**Supplementary material**

Supplemental Table 1. Characteristics of major bleeding events in patients with venous thromboembolism

|  |  |  |
| --- | --- | --- |
| Major bleeding site |  | % (n) |
|  Gastrointestinal |  | 36 (20) |
|  Intracranial |  | 18 (10) |
|  Intramuscular/compartment syndrome |  | 15 (8) |
|  Urogenital  |  | 13 (7) |
|  Retroperitoneal |  | 5 (3) |
|  Other\* |  | 13 (7) |
| ISTH major bleeding criteria |  |  |
|  Fatal bleedinga |  | 5 (3) |
|  Critical area or organb |  | 40 (22) |
|  Blood transfusionc ± hemoglobin falld | 55 (30) |

ISTH, International Society on Thrombosis and Haemostasis.

\*Pericardial, intra-abdominal and subcutaneous/intramuscular/hematoma.

aFatal outcome within one week after major bleeding, without other specified cause of death.

bIntracranial, retroperitoneal, pericardial and intramuscular with compartment syndrome.

cBleeding leading to transfusion of ≥ 2 units of whole blood or red cells.

dBleeding causing a fall in hemoglobin level of ≥20 g/L.

Supplemental Table 2.The one-year risk of major bleeding according to quartiles of platelet count measured at venous thromboembolism

diagnosis

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Quartiles of Platelet count (109/L)  | Major bleeding | IR (95% CI) | HR (95% CI)a | HR (95% CI)b | HR (95% CI)c | HR (95% CI)d |
| All VTE patients |  |  |  |  |  |  |
| ≤192  | 6 | 3.8 (1.7-8.6) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 193-239  | 15 | 9.2 (5.6-15.3) | 2.7 (1.0-6.9) | 2.7 (1.0-7.0) | 2.7 (1.0-7.0) | 2.6 (1.0-6.8) |
| 240-299  | 16 | 11.0 (6.7-17.9) | 3.1 (1.2-8.0) | 3.2 (1.2-8.2) | 3.3 (1.3-8.5) | 3.2 (1.2-8.2) |
| ≥300  | 18 | 12.8 (8.1-20.3) | 4.3 (1.7-10.9) | 4.4 (1.7-11.2) | 4.7 (1.8-12.0) | 4.3 (1.7-11.0) |
| p for trend |  |  | .002 | .002 | .001 | .002 |
| VTE patients without cancer |  |  |  |  |  |
| ≤192  | 5 | 4.1 (1.7-9.8) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 193-239  | 9 | 6.3 (3.3-12.2) | 1.9 (0.6-5.6) | 2.0 (0.7-5.9) | 2.0 (0.7-5.9) | 1.9 (0.6-5.7) |
| 240-299  | 9 | 7.2 (3.7-13.8) | 2.0 (0.7-6.1) | 2.1 (0.7-6.4) | 2.1 (0.7-6.5) | 2.1 (0.7-6.3) |
| ≥300  | 13 | 11.6 (6.8-20.0) | 4.0 (1.4-11.4) | 4.2 (1.5-12.1) | 4.3 (1.5-12.3) | 3.8 (1.3-11.1) |
| p for trend |  |  | .01 | .01 | .01 | .01 |

IR, incidence rate per 100 person-years; HR, hazard ratio; CI, confidence interval; SHR, sub-distribution hazard ratio.
aAdjusted for age and sex.

bAdjusted for age, sex, body mass index and planned duration of anticoagulant therapy.

cAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy and surgery.

dAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery and acute medical conditions (acute myocardial infarction, ischemic stroke, or major infectious disease).

Continued

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| HR (95% CI)e | HR (95% CI)f | HR (95% CI)g | HR (95% CI)h | SHR (95% CI)h |
|  |  |  |  |  |
| 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 2.4 (0.9-6.3) | 2.4 (0.9-6.3) | 2.2 (0.8-5.8) | 2.4 (0.9-6.3) | 2.5 (1.0-6.5) |
| 2.8 (1.1-7.3) | 2.8 (1.1-7.3) | 2.8 (1.0-7.3) | 2.8 (1.1-7.4) | 3.1 (1.2-8.0) |
| 3.9 (1.5-10.2) | 3.9 (1.5-10.2) | 3.6 (1.4-9.5) | 3.4 (1.3-8.8) | 3.2 (1.2-8.6) |
| .005 | .005 | .007 | .01 | .02 |
|  |  |  |  |  |
| 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 1.8 (0.6-5.4) | 1.8 (0.6-5.4) | 1.6 (0.5-5.0) | 1.8 (0.6-5.4) | 1.9 (0.6-5.7) |
| 1.5 (0.5-4.8) | 1.5 (0.5-5.0) | 1.6 (0.5-5.0) | 1.6 (0.5-5.2) | 1.8 (0.5-6.1) |
| 3.1 (1.0-9.2) | 3.0 (1.0-8.9) | 2.9 (1.0-8.6) | 2.8 (0.9-8.5) | 2.9 (0.9-9.5) |
| .05 | .07 | .07 | .08 | .09 |

eAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions and estimated glomerular filtration rate (eGFR).

fAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions, eGFR and hypertension (systolic blood pressure > 160 mmHg).

gAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions, eGFR, hypertension and
 history of bleeding (specifically noted in the medical records of VTE cases).

hAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions, eGFR, hypertension,
history of bleeding and anemia (hemoglobin level below 11.5 g/dL for women and below 13.0 g/dL for men at VTE diagnosis).

