

Review

Anticoagulant-Related Nephropathy Associated with Vitamin K Antagonists and Direct Oral Anticoagulants: Epidemiology, Pathophysiology, Clinical Features, and Outcomes

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Abstract

Background: Anticoagulant-related nephropathy (ARN) is an underrecognized cause of acute kidney injury (AKI) in patients receiving anticoagulants, classically vitamin K antagonists (VKAs) and increasingly direct oral anticoagulants (DOACs). ARN is characterized by glomerular hemorrhage, tubular obstruction by red blood cell casts, and oxidative tubular injury from hemoglobin, heme, and iron. Literature Search Strategy: A narrative literature review was performed using PubMed/MEDLINE, Scopus, and Web of Science from 2009 to February 2026. Observational studies, biopsy-based case series, systematic reviews, and experimental reports were included when they provided anticoagulant exposure, a defined renal outcome, and sufficient clinical detail. Results: ARN has been reported in approximately 19%-37% of anticoagulated patients who develop AKI, although estimates vary across heterogeneous cohorts. Risk is highest in older adults, patients with chronic kidney disease (CKD), and those with excessive anticoagulation. Observational studies and post hoc analyses suggest lower AKI rates with DOACs than VKAs, but these findings may be influenced by confounding by indication, healthy-user effects, and surveillance bias. Diagnosis remains challenging; renal biopsy is definitive and may reveal concomitant glomerular disease, including IgA deposits that do not necessarily indicate primary IgA nephropathy. Outcomes range from partial to complete recovery, with some patients progressing to CKD. Conclusions: Clinicians should recognize ARN in anticoagulated patients with unexplained AKI with hematuria, particularly when renal reserve is reduced or anticoagulant exposure is excessive. Prompt correction of excessive anticoagulation and individualized reassessment of therapy are essential. Prospective studies should validate diagnostic criteria, clarify comparative renal safety, and define anticoagulation resumption.

Keywords

Anticoagulant-related nephropathy, Warfarin-related nephropathy, Acute kidney injury, Renal hemorrhage, Direct oral anticoagulants, Chronic kidney disease, Renal biopsy

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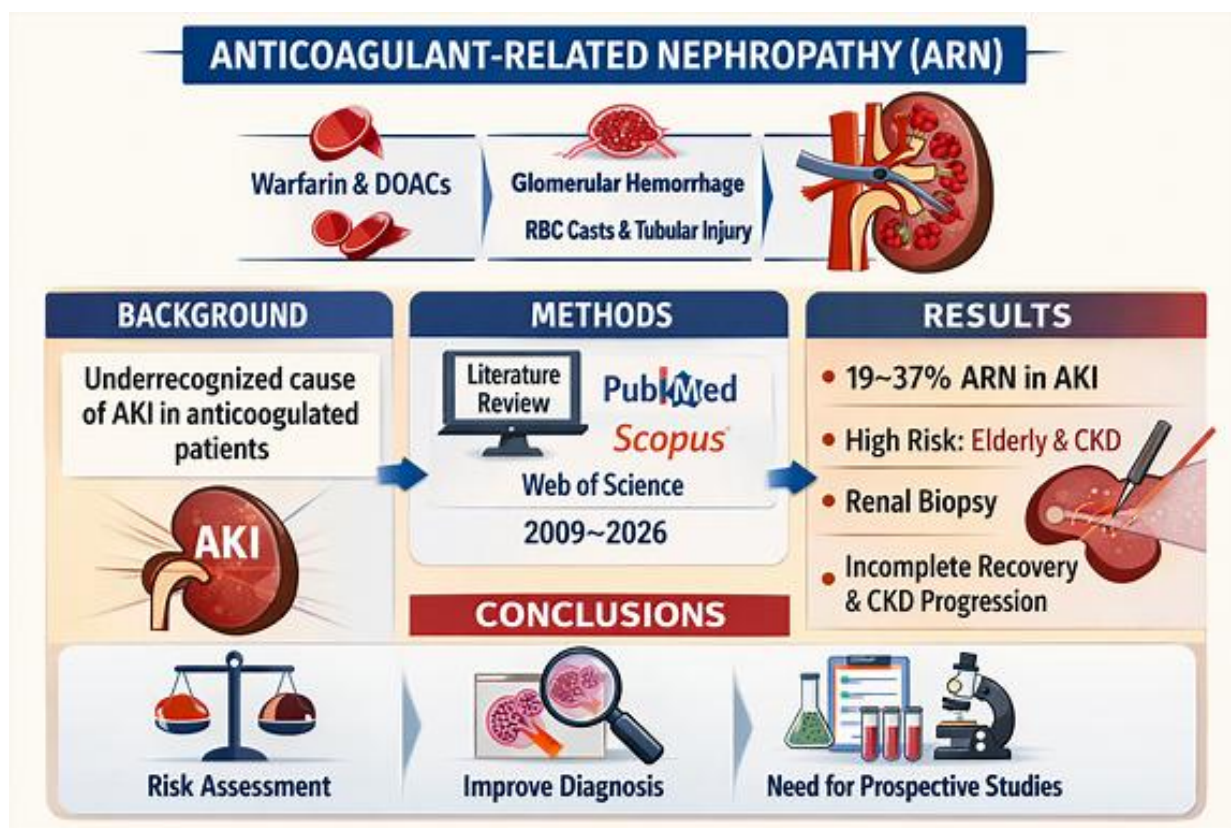
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Graphical Abstract



