

## Impact of cognitive impairment on clinical outcomes in elderly patients with atrial fibrillation: ANAFIE Registry

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**Table S1** Changes in MMSE scores over 2 years

	<b>Normal cognition (MMSE <math>\geq 24</math>) n=2377</b>	<b>Cognitive impairment (MMSE <math>\leq 23</math>) n=586</b>	<b>Total n=2963</b>	<b>p value*</b>
Number of repeated MMSE determination	1611 (67.8)	304 (51.9)	1915 (64.6)	<0.001
MMSE score decrease >2 points	526 (22.1)	116 (19.8)	642 (21.7)	0.062
Change in MMSE score	-1.2 $\pm$ 3.6	-0.4 $\pm$ 5.2	-1.1 $\pm$ 3.9	0.001

Data are n (%) or mean  $\pm$  standard deviation.

\*Normal cognition vs. cognitive impairment group.

MMSE, Mini-Mental State Examination.

**Table S2** Risk factors for cardiovascular death

Item	N	Event (%)			Univariate			Multivariate*		
					HR (95% CI)	P value		HR (95% CI)	P value	
Educational background	<9 years	1109	25	(2.25)	1.34	(0.79, 2.28)	0.271	1.06	(0.56, 2.00)	0.855
	≥9 years†	1822	31	(1.70)		-			-	
Volunteer activities	Nearly daily/ several times a week/once a week† or less	577	10	(1.73)		-			-	
	Not at all	2378	48	(2.02)	1.20	(0.61, 2.37)	0.599	0.63	(0.26, 1.57)	0.326
Employed	Nearly daily/several times a week†	605	9	(1.49)		-			-	
	Not more than once a week	2272	44	(1.94)	1.33	(0.65, 2.72)	0.436	0.77	(0.35, 1.66)	0.499
Participation in neighborhood associations and resident associations	Almost always/sometimes†	1432	18	(1.26)		-			-	
	Low participation/not interested	1523	40	(2.63)	2.20	(1.26, 3.83)	0.006	1.10	(0.54, 2.23)	0.795
Participation in learning activities such as open lectures for citizens	Participating/participated in the past†	1174	16	(1.36)		-			-	
	No participation	1776	41	(2.31)	1.73	(0.97, 3.08)	0.064	1.45	(0.69, 3.03)	0.325
Driving status	Currently driver/previous driver/an inexperienced driver†	1818	28	(1.54)		-			-	
	No driver's license	1128	30	(2.66)	1.77	(1.06, 2.96)	0.030	2.49	(1.11, 5.58)	0.027
	Used†	1809	29	(1.60)		-			-	

Mobile telephone use	Not used	1102	29	(2.63)	1.70	(1.02, 2.85)	0.043	0.76	(0.38, 1.53)	0.447
Frequency of calls (fixed-line phones and mobile phones)	Nearly daily/several times a week†	2095	32	(1.53)		-			-	
	Less than once a week/rarely used	862	26	(3.02)	2.05	(1.22, 3.44)	0.007	1.27	(0.62, 2.59)	0.518
Computer use	Daily/occasional use†	558	8	(1.43)		-			-	
	Little use/no interest	2393	50	(2.09)	1.52	(0.72, 3.20)	0.272	0.68	(0.19, 2.41)	0.555
Internet use	Daily/occasional use†	445	6	(1.35)		-			-	
	Little use/no interest	2505	51	(2.04)	1.58	(0.68, 3.67)	0.293	1.03	(0.26, 4.08)	0.970
Going out	Nearly daily/several times a week†	2427	38	(1.57)		-			-	
	Less than once a week/rarely go out	531	20	(3.77)	2.60	(1.51, 4.46)	<0.001	1.25	(0.59, 2.68)	0.558
Main means of going out	Public transportation†	644	13	(2.02)		-			-	
	Private car (driving oneself, driven by a household member)	1586	33	(2.08)	1.03	(0.54, 1.96)	0.921	1.04	(0.49, 2.21)	0.919
	Other	428	9	(2.10)	1.06	(0.45, 2.47)	0.899	0.88	(0.36, 2.18)	0.788
Shopping	Almost every day†	618	5	(0.81)		-			-	
	Several times a week	1255	18	(1.43)	1.79	(0.67, 4.83)	0.249	1.51	(0.54, 4.22)	0.431
	Less than once a week/rarely go out	1082	35	(3.23)	4.22	(1.65, 10.78)	0.003	1.50	(0.49, 4.59)	0.479
Monetary management (bank accounts and pensions)	Self-managed†	1989	28	(1.41)		-			-	
	Managed by relatives/others	942	30	(3.18)	2.40	(1.43, 4.01)	<0.001	1.15	(0.57, 2.31)	0.691

