Supplementary material

Lodziński P, Gawałko M, Budnik M, et al. Trends in antithrombotic management of patients with atrial fibrillation. A report from the Polish part of the EURObservational Research Programme – Atrial Fibrillation General Long-Term Registry. Pol Arch Intern Med. 2020; 130: 196-205. doi:10.20452/pamw.15157

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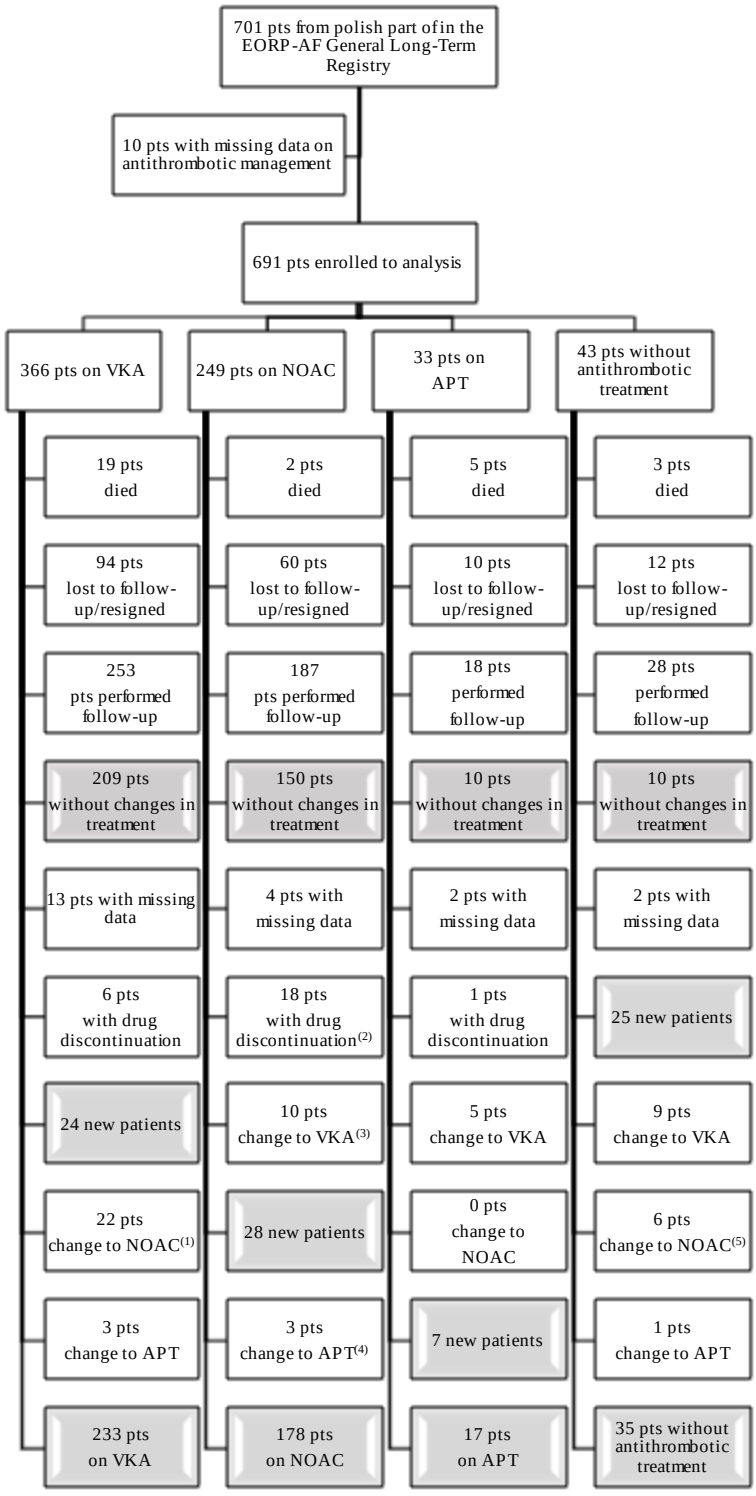
Figure S1. Flow chart of patient enrolment in the study.



