World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Intravenous iron therapy in chronic kidney disease–associated anemia: Current evidence on efficacy and safety

Ni Putu Yusica Maylasari * and Made Wirama Diyana

Department of Internal Medicine, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia.

World Journal of Biology Pharmacy and Health Sciences, 2026, 26(02), 304-312

Publication history: Received on 07 April 2026; revised on 22 May 2026; accepted on 25 May 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.26.2.0296

Abstract

Background: CKD–associated anemia is one of the most common and clinically significant complications of CKD, contributing to increased cardiovascular morbidity, and reduced quality of life. In addition to impaired erythropoietin production, iron dysregulation mediated by chronic inflammation and elevated hepcidin levels plays a central role in anemia pathogenesis. IV iron therapy has emerged as an increasingly important therapeutic strategy, particularly in patients with functional iron deficiency and inadequate response to oral iron supplementation.

Methods: A narrative review was conducted using literature from PubMed, Google Scholar, Scopus, and ScienceDirect published between 2015 and 2025. Studies discussing the efficacy and safety of IV iron therapy in CKD-associated anemia were included.

Results: Current evidence demonstrates that IV iron therapy provides superior hematologic efficacy compared with oral iron supplementation by improving hemoglobin levels, replenishing iron stores, and reducing erythropoiesis-stimulating agent (ESA) requirements. Landmark trials such as FIND-CKD and PIVOTAL further support the role of proactive IV iron administration in improving anemia-related outcomes without significantly increasing infection risk or serious adverse events. Modern IV iron formulations generally exhibit favorable safety profiles, although concerns regarding oxidative stress, iron overload, hypersensitivity reactions, and hypophosphatemia remain important clinical considerations.

Conclusion: Intravenous iron therapy has become a cornerstone in the management of CKD-associated anemia, particularly among patients with functional iron deficiency, ESA hyporesponsiveness, and dialysis dependence. Contemporary evidence supports its efficacy and acceptable safety profile when administered with appropriate monitoring and individualized treatment strategies.

Keywords: Anemia; Chronic Kidney Disease; Erythropoiesis-Stimulating Agents; Hepcidin; Intravenous Iron Therapy

1. Introduction

Chronic kidney disease (CKD) has emerged as one of the most significant global public health challenges, imposing substantial clinical, economic, and societal burdens worldwide. Recent estimates suggest that approximately 850 million individuals are affected by kidney disease globally, and CKD accounting for the vast majority of cases (1). Furthermore, the global age-standardized prevalence of CKD in adults has reached approximately 14.2%, this reflects a continuous increase over recent decades. Beyond its progressive decline in renal function, CKD is strongly associated with cardiovascular complications, impaired quality of life, increased hospitalization, and premature mortality, particularly in advanced disease stages (2).

* Corresponding author: Ni Putu Yusica Maylasari.

Among the numerous complications of CKD, anemia represents one of the most prevalent and clinically consequential disorders. The burden of CKD-associated anemia increases progressively with declining kidney function, affecting approximately 30–50% of patients with stage 3–4 CKD and exceeding 50% in stage 5 disease. A recent large-scale review from Asia further demonstrated an overall pooled anemia prevalence of 42% among individuals with CKD, with rates approaching 80% in end-stage kidney disease populations (3). Globally, the number of CKD-related anemia cases was estimated to exceed 63 million in 2021, nearly doubling compared with 1990. Importantly, anemia in CKD is not merely a laboratory abnormality; it is independently associated with worsening cardiovascular outcomes, accelerated CKD progression, reduced exercise tolerance, cognitive impairment, increased transfusion requirements, and diminished health-related quality of life(4).

The pathogenesis of anemia in CKD is multifactorial and complex. Although inadequate erythropoietin production remains the hallmark mechanism, increasing evidence highlights the pivotal contribution of iron dysregulation driven by chronic inflammation, elevated hepcidin, impaired intestinal iron absorption, reticuloendothelial iron sequestration. Consequently, many patients develop either absolute or functional iron deficiency, both of which substantially impair erythropoiesis and contribute to resistance to erythropoiesis-stimulating agents (ESAs). In parallel, the inflammatory milieu characteristic of CKD further limits the efficacy of oral iron supplementation, thereby complicating anemia management in routine clinical practice (5).

Over the past decade, therapeutic strategies for CKD-associated anemia have undergone substantial evolution. While ESAs previously dominated anemia management paradigms, concerns regarding cardiovascular and thromboembolic risks associated with aggressive hemoglobin correction have shifted increasing attention toward iron optimization strategies. Contemporary evidence now supports intravenous (IV) iron therapy not only as an adjunctive treatment, but also as a central component of anemia management in CKD, particularly among patients with dialysis dependence, functional iron deficiency, or ESA hyporesponsiveness. Several landmark trials, including FIND-CKD and PIVOTAL, have demonstrated that IV iron therapy can effectively improve hemoglobin levels, reduce ESA requirements, and potentially improve clinical outcomes compared with conservative or oral iron-based approaches (6).

