Supplementary material

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Table S1. Analyzed ICD-10 codes

Ischemic events	I63, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, I74, I65, I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.8, I63.9, I67.8, I67.9, I64, I74.0, I74.1 K55.0, M31.1, N28.0, H34.1, G45.8, G45.9, G45,
Bleeding events	I85.0, I84.4, I98.3, K22.1, K25.4, K26.4, K27.0, K29.0, K29.7, K31.8, K92.0, K57.3, K57.9, K62.5, K92.1, K92.2, K25.0, K25.2, K25.6, K26.0, K26.2, K26.6, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.2, K29.3, K29.4, K29.5, K29.6, K29.8, K55.2, K57.0, K57.1, K57.2, K57.4, K57.5, K57.8, K22.6, K66.1, K76.2, K62.6, K63.3, I62.0, I62.9, I60 , I60.0, I60.1, I60.2, I60.3, I60.4, I60.5, I60.6, I60.7, I60.8, I60.9, I61, I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I62.1, I62, S06.4, S06.5, S06.6, D62, D68.3, D69.8, D69.9, H05.2, H11.3, H21.0, H31.3, H31.4, H35.6, H43.1, H44.8, H45.0, H47.0, H92.2, I23.0, I31.2, I71.3, J94.2, M25.0, M79.8, N02, N02.0, N02.1, N02.2, N02.3, N02.4, N02.5, N02.6, N02.7, N02.8, N02.9, N42.1, N42.1, N83.7, N85.7, N89.7, N92.0, N92.1, N92.3, N92.4, N92.5, N93, N93.0, N93.8, N93.9, N95.0, O71.7, R04, R04.0, R04.1, R04.2, R04.8, R04.89, R04.9, R23.3, R31, R31.0, R31.9, R58, R58 , S26.0, S27.1, T79.2, T81.0, Y60

Table S2. Comparison of academic and district hospital groups after propensity score matching.

Variable	Academic hospital (n=712)	District hospital (n=712)	*P* value
Demographics			
Age (years)	77 [68-81]	76 [68-82]	0.96
Females	358 (50%)	352 (49%)	0.79
Atrial fibrillation type			
Paroxysmal	332 (47%)	296 (42%)	0.06
Non-paroxysmal	380 (53%)	416 (58%)	
Comorbidities			
Heart failure	430 (60%)	437 (61%)	0.74
Hypertension	556 (78%)	534 (75%)	0.19
Coronary artery disease	436 (61%)	450 (63%)	0.48
Diabetes mellitus	242 (34%)	263 (37%)	0.27
History of TBEs	134 (19%)	129 (18%)	0.78
History of HEs	164 (23%)	174 (24%)	0.58
Laboratory parameters			
eGFR <50 ml/min	165 (23%)	189 (27%)	0.16
eGFR ≥50 ml/min	547 (77%)	523 (73%)	
Thromboembolic and bleeding scores			
CHA2DS2-VASc	5 [3-6]	5 [3-6]	0.91
HAS-BLED	2 [2-3]	2 [2-3]	0.23

Table S3. Multiple logistic regression analysis for thromboembolic (A) and hemorrhagic events (B) in patients treated in university vs district hospital.

A)

Variable	Univariable analysis		Multivariable analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
A) academic hospital				
Female	1.444 (1.062-1.964)	**0.02**	1.612 (1.168-2.226)	**<0.001**
Non-paroxysmal (vs paroxysmal AF)	1.218 (0.889-1.669)	0.22		
Heart failure	1.156 (0.840-1.592)	0.37		
Hypertension	1.153 (0.771-1.724)	0.49		
Coronary artery disease	1.423 (1.047-1.933)	**0.02**	1.279 (0.899-1.818)	0.17
Diabetes mellitus	1.051 (0.744-1.485)	0.78		
History of TEs	2.592 (1.807-3.718)	**<0.001**	2.434 (1.691-3.505)	**<0.001**
COPD	1.130 (0.638-1.999)	0.68		
eGFR<50ml/min	1.379 (0.954-1.994)	0.09		
Smoking	2.343 (1.319-4.162)	**<0.001**	2.582 (1.421-4.691)	**<0.001**
VKA (vs NOAC)	1.155 (0.838-1.592)	0.38		
Antiplatelet drugs	1.544 (1.058-2.253)	**0.02**	1.347 (0.875-2.075)	0.18
B) district hospital				
Female	1.217 (0.789-1.876)	0.37		
Non-paroxysmal (vs paroxysmal AF)	1.025 (0.661-1.590)	0.91		
Heart failure	0.794 (0.510-1.235)	0.31		
Hypertension	0.971 (0.590-1.597)	0.91		
Coronary artery disease	1.462 (0.914-2.339)	0.11		
Diabetes mellitus	1.310 (0.842-2.038)	0.23		
History of TEs	6.828 (4.280-10.893)	**<0.001**	6.828 (4.280-10.893)	**<0.001**
COPD	1.639 (0.978-2.745)	0.06		
eGFR<50ml/min	0.953 0.580-1.566)	0.85		
Smoking	0.580 (0.244-1.380)	0.22		
VKA (vs NOAC)	0.910 (0.582-1.423)	0.68		
Antiplatelet drug	0.756 (0.365-1.566)	0.45		

