

Supplementary materials for “Association between diabetes and major bleeding complications of renal biopsy”

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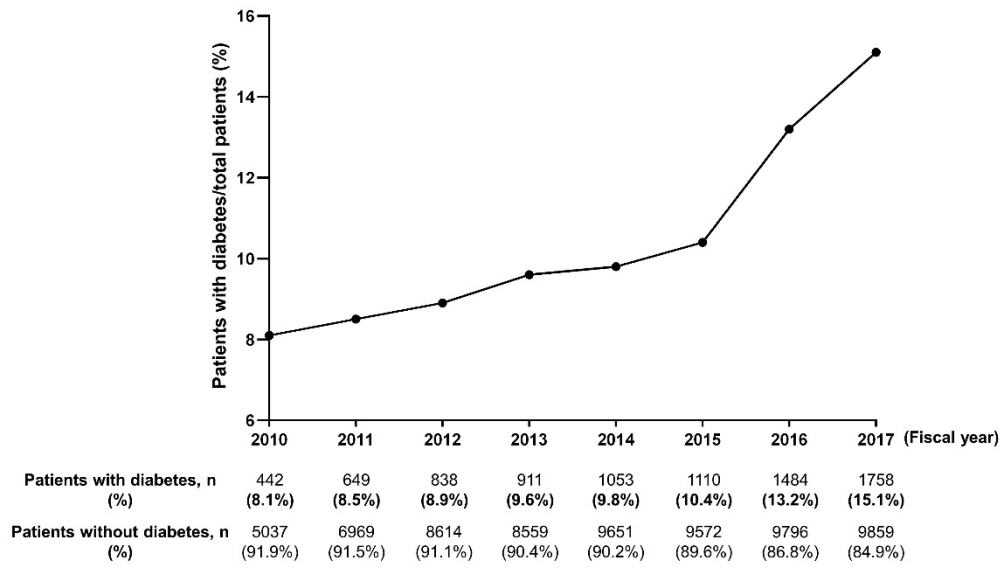
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Figure S1. Trend in the proportion of renal biopsies for patients with diabetes



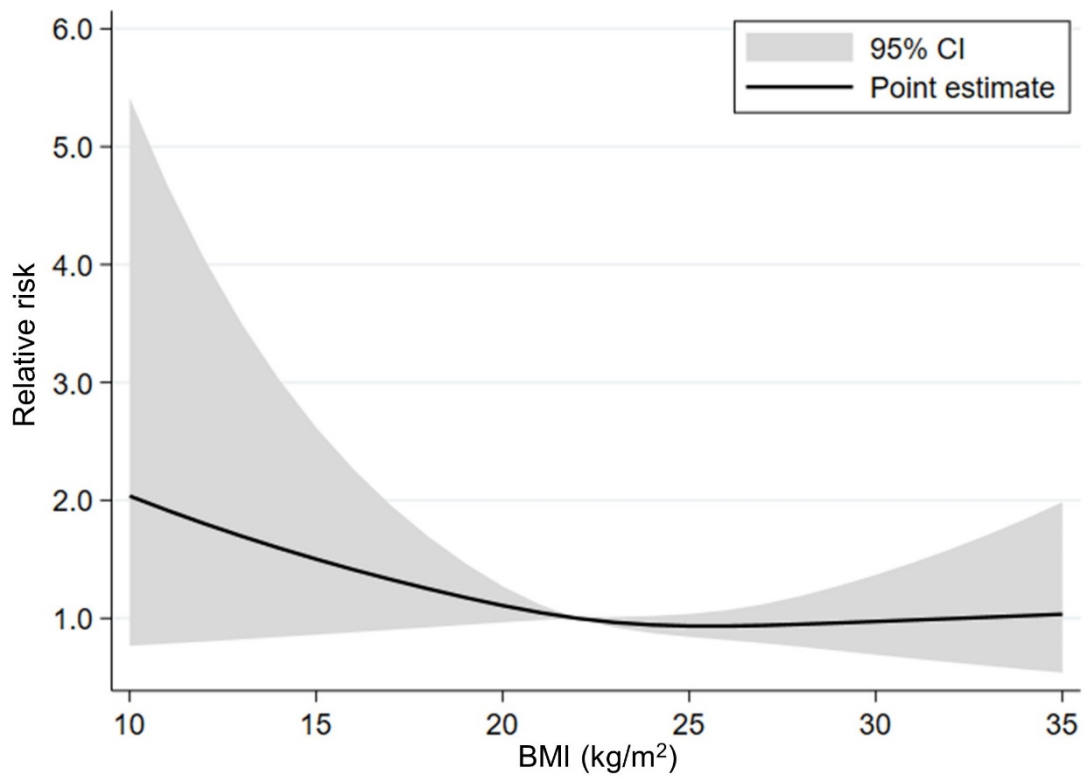
The horizontal axis denotes the fiscal year, and the vertical axis denotes the proportion of renal biopsies that were performed for patients with diabetes in each year.