1. Introduction

Anticoagulant therapy is among the most widely prescribed interventions worldwide for atrial fibrillation, venous thromboembolism, and mechanical heart valve disease. Despite its proven efficacy, anticoagulation carries the potential for serious organ-level complications beyond overt bleeding. Warfarin-related nephropathy (WRN), the most studied subtype of anticoagulant-related nephropathy (ARN), was first formally described by Brodsky and Satoskar in 2009 [1], characterized by glomerular hemorrhage and tubular obstruction with red blood cell (RBC) casts in patients with supratherapeutic anticoagulation. Retrospective studies later suggested that similar renal injury had likely been occurring for decades since the introduction of vitamin K antagonists (VKAs) in the mid-20th century [2].

With the widespread adoption of direct oral anticoagulants (DOACs)—including dabigatran, rivaroxaban, and apixaban—the concept was broadened to ARN, encompassing WRN and analogous renal lesions reported with DOACs and low-molecular-weight heparins [3,4]. Pathologically, ARN is defined by glomerular hemorrhage, tubular obstruction by RBC casts, and oxidative tubular injury mediated by hemoglobin, heme, and iron release. Population-based studies suggest ARN occurs in 19-37% among anticoagulated patients who develop AKI, though estimates vary substantially by study design, patient population, and diagnostic criteria [5].

The clinical significance of ARN has been further highlighted by retrospective analyses of major randomized trials, including RE-LY, ROCKET-AF, and ARISTOTLE, that have reported differences in renal risks associated with different anticoagulant regimens [6-8]. However, the renal safety of VKAs compared to DOACs in such high-risk patients is incompletely understood. This uncertainty may influence anticoagulant selection and monitoring strategies in patients at risk for renal complications.

However, many shortcomings have been observed in this regard. No validated blood or urinary biomarkers currently exist for the diagnosis of ARN; diagnosis is still inconsistent, and treatment strategies have not been standardized. Moreover, the prognosis after ARN is often poor because patients usually suffer from impaired recovery and the onset of chronic kidney disease (CKD). This review evaluates the recent research regarding ARN's pathophysiology and epidemiology and the differences between the VKAs and DOACs. Finally, we propose a diagnostic and management scheme for ARN, which is not meant to be validated but to be used in practice and guide future research.

2. Literature Search Strategy

An extensive search of the literature was performed using PubMed/MEDLINE, Scopus, and Web of Science databases from 2009, when Brodsky and colleagues first formally described WRN [1], until February 2026.

The keywords used were "anticoagulant-related nephropathy," "warfarin-related nephropathy," "anticoagulation AND acute kidney injury," and "direct oral anticoagulants AND nephropathy," together with secondary keywords that focused on the pathophysiology (oxidative tubular damage, heme nephrotoxicity), diagnosis (renal biopsy, urinalysis), and prognosis (progression to CKD, dialysis requirement, mortality) of the disorder [2,3]. Eligible studies included observational studies, biopsy-based case series, systematic reviews, and experimental models reporting, at minimum, anticoagulant type/intensity, a defined renal outcome (e.g., creatinine change, biopsy finding, or dialysis requirement), and patient-level or aggregate cohort demographics—operationalized here as “sufficient clinical detail”—while non-English publications, pediatric-only populations, and conference abstracts without full reports were excluded [5,9]. Screening was performed in two stages (title/abstract and full text) by a single reviewer, and data were extracted on study design, patient characteristics, anticoagulant type and intensity, renal outcomes, histopathological findings, and reported ARN risk factors. Due to heterogeneity in study design and diagnostic criteria, results were narratively synthesized and therefore did not follow a formal systematic-review framework such as PRISMA. The literature mainly consists of retrospective and biopsy studies that may overrepresent severe cases, with some methodology issues, including single-reviewer screening and data extraction, limitation by language and using only observational data. There might also be publication bias, especially concerning DOAC-related ARN [9-11].

