

Table 1: Characteristics of patients by presence or absence of heart failure and classified by right atrial pressure measured using near-infrared spectroscopy

Variable	Missing values	Controls	HF	P-value	HF and	HF and	HF and	P-value
		(n = 49)	(n = 243)		RAP ≤5 (n = 80)	RAP 6–9 (n = 88)	RAP ≥10 (n = 75)	
RAP by NIRS, mmHg	0	4 (3–8)	7 (4–11)	<0.001	4 (2–4)	7 (6–8)	12 (11–14)	NA
RAP by NIRS range, mmHg	0	1–13	1–20	NA	NA	NA	NA	NA
Demographics								
Age, years	0	72 (8)	71 (10)	0.53	69 (10)	72 (10)	72 (10)	0.033
Men, no. (%)	0	24 (49)	155 (64)	0.052	54 (68)	55 (63)	46 (61)	0.69
NYHA class I	0	41 (84)	70 (29)	<0.001	30 (37)	24 (28)	16 (21)	0.016
NYHA class II		7 (14)	112 (46)		40 (50)	39 (44)	33 (44)	
NYHA class III		1 (2)	61 (25)		10 (13)	25 (28)	26 (35)	
IHD, no. (%)	0	8 (16)	142 (58)	<0.001	43 (54)	52 (59)	47 (63)	0.52
DM, no. (%)	0	41 (84)	100 (41)	<0.001	29 (36)	42 (48)	29 (39)	0.27
Hypertension, no. (%)	0	34 (69)	108 (44)	0.001	30 (37)	43 (49)	35 (47)	0.30
Atrial fibrillation, no. (%)	0	0 (0)	69 (28)	<0.001	12 (15)	25 (28)	32 (43)	0.001
COPD, no. (%)	0	3 (6)	13 (5)	0.83	1 (1)	7 (8)	5 (7)	0.12
SBP, mmHg	0	144 (18)	127 (23)	<0.001	125 (21)	129 (26)	127 (22)	0.55
Heart rate, b.p.m.	0	76 (15)	68 (14)	0.001	68 (12)	69 (15)	67 (14)	0.74
BMI, kg/m ²	0	31 (6)	30 (6)	0.23	31 (6)	30 (7)	28 (5)	0.10
BSA, m ²	0	1.9 (0.3)	1.9 (0.2)	0.32	2.0 (0.2)	1.9 (0.2)	1.9 (0.2)	0.25
Congestion ≥3, no. (%)	0	2 (4)	25 (10)	0.17	1 (1)	5 (6)	19 (25)	<0.001
JVP not visible (=0), no. (%)	0	48 (96)	193 (80)	0.008	79 (99)	70 (80)	44 (59)	<0.001
JVP raised 1–4 cm (=1), no. (%)	0	1 (2)	42 (17)		1 (1)	18 (2)	23 (31)	
JVP raised to earlobe (=2), no. (%)	0	0 (0)	8 (3)		0 (0)	0 (0)	8 (10)	
Bloods								
Creatinine, μmol/L	0	76 (66–88)	97 (81–130)	<0.001	96 (77–117)	95 (76–132)	102 (85–156)	0.10
Urea, mmol/L	0	5.9 (5.2–7.0)	7.7 (5.8–11.0)	<0.001	7.4 (5.5–9.1)	7.4 (5.5–11)	8.7 (6.4–13)	0.03
eGFR, mL/min/1.73 m ²	0	91 (25)	66 (27)	<0.001	69 (28)	69 (28)	60 (24)	0.04
Haemoglobin, g/dL	1	13.6 (1.5)	13.3 (1.6)	0.25	13.7 (1.3)	13.4 (1.5)	12.7 (1.7)	<0.001
Albumin, g/L	0	39 (3)	38 (3)	0.06	38 (3)	39 (3)	38 (4)	0.32
Bilirubin, μmol/L	0	14.7 (4.8)	17.2 (6.6)	0.011	17.0 (7.6)	16.9 (5.6)	17.7 (6.3)	0.73
NT-proBNP, ng/L	1	72 (45–104)	788 (280–1841)	<0.001	406 (191–892)	903 (276–1922)	1549 (703–3058)	<0.001
NT-proBNP, ng/L (patients in sinus rhythm only)	0	72 (45–104)	441 (223–1284)	<0.001	347 (183–836)	421 (216–1452)	957 (311–2897)	0.001