Abbreviations: AF, atrial fibrillation; CKD, chronic kidney disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NOAC, non-vitamin K oral anticoagulant; TIA, transient ischemic attack; VKA, vitamin K antagonist

B)

Variable	Univariable analysis		Multivariable analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
A) academic hospital				
Female	1.231 (0.975-1.556)	0.08		
Non-paroxysmal (vs paroxysmal AF)	0.960 (0.756-1.220)	0.74		
Heart failure	0.709 (0.548-0.917)	**<0.001**	0.535 (0.398-0.720)	**<0.001**
Hypertension	1.118 (0.829-1.508)	0.46		
Coronary artery disease	1.103 (0.873-1.393)	0.41		
Diabetes mellitus	1.138 (0.880-1.472)	0.32		
Ischemic stroke/TIA/ thromboembolism	1.225 (0.884-1.698)	0.22		
COPD	1.329 (0.878-2.012)	0.18		
eGFR<50ml/min	1.482 (1.112-1.974)	**<0.001**	1.606 (1.191-2.166)	**<0.001**
Smoking	0.518 (0.249-1.079)	0.08		
VKA (vs NOAC)	1.561 (1.215-2.005)	**<0.001**	1.709 (1.285-2.274)	**<0.001**
Antiplatelet drug	1.208 (0.890-1.639)	0.23		
B) district hospital				
Female	0.860 (0.568-1.300)	0.47		
Paroxysmal (vs non-paroxysmal AF)	1.152 (0.755-1.758)	0.51		
Heart failure	1.240 (0.803-1.914)	0.33		
Hypertension	1.017 (0.629-1.642)	0.95		
Coronary artery disease	2.350 (1.440-3.835)	**<0.001**	2.350 (1.440-3.835)	**<0.001**
Diabetes mellitus	1.343 (0.883-2.041)	0.17		
Ischemic stroke/TIA/ thromboembolism	1.377 (0.834-2.274)	0.22		
COPD	1.299 (0.776-2.176)	0.32		
eGFR<50ml/min	1.124 (0.709-1.780)	0.62		
Smoking	1.183 (0.612-2.286)	0.62		
VKA (vs NOAC)	1.198 (0.788-1.820)	0.40		
Antiplatelet drug	0.845 (0.432-1.653)	0.62		

Abbreviations: AF, atrial fibrillation; CKD, chronic kidney disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NOAC, non-vitamin K oral anticoagulant; TIA, transient ischemic attack; VKA, vitamin K antagonist

Table S4. Comparison of patients treated in academic and district hospitals with OAC aspect.

