Supplementary Table 1. Baseline characteristics and medications in patients with and without creatinine clearance data

	Overall (n=7406)	CrCl (–) (n=1354)	CrCl (+) (n=6052)	P value*
Age, years	69.8±10.0	69.7±10.0	69.8±10.0	0.823
Female	2165 (29.2)	419 (30.9)	1746 (28.8)	0.125
Body weight, kg	62.4±12.8 [n=6432]	63.1±11.4 [n=380]	62.3±12.9	0.248
Renal function				
Serum creatinine, mg/dL	1.0±0.6 [n=6578]	0.9±0.4 [n=526]	1.0±0.6	0.098
CrCl, mL/min	68.3±27.7 [n=6052]	-	68.3±27.7	-
Type of atrial fibrillation				
Paroxysmal	2835 (38.3)	553 (40.8)	2282 (37.7)	
Persistent	1081 (14.6)	235 (17.4)	846 (14.0)	<0.001
Permanent	3490 (47.1)	566 (41.8)	2924 (48.3)	
Comorbidities				
Coronary artery disease	781 (10.5)	105 (7.8)	676 (11.2)	<0.001
Cardiomyopathy	634 (8.6)	87 (6.4)	547 (9.0)	0.002
HCM	264 (3.6)	33 (2.4)	231 (3.8)	0.013
DCM	370 (5.0)	54 (4.0)	316 (5.2)	0.060
COPD	131 (1.8)	15 (1.1)	116 (1.9)	0.041
Hyperthyroidism	131 (1.8)	29 (2.1)	102 (1.7)	0.249
Risk factors for stroke				
Heart failure	2055 (27.7)	303 (22.4)	1752 (28.9)	<0.001
Hypertension	4477 (60.5)	788 (58.2)	3689 (61.0)	0.061
Age (≥75 years)	2565 (34.6)	478 (25.3)	2087 (34.5)	0.567
Diabetes mellitus	1359 (18.3)	198 (14.6)	1161 (19.2)	<0.001
Stroke/TIA	1022 (13.8)	163 (12.0)	859 (14.2)	0.038
$CHADS_2$ score	1.7±1.2	1.6±1.2	1.7±1.2	<0.001
CHA_2DS_2-VASc score	2.8±1.6	2.6±1.6	2.8±1.6	<0.001
HAS-BLED score	1.5±1.0	1.4±1.0	1.5±1.0	<0.001
Heart rate, /min	72.5±13.2	72.4±13.5	72.5±13.1	0.905
Systolic BP, mmHg	126.0±16.2	126.1±15.2	126.0±16.4	0.689
Diastolic BP, mmHg	73.5±17.0	74.1±22.4	73.4±15.5	0.148
Warfarin	6404 (86.5)	1116 (82.4)	5288 (87.4)	<0.001
Dosage, mg/day	2.9±1.2	2.9±1.2	2.9±1.2	0.088
INR	1.91±0.49	1.92±0.49	1.90±0.49	0.205
TTR**, %	59.3±29.2 [n=6064]	59.3±29.8 [n=1068]	59.3±29.0 [n=4996]	0.965
Antiplatelet	1937 (26.2)	327 (24.2)	1610 (26.6)	0.063
Aspirin	1675 (22.6)	282 (20.8)	1393 (23.0)	0.082
Others	433 (5.8)	72 (5.3)	361 (6.0)	0.356
Warfarin+antiplatelet	1358 (18.3)	204 (15.1)	1154 (19.1)	<0.001

Data are number of patients (%) or mean±SD.

CrCl, creatinine clearance; HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; COPD, chronic obstructive pulmonary disease; CHADS$_2$, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and history of stroke or TIA; CHA$_2$DS$_2$-VASc, CHADS$_2$ components plus vascular disease (coronary artery disease), age 65–74 years, and female sex; HAS-BLED, hypertension (systolic BP ≥140 mmHg), abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR (episodes of INR ≥3.5), elderly (age >65 years), drugs (use of antiplatelets)/alcohol concomitantly; TIA, transient ischemic attack; BP, blood pressure; INR, international normalized ratio of prothrombin time; TTR, time in therapeutic range.