(1) 11 pts for dabigatran, 11 pts for rivaroxaban;

(2) 8 pts on dabigatran, 10 pts on rivaroxaban;

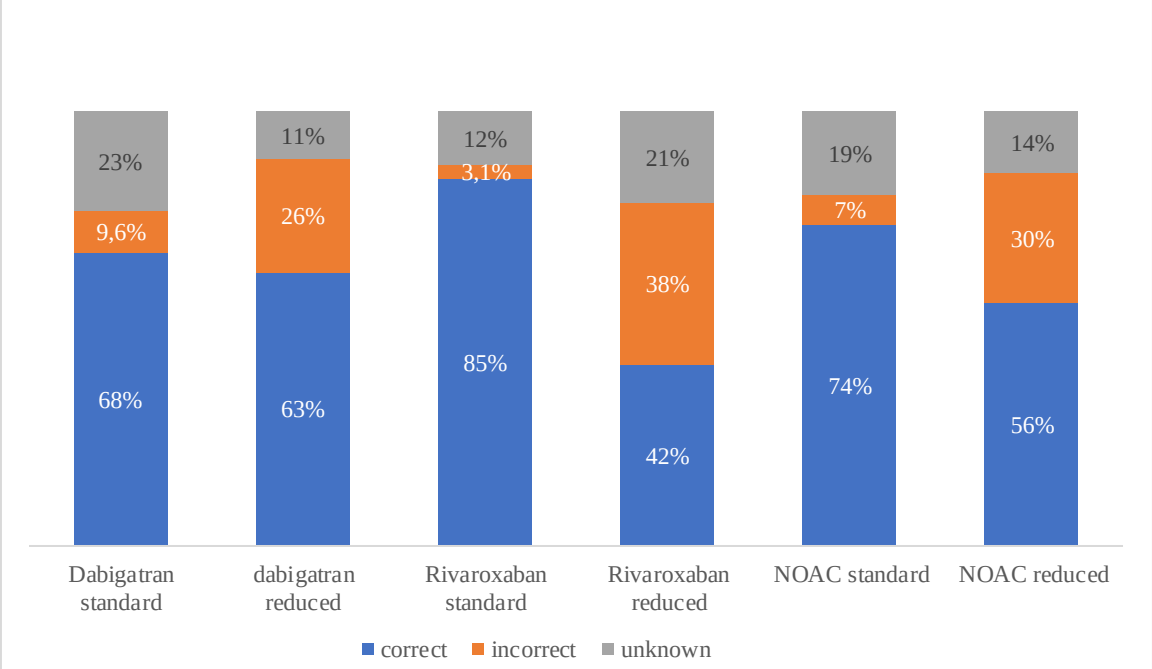
(3) 9 pts on dabigatran, 1 pts on rivaroxaban;

(4) all on dabigatran;

(5) all for dabigatran

ATP – antiplatelet therapy, EORP-AF - EURObservational Research Programme Atrial Fibrillation, NOAC – non-vitamin K antagonist anticoagulants, pts – patients, VKA – vitamin K antagonists

Figure S2 Percentage of patients who received correct, incorrect, and unknown doses of non–vitamin K antagonist oral anticoagulants according to the current recommendation for patients receiving standard and reduced dosing regimens



Abbreviations: see Table 1

Table S1. Distribution of non-vitamin K antagonist oral anticoagulants according the recommendation for patients receiving reduced (A) and standard (B) dosing.

