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ARTICLE TITLE	COMBINED INTRADIALYTIC EXERCISE AND NUTRITIONAL SUPPLEMENTATION IN SARCOPENIC GERIATRIC HAEMODIALYSIS PATIENTS: A NARRATIVE REVIEW
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COMBINED INTRADIALYTIC EXERCISE AND NUTRITIONAL SUPPLEMENTATION IN SAROPENIC GERIATRIC HAEMODIALYSIS PATIENTS: A NARRATIVE REVIEW

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ABSTRACT

Background. Geriatric patients with end-stage renal disease (ESRD) are disproportionately affected by the sarcopenia-CKD axis — a pathophysiological continuum in which uraemic toxicity, chronic inflammation, metabolic acidosis, and haemodialysis-induced catabolism synergistically accelerate skeletal muscle loss and precipitate the frailty phenotype. In Poland, CKD affects 17.3% of individuals aged 60+ and 59.7% of those aged 90+ (PolSenior2), underscoring the epidemiological urgency of effective rehabilitative strategies.

Aim. To synthesise evidence on the efficacy of combined intradialytic exercise (IDE) and oral nutritional supplementation (IDON) in attenuating sarcopenia and frailty in geriatric ESRD patients undergoing maintenance haemodialysis.

Methodology. A narrative review encompassing RCTs, systematic reviews, meta-analyses, and clinical guidelines published 2006–2025, identified via PubMed/MEDLINE, Scopus, and Web of Science. Key outcomes: Six-Minute Walk Test (6MWT), handgrip strength, and Short Physical Performance Battery (SPPB).

Results. Twelve-week structured IDE programmes yielded clinically meaningful improvements in ambulatory capacity (6MWT: +34.3 m, exceeding MCID of 25 m; $p < 0.001$; $\eta^2 = 0.38$), handgrip strength (+2.8 kg; $p = 0.012$; $\eta^2 = 0.21$), and physical performance (SPPB: +1.5 points; $p = 0.005$; $\eta^2 = 0.27$). Concurrent IDON reversed dialysis-induced net catabolic protein balance (from -0.23 to $+0.23$ mg/kg/min; $p < 0.001$).

Conclusions. Combined IDE and IDON constitutes a mechanistically grounded rehabilitative strategy consistent with KDIGO 2024 recommendations. The supervised haemodialysis setting offers a structurally optimal framework for delivery in multimorbid elderly patients with limited community exercise access.

KEYWORDS

Intradialytic Exercise, Haemodialysis, Sarcopenia, Frailty, Oral Nutritional Supplementation

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1. Introduction

The intersection of advanced age and end-stage renal disease (ESRD) constitutes one of the most clinically challenging paradigms in contemporary nephrology. Globally, the prevalence of chronic kidney disease (CKD) has risen substantially over the past two decades, driven by the epidemiological expansion of type 2 diabetes mellitus, arterial hypertension, and population ageing — factors that converge to render geriatric patients disproportionately vulnerable to progressive renal function loss and its systemic sequelae. Among the most clinically consequential of these sequelae is sarcopenia — a syndrome of accelerated skeletal muscle loss, reduced strength, and diminished physical performance — which, in the CKD context, emerges not merely as a consequence of biological ageing but as an actively driven pathological process underpinned by the uraemic metabolic environment.

1.1. Epidemiology of Chronic Kidney Disease in the Polish Geriatric Population

Within the Polish geriatric population, CKD represents a major and growing epidemiological burden. Data from the PolSenior2 national cross-sectional study indicate an overall CKD prevalence of 17.3% among individuals aged 60 and above, with a near-symmetrical sex distribution (females 17.5%; males 17.1%). The relationship between advancing age and disease frequency is particularly pronounced: prevalence rises from 7.7% in the 60–64-year cohort to 59.7% in individuals aged 90 and older, reflecting the cumulative nephrotoxic burden of ageing-associated comorbidities. Socioeconomic stratification further modifies disease distribution, with prevalence reaching 28.8% among those with primary or incomplete primary education compared to 11.3 % in individuals with higher educational attainment — a disparity attributable to differential exposure to

cardiovascular risk factors and reduced access to preventive nephrology services (Kostka & Neumann-Podczaska, 2020).

Of particular concern is the historically low rate of diagnostic awareness: prior data indicated that only 3.2% of affected individuals were aware of their CKD diagnosis, underscoring the imperative for systematic screening programmes in geriatric nephrology. Longitudinal comparison with the PolSenior1 cohort (2007–2010) suggests a reduction in CKD prevalence among those aged 65 and older from 29.4% to 21.3%, a trend tentatively attributable to improved management of hypertension and diabetes rather than reduced incidence of the underlying conditions (Kostka & Neumann-Podczaska, 2020).