Travel and business trips to other prefectures	Monthly, several times a year, not more than once a year†	1497	19	(1.27)		-			-	
	Little travel	1458	39	(2.67)	2.20	(1.27, 3.81)	0.005	1.32	(0.62, 2.79)	0.468
Exercise habits	None	1081	34	(3.15)	2.44	(1.44, 4.11)	<0.001	1.54	(0.80, 2.96)	0.195
	Other†	1784	24	(1.35)		-			-	
Use of long-term care services	None	2385	37	(1.55)	0.38	(0.22, 0.66)	<0.001	0.72	(0.35, 1.49)	0.376
	Other†	538	20	(3.72)		-			-	
Sex	Male†	1657	34	(2.05)		-			-	
	Female	1306	24	(1.84)	0.90	(0.53, 1.51)	0.686	0.31	(0.14, 0.70)	0.005
Age	<85 years†	2216	33	(1.49)		-			-	
	≥85 years	747	25	(3.35)	2.38	(1.41, 4.00)	0.001	0.91	(0.45, 1.82)	0.789
BMI (kg/m <sup>2</sup> )	<18.5	178	10	(5.62)	3.18	(1.55, 6.50)	0.002	2.14	(0.89, 5.16)	0.090
	≥18.5 to <25.0†	1641	30	(1.83)		-			-	
	≥25.0	775	11	(1.42)	0.76	(0.38, 1.52)	0.445	1.00	(0.45, 2.22)	0.994
Anticoagulants	Warfarin†	685	19	(2.77)		-			-	
	None	228	5	(2.19)	0.79	(0.29, 2.10)	0.632	1.04	(0.33, 3.27)	0.945
	DOAC	2050	34	(1.66)	0.59	(0.34, 1.04)	0.066	0.77	(0.40, 1.50)	0.442
Hypertension	Systolic BP <130 mmHg†	1382	34	(2.46)		-			-	
	Systolic BP ≥130 mmHg to <140 mmHg	696	10	(1.44)	0.57	(0.28, 1.16)	0.124	0.64	(0.29, 1.43)	0.280
	Systolic BP ≥140 mmHg	655	9	(1.37)	0.55	(0.26, 1.15)	0.111	0.62	(0.27, 1.44)	0.264
Diabetes mellitus	Presence (HbA1c: <6.0%)	88	2	(2.27)	1.10	(0.27, 4.55)	0.892	0.63	(0.08, 4.73)	0.652
	Presence (HbA1c: ≥6.0%)	513	9	(1.75)	0.85	(0.42, 1.74)	0.664	0.71	(0.31, 1.63)	0.418
	None†	2234	46	(2.06)		-			-	

Heart disease: heart failure, left ventricular systolic dysfunction	Yes	976	27	(2.77)	1.84	(1.10, 3.08)	0.021	1.36	(0.74, 2.50)	0.326
	None†	1987	31	(1.56)		-			-	
Cerebrovascular disorders	Yes	754	20	(2.65)	1.62	(0.94, 2.78)	0.082	1.88	(1.01, 3.51)	0.047
	None†	2209	38	(1.72)		-			-	
Creatinine clearance	<30 mL/min/severe renal dysfunction/dialysis	337	18	(5.34)	7.85	(3.41, 18.05)	<0.001	3.34	(1.12, 9.97)	0.031
	30 mL/min to <50 mL/min	953	23	(2.41)	3.34	(1.49, 7.47)	0.003	2.97	(1.26, 7.01)	0.013
	≥50 mL/min†	1076	8	(0.74)		-			-	

\*All of the items listed in the column were included in the model.