A. Reduced doses of non-vitamin K antagonist oral anticoagulants		
Variable	**Dabigatran (n=46)**	**Rivaroxaban (n=24)**
Correct prescription		
All	**29 (63%)**	**10 (42%)**
Recommended indications for dose reduction	25 (54%)	7 (29%)
- CrCl 30-49ml/min	4 (8.7%)	Not applicable
- CrCl 15-49ml/min	Not applicable	7 (29%)
- Age ≥ 80 years	9 (20%)	Not applicable
- CrCl 30-49ml/min +age ≥ 80 years	12 (26%)	Not applicable
Indications to be considered		
- ≥ 2 indications	4[a] (8.7%)	3[b] (13%)
Incorrect prescription		
All	**12 (26%)**	**9 (38%)**
Unknown reason	6 (13%)	1 (4.2%)
Indications to be considered	6 (13%)	8 (33%)
- HAS-BLED ≥ 3	0 (0%)	0 (0%)
- Age ≥ 75 years	1 (2.2%)	0 (0%)
- Antiplatelet drugs	0 (0%)	7 (29%)
- NSAIDs	2 (4.3%)	0 (0%)
- Amiodarone	1 (2.2%)	0 (0%)
- History of GI bleeding	2 (4.3%)	1 (4.2%)
- Weight ≤60kg	0 (0%)	0 (0%)
Unknown appropriate prescriptions		
- No data regarding CrCl or type of DHP-CCB	5 (11%)	5 (21%)

[a] *age ≥ 75 years + antiplatelets + HAS-BLED ≥ 3 (2 patients), amiodarone + antiplatelets + HAS-BLED ≥ 3 (1 patient), amiodarone +NSAIDs (1 patient)*

[b] *age ≥ 75 years + NSAIDs (1 patient), age ≥ 75 years + antiplatelets (1 patient), age ≥ 75 years + HAS-BLED ≥ 3 (1 patient)*

B. Standard doses of non-vitamin K antagonist oral anticoagulants		
Variable	**Dabigatran (n=114)**	**Rivaroxaban (n=65)**
Incorrect prescription		
Recommended indications for dose reduction	**11 (9.6%)**	**2 (3.1%)**
- CrCl 30-49ml/min	9 (7.9%)	Not applicable
- CrCl 15-49ml/min	Not applicable	2 (3.1%)
- Age ≥ 80 years	1 (0.9%)	Not applicable
- CrCl 30-49ml/min +age ≥ 80 years	1 (0.9%)	Not applicable
Correct prescription		
All	**77 (68%)**	**55 (85%)**
Indications to be considered	**26 (23%)**	**12 (18%)**
- ≥ 2 indications	4 [a] (3.5%)	2 [b] (3.1%)
- HAS-BLED ≥ 3	0 (0%)	1 (1.5%)
- Age ≥ 75 years	4 (3.5%)	6 (9.2%)
- Antiplatelet drugs	5 (4.4%)	1 (1.5%)
- NSAIDs	3 (2.6%)	0 (0%)
- Amiodarone	9 (7.9%)	2 (3.1%)
- History of GI bleeding	0 (0%)	0 (0%)
- Weight ≤60kg	1 (0.9%)	0 (0%)
None of indications	**51 (45%)**	**43 (66%)**
Unknown appropriate prescriptions		
No data regarding CrCl or type of DHP-CCB	26 (23%)	8 (12%)

[a] *age ≥ 75 years + antiplatelets (2 patients), age ≥ 75 years + HAS-BLED ≥ 3 + amiodarone (2 patients)*
[b] *age > 75 years + APT + HAS-BLED > 3, HAS-BLED > 3 + NSAIDs*

CrCl - Creatinine Clearance, DHP-CCB – dihydropyridine calcium canal blockers, GI – gastrointestinal, NSAID - nonsteroidal anti-inflammatory drugs

Table S2. Detailed clinical characteristics of patients with atrial fibrillation treated with different oral antithrombotic regiments.