Table S1. Multivariable regression analysis for massive red blood cell transfusion

Generalized Estimating Equations (Group variable: hospital code)	Multivariable Analysis	
	RR (95% CI)	p-value
Diabetes mellitus	7.47 (5.25-10.63)	< 0.001
Age, years	1.03 (1.02-1.04)	< 0.001
Female, sex	1.19 (0.90-1.58)	0.22
BMI (kg/m²)	See Figure S2	
Main diagnosis		
AKI or RPGN	3.38 (2.27-5.04)	< 0.001
Nephrosis	1.22 (0.83-1.81)	0.31
Others	1 (base)	
Presence of CKD	2.25 (1.62-3.12)	< 0.001
Hospital volume		
1–24/year	1 (base)	
25–44/year	0.75 (0.52-1.11)	0.15
≥ 45/year	0.75 (0.50-1.13)	0.17
Academic hospital	1.75 (1.21-2.53)	0.003
Fiscal year period		0.001
2010–2015	1 (base)	
2016–2017	0.57 (0.41-0.81)	
ADL		< 0.001
Dependent	3.47 (2.35-5.13)	
Independent	1 (base)	
Corticosteroid use	1.59 (0.997-2.55)	0.052
Immunosuppressant use	0.48 (0.065-3.48)	0.47
Antithrombotic use	1.57 (0.83-3.00)	0.17

Abbreviations: RR, relative risk; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Figure S2. Cubic spline estimation of body mass index and relative risk of massive red blood cell transfusion



The horizontal axis denotes the body mass index (BMI, kg/m²), and the vertical axis denotes the relative risk of massive red blood cell transfusion.

Table S2. Baseline characteristics of patients with and without diabetes (when patients with anemia defined using ICD-10 codes on admission were excluded)

	Total patients (n = 73632)	Patients without diabetes (n = 65758)	Patients with diabetes (n = 7874)	p-value
Age, years	50 (34–65)	48 (33–63)	65 (55–72)	< 0.001
Male, n (%)	38683 (52.5%)	33866 (51.5%)	4817 (61.2%)	< 0.001
BMI (kg/m²)				< 0.001
BMI < 18.5, n (%)	6093 (8.3%)	5694 (8.7%)	399 (5.1%)	
18.5 ≤ BMI < 23.0, n (%)	31561 (42.9%)	28954 (44.0%)	2607 (33.1%)	
23.0 ≤ BMI < 25.0, n (%)	13875 (18.8%)	12257 (18.6%)	1618 (20.5%)	
25.0 ≤ BMI < 30.0, n (%)	17130 (23.3%)	14709 (22.4%)	2421 (30.7%)	
BMI ≥ 30.0, n (%)	4973 (6.8%)	4144 (6.3%)	829 (10.5%)	
Main diagnosis				< 0.001
AKI or RPGN, n (%)	3185 (4.3%)	2241 (3.4%)	944 (12.0%)	
Nephrosis, n (%)	13301 (18.1%)	10501 (16.0%)	2800 (35.6%)	
Others, n (%)	57146 (77.6%)	53016 (80.6%)	4130 (52.5%)	
Presence of CKD, n (%)	8345 (11.3%)	6886 (10.5%)	1459 (18.5%)	< 0.001
Hospital volume per year				0.38
1–24 cases, n (%)	27833 (37.8%)	24867 (37.8%)	2966 (37.7%)	
25–44 cases, n (%)	24324 (33.0%)	21672 (33.0%)	2652 (33.7%)	
≥ 45 cases, n (%)	21475 (29.2%)	19219 (29.2%)	2256 (28.7%)	
Academic hospital, n (%)	19095 (25.9%)	17014 (25.9%)	2081 (26.4%)	0.29
Fiscal year period				< 0.001
2010–2015, n (%)	51628 (70.1%)	46845 (71.2%)	4783 (60.7%)	
2016–2017, n (%)	22004 (29.9%)	18913 (28.8%)	3091 (39.3%)	
ADL				< 0.001
Independent	72550 (98.5%)	64987 (98.8%)	7563 (96.1%)	
Dependent	1082 (1.5%)	771 (1.2%)	311 (3.9%)	
Corticosteroid use, n (%)	2250 (3.1%)	1666 (2.5%)	584 (7.4%)	< 0.001
Immunosuppressant use, n (%)	760 (1.0%)	654 (1.0%)	106 (1.3%)	0.004
Antithrombotic use, n (%)	985 (1.3%)	687 (1.0%)	298 (3.8%)	< 0.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Table S3. Major bleeding complications of patients with and without diabetes (when patients with anemia defined using ICD-10 codes on admission were excluded)

