A Patient on hemodialysis with Paroxysmal Atrial Fibrillation: Case Discussion

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Disclosure Information

Sagar Nigwekar, MD, MMSc

Disclosure of Relevant Financial Relationships

I have the following financial relationships to disclose:

- Consultant for: *Epizon Pharma, Fresenius Renal Therapies Group, Laboratoris Sanifit, Guidepoint*
- Speaker’s Bureau for: *None*
- Grant/Research support from: *Hope Pharmaceuticals, Duke University (RENAL-AF trial)*
Objectives

1. To discuss the relevance and risks of anticoagulation in hemodialysis

2. To review literature regarding novel anticoagulants in hemodialysis patients
Case presentation

- 67 year old man
- ESRD on peritoneal dialysis
- Diabetes mellitus, hypertension, coronary artery disease, atrial fibrillation (on chronic stable dose warfarin), temporal arteritis (on prednisone)
Calciphylaxis is a disorder of microvascular calcification and occlusion involving subcutaneous adipose tissue and dermis leading to painful skin lesions (50-80% one-year mortality).

Warfarin (vitamin K antagonist) is a risk factor for calciphylaxis (n=1030 cases; 2060 controls)

Demographic and clinical characteristics of calciphylaxis patients: Mayo Clinic experience (n=101)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 ± 14</td>
</tr>
<tr>
<td>Sex, female (%)</td>
<td>80</td>
</tr>
<tr>
<td>CKD, stage (%)</td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>68</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>54</td>
</tr>
<tr>
<td>Warfarin (%)</td>
<td>62</td>
</tr>
<tr>
<td>Hyperparathyroidism (%)</td>
<td>27</td>
</tr>
</tbody>
</table>

**Table 1. Risk Factors for Calciphylaxis.**

- End-stage renal disease
- Female sex
- Obesity
- Diabetes mellitus
- Hypercalcemia
- Hyperphosphatemia
- Hyperparathyroidism (both primary and secondary)
- Oversuppressed PTH with adynamic bone disease (low bone turnover)
- Elevated alkaline phosphatase
- Vitamin K deficiency
- Hepatobiliary disease
- Thrombophilia (e.g., antithrombin deficiency, protein C deficiency, or lupus anticoagulant)
- Autoimmune disorders (e.g., systemic lupus erythematosus)
- Hypoalbuminemia
- Metastatic cancers (e.g., colon or lung cancer)
- POEMS syndrome
- Genetic polymorphisms (e.g., rs4431401 and rs944348)
- Skin trauma (e.g., from subcutaneous injections)
- Recurrent hypotension
- Rapid weight loss
- Exposure to ultraviolet light
- Exposure to aluminum
- Medications (e.g., warfarin, calcium, vitamin D, iron, and recombinant PTH)

Vitamin K deficiency is more prevalent in dialysis-dependent calciphylaxis patients than in dialysis patients without calciphylaxis (n=20 cases; 20 controls).

Proposed pathogenesis of calciphylaxis - imbalance between calcification inhibitors and promoters.
Clinical questions

• Is anticoagulation indicated?

• Which anticoagulant agent? Dose?

• Duration of anticoagulation?

• Monitoring?

• Prevention and treatment of adverse effects?
Patients with CKD have increased risk of bleeding

Coagulation cascade

- Intrinsic system: XII → X → Xa
- Extrinsic system: tissue injury → tissue thromboplastin → VIIa → II

Platelet dysfunction

- Accumulation of anticoagulants in patients with renal failure

Anemia

- Reduced platelet vessel wall interaction
- Reduced ADP release/PGI2 inactivation
- Reduced scavenging of NO

Medications

- Prostaglandin metabolism
- Dysregulated arachidonic acid metabolism

Procedures

- Decreased function of GP IIb/IIIa
- Increased binding of vWF and fibrinogen
- Changed Ca++ metabolism

Platelets

- Activation of the fibrinolytic system

Vessel wall

- Increased expression of vWF and fibrinogen
- GP Ib reduced
- Increase of vasoactive substances (i.e., NO)
Patients with CKD have increased risk of thrombosis

- **Vascular endothelial alterations**
- **Increase in coagulation factors and anti-fibrinolytic proteins**
- **Platelet membrane alterations**
- **Hyperlipidemia**
Arterial thrombotic events

- Cerebrovascular disease
- Myocardial infarction
- Peripheral arterial disease
- Micro-vascular events
Venous thrombotic events

- Deep venous thrombosis
- Pulmonary embolism
- Access thrombosis
Anti-platelet therapy did not improve all cause mortality rate in CKD and dialysis patients.

