Supplementary Online Content

Goto S, Haas S, Ageno W, et al; GARFIELD-VTE Investigators. Assessment of outcomes among patients with venous thromboembolism with and without chronic kidney disease. JAMA Netw Open. 2020;3(10):e2022886. doi:10.1001/jamanetworkopen.2020.22886

eTable 1 Covariates Considered for the Adjustment of 12-Month Outcomes

eTable 2. Chronic Kidney Disease Classification Using the Modification of Diet in Renal Disease Equation and the Cockcroft Gault Calculation of Renal Function

eTable 3. Unadjusted 12-Month Clinical Outcomes

eTable 4. Cause of Death Over 12 Months of Follow-Up

eTable 5. Site of Major Bleeding in Patients With Moderate to Severe Chronic Kidney Disease and Mild to No Chronic Kidney Disease

eTable 6. Incidence Rates of Outcomes at 12 Months in Patients With Mild to No Chronic Kidney Disease and Moderate to Severe Chronic Kidney Disease According to Type of Lower Limb Deep Vein Thrombosis

eFigure 1. Spearman Correlation for Association Between Glomerular Filtration Rate and Creatinine Clearance Among Patients With Mild to No Chronic Kidney Disease and Moderate to Severe Chronic Kidney Disease

eFigure 2. Sensitivity Analysis for Standardized Differences Between Baseline Characteristics for Missing Patients and Patients Included in the Study

This supplementary material has been provided by the authors to give readers additional information about their work.

© 2020 Goto S et al. JAMA Network Open.
eTable 1. Covariates Considered for the Adjustment of 12-Month Outcomes

| Outcome                  | Covariates                                                                                                                                                                                                 |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| All-cause mortality      | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, prior episode of VTE, family history of VTE, history of cancer, chronic immobilization, chronic heart failure, renal insufficiency, surgery*, trauma of the lower limb*, acute medical illness*, hospitalization*, active cancer and recent bleeding or anemia. |
| Recurrent VTE            | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, prior episode of VTE, family history of VTE, history of cancer, oral contraception, known thrombophilia, chronic immobilization, renal insufficiency, surgery*, trauma of the lower limb*, acute medical illness*, hospitalization*, long-haul travel*, active cancer and recent bleeding or anemia. |
| Major bleeding           | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, prior episode of VTE, history of cancer, chronic immobilization, chronic heart failure, renal insufficiency, surgery*, acute medical illness*, hospitalization*, active cancer and recent bleeding or anemia. |
| Any bleeding             | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, prior episode of VTE, family history of VTE, history of cancer, oral contraception, hormonal replacement therapy, known thrombophilia, chronic immobilization, chronic heart failure, renal insufficiency, surgery*, trauma of the lower limb*, acute medical illness*, hospitalization*, long-haul travel*, active cancer, pregnancy or postpartum and recent bleeding or anemia. |
| Myocardial Infarction    | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, history of cancer, chronic immobilization, chronic heart failure, renal insufficiency, surgery*, acute medical illness*, hospitalization* and active cancer. |
| Stroke/TIA               | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, history of cancer, chronic heart failure, surgery*, hospitalization* and active cancer. |
| Cancer                   | Age, sex, ethnicity, BMI, tobacco, VTE type, Haemoglobin, Platelets, region, family history of VTE, history of cancer, chronic immobilization, renal insufficiency, surgery*, acute medical illness*, hospitalization*, active cancer and recent bleeding or anemia. |

*Within 3 months before VTE diagnosis
**eTable 2. Chronic Kidney Disease Classification Using the Modification of Diet in Renal Disease Equation and the Cockcroft Gault Calculation of Renal Function**

| CKD Stage | Modification of Diet in Renal Disease: GFR (ml/min) | n  | Cockcroft Gault: CrCl (ml/min) | n  |
|-----------|---------------------------------------------------|----|-------------------------------|----|
| None      | ≥90                                               | 6,924 | >50                           | 7,411 |
| 1 – Normal|                                                   |      |                               |     |
| 2 – Mild  | 60-89                                             |      |                               |     |
| 3 – Moderate | 30-59                                        | 2,055 | 30-49                         | 1,136 |
| 4 - Severe| 15-29                                             |      | 15-29                         |     |
| 5 - Failure| <15                                              |      | <15                           |     |

