

Supplementary material

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Supplementary Table S1. Baseline characteristics in the overall study population depending on the success of pharmacological cardioversion

Variable	Successful rhythm conversion N=965	Cardioversion failure N=400	<i>P</i>
Male sex	508 (52.6%)	217 (54.3%)	0.59*
Age [years]	69.0 (60.0 – 76.0)	69.0 (61.0 – 77.0)	0.13‡
Weight [kg]	78.0 (68.5 – 91.0)	80.0 (70.0 – 88.5)	0.36‡
BMI [kg/m²]	27.8 (4.58)	28.2 (4.07)	0.46†
Arterial hypertension	662 (68.6%)	285 (71.3%)	0.21*
Diabetes mellitus	179 (18.5%)	83 (20.8%)	0.65*
CAD/PAD	338 (35.0%)	105 (26.3%)	0.001*
Ischaemic stroke/TIA	50 (5.2%)	14 (3.5%)	0.01*

Variable	Successful rhythm conversion N=965	Cardioversion failure N=400	<i>P</i>
Structural heart disease	368 (38.1%)	137 (34.3%)	0.18*
LVEF [%]	58.0 (52.0 – 60.0)	55.0 (50.0 – 60.0)	<0.001‡
LVEF <50%	73 (7.6%)	55 (13.8%)	0.02*
LAd [mm]	43.09 (5.27)	45.08 (6.44)	<0.001†
SCr [mg/dl]	0.97 (0.81 – 1.13)	1.03 (0.86 – 1.21)	0.01‡
eGFR [ml/min]	74.0 (57.0 – 88.0)	68.8 (52.7 – 83.0)	0.01‡
eGFR <60 ml/min/1.73 m2	144 (14.9%)	89 (22.3%)	0.05*
K⁺ level [mEq/l]	4.22 (0.46)	4.30 (0.43)	0.003†
WBC [x1000/μl]	7.5 (6.25 – 9.13)	7.6 (6.5 – 8.9)	0.37‡
Haemoglobin [g/dl]	14.3 (13.1 – 15.2)	14.4 (13.5 – 15.4)	0.11‡
Persistent AF	20 (2.1%)	83 (20.8%)	<0.001*
CHA₂DS₂-VASc score	3 (2 – 4)	3 (2 – 4)	0.30‡
EHRA class	2.5 (2 – 3)	3 (2 – 3)	<0.001‡
History of PVI	91 (9.4%)	30 (7.5%)	0.17*

Variable	Successful rhythm conversion N=965	Cardioversion failure N=400	<i>P</i>
Chronic anticoagulation	437 (45.3%)	216 (54.0%)	0.05*
HR ≥130 bpm	236 (24.5%)	83 (20.8%)	0.09*
Time of ED admission	13.00 (9.00 - 18.00)	13.00 (10.00 - 17.50)	0.75‡
Beta-blocker use	390 (40.4%)	168 (42.0%)	0.92*
IV potassium	441 (45.7%)	152 (38.0%)	<0.001*
Amiodarone ^Δ	323 (33.5%)	185 (46.3%)	<0.001*
Propafenone ^Δ	190 (19.7%)	101 (25.3%)	0.03*
Antazoline ^Δ	643 (66.6%)	254 (63.5%)	0.27*
Dose of antazoline [mg]	200 (100 - 200)	200 (200 - 300)	<0.001‡
Dose of amiodarone [mg]	450 (300 - 600)	375 (300 - 600)	0.45‡
Dose of propafenone [mg]	150 (70 - 370)	300 (70 - 300)	0.78‡

* – Chi² test; † – student's t test; ‡ – Mann-Whitney U test; ^Δ - drugs used also alone or in combination

AF – atrial fibrillation; BMI – body mass index; bpm – beats per minute; CAD – coronary artery disease; ED – emergency department; EHRA – European Heart Rhythm Association classification; HR – heart rate; PAD – peripheral artery disease; TIA- transient ischaemic attack; LAd – left atrial diameter; LVEF – left ventricular ejection fraction; eGFR – estimated glomerular filtration rate; SCr – serum creatinine concentration; SD – standard deviation; TSH – thyroid-stimulating hormone concentration; TnT – troponin T concentration; WBC – white blood cell count

Supplementary Table S2. Clinical characteristics and cardioversion outcome per antiarrhythmic drug used for pharmacological cardioversion

Variable	Amiodarone (1) N=287	Propafenone (2) N=150	Antazoline (3) N=600	Overlapping treatment (4) N=328	<i>P</i>* Δ 1 vs 2	<i>P</i>* Δ 1 vs 3	<i>P</i>* Δ 1 vs 4	<i>P</i>* Δ 2 vs. 3	<i>P</i>* Δ 2 vs. 4	<i>P</i>*Δ 3 vs 4	<i>P</i>**Δ
Male sex	123 (42.9%)	68 (45.3%)	350 (58.3%)	184 (56.1%)	0.57	<0.001	0.001	0.004	0.03	0.55	<0.001
Age [years]	69.0 (61.0 - 76.0)	70.0 (60.0 – 77.0)	68.0 (61.0 – 76.0)	68.0 (59.0 – 76.0)	0.96	0.17	0.13	0.30	0.21	0.61	0.31
Weight [kg]	86.0 (72.0 – 99.0)	65.0 (62.0 – 90.0)	80.0 (71.0 – 91.5)	78.0 (67.0 - 90.0)	0.21	0.33	0.15	0.29	0.46	0.22	0.28
BMI [kg/m²]	28.74 (4.79)	26.41 (3.35)	28.06 (4.24)	27.98 (4.49)	0.59	0.80	0.87	0.57	0.58	0.97	0.94

