Risk Factors for Incident Heart Failure in Age and Sex Specific Strata: a Population-Based cohort using linked Electronic Health Records

Alicia Uijl[1,2], Stefan Koudstaal[2,3], Kenan Direk[2], Spiros Denaxas[2], Rolf H.H. Groenwold[1, 2], A. Banerjee[2], Arno W. Hoes[1,2], Harry Hemingway[2,3], Folkert W. Asselbergs[2, 4, 5]

1. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, the Netherlands

2. Farr Institute of Health Informatics Research, Institute of Health Informatics, University College London, United Kingdom

3. The National Institute for Health Research, Biomedical Research Centre, University College London Hospitals NHS Foundation Trust

4. Department of Cardiology, Division Heart & Lungs, University Medical Center Utrecht, Utrecht University, the Netherlands

5. Institute of Cardiovascular Science, Faculty of Population Health Sciences, University College London, United Kingdom

Tables

Table 1 – Baseline characteristics stratified by age and heart failure status in men

	55 – 64 years		65 – 74 years		> 75 years	
	Incident HF patients	Individuals without HF	Incident HF patients	Individuals without HF	Incident HF patients	Individuals without HF
Number of patients	5,408	252,290	8,047	80,369	9,859	48,672
Demographics						
Ethnicity (% Caucasian)	96.1	95.1	96.6	95.8	98.2	97.4
Most deprived fifth (%)*	26.2	17.2	22.8	18.1	19.4	19.3
Lifestyle (%) †						
Smoking						
Current Smoking	32.4	27.9	19.7	18.8	12.5	13
Ex-smoker	31.9	29.3	38.7	36.5	39.5	38.7
Never smoked	35.7	42.8	41.6	44.7	48	48.3
Sedentary lifestyle	43.5	36.4	48.1	41.2	62.3	58.1
Clinical measures in mean (sd)						
or median [IQR] †						
Body Mass Index (kg/m2)	28.5 (5.2)	27.5 (4.5)	27.3 (4.4)	26.6 (4.0)	25.7 (4.0)	25.1 (3.9)
Total cholesterol (mmol/L)	5.4 (1.2)	5.5 (1.0)	5.2 (1.0)	5.3 (1.0)	5.1 (1.0)	5.1 (1.0)
Triglycerides (mmol /L)	1.9 (1.4)	1.8 (1.2)	1.7 (1.1)	1.7 (1.0)	1.5 (0.9)	1.5 (0.9)

SBP (mmHg)	142.0 (19.3)	138.4 (16.9)	146.7 (19.2)	145.4 (18.3)	147.9 (19.8)	146.5 (19.5)
DBP (mmHg)	83.5 (10.2)	83.2 (9.5)	81.4 (9.6)	82.0 (9.4)	79.8 (9.8)	79.6 (9.7)
Heamoglobin (g/dL)	14.7 (1.4)	14.8 (1.2)	14.2 (1.6)	14.3 (1.5)	13.5 (1.7)	13.5 (1.7)
Platelets (10^9/L)	240.7 [80.5]	243.0 [77.4]	229.3 [82.1]	231.1 [80.9]	226.8 [87.1]	230.1 [89.3]
Total WBC count (10^9 / L)	7.5 (2.4)	7.0 (2.2)	7.5 (2.6)	7.2 (2.5)	7.6 (2.8)	7.5 (2.7)
Albumin (g/L)	41.8 (3.9)	42.4 (3.6)	40.8 (3.9)	40.9 (3.9)	39.3 (4.3)	39.2 (4.4)
Creatinine (micromol/L)	94.4 [21.6]	93.0 [18.25]	100.0 [25.0]	98.0 [22.35]	104.2 [30.5]	108.3 [35.0]
Comorbidity (%) §						
Atrial fibrillation	6.5	0.9	8.8	2.4	11.1	4.6
COPD	22.4	10.2	25.4	13.8	27.7	18.1
Diabetes mellitus	5.5	1.6	5.3	2.3	3.7	2.4
Myocardial infarction	5.3	0.9	4.2	1.3	3.8	1.5
Hypertension	72.1	54.9	80.0	71.6	80.8	72.9
Obesity	42.6	26.6	24.0	17.4	13.7	10.3
Medication use (%) ¤						
Blood pressure lowering medication	37.3	15.9	48.7	26.4	59.0	34.9
Lipid regulating drugs	29.6	13.6	26.2	17.2	11.5	10.7

*assessed by index of multiple deprivation † measurement closest to and within 3 years before baseline. § denotes prior medical history of given comorbidity 3 years before baseline, ¤ prescription use 3 years before baseline. SD = Standard Deviation; LDL = Low Density Lipoprotein; HDL = High Density Lipoprotein ; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; total WBC count = total White Blood Cell count; eGFR = estimated Glomerular Filtration Rate; COPD = Chronic Obstructive Pulmonary Disease.