Variable	Academic hospital				P [1] value	District hospital				P [2] value
	Overall (n=2271)	**Rivaroxaban (n=576)**	**Dabigatran (n=285)**	**VKA (n=1410)**		**Overall (n=712)**	**Rivaroxaban (n=315)**	**Dabigatran (n=121)**	**VKA (n=276)**	
Demographics										
Age (years)	68 [61-78]	72 [64-80]	67 [59-77]	67 [60-76]	<0.001	76 [68-82]	77 [69-82]	72 [66-80]	77 [68-82]	0.007
Females	872 (38%)	246 (43%)	109 (38%)	517 (37%)	0.04	352 (49%)	174 (55%)	57 (47%)	121 (44%)	0.02
Atrial fibrillation type*										
Paroxysmal	1201 (56%) *n=2156*	309 (60%) *n=519*	157 (58%) *n=271*	735 (54%) *n=1366*	0.02	296 (42%)	158 (50%)	51 (42%)	87 (32%)	<0.001
Long-standing persistent	99 (4.6%) *n=2156*	8 (1.5%) *n=519*	10 (3.7%) *n=271*	81 (5.9%) *n=1366*	<0.001	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.25
Persistent	276 (13%) *n=2156*	69 (13%) *n=519*	42 (16%) *n=271*	165 (12%) *n=1366*	0.07	104 (15%)	30 (9.5%)	36 (30%)	38 (14%)	<0.001
Permanent	556 (26%) *n=2156*	69 (13%) *n=519*	42 (16%) *n=271*	165 (12%) *n=1366*	0.14	312 (44%)	127 (40%)	34 (28%)	151 (55%)	<0.001
Comorbidities										
Heart failure	748 (33%)	184 (32%)	86 (30%)	478 (34%)	0.40	437 (62%) *n=707*	197 (63%)	63 (53%) *n=119*	177 (65%) *n=273*	0.08
Hypertension	1829 (81%) *n=2269*	455 (79%)	232 (81%)	1142 (81%) *n=1408*	0.52	5334 (75%) *n=710*	234 (75%) *n=314*	94 (78%)	206 (75%) *n=275*	0.78
Coronary artery disease	916 (40%)	248 (43%)	97 (34%)	571 (41%)	0.04	450 (63%)	199 (63%)	63 (52%)	188 (68%)	0.01
Diabetes mellitus	591 (26%) *n=2267*	155 (27%)	61 (21%)	375 (27%) *n=1406*	0.16	263 (37%) *n=703*	119 (38%) *n=311*	33 (28%) *n=120*	111 (41%) *n=272*	0.04
History of TEs	294 (13%) *n=2270*	84 (15%)	38 (13%)	172 (12%) *n=1409*	0.35	129 (18%) *n=705*	73 (23%) *n=313*	20 (17%) *n=119*	36 (13%) *n=273*	0.006
History of bleeding	67 (3.0%)	22 (3.8%)	8 (2.8%)	37 (2.6%)	0.36	174 (25%) *n=710*	76 (24%)	22 (18%)	76 (28%) *n=274*	0.12
COPD	161 (7.1%) *n=2270*	57 (9.9%)	9 (3.2%)	95 (6.7%) *n=1409*	0.001	123 (17%) *n=708*	57 (18%) *n=314*	19 (16%) *n=120*	47 (17%) *n=274*	0.84
Smoking	94 (4.1%) *n=2268*	35 (6.1%)	13 (4.6%)	46 (3.3%) *n=1407*	0.02	71 (10%) *n=705*	22 (7.0%)	19 (16%) *n=120*	30 (11%) *n=270*	0.02
Laboratory parameters										
Hemoglobin (g/dl)	14 [13-15] *n=2258*	14 [13-15] *n=574*	14 [13-15]	14 [13-15] *n=1399*	0.005	NA	NA	NA	NA	NA
Platelet count (10^3/mm3)	204 [168-239] *n=2262*	205 [172-242] *n=574*	210 [174-248]	202 [166-237] *n=1403*	0.01	NA	NA	NA	NA	NA
eGFR $\geq$50 ml/min/1.73m2	1195 (73%) *n=1646*	404 (78%) *n=517*	184 (79%) *n=232*	607 (68%) *n=897*	<0.001	523 (74%) *n=710*	228 (74%) *n=314*	99 (83%) *n=120*	196 (71%)	0.05
Thromboembolic and bleeding scores										
CHA2DS2-VASc	3 [2-5]	4 [2-5]	3 [2-5]	3 [2-5]	<0.001	5 [3-6]	2 [2-3]	2 [1-3]	2 [2-3]	<0.001
HAS-BLED	2 [1-2]	2 [1-2]	2 [1-2]	2 [1-2]	0.007	2 [2-3]	5 [4-6]	4 [3-5]	5 [4-6]	0.08
Antithrombotic treatment										
Antiplatelet drugs	351 (16%)	68 (12%)	27 (9.5%)	256 (18%)	<0.001	84 (12%)	26 (8.3%)	7 (5.8%)	51 (18%)	<0.001
Other medications										
Beta-blockers	1907 (84%) *n=2270*	478 (83%)	230 (81%)	1199 (85%) *n=1409*	0.13	NA	NA	NA	NA	NA

