Appendix

Supplementary Table 1.

Comparison of baseline characteristics according to presence or absence of heart failure requiring hospitalisation

	HF (n=880)	Non-HF (n=6,728)	P-value
Age, y	70±10	67±10	<0.001
Male, n (%)	603 (68.5)	4863 (72.3)	0.021
BMI, kg/m^2	25.0±4.3	25.3±3.9	0.047
LVEF, %	52.0±15.3	60.9±13.0	<0.001
Current smoker, %	174 (19.7)	1461 (21.7)	0.19
Ex-smoker, %	262 (29.8)	1864 (27.7)	0.2
Never smoker, %	444 (50.5)	3,403 (50.6)	0.94
WBC count, cells/µL	7015±2231	6663±2038	<0.001
History of hypertension, n (%)	766 (87.1)	5515 (82.0)	<0.001
History of stroke, n (%)	185 (21.0)	1092 (16.2)	<0.001
History of acute myocardial infarction, n (%)	359 (40.8)	2311 (34.4)	<0.001
History of malignancy, n (%)	54 (6.1)	306 (4.6)	0.044
History of PCI, n (%)	384 (43.6)	3029 (45.0)	0.44
History of CABG, n (%)	159 (18.1)	699 (10.4)	<0.001
Duration of diabetes, median (IQR), y	11.7 (3-17)	10.5 (2-16)	0.001
Triglycerides, median (IQR), mg/dL	125 (89-194)	132 (91-193)	0.085
HDL cholesterol, mg/dL	45±13	47±13	<0.001

LDL cholesterol, mg/dL	107±35	103±33	0.012
Systolic blood pressure, mmHg	134±22	134±20	0.64
Haemoglobin A1c, %	7.5±1.5	7.2±1.3	<0.001
eGFR, L/min/1.73^2	48.1±26.7	60.7±26.2	<0.001
End-stage renal failure on maintenance Dialysis, n (%)	133 (15.1)	641 (9.53)	<0.001
Statin, n (%)	457 (51.9)	4393 (65.3)	<0.001
Insulin, n (%)	218 (24.8)	1292 (19.2)	<0.001
Metformin, n (%)	145 (16.5)	1106 (16.4)	0.98
Aspirin, n (%)	753 (85.6)	5963 (88.6)	0.009
Beta blocker, n (%)	378 (43.0)	2540 (37.8)	0.003
ARB, n (%)	414 (47.1)	2915 (43.3)	0.037
ACEi, n (%)	252 (28.6)	1496 (22.2)	<0.001
Diuretics, n (%)	499 (56.7)	1611 (24.0)	<0.001

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HF, heart failure; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; WBC, white blood cell

Supplementary Table 2. Hazard ratio for heart failure requiring hospitalisation in the sub-group excluding patients who showed baseline WBC more than 10,600 (mean+2SD) adjusted for confounders in a multivariate Cox-regression model (n=7,277)

Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
WBC 500	1.04	1.02	1.07	<0.001
Age (y) ≥65	1.45	1.21	1.73	<0.001
Male	0.79	0.66	0.94	0.009
BMI ≤25	1.20	1.03	1.40	0.019
LVEF ≥40	0.31	0.26	0.38	<0.001
eGFR ≥60	0.47	0.40	0.56	<0.001
End-stage renal failure on maintenance Dialysis	1.39	1.09	1.78	0.008
Current Smoker	1.11	0.90	1.38	0.33
Past Smoker	1.21	1.01	1.45	0.043
History of Malignancy	1.25	0.92	1.70	0.15
History of Stroke	1.41	1.18	1.69	<0.001
History of AMI	1.19	1.00	1.41	0.06
History of PCI	0.91	0.77	1.08	0.28
History of CABG	1.51	1.24	1.84	<0.001
ACEi	1.42	1.19	1.70	<0.001
ARB	1.21	1.03	1.42	0.021
βblocker	1.24	1.06	1.45	0.006

Biganide	**1.12**	**0.91**	**1.38**	**0.27**
Aspirin	**0.80**	**0.65**	**0.99**	**0.044**
Statin	**0.70**	**0.60**	**0.81**	**<0.001**
Haemoglobin A1c ≥7.0	**1.34**	**1.15**	**1.56**	**<0.001**
LDL-cholesterol ≥100	**0.93**	**0.80**	**1.08**	**0.34**
SBP ≥140	**1.03**	**0.88**	**1.20**	**0.72**

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HF, heart failure; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; WBC, white blood cell

Supplementary Table 3. **Cochran-Armitage trend test**

Event	P-value for trend
HF requiring hospitalisation	<0.0001
Death	<0.0001
AMI	0.008
Stroke	0.65
3 points MACE (Death/AMI/Stroke)	<0.0001
4 points MACE (Death/AMI/ Stroke /HF)	<0.0001