Variable	VKA (n=366)	NOAC (n=249)	APT (n=33)	Without OAT (n=43)	p
Demographics					
Age, years	67 [61-74]	68 [61-76]	73 [63-80]	68 [51-73]	0.07
Female [n (%)]	156 (43%)	110 (44%)	11 (33%)	17 (40%)	0.67
Site of patient inclusion [n (%)]					
Hospitalized	318 (87%)	233 (94%)	29 (88%)	40 (93%)	0.05
Outpatient/ office based	48 (13%)	16 (6.4%)	4 (12%)	3 (7.0%)	0.05
Atrial fibrillation [n (%)]					
First diagnosed	10 (2.7%) *n=365*	24 (9.6%) *n=248*	5 (15%)	2 (4.7%)	**<0.0001**
Paroxysmal	107 (29%) *n=365*	80 (32%) *n=248*	10 (30%)	20 (46%)	0.14
Long-standing persistent	38 (10%) *n=365*	20 (8.0%) *n=248*	1 (3.0%)	3 (7.0%)	0.43
Persistent	67 (18%) *n=365*	67 (27%) *n=248*	1 (3.0%)	5 (12%)	**0.001**
Permanent	143 (39%) *n=365*	57 (23%) *n=248*	16 (49%)	13 (30%)	**<0.0001**
Lone	18 (4.9%)	20 (8.0%)	3 (9.1%)	10 (23%)	**<0.0001**
EHRA I	168 (46%) *n=364*	93 (37%) *n=248*	18 (55%)	21 (49%)	0.08
EHRA II	115 (31%)	92 (37%)	8 (24%)	13 (30%)	0.31

	n=364	*n=248*			
EHRA III	76 (21%) *n=364*	63 (25%) *n=248*	6 (18%)	8 (19%)	0.58
EHRA IV	5 (1.4%) *n=364*	1 (0.4%) *n=248*	1 (3.0%)	1 (2.3%)	0.41
Concomitant cardiac diseases [n (%)]					
Hypertension	208 (57%) *n=364*	157 (64%) *n=247*	16 (49%) *n=32*	17 (40%)	**0.02**
CAD	135 (39%) *n=350*	80 (34%) *n=237*	21 (64%)	8 (21%) *n=39*	**0.001**
Previous MI	66 (19%) *n=350*	32 (14%) *n=237*	15 (46%)	5 (13%) *n=39*	**<0.0001**
Previous PCI/PTCA	65 (19%) *n=350*	28 (12%) *n=237*	12 (36%)	3 (7.7%) *n=39*	**0.001**
Previous CABG	17 (5.1%) *n=350*	8 (3.4%) *n=237*	2 (6.1%)	1 (2.6%) *n=39*	0.67
Angina	48 (14%) *n=350*	39 (17%) *n=247*	5 (15%)	2 (5.1%) *n=39*	0.29
Heart failure	201 (55%) *n=364*	107 (43%) *n=247*	24 (73%)	18 (42%)	**0.001**
NYHA III/IV	75 (21%) *n=364*	36 (15%) *n=247*	10 (30%)	10 (23%)	0.07
Valvular alterations moderate/severe	133 (36%) *n=359*	71 (29%) *n=245*	13 (39%) *n=32*	16 (37%)	0.30
Cardiomyopathy dilated	35 (9.6%) *n=364*	14 (5.6%) *n=245*	3 (9.1%)	3 (7.0%)	0.37

Cardiomyopathy hyperothtophic	11 (3.0%) *n=364*	2 (0.8%) *n=245*	0 (0%)	2 (4.7%)	0.15
Cardiomyopathy restrictive	0 (0%) *n=364*	0 (0%) *n=245*	0 (0%)	1 (2.3%)	**0.002**
Device therapy (PM/CRT/ICD)	88 (24%) *n=361*	27 (11%) *n=248*	7 (21%)	4 (10%) *n=39*	**<0.0001**
Concomitant non-cardiac diseases [n (%)]					
COBP	22 (6.3%) *n=364*	16 (6.4%)	5 (16%) *n=32*	3 (7.0%)	0.25
Hyperthyroidism	24 (6.7%) *n=358*	20 (8.1%) *n=247*	1 (3.0%)	6 (14%)	0.26
Hypothyroidism	41 (12%) *n=358*	24 (9.7%) *n=248*	3 (9.1%)	4 (9.3%)	0.88
Previous TBE	52 (14%) *n=363*	23 (9.2%)	3 (9.1%)	2 (4.7%)	0.08
Ischaemic stroke	35 (9.6%) *n=363*	14 (5.6%)	1 (3.0%)	1 (2.3%)	0.07
TIA	5 (1.4%) *n=363*	8 (3.2%)	1 (3.0%)	1 (2.3%)	0.63
Peripheral embolism	6 (1.6%) *n=363*	3 (1.2%)	1 (3.0%)	1 (2.3%)	0.84
Pulmonary embolism/DVT	10 (2.7%) *n=363*	1 (0.4%)	0 (0%)	0 (0%)	0.09
Haemorrhagic events	23 (6.0%) *n=364*	19 (7.6%) *n=248*	8 (24%)	6 (14%)	**0.001**
Current malignancy	4 (1.1%) *n=360*	2 (0.8%)	2 (6.1%)	2 (4.7%)	**0.03**

