

Supplementary Table 5. Grade Recommendation.

A. The quality of evidence for each outcome of RCTs assessed by GRADE framework.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	I-TA	PA	Relative (95% CI)	Absolute (95% CI)		
Mortality												
11	randomised trials	serious ^a	no serious	no serious	no serious	none	482/2874 (16.8%)	481/2745 (17.5%)	OR 0.93 (0.71 to 1.22)	10 fewer per 1000 (from 44 fewer to 31 more)	⊕⊕⊕O	CRITICAL
								8.2%		5 fewer per 1000 (from 22 fewer to 16 more)	MODERATE	
Major bleeding												
10	randomised trials	serious ^a	no serious	no serious	no serious	none	64/2790 (2.3%)	37/2703 (1.4%)	OR 1.73 (1.15 to 2.6)	10 more per 1000 (from 2 more to 21 more)	⊕⊕⊕O	CRITICAL
								1.2%		9 more per 1000 (from 2 more to 19 more)	MODERATE	
Thrombotic events												
6	randomised trials	serious ^a	no serious	no serious	no serious	none	81/2108 (3.8%)	127/2002 (6.3%)	OR 0.62 (0.46 to 0.83)	23 fewer per 1000 (from 10 fewer to 33 fewer)	⊕⊕⊕O	IMPORTANT
								8.9%		32 fewer per 1000 (from 14 fewer to 46 fewer)	MODERATE	
Pulmonary embolism												

3	randomised trials	serious ^a	no serious	no serious	serious ^b	none	8/539 (1.5%)	18/541 (3.3%)	OR 0.45 (0.19 to 1.05)	18 fewer per 1000 (from 27 fewer to 2 more)	⊕⊕OO LOW	IMPORTANT
								3.2%		17 fewer per 1000 (from 26 fewer to 2 more)		
Myocardial infarction												
2	randomised trials	serious ^a	no serious	no serious	serious ^b	none	13/539 (2.4%)	15/541 (2.8%)	OR 0.85 (0.4 to 1.79)	4 fewer per 1000 (from 16 fewer to 21 more)	⊕⊕OO LOW	IMPORTANT
								2.5%		4 fewer per 1000 (from 15 fewer to 19 more)		
Stroke												
2	randomised trials	serious ^a	no serious	no serious	serious ^b	none	1/402 (0.2%)	1/396 (0.3%)	OR 0.99 (0.14 to 7.12)	0 fewer per 1000 (from 2 fewer to 15 more)	⊕⊕OO LOW	IMPORTANT
								0.5%		0 fewer per 1000 (from 4 fewer to 30 more)		
Venous thromboembolism												
5	randomised trials	serious ^a	no serious	no serious	no serious	none	29/993 (2.9%)	47/1005 (4.7%)	OR 0.65 (0.37 to 1.16)	16 fewer per 1000 (from 29 fewer to 7 more)	⊕⊕⊕O MODERATE	IMPORTANT
								5.9%		20 fewer per 1000 (from 36 fewer to 9 more)		

I-TA = intermediate-to-therapeutic anticoagulation; PA = prophylactic anticoagulation; RCT = randomized controlled trial; OR = odds ratio, CI = confidence interval; a: mainly due to open label approach; b: low numbers of cases.

B. The quality of evidence for each outcome of Cohort studies assessed by GRADE framework.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	I-TA	PA	Relative (95% CI)	Absolute (95% CI)		
Mortality												
32	observational studies	no serious	no serious	no serious	no serious	none	1891/6688 (28.3%)	2383/12778 (18.6%)	OR 1.55 (1.27 to 1.9)	76 more per 1000 (from 39 more to 117 more)	⊕⊕⊕⊕ LOW	CRITICAL
								19.4%		78 more per 1000 (from 40 more to 120 more)		
Major bleeding												
19	observational studies	no serious	no serious	no serious	no serious	strong association ^a	223/3600 (6.2%)	185/7449 (2.5%)	OR 2.4 (1.96 to 2.94)	33 more per 1000 (from 23 more to 45 more)	⊕⊕⊕⊕⊕ MODERATE	CRITICAL
								3.3%		43 more per 1000 (from 30 more to 58 more)		
Thrombotic events												
10	observational studies	no serious	no serious	no serious	serious ^b	none	144/1438 (10%)	186/2621 (7.1%)	OR 1.4 (0.7 to 2.82)	26 more per 1000 (from 20 fewer to 106 more)	⊕⊕⊕⊕⊕ VERY LOW	IMPORTANT
								8%		29 more per 1000 (from 23 fewer to 117 more)		
Pulmonary embolism												
12	observational studies	no serious	no serious	no serious	serious ^b	none	83/1551 (5.4%)	93/3641 (2.6%)		25 more per 1000 (from 3 fewer to 87 more)	⊕⊕⊕⊕⊕ VERY LOW	IMPORTANT

								0.7%	OR 2.04 (0.86 to 4.84)	7 more per 1000 (from 1 fewer to 26 more)		
Myocardial infarction												
4	observational studies	no serious	no serious	no serious	serious ^{b, c}	none	15/686 (2.2%)	17/1819 (0.9%)	OR 2.83 (1.37 to 5.86)	17 more per 1000 (from 3 more to 43 more)	⊕○○○ VERY LOW	IMPORTANT
								0.7%		13 more per 1000 (from 3 more to 33 more)		
Stroke												
7	observational studies	no serious	no serious	no serious	serious ^c	none	9/944 (1%)	26/2283 (1.1%)	OR 0.77 (0.37 to 1.58)	3 fewer per 1000 (from 7 fewer to 6 more)	⊕○○○ VERY LOW	IMPORTANT
								2%		5 fewer per 1000 (from 13 fewer to 11 more)		
Venous thromboembolism												
11	observational studies	no serious	no serious	no serious	serious ^b	none	136/1517 (9%)	100/3482 (2.9%)	OR 2.09 (0.98 to 4.45)	29 more per 1000 (from 1 fewer to 88 more)	⊕○○○ VERY LOW	IMPORTANT
								2.5%		26 more per 1000 (from 0 fewer to 77 more)		

I-TA = intermediate-to-therapeutic anticoagulation; PA = prophylactic anticoagulation; RCT = randomized controlled trial; OR = odds ratio, CI = confidence interval; a: large effect value; b: large 95% CI; c: low numbers of cases.