Table 2 - Baseline characteristics stratified by age and heart failure status in women

	55 – 64 years		65 – 74 years		> 75 years	
	Incident HF patients	Individuals without HF	Incident HF patients	Individuals without HF	Incident HF patients	Individuals without HF
Number of patients	2,878	254,486	6,624	94,568	15,171	93,315
Demographics						
Ethnicity (% Caucasian)	94.8	94.5	96.7	96.0	98.8	98.2
Most deprived fifth (%)*	29.4	16.4	25.4	18.6	22.2	19.1
Lifestyle (%) †						
Smoking						
Current Smoking	26.2	21.3	16.5	14.4	7.3	7.4
Ex-smoker	23.3	21.1	23.8	22.5	20.7	20.4
Never smoked	50.5	57.6	59.7	63.1	72.0	72.2
Sedentary lifestyle	52.8	41.7	60.3	51.3	75.5	71.3
Clinical measures in mean (sd) or median [IQR] †						
Body Mass Index (kg/m2)	29.8 (7.2)	27.3 (5.7)	28.1 (5.8)	26.8 (5.2)	25.5 (5.0)	24.7 (4.7)
Total cholesterol (mmol/L)	5.8 (1.2)	5.8 (1.1)	5.9 (1.2)	6.0 (1.1)	5.8 (1.2)	5.8 (1.2)

Triglycerides (mmol /L)	1.8 (1.1)	1.5 (0.9)	1.8 (1.0)	1.6 (0.9)	1.7 (1.1)	1.6 (0.9)
SBP (mmHg)	144.0 (19.5)	136.3 (17.5)	150.7 (19.8)	147.3 (18.7)	152.0 (20.9)	149.5 (20.8)
DBP (mmHg)	82.8 (9.8)	81.3 (9.2)	82.5 (9.7)	82.4 (9.3)	81.2 (9.9)	80.5 (10.0)
Heamoglobin (g/dL)	13.4 (1.3)	13.5 (1.1)	13.2 (1.4)	13.3 (1.3)	12.7 (1.5)	12.7 (1.5)
Platelets (10^9/L)	268.1 [85.2]	268.7 [87.1]	263.8 [91.2]	263.5 [88.5]	260.6 [96.7]	264.0 [97.4]
Total WBC count (10^9 / L)	7.3 (2.3)	6.7 (2.0)	7.3 (2.4)	7.0 (2.3)	7.5 (2.6)	7.3 (2.5)
Albumin (g/L)	41.2 (3.8)	41.9 (3.5)	40.5 (3.8)	40.7 (3.8)	39.0 (4.4)	38.9 (4.5)
Creatinine (micromol/L)	78.9 [18.8]	76.7 [16.5]	84.0 [23.2]	81.0 [20.0]	90.2 [29.3]	86.2 [25.6]
Comorbidity (%) §						
Atrial fibrillation	5.4	0.4	7.7	1.4	10.9	3.7
COPD	29.4	13.1	27.4	14.1	24.6	15.2
Diabetes mellitus	6.5	1.1	4.9	1.7	3.4	1.9
Myocardial infarction	2.6	0.2	2.6	0.5	2.3	0.9
Hypertension	82.6	47.6	81.7	72.3	70.2	75.3
Obesity	42.6	26.6	32.4	23.1	16.8	12.7
Medication use (%) ¤						
Blood pressure lowering medication	47.2	18.9	58.6	31.8	69.1	44.2
Lipid regulating drugs	22.9	9.4	21.6	14.3	8.8	8.7

*assessed by index of multiple deprivation † measurement closest to and within 3 years before baseline. § denotes prior medical history of given comorbidity 3 years before baseline, ¤ prescription use 3 years before baseline. SD = Standard Deviation; LDL = Low Density Lipoprotein; HDL = High Density Lipoprotein; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; total WBC count = total White Blood Cell count; eGFR = estimated Glomerular Filtration Rate; COPD = Chronic Obstructive Pulmonary Disease.

Table 3 – Relative contributions of risk factors for incident heart failure stratified by age in men