For transparency, the search combined the primary terms above using Boolean logic as follows: (“anticoagulant-related nephropathy” OR “warfarin-related nephropathy”) AND (“acute kidney injury” OR “nephropathy”) OR (“direct oral anticoagulants” AND “nephropathy”), each combined with the secondary pathophysiology, diagnosis, and prognosis terms listed above using the AND operator and applied to titles, abstracts, and keywords in PubMed/MEDLINE, Scopus, and Web of Science. No gray literature (conference proceedings, trial registries, dissertations) was searched, and reference lists of included articles were not systematically hand-searched; both are acknowledged as limitations. No formal quality-assessment or risk-of-bias instrument (e.g., Newcastle-Ottawa Scale, QUADAS-2) was applied to included studies, and no quality weighting was incorporated into the narrative synthesis. Consistent with its narrative rather than systematic design, this review was not registered in a protocol registry (e.g., PROSPERO), and no PRISMA flow diagram is presented, as study identification did not follow a systematic, reproducible screening pipeline amenable to such reporting.

3. Epidemiology

The reported incidence of ARN among anticoagulated patients who develop AKI ranges from 19% to 37%, though estimates vary considerably depending on study design, diagnostic criteria, and population characteristics, and should therefore be interpreted with caution [2,12]. Risk (Table 1) is highest in elderly patients, those with CKD, and individuals with supratherapeutic anticoagulation, and large pharmacoepidemiologic analyses have reported findings broadly consistent with this range, although heterogeneity persists [5]. ARN's true prevalence remains uncertain, especially in regions that lack access to adequate diagnostic resources for ARN, including those that limit access to facilities equipped to conduct renal biopsies. Established risk factors for ARN include advanced age, CKD, and excessive anticoagulation; additionally, pharmacogenomic determinants—such as CYP2C9 and VKORC1 gene variants—contribute to susceptibility [13,14].

Renal biopsy is considered the gold standard, commonly demonstrating glomerular hemorrhages, as well as the underlying cause such as IgA nephropathy, in some cases. Renal prognosis is frequently unfavorable, with incomplete renal recovery and progression to CKD frequently observed. Observational comparisons of VKAs and DOACs indicate lower AKI rates among users of the latter drug class; however, it should be emphasized that the available literature primarily comes from observational cohort designs or secondary analyses of clinical trials [6-8,15-17]. The chief disadvantage of such studies includes residual confounding as a result of disparity in the baseline characteristics among patients, in which VKA had been mainly prescribed for aged and/or renal-impaired patients with other diseases or mechanical heart valves; however, DOACs were usually prescribed for patients with fewer comorbidities. Some investigators attempted to overcome the influence of confounders by making use of various causality inference methods, such as propensity score matching and regression models, and concluded lower incidences of AKI related to the use of DOACs [5]. This apparent difference should also be interpreted in light of surveillance bias: patients on VKAs undergo frequent INR monitoring, which entails correspondingly frequent serum creatinine measurement and therefore a substantially higher likelihood of detecting incidental or subclinical creatinine elevations than in DOAC users, who are not subject to routine coagulation monitoring.

Table 1. Risk factors for anticoagulant-related nephropathy.

Risk Factor	Description	Strength of Evidence	Ref.
Supratherapeutic INR	INR >3.0 is associated with significantly higher glomerular bleeding risk	Strong (multiple biopsy and cohort studies)	[1,12]
Chronic Disease	Kidney Pre-existing CKD reduces renal reserve and impairs tubular repair mechanisms	Strong (consistent across cohorts and mechanistic studies)	[12,18]
Diabetes Mellitus	Microvascular damage increases glomerular fragility and susceptibility to hemorrhage	Moderate (observational data, mechanistic plausibility)	[5,13]
Advanced Age	Reduced renal reserve and altered drug metabolism heighten ARN risk	Strong (epidemiologic consistency)	[5,13]
Hypertension	Baseline vascular injury and nephrosclerosis increase glomerular vulnerability	Moderate (observational, less biopsy confirmation)	[12,13]
Nephrotoxic Drugs	Concomitant NSAIDs, aminoglycosides, or contrast agents amplify tubular injury	Strong (well established nephrotoxic synergy)	[18,19]
Underlying Glomerulopathy	IgA nephropathy, membranous nephropathy, and diabetic nephropathy, among others, predispose to glomerular hemorrhage; hypertensive nephrosclerosis increases glomerular fragility through baseline vascular injury	Strong (biopsy confirmed associations)	[20,21]
Recent Invasive Procedures	Surgical or endovascular procedures may precipitate acute hemodynamic changes, amplifying ARN risk in anticoagulated patients	Limited (case reports, small series)	[5]
DOAC-Specific Triggers	Peak drug exposure, drug accumulation with renal impairment, and P-glycoprotein/CYP3A4 drug-drug interactions raise effective DOAC anticoagulant intensity independent of supratherapeutic INR	Moderate (pharmacokinetic studies, limited clinical data)	[4,6]

Note: Patient-level, pharmacogenomic, and drug-related determinants associated with increased susceptibility to glomerular hemorrhage and tubular injury, with relevance to clinical risk stratification.