†Reference

BMI, body mass index; BP, blood pressure; CI, confidence interval; DOAC, direct oral anticoagulant; HbA1c, glycated hemoglobin; HR, hazard ratio.

**Table S3** Risk factors for all-cause death

Item	N	Event (%)			Univariate			Multivariate*		
					HR (95% CI)	P value	HR (95% CI)	P value		
Educational background	<9 years	1109	90	(8.12)	1.35	(1.02, 1.78)	0.035	1.11	(0.80, 1.55)	0.518
	≥9 years†	1822	111	(6.09)		-			-	
Volunteer activities	Nearly daily/several times a week/ once a week† or less	577	26	(4.51)		-			-	
	Not at all	2378	178	(7.49)	1.71	(1.13, 2.58)	0.010	0.91	(0.55, 1.50)	0.698
Employed	Nearly daily/several times a week†	605	22	(3.64)		-			-	
	Not more than once a week	2272	172	(7.57)	2.14	(1.37, 3.33)	<0.001	1.28	(0.79, 2.08)	0.320
Participation in neighborhood associations and resident associations	Almost always/sometimes†	1432	58	(4.05)		-			-	
	Low participation/not interested	1523	145	(9.52)	2.47	(1.82, 3.35)	<0.001	1.36	(0.93, 2.00)	0.118
Participation in learning activities such as open lectures for citizens	Participating/having participated in the past†	1174	64	(5.45)		-			-	
	Do not participate	1776	139	(7.83)	1.47	(1.09, 1.97)	0.011	0.71	(0.50, 1.01)	0.057
Driving status	Currently driver/previous driver operation/an inexperienced driver†	1818	105	(5.78)		-			-	



	No driver's license	1128	98	(8.69)	1.54	(1.17, 2.03)	0.002	1.69	(1.10, 2.60)	0.016
Mobile telephone use	Used†	1809	94	(5.20)		-			-	
	Not used	1102	109	(9.89)	1.97	(1.50, 2.60)	<0.001	0.85	(0.59, 1.22)	0.373
Frequency of calls (fixed-line phones and mobile phones)	Nearly daily/several times a week†	2095	113	(5.39)		-			-	
	Less than once a week/rarely used	862	91	(10.56)	2.03	(1.54, 2.67)	<0.001	0.97	(0.67, 1.42)	0.893
Computer use	Daily/occasional use†	558	16	(2.87)		-			-	
	Little use/no interest	2393	187	(7.81)	2.84	(1.70, 4.73)	<0.001	1.29	(0.59, 2.82)	0.530
Internet use	Daily/occasional use†	445	12	(2.70)		-			-	
	Little use/no interest	2505	190	(7.58)	2.93	(1.63, 5.25)	<0.001	1.38	(0.57, 3.34)	0.474
Going out	Nearly daily/several times a week†	2427	133	(5.48)		-			-	
	Less than once a week/rarely go out	531	71	(13.37)	2.63	(1.97, 3.51)	<0.001	1.17	(0.79, 1.75)	0.433
Main means of going out	Public transportation†	644	43	(6.68)		-			-	
	Private car (driving oneself, driven by a household member)	1586	113	(7.12)	1.07	(0.75, 1.51)	0.724	1.10	(0.73, 1.66)	0.635
	Other	428	36	(8.41)	1.28	(0.82, 1.99)	0.273	0.93	(0.56, 1.53)	0.768
Shopping	Almost every day†	618	19	(3.07)		-			-	
	Several times a week	1255	64	(5.10)	1.68	(1.00, 2.80)	0.048	1.43	(0.82, 2.48)	0.205