Treatment								
Beta-blocker, no. (%)	0	13 (27)	195 (80)	<0.001	64 (80)	74 (84)	57 (76)	0.43
ACE-I/ARB, no (%)	0	21 (43)	186 (77)	<0.001	60 (75)	69 (78)	57 (76)	0.86
Aldosterone antagonist, no. (%)	0	4 (8)	115 (47)	<0.001	37 (46)	43 (49)	35 (47)	0.93
Loop diuretic, no. (%)	0	5 (10)	152 (63)	<0.001	46 (57)	55 (63)	51 (68)	0.40
Loop >40 mg furosemide, no. (%)	0	0 (0)	50 (21)	<0.001	14 (18)	15 (17)	21 (28)	0.16
Ultrasound								
LVEDD, cm	0	4.6 (0.6)	5.5 (0.9)	<0.001	5.5 (0.8)	5.4 (0.9)	5.7(1.0)	0.057
LVEDV, mL	0	92 (29)	139 (64)	<0.001	134 (49)	130 (59)	154 (80)	0.04
LVEF, %	0	60 (5)	45 (13)	<0.001	46 (12)	46 (12)	45 (14)	0.77
LVEF ≤40%, no. (%)	0	0 (0)	86 (35)	<0.001	28 (35)	31 (35)	27 (36)	0.99
LAVI, mL/m ²	1	26 (9)	39 (17)	<0.001	33 (13)	38 (15)	46 (20)	<0.001
Mitral E/E'	7	8.9 (2.8)	12.2 (6.3)	0.001	11.4 (6.7)	11.7 (4.5)	13.7 (7.4)	0.058
TAPSE, cm	2	2.2 (0.3)	1.8 (0.4)	<0.001	1.9 (0.3)	1.9 (0.4)	1.7 (0.5)	0.001
TR gradient, mmHg	37	22 (5)	27 (11)	<0.001	24 (9)	26 (8)	34 (13)	<0.001
IVC, cm	12	1.5 (0.3)	1.9 (0.4)	<0.001	1.7 (0.3)	1.9 (0.4)	2.1 (0.5)	<0.001
IVC ≤16 mm, no. (%)	12	28 (61)	68 (29)	<0.001	37 (50)	22 (26)	9 (12)	<0.001
IVC 17–20 mm, no. (%)		15 (33)	89 (38)		24 (33)	37 (43)	28 (38)	
IVC >20 mm, no. (%)		3 (6)	77 (33)		13 (17)	27 (31)	37 (50)	
Mitral regurgitation				<0.001				0.014
Mild	0	11 (22)	105 (43)		32 (40)	39 (44)	34 (45)	
Moderate/severe		0 (0)	31 (13)		4 (5)	11 (12)	16 (21)	
Tricuspid regurgitation				<0.001				<0.001
Mild	0	6 (12)	82 (34)		22 (27)	28 (32)	32 (43)	
Moderate/severe		0 (0)	32 (13)		2 (3)	11 (13)	19 (25)	
JVD rest, cm	7	0.15 (0.04)	0.25 (0.24)	<0.001	0.18 (0.08)	0.19 (0.1)	0.40 (0.37)	<0.001
JVD deep inspiration, cm	7	0.09 (0.03)	0.18 (0.23)	<0.001	0.11 (0.08)	0.13 (0.08)	0.32 (0.40)	<0.001
JVD maximal, cm	7	1.02 (0.17)	1.07 (0.22)	0.09	1.05 (0.18)	1.04 (0.19)	1.12 (0.27)	0.057
JVD ratio (max/baseline)	7	6.9 (1.3)	5.8 (2.3)	<0.001	6.4 (2.0)	6.1 (2.0)	4.7 (2.6)	<0.001
JVD ratio >4, no. (%)	7	46 (98)	189 (79)	0.002	72 (90)	73 (86)	44 (60)	<0.001
JVD ratio ≤4, no. (%)		1 (2)	49 (21)		8 (10)	12 (14)	29 (40)	

ACE-I, ACE inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index; BSA, body surface area; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; IHD, ischaemic heart disease; IVC, inferior vena cava; JVD, jugular vein diameter; JVP, jugular venous pressure; LAVI, left atrial volume index; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; NA, not applicable; NIRS, near-infrared spectroscopy; NT-proBNP, N-terminal B-type natriuretic peptide; RAP, right atrial pressure; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; TR gradient, trans-tricuspid systolic gradient.