Nat Rev Nephrol 2013
Anticoagulant agents

- Unfractionated heparin
- Low-molecular weight heparins
- Fondaparinux
- Warfarin
- Direct factor Xa inhibitors
- Direct thrombin inhibitors

LMW heparins include enoxaparin, dalteparin, and tinzaparin. Unfractionated heparin and LMW heparin inhibit both factor Xa and thrombin; the effect of LMW heparins on thrombin is less than that of unfractionated heparin. Fondaparinux is a synthetic pentasaccharide based on the minimal antithrombin-binding region of heparin that inhibits factor Xa. LMW heparins, unfractionated heparin, and fondaparinux inhibit clotting factors by binding to antithrombin.

Oral direct factor Xa inhibitors include apixaban, rivaroxaban, and edoxaban. Parenteral direct thrombin inhibitors include argatroban and lepirudin. Oral direct thrombin inhibitors include dabigatran. Coagulation factors are shown as Roman numerals. Only the activated forms (with the suffix "a") are shown for simplicity. Thrombin is also known as factor IIa.

LMW: low molecular weight.
Unfractionated heparin

-sulfated polysaccharide

-metabolized primarily in reticular endothelial system but has secondary renal clearance; hence, maximal dose in CKD at 60 units/kg for loading and 12 units/kg/hr for maintenance

-short half life- 30 to 150 minutes

-risk of major bleeding higher in CKD compared with enoxaparin; however, monitoring and reversibility is easily available

-limitations- HIT and osteopenia risks, monitoring requirement
Low molecular weight heparin

- Shorter heparin chains with greater affinity for factor Xa

- Advantages: less risk for HIT and osteopenia, predictable bioavailability, monitoring may not be necessary

- Renal clearance so dose adjustment necessary

- Underdosing is a concern

- Twice daily dosing with monitoring of anti-Xa is recommended
Monitoring anti-Xa levels with low molecular weight heparin

<table>
<thead>
<tr>
<th>Initial anti-Xa test</th>
<th>Pre-dose level (trough)</th>
<th>Before and after the third dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 hour post-dose (peak)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subsequent monitoring once in therapeutic range</strong></td>
<td>(Peak and trough) twice a week</td>
<td></td>
</tr>
</tbody>
</table>
| **Target anti-Xa level**             | Pre-dose level (trough)  
<0.1-0.3 IU/ml 2-4 hour post dose                                                        | 0.5-1 IU/ml (peak)              |
Warfarin

\[ \text{Target proteins} \]

\[ \gamma\text{-Carboxylated proteins:} \]
- Coagulation factors
- Inhibitors of coagulation
- Matrix-Gla Protein
- Growth arrest-specific protein 6

\[ \text{Vitamin K dependent carboxylase} \]

\[ \text{Reduced Vitamin K} \]

\[ \text{Oxidized Vitamin K} \]

\[ \text{Vitamin K} \]

\[ \text{Vitamin K quinone reductase} \]

\[ \text{Vitamin K epoxide reductase} \]

\[ \text{Inhibition by warfarin} \]
Warfarin

- narrow therapeutic index
- drug, food interactions
- lower dose in CKD: 10% dose reduction in CKD, 3 and 20% reduction in CKD, 4 and 5
- labile INR in CKD
- start low and go slow
Proportion of patients in different time-in-therapeutic ranges (TTR) across eGFR strata

Szummer et al. J Am Heart Assoc. 2017;6:e004925
Comparison between warfarin and different NOACs

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Mechanism of Action</th>
<th>$T_{1/2}$ (h)</th>
<th>Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin)</td>
<td>Vitamin K antagonist (factors II, VII, IX, and X)$^a$</td>
<td>25–60 (mean 40)$^b$</td>
<td>CYP450 2C9$^c$</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>Factor II (thrombin) inhibitor</td>
<td>12–14</td>
<td>P-gp</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>Factor Xa inhibitor</td>
<td>12</td>
<td>CYP450 3A4 P-gp</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>Factor Xa inhibitor</td>
<td>7–11</td>
<td>CYP450 3A4-P-gp</td>
</tr>
<tr>
<td>Edoxaban (Savaysa)</td>
<td>Factor Xa inhibitor</td>
<td>8–10</td>
<td>CYP450 3A4 P-gp</td>
</tr>
</tbody>
</table>