PAD	26 (7.2%) *n=359*	13 (5.3%) *n=244*	2 (6.2%) *n=32*	4 (9.3%)	0.71
CKD	55 (15%) *n=364*	38 (15%)	8 (24%)	7 (16%)	0.58
Diabetes mellitus	107 (30%) *n=361*	62 (25%) *n=247*	14 (42%)	10 (23%)	0.15
Hyper cholesterolemia	174 (49%) *n=357*	129 (53%) *n=242*	13 (41%) *n=32*	13 (35%) *n=37*	0.14
Smoking	112 (32%) *n=356*	73 (31%) *n=237*	11 (36%) *n=31*	18 (43%) *n=42*	0.46
None exercise	153 (47%) *n=328*	94 (50%) *n=188*	18 (55%) *n=32*	18 (47%) *n=38*	0.76
Exercise occasionally	118 (36%) *n=328*	64 (34%) *n=188*	9 (27%) *n=32*	12 (32%) *n=38*	0.76
Exercise regularly	51 (15%) *n=328*	26 (14%) *n=188*	5 (15%) *n=32*	6 (16%) *n=38*	0.98
Exercise intensely	6 (1.8%) *n=328*	4 (2.1%) *n=188*	0 (0%) *n=32*	2 (5.3%) *n=38*	0.43
Thromboembolic and bleeding risk					
CHA_2DS_2-VASc score	3 [2-4]	3 [2-4]	4 [3-6]	3 [1-3]	**0.01**
CHA_2DS_2-VASc score 0 [n (%)]	22 (6.0%)	16 (6.4%)	6 (18%)	5 (12%)	0.16
CHA_2DS_2-VASc score 1 [n (%)]	47 (13%)	36 (15%)	0 (0%)	10 (23%)	0.05
CHA_2DS_2-VASc score $\geq$2 [n (%)]	297 (81%)	197 (79%)	27 (82%)	28 (65%)	0.09

HAS-BLED score	1,5 [1-2]	1 [0-2]	2 [1-3]	1 [0-2]	**0.02**
HAS-BLED score 0 [n (%)]	54 (15%)	65 (26%)	2 (6.1%)	13 (30%)	0.31
HAS-BLED score 1-2 [n (%)]	242 (66%)	161 (65%)	19 (58%)	23 (54%)	**0.007**
HAS-BLED score $\geq$3 [n (%)]	70 (15%)	23 (9.2%)	12 (36%)	7 (16%)	**0.003**
Treatment [n (%)]					
ACE inhibitors	207 (57%) *n=364*	142 (57%)	17 (52%)	13 (32%) *n=41*	**0.02**
ARBs	65 (18%) *n=364*	50 (20%)	2 (6.1%)	5 (12%) *n=41*	0.2
Diuretics	220 (60%) *n=364*	138 (55%)	20 (61%)	14 (34%) *n=41*	**0.01**
Aldosterone blockers	140 (39%) *n=364*	67 (27%)	10 (30%)	12 (29%) *n=41*	**0.03**
Beta-blockers	308 (85%)	189 (76%)	31 (94%)	23 (58%) *n=40*	**<0.0001**
DHP-CCB	53 (14%) *n=364*	51 (20%)	5 (15%)	2 (4.7%) *n=41*	0.31
Non-DHP-CCB	6 (1.6%) *n=364*	8 (3.2%)	0 (0%)	0 (0%) *n=41*	0.32
Digoxin	66 (18%) *n=364*	24 (9.6%)	8 (24%)	3 (7.3%) *n=41*	**0.005**
Any antiarrhythmic	102 (28%) *n=364*	89 (36%)	4 (12%)	10 (23%) *n=41*	**0.01**