Variable	Amiodarone (1) N=287	Propafenone (2) N=150	Antazoline (3) N=600	Overlapping treatment (4) N=328	<i>P</i> * Δ 1 vs 2	<i>P</i> * Δ 1 vs 3	<i>P</i> * Δ 1 vs 4	<i>P</i> * Δ 2 vs. 3	<i>P</i> * Δ 2 vs. 4	<i>P</i> *Δ 3 vs 4	<i>P</i> **Δ
Arterial hypertension	210 (73.2%)	80 (53.3%)	401 (66.8%)	256 (78.0%)	<0.001	0.14	0.19	<0.001	<0.001	0.04	<0.001
Diabetes mellitus	50 (17.4%)	17 (11.3%)	111 (18.5%)	84 (25.6%)	0.002	0.35	<0.001	0.02	<0.001	0.02	<0.001
CAD/PAD	82 (28.6%)	35 (23.3%)	231 (38.5%)	95 (29.0%)	0.03	<0.001	0.40	<0.001	0.01	0.001	<0.001
Ischaemic stroke/TIA	14 (4.9%)	3 (2.0%)	19 (3.2%)	28 (8.5%)	0.46	0.14	0.02	0.67	<0.001	0.03	0.07
Structural heart disease	102 (35.5%)	38 (25.3%)	247 (41.2%)	118 (36.0%)	0.03	0.11	0.91	<0.001	0.02	0.12	0.003
LVEF [%]	55.0 (50.0 - 60.0)	60.0 (55.0 – 60.0)	57.0 (51.0 – 60.0)	55.0 (50.0 - 60.0)	0.003	0.44	0.88	0.01	0.002	0.34	0.02
LAd [mm]	42.62 (4.95)	39.57 (5.93)	44.34 (6.27)	45.13 (5.56)	0.002	0.002	<0.001	<0.001	<0.001	0.04	<0.001
SCr [mg/dl]	0.92 (0.79 – 1.12)	0.94 (0.75 – 1.10)	0.98 (0.82 – 1.15)	1.06 (0.88 – 1.25)	0.58	0.20	<0.001	0.19	0.002	0.001	<0.001
eGFR [ml/min]	74.0 (57.0 - 86.0)	75.0 (56.0 – 90.0)	73.7 (57.8 - 86.0)	69.8 (52.7; 84.0)	0.77	0.42	0.23	0.80	0.36	0.04	0.23
eGFR <60 ml/min/1.73 m2	68 (23.7%)	16 (10.7%)	69 (11.5%)	80 (24.4%)	<0.001	<0.001	0.97	0.87	<0.001	<0.001	<0.001

Variable	Amiodarone (1) N=287	Propafenone (2) N=150	Antazoline (3) N=600	Overlapping treatment (4) N=328	<i>P</i>* Δ 1 vs 2	<i>P</i>* Δ 1 vs 3	<i>P</i>* Δ 1 vs 4	<i>P</i>* Δ 2 vs. 3	<i>P</i>* Δ 2 vs. 4	<i>P</i>* Δ 3 vs 4	<i>P</i>**Δ
K⁺ level [mEq/l]	4.28 (0.48)	4.27 (0.41)	4.20 (0.45)	4.25 (0.44)	0.68	0.03	0.65	0.24	0.95	0.09	0.13
WBC [x1000/μl]	7.80 (6.54 – 9.40)	7.40 (6.48 – 8.91)	7.30 (6.10 – 8.77)	7.41 (6.25 – 9.02)	0.49	0.04	0.08	0.50	0.66	0.73	0.16
Hemoglobin [g/dl]	14.2 (13.1 - 15.1)	14.6 (13.7 – 15.6)	14.5 (13.4 – 15.3)	14.2 (12.8 - 15.3)	0.02	0.01	0.84	0.36	0.02	0.02	0.007
Persistent AF	14 (4.9%)	3 (2.0%)	44 (7.33%)	42 (12.8%)	0.14	0.22	<0.001	0.02	<0.001	0.03	<0.001
CHA₂DS₂-VASc score	3 (2 - 4)	3 (1 - 3)	3 (2 - 4)	3 (2 - 4)	0.01	0.16	0.67	0.12	0.01	0.09	0.03
EHRA class	3 (2 - 3)	2 (2 - 3)	3 (2 - 3)	2 (1 - 3)	0.59	0.20	<0.001	0.19	0.11	<0.001	<0.001
History of PVI	12 (4.2%)	13 (8.7%)	71 (11.8%)	25 (7.6%)	0.001	<0.001	0.048	0.31	0.43	0.001	<0.001
Chronic anticoagulation	191 (66.6%)	47 (31.3%)	199 (33.2%)	216 (65.9%)	<0.001	<0.001	0.88	0.69	<0.001	<0.001	<0.001
HR ≥130 bpm	94 (32.8%)	30 (20.0%)	109 (18.2%)	86 (26.2%)	<0.001	<0.001	0.04	0.56	0.03	0.02	0.02
Beta-blocker use	77 (26.8%)	37 (24.7%)	333 (55.5%)	111 (33.8%)	0.51	<0.001	0.046	<0.001	0.02	<0.001	<0.001
IV potassium	160 (55.7%)	33 (22.0%)	225 (37.5%)	175 (53.3%)	<0.001	0.001	0.55	<0.001	<0.001	0.001	<0.001
Successful	192 (66.9%)	109 (72.7%)	470 (78.3%)	194 (59.2%)	0.22	<0.001	0.047	0.14	0.004	<0.001	<0.001