SHR denotes the HR after taking competing risk by death into account.

Supplemental Table 3. The one-year risk of major bleeding according to quartiles of platelet count measured at venous

thromboembolism diagnosis stratified by planned type of anticoagulant

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Quartiles of Platelet count (109/L)  | Major bleeding | IR (95% CI) | HR (95% CI)a | HR (95% CI)b | HR (95% CI)c | SHR (95% CI)c |
| Heparin and VKA (n=488) |  |  |  |  |  |
| ≤192  | 3 | 2.8 (0.9-8.6) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 193-239  | 9 | 7.4 (3.8-14.2) | 3.2 (0.9-12.0) | 3.3 (0.9-12.3) | 3.5 (0.9-13.0) | 3.4 (09-13.0) |
| 240-299  | 11 | 10.5 (5.8-19.0) | 4.1 (1.1-14.6) | 4.2 (1.2-15.0) | 3.1 (0.8-11.5) | 3.2 (0.8-12.3) |
| ≥300  | 10 | 10.0 (5.4-18.6) | 5.3 (1.4-19.5) | 5.4 (1.5-20.0) | 4.5 (1.2-17.1) | 4.4 (1.1-17.1) |
| p for trend |  |  | .008 | .007 | .04 | .03 |
| Heparin (n=145) |  |  |  |  |  |
| ≤192  | 1 | 4.1 (0.6-28.9) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 193-239  | 4 | 18.2 (6.8-48.4) | 5.2 (0.6-48.5) | 5.0 (0.5-47.5) | 3.4 (0.3-36.7) | 5.5 (0.7-43.3) |
| 240-299  | 2 | 10.7 (2.7-42.6) | 3.1 (0.3-35.5) | 3.2 (0.3-36.8) | 6.0 (0.4-92.8) | 5.3 (0.5-56.8) |
| ≥300  | 6 | 28.1 (12.6-62.6) | 6.8 (0.8-57.2) | 6.6 (0.8-55.0) | 4.1 (0.4-47.3) | 4.3 (0.6-31.0) |
| p for trend |  |  | .09 | .1 | .3 | .2 |

IR, incidence rate per 100 person-years; HR, hazard ratio; CI, confidence interval; SHR, sub-distribution hazard ratio; VKA, vitamin k antagonist.
\*Information on anticoagulation type was missing in 34 subjects.

aAdjusted for age and sex.

bAdjusted for age, sex, body mass index and planned duration of anticoagulant therapy.

cAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions (acute myocardial infarction,

 ischemic stroke, or major infectious disease), estimated glomerular filtration rate, hypertension (systolic blood pressure > 160 mmHg),
history of bleeding (specifically noted in the medical records of VTE cases), and anemia (hemoglobin level below 11.5 g/dL for women and below 13.0 g/dL for men at VTE diagnosis).

SHR denotes the HR after taking competing risk by death into account

Supplemental Table 4**.** The one-year risk of major bleeding according to quartiles of platelet count measured at venous

thromboembolism diagnosis after excluding subjectswith previous myocardial infarction or stroke

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Quartiles of Platelet count (109/L)  | Major bleeding | IR (95% CI) | HR (95% CI)a | HR (95% CI)b | HR (95% CI)c | SHR (95% CI)c |
| All VTE patients (n=613) |  |  |  |  |  |
| ≤192  | 5 | 4.1 (1.7-10.0) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| 193-239  | 11 | 7.8 (4.3-14.1) | 1.9 (0.7-5.6) | 2.0 (0.7-5.7) | 1.9 (0.6-5.5) | 2.0 (0.7-6.0) |
| 240-299  | 12 | 9.9 (5.6-17.4) | 2.4 (0.8-6.9) | 2.4 (0.9-7.0) | 2.4 (0.8-7.1) | 2.7 (0.9-8.1) |
| ≥300  | 16 | 13.2 (8.1-21.5) | 3.8 (1.4-10.5) | 3.9 (1.4-10.6) | 3.1 (1.1-8.7) | 2.9 (1.0-8.7) |
| p for trend |  |  | .006 | .005 | .03 | .04 |

IR, incidence rate per 100 person-years; HR, hazard ratio; CI, confidence interval; SHR, sub-distribution hazard ratio.
aAdjusted for age and sex.

bAdjusted for age, sex, body mass index and planned duration of anticoagulant therapy.

cAdjusted for age, sex, body mass index, planned duration of anticoagulant therapy, surgery, acute medical conditions (acute myocardial infarction,

 ischemic stroke, or major infectious disease), estimated glomerular filtration rate, hypertension (systolic blood pressure > 160 mmHg),
history of bleeding (specifically noted in the medical records of VTE cases), and anemia (hemoglobin level below 11.5 g/dL for women and below 13.0 g/dL for men at VTE diagnosis).

SHR denotes the HR after taking competing risk by death into account.