Nevertheless, despite its growing utilization and therapeutic promise, the administration of IV iron remains accompanied by important safety considerations and ongoing controversies. Concerns regarding oxidative stress, iron overload, infection risk, hypersensitivity reactions, and long-term cardiovascular consequences continue to generate debate within nephrology practice. Moreover, heterogeneity among available IV iron formulations, dosing strategies, and patient populations further complicates therapeutic decision-making. As a result, optimizing the balance between efficacy and safety remains a major challenge in contemporary CKD anemia management. Given the rapidly evolving evidence base and the expanding role of iron-centered therapeutic strategies, a comprehensive understanding of the efficacy and safety profile of IV iron therapy in CKD-associated anemia is increasingly essential. Therefore, this narrative review aims to critically evaluate the current evidence regarding the therapeutic efficacy, safety considerations, clinical limitations, and future perspectives of intravenous iron therapy in patients with CKD-associated anemia (7).

2. Methods

This narrative review was conducted through a comprehensive literature search of electronic databases, including PubMed, Google Scholar, Scopus, and ScienceDirect. Relevant studies discussing intravenous iron therapy in chronic kidney disease (CKD)–associated anemia were identified using combinations of the following keywords: “chronic kidney disease,” “CKD-associated anemia,” “intravenous iron therapy,” “iron deficiency,” “functional iron deficiency,” “hepcidin,” “erythropoiesis-stimulating agents,” and “dialysis anemia.”

Articles included in this narrative review were selected based on several predefined inclusion and exclusion criteria. The inclusion criteria comprised studies published within the last 10 years (2015–2025) and articles written in English. Meanwhile, articles available only in abstract form without accessible full-text manuscripts were excluded from this review. Studies considered irrelevant to the topic of intravenous iron therapy in CKD-associated anemia were also excluded. Additional exclusion criteria included duplicate publications.

3. Pathophysiology of Iron Deficiency in CKD

Anemia in CKD arises through a multifactorial and highly complex pathophysiological process involving impaired erythropoiesis, chronic inflammation, dysregulated iron metabolism, and reduced red blood cell survival. Among these mechanisms, iron deficiency has emerged as one of the most critical contributors to CKD-associated anemia and plays a central role in therapeutic decision-making. Importantly, iron deficiency in CKD is not solely attributable to absolute

depletion of iron stores, but also to profound disturbances in iron homeostasis driven by inflammation-mediated pathways (8).

Under normal physiological conditions, erythropoiesis is regulated primarily by erythropoietin (EPO), a glycoprotein hormone predominantly synthesized by peritubular fibroblast-like cells in the renal cortex in response to tissue hypoxia. In CKD, progressive nephron loss and tubulointerstitial fibrosis impair endogenous EPO production, resulting in inadequate bone marrow stimulation and reduced red blood cell production. However, increasing evidence suggests that EPO deficiency alone cannot fully explain the severity of anemia observed in CKD patients. Disturbances in iron metabolism, particularly functional iron deficiency mediated by elevated hepcidin levels, have now been recognized as equally important pathogenic mechanisms. Iron homeostasis in CKD is profoundly influenced by hepcidin, a peptide hormone synthesized primarily by hepatocytes and regarded as the master regulator of systemic iron metabolism. Hepcidin controls iron availability by binding to ferroportin, the major cellular iron exporter expressed on enterocytes, macrophages, and hepatocytes. This interaction induces ferroportin internalization and degradation, thereby inhibiting intestinal iron absorption and preventing the release of stored iron into the circulation (9).