4. Pathophysiology

ARN is characterized by kidney injury resulting from excessive anticoagulation, which causes a disturbance to the glomerular capillary wall that results in leaking of RBCs into Bowman's space and into the renal tubules [1,22]. The glomerular filtration rate decreases, further contributing to tubular injury through ischemic and oxidative stress [12,18]. Histopathologic findings (Table 2) reveal RBC casts—with or without fragmentation—acute tubular necrosis (ATN), and interstitial inflammation with neutrophil and macrophage infiltration; these lesions reflect mechanical tubular obstruction by erythrocytes and subsequent inflammatory injury [20].

Table 2. Histopathological features of anticoagulant-related nephropathy.

Histopathological Feature	Description	Strength of Evidence	Ref.
RBC Casts	Occlusive RBC casts within renal tubules, hallmark finding of ARN	Strong (biopsy confirmed hallmark)	[1,18]
Acute Tubular Injury	Tubular epithelial cell necrosis and degeneration secondary to ischemia and oxidative stress	Strong (consistent biopsy and mechanistic studies)	[18,20]
Glomerular Hemorrhage	RBCs present in Bowman's space without immune complex deposition	Strong (multiple biopsy series)	[12,18]
Absent or Non-Specific Immune Deposits	Negative immunofluorescence for IgA, IgG, IgM, C3, and C1q; differentiates ARN from immune-mediated glomerulonephritis	Strong (diagnostic differentiation)	[18,21]
Interstitial Inflammation	Variable neutrophil and macrophage infiltration contributing to tubulointerstitial injury	Moderate (observational biopsy data)	[20]

Note: Light microscopy shows RBC casts, ATN, and interstitial inflammation; immunofluorescence is variable, often negative or with mild, nonspecific IgA deposits not indicative of primary glomerulonephritis. RBC casts undergo rapid lytic degradation in alkaline urine, so their absence on urinalysis does not exclude a diagnosis of ARN; repeat or expedited microscopy of fresh, acidified urine improves sensitivity (see Figure 2).

Studies using animal models have shown that hemoglobin, heme, and iron released through lysis of RBC casts cause oxidative stress through reactive oxygen species (ROS), adding insult to injury by causing a mechanical obstruction [23,24]. To elucidate the role of oxidative injury in ARN versus mechanical obstruction, future animal models would benefit from assessing if chelators of iron (such as deferoxamine) and scavengers of ROS (such as N-acetylcysteine) can prevent tubular necrosis in the absence of a significant load of RBC casts [25]. The inability of the cells to repair themselves and the decreased antioxidants in patients with CKD make the condition more difficult to manage. Similar histopathology has been seen in patients receiving DOACs and heparin; however, there is limited understanding of how much of an overlap exists between them and VKAs [4].

Apart from mechanical and oxidative mechanisms, there is growing evidence that coagulation plays an important role in receptor-mediated pathogenesis, although this mechanism likely differs across DOAC subclasses rather than applying uniformly. Direct thrombin inhibitors, of which dabigatran is the prototype, act at the final common step of the coagulation cascade and therefore directly block thrombin-mediated activation of protease-activated receptor-1 (PAR-1) on glomerular endothelial cells and podocytes; this effect has been demonstrated experimentally, with dabigatran inducing glomerular hemorrhage in rodent models independent of a systemic bleeding diathesis [25]. Factor Xa inhibitors such as apixaban and rivaroxaban act upstream of thrombin generation and reduce thrombin formation indirectly, so their effect on PAR-1 signaling is expected to be less direct, although residual thrombin generation through Factor Xa-independent pathways may still permit some receptor activation. Disruption of PAR-1 signaling, however it is achieved, affects the integrity of the endothelial cells and podocytes in the glomerulus, resulting in glomerular damage and increasing the vulnerability of this area to bleeding, but head-to-head comparisons of PAR-1-mediated injury across DOAC subclasses have not been performed in clinical studies [26,27]. All these pieces of evidence point to a dual mechanism of ARN: mechanical occlusion caused by erythrocyte casts as well as oxidative damage to tubules due to hemoglobin, heme, and iron [23,24].

5. Clinical Presentation

In the clinical scenario, ARN is characterized by acute onset of elevated serum creatinine in anticoagulant therapy, usually with no obvious gross hematuria [1,28]. Subclinical hematuria is commonly detected and more readily identified through urine dipstick analysis rather than microscopy, whereas microscopy remains necessary as a confirmatory test for RBCs and casts [3,19,29]. Constitutional symptoms such as fatigue and nausea are often non-specific; imaging is usually done in order to rule out structural causes of AKI (Table 3) [3].

Table 3. Comparison of ARN with other common causes of acute kidney injury.