* Comparison between patients with and without CrCl data.

** Target INR was 2.0–3.0 (<70 years) or 1.6–2.6 (≥70 years).

Supplementary Table 2. Baseline characteristics of patients characterized by creatinine clearance and warfarin at baseline

	Creatinine clearance values											
	<30 mL/min			30–49.9 mL/min			50–79.9 mL/min			≥80 mL/min		
	W (−) (n=34)	W (+) (n=322)	P value*	W (−) (n=137)	W (+) (n=1064)	P value*	W (−) (n=322)	W (+) (n=2364)	P value*	W (−) (n=271)	W (+) (n=1538)	P value*
Age, years	82.1±8.7	79.6±7.8	0.078	78.8±7.3	77.5±6.3	0.028	70.1±7.5	70.8±6.9	0.093	58.3±9.7	61.6±8.9	<0.001
Female	13 (38.2)	168 (52.2)	0.122	54 (39.4)	427 (40.1)	0.872	104 (32.3)	660 (27.9)	0.102	47 (17.3)	213 (17.8)	0.871
CrCl, mL/min	20.2±7.3	22.0±6.5	0.137	40.7±5.6	41.4±5.6	0.177	65.5±8.6	64.6±8.3	0.057	103.1±26.7	100.4±20.4	0.056
Comorbidities												
Coronary artery disease	7 (20.6)	70 (21.7)	0.877	15 (10.9)	165 (15.5)	0.159	37 (11.5)	239 (10.1)	0.444	17 (6.3)	126 (8.2)	0.280
Cardiomyopathy	3 (8.8)	42 (13.0)	0.481	9 (6.6)	91 (8.6)	0.429	13 (4.0)	217 (9.2)	0.002	12 (4.4)	160 (10.4	0.002
COPD	1 (2.9)	4 (1.2)	0.423	5 (3.6)	38 (3.6)	0.963	5 (1.6)	48 (2.0)	0.563	0 (0.0)	15 (1.0)	<0.001
Hyperthyroidism	0 (0.0)	7 (2.2)	0.385	2 (1.5)	12 (1.1)	0.733	4 (1.2)	32 (1.4)	0.870	6 (2.2)	39 (2.5)	0.754
Risk factors for stroke												
Heart failure	18 (58.8)	205 (63.7)	0.219	40 (29.2)	422 (41.5)	0.006	47 (14.6)	619 (26.2)	<0.001	17 (6.3)	364 (23.7)	<0.001
Hypertension	20 (52.9)	214 (66.5)	0.372	91 (66.4)	694 (65.2)	0.782	185 (57.5)	1465 (62.0)	0.118	128 (47.2)	892 (58.0)	0.001
Age (≥75 years)	28 (82.4)	254 (78.9)	0.635	108 (78.8)	758 (71.2)	0.062	97 (69.9)	744 (31.5)	0.625	8 (3.0)	90 (5.9)	0.052
Diabetes mellitus	7 (20.6)	74 (23.0)	0.752	26 (19.0)	216 (20.3)	0.716	44 (13.7)	448 (19.0)	0.021	39 (14.4)	307 (20.0)	0.032
Stroke/TIA	10 (29.4)	55 (17.1)	0.077	20 (14.6)	198 (18.6)	0.252	21 (6.5)	364 (15.4)	<0.001	5 (1.8)	186 (12.1)	<0.001
CHADS$_2$ score	2.7±1.3	2.7±1.2	0.728	2.2±1.2	2.4±1.2	0.240	1.3±1.1	1.7±1.2	<0.001	0.7±0.8	1.3±1.1	<0.001
CHA$_2$DS$_2$-VASc score	4.3±1.5	4.4±1.4	0.694	3.7±1.4	3.9±1.4	0.087	2.5±1.4	2.9±1.4	<0.001	1.3±1.2	2.0±1.4	<0.001
HAS-BLED score	2.5±0.9	2.2±1.0	0.053	2.0±0.8	1.9±0.9	0.095	1.7±0.9	1.5±0.9	0.001	1.0±0.9	1.0±1.0	0.870
INR	-	1.89±0.52	-	-	1.92±0.53	-	-	1.90±0.47	-	-	1.90±0.49	-
TTR**, %	-	61.7±26.5 [n=299]	-	-	69.8±24.8 [n=997]	-	-	61.9±28.3 [n=2251]	-	-	47.5±29.5 [n=1449]	-
Antiplatelet use	24 (70.6)	99 (30.7)	<0.001	89 (65.0)	298 (28.0)	<0.001	200 (62.1)	500 (21.2)	<0.001	143 (52.0)	257 (16.7)	<0.001

Data are number of patients (%) or mean±SD.