Age category	Risk Factors	Hazard ratio (95% CI)*	Prevalence	Relative contribution (95% CI)
55 - 64 years	COPD	1.93 (1.81; 2.06)	0.22	17.24 (15.36; 19.19)
	Atrial fibrillation	4.04 (3.62; 4.52)	0.07	16.50 (14.55; 18.62)
	Obesity	1.21 (1.11; 1.31)	0.48	9.07 (4.97; 12.84)
	Sedentary lifestyle	1.06 (0.99; 1.14)	0.44	2.54 (-0.44; 5.74)
	Diabetes	1.85 (1.64; 2.10)	0.06	4.47 (3.40; 5.70)
	Current-smokers	1.27 (1.14; 1.40)	0.32	8.04 (4.34; 11.47)
	Hypertension	1.14 (1.07; 1.22)	0.72	9.17 (4.80; 13.69)
65 - 74 years	COPD	1.81 (1.72; 1.90)	0.25	17.06 (15.46; 18.61)
	Atrial fibrillation	2.54 (2.35; 2.75)	0.09	11.93 (10.62; 13.34)
	Obesity	1.25 (1.18; 1.34)	0.24	5.66 (4.14; 7.54)
	Sedentary lifestyle	1.11 (1.05; 1.18)	0.48	5.03 (2.35; 7.97)
	Diabetes	1.73 (1.57; 1.92)	0.05	3.72 (2.93; 4.65)
	Current-smokers	1.15 (1.07; 1.24)	0.20	2.87 (1.36; 4.51)
	Hypertension	1.03 (0.97; 1.09)	0.80	n.e.
> 75 years	COPD	1.69 (1.61; 1.76)	0.28	16.05 (14.45; 17.39)
	Atrial fibrillation	2.16 (2.02; 2.30)	0.11	11.41 (10.17; 12.61)
	Obesity	1.15 (1.07; 1.25)	0.14	2.01 (0.95; 3.31)
	Sedentary lifestyle	1.09 (1.03; 1.16)	0.62	5.31 (1.83; 9.06)
	Diabetes	1.45 (1.31; 1.62)	0.04	1.64 (1.13; 2.24)
	Current-smokers	1.05 (0.95; 1.16)	0.19	n.e.
	Hypertension	1.10 (1.05; 1.15)	0.81	7.48 (3.88; 10.81)

* Independent HRs of other variables shown and further adjusted for age, haemoglobin, platelets, total white blood cell count, total cholesterol, triglycerides, albumin, creatinine, ethnicity, smoking habits, index of multiple deprivation, blood pressure lowering medication and lipid lowering drugs. N.E.= not estimable, Obesity = Body Mass Index $\geq$ 30 kg/m^2, 95% CI = 95% Confidence Interval. Hazard ratios were considered statistically significant if p-value < 0.001 (Bonferroni corrected threshold).

Table 4 – Relative contributions of risk factors for incident heart failure stratified by age in women

Age category	Risk Factors	Hazard ratio (95% CI)*	Prevalence	Relative contribution (95% CI)
55 - 64 years	COPD	2.07 (1.91; 2.25)	0.29	23.93 (21.11; 26.87)
	Atrial fibrillation	6.78 (5.73; 8.01)	0.05	23.79 (20.35; 27.46)
	Obesity	1.39 (1.25; 1.54)	0.43	14.25 (9.62; 18.70)
	Sedentary lifestyle	1.12 (1.03; 1.22)	0.52	5.96 (1.56; 10.41)
	Diabetes	2.77 (2.36; 3.24)	0.07	10.32 (8.12; 12.71)
	Current-smokers	1.33 (1.18; 1.49)	0.26	7.96 (4.50; 11.38)
	Hypertension	1.09 (1.00; 1.19)	0.83	n.e.
65 - 74 years	COPD	1.89 (1.79; 2.00)	0.27	19.61 (17.79; 21.51)
	Atrial fibrillation	3.49 (3.18; 3.83)	0.08	16.09 (14.37; 17.89)
	Obesity	1.25 (1.17; 1.34)	0.32	7.49 (5.22; 9.92)
	Sedentary lifestyle	1.10 (1.02; 1.18)	0.60	5.69 (1.19; 9.79)
	Diabetes	1.91 (1.70; 2.15)	0.05	4.27 (3.32; 5.02)
	Current-smokers	1.21 (1.11; 1.32)	0.24	3.35 (1.78; 5.02)
	Hypertension	0.98 (0.92; 1.04)	0.82	n.e.
> 75 years	COPD	1.65 (1.59; 1.71)	0.25	13.79 (12.67; 14.87)
	Atrial fibrillation	2.69 (2.55; 2.84)	0.11	15.56 (14.45; 16.71)
	Obesity	1.14 (1.08; 1.20)	0.17	2.30 (1.33; 3.25)
	Sedentary lifestyle	1.09 (1.02; 1.16)	0.76	6.36 (1.49; 10.78)
	Diabetes	1.70 (1.56; 1.86)	0.03	2.32 (1.87; 2.84)
	Current-smokers	1.08 (0.99; 1.19)	0.07	n.e.
	Hypertension	1.02 (0.99; 1.07)	0.70	n.e.

* Independent HRs of other variables shown and further adjusted for age, haemoglobin, platelets, total white blood cell count, total cholesterol, triglycerides, albumin, creatinine, ethnicity, smoking habits, index of multiple deprivation, blood pressure lowering medication and lipid lowering drugs. N.E.= not estimable, Obesity = Body Mass Index $\geq$ 30 kg/m^2, 95% CI = 95% Confidence Interval. Hazard ratios were considered statistically significant if p-value < 0.001 (Bonferroni corrected threshold).