© 2020 Goto S et al. *JAMA Network Open.*
**eTable 3. Unadjusted 12-Month Clinical Outcomes**

| Event                          | Mild-to-no CKD (N = 6,924) | Moderate-to-severe CKD (N = 2,055) |
|--------------------------------|----------------------------|-----------------------------------|
|                                | Event rate (95% CI)        | Event rate (95% CI)               |
| All-cause mortality            | 425                        | 6.7 (6.1 to 7.3)                  |
|                                |                            | 234                               | 12.8 (11.3 to 14.5)              |
| Recurrent VTE                  | 311                        | 5.0 (4.5 to 5.6)                  |
|                                |                            | 115                               | 6.6 (5.5 to 7.9)                 |
| Major bleed                    | 153                        | 2.4 (2.1 to 2.8)                  |
|                                |                            | 82                                | 4.6 (3.7 to 5.7)                 |
| Any bleed                      | 653                        | 10.9 (10.1 to 11.8)               |
|                                |                            | 250                               | 14.8 (13.1 to 16.8)              |
| MI/ACS                         | 42                         | 0.7 (0.5 to 0.9)                  |
|                                |                            | 23                                | 1.3 (0.8 to 1.9)                 |
| Stroke/TIA                     | 37                         | 0.6 (0.4 to 0.8)                  |
|                                |                            | 17                                | 0.9 (0.6 to 1.5)                 |
| Cancer                         | 144                        | 2.3 (1.9 to 2.7)                  |
|                                |                            | 63                                | 3.5 (2.7 to 4.5)                 |

Event rates are shown per 100 person-year (95% confidence interval)
**eTable 4.** Cause of Death Over 12 Months of Follow-Up

| Cause of Death | Mild-to-no CKD, n (%) | Moderate-to-severe CKD, n (%) |
|----------------|----------------------|-----------------------------|
| Bleed          | 10 (2.4)             | 5 (2.1)                     |
| Cancer         | 254 (59.8)           | 104 (44.4)                  |
| Cardiac        | 21 (4.9)             | 21 (9.0)                    |
| VTE            | 21 (5.0)             | 9 (3.9)                     |
| Stroke         | 6 (1.4)              | 6 (2.6)                     |
| Other          | 70 (16.5)            | 50 (21.4)                   |
| Unknown        | 43 (10.1)            | 39 (16.7)                   |
| Total          | 425                  | 234                         |
**eTable 5. Site of Major Bleeding in Patients With Moderate to Severe Chronic Kidney Disease and Mild to No Chronic Kidney Disease**

| Site, n (%)                                      | Mild-to-no CKD (n=153) | Moderate-to-severe CKD (n=82) |
|-------------------------------------------------|------------------------|-------------------------------|
| GI upper                                        | 20 (13.1)              | 19 (23.2)                     |
| GI lower                                        | 20 (13.1)              | 15 (18.3)                     |
| Macroscopic hematuria                           | 10 (6.5)               | 4 (4.9)                       |
| Abnormal uterine (metorrhagia)                  | 16 (10.5)              | 3 (3.7)                       |
| Hemorrhagic stroke                              | 9 (5.9)                | 3 (3.7)                       |
| Intra peritoneal                                | 2 (1.3)                | 3 (3.7)                       |
| Hemopericardium                                 | 2 (1.3)                | 2 (2.4)                       |
| Hemoptysis                                      | 5 (3.3)                | 2 (2.4)                       |
| Intra-muscular (with compartment syndrome)      | 3 (2.0)                | 2 (2.4)                       |
| Intra-muscular (no compartment syndrome)        | 5 (3.3)                | 2 (2.4)                       |
| Intra-ocular/ Retinal                           | 5 (3.3)                | 2 (2.4)                       |
| Menorrhagia                                     | 9 (5.9)                | 2 (2.4)                       |
| Retro-peritoneal                                | 5 (3.3)                | 2 (2.4)                       |
| Puncture site                                   | 1 (0.7)                | 0 (0.0)                       |
| Skin (ecchymosis other than instrument site)    | 2 (1.3)                | 2 (2.4)                       |
| Gingival                                        | 1 (0.7)                | 1 (1.2)                       |
| Hemothorax                                      | 3 (2.0)                | 1 (1.2)                       |
| Intra-spinal                                    | 2 (1.3)                | 1 (1.2)                       |
| Intra-articular                                 | 2 (1.3)                | 1 (1.2)                       |
| Epistaxis                                       | 3 (2.0)                | 0 (0.0)                       |
| Other                                           | 24 (15.7)              | 10 (12.2)                     |
| Unknown                                         | 4 (2.6)                | 5 (6.1)                       |
**eTable 6. Incidence Rates of Outcomes at 12 Months in Patients With Mild to No Chronic Kidney Disease and Moderate to Severe Chronic Kidney Disease According to Type of Lower Limb Deep Vein Thrombosis**