	Total patients (n = 73632)	Patients without diabetes (n = 65758)	Patients with diabetes (n = 7874)	p-value
Major bleeding complications, n (%)	499 (0.7%)	304 (0.5%)	195 (2.5%)	< 0.001
RBC transfusion, n (%)	448 (0.6%)	264 (0.4%)	184 (2.3%)	< 0.001
Invasive hemostasis, n (%)	93 (0.1%)	68 (0.1%)	25 (0.3%)	< 0.001
Massive RBC transfusion, n (%)	162 (0.2%)	51 (0.1%)	111 (1.4%)	< 0.001

Abbreviation: RBC, red blood cell.

Footnote: Some patients have received both RBC transfusion and invasive hemostasis.

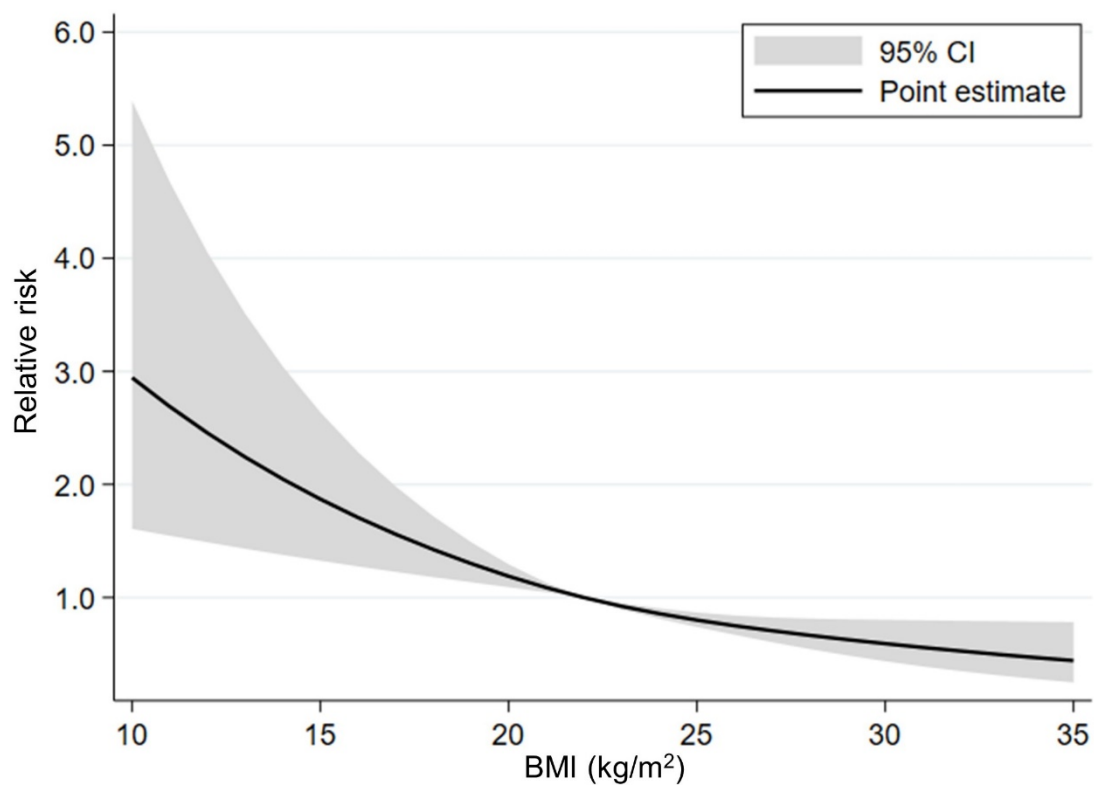
Thus, they are not mutually exclusive.