A. Apixaban
- Parent drug (87% bound)
- CYP3A4/5 and P-glycoprotein
- 6% cleared with dialysis
- Inactive metabolite (~50% in feces)
- 27% renal elimination

B. Rivaroxaban
- Parent drug (95% bound)
- CYP3A4/5 and CYP2J2 metabolized
- 51% inactive metabolite
- 7% feces
- 36% renal elimination

C. Dabigatran etexilate
- Dabigatran active (35% bound)
- 50-60% cleared with dialysis
- 80% renal elimination

D. Edoxaban
- Parent drug (55% bound)
- 10% metabolite
- 9% cleared with dialysis
- 40% bile elimination
- 50% renal elimination
Comparison between warfarin and NOACs

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Kidney Clearance (%)</th>
<th>Dose eCrCl≥51 ml/min</th>
<th>Dose eCrCl&lt;51–31 ml/min</th>
<th>Dose eCrCl&lt;31 ml/min and Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin)</td>
<td>0</td>
<td>INR 2–3</td>
<td>INR 2–3</td>
<td>INR 2–3</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>80</td>
<td>150 mg twice daily</td>
<td>150 mg twice daily&lt;sup&gt;d&lt;/sup&gt;</td>
<td>75 mg twice daily (eCrCl 30–15 ml/min)</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>25</td>
<td>5 mg twice daily</td>
<td>2.5 mg twice daily if 2 of 3 criteria&lt;sup&gt;f&lt;/sup&gt;</td>
<td>2.5 mg twice daily if 2 of 3 criteria&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>35</td>
<td>20 mg once daily</td>
<td>15 mg once daily</td>
<td>15 mg once daily (eCrCl 30–15 ml/min)</td>
</tr>
<tr>
<td>Edoxaban (Savaysa)</td>
<td>40</td>
<td>60 mg once daily&lt;sup&gt;g&lt;/sup&gt;</td>
<td>30 mg once daily</td>
<td>No</td>
</tr>
</tbody>
</table>

Comparison between warfarin and NOACs

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Approved Reversal Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin)</td>
<td>Yes: Vitamin K (oral or intravenous)</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>Yes: Idarucizumab (intravenous) e</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>Yes: Andexanet alfa (intravenous)</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>Yes: Andexanet alfa (intravenous)</td>
</tr>
<tr>
<td>Edoxaban (Savaysa)</td>
<td>Yes: Andexanet alfa (intravenous) h</td>
</tr>
</tbody>
</table>

CKD and atrial fibrillation

Shared risk factors
Age, male sex, obesity, smoking, low physical activity, hypertension, heart failure, CVD

Systemic processes
Inflammation, oxidative stress, fibrosis

Detection bias
More exposure to healthcare

Warfarin for atrial fibrillation in patients without CKD (pooled data from clinical trials; n=2,900)

- Reduction in
  - ischemic stroke by 67% (95% CI, 54–77),
  - all stroke (ischemic and hemorrhagic) by 64% (95% CI, 49–74)
  - all-cause mortality by 26% (95% CI, 3–43)

- The absolute increase in major extra-cranial hemorrhage less than the absolute reduction in strokes

- The number needed to treat for 1 year to prevent 1 stroke is 37
ARISTOTLE trial:
- Over 18,000 patients
- Atrial fibrillation with one risk factor for stroke
- Apixaban vs. warfarin (INR 2-3)

**A Primary Outcome: Stroke or Systemic Embolism**

Hazard ratio, 0.79 (95% CI, 0.66–0.95)  
\[ P=0.01 \]

<table>
<thead>
<tr>
<th>Months</th>
<th>Apixaban</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9120</td>
<td>9081</td>
</tr>
<tr>
<td>6</td>
<td>8726</td>
<td>8620</td>
</tr>
<tr>
<td>12</td>
<td>8440</td>
<td>8301</td>
</tr>
<tr>
<td>18</td>
<td>6051</td>
<td>5972</td>
</tr>
<tr>
<td>24</td>
<td>3464</td>
<td>3405</td>
</tr>
<tr>
<td>30</td>
<td>1754</td>
<td>1768</td>
</tr>
</tbody>
</table>