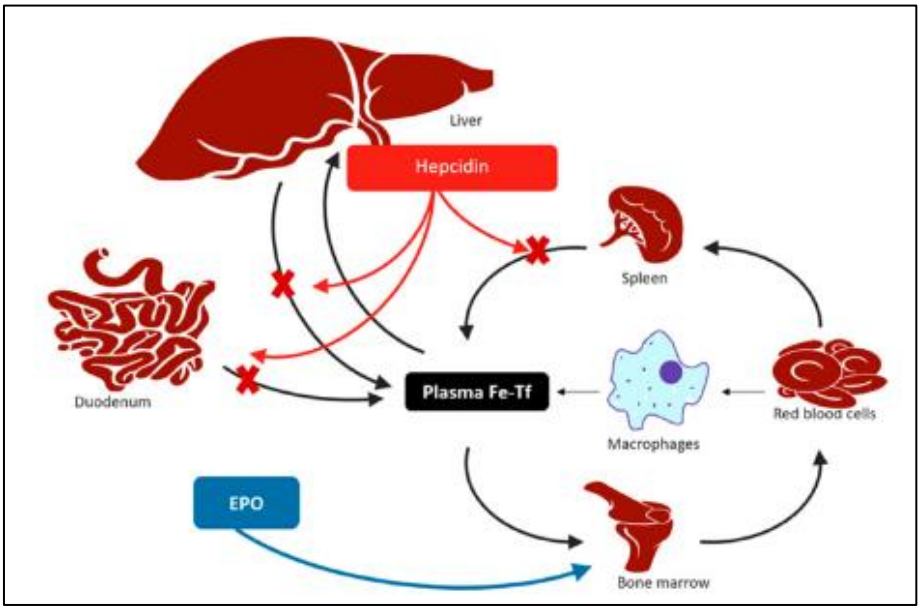

Figure 1 Hepcidin-mediated dysregulation of iron metabolism in CKD (8)

In patients with CKD, circulating hepcidin levels are markedly elevated due to several interrelated mechanisms. First, reduced renal clearance contributes directly to hepcidin accumulation as kidney function declines. Second, chronic low-grade inflammation characteristic of CKD stimulates hepatic hepcidin synthesis through inflammatory cytokines, particularly interleukin-6 (IL-6). Elevated hepcidin subsequently leads to iron sequestration within macrophages and reticuloendothelial cells, limiting iron bioavailability for erythropoiesis despite adequate or even increased total body iron stores. This phenomenon is commonly referred to as functional iron deficiency (10).

Two distinct forms of iron deficiency may therefore occur in CKD patients: absolute iron deficiency and functional iron deficiency. Absolute iron deficiency results from true depletion of total body iron stores, which may occur secondary to poor dietary intake, impaired gastrointestinal absorption, chronic blood loss, or frequent phlebotomy and dialysis-related blood loss. In contrast, functional iron deficiency is characterized by adequate iron stores with insufficient mobilization of iron to support erythropoiesis, primarily due to hepcidin-mediated iron restriction. Functional iron deficiency is particularly common among patients receiving erythropoiesis-stimulating agents (ESAs), in whom iron demand exceeds the capacity of iron mobilization from storage sites. Chronic inflammation further exacerbates iron dysregulation and anemia severity in CKD. Inflammatory cytokines not only stimulate hepcidin production but also directly suppress erythroid progenitor cell proliferation within the bone marrow. Additionally, inflammation contributes to erythropoietin resistance and shortens erythrocyte lifespan through enhanced oxidative stress and eryptosis. Consequently, CKD-associated anemia frequently demonstrates features of both iron-restricted erythropoiesis and anemia of chronic inflammation (11).

Several additional factors may aggravate iron deficiency and anemia in CKD patients. Uremic toxins have been shown to impair bone marrow responsiveness and erythrocyte survival, while nutritional deficiencies, gastrointestinal edema,

and concurrent medications may reduce intestinal iron absorption. Hemodialysis patients are particularly susceptible to ongoing iron loss due to repeated extracorporeal circulation, frequent laboratory testing, occult gastrointestinal bleeding, and blood retention within dialysis tubing systems. Collectively, these pathophysiological mechanisms create a state of persistent iron-restricted erythropoiesis that substantially contributes to anemia progression in CKD. Understanding the complex interplay between inflammation, hepcidin dysregulation, impaired erythropoietin production, and iron sequestration is therefore essential for optimizing therapeutic strategies. This evolving understanding also provides the biological rationale for the increasing use of intravenous iron therapy, particularly in CKD patients in whom oral iron supplementation is often insufficient to overcome inflammation-mediated impairment of iron absorption and mobilization (4).

