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OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

**Serum total bilirubin concentration is
negatively associated with increasing severity
in patients with type 2 diabetes mellitus**

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Aims

- **Serum bilirubin concentration is associated with diabetic retinopathy in patients with type 2 diabetes.**
- **This study investigated the relationships between serum bilirubin concentration and the severity of diabetic retinopathy.**
- **The importance of bilirubin was compared with the factors which were previously shown to be associated with the incidence of diabetic retinopathy (duration of diabetes, body mass index, systolic blood pressure, and HbA1c).**

Methods

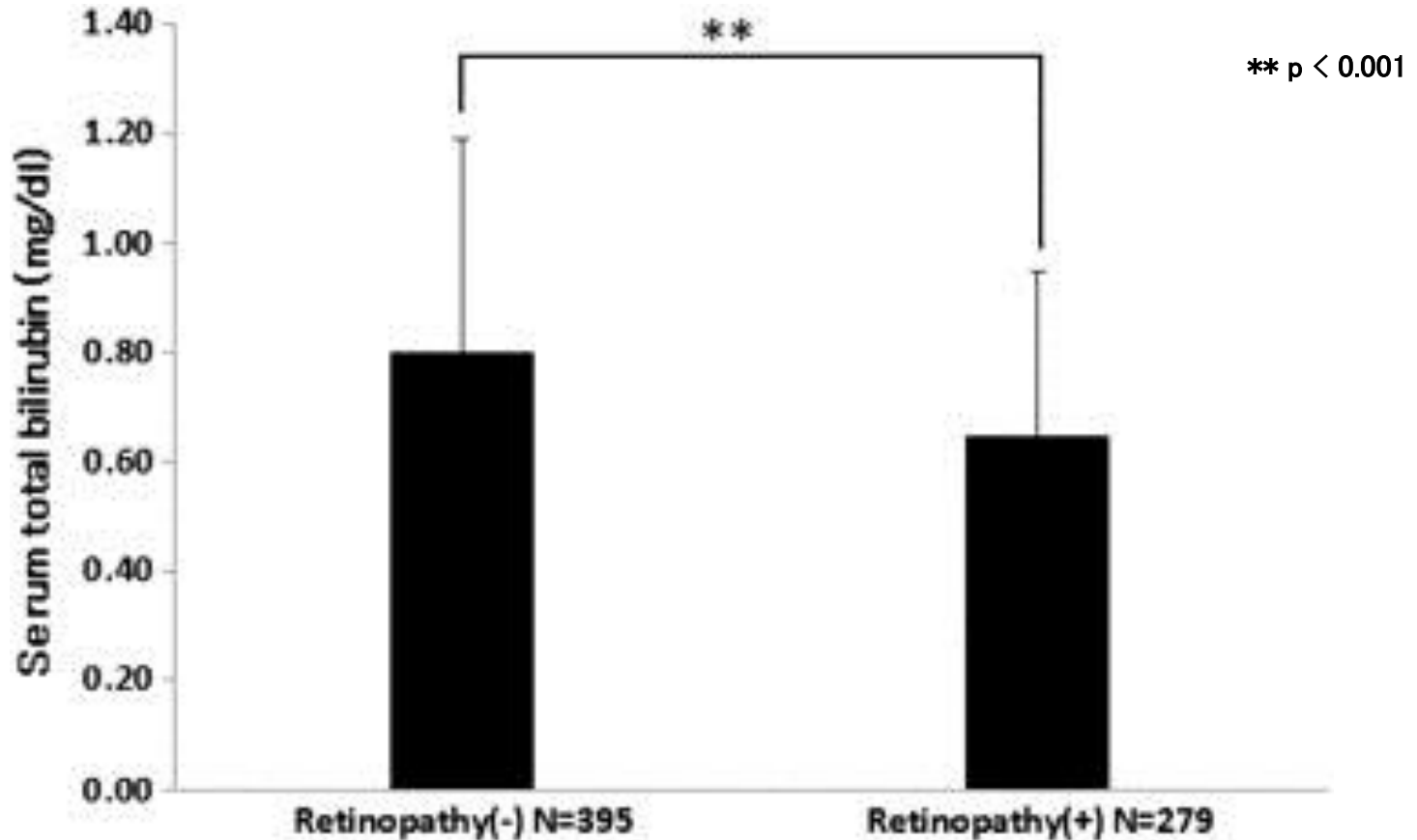
- **A total of 674 patients with type 2 diabetes are investigated in this cross-sectional study.**
- **Serum total bilirubin concentrations are compared between patients with and without diabetic retinopathy, and according to the severity of the retinopathy.**
- **Multivariate analyses are performed to evaluate the association of retinopathy with total bilirubin concentration, duration of diabetes, body mass index, systolic blood pressure, and HbA1c.**