**B Major Bleeding**

Hazard ratio, 0.69 (95% CI, 0.60–0.80)  
\[ P<0.001 \]

<table>
<thead>
<tr>
<th>Months</th>
<th>Apixaban</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9088</td>
<td>9052</td>
</tr>
<tr>
<td>6</td>
<td>8103</td>
<td>7910</td>
</tr>
<tr>
<td>12</td>
<td>7564</td>
<td>7335</td>
</tr>
<tr>
<td>18</td>
<td>5365</td>
<td>5196</td>
</tr>
<tr>
<td>24</td>
<td>3048</td>
<td>2956</td>
</tr>
<tr>
<td>30</td>
<td>1515</td>
<td>1491</td>
</tr>
</tbody>
</table>
NOACs are non-inferior to warfarin in the general population in terms of their efficacy and have a superior safety profile.
What about non-dialysis dependent CKD patients?

- Risks vs. benefits?
Warfarin in patients with CKD, stage 3 (pooled data from clinical trials; n=516)

- Ischemic stroke/systemic embolism reduced by 76% (95% CI 42, 90) by adjusted-dose warfarin compared with aspirin/low-dose warfarin

- No difference in major hemorrhage

Efficacy and safety of NOACs versus warfarin in a subgroup of patients with moderate CKD from randomized controlled trials in atrial fibrillation
### CHADS2 score, thromboembolic risk, and effect of warfarin anticoagulation

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure (any history)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Hypertension</strong> (prior history)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Age ≥75 years</strong></td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td><strong>Secondary prevention in patients with a prior ischemic stroke or a transient ischemic attack; most experts also include patients with a systemic embolic event</strong></td>
<td>2</td>
</tr>
</tbody>
</table>
Clinical risk factors for stroke, transient ischemic attack, and systemic embolism in the CHA$_2$DS$_2$-VASc score

(A) The risk factor-based approach expressed as a point based scoring system, with the acronym CHA$_2$DS$_2$-VASc

(NOTE: maximum score is 9 since age may contribute 0, 1, or 2 points)

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc risk factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure&lt;br&gt;Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction</td>
<td>+1</td>
</tr>
<tr>
<td>Hypertension&lt;br&gt;Resting blood pressure $&gt;$140/90 mmHg on at least two occasions or current antihypertensive treatment</td>
<td>+1</td>
</tr>
<tr>
<td>Age 75 years or older</td>
<td>+2</td>
</tr>
<tr>
<td>Diabetes mellitus&lt;br&gt;Fasting glucose $&gt;$125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin</td>
<td>+1</td>
</tr>
<tr>
<td>Previous stroke, transient ischaemic attack, or thromboembolism</td>
<td>+2</td>
</tr>
<tr>
<td>Vascular disease&lt;br&gt;Previous myocardial infarction, peripheral artery disease, or aortic plaque</td>
<td>+1</td>
</tr>
<tr>
<td>Age 65-74 years</td>
<td>+1</td>
</tr>
<tr>
<td>Sex category (female)</td>
<td>+1</td>
</tr>
<tr>
<td>Letter</td>
<td>Clinical characteristic*</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>H</td>
<td>Hypertension (ie, uncontrolled blood pressure)</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function (1 point each)</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding tendency or predisposition</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs (for patients taking warfarin)</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (age greater than 65 years)</td>
</tr>
<tr>
<td>D</td>
<td>Drugs (concomitant aspirin or NSAIDs) or excess alcohol use (1 point each)</td>
</tr>
</tbody>
</table>
What about ESRD patients?

• Risks vs. benefits?
Receiver operating characteristic curves of CHADS2 and CHA2DS2-VASc scores in predicting ischemic stroke in patients with ESRD
Warfarin use and the risk for stroke in patients with atrial fibrillation undergoing dialysis

Warfarin use and the risk for bleeding in patients with atrial fibrillation undergoing dialysis

Thrombosis and bleeding rate in ESRD patients initiated on subcutaneous enoxaparin or heparin for thromboprophylaxis (n=7,721)

![Graph showing event rates for serious bleeding and thrombosis with comparison between enoxaparin and heparin.]