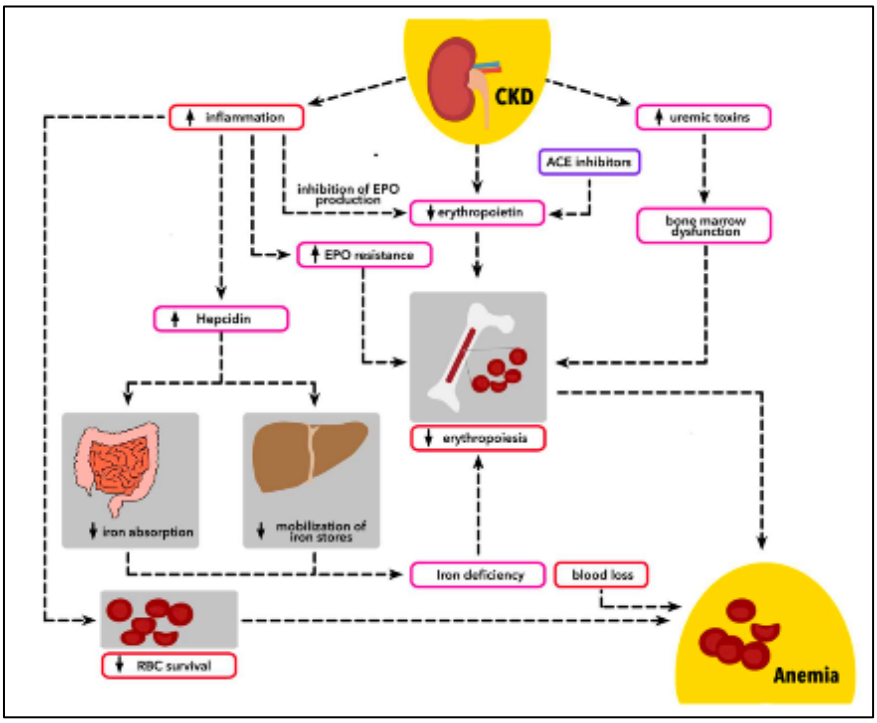

Figure 2 Pathophysiology of Anemia in CKD (4)

4. Efficacy of Intravenous Iron Therapy

Intravenous (IV) iron therapy has become a cornerstone in the management of CKD–associated anemia, particularly in patients with functional iron deficiency, inadequate response to oral iron supplementation, or increased erythropoietic demand during erythropoiesis-stimulating agent (ESA) therapy. Over the past decade, accumulating evidence from randomized controlled trials, observational studies, and international guidelines has consistently demonstrated that IV iron provides superior hematologic efficacy compared with oral iron therapy, while simultaneously reducing ESA requirements and improving anemia-related clinical outcomes. Consequently, IV iron has progressively shifted from an adjunctive strategy toward a central therapeutic component in contemporary CKD anemia management (12).

The therapeutic rationale for IV iron administration in CKD is strongly linked to the underlying pathophysiology of iron dysregulation. Elevated hepcidin levels in CKD impair intestinal iron absorption and inhibit mobilization of stored iron from macrophages and hepatocytes, thereby limiting the efficacy of oral iron preparations. As a result, oral iron often fails to adequately replenish bioavailable iron, particularly in patients with advanced CKD, chronic inflammation, or dialysis dependence. In contrast, IV iron bypasses gastrointestinal absorption barriers and delivers iron directly into the reticuloendothelial system and circulation, allowing more rapid iron utilization for erythropoiesis. This mechanistic advantage explains the consistently superior hematologic response observed with IV iron therapy in CKD populations (13).

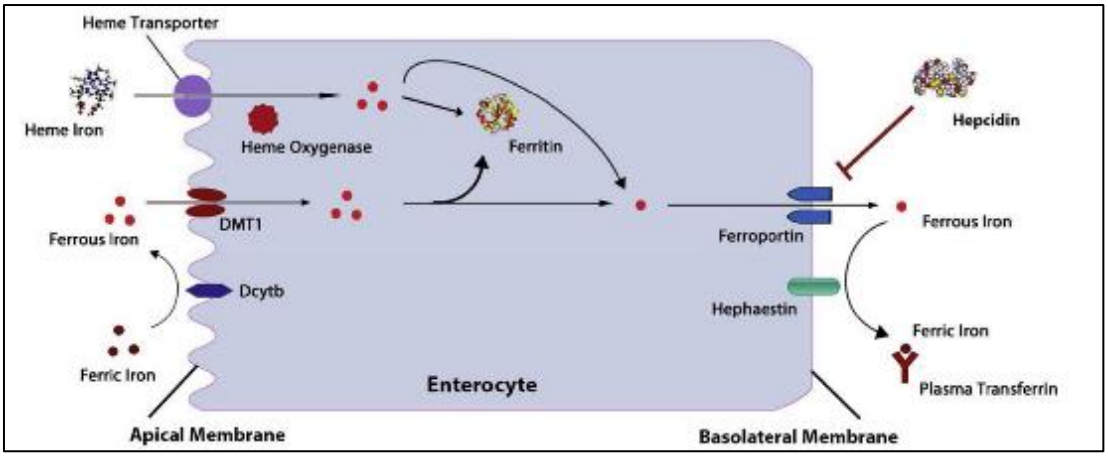

Figure 3 Intestinal iron absorption and inhibitory of hepcidin in CKD (13)