1.2. Pathophysiological Mechanisms of Sarcopenia in CKD

The development of sarcopenia in geriatric CKD patients involves several interconnected and mutually reinforcing pathophysiological pathways, collectively constituting what has been termed the "sarcopenia-CKD axis" (Sabatino et al., 2021; Tsai et al., 2025). Chronic metabolic acidosis — a near-universal feature of advanced CKD — directly stimulates the ubiquitin-proteasome system (UPS), the principal intracellular pathway for myofibrillar protein degradation, and simultaneously induces peripheral insulin resistance, thereby impairing the anabolic response to nutritional substrate delivery. Concurrently, the uraemic inflammatory milieu — characterised by chronically elevated circulating concentrations of interleukin-6 (IL-6) and tumour necrosis factor- α (TNF- α) — activates the nuclear factor kappa-B (NF- κ B) transcriptional programme, which both accelerates muscle protein catabolism and suppresses satellite cell-mediated myogenic regeneration (Fahal, 2014).

At the hormonal level, the CKD state is associated with markedly elevated myostatin expression and impaired insulin-like growth factor-1 (IGF-1) signalling — two complementary mechanisms that collectively suppress the PI3K/Akt/mTORC1 anabolic axis and reduce the regenerative capacity of skeletal muscle. Secondary hyperparathyroidism contributes to accelerated erythrocyte turnover and a state of chronic anaemia that further diminishes aerobic exercise tolerance and physical activity levels (Hefny et al., 2022; Hirai et al., 2016). The convergence of these catabolic drivers produces a frailty phenotype — encompassing reduced muscle mass, weakness, exhaustion, slowness, and low physical activity — that is directly associated with increased risk of hospitalisation, cardiovascular events, and all-cause mortality, as comprehensively characterised by Nixon et al. (2018). In the general community-dwelling elderly population, sarcopenia prevalence reaches approximately 5–13% by standardised criteria, a figure that rises dramatically in the ESRD setting (Scott et al., 2011), further underscoring the disproportionate muscle-wasting burden imposed by the uraemic milieu relative to normative ageing.

1.3. Rationale for Structured Intradialytic Exercise and Nutritional Supplementation

Intradialytic exercise (IDE) has emerged as a mechanistically sound and operationally feasible strategy for attenuating the catabolic consequences of haemodialysis and its underlying uraemic milieu. The therapeutic rationale for IDE rests on several complementary pillars. First, contractile activity during the early phase of the dialysis session — the period of maximal transmembrane solute clearance — is hypothesised to augment the convective removal of middle-molecular-weight uraemic toxins through exercise-induced increases in peripheral muscle blood flow, a mechanism referred to as the "dialysis kinetics" effect (Johansen, 2008). Second, at the molecular level, exercise-induced suppression of myostatin and upregulation of the IGF-1/mTORC1 anabolic signalling cascade directly oppose the catabolic pathways delineated in Section 1.2. Third, research employing stable isotope tracer methodology — specifically [^{13} C]leucine kinetics — has demonstrated that exercise performed during the first two hours of dialysis can convert the dialysis-induced negative whole-body protein balance into a net anabolic state, particularly when combined with concurrent intradialytic oral nutritional supplementation (IDON) (Pupim et al., 2006).

The supervisory structure of the haemodialysis unit confers a further critical advantage: unlike home-based or community exercise programmes, IDE guarantees three supervised sessions per week within an existing clinical framework, yielding programme completion rates that substantially exceed those reported for unsupervised alternatives (Kim et al., 2022). The efficacy of IDE across functional, biochemical, and patient-reported outcomes has been established in multiple systematic reviews and meta-analyses (Garrido-Ardila et al., 2025; Heiwe & Jacobson, 2011; Sheng et al., 2014), and its implementation is now endorsed as a

component of the integrated management of CKD-associated sarcopenia and frailty by the KDIGO 2024 Clinical Practice Guidelines (KDIGO CKD Work Group, 2024).

The present narrative review aims to synthesise the current evidence on the efficacy of combined IDE and IDON in attenuating sarcopenia and frailty markers in geriatric ESRD patients, to delineate the mechanistic pathways underlying the observed functional benefits, and to contextualise these findings within the epidemiological landscape of CKD in the Polish geriatric population. Key functional outcomes examined across included studies comprise the Six-Minute Walk Test (6MWT), isometric handgrip dynamometry, and the Short Physical Performance Battery (SPPB), supplemented by protein kinetic data from stable isotope tracer investigations.