Statins	223 (61%) *n=364*	154 (62%)	21 (64%) *n=32*	9 (22%) *n=41*	**<0.0001**
Antiplatelet drugs	63 (17%)	18 (7.2%)			**<0.0001**

ACE - angiotensin-converting enzyme, AF - atrial fibrillation, APT – antiplatelet therapy, ARB - angiotensin receptor blocker, CABG - coronary artery bypass graft, CAD - coronary artery disease, CCB - calcium-channel blockers, CKD - chronic kidney disease, COBP - chronic obstructive pulmonary disease, CRT – cardiac resynchronization therapy, DHP - dihydropyridine, DVT - deep vein thrombosis, EHRA - European Heart Rhythm Association, ICD - implantable cardioverter defibrillator, MI - myocardial infraction, NOAC - non vitamin K antagonists oral anticoagulants, NYHA - New York Heart Association, OAT – oral antithrombotic treatment, PAD - peripheral artery disease, PCI - percutaneous coronary intervention, PM - pacemaker, PTCA - percutaneous transluminal coronary angioplasty, TBE - thromboembolic, TIA - transient ischemic attack, VKA - vitamin K antagonists

Table S3. Detailed clinical characteristics of patients with atrial fibrillation depending on the dose of dabigatran or rivaroxaban.

Variable	Rivaroxaban		Dabigatran		p
	Standard (n=65)	**Reduced (n=24)**	**Standard (n=114)**	**Reduced (n=46)**	
Demographics					
Age [years]	67 [62-73]	80 [75-84]	64 [57-71]	78 [70-83]	**<0.0001**
Female [n (%)]	26 (40%)	15 (63%)	44 (39%)	25 (54%)	**0.02**
Site of patient inclusion [n (%)]					
Hospitalized	63 (97%)	20 (83%)	107 (94%)	43 (93%)	0.14
Outpatient/ office based	2 (3.1%)	4 (17%)	7 (6.1%)	3 (6.5%)	0.14
Atrial fibrillation [n (%)]					
First diagnosed	6 (9.2%) *n=64*	2 (8.3%)	14 (12%)	2 (4.3%)	0.28
Paroxysmal	24 (37%) *n=64*	9 (38%)	34 (30%)	13 (28%)	0.61
Long-standing persistent	5 (7.7%) *n=64*	2 (8.3%)	11 (9.6%)	2 (4.3%)	0.47
Persistent	9 (14%) *n=64*	2 (8.3%)	43 (38%)	13 (28%)	**0.001**
Permanent	20 (31%) *n=64*	9 (38%)	12 (11%)	16 (35%)	**<0.0001**