MACE, major adverse cardiovascular event; HF, heart failure; AMI, acute myocardial infarction

Supplementary Table 4. Hazard ratio for heart failure requiring hospitalisation in the sub-group excluding patients on maintenance dialysis (n=6,834), adjusted for confounders in a multivariate Cox-regression model, compared to the lowest quartile white blood cell count of <5,300 cells/μL

Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
5,300 ≤WBC <6,400	1.26	0.99	1.60	0.07
6,400 ≤WBC <7,700	1.40	1.10	1.78	0.006
7,700 ≤WBC	1.62	1.28	2.05	<0.001
Age ≥65 years	1.47	1.22	1.79	<0.001
Male	0.81	0.67	0.98	0.027
BMI ≤25	1.20	1.03	1.41	0.020
EF ≥40	0.30	0.25	0.37	<0.001
eGFR ≥60	0.47	0.40	0.55	<0.001
Current Smoker	1.14	0.91	1.41	0.25
Past Smoker	1.19	0.98	1.44	0.079
History of Malignancy	1.22	0.89	1.66	0.21
History of Stroke	1.30	1.07	1.58	0.007
History of AMI	1.08	0.90	1.29	0.41
History of PCI	0.94	0.79	1.12	0.48
History of CABG	1.66	1.36	2.04	<0.001
ACEi	1.41	1.17	1.70	<0.001
ARB	1.31	1.11	1.56	0.0018
βblocker	1.32	1.13	1.55	<0.001

Biguanide	1.17	0.96	1.43	0.11
Aspirin	0.76	0.61	0.95	0.015
Statin	0.67	0.57	0.78	<0.001
HbA1c ≥7.0	1.30	1.11	1.53	0.0014
LDL ≥100	0.95	0.81	1.11	0.50
SBP ≥140	0.96	0.82	1.14	0.66

ACEi, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin-II receptor blocker; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HF, heart failure; HR, hazard ratio; HbA1c, glycated haemoglobin; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; WBC, white blood cell

Supplementary Table 5a. Hazard ratio for acute myocardial infarction, adjusted for confounders in a multivariate Cox-regression model, compared to the lowest quartile white blood cell count of <5300 cells/μL

Variables	HR	95% Confidence Interval		P value
		Lower	Upper	
5300≤WBC<6400	1.35	0.87	2.07	0.18
6400≤WBC<7700	1.39	0.90	2.16	0.14
7700≤WBC	1.59	1.04	2.44	0.034

WBC, white blood cell; HR, hazard ratio

Supplementary Table 5b. Hazard ratio for stroke, adjusted for confounders in a multivariate Cox-regression model, compared to the lowest quartile white blood cell count of <5,300 cells/μL

Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
5,300 ≤WBC <6,400	1.08	0.79	1.47	0.65
6,400 ≤WBC <7,700	1	0.72	1.38	0.98
7,700 ≤WBC	1.09	0.79	1.49	0.61

WBC, white blood cell; HR, hazard ratio

Supplementary Table 5c. Hazard ratio for all-cause death, adjusted for confounders in a multivariate Cox-regression model, compared to the lowest quartile white blood cell count of <5300 cells/µL

| Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
5,300 ≤WBC <6,400	0.98	0.79	1.22	0.87
6,400 ≤WBC <7,700	1.17	0.95	1.45	0.14
7,700 ≤WBC	1.62	1.33	1.98	<0.001

WBC, white blood cell; HR, hazard ratio

Supplementary Table 5d. Hazard ratio for the 3-point major adverse cardiovascular events (acute myocardial infarction, stroke, death), adjusted for confounders in a multivariate Cox-regression model, and compared to the lowest quartile white blood cell count of <5,300 cells/µL

Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
5,300 ≤WBC <6,400	1.03	0.86	1.23	0.74
6,400 ≤WBC <7,700	1.14	0.96	1.36	0.13
7,700 ≤WBC	1.49	1.26	1.76	<0.001

WBC, white blood cell; HR, hazard ratio

Supplementary Table 5e. Hazard ratio for the 4-point major adverse cardiovascular events (acute myocardial infarction, stroke, death, heart failure event requiring hospitalisation), adjusted for confounders in a multivariate Cox-regression model, and compared to the lowest quartile white blood cell count of <5,300 cells/µL

| Variables	HR	95% Confidence Interval		P-value
		Lower	Upper	
5,300 ≤WBC <6,400	1.11	0.95	1.29	0.17
6,400 ≤WBC <7,700	1.22	1.04	1.42	0.012
7,700 ≤WBC	1.6	1.38	1.85	<0.001