Calcium channel blockers	524 (23%) *n=2270*	162 (28%)	68 (24%)	294 (21%) *n=1409*	0.002	NA	NA	NA	NA	NA
Antiarrhythmic drugs	392 (17%) *n=2269*	101 (18%)	50 (18%)	241 (17%) *n=1408*	0.97	119 (17%) *n=711*	62 (20%)	24 (20%) *n=120*	33 (12%)	0.02
RAS inhibitors	1848 (81%)	457 (79%)	225 (79%)	1166 (83%)	0.12	NA	NA	NA	NA	NA
Statins	1539 (68%)	397 (69%)	172 (60%)	970 (69%)	0.02	NA	NA	NA	NA	NA
Long-term outcomes										
MAEs	849 (37%)	203 (35%)	80 (28%)	566 (40%)	<0.001	379 (53%)	170 (54%)	46 (38%)	163 (59%)	<0.001
All-cause death	541 (24%)	129 (22%)	54 (19%)	358 (25%)	<0.001	287 (40%)	121 (38%)	35 (29%)	131 (47%)	0.002
TEs	178 (7.8%)	44 (7.6%)	18 (6.3%)	116 (8.2%)	0.54	95 (13%)	48 (15%)	12 (9.9%)	35 (13%)	0.31
HEs	3339 (15%)	77 (13%)	23 (8.1%)	239 (17%)	0.04	106 (15%)	51 (16%)	10 (8.3%)	45 (16%)	0.08

Number provided after in italic indicates the total number of patients available for that variable.

**The Bonferroni correction was applied to address the multiple comparison issue*.

Abbreviations: see Table 1

P [1] value for comparison between different anticoagulant regimens (vitamin K antagonist vs rivaroxaban vs dabigatran) within academic hospital conditions (*Chi-square test for categorical variables and Kruskal-Wallis test for continuous variables comparison)*

P [2] value for comparison between different anticoagulant regimens (vitamin K antagonist vs rivaroxaban vs dabigatran) within district hospital conditions (*Chi-square test for categorical variables and Kruskal-Wallis test for continuous variables comparison)*

Table S5. Primary outcome event rates and hazard ratios for the rivaroxaban and dabigatran (A) rivaroxaban and VKA (B) and dabigatran and VKA (C) cohorts, after propensity score matching.

A)	Major adverse event		All-cause death		Thromboembolic events		Haemorrhagic events	
	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)
District hospital (n=242)								
Rivaroxaban	0.859 [0.564-1.308]	44 (36%)	0.761 [0.566-1.245]	31 (26%)	0.936 [0.419-2.088]	12 (9.9%)	0.789 [0.319-1.951]	9 (7.4%)
Dabigatran	reference	46 (38%)	reference	35 (29%)	reference	12 (9.9%)	reference	10 (8.3%)
University hospital (n=570)								
Rivaroxaban	1.018 [0.748-1.385]	82 (29%)	0.878 [0.594-1.298]	47 (16%)	1.311 [0.712-2.416]	24 (8.4%)	1.183 [0.679-2.064]	27 (9.5%)
Dabigatran	reference	80 (28%)	reference	54 (19%)	reference	18 (6.3%)	reference	23 (8.1%)

B)	Major adverse event		All-cause death		Thromboembolic events		Haemorrhagic events	
	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)
District hospital (n=630)								
VKA	0.928 (0.752-1.145)	184 (58%)	0.858 (0.669-1.101)	130 (41%)	1.290 (0.890-1.871)	67 (21%)	**0.651 (0.428-0.989)***	39 (12%)
Rivaroxaban	reference	170 (54%)	reference	121 (38%)	reference	48 (15%)	reference	51 (16%)
University hospital (n=1152)								
VKA	1.040 (0.862-1.256)	246 (43%)	0.971 (0.766-1.231)	162 (28%)	0.981 (0.652-1.475)	52 (9.0%)	1.201 (0.893-1.616)	106 (18%)
Rivaroxaban	reference	203 (35%)	reference	129 (22%)	reference	44 (7.6%)	reference	77 (13%)

C)	Major adverse event		All-cause death		Thromboembolic events		Haemorrhagic events	
	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)	HR [95% CI]	n (%)
District hospital (n=121)								
VKA	**1.601 (1.094-2.342)***	68 (56%)	1.318 (0.848-2.051)	51 (42%)	1.181 (0.546-2.555)	14 (12%)	**2.308 (1.093-4.876)***	22 (18%)
Dabigatran	reference	46 (38%)	reference	35 (29%)	reference	12 (9.9%)	reference	10 (8.3%)
University hospital (n=285)								
VKA	1.142 (0.854-1.528)	117 (41%)	1.157 (0.815-1.543)	87 (31%)	1.072 (0.576-1.996)	23 (8.1%)	1.426 (0.847-2.402)	38 (13%)
Dabigatran	reference	80 (28%)	reference	54 (19%)	reference	18 (6.3%)	reference	23 (8.1%)

**(asterisk) means statistically significant difference between groups*

Abbreviations: CI, coincidence interval; HR, hazard ration; VKA, vitamin K antagonist