Lone	4 (6.2%)	0 (0%)	14 (12%)	2 (4.3%)	0.15
EHRA [class]					
I	29 (45%)	9 (38%)	32 (28%)	23 (50%)	0.05
II	24 (37%)	9 (38%)	47 (41%)	12 (26%)	0.43
III	12 (18%)	6 (25%)	35 (31%)	10 (22%)	0.31
IV	0 (0%)	0 (0%)	0 (0%)	1 (2.2%)	0.18
Concomitant cardiac diseases [n (%)]					
Hypertension	44 (69%) *n=64*	13 (54%)	70 (61%) *n=113*	30 (65%)	0.57
CAD	24 (38%) *n=63*	12 (55%) *n=22*	24 (21%) *n=108*	20 (44%) *n=44*	**0.001**
Previous MI	5 (7.7%) *n=63*	6 (25%) *n=22*	10 (8.8%) *n=108*	11 (24%) *n=44*	**0.003**
Previous PCI/PTCA	5 (7.7%) *n=63*	5 (23%) *n=22*	9 (7.9%) *n=108*	9 (20%) *n=44*	**0.03**
Previous CABG	4 (6.3%) *n=63*	1 (4.5%) *n=22*	1 (0.9%) *n=108*	2 (4.3%) *n=44*	0.24
Angina	16 (25%) *n=63*	8 (36%) *n=22*	5 (4.4%) *n=108*	10 (22%) *n=44*	**<0.0001**
Heart failure	26 (40%) *n=64*	12 (50%)	47 (41%) *n=113*	22 (48%)	0.65
NYHA III/IV	8 (12%) *n=64*	6 (25%)	13 (11%) *n=113*	9 (20%)	0.17
Valvular alterations	21 (32%)	14 (58%)	20 (18%)	16 (35%)	**0.007**

moderate/severe	*n=64*		*n=111*		
Cardiomyopathy dilated	6 (9.5%) *n=63*	0 (0%)	6 (5.3%) *n=112*	2 (4.3%)	0.35
Cardiomyopathy hyperothtophic	0 (0%) *n=63*	1 (4.2%)	0 (0%) *n=112*	1 (2.2%)	0.11
Cardiomyopathy restrictive	0 (0%) *n=63*	0 (0%)	0 (0%) *n=112*	0 (0%)	1.00
Device therapy (PM/ICD/CRT)	7 (11%) *n=64*	3 (13%)	8 (7.0%)	9 (20%)	0.08
Concomitant non-cardiac diseases [n (%)]					
COBP	4 (6.2%)	2 (8.3%)	5 (4.4%)	5 (11%)	0.37
Hyperthyroidism	10 (15%)	0 (0%)	6 (5.3%)	4 (8.7%) *n=44*	0.04
Hypothyroidism	5 (7.7%)	5 (21%)	8 (7.0%)	6 (13%) *n=45*	0.21
Previous thromboembolic events	2 (3.1%)	1 (4.2%)	16 (14%)	4 (8.7%)	0.14
TIA	0 (0%)	1 (4.2%)	6 (5.3%)	1 (2.2%)	0.40
Peripheral embolism	0 (0%)	0 (0%)	3 (2.6%)	0 (0%)	0.34
Pulmonary embolism/DVT	1 (1.5%)	0 (0%)	0 (0%)	0 (0%)	0.42
Hemorrhagic events	4 (6.2%) *n=64*	2 (8.3%)	7 (6.1%)	6 (13%)	0.26

Current malignancy	1 (1.5%)	0 (0%)	1 (0.9%)	0 (0%)	0.81
PAD	5 (7.7%) *n=63*	1 (4.2%) *n=23*	6 (5.3%) *n=112*	1 (2.2%)	0.66
CKD	3 (4.6%)	5 (21%)	12 (11%)	18 (39%)	**<0.0001**
Diabetes mellitus	18 (28%)	8 (33%)	26 (23%) *n=112*	10 (22%)	0.66
Hyper-cholesterolemia	32 (49%) *n=63*	9 (38%) *n=23*	64 (56%) *n=112*	24 (52%) *n=44*	0.45
Smoking	20 (31%) *n=63*	3 (13%) *n=22*	38 (33%) *n=108*	12 (26%) *n=44*	0.11
None exercise	18 (40%) *n=45*	9 (56%) *n=16*	43 (48%) *n=90*	24 (67%) *n=37*	0.17
Exercise occasionally	18 (40%) *n=45*	3 (19%) *n=16*	34 (38%) *n=90*	9 (25%) *n=37*	0.32
Exercise regularly	9 (20%) *n=45*	3 (19%) *n=16*	10 (11%) *n=90*	4 (11%) *n=37*	0.43
Exercise intensely	0 (0%) *n=45*	1 (6.2%) *n=16*	3 (3.3%) *n=90*	0 (0%) *n=37*	0.32
Thromboembolic and bleeding risk					
CHA_2DS_2-VASc score	3 [2-4]	4 [3-5]	2 [1-4]	4 [3-5]	**<0.0001**
CHA_2DS_2-VASc score 0 [n (%)]	5 (7.7%)	0 (0%)	10 (8.8%)	1 (2.2%)	0.10