Table S4. Multivariable regression analysis for major bleeding complications (when patients with anemia defined using *ICD-10* codes on admission were excluded)

Generalized Estimating Equations (Group variable: hospital code)	Multivariable Analysis	
	RR (95% CI)	p-value
Diabetes mellitus	2.63 (2.12-3.28)	< 0.001
Age, years	1.03 (1.03-1.04)	< 0.001
Female, sex	1.48 (1.23-1.79)	< 0.001
BMI (kg/m²)	See Figure S3	
Main diagnosis		
AKI or RPGN	3.96 (3.09-5.08)	< 0.001
Nephrosis	0.87 (0.66-1.15)	0.33
Others	1 (base)	
Presence of CKD	2.59 (2.11-3.17)	< 0.001
Hospital volume		
1–24/year	1 (base)	
25–44/year	0.88 (0.70-1.11)	0.29
≥ 45/year	0.91 (0.70-1.17)	0.44
Academic hospital	1.47 (1.18-1.84)	0.001
Fiscal year period		0.13
2010–2015	1 (base)	
2016–2017	0.86 (0.70-1.05)	
ADL		< 0.001
Dependent	2.62 (1.95-3.54)	
Independent	1 (base)	
Corticosteroid use	1.37 (0.97-1.93)	0.075
Immunosuppressant use	1.09 (0.42-2.83)	0.86
Antithrombotic use	1.27 (0.80-2.04)	0.31

Abbreviations: RR, relative risk; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Figure S3. Cubic spline estimation of body mass index and relative risk of major bleeding complications (when patients with anemia defined using *ICD-10* codes on admission were excluded)



The horizontal axis denotes the body mass index (BMI, kg/m²), and the vertical axis denotes the relative risk of major bleeding complications.

Table S5. Baseline characteristics of patients with and without diabetes (when diabetes was defined using ICD-10 codes)

	Total patients (n = 76302)	Patients without diabetes (n = 65101)	Patients with diabetes (n = 11201)	p-value
Age, years	50 (35–65)	47 (33–63)	63 (50–71)	< 0.001
Male, n (%)	39555 (51.8%)	32557 (50.0%)	6998 (62.5%)	< 0.001
BMI (kg/m²)				< 0.001
BMI < 18.5, n (%)	6409 (8.4%)	5896 (9.1%)	513 (4.6%)	
18.5 ≤ BMI < 23.0, n (%)	32871 (43.1%)	29316 (45.0%)	3555 (31.7%)	
23.0 ≤ BMI < 25.0, n (%)	14330 (18.8%)	12032 (18.5%)	2298 (20.5%)	
25.0 ≤ BMI < 30.0, n (%)	17608 (23.1%)	14056 (21.6%)	3552 (31.7%)	
BMI ≥ 30.0, n (%)	5084 (6.7%)	3801 (5.8%)	1283 (11.5%)	
Main diagnosis				< 0.001
AKI or RPGN, n (%)	3425 (4.5%)	2544 (3.9%)	881 (7.9%)	
Nephrosis, n (%)	13708 (18.0%)	10606 (16.3%)	3102 (27.7%)	
Others, n (%)	59169 (77.5%)	51951 (79.8%)	7218 (64.4%)	
Presence of CKD, n (%)	8837 (11.6%)	6811 (10.5%)	2026 (18.1%)	< 0.001
Hospital volume per year				0.03
1–24 cases, n (%)	28808 (37.8%)	24694 (37.9%)	4114 (36.7%)	
25–44 cases, n (%)	25197 (33.0%)	21478 (33.0%)	3719 (33.2%)	
≥ 45 cases, n (%)	22297 (29.2%)	18929 (29.1%)	3368 (30.1%)	
Academic hospital, n (%)	19831 (26.0%)	17178 (26.4%)	2653 (23.7%)	< 0.001
Fiscal year period				< 0.001
2010–2015, n (%)	53405 (70.0%)	46013 (70.7%)	7392 (66.0%)	
2016–2017, n (%)	22897 (30.0%)	19088 (29.3%)	3809 (34.0%)	
ADL				< 0.001
Independent	75145 (98.5%)	64230 (98.7%)	10915 (97.4%)	
Dependent	1157 (1.5%)	871 (1.3%)	286 (2.6%)	
Corticosteroid use, n (%)	2365 (3.1%)	1866 (2.9%)	499 (4.5%)	< 0.001
Immunosuppressant use, n (%)	802 (1.1%)	694 (1.1%)	108 (1.0%)	0.33
Antithrombotic use, n (%)	1016 (1.3%)	752 (1.2%)	264 (2.4%)	< 0.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