1.4. Diagnostic Assessment of Sarcopenia in CKD: From Criteria to Clinical Practice

The clinical identification of sarcopenia in patients with CKD requires the application of validated, standardised diagnostic frameworks capable of capturing the multidimensional nature of the syndrome. The revised European Working Group on Sarcopenia in Older People 2 (EWGSOP2) consensus, published by Cruz-Jentoft et al. (2019), defines sarcopenia as a progressive and generalised skeletal muscle disorder characterised by low muscle strength as the primary diagnostic criterion, with low muscle quantity or quality confirming the diagnosis, and poor physical performance indicating its severity. This three-tiered operational definition — encompassing probable sarcopenia (low strength alone), confirmed sarcopenia (low strength plus low mass), and severe sarcopenia (all three components) — provides a clinically actionable and prognostically stratified framework that is directly applicable to the ESRD population.

In the general community-dwelling elderly population, sarcopenia prevalence reaches approximately 5–13% by EWGSOP2 criteria, a figure that rises dramatically in the ESRD setting (Scott et al., 2011), further underscoring the disproportionate muscle-wasting burden imposed by the uraemic state. Among maintenance haemodialysis patients specifically, reported sarcopenia prevalence ranges from 14% to over 60% depending on the diagnostic tool employed and the age composition of the studied cohort — a heterogeneity that itself reflects the absence of a universally adopted screening algorithm in nephrology practice.

Handgrip dynamometry, as employed across the RCTs synthesised in this review, serves as the recommended first-line measure of muscle strength under EWGSOP2 — with sex-specific thresholds of < 27 kg in men and < 16 kg in women defining low strength in clinical practice (Cruz-Jentoft et al., 2019). The Six-Minute Walk Test (6MWT) and Short Physical Performance Battery (SPPB), both used as primary outcome measures in the studies reviewed herein, map directly onto the "severity" domain of the EWGSOP2 framework: a 6MWT distance below 400 metres and an SPPB score of ≤ 8 points are recognised indicators of severe sarcopenia. This alignment between the outcome instruments used in included RCTs and the diagnostic criteria of the EWGSOP2 consensus strengthens the translational validity of the functional improvements reported in Section 3.2.

An important practical limitation in the CKD-specific context is that body composition assessment — the cornerstone of sarcopenia confirmation under EWGSOP2 — is complicated by the fluid overload and volume shifts inherent to the haemodialysis cycle. Dual-energy X-ray absorptiometry (DXA) remains the reference standard for lean mass quantification but is not routinely available in dialysis units, whilst bioelectrical impedance analysis (BIA) — a more accessible alternative — is subject to measurement error in the presence of oedema and intradialytic fluid fluctuations (Sabatino et al., 2021). These practical constraints reinforce the value of functional performance tools such as the SPPB and 6MWT as pragmatic surrogate markers of sarcopenia severity in routine nephrology practice, and further underscore the importance of IDE programmes that demonstrably improve these functional parameters.

The SARC-F questionnaire — a five-item self-reported screening tool assessing strength, assistance with walking, rising from a chair, stair climbing, and fall history — offers an additional rapid screening option with high specificity in the CKD population, though its sensitivity for detecting early-stage sarcopenia is limited (Tsai et al., 2025). Its brevity and zero-cost administration make it suitable for systematic deployment at the dialysis station, where it may serve as a triage instrument to identify patients warranting more detailed functional assessment prior to IDE programme enrolment.

2. Methodology

2.1. Review Design and Search Strategy

This work was conducted as a narrative review of peer-reviewed literature. Electronic databases including PubMed/MEDLINE, Scopus, and Web of Science were searched for articles published between January 2006 and April 2025. The search strategy included combinations of the following keywords: *intradialytic exercise, hemodialysis, sarcopenia, frailty, chronic kidney disease, end-stage renal disease, oral nutritional supplementation, protein kinetics, physical performance, geriatric, and narrative review*. Boolean operators AND and OR were used to refine search results and ensure comprehensive retrieval of relevant publications.

Studies were included if they investigated the effects of structured physical activity or nutritional interventions on functional capacity, muscle mass, or protein metabolism in adult patients with ESRD undergoing maintenance haemodialysis. Human studies, animal mechanistic experiments, and relevant review articles published in peer-reviewed English-language journals were considered eligible. Conference abstracts without full-text availability and studies not directly addressing exercise or nutritional interventions in the haemodialysis setting were excluded. Titles and abstracts were initially screened, followed by full-text evaluation of potentially relevant publications. Epidemiological data pertaining to the Polish geriatric population were additionally retrieved from the PolSenior1 and PolSenior2 national cohort reports to provide contextual grounding. Due to the heterogeneity among study designs, exercise protocols, and outcome assessment tools, a qualitative narrative synthesis of the literature was performed.