Table 2: Variables associated with right atrial pressure measured by near-infrared spectroscopy only in patients with heart failure

Variable	Univariable analysis		Multivariable analysis	
	Correlation coefficient	P-value	Unstandardized coefficients (95% CI)	t-stat (P-value)
Demographics				
Age, years	0.166	0.010		
SBP, mmHg	0.000	0.999		
Heart rate, b.p.m.	-0.007	0.916		
BMI, kg/m ²	-0.076	0.239		
BSA, m ²	-0.091	0.157		
Bloods				
log(creatinine)	0.150	0.019		
log(urea)	0.180	0.005		
eGFR, mL/min/1.73 m ²	-0.167	0.009		
Haemoglobin, g/dL	-0.284	<0.001	-0.043 (-0.073;-0.013)	-2.824 (0.005)
Albumin, g/L	0.011	0.859		
Bilirubin, μmol/L	0.035	0.584		
log(NT-proBNP)	0.370	<0.001	1.222 (0.085;2.358)	2.119 (0.035)
Ultrasound				
LVEDV, mL	0.073	0.258		
LVEDD, cm	0.101	0.115		
LVEF, %	-0.040	0.536		
Mitral E/E'	0.091	0.161		
LAVI, mL/m ²	0.291	<0.001		
TAPSE, cm	-0.178	0.006		
TR gradient, mmHg	0.354	<0.001		
IVC, cm	0.461	<0.001	3.313 (2.207;4.419)	5.903 (<0.001)
JVD rest, cm	0.348	<0.001		
JVD deep inspiration, cm	0.354	<0.001		
JVD maximal, cm	0.108	0.097		
JVD ratio (max/baseline)	-0.306	<0.001		

Results were obtained from univariable and multivariable linear regression models. The first column on the left (univariable analysis) represents the correlation between RAP measured by NIRS and the variables studied. The column for the multivariable analysis (left) shows the coefficients for slope of the linear relation between all the variables independently associated with RAP measured by NIRS [$R^2 = 0.33$, adjusted $R^2 = 0.31$; variables entered in multivariable analysis: age, log(NT-proBNP), log(creatinine), TAPSE, IVC, haemoglobin, LAVI].

BMI, body mass index; BSA, body surface area; eGFR, estimated glomerular filtration rate; IVC, inferior vena cava; JVD, jugular vein diameter; LAVI, left atrial volume index; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal B-

type natriuretic peptide; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; TR gradient, trans-tricuspid systolic gradient.

Table 3: Univariable Cox regression model for the composite endpoint of death from all causes or heart failure hospitalization in patients with heart failure (n = 243 patients with heart failure who had 49 events)