Patient demographic and laboratory data

• <i>N</i>	674
• Age (years)	64.7 ± 13.9
• Sex (men/women)	446/228
• Duration of diabetes (years)	13.9 ± 10.9
• BMI (kg/m ²)	25.5 ± 6.3
• HbA1c (%)	9.13 ± 2.16
• Total bilirubin (mg/dL)	0.74 ± 0.36
• AST (IU/L)	26.8 ± 17.0
• ALT (IU/L)	26.8 ± 20.1
• eGFR (mL min ⁻¹ 1.73 m ⁻²)	61.7 ± 31.6
• Smoking, <i>n</i> (%)	324 (48.1)
• Hypertension, <i>n</i> (%)	498 (73.9)
• Dyslipidaemia, <i>n</i> (%)	520 (77.2)
• Diabetic retinopathy, <i>n</i> (%)	279 (41.4)
• NDR/SDR/PPDR/PDR, <i>n</i> (%)	395 (58.6)/132 (19.6)/43 (6.4)/104 (21.8)
• Diabetic nephropathy, <i>n</i> (%)	323 (47.9)
• Cerebrovascular disease, <i>n</i> (%)	101 (15.0)
• Cardiovascular disease, <i>n</i> (%)	128 (19.0)

NDR, no diabetic retinopathy
SDR, simple DR
PPDR, preproliferative DR
PDR, proliferative DR

Result 1: Serum total bilirubin concentration of patients with and without retinopathy



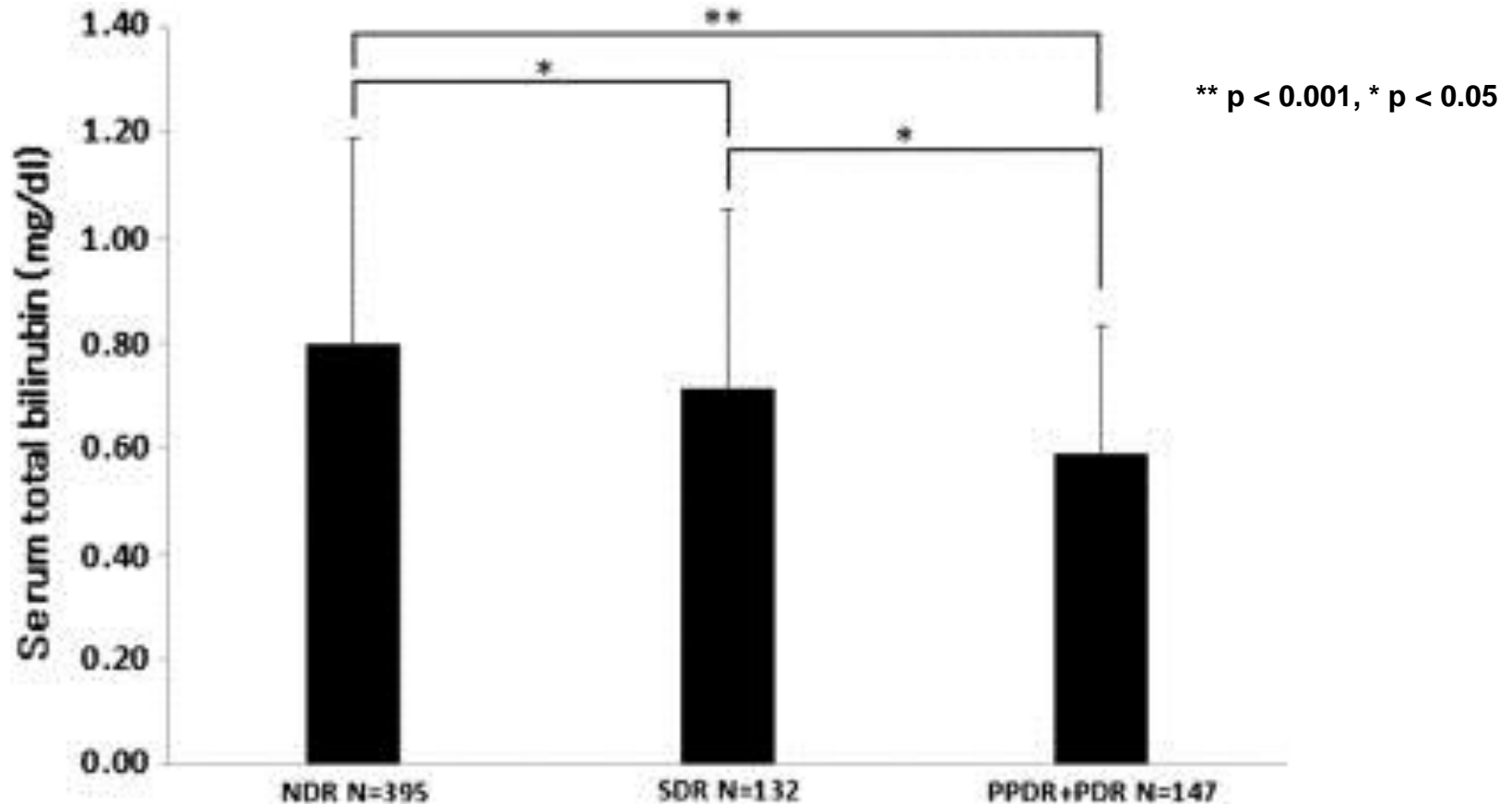
Sekioka R, Tanaka, M, et al.