**Table S6. Major bleeding complications of patients with and without diabetes
(when diabetes was defined using ICD-10 codes)**

	Total patients (n = 76302)	Patients without diabetes (n = 65101)	Patients with diabetes (n = 11201)	p-value
Major bleeding complications, n (%)	678 (0.9%)	495 (0.8%)	183 (1.6%)	< 0.001
RBC transfusion, n (%)	622 (0.8%)	447 (0.7%)	175 (1.6%)	< 0.001
Invasive hemostasis, n (%)	109 (0.1%)	90 (0.1%)	19 (0.2%)	< 0.001
Massive RBC transfusion, n (%)	201 (0.3%)	145 (0.2%)	56 (0.5%)	< 0.001

Abbreviation: RBC, red blood cell.

Footnote: Some patients have received both RBC transfusion and invasive hemostasis.

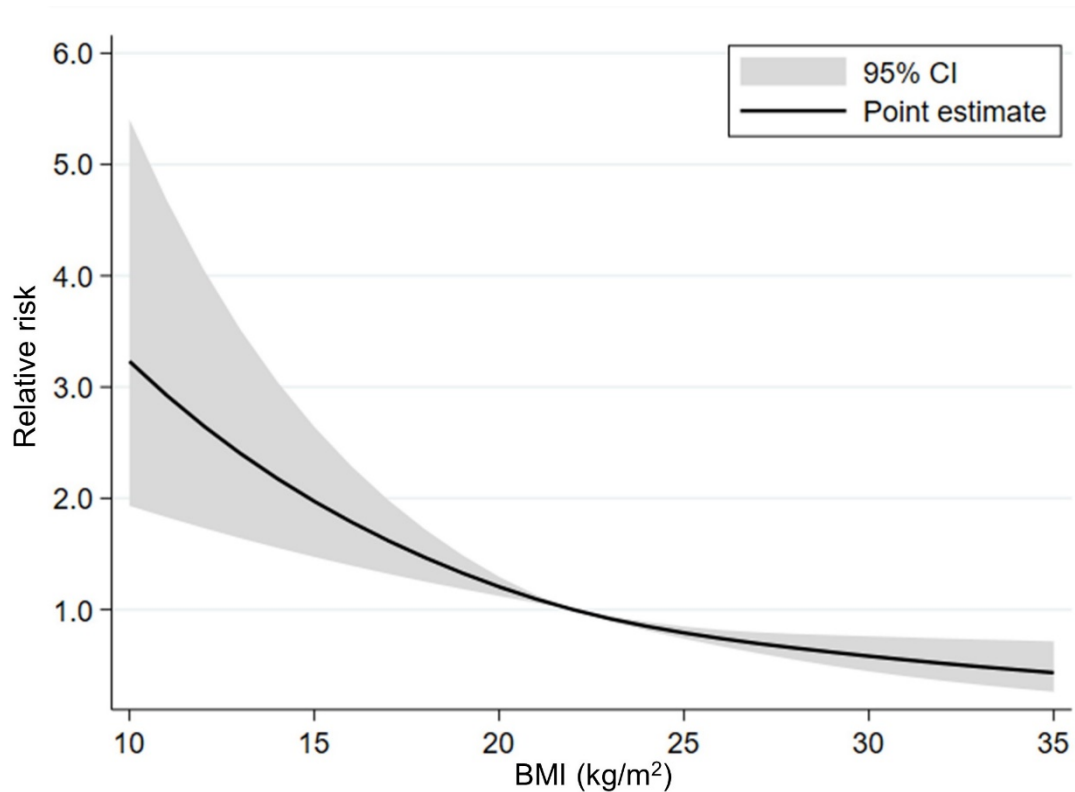
Thus, they are not mutually exclusive.