Variables	Univariable analysis		
	HR (95% CI)	χ^2	P-value
RAP by NIRS, mmHg	1.10 (1.04–1.18)	10.06	0.002
Demographics			
Age, years	1.03 (0.99–1.06)	3.18	0.08
Sex (men vs. women)	1.47 (0.79–2.73)	1.46	0.23
NYHA class III vs. I/II	2.51 (1.43–4.43)	10.19	0.001
IHD (yes vs. no)	2.45 (1.27–4.70)	7.27	0.007
DM (yes vs. no)	1.18 (0.67–2.08)	0.35	0.55
Hypertension (yes vs. no)	1.21 (0.69–2.12)	0.46	0.49
Atrial fibrillation (yes vs. no)	1.59 (0.79–3.11)	1.72	0.19
COPD (yes vs. no)	1.58 (0.57–4.38)	0.76	0.38
SBP, mmHg	0.99 (0.98–1.00)	0.74	0.39
Heart rate, b.p.m.	1.01 (0.99–1.03)	0.94	0.33
BMI, kg/m ²	1.01 (0.97–1.06)	0.33	0.57
BSA, m ²	1.75 (0.52–5.87)	0.83	0.36
Congestion \geq 3 signs	3.56 (1.86–6.84)	14.60	<0.001
Clinical JVP (2/1 vs. 0)	2.20 (1.21–4.01)	6.71	0.01
Bloods			
Creatinine, μ mol/L	1.01 (1.00–1.01)	3.66	0.056
Urea, mmol/L	1.06 (1.01–1.10)	5.17	0.02
eGFR, mL/min/1.73 m ²	0.99 (0.98–1.00)	3.41	0.065
Haemoglobin, g/dL	0.98 (0.96–1.00)	6.22	0.013
Albumin, g/L	0.88 (0.81–0.94)	11.50	0.001
Bilirubin, μ mol/L	1.02 (0.98–1.06)	1.29	0.26
log(NT-proBNP)	4.01 (2.30–6.99)	23.97	<0.001
Ultrasound			
LVEDV, mL	1.01 (1.00–1.01)	11.77	0.001
LVEDD, cm	1.77 (1.32–2.37)	14.72	<0.001
LVEF, %	0.97 (0.95–0.99)	8.70	0.003
E/E'	1.04 (1.01–1.08)	7.99	0.005
LAVI, mL/m ²	1.02 (1.01–1.04)	8.13	0.004
TAPSE, cm	0.42 (0.21–0.87)	5.40	0.02
TR gradient, mmHg	1.04 (1.02–1.06)	16.28	<0.001
IVC, cm	3.94 (2.18–7.11)	20.55	<0.001

MR, moderate vs. none/mild	2.92 (1.55–5.51)	10.94	0.001
TR, moderate vs. none/mild	2.66 (1.38–5.12)	8.60	0.003
JVD rest, cm	4.56 (2.26–9.21)	17.94	<0.001
JVD deep inspiration, cm	4.26 (2.11–8.60)	16.30	<0.001
JVD maximal, cm	2.77 (0.84–9.10)	2.81	0.09
JVD ratio (max/baseline)	0.79 (0.70–0.90)	12.66	<0.001

For continuous variables, the values are the hazard ratios associated with a unitary increase in that variable.

BMI, body mass index; BSA, body surface area; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; IHD, ischaemic heart disease; IVC, inferior vena cava; JVD, jugular vein diameter; JVP, jugular venous pressure; LAVI, left atrial volume index; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; NIRS, near-infrared spectroscopy; NT-proBNP, N-terminal B-type natriuretic peptide; RAP, right atrial pressure; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; TR gradient, trans-tricuspid systolic gradient.

Table 4: Multivariable Cox regression model for the composite endpoint of death from all causes or heart failure hospitalization in patients with heart failure (n = 243 patients with heart failure who had 49 events)

	Model A-1			Model A-2		
	HR (95% CI)	χ^2	P-value	HR (95% CI)	χ^2	P-value
Age, years	1.01 (0.98–1.05)	0.65	0.42	1.02 (0.99–1.06)	2.15	0.15
NYHA III vs. II/I	1.43 (0.76–2.71)	1.21	0.27	1.56 (0.83–2.92)	1.94	0.16
RAP by NIRS, mmHg	1.04 (0.97–1.11)	1.17	0.28	1.08 (1.01–1.15)	5.01	0.03
Creatinine, $\mu\text{mol/L}$	1.01 (1.00–1.01)	0.01	0.97	1.01 (1.00–1.01)	0.18	0.67
LVEF, %	0.99 (0.96–1.01)	1.20	0.27	0.97 (0.95–0.99)	5.37	0.02
log(NT-proBNP)	2.40 (1.13–5.10)	5.17	0.02	–	–	–
	Model B-1			Model B-2		
Age, years	1.00 (0.97–1.03)	0.02	0.88	1.01 (0.97–1.04)	0.10	0.76
Urea, mmol/L	1.01 (0.95–1.07)	0.09	0.76	1.04 (0.99–1.09)	1.85	0.17
Haemoglobin, g/dL	0.99 (0.98–1.01)	0.38	0.54	0.99 (0.98–1.01)	0.33	0.56
Albumin, g/L	0.90 (0.84–0.99)	5.31	0.02	0.90 (0.83–0.97)	7.34	0.007
log(NT-proBNP)	2.89 (1.47–5.65)	9.54	0.002	–	–	–
RAP by NIRS, mmHg	1.03 (0.96–1.11)	0.71	0.40	1.08 (1.01–1.16)	5.63	0.02
	Model C-1			Model C-2		
Age, years	1.03 (0.00–1.06)	2.36	0.12	1.01 (0.98–1.04)	0.52	0.47
LVEF, %	0.98 (0.95–1.00)	3.28	0.07	0.98 (0.95–1.00)	3.42	0.06
E/E'	1.02 (0.98–1.07)	0.79	0.37	1.02 (0.98–1.06)	1.07	0.30
LAVI, mL/m ²	1.01 (0.99–1.03)	0.98	0.32	1.01 (0.99–1.02)	0.57	0.45
TAPSE, cm	0.86 (0.40–1.86)	0.14	0.71	–	–	–
IVC, cm	–	–	–	2.73 (1.29–5.74)	7.01	0.008
RAP by NIRS, mmHg	1.08 (1.01–1.15)	4.40	0.036	1.03 (0.95–1.11)	0.38	0.54