Serum total bilirubin concentration is negatively associated with increasing severity of retinopathy in patients with type 2 diabetes mellitus

Journal of Diabetes and its Complications, Volume 29, Issue 2, 2015, 218–221

Result 2:

Serum total bilirubin concentration of patients with NDR, SDR, and PPDR + PDR



NDR, no diabetic retinopathy;
SDR, simple diabetic retinopathy;
PPDR, preproliferative diabetic retinopathy
PDR, proliferative diabetic retinopathy

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Result 3:

Multivariate logistic regression analysis of diabetic retinopathy

	Wald	Odds ratio	95%CI	p
Sex (Female = 1, Male = 0)	2.620	1.419	0.929–2.168	0.106
Age	0.327	0.995	0.980–1.011	0.568
BMI	0.295	0.992	0.962–1.022	0.587
Duration of diabetes	57.419	1.079	1.058–1.100	0.000
Systolic blood pressure	8.100	1.012	1.004–1.021	0.004
HbA1c	0.002	1.002	0.917–1.095	0.961
Total bilirubin	18.112	0.262	0.142–0.486	0.000
Smoking	1.005	1.225	0.824–1.822	0.316

CI : confidence interval

Summary of results

- ▶ Total bilirubin concentration is lower in type 2 diabetic patients with retinopathy.
- ▶ Total bilirubin concentration decreases with increasing severity of diabetic retinopathy.
- ▶ Patients with retinopathy have high blood pressure and long diabetes duration.



Serum total bilirubin concentration is negatively associated with increasing severity of retinopathy in patients with type 2 diabetes mellitus

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Discussion

- **It is already shown that bilirubin concentration is lower in patients with type 1 and 2 diabetes with vascular complications.**

Low serum total bilirubin concentration in patients with type 1 or type 2 diabetes mellitus complicated by vascular complication

Masami Tanaka, Takeshi Nishimura, Risa Sekioka, Hiroshi Itoh

ADA2015 Boston

1) 131 patients with type 1 DM

serum TBC is compared between patients with and without retinopathy/nephropathy, and among groups stratified according to the severity of retinopathy/nephropathy.

2) 293 patients with type 2 DM

TBC is compared between patients with and without diabetic microangiopathy, and between patients with and without macroangiopathy (cerebral infarction, coronary artery disease, and peripheral arterial disease).