One of the most consistently reported benefits of IV iron therapy is improvement in hemoglobin (Hb) concentration. Multiple studies have demonstrated that IV iron produces faster and greater Hb increases than oral iron supplementation, particularly among patients with moderate-to-severe iron deficiency. The FIND-CKD trial, a multicenter randomized controlled trial involving 626 patients with non–dialysis-dependent CKD, compared high-ferritin-target intravenous ferric carboxymaltose (FCM), low-ferritin-target FCM, and oral iron therapy over 56 weeks. The study demonstrated that patients receiving high-dose IV ferric carboxymaltose experienced a significantly delayed need for additional anemia management, including ESA initiation or blood transfusion, compared with those receiving oral iron therapy. Furthermore, IV iron therapy achieved superior and more sustained hemoglobin improvement with fewer treatment failures (14).

Similarly, the Randomized Trial Comparing Proactive, High-Dose versus Reactive, Low-Dose IV Iron Supplementation in Hemodialysis (PIVOTAL) substantially reshaped contemporary perspectives regarding IV iron therapy in dialysis-dependent CKD patients. This landmark trial enrolled 2,141 incident hemodialysis patients randomized to either proactive high-dose IV iron sucrose (400 mg monthly unless safety thresholds were exceeded) or reactive low-dose iron administration based on ferritin and transferrin saturation (TSAT) levels. Remarkably, proactive high-dose IV iron not only reduced ESA requirements but also significantly lowered the composite risk of myocardial infarction, stroke, hospitalization for heart failure, and all-cause mortality compared with the reactive low-dose strategy. Importantly, these benefits were achieved without an increased incidence of infection or serious adverse events. The PIVOTAL trial therefore provided strong evidence supporting a more proactive IV iron replacement strategy in hemodialysis populations (15).

Beyond hemoglobin correction alone, IV iron therapy also demonstrates substantial ESA-sparing effects. Functional iron deficiency frequently limits the effectiveness of ESA therapy because erythropoietic stimulation rapidly increases iron demand beyond the capacity of endogenous iron mobilization. Inadequate iron availability subsequently contributes to ESA hyporesponsiveness, necessitating escalating ESA doses that may increase cardiovascular and thromboembolic risk. Several clinical trials have shown that IV iron supplementation improves ESA responsiveness and permits significant ESA dose reduction while maintaining target hemoglobin levels. The DRIVE I and DRIVE II studies, conducted in hemodialysis patients with elevated ferritin levels but low TSAT, demonstrated that administration of IV ferric gluconate significantly improved hemoglobin response and reduced epoetin requirements despite baseline ferritin concentrations traditionally considered "adequate." These findings challenged the conventional assumption that elevated ferritin reliably excludes iron-responsive anemia in CKD (16).

The superiority of IV iron over oral formulations is particularly evident in advanced CKD and dialysis populations. Oral iron therapy is frequently limited by poor gastrointestinal absorption, high pill burden, gastrointestinal adverse effects, and poor long-term adherence. Moreover, chronic inflammation and elevated hepcidin levels substantially diminish intestinal iron uptake, rendering oral supplementation insufficient in many CKD patients. In contrast, IV iron circumvents these barriers and achieves more efficient iron delivery. Meta-analyses comparing IV and oral iron consistently demonstrate greater increases in hemoglobin, ferritin, and TSAT with IV therapy, alongside reduced ESA utilization and lower transfusion requirements. These benefits are especially pronounced among patients receiving hemodialysis, in whom ongoing extracorporeal blood loss and repeated phlebotomy contribute to persistent iron depletion (13).

Several IV iron formulations are currently available, each characterized by distinct pharmacokinetic properties, dosing schedules, and stability profiles. Commonly utilized formulations include iron sucrose, ferric carboxymaltose, ferric derisomaltose, sodium ferric gluconate, ferumoxytol, and low-molecular-weight iron dextran. Newer formulations such as ferric carboxymaltose and ferric derisomaltose allow administration of larger single doses with improved convenience and reduced infusion frequency, which may enhance treatment adherence and healthcare efficiency. Comparative studies generally suggest similar hematologic efficacy among modern IV iron preparations, although differences in infusion protocols, hypophosphatemia risk, and hypersensitivity profiles remain clinically relevant. Importantly, emerging evidence suggests that the benefits of IV iron therapy may extend beyond correction of anemia alone. Iron deficiency itself has been associated with impaired skeletal muscle function, reduced exercise tolerance, fatigue, cognitive dysfunction, and diminished quality of life independent of hemoglobin concentration. Several studies have reported improvements in fatigue scores, physical functioning, and patient-reported outcomes following IV iron administration in CKD populations. Additionally, by reducing transfusion dependence and minimizing high ESA exposure, IV iron therapy may indirectly contribute to improved long-term cardiovascular safety and transplantation eligibility (12).