Different models were tested to explore how the inclusion or exclusion of known predictors of outcome affects the impact of RAP by NIRS. This is relevant to the clinical setting, when information is often incomplete. It also shows whether variables that are associated with RAP also provide similar prognostic information.

IVC, inferior vena cava; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; NIRS, near-infrared spectroscopy; NT-proBNP, N-terminal B-type natriuretic peptide; RAP, right atrial pressure; TAPSE, tricuspid annular plane systolic excursion.



Figure 1: Measurement of right atrial pressure using near-infrared spectroscopy. With the patient reclining and head and neck elevated at 45° , the external jugular vein was identified and right atrial pressure measured using near-infrared spectroscopy (Venus 1000, Mespere LifeSciences, Canada), a portable device that includes adhesive patches connected to a reading electrode placed over the external jugular vein on the right side of the neck and a reference point aligned with the right atrium (the fourth intercostal space at the mid-anteroposterior diameter of the chest wall). Once stable waveforms and readings are obtained, the device records right atrial pressure (in mmHg).

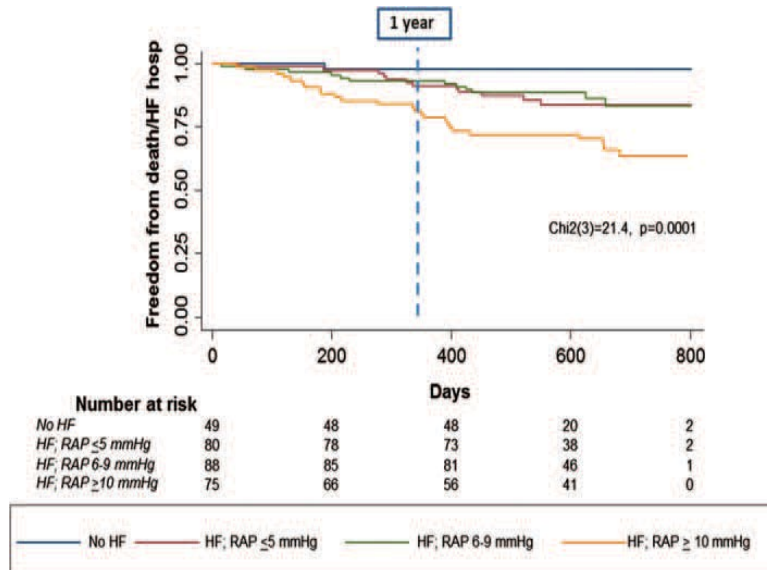


Figure 2: Kaplan-Meier curves for the primary outcome of death from all causes and heart failure (HF) hospitalizations. Compared with those with normal right atrial pressure (RAP) by near-infrared spectroscopy (≤ 5 mmHg, in red), HF patients with high RAP (≥ 10 mmHg, in yellow) had more than a two-fold higher risk of dying or being hospitalized for HF (hazard ratio 2.38, 95% confidence interval: 1.19 - 4.75, $P = 0.014$).