| Outcome       | Type of LLDVT | Mild-to-no | Event rate (95% CI) | Moderate-to-severe | Event rate (95% CI) |
|---------------|---------------|------------|---------------------|--------------------|---------------------|
|               |               | n          |                     | n                  |                     |
| All-cause mortality | Distal    | 71         | 4.6 (3.6 to 5.8)    | 39                 | 10.2 (7.5 to 14.0)  |
|                | Proximal     | 127        | 7.9 (6.7 to 9.4)    | 81                 | 16.7 (13.4 to 20.7) |
|                | Both         | 61         | 4.9 (3.8 to 6.3)    | 46                 | 12.0 (9.0 to 16.0)  |
| Recurrent VTE  | Distal       | 80         | 5.3 (4.3 to 6.6)    | 17                 | 4.6 (2.9 to 7.4)    |
|                | Proximal     | 98         | 6.3 (5.2 to 7.7)    | 41                 | 8.9 (6.5 to 12.1)   |
|                | Both         | 54         | 4.5 (3.4 to 5.9)    | 25                 | 6.8 (4.6 to 10.1)   |
| Major bleed    | Distal       | 25         | 1.6 (1.1 to 2.4)    | 12                 | 3.2 (1.8 to 5.6)    |
|                | Proximal     | 41         | 2.6 (1.9 to 3.5)    | 21                 | 4.4 (2.9 to 6.8)    |
|                | Both         | 30         | 2.5 (1.7 to 3.5)    | 24                 | 6.4 (4.3 to 9.6)    |
**eFigure 1.** Spearman Correlation for Association Between Glomerular Filtration Rate and Creatinine Clearance Among Patients With Mild to No Chronic Kidney Disease and Moderate to Severe Chronic Kidney Disease

| Categories based on GFR                             | Categories based on CrCl                             |
|-----------------------------------------------------|-----------------------------------------------------|
| Mild-to-no CKD, n                                   | Moderate-to-severe CKD                              |
| Mild-to-no CKD                                      | 6,423                                               |
| Moderate-to-severe CKD                             | 988                                                 |
| Moderate-to-severe CKD/Mild-to-no CKD               | 154                                                 |
|                                                     | 982                                                 |

Scatterplot of GFR as a Function of CrCl. The diagonal line has slope 1. The four quadrants show the agreement (green and red) and disagreement (blue and purple) for CKD classification between the measures. Spearman’s rho statistic was used to estimate a rank-based association between GFR and CrCl (rho=0.75, p<0.001).
eFigure 2. Sensitivity Analysis for Standardized Differences Between Baseline Characteristics for Missing Patients and Patients Included in the Study

| Outcome                  | Adjusted HR (95% CI) | p-value |
|--------------------------|-----------------------|---------|
| All-cause mortality      | 1.52 (1.29 to 1.81)   | <0.001  |
| Recurrent VTE            | 1.45 (1.16 to 1.80)   | <0.001  |
| Major Bleeding           | 1.49 (1.11 to 1.99)   | 0.01    |

Moderate-to-severe vs. mild-to-no CKD.