Feature	ARN	ATN	AIN	GN
Primary Cause	Supratherapeutic anticoagulation [1,2]	Ischemia or nephrotoxins	Drug hypersensitivity	Immune-mediated glomerular injury
Key Pathology	Glomerular hemorrhage, RBC casts [12,18]	Tubular epithelial necrosis	Interstitial inflammation, eosinophils	Endocapillary proliferation, immune deposits
Urine Findings	Hematuria, RBC casts [19,29]	Muddy brown casts	Pyuria, eosinophiluria	Proteinuria, RBC casts
Biopsy Findings	Intact RBC casts, ATN, no immune deposits [18,20]	Tubular epithelial necrosis, loss of brush border, cytoplasmic vacuolation	Interstitial edema, inflammatory infiltrates	Immune deposits, complex glomerular hypercellularity
Reversibility	Possible with anticoagulation correction [18,19]	Possible if cause removed	Possible with drug withdrawal ± steroids	Variable; depends on type and severity

Note: Differential features across primary etiology, urinalysis, histopathology, and reversibility to support the diagnostic workup of anticoagulated patients presenting with unexplained AKI. ARN, anticoagulant-related nephropathy; ATN, acute tubular necrosis; AIN, acute interstitial nephritis; GN, glomerulonephritis. Immunofluorescence in pure ARN is typically negative; when immune deposits such as IgA are identified on biopsy, they reflect an underlying primary glomerulopathy (e.g., IgA nephropathy) unmasked or exacerbated by anticoagulation, rather than a direct feature of ARN itself.

Glomerular diseases, particularly IgA nephropathy, membranous nephropathy, and diabetic nephropathy, significantly predispose patients to developing ARN [13,21]. Clinical data indicate that 33% of patients with supratherapeutic INR levels (> 3.0) may experience subclinical WRN [9,12]. In recent years, a novel mechanism of ARN development other than glomerular hemorrhage has been proposed, whereby anticoagulant therapy induces weakening of the glomerular filtration barrier in the presence of mesangial hypercellularity and compromised integrity of the capillary walls [26,30]. In addition, thrombin inhibition might affect podocytes and compromise platelet-endothelial adhesion, leading to glomerular bleeding [27,31].

Although DOACs generally demonstrate favorable renal safety profiles compared with VKAs, ARN has also been reported with rivaroxaban and apixaban [2,11]. Risk may be further increased by genetic factors such as the presence of CYP2C9 and VKORC1 polymorphism affecting warfarin metabolism and predisposing one to ARN [13]. Patients who are older and those suffering from CKD are at greater risk owing to the loss of renal reserve, and in resource-limited settings, diagnosis of the condition may rely entirely on clinical presentation.

Renal biopsy remains the definitive diagnostic tool in case of accessibility, usually demonstrating glomerular hemorrhage, ATN, and tubular obstruction with RBC casts. RBCs may be present in Bowman's space without significant immune complex deposition, although mild deposits—most commonly IgA—may be observed; these do not necessarily indicate primary IgA nephropathy and must be interpreted in context [21,22]. Biopsy is often precluded by bleeding risk in patients with supratherapeutic anticoagulation. Interestingly, the absence of casts of RBCs on urinalysis tests cannot be considered as ruling out ARN since the deterioration of the casts may have led to their absence. No specific laboratory test is available for the condition, and the difficulty of its diagnosis often lies in the lack of clinical suspicion and availability of biopsies [2]. In many cases, the clinical diagnosis of ARN comprises AKI, which is characterized by an elevation in serum creatinine levels ≥ 0.3 mg/dL, and hematuria. Figure 1 outlines a proposed diagnostic framework, intended as a practical clinical aid but not yet validated against biopsy-confirmed ARN. The framework addresses the diagnostic approach to ARN across VKAs, DOACs, and low-molecular-weight heparins, directing clinical suspicion toward ARN in anticoagulated patients presenting with AKI and hematuria while helping to distinguish it from ATN, acute interstitial nephritis, and glomerulonephritis.