Table S7. Multivariable regression analysis for major bleeding complications (when diabetes was defined using ICD-10 codes)

Generalized Estimating Equations (Group variable: hospital code)	Multivariable Analysis	
	RR (95% CI)	p-value
Diabetes mellitus	1.34 (1.11-1.62)	0.002
Age, years	1.04 (1.03-1.05)	< 0.001
Female, sex	1.48 (1.25-1.75)	< 0.001
BMI (kg/m²)	See Figure S4	
Main diagnosis		
AKI or RPGN	4.57 (3.79-5.52)	< 0.001
Nephrosis	0.97 (0.76-1.23)	0.79
Others	1 (base)	
Presence of CKD	2.62 (2.21-3.11)	< 0.001
Hospital volume		
1–24/year	1 (base)	
25–44/year	0.87 (0.71-1.05)	0.15
≥ 45/year	0.87 (0.72-1.07)	0.19
Academic hospital	1.46 (1.20-1.77)	< 0.001
Fiscal year period		
2010–2015	1 (base)	
2016–2017	0.92 (0.78-1.09)	
ADL		< 0.001
Dependent	2.75 (2.14-3.54)	
Independent	1 (base)	
Corticosteroid use	1.65 (1.23-2.22)	0.001
Immunosuppressant use	1.11 (0.51-2.44)	0.79
Antithrombotic use	1.25 (0.81-1.91)	0.31

Abbreviations: RR, relative risk; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Figure S4. Cubic spline estimation of body mass index and relative risk of major bleeding complications (when diabetes was defined using *ICD-10* codes)



The horizontal axis denotes the body mass index (BMI, kg/m²), and the vertical axis denotes the relative risk of major bleeding complications.

Table S8. Baseline characteristics of the subgroups of patients with diabetes

	Single-agent (n = 2562)	Multi-agent or Insulin (n = 5683)	p-value
Age, years	64 (53-72)	65 (55-72)	< 0.001
Male, n (%)	1545 (60.3%)	3449 (60.7%)	0.74
BMI (kg/m²)			0.40
BMI < 18.5, n (%)	130 (5.1%)	299 (5.3%)	
18.5 ≤ BMI < 23.0, n (%)	824 (32.2%)	1926 (33.9%)	
23.0 ≤ BMI < 25.0, n (%)	552 (21.5%)	1135 (20.0%)	
25.0 ≤ BMI < 30.0, n (%)	795 (31.0%)	1734 (30.5%)	
BMI ≥ 30.0, n (%)	261 (10.2%)	589 (10.4%)	
Main diagnosis			< 0.001
AKI or RPGN, n (%)	210 (8.2%)	822 (14.5%)	
Nephrosis, n (%)	865 (33.8%)	2027 (35.7%)	
Others, n (%)	1487 (58.0%)	2834 (49.9%)	
Presence of CKD, n (%)	532 (20.8%)	1027 (18.1%)	0.004
Hospital volume per year			0.002
1–24 cases, n (%)	904 (35.3%)	2190 (38.5%)	
25–44 cases, n (%)	862 (33.6%)	1923 (33.8%)	
≥ 45 cases, n (%)	796 (31.1%)	1570 (27.6%)	
Academic hospital, n (%)	740 (28.9%)	1434 (25.2%)	< 0.001
Fiscal year period			0.002
2010–2015, n (%)	1490 (58.2%)	3513 (61.8%)	
2016–2017, n (%)	1072 (41.8%)	2170 (38.2%)	
ADL			< 0.001
Independent	2498 (97.5%)	5409 (95.2%)	
Dependent	64 (2.5%)	274 (4.8%)	
Corticosteroid use, n (%)	143 (5.6%)	478 (8.4%)	< 0.001
Immunosuppressant use, n (%)	44 (1.7%)	67 (1.2%)	0.05
Antithrombotic use, n (%)	76 (3.0%)	232 (4.1%)	0.013