Results: T1DM-1

Comparison of serum total bilirubin concentration according to severity of diabetic retinopathy and nephropathy

MA	Severity	n	Total bilirubin (mg/dl)	J-T, p value
R	NDR	82	0.8 (0.6-1.0)	<0.001
	SDR	24	0.6 (0.5-0.775)	
	PPDR+PDR	25	0.5 (0.4-0.75)	
N	Without nephropathy	88	0.8 (0.6-1.0)	<0.001
	Microalbuminuria	12	0.75 (0.525-1.0)	
	Macroalbuminuria and/or renal failure including dialysis	31	0.5 (0.4-0.7)	

Values are expressed as number or median (interquartile range).

Abbreviation: MA, Microangiopathy; R, Retinopathy; N, Nephropathy; J-T, Jonckheere-Terpstra test; NDR, no diabetic retinopathy; SDR, simple DR; PPDR, preproliferative DR; PDR, proliferative DR.

Logistic-regression analysis of diabetic retinopathy and nephropathy

Retinopathy

	Odds ratio	95%CI	p value
Gender (Female = 1, Male = 0)	0.879	0.347-2.228	0.786
Age	1.007	0.976-1.038	0.672
Duration of diabetes	1.067	1.022-1.114	0.003
HbA1c	1.064	0.813-1.394	0.650
Systolic blood pressure	1.025	0.998-1.053	0.067
Total bilirubin	0.047	0.007-0.310	0.001
Smoking	0.538	0.209-1.380	0.197

Nephropathy

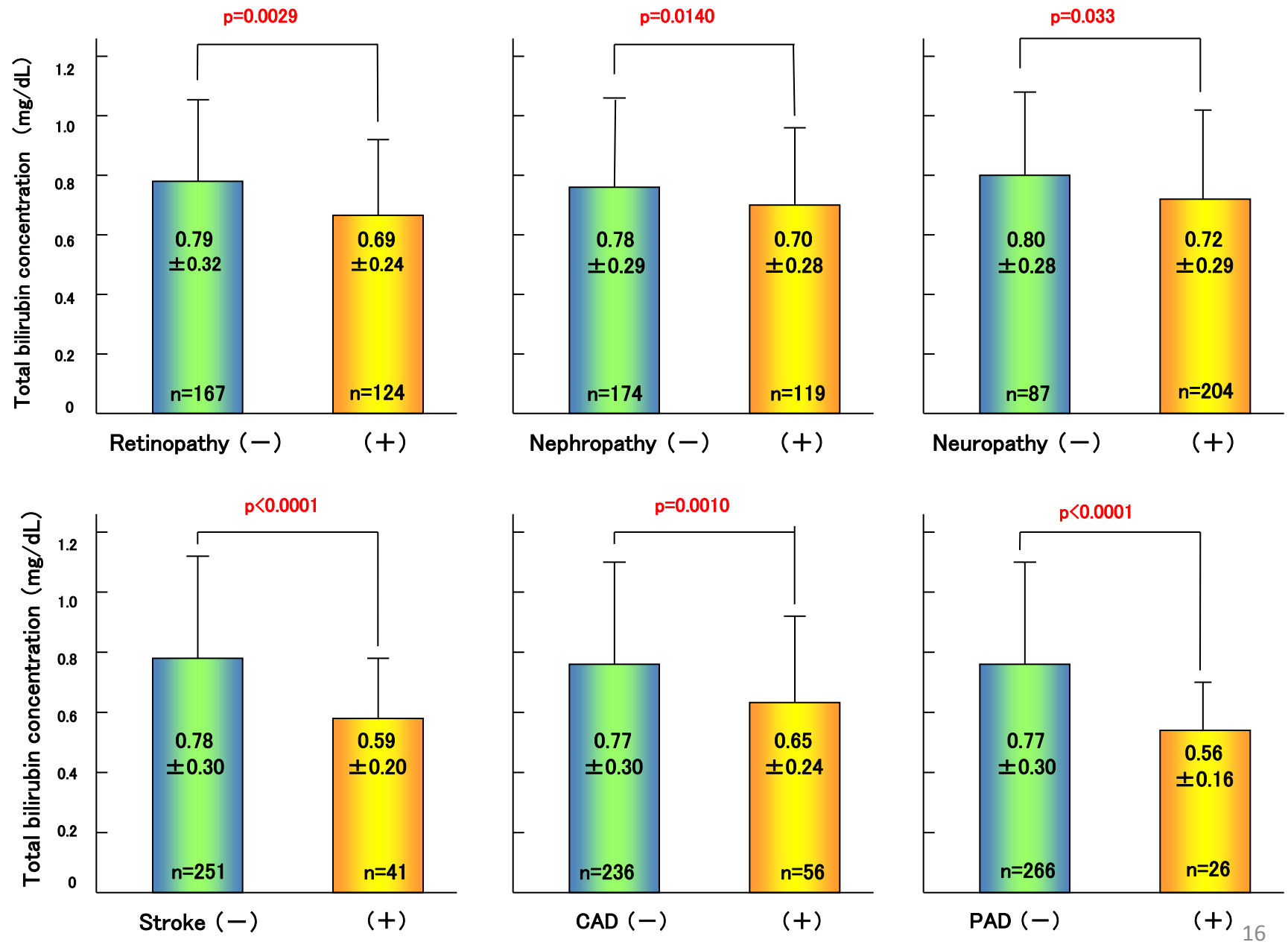
	Odds ratio	95%CI	p value
Gender (Female = 1, Male = 0)	0.474	0.176-1.278	0.140
Age	1.061	1.025-1.099	0.001
Duration of diabetes	1.011	0.972-1.051	0.593
HbA1c	1.074	0.813-1.418	0.616
Systolic blood pressure	1.020	0.993-1.048	0.142
Total bilirubin	0.017	0.002-0.158	0.000
Smoking	0.818	0.316-2.118	0.679