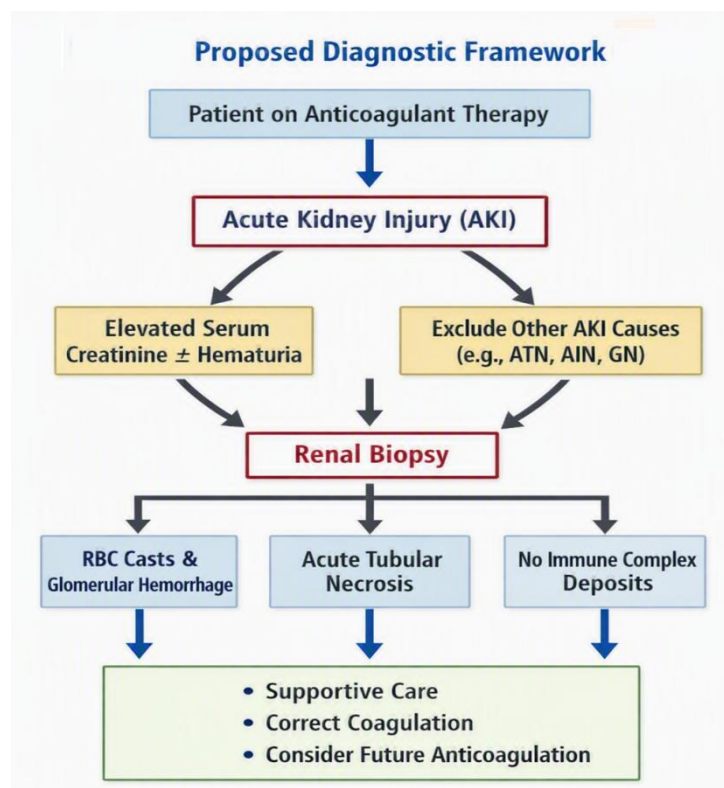


Figure 1. Proposed (Not Validated) Diagnostic Framework for ARN.

Note: A practical, unvalidated clinical framework for the diagnostic evaluation of suspected ARN in anticoagulated patients. This proposed, unvalidated framework should not be used as a formal diagnostic rule. Absence of red blood cell casts does not exclude ARN because they may lyse rapidly in alkaline urine. Renal biopsy continues to be the definitive diagnostic procedure where possible, confirming ARN and uncovering the underlying glomerulopathy.

6. Management and Outcomes

Renal recovery following ARN ranges from partial to complete after correction of over-anticoagulation; however, pre-existing CKD portends a worse prognosis [5,12]. ARN has consistently been associated with longer hospitalization, increased complications, and higher mortality [12,32].

From a clinical management perspective, early identification and reversal of supratherapeutic anticoagulation is key to preventing irreversible nephron loss [18]. For warfarin, treatment includes vitamin K administration and, in severe cases, prothrombin complex concentrates [2]. For DOACs, specific reversal agents—idarucizumab for dabigatran and andexanet alfa for factor Xa inhibitors—may be potentially lifesaving in severe hemorrhagic complications associated with AKI [6,7,28].

In patients with advanced CKD, standard DOAC dose-adjustment principles should be applied proactively to reduce the risk of drug accumulation and secondary renal injury: agents are typically dose-reduced or avoided below defined renal-function thresholds (e.g., dabigatran is generally avoided at low creatinine clearance, and apixaban and rivaroxaban require dose reduction according to labeled renal-function, age, and weight criteria), and renal function should be reassessed at regular intervals in patients with fluctuating creatinine, since a declining glomerular filtration rate can itself precipitate supratherapeutic DOAC exposure even without a dosing change [6-8].

In the long run, ARN leads to CKD progression, increases reliance on dialysis and raises overall mortality as well as cardiac mortality [10,11,33]. The role of iron chelation or antioxidant therapy has yet to be determined; however, these treatments represent experimental options and shed light on modifiable factors that may lead to positive patient outcomes [23,24].

7. Discussion

The available epidemiological evidence suggests that ARN is a clinically significant and likely underdiagnosed complication of anticoagulation, affecting 19% to 37% of anticoagulated patients who develop AKI [2,12]. Population-based pharmacoepidemiologic data and post-hoc analyses of the RE-LY, ROCKET-AF, and ARISTOTLE trials converge on the finding that DOACs are associated with a lower risk of AKI and more favorable long-term renal outcomes compared with VKAs [6-8,15-17]. While this pattern is consistent across datasets, it should be interpreted with caution: renal endpoints were secondary outcomes, and residual confounding by indication—most notably the preferential use of VKAs in patients with advanced CKD and mechanical heart valves—cannot be fully excluded even after propensity score adjustment [10,15,16]. This pattern is consistent with a broader “healthy-user effect,” whereby patients selected for DOAC therapy tend to be systematically healthier, more adherent, and to carry fewer comorbidities than those maintained on VKAs, independent of formal comorbidity indices; propensity-score and regression-based adjustments can account only for measured confounders and cannot fully correct for this unmeasured selection, so indication bias should be regarded as a structural limitation of the comparative renal-safety literature rather than a fully resolvable statistical artifact. Nevertheless, the consistency of direction across heterogeneous populations lends sufficient credibility to inform clinical decision-making, particularly in CKD patients requiring long-term anticoagulation, where renal outcomes should be weighted alongside thromboembolic risk.