5. Safety and Limitations of Intravenous Iron Therapy

Despite its proven efficacy in improving anemia outcomes, IV iron therapy remains associated with several important safety considerations in patients with CKD. Nevertheless, contemporary evidence indicates that modern IV iron formulations are generally safe and well tolerated when administered appropriately under guideline-based monitoring. Historically, concerns regarding IV iron therapy originated from older high-molecular-weight iron dextran preparations, which were associated with severe hypersensitivity and anaphylactoid reactions. However, these formulations have largely been replaced by newer-generation agents such as iron sucrose, ferric carboxymaltose, ferric derisomaltose, and ferumoxytol, all of which demonstrate substantially improved safety profiles with relatively low rates of serious adverse reactions (17).

One major concern surrounding IV iron therapy involves oxidative stress and tissue injury. Because iron can catalyze reactive oxygen species formation, excessive iron exposure has theoretically been linked to endothelial dysfunction, inflammation, and cardiovascular injury. This concern is particularly relevant in CKD patients who already exhibit chronic inflammatory and oxidative states. However, current large-scale clinical trials have not consistently demonstrated increased cardiovascular morbidity or mortality associated with modern IV iron therapy when administered within recommended dosing strategies. The potential relationship between IV iron therapy and infection risk has also been extensively debated. Iron availability may theoretically promote bacterial proliferation and impair immune defense mechanisms. Nonetheless, findings from the landmark PIVOTAL trial demonstrated that proactive high-dose IV iron administration did not increase rates of infection, infection-related hospitalization, or infection-related mortality compared with reactive low-dose strategies. These findings provide important reassurance regarding the infectious safety of contemporary IV iron therapy (18).

Another important consideration is iron overload, particularly in patients receiving long-term repeated iron administration. Interpretation of iron biomarkers in CKD remains challenging because ferritin may increase not only due to iron accumulation but also secondary to chronic inflammation. Consequently, differentiating functional iron deficiency from excessive iron storage may be difficult in certain clinical settings. Current KDIGO recommendations therefore emphasize careful monitoring of transferrin saturation (TSAT) and ferritin levels during therapy to minimize the risk of overtreatment. Differences among IV iron formulations also represent an important clinical consideration. Although most preparations exhibit comparable hematologic efficacy, variations exist in dosing schedules, infusion protocols, and adverse-effect profiles. Ferric carboxymaltose and ferric derisomaltose permit larger single-dose administration and reduced infusion frequency, improving treatment convenience and adherence. However, ferric carboxymaltose has been associated with hypophosphatemia mediated by fibroblast growth factor-23 (FGF-23), particularly following repeated administration (12).

Practical limitations additionally influence the implementation of IV iron therapy. Intravenous administration requires infusion facilities, trained personnel, monitoring systems, and venous access, which may increase healthcare costs and reduce accessibility in resource-limited settings. Furthermore, repeated hospital visits may decrease convenience for non–dialysis-dependent CKD patients. Despite these limitations, the overall balance of evidence strongly supports the safety of IV iron therapy when used judiciously and individualized according to patient characteristics and laboratory monitoring. Current nephrology practice increasingly recognizes that untreated iron deficiency itself carries substantial clinical consequences, including worsening anemia, ESA hyporesponsiveness, reduced quality of life, and increased transfusion requirements. Therefore, the modern challenge is not whether IV iron should be used, but rather how to

optimize dosing strategies, monitoring protocols, and patient selection to maximize therapeutic benefit while minimizing potential risk (19).

6. Current Recommendations and Future Perspectives

Current international guidelines increasingly recognize IV iron therapy as a fundamental component in the management of CKD–associated anemia, particularly in patients with functional iron deficiency, inadequate response to oral supplementation, or increased erythropoietic demand. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend consideration of iron therapy in CKD patients with transferrin saturation (TSAT) ≤30% and serum ferritin ≤500 ng/mL when the therapeutic goal is to increase hemoglobin levels, reduce erythropoiesis-stimulating agent (ESA) requirements, or minimize transfusion dependence. Importantly, contemporary recommendations increasingly emphasize individualized treatment strategies rather than rigid laboratory thresholds alone (3).