Low serum total bilirubin concentration in patients with type 1 diabetes mellitus complicated by retinopathy and nephropathy

**Risa Sekioka · Masami Tanaka · Takeshi Nishimura ·
Hiroshi Itoh**

Results: T2DM-1

Diabetic micro/macro angiopathy and serum total bilirubin concentration



CAD: Coronary artery disease, PAD: Peripheral artery disease

Logistic regression analysis examining the effect of various factors on micro/macro angiopathy

Microangiopathy

Characteristics	Odds ratio	P
TBC	0.652	0.49
BMI	1.05	0.24
Age	1.02	0.35
Gender	0.788	0.57
Duration of diabetes	1.18	0.0000
HbA1c	1.01	0.94
Smoking	1.60	0.29
Alcohol	1.06	0.90
LDL-C	0.999	0.88
HDL-C	0.993	0.59
TG	1.00	0.32
SBP	1.01	0.63

Macroangiopathy

Characteristics	Odds ratio	P
TBC	0.1051	0.0004
BMI	1.0567	0.0851
Age	1.0512	0.0022
Gender	1.1601	0.6896
Duration of diabetes	1.0359	0.0482
HbA1c	0.8849	0.2088
Smoking	1.5366	0.2523
Alcohol	1.6685	0.1799
LDL-C	0.9906	0.0297
HDL-C	0.9978	0.8419
TG	1.0010	0.1597
SBP	1.0049	0.5311



Contents lists available at ScienceDirect

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journal homepage: WWW.JDCJOURNAL.COM



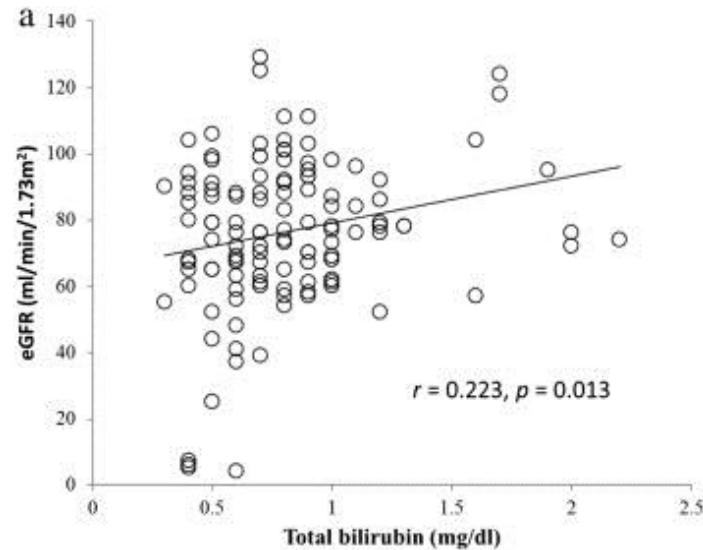
Serum bilirubin concentration is associated with eGFR and urinary albumin excretion in patients with type 1 diabetes mellitus