- **Serious bleeding**
  - Enoxaparin: Event rate of 15 (95% CI: 12-18)
  - Heparin: Event rate of 15 (95% CI: 12-18)
  - P-value: 0.59

- **Thrombosis**
  - Enoxaparin: Event rate of 5 (95% CI: 4-6)
  - Heparin: Event rate of 5 (95% CI: 4-6)
  - P-value: 0.34
Dabigatran and rivaroxaban in hemodialysis patients associated with significant risk of bleeding (n= 29997)

6% of dialysis patients were started on dabigatran or rivaroxaban with a statistically significant 48% and 38% increased risk for serious bleeding referent to warfarin.

*Chan et al. Circulation. 2015;131:972-979*

Kaplan–Meier curves for the apixaban group and a prognostic score–matched warfarin cohort

Association estimates from dose-specific comparisons of apixaban versus warfarin

Comparison of the pharmacokinetic parameters at steady state (i.e., after 8 days of apixaban administration) achieved with the reduced dose (2.5 mg twice daily) and with the standard dose (5 mg twice daily) of apixaban

Mavrakanas et al. JASN doi:10.1681/ASN.2016090980
Guidelines

KDIGO Controversies Conference, 2018

CKD, stages 1, 2 and 3

- NOACs non-inferior to warfarin in terms of efficacy and likely superior (or comparable) to warfarin in terms of safety

CKD, stages 4, 5 and 5D

- Efficacy and safety of anticoagulation not established
- No high quality evidence regarding comparison between among different anticoagulant agents

# Recommendations for discontinuation of novel anticoagulants prior to elective procedures

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Apixaban–Edoxaban–Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. $\geq 12$ or 24 h after last intake)</td>
<td></td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl $\geq 80$ mL/min</td>
<td>$\geq 24$ h</td>
<td>$\geq 24$ h</td>
</tr>
<tr>
<td>CrCl 50–80 mL/min</td>
<td>$\geq 36$ h</td>
<td>$\geq 72$ h</td>
</tr>
<tr>
<td>CrCl 30–50 mL/min$^a$</td>
<td>$\geq 48$ h</td>
<td>$\geq 96$ h</td>
</tr>
<tr>
<td>CrCl 15–30 mL/min$^a$</td>
<td>No official indication</td>
<td>No official indication</td>
</tr>
<tr>
<td>CrCl $&lt; 15$ mL/min</td>
<td>No official indication for use</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>There is no need for bridging with LMWH/UFH</td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CrCl*: creatinine clearance; *LMWH*: low-molecular-weight heparin; *UFH*: unfractionated heparin.

*For CrCl $< 15$ mL/min, no official indication for use.*

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Summary: Do’s and Don’ts

• Active participation in anticoagulation decisions for CKD patients
  – Assess indication
  – Assess the risk for adverse events
  – Assess renal elimination issues
  – Understand the duration of anticoagulation and monitoring

• Management of adverse effects
  – Reversal
  – Discontinuation
Current evidence on oral anticoagulant therapy for patients with atrial fibrillation across the spectrum of chronic kidney disease

<table>
<thead>
<tr>
<th>Indication for oral anticoagulation as stroke prevention in AF (if risk factor[s] present)</th>
<th>RCT(s) in the general population: Broad evidence that OAT reduces stroke risk</th>
<th>Cohort studies: Contradictory data and potentially more strokes in CKD stage G5 with OAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy and safety of NOACs versus vitamin K antagonists (VKA)</td>
<td>RCT: NOACs noninferior (in some cases superior) to VKAs</td>
<td>RCT initiated Results not yet available in 2017 Mind potential risk of accumulation of NOAC</td>
</tr>
<tr>
<td>Association between stroke risk and renal function in AF</td>
<td>Risk of stroke and systemic embolism</td>
<td></td>
</tr>
<tr>
<td>Association between bleeding risk and renal function in AF</td>
<td>Bleeding risk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prevalence of atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>NKD CKD G1 CKD G2</td>
<td>CKD G3a CKD G3b CKD G4 CKD G5</td>
<td></td>
</tr>
</tbody>
</table>

Kidney International 2017
Anticoagulation is a shared decision between patients and physicians


---

**Step 1:** Elicit patient's values, preferences, and goals

**Step 2:** Determine individual baseline risk of stroke and bleeding

**Step 3:** Compare benefit in stroke prevention and risk of bleeding anti-coagulation

**Step 4:** Discuss how anticoagulation modifies the risk: benefit of stroke and bleeding

---

Patient wishes to have anticoagulation
- Communicate with family members
- Close loop with other providers

Patient wishes not to have anticoagulation
- Communicate with family members
- Close loop with other providers

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Thank you