Supplementary Table 2. Evidence profile for bleeding-related prognostic factors

No. of studies	Certainty assessment domains						Overall certainty in the evidence about this prognostic factor	Relative effect, OR (95% CI)
	Study design	Risk of bias	Indirect	Inconsistent	Imprecise	Publication bias		
History of peptic ulcer/GIB (yes vs. no) [19,23,24,28,30,39,41,45,47,48,50-52]								
13	Observational	Serious	Not serious	Serious	Not serious	Serious	⊕⊙⊙⊙ VERY LOW	5.26 (2.76–10.05)
Concomitant therapy with clopidogrel (yes vs. no) [19]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	2.37 (1–5.65)
HasBled-Score (≥ 3 vs. < 3) [19,41]								
2	Observational	Serious	Not serious	Serious	Serious	Undetected	⊕⊙⊙⊙ VERY LOW	1.20 (0.06–22.63)
Older age (yes vs. no) [19,23,24,28,33,36,45,47]								
8	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.95 (1.36–2.79)
Age: for each 1-year increase (yes vs. no) [40,51]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.03 (1.01–1.06)
Age: for each 5-year increase (yes vs. no) [50]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	1.11 (1.06–1.17)
Kidney disease (yes vs. no) [19,36,45,46,52]								
5	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.69 (1.24–2.31)
Combination of corticosteroid (yes vs. no) [19,41]								
2	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	2.14 (0.98–4.72)
Dabigatran dose (dabigatran 150 mg twice daily vs. warfarin) [21,35]								
2	Observational	Serious	Not serious	Serious	Not serious	Undetected	⊕⊕⊙⊙ LOW	1.53 (1.39–1.69)
Concomitant use of aspirin (yes vs. no) [22,23,26,27,47]								
5	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	2.07 (1.17–3.66)
INR (> 2.1 vs. ≤ 2.1; ≥ 4 vs. < 4) [24,41]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	INR > 2.1: 2.05 (1.00–4.20) INR < 4: 4.09 (1.17–14.27)
Cirrhosis (yes vs. no) [24,52]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	6.24 (2.63–14.83)
Obesity (weight > 120 vs. ≤ 120 kg) [25]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.44 (1.01–2.05)
Alcohol use (yes vs. no) [26,36]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	3.46 (2.30–5.19)

Supplementary Table 2. Continued

No. of studies	Certainty assessment domains						Overall certainty in the evidence about this prognostic factor	Relative effect, OR (95% CI)
	Study design	Risk of bias	Indirect	Inconsistent	Imprecise	Publication bias		
Smoking (yes vs. no) [26,50]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.26 (1.18–1.35)
Liver failure (yes vs. no) [26]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	7.01 (4.78–10.27)
Concomitant with NSAIDs: including paracetamol, COX-2 inhibitor (yes vs. no) [26,39,43,47]								
4	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	NSAIDs use: 2.37 (1.61–3.50) Paracetamol use: 1.47 (1.35–1.60) COX-2 inhibitor use: 1.97 (1.59–2.40)
Antiplatelet agent use (yes vs. no) [19,27,36,39,42,47,48,50,51]								
9	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.45 (1.11–1.90)
HF (congestive HF vs. no congestive HF; chronic HF vs. no chronic HF) [28,36,46]								
3	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	Any HF: 1.30 (1.14–1.49) Chronic HF: 1.31 (1.09–1.58) Congestive HF: 1.29 (1.06–1.57)
History of bleeding (yes vs. no) [28]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	History of bleeding: 3.26 (1.86–5.73)
Sex (male vs. female) [20,26,28,36,39,40,47]								
2	Observational	Serious	Not serious	Serious	Not serious	Undetected	⊕⊕⊙⊙ LOW	0.95 (0.72–1.26)
Myocardial infarction (yes vs. no) [28]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	2.23 (1.12–4.43)
Peripheral vascular disease: including peripheral artery disease (yes vs. no) [28,36]								
2	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	2.33 (0.66–8.20)
Concomitant use of dronedarone (yes vs. no) [29]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.29 (1.04–1.62)
Combination of CYP3A4 and/or P-gp-inhibitors (yes vs. no) [31]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.47 (1.15–1.88)
Oral glucocorticoid use (yes vs. no) [32]								
1	Observational	Serious	Not serious	Serious	Not serious	Undetected	⊕⊕⊙⊙ LOW	1.83 (1.30–2.59)