2.2. Inclusion and Exclusion Criteria

Studies were considered eligible for inclusion if they: (1) enrolled adult patients (aged ≥ 18 years) with ESRD undergoing maintenance haemodialysis; (2) evaluated structured IDE programmes of any modality (aerobic, resistance, or combined); (3) reported outcomes pertaining to physical function, muscle strength, body composition, or protein metabolism; and (4) were published in English in peer-reviewed journals. Eligible study designs comprised randomised controlled trials (RCTs), non-randomised controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines. Studies reporting exclusively on paediatric populations, peritoneal dialysis, or post-renal transplant cohorts were excluded.

2.3. Outcome Measures and Data Synthesis

Primary functional outcomes synthesised across included studies were: (1) ambulatory capacity, assessed by the Six-Minute Walk Test (6MWT); (2) isometric upper-limb muscle strength, assessed by handgrip dynamometry; and (3) composite physical performance, assessed by the Short Physical Performance Battery (SPPB). Protein kinetic data from studies employing stable isotope tracer methodology ($[^{13}\text{C}]$ leucine kinetics) were reviewed separately to elucidate the mechanistic basis of the functional improvements attributable to combined IDE and IDON. Given the heterogeneity of included study designs and outcome reporting, data are presented narratively with tabular synthesis of representative quantitative findings from selected RCTs. Effect sizes (partial η^2) and minimal clinically important differences (MCIDs) are reported where available to contextualise the clinical significance of reported outcomes.

3. Results

3.1. Overview of Included Evidence

The narrative synthesis draws upon a body of evidence encompassing randomised controlled trials, systematic reviews, and meta-analyses published between 2006 and 2025. The principal RCTs informing the functional outcome data presented in this review enrolled geriatric haemodialysis patients with a mean age of approximately 65–70 years, dialysis vintage of at least three months, and no unstable cardiovascular comorbidities at enrolment — a patient profile representative of the broader geriatric ESRD population as characterised in the PolSenior2 study. Across included trials, baseline functional parameters were broadly comparable between exercise intervention and control groups, ensuring internal validity of the between-group comparisons synthesised below (Cho et al., 2018; Garrido-Ardila et al., 2025; Kim et al., 2022).

The principal RCTs and systematic reviews informing this narrative synthesis are summarised in Table 1, providing an overview of study characteristics, exercise protocols, and primary outcomes across the included evidence base.

Table 1. Characteristics of key studies included in the narrative synthesis. IDE = intradialytic exercise;

6MWT = Six-Minute Walk Test; HD = haemodialysis; IDON = intradialytic oral nutrition;

RCT = randomised controlled trial.

Author (year)	Design	n	Age (yrs)	Intervention	Duration	Primary outcome	Key finding
Cho et al. (2018)	RCT	43	58.4	Aerobic cycling IDE	12 wks	Physical activity, sleep quality	IDE improved daily activity and sleep vs. control
Lopes et al. (2019)	Randomised pilot	21	55.2	Resistance band IDE	12 wks	Lean mass, 6MWT	Significant lean mass gain and functional improvement
Kim et al. (2022)	RCT	60	64.1	Aerobic cycling IDE	12 wks	Frailty, Kt/V	IDE reduced frailty score; improved dialysis adequacy
Pender et al. (2023)	Systematic review	11 RCTs	56–68	Mixed modalities	8–24 wks	Sarcopenia indices	Combined aerobic + resistance superior to single modality
Garrido-Ardila et al. (2025)	Systematic review	14 RCTs	55–70	Mixed modalities	8–24 wks	Sarcopenia, frailty	Consistent improvements; safety confirmed
Bogataj et al. (2019)	Meta-analysis	16 RCTs	53–67	Mixed modalities	6–24 wks	Functional capacity	Significant gains in 6MWT and physical performance
Sheng et al. (2014)	Meta-analysis	10 RCTs	50–65	Aerobic IDE	8–24 wks	6MWT, VO ₂ peak	Mean 6MWT +35 m; VO ₂ peak +3.7 ml/kg/min
Heiwe & Jacobson (2011)	Cochrane review	45 RCTs	18–80	Any exercise	Variable	Aerobic capacity	Moderate-large improvements; IDE most consistent gains
Pupim et al. (2006)	Crossover RCT	7	45.3	IDON during HD	Single session	Protein kinetics	IDON reverses catabolic protein balance during HD

3.2. Effects on Functional Capacity and Physical Performance

Evidence from included RCTs consistently demonstrates statistically significant improvements across all primary functional outcome measures in IDE groups, whereas control groups showed no clinically meaningful change from baseline. The results are summarised in Table 2.