Takeshi Nishimura^{*}, Masami Tanaka, Risa Sekioka¹, Hiroshi Itoh

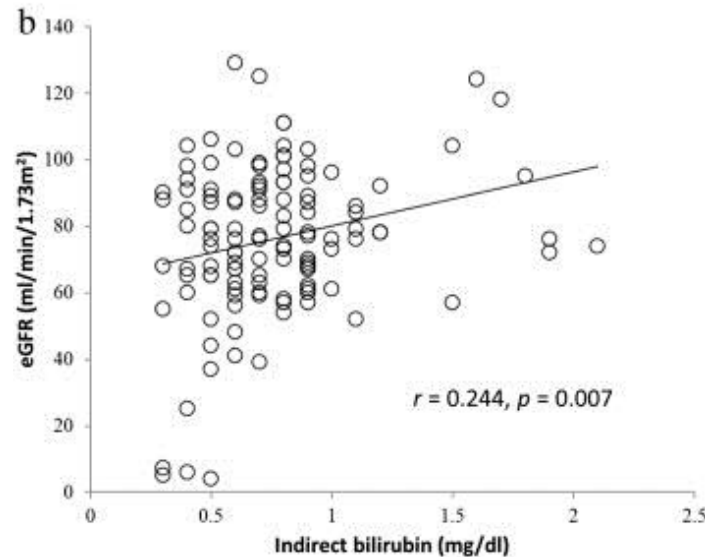
Division of Endocrinology, Metabolism and Nephrology, Department of Internal Medicine, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan

Correlation between serum bilirubin concentration and estimated glomerular filtration rate (eGFR) in patients with type 1 diabetes

(a) Total bilirubin



(b) Indirect bilirubin



Nishimura T, Tanaka M, et al

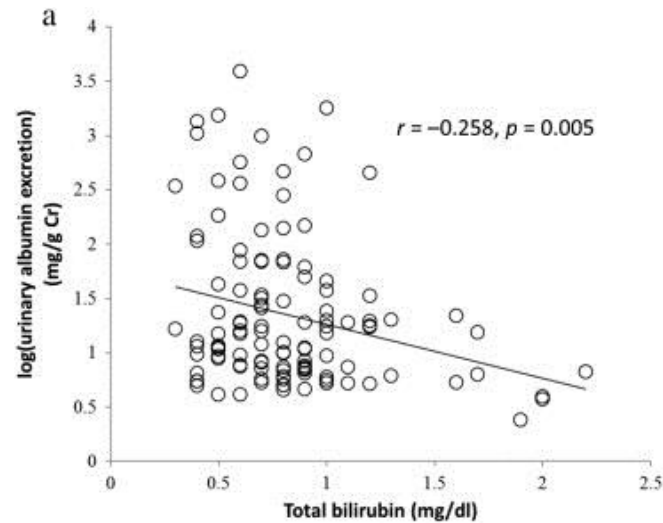
Serum bilirubin concentration is associated with eGFR and urinary albumin excretion in patients with type 1 diabetes mellitus