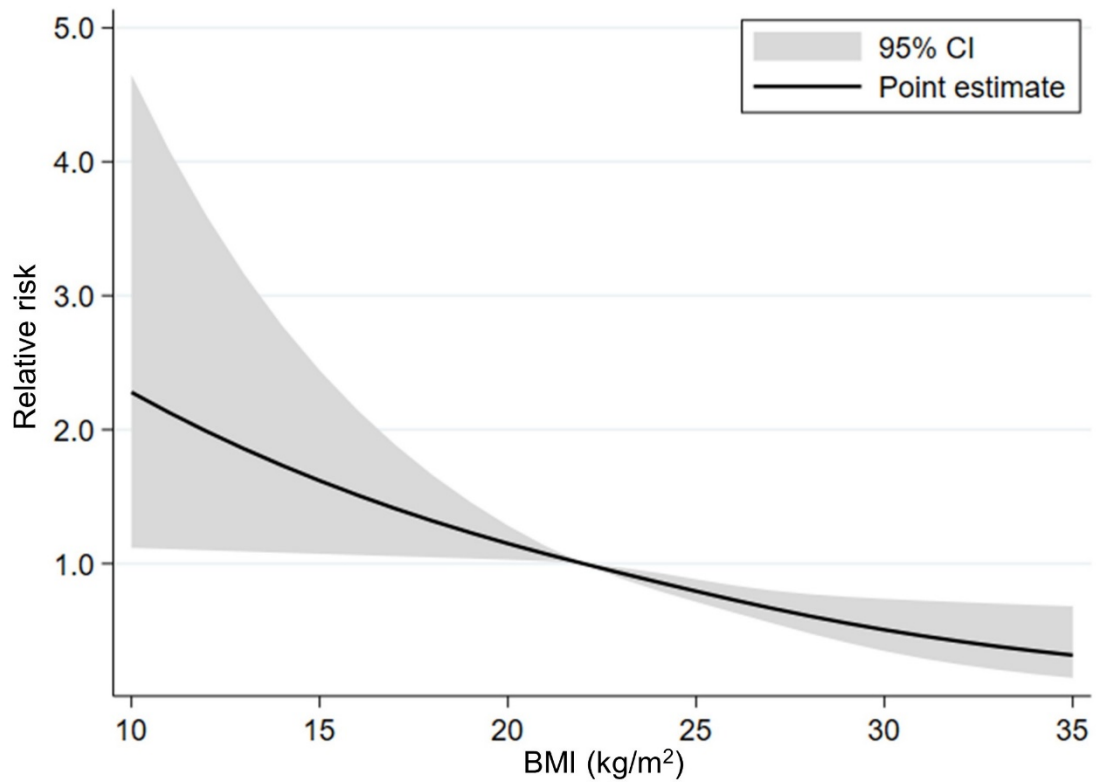
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Table S9. Multivariable regression analysis for major bleeding complications in the subgroup of patients with diabetes

Generalized Estimating Equations (Group variable: hospital code)	Multivariable Analysis	
	RR (95% CI)	p-value
Treatment regimen for diabetes		0.002
Single-agent	1 (base)	
Multi-agent or insulin use	1.57 (1.18-2.10)	
Age, years	1.03 (1.02-1.04)	< 0.001
Female, sex	1.53 (1.20-1.94)	0.001
BMI (kg/m²)	See Figure S5	
Main diagnosis		
AKI or RPGN	2.20 (1.72-2.82)	< 0.001
Nephrosis	0.55 (0.39-0.77)	0.001
Others	1 (base)	
Presence of CKD	2.09 (1.61-2.70)	< 0.001
Hospital volume		
1–24/year	1 (base)	
25–44/year	1.00 (0.75-1.33)	0.99
≥ 45/year	0.71 (0.51-1.00)	0.047
Academic hospital	1.23 (0.91-1.67)	0.18
Fiscal year period		0.23
2010–2015	1 (base)	
2016–2017	0.85 (0.65-1.11)	
ADL		< 0.001
Dependent	2.14 (1.53-3.00)	
Independent	1 (base)	
Corticosteroid use	1.36 (0.95-1.96)	0.096
Immunosuppressant use	1.04 (0.33-3.25)	0.95
Antithrombotic use	1.25 (0.75-2.10)	0.39

Abbreviations: RR, relative risk; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); AKI, acute kidney injury; RPGN, rapidly progressive glomerulonephritis; ADL, activities of daily living.

Figure S5. Cubic spline estimation of body mass index and relative risk of major bleeding complications in patients with diabetes



The horizontal axis denotes the body mass index (BMI, kg/m²), and the vertical axis denotes the relative risk of major bleeding complications in patients with diabetes.