Mechanistically (Figure 2), ARN involves two major processes: mechanical tubular obstruction by RBC casts and oxidative tubular injury driven by hemoglobin, heme, and iron released from lysed erythrocytes [23,24]. Whether oxidative injury is a primary driver or secondary to glomerular hemorrhage remains unclear; nonetheless, antioxidant approaches such as iron chelation or free radical scavenging may offer therapeutic potential beyond anticoagulation reversal, though this hypothesis remains untested in clinical ARN and is supported only by experimental rodent models [25]. The impaired antioxidant defenses and reduced tubular regenerative capacity characteristic of CKD amplify both pathways, explaining the consistently worse prognosis in patients with pre-existing renal disease [12,18]. Current management remains focused on prompt correction of supratherapeutic anticoagulation, with vitamin K and prothrombin complex concentrates for VKAs [19] and specific reversal agents—idarucizumab for dabigatran and andexanet alfa for factor Xa inhibitors—for DOACs [28].

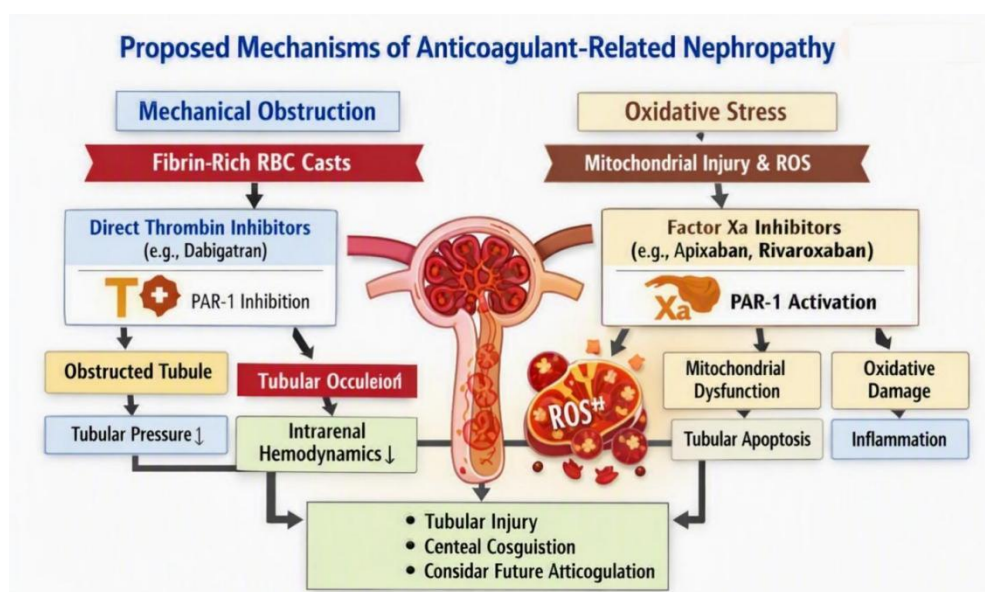


Figure 2. Comparative histology and mechanistic pathways in anticoagulant-related nephropathy.

Note: Histological correlates and the two-part mechanistic pathway (mechanical obstruction and oxidative tubular injury) underlying ARN, as detailed in the main text above.

Diagnosis of ARN remains one of the most clinically challenging aspects of its management. The pragmatic three-component clinical criteria—AKI with a serum creatinine rise ≥ 0.3 mg/dL, concurrent hematuria, and supratherapeutic anticoagulation without an alternative explanation—have not been validated against biopsy-confirmed ARN, and their sensitivity and specificity remain unknown. The diagnostic framework proposed above in Figure 1 is intended as a practical clinical aid rather than a validated decision rule, and should be applied with recognition that RBC casts may be absent on routine urinalysis due to rapid degradation. Renal biopsy, while definitive, is frequently precluded by bleeding risk inherent in supratherapeutic anticoagulation. When feasible, biopsy provides dual diagnostic value: confirming ARN and detecting underlying glomerular disease such as IgA nephropathy or membranous nephropathy, which may require specific immunosuppressive therapy.

A clinically consequential question that remains unanswered is when and whether anticoagulation should be resumed following an episode of ARN. Reversing or withholding anticoagulation protects the kidney from ongoing hemorrhagic injury but exposes the patient to thromboembolic risk. No prospective study, randomized trial, or validated protocol addresses this dilemma. Current practice is extrapolated from general anticoagulation management principles, with individualized decisions based on indication, severity of renal injury, creatinine trajectory, and bleeding-versus-thrombosis risk balance. In atrial fibrillation, CHA₂DS₂-VASc and HAS-BLED scores provide a framework, but neither was validated in ARN. If anticoagulation is resumed, a DOAC at the lowest effective dose appears most defensible given comparative renal safety, though this recommendation rests on indirect evidence. Prospective registry data specifically capturing anticoagulation resumption decisions and renal and thromboembolic outcomes after ARN are urgently needed.