Recent evidence, particularly from landmark trials such as PIVOTAL, has substantially influenced modern nephrology practice by supporting more proactive iron replacement approaches in carefully monitored patients undergoing hemodialysis. These findings have shifted clinical perspectives away from excessive concern regarding iron administration toward a more balanced recognition that untreated iron deficiency itself contributes significantly to morbidity, impaired quality of life, ESA hyporesponsiveness, and cardiovascular burden in CKD populations. Nevertheless, several unresolved challenges remain in optimizing IV iron therapy. Current biomarkers, including ferritin and TSAT, possess important limitations in inflammatory states and may not accurately reflect true iron bioavailability. Consequently, growing attention has been directed toward the development of more precise biomarkers, including hepcidin measurement, reticulocyte hemoglobin content, and hypochromic red blood cell indices, which may improve individualized assessment of iron status and therapeutic responsiveness in the future (20).

In parallel, emerging therapeutic advances are reshaping the landscape of anemia management in CKD. Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), such as roxadustat and daprodustat, have demonstrated the ability to improve erythropoiesis while simultaneously modulating iron metabolism through hepcidin suppression and enhanced endogenous iron utilization. These agents may potentially reduce IV iron requirements in selected patients and represent an important future direction in integrated anemia therapy. Future research should continue to focus on long-term cardiovascular safety, optimal iron dosing strategies, individualized treatment targets, and the identification of patient populations most likely to benefit from proactive iron replacement. Furthermore, additional studies evaluating patient-reported outcomes, physical function, and quality of life are necessary to better understand the broader clinical impact of iron therapy beyond hemoglobin correction alone (21).

7. Conclusion

CKD–associated anemia remains a major clinical challenge driven by complex disturbances in erythropoiesis, iron metabolism, inflammation, and hepcidin dysregulation. Contemporary evidence strongly supports IV iron therapy as an effective and increasingly central strategy in anemia management, particularly in patients with functional iron deficiency, ESA hyporesponsiveness, and dialysis dependence. Landmark studies such as FIND-CKD and PIVOTAL have demonstrated that IV iron not only improves hemoglobin levels and replenishes iron stores more effectively than oral therapy, but may also reduce ESA requirements, transfusion dependence, and adverse cardiovascular outcomes when appropriately administered. Although concerns regarding oxidative stress, infection risk, and iron overload remain important considerations, modern IV iron formulations generally exhibit favorable safety profiles under careful monitoring and individualized treatment approaches. As understanding of CKD-related iron dysregulation continues to evolve, future advances in biomarker-guided therapy and emerging agents such as HIF-prolyl hydroxylase inhibitors may further refine personalized anemia management. Ultimately, IV iron therapy represents a pivotal component of contemporary CKD care, with the potential not only to correct anemia, but also to improve overall clinical outcomes and quality of life in patients living with CKD.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Li PKT, Garcia-Garcia G, Lui SF, Andreoli S, Fung WWS, Hradsky A, et al. Kidney Health for Everyone Everywhere—From Prevention to Detection and Equitable Access to Care. Kidney International Reports. Elsevier Inc.; 2020. p. 245–51. doi:10.1016/j.ekir.2020.01.023

[2] Mark PB, Stafford LK, Grams ME, Aalruz H, Abd ElHafeez S, Abdelgalil AA, et al. Global, regional, and national burden of chronic kidney disease in adults, 1990–2023, and its attributable risk factors: a systematic analysis for the Global Burden of Disease Study 2023. The Lancet. 2025 Nov 22;406(10518):2461–82. doi:10.1016/S0140-6736(25)01853-7 PubMed PMID: 41213283.

[3] Kidney Disease Improving Global Outcomes. KDIGO 2025 CLINICAL PRACTICE GUIDELINE FOR ANEMIA IN CHRONIC KIDNEY DISEASE (CKD). 2024.

[4] Badura K, Janc J, Wąsik J, Gnitecki S, Skwira S, Młynarska E, et al. Anemia of Chronic Kidney Disease—A Narrative Review of Its Pathophysiology, Diagnosis, and Management. Biomedicines. Multidisciplinary Digital Publishing Institute (MDPI); 2024. doi:10.3390/biomedicines12061191 PubMed PMID: 38927397.

[5] Gutiérrez OM. Treatment of Iron Deficiency Anemia in CKD and End-Stage Kidney Disease. Kidney International Reports. Elsevier Inc.; 2021. p. 2261–9. doi:10.1016/j.ekir.2021.05.020

[6] Babitt JL, Eisenga MF, Haase VH, Kshirsagar A V., Levin A, Locatelli F, et al. Controversies in optimal anemia management: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Conference. In: Kidney International. Elsevier B.V.; 2021. p. 1280–95. doi:10.1016/j.kint.2021.03.020 PubMed PMID: 33839163.