W, warfarin; CrCl, creatinine clearance; COPD, chronic obstructive pulmonary disease; CHADS$_2$, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and history of stroke or TIA; CHA$_2$DS$_2$-VASc, CHADS$_2$ components plus vascular disease (coronary artery disease), age 65–74 years, and female sex; HAS-BLED, hypertension (systolic BP ≥140 mmHg), abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR (episodes of INR ≥3.5), elderly (age >65 years), drugs (use of antiplatelets)/alcohol concomitantly; TIA, transient ischemic attack; INR, international normalized ratio of prothrombin time; TTR, time in therapeutic range.

* Comparison between W (−) and W (+).

** Target INR was 2.0–3.0 (<70 years) or 1.6–2.6 (≥70 years).

Supplementary Table 3. Two-year event rates in patients with and without creatinine clearance data

	Overall (n=7406)	CrCl (–) (n=1354)	CrCl (+) (n=6052)	P value*
Thromboembolism	126 (1.7%)	17 (1.3%)	109 (1.8%)	0.198
Major hemorrhage	140 (1.9%)	22 (1.6%)	118 (1.9%)	0.494
All-cause death	195 (2.6%)	35 (2.6%)	160 (2.6%)	0.979
Cardiovascular death	68 (0.9%)	13 (1.0%)	55 (0.9%)	0.983
Composite events**	461 (6.2%)	74 (5.5%)	387 (6.4%)	0.224

Data are number of patients (%).

* Comparison between patients with and without CrCl data.

** Thromboembolism, major hemorrhage, and all-cause death.

Supplementary Table 4. Two-year event rates characterized by warfarin treatment at the time of events or the end of follow up period and creatinine clearance.

	Creatinine clearance values											
	<30 mL/min			30–49.9 mL/min			50–79.9 mL/min			≥80 mL/min		
	W (–) (n=48)	W (+) (n=308)	P value*	W (–) (n=170)	W (+) (n=1031)	P value*	W (–) (n=341)	W (+) (n=2325)	P value*	W (–) (n=322)	W (+) (n=1487)	P value*
Thromboembolism	0.0	2.3	0.291	5.3	2.3	0.028	3.8	1.7	0.009	1.9	0.7	0.039
Major hemorrhage	2.1	3.9	0.533	1.2	3.1	0.160	1.5	1.8	0.669	0.9	1.4	0.494
All-cause death	41.7	6.8	<0.001	15.9	3.1	<0.001	3.8	1.4	0.004	1.2	0.6	0.388
Cardiovascular death	14.6	2.6	<0.001	4.1	1.6	0.024	0.6	0.3	0.487	0.6	0.3	0.455
Composite events**	43.8	13.0	<0.001	22.4	8.5	<0.001	9.1	4.9	0.002	4.0	2.7	0.194

Data are % per 2 years.

W, warfarin.

* Comparison between W (–) and W (+).

** Thromboembolism, major hemorrhage, and all-cause death.

Supplementary Table 5. Sensitivity and specificity of cutoff creatinine clearance values for events

	Creatinine clearance values (mL/min)					
	<30		**<50**		**<80**	
	Sensitivity	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Thromboembolism	6.4%	94.1%	36.7%	74.5%	85.3%	30.2%
Major hemorrhage	21.2%	86.5%	39.8%	74.6%	79.7%	30.1%
All-cause death	25.6%	94.7%	62.5%	75.3%	91.9%	30.5%
Cardiovascular death	27.3%	94.3%	69.1%	74.7%	87.3%	30.0%
Composite events*	16.8%	94.1%	48.3%	75.8%	86.3%	31.0%

* Thromboembolism, major hemorrhage, and all-cause death.