Journal of Diabetes and its Complications, 2015, Available online 9 July 2015

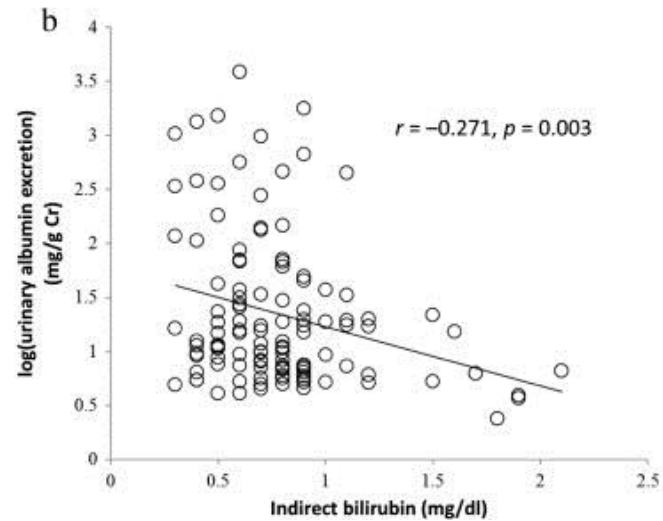
<http://dx.doi.org/10.1016/j.jdiacomp.2015.07.007>

Correlation between serum bilirubin concentration and log(urinary albumin excretion) in patients with type 1 diabetes

(a) Total bilirubin



(b) Indirect bilirubin



Factors contributing to the estimated glomerular filtration rate

	Estimated	SE	t value	p value
Total bilirubin				
Total bilirubin level (mg/dL)	0.160	5.490	1.837	0.069
Duration of diabetes (years)	-0.110	0.176	-1.252	0.213
BMI (kg/m ²)	-0.116	0.592	-1.318	0.190
HbA1c (%)	0.099	1.332	1.122	0.264
Use of ARB or ACEI (yes = 1, no = 0)	-0.290	4.611	-3.285	0.001
Systolic blood pressure (mmHg)	-0.006	0.105	-0.069	0.945
Indirect bilirubin				
Indirect bilirubin level (mg/dL)	0.174	5.752	2.012	0.047
Duration of diabetes (years)	-0.108	0.175	-1.234	0.220
BMI (kg/m ²)	-0.113	0.591	-1.280	0.203
HbA1c (%)	0.095	1.324	1.085	0.280
Use of ARB or ACEI (yes = 1, no = 0)	-0.288	4.599	-3.279	0.001
Systolic blood pressure (mmHg)	-0.004	0.104	-0.041	0.968

“Estimated” refers to the estimated value of the standardized regression coefficient.
 Abbreviations: SE, standard error; BMI; body mass index; HbA1c, haemoglobin A1c; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

Factors contributing to urinary albumin excretion

	Estimated	SE	t value	p value
Total bilirubin				
Total bilirubin level (mg/dL)	-0.186	0.169	-2.095	0.038
Sex (male = 1, female = 0)	0.052	0.123	0.586	0.559
Age (years)	0.233	0.004	2.699	0.009
Duration of diabetes (years)	0.111	0.005	1.271	0.206
BMI (kg/m ²)	0.009	0.017	0.107	0.915
HbA1c (%)	0.222	0.039	2.617	0.010
Use of ARB or ACEI (yes = 1, no = 0)	0.230	0.137	2.661	0.009
Systolic blood pressure (mmHg)	0.110	0.003	1.223	0.224
Indirect bilirubin				
Indirect bilirubin level (mg/dL)	-0.196	0.177	-2.242	0.027
Sex (male = 1, female = 0)	0.050	0.121	0.576	0.566
Age (years)	0.231	0.004	2.651	0.009
Duration of diabetes (years)	0.110	0.005	1.260	0.210
BMI (kg/m ²)	0.006	0.017	0.068	0.946
HbA1c (%)	0.226	0.039	2.682	0.008
Use of ARB or ACEI (yes = 1, no = 0)	0.230	0.137	2.668	0.009
Systolic blood pressure (mmHg)	0.107	0.003	1.199	0.233

“Estimated” refers to the estimated value of the standardized regression coefficient.

Abbreviations: SE, standard error; BMI, body mass index; HbA1c, haemoglobin A1c; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

Serum bilirubin concentration is negatively associated with micro/macro vascular complications in both type 1 and type 2 diabetes.

Bilirubin

- 1) **Antioxidant** properties by scavenging reactive oxygen species,
- 2) **Anti-inflammatory** properties by inhibiting the TNF α -related induction of endothelial adhesion molecules (E-selectin, VCAM-1, ICAM-1)

Conclusion

- **Bilirubin might function protectively against vascular complications in both type 1 and type 2 DM patients.**

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