WBC, white blood cell; HR, hazard ratio
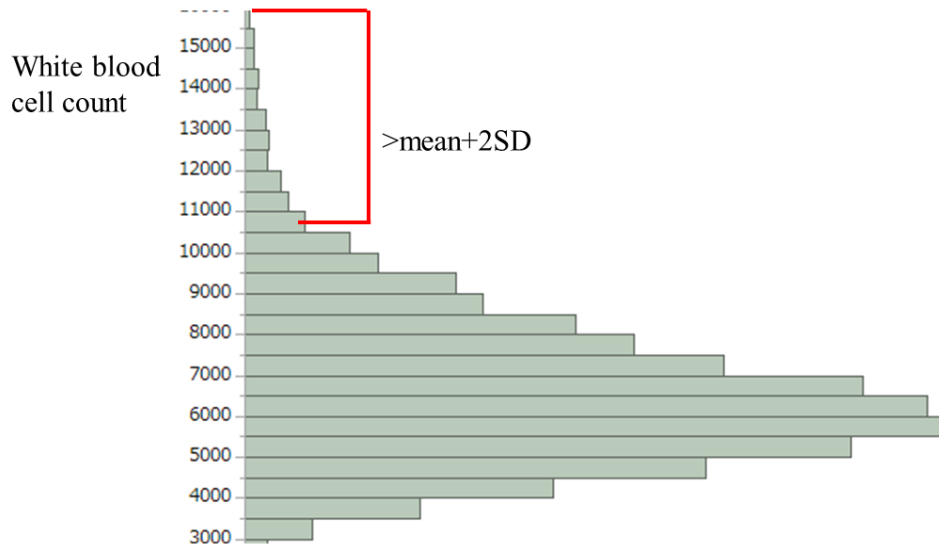
Graphical distribution of the baseline white blood cell (WBC) count does not show normal distribution due to outliers (WBC>mean+2SD=10,600) according to Lilliefors test (P<0.01).

Supplementary Figure 2

HF event requiring hospitalisation in the sub-group excluding patients on maintenance dialysis
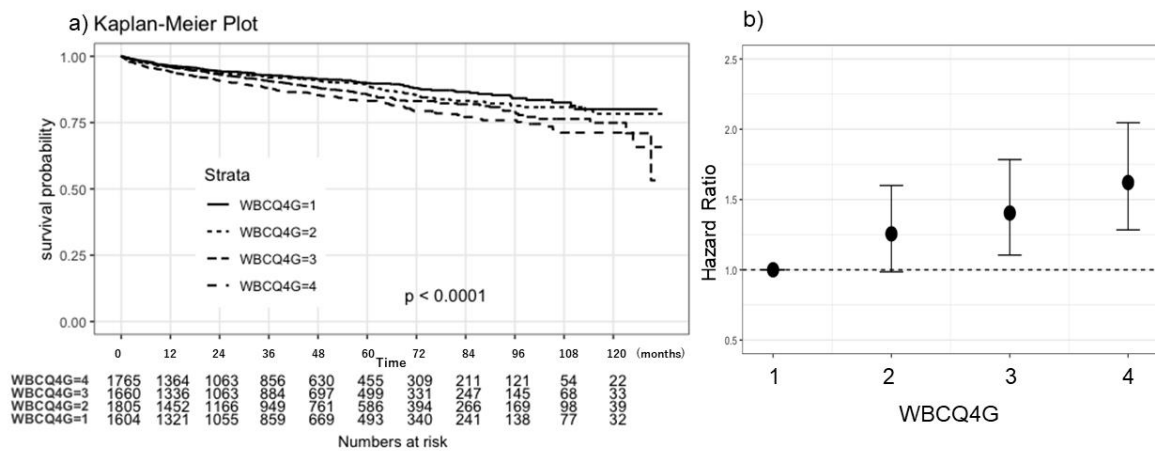
(a) Kaplan–Meier curves for heart failure hospitalisation event-free survival rate and relative hazard ratio stratified by the baseline white blood cell (WBC) count in the subgroup excluding patients on maintenance dialysis (n=6,834). Patients with the highest in the fourth WBC quartile (WBC ≥7,700 cells/µL) had a significantly lower cumulative survival rate without heart failure hospitalisation events, compared to patients with the lowest in the fourth WBC quartile (WBC <5,300 cells/µL, P<0.0001). Relative hazard ratio of heart failure hospitalisation event during the follow-up period adjusted for confounders in a multivariate Cox-regression model, compared to the lowest quartile WBC count of <5,300 cells/µL. WBCQG=white blood cell quartile group. WBCQG1=(WBC counts<5,300 cells/µL), WBCQG2=(5,300≤WBC<6,400), WBCQG3=(6,400≤WBC<7,700), WBCQG4=(≥7,700 cells/µL).

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