[7] Del Vecchio L, Longhi S, Locatelli F. Safety concerns about intravenous iron therapy in patients with chronic kidney disease. Clinical Kidney Journal. Oxford University Press; 2016. p. 260–7. doi:10.1093/ckj/sfv142

[8] Batchelor EK, Kapitsinou P, Pergola PE, Kovesdy CP, Jalal DI. Iron deficiency in chronic kidney disease: Updates on pathophysiology, diagnosis, and treatment. Journal of the American Society of Nephrology. American Society of Nephrology; 2020. p. 456–68. doi:10.1681/ASN.2019020213 PubMed PMID: 32041774.

[9] Zumbrennen-Bullough K, Babitt JL. The iron cycle in chronic kidney disease (CKD): from genetics and experimental models to CKD patients. Nephrology Dialysis Transplantation. 2020. p. 263–73. doi:10.1093/ndt/gft443 PubMed PMID: 24235084.

[10] Ganz T, Nemeth E. Iron Balance and the Role of Hepcidin in Chronic Kidney Disease. Seminars in Nephrology. W.B. Saunders; 2016. p. 87–93. doi:10.1016/j.semnephrol.2016.02.001 PubMed PMID: 27236128.

[11] Hain D, Bednarski D, Cahill M, Dix A, Foote B, Haras MS, et al. Iron-Deficiency Anemia in CKD: A Narrative Review for the Kidney Care Team. Kidney Medicine. Elsevier Inc.; 2023. doi:10.1016/j.xkme.2023.100677 PubMed PMID: 37415621.

[12] Macdougall IC. Intravenous iron therapy in patients with chronic kidney disease: Recent evidence and future directions. Clinical Kidney Journal. Oxford University Press; 2017. p. i16–24. doi:10.1093/ckj/sfx043 PubMed PMID: 29225819.

[13] Gutiérrez OM. Treatment of Iron Deficiency Anemia in CKD and End-Stage Kidney Disease. Kidney International Reports. Elsevier Inc.; 2021. p. 2261–9. doi:10.1016/j.ekir.2021.05.020

[14] Macdougall IC, Bock AH, Carrera F, Eckardt KU, Gaillard C, Van Wyck D, et al. FIND-CKD: A randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anaemia. Nephrology Dialysis Transplantation. 2015 Nov 1;29(11):2075–84. doi:10.1093/ndt/gfu201 PubMed PMID: 24891437.

[15] Macdougall IC, White C, Anker SD, Bhandari S, Farrington K, Kalra PA, et al. Intravenous Iron in Patients Undergoing Maintenance Hemodialysis. New England Journal of Medicine. 2019 Jan 31;380(5):447–58. doi:10.1056/nejmoa1810742 PubMed PMID: 30365356.

[16] Kapoian T, O'Mara NB, Singh AK, Moran J, Rizkala AR, Geronemus R, et al. Ferric gluconate reduces epoetin requirements in hemodialysis patients with elevated ferritin. Journal of the American Society of Nephrology. 2016;19(2):372–9. doi:10.1681/ASN.2007050606 PubMed PMID: 18216316.

[17] Del Vecchio L, Longhi S, Locatelli F. Safety concerns about intravenous iron therapy in patients with chronic kidney disease. Clinical Kidney Journal. Oxford University Press; 2016. p. 260–7. doi:10.1093/ckj/sfv142

[18] Greenland JC, Cutting E, Kadyan S, Bond S, Chhabra A, Williams-Gray CH. Azathioprine immunosuppression and disease modification in Parkinson's disease (AZA-PD): a randomised double-blind placebo-controlled phase II trial protocol. BMJ Open. 2020 Nov 23;10(11). doi:10.1136/bmjopen-2020-040527 PubMed PMID: 33234645.

[19] Balogun M, Kumah EA, Adaramoye VO, Eboreime E, Ameh C, Afolabi BB. Implementation strategies and outcomes of intravenous iron use for treatment of anaemia during and after pregnancy in low- and middle-income countries: A scoping review. PLOS Global Public Health. 2026 Jan 1;6(1). doi:10.1371/journal.pgph.0004858

[20] Macdougall IC, White C, Anker SD, Bhandari S, Farrington K, Kalra PA, et al. Randomized trial comparing proactive, high-dose versus reactive, low-dose intravenous iron supplementation in hemodialysis (PIVOTAL): Study design and baseline data. Am J Nephrol. 2018 Nov 1;48(4):260–8. doi:10.1159/000493551 PubMed PMID: 30304714.

[21] Haase VH. Hypoxia-inducible factor–prolyl hydroxylase inhibitors in the treatment of anemia of chronic kidney disease. Kidney Int Suppl (2011). 2021 Apr 1;11(1):8–25. doi:10.1016/j.kisu.2020.12.002