP-4 inhibitors	6 (19.4)	12 (26.7)	225 (72.1)	189 (71.9)
Glinides	0 (0)	0 (0)	31 (9.9)	18 (6.8)
SGLT2 inhibitors	0 (0)	0 (0)	5 (1.6)	5 (1.9)
Anti-dyslipidemic drugs				
Statin	8 (25.8)	21 (46.7)	154 (49.4)	148 (56.3)
Biochemical data				
Total protein, g/dL	7.0 ± 0.4	7.3 ± 0.4	7.3 ± 0.5	7.3 ± 0.5
AST, IU/L	22 [19-26]	20 [16-25]	22 [17-29]	21 [17-26]
ALT, IU/L	19 [15-25]	16 [11-22]	20 [14-29]	18 [13-28]
γGTP, IU/L	28 [18-53]	16 [12-26]	30 [20-55]	22 [16-36]
BUN, mg/dL	17 ± 7	18 ± 7	18 ± 9	16 ± 7
Creatinine, mg/dL	0.80 [0.72-0.90]	0.70 [0.60-0.80]	0.90 [0.80-1.10]	0.64 [0.57-0.80]
eGFR, mL/min/1.73m <sup>2</sup>	73 ± 18	68 ± 28	64 ± 21	70 ± 25
Uric acid, mg/dL	5.4 ± 1.2	4.3 ± 1.5	5.7 ± 1.3	5.0 ± 1.2
TC, mg/dL	189 ± 31	193 ± 29	177 ± 36	187 ± 33
LDL-C, mg/dL	108 ± 25	114 ± 21	102 ± 29	110 ± 27
HDL-C, mg/dL	65 ± 16	62 ± 17	49 ± 14	54 ± 13
Non-HDL-C, mg/dL	121 ± 26	131 ± 25	128 ± 35	133 ± 32
Triglycerides, mg/dL	72 [50-85]	81 [58-110]	118 [80-172]	103 [75-159]
CRP, mg/dL	0.06 [0.04-0.11]	0.08 [0.06-0.21]	0.11 [0.06-0.23]	0.10 [0.06-0.17]
Glucose, mg/dL	124 [101-175]	179 [135-225]	141 [118-172]	139 [118-169]
Hemoglobin A1c, %	7.1 [6.5-7.5]	7.8 [7.1-8.4]	7.1 [6.5-7.8]	7.2 [6.7-8.1]
C-peptide, ng/mL	0.15 [0.15-0.47]	0.15 [0.06-0.21]	1.75 [1.12-2.62]	1.51 [1.13-2.45]
TNFR1, ng/mL	1.34 [1.04-1.74]	1.32 [1.06-2.10]	1.74 [1.40-2.35]	1.45 [1.16-1.97]
TNFR2, ng/mL	3.10 [2.36-3.94]	2.93 [2.43-4.61]	3.67 [2.99-4.81]	3.08 [2.52-4.28]
FABP4, ng/mL	13.9 [8.2-16.1]	14.3 [9.6-21.8]	15.7 [10.6-22.3]	18.9 [13.2-25.7]

Variables are expressed as number (%), means ± standard deviation or medians [interquartile ranges].

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; CRP, C-reactive protein; DM, diabetes mellitus; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; FABP4, fatty acid-binding protein 4; GLP-1, glucagon-like peptide-1; γGTP, γ-glutamyl transpeptidase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SGLT2, sodium-glucose co-transporter-2; TC, total cholesterol; TNFR, tumor necrosis factor receptor; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

## Supplementary Table S3

Supplementary Table S3. Correlation analyses for Log FABP4 in patients with DM divided by sex

	T1DM				T2DM			
	Men		Women		Men		Women	
	(n = 31)		(n = 45)		(n = 312)		(n = 263)	
	r	P	r	P	r	P	r	P
Age	0.089	0.632	0.018	0.905	-0.027	0.636	0.030	0.625
BMI	0.081	0.677	0.526	<0.001	0.277	<0.001	0.331	<0.001
Systolic BP	0.385	0.033	0.086	0.573	0.034	0.545	0.073	0.237
Diastolic BP	0.382	0.034	-0.039	0.799	0.027	0.631	0.062	0.317
Heart rate	0.301	0.099	-0.275	0.067	0.085	0.136	0.034	0.584
Log [Duration of DM]	-0.025	0.893	0.328	0.052	0.089	0.129	0.056	0.375
Total protein	-0.161	0.386	-0.081	0.599	-0.016	0.778	-0.087	0.160
Log AST	0.392	0.029	0.277	0.065	0.039	0.492	0.057	0.357
Log ALT	0.410	0.022	0.268	0.075	0.079	0.164	0.077	0.212
Log $\gamma$ GTP	0.459	0.009	0.322	0.031	0.088	0.120	0.120	0.051
BUN	0.043	0.817	0.649	<0.001	0.200	<0.001	0.344	<0.001
Log Creatinine	-0.013	0.946	0.696	<0.001	0.389	<0.001	0.414	<0.001
eGFR	-0.068	0.718	-0.640	<0.001	-0.319	<0.001	-0.343	<0.001
Uric acid	0.158	0.394	0.329	0.026	0.259	<0.001	0.273	<0.001
TC	-0.037	0.846	-0.005	0.975	0.039	0.494	-0.105	0.089
LDL-C	0.072	0.702	-0.067	0.664	0.019	0.740	-0.065	0.296
HDL-C	-0.275	0.134	-0.109	0.478	-0.078	0.165	-0.269	<0.001
Non-HDL-C	0.126	0.498	0.069	0.652	0.072	0.205	-0.001	0.994
Log Triglycerides	0.333	0.067	0.309	0.039	0.135	0.017	0.158	0.010
Log CRP	0.083	0.656	0.187	0.224	0.143	0.011	0.109	0.079
Log Glucose	-0.055	0.770	0.067	0.666	0.014	0.800	-0.056	0.362
Log [Hemoglobin A1c]	-0.195	0.294	0.290	0.054	0.071	0.214	0.039	0.530
Log C-peptide	0.165	0.374	0.164	0.280	0.186	<0.001	0.245	<0.001
Log TNFR1	0.330	0.070	0.546	<0.001	0.394	<0.001	0.607	<0.001
Log TNFR2	0.347	0.056	0.578	<0.001	0.350	<0.001	0.423	<0.001