CHA_2DS_2-VASc score 1 [n (%)]	8 (12%)	0 (0%)	22 (19%)	6 (13%)	0.06
CHA_2DS_2-VASc score $\geq$2 [n (%)]	52 (80%)	24 (100%)	82 (72%)	39 (85%)	**0.003**
HAS-BLED score	1 [0-2]	2 [1-2]	1 [0-2]	2 [1-2]	**0.001**
HAS-BLED score 0 [n (%)]	23 (35%)	0 (0%)	39 (34%)	3 (6.5%)	**0.03**
HAS-BLED score 1-2 [n (%)]	39 (60%)	21 (88%)	68 (60%)	33 (72%)	**0.02**
HAS-BLED score $\geq$3 [n (%)]	3 (4.6%)	3 (13%)	7 (6.1%)	10 (22%)	**0.003**
Treatment [n (%)]					
ACE inhibitors	32 (49%)	17 (71%)	65 (57%)	28 (61%)	0.28
ARBs	19 (29%)	2 (8.3%)	19 (17%)	10 (22%)	0.10
Diuretics	36 (55%)	16 (67%)	53 (47%)	33 (72%)	**0.01**
Aldosterone blockers	19 (29%)	8 (33%)	25 (22%)	15 (33%)	0.40
Beta-blockers	51 (78%)	18 (75%)	82 (72%)	38 (83%)	0.70
DHP-CCB	16 (25%)	6 (25%)	22 (19%)	7 (16%)	0.66
Non-DHP-CCB	3 (4.6%)	1 (4.2%)	2 (1.8%)	2 (4.3%)	0.64
Digoxin	9 (14%)	5 (21%)	5 (4.4%)	5 (11%)	**0.03**
Any	21 (32%)	4 (17%)	49 (43%)	15 (33%)	0.09

antiarrhythmic					
Statins	35 (54%)	14 (58%)	69 (61%)	36 (78%)	**0.04**
Antiplatelet drugs	4 (6.2%)	1 (4.2%)	7 (6.1%)	6 (13%)	0.51

ACE - angiotensin-converting enzyme, AF - atrial fibrillation, APT – antiplatelet therapy, ARB - angiotensin receptor blocker, CABG - coronary artery bypass graft, CAD - coronary artery disease, CCB - calcium-channel blockers, CKD - chronic kidney disease, COBP - chronic obstructive pulmonary disease, CRT – cardiac resynchronization therapy, DHP - dihydropyridine, DVT - deep vein thrombosis, EHRA - European Heart Rhythm Association, ICD - implantable cardioverter defibrillator, MI - myocardial infraction, NYHA - New York Heart Association, *PAD* - peripheral artery disease, PCI - percutaneous coronary intervention, PM - pacemaker, PTCA - percutaneous transluminal coronary angioplasty, TIA - transient ischemic attack

Table S4. Antithrombotic (A) and no antithrombotic treatment (B) analysis of bleeding and stroke risk.

A)

		CHA2DS2-VASc score		
		0 (n=44)	1 (n=83)	≥2 (n=521)
HAS-BLED score	0	23 (52%)	39 (47%)	59 (11%)
	1-2	21 (48%)	42 (51%)	359 (69%)
	≥3	0 (0%)	2 (2.4%)	103 (20%)

B)

		CHA2DS2-VASc score		
		0 (n=5)	1 (n=10)	≥2 (n=28)
HAS-BLED score	0	4 (80%)	7 (70%)	2 (7.1%)
	1-2	1 (20%)	3 (10%)	19 (68%)
	≥3	0	0	7 (25%)

Table S5. Participating centers, investigators, and data collection officers.

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