Supplementary Table 2. Continued

No. of studies	Certainty assessment domains						Overall certainty in the evidence about this prognostic factor	Relative effect, OR (95% CI)
	Study design	Risk of bias	Indirect	Inconsistent	Imprecise	Publication bias		
Renal failure (yes vs. no) [34,47]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	Total: 3.18 (1.44–6.99) GFR 50–80 mL/min /1.73 m^2: 2.95 (1.24–7.02) GFR ≤ 30 mL/min/1.73 m^2: 4.53 (0.68–30.14)
Coronary artery disease (yes vs. no) [36]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.36 (1.10–1.69)
Helicobacter pylori infection (yes vs. no) [36]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	4.75 (1.93–11.68)
Combination of digoxin (yes vs. no) [36]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.50 (1.19–1.88)
Combination of gemfibrozil (yes vs. no) [38]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	2.29 (1.61–3.25)
Creatinine level (per 1 mg/dL increase) (yes vs. no) [40]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.38 (1.09–1.74)
Creatinine clearance < 60 mL/min (yes vs. no) [50]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	1.06 (1.01–1.12)
Combination of verapamil or diltiazem (yes vs. no) [44]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	2.33 (1.82–2.98)
Mechanical valve implant (yes vs. no) [45]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	1.97 (0.43–9.07)
Substance abuse: defined as alcohol dependence, drug dependence, or non-dependent abuse, excluding tobacco use disorder (presence vs. absence) [46]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.41 (1.07–1.87)
Psychiatric illness: defined as schizophrenia, affective psychosis, paranoia, or other nonorganic psychosis (presence vs. absence) [46]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.20 (1.03–1.39)
Social risk factors: defined as lack of housing, inadequate housing, inadequate material resources, persons living alone, no other household member able to render care, or non-compliance with medical treatment [46]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.29 (1.12–1.48)

Supplementary Table 2. Continued

No. of studies	Certainty assessment domains						Overall certainty in the evidence about this prognostic factor	Relative effect, OR (95% CI)
	Study design	Risk of bias	Indirect	Inconsistent	Imprecise	Publication bias		
Liver disease (yes vs. no) [46]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	1.31 (0.99–1.74)
Venous thromboembolism: including deep vein thrombosis (yes vs. no) [36,46]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.21 (1.02–1.44)
Diabetes (yes vs. no) [36,46]								
2	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	1.08 (0.96–1.21)
Anticoagulant treatment time (≤ 100 vs. > 100 d) [47-49]								
3	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	4.94 (2.66–9.17)
Combination of thienopyridines use (yes vs no) [47]								
1	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	2.37 (0.75–7.44)
Long-term ASA use at screening (yes vs. no) [50]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.47 (1.26–1.72)
Anemia (yes vs. no) [36,50]								
2	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.48 (1.10–1.98)
Diastolic BP (for each 5 mmHg decrease to < 80 mmHg) (presence vs. absence) [50]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.10 (1.05–1.16)
History of sleep apnea (presence vs. absence) [50]								
1	Observational	Serious	Not serious	Not serious	Not serious	Undetected	⊕⊕⊕⊙ MODERATE	1.60 (1.22–2.10)
COPD (yes vs. no) [50,52]								
2	Observational	Serious	Not serious	Not serious	Serious	Undetected	⊕⊕⊙⊙ LOW	2.01 (0.69–5.83)

GRADE Working Group grades of evidence:

1. High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

2. Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

3. Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

4. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations:

1. Risk of bias: The retrospective enrollment of patients may have introduced classification bias, certainty in evidence was downgraded for risk of bias.

2. Certainty in evidence was downgraded for high heterogeneity.

3. Imprecise: Certainty in evidence was downgraded for imprecision, given that the 95% CI suggests that there may be no association.