	Less than once a week/rarely go out	1082	121	(11.18)	3.84	(2.37, 6.23)	<0.001	1.37	(0.75, 2.50)	0.302
Monetary management (bank accounts and pensions)	Self-managed†	1989	85	(4.27)		-			-	
	Managed by a family member/others	942	118	(12.53)	3.11	(2.35, 4.11)	<0.001	1.54	(1.07, 2.21)	0.020
Travel and business trips to other prefectures	Monthly, several times a year, not more than once a year†	1497	62	(4.14)		-			-	
	Little travel	1458	142	(9.74)	2.45	(1.82, 3.31)	<0.001	1.24	(0.84, 1.83)	0.270
Exercise habits	None	1081	112	(10.36)	2.21	(1.67, 2.92)	<0.001	1.21	(0.86, 1.71)	0.275
	Other†	1784	87	(4.88)		-			-	
Use of long-term care services	None	2385	127	(5.32)	0.37	(0.28, 0.50)	<0.001	0.73	(0.49, 1.06)	0.101
	Other†	538	71	(13.20)		-			-	
Sex	Male†	1657	125	(7.54)		-			-	
	Female	1306	79	(6.05)	0.80	(0.61, 1.07)	0.131	0.42	(0.27, 0.65)	<0.001
Age	<85 years†	2216	121	(5.46)		-			-	
	≥85 years	747	83	(11.11)	2.16	(1.63, 2.85)	<0.001	1.18	(0.82, 1.69)	0.382
BMI (kg/m <sup>2</sup> )	<18.5	178	23	(12.92)	1.94	(1.24, 3.04)	0.004	1.66	(0.99, 2.78)	0.054
	≥18.5 to <25.0†	1641	113	(6.89)		-			-	
	≥25.0	775	39	(5.03)	0.72	(0.50, 1.03)	0.076	0.95	(0.62, 1.45)	0.818
Anticoagulants	Warfarin†	685	57	(8.32)		-			-	
	None	228	17	(7.46)	0.89	(0.52, 1.53)	0.670	1.15	(0.63, 2.08)	0.656
	DOAC	2050	130	(6.34)	0.75	(0.55, 1.03)	0.072	0.88	(0.62, 1.26)	0.488
Hypertension	Systolic BP <130 mmHg†	1382	120	(8.68)		-			-	
	Systolic BP ≥130 mmHg to <140 mmHg	696	39	(5.60)	0.64	(0.44, 0.91)	0.014	0.75	(0.51, 1.13)	0.169

	Systolic BP $\geq$ 140 mmHg	655	36	(5.50)	0.62	(0.43, 0.90)	0.013	0.74	(0.49, 1.13)	0.166
Diabetes mellitus	Presence (HbA1c: $<$ 6.0%)	88	6	(6.82)	0.97	(0.43, 2.20)	0.948	0.56	(0.18, 1.78)	0.328
	Presence (HbA1c: $\geq$ 6.0%)	513	31	(6.04)	0.86	(0.59, 1.27)	0.447	0.82	(0.53, 1.27)	0.380
	None <sup>†</sup>	2234	157	(7.03)		-			-	
Heart disease: heart failure, left ventricular systolic dysfunction	Yes	976	92	(9.43)	1.74	(1.32, 2.29)	$<$ 0.001	1.21	(0.88, 1.68)	0.242
	None <sup>†</sup>	1987	112	(5.64)		-			-	
Cerebrovascular disorders	Yes	754	77	(10.21)	1.86	(1.40, 2.46)	$<$ 0.001	1.63	(1.17, 2.27)	0.004
	None <sup>†</sup>	2209	127	(5.75)		-			-	
Creatinine clearance	$<$ 30 mL/min/severe renal dysfunction/dialysis	337	55	(16.32)	4.58	(3.07, 6.85)	$<$ 0.001	2.30	(1.34, 3.96)	0.003
	30 mL/min to $<$ 50 mL/min	953	62	(6.51)	1.71	(1.16, 2.54)	0.007	1.34	(0.86, 2.10)	0.197
	$\geq$ 50 mL/min <sup>†</sup>	1076	42	(3.90)		-			-	

\*All of the items listed in the column were included in the model.

<sup>†</sup>Reference

BMI, body mass index; BP, blood pressure; CI, confidence interval; DOAC, direct oral anticoagulant; HbA1c, glycated hemoglobin; HR, hazard ratio.