Variable	Amiodarone (1) N=287	Propafenone (2) N=150	Antazoline (3) N=600	Overlapping treatment (4) N=328	<i>P</i> * Δ 1 vs 2	<i>P</i> * Δ 1 vs 3	<i>P</i> * Δ 1 vs 4	<i>P</i> * Δ 2 vs. 3	<i>P</i> * Δ 2 vs. 4	<i>P</i> *Δ 3 vs 4	<i>P</i> **Δ
pharmacological cardioversion											
Composite safety endpoint	6 (2.09%)	11 (7.33%)	31 (5.17%)	18 (5.49%)	0.01	0.03	0.03	0.30	0.43	0.83	0.07
Death	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	-	-	-	-	-	-	-
Bradycardia ≤45 bpm	5 (1.7%)	8 (5.3%)	29 (4.8%)	14 (4.3%)	0.04	0.03	0.10	0.80	0.50	0.54	0.14
Syncope	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0.17	-	-	0.045	0.14	-	0.04
Hypotension	2 (0.7%)	3 (2.0%)	5 (0.8%)	4 (1.2%)	0.23	0.83	0.51	0.21	0.51	0.57	0.56

* – Chi² test with Bonferroni adjustment or Mann-Whitney U test or Student's t test; **- Chi-square test for multiple comparisons or Kruskal-Wallis test or analysis of variance (ANOVA) test; Δ - Bonferroni adjustment for multiple testing was performed and the p-value threshold was set for 0.008; AF – atrial fibrillation; BMI – body mass index; bpm – beats per minute; CAD – coronary artery disease; ED – emergency department; EHRA – European Heart Rhythm Association classification; HR – heart rate; PAD – peripheral artery disease; TIA- transient ischaemic attack; LAd – left atrial diameter; LVEF – left ventricular ejection fraction; eGFR – estimated glomerular filtration rate; IV – intravenous; SCr – serum creatinine concentration; SD – standard deviation; TSH – thyroid-stimulating hormone concentration; TnT – troponin T concentration; WBC – white blood cell count

Supplementary file: *Definitions*

Data acquisitions and definitions

Baseline evaluation of clinical variables was conducted by the review of electronic health records and diligent clinical interview. The acquisition of blood samples was performed on admission in all patients. Laboratory test involved complete blood count, serum creatinine concentration, plasma sodium and potassium level, thyroid-stimulating hormone and high-sensitivity troponin T.

Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73 m² based on Modification of Diet in Renal Disease formula. The risk of ischemic stroke in patients with AF was assessed using CHA₂DS₂-VASc score. The arrhythmia-related symptoms were classified according to Heart Rhythm Association (EHRA) classification. The AF was categorized into two types depending on the duration of the current episode: paroxysmal < 7 days and persistent ≥ 7 days. Coronary artery disease (CAD) comprised cases of chronic coronary syndrome confirmed by positive non-invasive stress test or history of acute coronary syndrome or any myocardial revascularization. Peripheral artery disease (PAD) was diagnosed in case of symptomatic lower limb ischemia or the history of peripheral artery revascularization or ankle-brachial index < 0.9 or visible atheromatous plaque during Doppler imaging of carotid arteries. Structural heart disease was defined as the history of CAD or LVEF $< 50\%$ or severe valvular heart disease or left ventricular hypertrophy.

Screening transthoracic echocardiography was conducted on admission so as to evaluate left ventricular ejection fraction (LVEF) and left atrial diameter (LAd, parasternal long axis view) and to exclude presence of severe valvular heart disease. Depressed left ventricular systolic function was defined as LVEF $< 50\%$. Left ventricular hypertrophy was consistent with myocardial thickness ≥ 12 mm in any transthoracic view. Left atrial enlargement was defined as LAd ≥ 40 mm. Transesophageal echocardiography was not a routine examination and was performed only in selected patients who were not adequately anticoagulated.