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Dose Adjustment of Direct Oral Anticoagulants in Elderly Institutionalized Patients

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Name of Author:
Claudia L.G., Virginia S.A., Jesica N.R., Alicia C.G., Maria Jose N.V., Ricardo Z.M., Yared G.P. and Maria Teresa B.S.

Corresponding Author:
Claudia L.G.

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Abstract: Direct oral anticoagulants (DOACs) have transformed anticoagulation therapy in elderly populations due to predictable pharmacokinetics and less stringent monitoring. However, elderly institutionalized patients present particular challenges, including frailty, multiple comorbidities, altered pharmacodynamics, renal impairment, polypharmacy, and risk of bleeding. This article reviews the principles, evidence, and practical considerations for the optimal dose adjustment of DOACs—apixaban, rivaroxaban, dabigatran, and edoxaban—in elderly residents of long-term care facilities.

Keywords: Direct Oral Anticoagulants (DOACs), Elderly Patients, Dose Adjustment, Long-Term Care Facilities, Bleeding Risk.

INTRODUCTION

Atrial fibrillation and venous thromboembolism are particularly prevalent among the institutionalized elderly, making anticoagulation common. The risk-benefit balance for DOACs in this group is sensitive to dosing errors, with both over- and under-dosing associated with serious adverse events. Dose adjustments are essential due to age-associated changes in renal and hepatic function, body weight, and a high prevalence of drug–drug interactions.

PHARMACOLOGICAL OVERVIEW OF DOACS

- **Apixaban** (Factor Xa inhibitor)
- **Rivaroxaban** (Factor Xa inhibitor)
- **Dabigatran** (Direct thrombin inhibitor)
- **Edoxaban** (Factor Xa inhibitor)

All DOACs are partially eliminated renally, to a variable extent, and all have potential interactions with P-glycoprotein and CYP3A4-modifying drugs.

Agent	% Renal Excretion	Key Considerations in Elderly
Apixaban	27	Flexible dosing, safest in renal impairment
Rivaroxaban	33	Once daily, avoid in severe renal impairment
Dabigatran	80	Highest renal excretion, not preferable if CrCl <30 mL/min
Edoxaban	50	Contraindicated if CrCl >95 or <15 mL/min

Physiology and Risk Factors in the Institutionalized Elderly

- **Decreased renal function:** Reduced GFR common and may fluctuate rapidly, especially with acute illness and dehydration.
- **Low body weight:** Both an independent risk for bleeding and impacts dosing thresholds.
- **Drug interactions:** Polypharmacy increases chances of contraindicated or interactive agents.
- **Frailty, cognitive and swallowing difficulties, risk of falls:** Increased bleeding risk and adherence challenges.

DOSE ADJUSTMENT: GUIDELINE OVERVIEW

Main Factors

1. **Renal Function:** Dosage should be adjusted based on creatinine clearance (CrCl), calculated ideally using the Cockcroft–Gault formula. The Cockcroft–Gault equation is routinely recommended despite chronic comorbidity and muscle-wasting potentially complicating accuracy in the elderly[1][2].
2. **Age & Body Weight:** Most agents have dose-reduction cutoffs for advanced age (≥80 years) and low body weight (<60kg)[3].
3. **Drug–Drug Interactions:** Caution with strong P-gp/CYP3A4 inhibitors or inducers.
4. **Clinical Status:** Changes in hydration, acute illness, or other organ dysfunctions require re-evaluation.

Dose Adjustments for Common DOACs in Elderly

Drug	Standard Dose	Reduced Dose & Criteria
Apixaban	5mg BID	2.5mg BID if ≥80y AND/OR Cr ≥1.5mg/dL AND/OR weight ≤60kg (if ≥2 criteria met)[2][3]
Rivaroxaban	20mg QD w/food	15mg QD if CrCl 15–49ml/min; Avoid <15ml/min[2]
Dabigatran	150mg BID	110mg BID if ≥80y or high bleeding risk; Avoid CrCl <30ml/min[4]
Edoxaban	60mg QD	30mg QD if CrCl 15–50ml/min or weight ≤60kg; Avoid <15ml/min[2]

Note: Dose reductions outside these criteria ("off-label underdosing") increase thrombotic risk without clear bleeding benefit[5][6].

CLINICAL EVIDENCE AND REAL-WORLD DATA

Adherence to Dose Guidance

- Inappropriate dosing (especially underdosing) is common, seen in up to 25% of elderly patients on DOACs, more frequent with advancing age, renal impairment, and higher comorbidity[7].
- Underdosing correlates with increased rates of stroke and does not necessarily reduce bleeding risk[5][6].

Age-Stratified Outcomes

- Patients aged ≥85 have higher rates of both thrombotic events and major bleeds within the first year after DOAC initiation versus those 75–84 years old, regardless of label-based dosing[5].
- Chronic kidney disease, polypharmacy, prior bleeding, and the absence of a caregiver have been independently associated with increased adverse events in this group.

Risk of Renal Function Decline

- DOACs in elderly patients may be associated with smaller long-term renal function declines compared to warfarin, but ongoing monitoring is critical[8][9].

PRACTICAL MANAGEMENT IN INSTITUTIONS

Best Practices:

- Baseline & periodic renal function assessment (at least annually, or more frequently if instability expected)[2][1].
- Weight monitoring and nutritional assessment to catch body habitus changes.
- Regular medication review for drug–drug interactions.
- Vigilance for AKI (dehydration, infection).

Dosing Errors:

- Dosing incorrectly for renal fluctuations is more common with rivaroxaban and dabigatran (CrCl-sensitive agents)[2][10].
- Apixaban is favored when renal function is borderline[2].

Education & Monitoring:

- Staff training in DOAC handling, recognition of bleeding and thrombosis, and documentation.
- Use of protocols for rapid re-evaluation of dosing after acute illness, dehydration, or renal change.

Table: Clinical Decision Pathway for DOAC Dosing in Elderly

Patient Factor	Action
CrCl <15 mL/min	DOACs generally contraindicated
CrCl 15–30 mL/min	Reduce dose as per specific agent
Age ≥80 years	Apixaban/Dabigatran dose reduction; Review for frailty
Weight ≤60kg	Dose reduction for Apixaban/Edoxaban
Polypharmacy	Check for P-gp/CYP3A4 interactions
Recent major bleed	Consider extra caution or alternative therapy

Graph: Prevalence of Inappropriate DOAC Dosing in Elderly Institutionalized Patients

A bar graph would demonstrate:

- Percentage of elderly (≥75 years) on inappropriate DOAC doses.
- Division by underdose, overdose, and on-label dosing.

Dosing Type	Prevalence (%)
On-label	72
Underdosed	21
Overdosed	7

Illustrative only; actual prevalence varies by region and setting[7].

DISCUSSION

Elderly institutionalized patients are high benefit/high risk candidates for DOAC therapy. Appropriate dose adjustments having adherence to guidelines are crucial. Over- and underdosing lead to poor outcomes. Periodic reassessment of renal function and individualized approach—factoring clinical status, comorbidity, caregiver involvement, and drug interaction—is vital. Interdisciplinary collaboration and standardized, protocol-driven practices can significantly mitigate harm.

CONCLUSION

DOACs are effective and generally safe for elderly residents of long-term care settings when dosing is individualized, routinely reassessed, and guideline-concordant. Avoidance of off-label dose reductions and vigilant monitoring—especially regarding renal function—are keys to maximizing benefits and minimizing harms.

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