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; CRP, C-reactive protein; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FABP4, fatty acid-binding protein 4;  $\gamma$ GTP,  $\gamma$ -glutamyl transpeptidase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TNFR, tumor necrosis factor receptor; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

## Supplementary Table S4

Supplementary Table S4. Additional multivariable regression analyses for Log FABP4 in patients with DM

	T1DM (n = 76)				T2DM (n = 575)			
	Model 3		Model 4		Model 3		Model 4	
	$\beta$	P	$\beta$	P	$\beta$	P	$\beta$	P
Age	-0.052	0.688	-0.073	0.569	-0.110	0.016	-0.124	0.007
Sex (Men)	-0.097	0.364	-0.090	0.401	-0.235	<0.001	-0.235	<0.001
BMI	0.363	0.006	0.366	0.006	0.281	<0.001	0.287	<0.001
eGFR	-0.191	0.295	-0.241	0.143	-0.251	<0.001	-0.284	<0.001
Log Triglycerides	0.101	0.398	0.136	0.231	0.010	0.789	0.014	0.713
Current smoking habit	-0.004	0.970	-0.006	0.952	0.032	0.410	0.044	0.257
Insulin	-	-	-	-	0.056	0.175	0.065	0.115
GLP-1 analogs	-0.096	0.372	-0.106	0.332	-0.032	0.406	-0.032	0.433
Sulfonylureas	-	-	-	-	0.061	0.154	0.063	0.146
Biguanides	-0.080	0.502	-0.076	0.524	0.022	0.589	0.013	0.760
$\alpha$ -glucosidase inhibitors	0.098	0.335	0.095	0.349	0.008	0.825	0.001	0.969
DPP-4 inhibitors	0.210	0.183	0.106	0.372	0.069	0.083	0.069	0.084
Glinides	-	-	-	-	-0.076	0.039	-0.075	0.042
SGLT2 inhibitors	-	-	-	-	0.033	0.362	0.038	0.296
Log TNFR1	0.210	0.183	-	-	0.277	<0.001	-	-
Log TNFR2	-	-	0.170	0.225	-	-	0.239	<0.001
AIC	100		100		723		729	
R <sup>2</sup>	0.443		0.440		0.326		0.319	
Adjusted R <sup>2</sup>	0.342		0.339		0.308		0.301	
Statistical power (1 - $\beta$ error)	0.991		0.990		1.000		1.000	

AIC, Akaike's information criterion;  $\beta$ , standardized regression coefficient; BMI, body mass index; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; FABP4, fatty acid-binding protein 4; SGLT2, sodium-glucose co-transporter-2; TNFR, tumor necrosis factor receptor; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

## Supplementary Table S5

Supplementary Table S5. Multivariable regression analyses for Log FABP4 in patients with DM

	T1DM (n = 76)				T2DM (n = 575)			
	Model 5		Model 6		Model 5		Model 6	
	$\beta$	P	$\beta$	P	$\beta$	P	$\beta$	P
Age	-0.614	0.207	-0.192	0.312	-0.102	0.022	-0.122	0.007
Sex (Men)	-0.137	0.182	-0.126	0.219	-0.227	<0.001	-0.215	<0.001
BMI	0.180	0.134	0.181	0.132	0.284	<0.001	0.288	<0.001
eGFR	-0.305	0.077	-0.361	0.020	-0.221	<0.001	-0.261	<0.001
Log Triglycerides	0.175	0.156	0.183	0.140	0.012	0.754	0.015	0.710
Log Glucose	0.020	0.851	0.017	0.875	-0.037	0.324	-0.031	0.411
Log CRP	-0.214	0.086	-0.203	0.099	0.014	0.178	-0.008	0.847
Cardiovascular disease	0.121	0.257	0.114	0.286	-0.005	0.890	0.001	0.977
Statin	0.099	0.345	0.105	0.318	0.016	0.662	0.012	0.753
Log TNFR1	0.326	0.053	-	-	0.293	<0.001	-	-
Log TNFR2	-	-	0.281	0.057	-	-	0.253	<0.001
AIC	103		103		742		749	
R <sup>2</sup>	0.464		0.463		0.305		0.296	
Adjusted R <sup>2</sup>	0.380		0.379		0.293		0.284	
Statistical power (1 - $\beta$ error)	0.998		0.998		1.000		1.000	

AIC, Akaike's information criterion;  $\beta$ , standardized regression coefficient; BMI, body mass index; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; FABP4, fatty acid-binding protein 4; TNFR, tumor necrosis factor receptor; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.