11
CHAPTER

CONSIDERATIONS IN SPECIAL POPULATIONS

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INTRODUCTION

It is widely known that giving various patient populations the same dose of the same drug may lead to different treatment outcomes. Differences in dose and response relationships of anticoagulants within various populations may lead to a decreased thromboembolic effect or increased rates of bleeding. The "one dose fits all" strategy may not be appropriate for all patient populations. Independently, these special populations can have risks for bleeding or thrombosis. This chapter will outline special patient populations in renal dysfunction, hepatic dysfunction, elderly, obesity, low body weight, and malignancy.

RENAL IMPAIRMENT[1-5]

- The majority of anticoagulant agents are partially or fully eliminated by the kidneys.
- Patients with renal impairment may be at risk for drug accumulation and increased rates of bleeding, and the clinician can play a significant role in recommending alternative agents or recommend dose adjustments.
- The majority of data concerning anticoagulants in renal disease are in patients with stable chronic kidney disease, and data are limited regarding the use of anticoagulants in patients with altering degrees of renal impairment because this population was frequently excluded.
- None of the agents has been formally studied in patients with end-stage renal disease (ESRD) for their U.S. Food and Drug Administration (FDA)-approved indications, and patients generally were excluded from clinical trials involving direct-acting oral anticoagulants (DOACs) with a creatinine clearance (CrCl) <25–30 mL/min.
- In general, as CrCl decreases, bleeding rates increase with anticoagulant therapy. Renal failure is also associated with drivers for both thrombosis and bleeding (**Table 11-1**). Other factors less expressive in normal renal function can accumulate to exert influence (e.g., plasminogen activator inhibitor [PAI-1]).
- CrCl should be calculated using the Cockcroft-Gault equation using actual body weight in accordance with the majority of clinical trials; however, use caution in morbidly obese patients since they weren't commonly represented in clinical trials.
- Studies and recommendations for CrCl <30 mL/min may not have included patients requiring renal replacement therapy, for which dosing should be separately considered.
- Anticoagulant dosing is specifically impacted by both indication and renal function (**Tables 11-2**, **11-3**, **11-4**, **11-5**, **11-6**, and **11-7**).

TABLE 11-1: Examples of Factors Influencing Hypercoagulable or Hemorrhagic Risk in Renal Failure

Drivers for Thrombosis

- Increased
  - PAI-1, vWF, homocysteine, fibrinogen, clotting factors, tissue factor expression, antiphospholipid antibodies
- Decreased
  - Antithrombin, protein C and S, p-selectin, phosphatidylserine
- High Hgb with ESA use
- Prothrombotic microparticles
- Hemodialysis-induced platelet aggregation
- Endothelial changes
- History of thrombotic event
- Factors associated with stroke in the setting of atrial arrhythmias
- Inadequate prophylaxis during acute risk periods (acute illness)
- Heparin-induced thrombocytopenia (HIT)
- Nephrotic syndrome
- Graft thrombosis
  - Low albumin
  - Shear stress
  - Stenosis
  - Blood stasis

Drivers for Bleeding

- Systemic anticoagulation
- Excessive anticoagulation (including excessing dosing as elimination declines, drug interactions)
- Antiplatelet therapy
- Recent use of systemic thrombolytic agent
- Anemia (hereditary and acquired), frequent blood draws
- Impaired platelet function (uremia, oxidative, and mechanical stress)
- Vascular tone modulation (increased NO and prostacyclin, inflammation)
- Dialysis circuit (sheer wall stress by dialyzer on platelets)
- Severe hypocalcemia
- Increased fibrinogen fragments
- Defect in vWF
- Advanced age
- Poorly controlled high blood pressure
- History of bleeding events
- Trauma, increased risks for traumatic events

ESA: erythrocyte-stimulating agent, HgB: hemoglobin, NO: nitrous oxide, PAI-1: plasminogen activator inhibitor – 1, vWF: von Willibrand factor