In the absence of validated criteria, a pragmatic framework for this decision can integrate four elements: (1) thromboembolic risk, estimated using CHA₂DS₂-VASc in atrial fibrillation or the specific indication (mechanical valve, venous thromboembolism) in other settings; (2) bleeding risk, estimated using HAS-BLED or an equivalent score, acknowledging that neither instrument was derived in ARN populations; (3) renal trajectory, favoring resumption once creatinine has returned to baseline or a stable plateau and hematuria has resolved, and favoring continued avoidance if renal function remains actively declining; and (4) anticoagulant choice, favoring a DOAC at the lowest effective, renal-function-adjusted dose over VKA resumption where comparative renal safety data support it. This framework is offered to structure clinical decision-making pending prospective validation and should not be regarded as a validated algorithm.

However, the risk profile of ARN is varied. Pharmacogenomic difference in CYP2C9 and VKORC1 influences anticoagulant metabolism and may affect ARN risk [13,14,34]. Older adults and diabetics, hypertensives, or patients with pre-existing CKD have an increased risk because of diminished renal functional reserve, predisposition for glomerular fragility, and changed pharmacokinetics of drugs. In developing countries, only clinical criteria can be used to diagnose ARN as biopsy and laboratory tests cannot be done, resulting in possible underreporting. These observations highlight the importance of anticoagulant selection, dose optimization, and renal function monitoring as key components of individualized pharmacotherapy aimed at minimizing ARN risk.

8. Limitations

This review has several limitations that should inform interpretation of its conclusions. First, it is a single-author narrative review: screening and data extraction were performed by one reviewer without independent duplicate verification, so the risk of selective study identification, data-extraction error, and interpretive bias cannot be fully excluded. Second, the search was restricted to English-language, peer-reviewed sources identified in PubMed/MEDLINE, Scopus, and Web of Science; gray literature and reference-list (backward) screening were not performed, and relevant studies may have been missed. Third, publication bias is likely, particularly for DOAC-related ARN, where case-level and mechanistic reports may be more likely to be published when positive or novel, potentially skewing the apparent comparative renal safety of DOACs. Fourth, no formal quality-assessment or risk-of-bias instrument was applied to included studies, and no quality weighting was incorporated into the narrative synthesis, so the evidence base is presented without a formal hierarchy of certainty. Fifth, the literature is dominated by retrospective, biopsy-based, and observational studies that likely overrepresent clinically severe cases and are subject to residual confounding by indication and a healthy-user effect, as VKA users are systematically older and have greater baseline renal impairment than DOAC users. Finally, this review did not follow a PRISMA-based systematic methodology, was not registered in a protocol registry, and does not include a PRISMA flow diagram; its findings should therefore be interpreted as a structured narrative synthesis rather than as a systematic review.

9. Conclusion

ARN is an underrecognized but clinically important cause of AKI in anticoagulated patients. Not only does ARN involve glomerular bleeding but also represents oxidative stress-induced tubular cell injury, a novel and treatable factor contributing to kidney dysfunction. Available evidence suggests that DOACs may offer a more favorable renal safety profile than VKAs in appropriately selected patients, from real-world observations and post hoc analyses of the RE-LY, ROCKET-AF, and ARISTOTLE trials.

The lack of any characteristic biomarker makes the diagnosis dependent on suspicion and clinical findings confirmed by laboratory tests. The presence of red cell casts on urine examination is a significant clue for making the diagnosis, and

renal biopsy is confirmatory and diagnostic of any underlying glomerulonephritis. Physicians should be highly suspicious of ARN when managing AKI and hematuria in anticoagulated patients. Urgent microscopic urinalysis should be conducted, and any supratherapeutic anticoagulation should be managed appropriately. The available literature suggests that DOACs may offer renal safety advantages over VKAs in appropriately selected patients.

Future research priorities include prospective cohort studies incorporating systematic urine microscopy and selective renal biopsy to validate diagnostic criteria and assess their performance; rigorously controlled comparative studies with renal outcomes as primary endpoints; and mechanistic investigations to determine whether oxidative tubular injury is independently targetable. Dedicated registry data are also needed to clarify optimal timing and outcomes of anticoagulation resumption following confirmed ARN.

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Ethics Statement

This review is based entirely on previously published studies. No individual patient data were collected or analyzed, and no institutional review board approval was required.

Informed Consent

Not applicable.

Data Availability Statement

All data are from published sources.

Author Contributions

Conceptualization, original draft preparation, review and editing: A.Z. The author has read and approved the final manuscript.

Conflict of Interest

The author declares no conflict of interest related to the publication of this manuscript.

Generative AI Statement

Generative AI (Paperpal) was used to assist with language and grammar editing, formatting to meet the journal word limit. The AI tool was not used to generate primary scientific data or replace the author's scientific judgment. The author reviewed and approved the AI-assisted revisions and remains responsible for the accuracy, integrity, and final content of the manuscript.

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