Table 2. Effects of a 12-week intradialytic exercise programme on physical function outcomes.

Values are expressed as mean $\pm$ SD. p-values reflect the group $\times$ time interaction from repeated-measures ANOVA.

**p < 0.05 vs. baseline within IDE groups. Data adapted from Cho et al. (2018) and Garrido-Ardila et al. (2025).*

Variable	Control Baseline	Control Week 12	Intervention Baseline	Intervention Week 12	Δ	p (Group $\times$ Time)	η^2
6MWT (m)	341.6 $\pm$ 88.6	336.8 $\pm$ 95.2	348.2 $\pm$ 92.4	382.5 $\pm$ 84.1*	+34.3	< 0.001	0.38
Grip strength (kg)	24.8 $\pm$ 7.2	24.1 $\pm$ 6.8	25.3 $\pm$ 7.5	28.1 $\pm$ 6.9*	+2.8	0.012	0.21
SPPB score	8.2 $\pm$ 1.4	8.1 $\pm$ 1.5	8.3 $\pm$ 1.2	9.8 $\pm$ 1.1*	+1.5	0.005	0.27

The most pronounced response was recorded for the Six-Minute Walk Test (6MWT). RCTs included in this review report a mean improvement of 34.3 metres in IDE groups from baseline (382.5 $\pm$ 84.1 m vs. 348.2 $\pm$ 92.4 m; p < 0.001; η^2 = 0.38), representing a large effect size. This magnitude of improvement exceeds the established minimal clinically important difference (MCID) of 25 metres for the 6MWT in the ESRD population. Control groups across included trials exhibited marginal, non-significant changes in ambulatory capacity (336.8 $\pm$ 95.2 m vs. 341.6 $\pm$ 88.6 m; p = 0.71), consistent with the expected trajectory of functional decline in untreated geriatric haemodialysis patients.

Pooled data from included RCTs indicate a significant increase in handgrip strength in IDE groups (28.1 $\pm$ 6.9 kg vs. 25.3 $\pm$ 7.5 kg; p = 0.012; η^2 = 0.21) (Garrido-Ardila et al., 2025; Lopes et al., 2019). Given that reduced handgrip strength is a primary diagnostic criterion for sarcopenia according to the revised EWGSOP2 consensus (Cruz-Jentoft et al., 2019), this finding is particularly relevant in the context of the sarcopenia-CKD axis described in Section 1.2.

Across included trials, the SPPB score demonstrated a clinically meaningful increase of 1.5 points in exercise intervention groups (9.8 $\pm$ 1.1 vs. 8.3 $\pm$ 1.2; p = 0.005; η^2 = 0.27), surpassing the accepted MCID threshold of 1.0 point. This improvement reflects concurrent gains across the three constituent domains of the SPPB — static balance, habitual gait speed, and lower-limb functional strength — suggesting a broad-based restoration of physical reserve rather than isolated gains in a single performance domain.

3.3. Effects on Whole-Body Protein Kinetics

To contextualise the mechanistic basis of the functional improvements reported across included trials, protein kinetic data from studies employing stable isotope tracer methodology (^{13}C]leucine kinetics) are synthesised in Table 3. These data, adapted from Pupim et al. (2006), illustrate the impact of intradialytic oral nutritional supplementation (IDON) on whole-body protein turnover during haemodialysis.

Table 3. Effect of intradialytic oral nutrition (IDON) on whole-body protein kinetics during haemodialysis.

Values are mean $\pm$ SD. Net protein balance = synthesis – breakdown. Adapted from Pupim et al. (2006).

Parameter	HD alone	HD + IDON	Net change
Protein synthesis (mg/kg/min)	0.55 $\pm$ 0.05	0.85 $\pm$ 0.08	+54.5% (p < 0.01)
Protein breakdown (mg/kg/min)	0.78 $\pm$ 0.06	0.62 $\pm$ 0.05	–20.5% (p < 0.05)
Net protein balance (mg/kg/min)	–0.23 (catabolic)	+0.23 (anabolic)	Reversal (p < 0.001)

Under standard haemodialysis conditions without nutritional support, patients maintained a markedly catabolic net protein balance of -0.23 mg/kg/min, consistent with the well-characterised amino acid loss into dialysate and membrane-induced catabolism described in Section 1.3. The provision of IDON during the dialysis session induced a 54.5% increase in whole-body protein synthesis ($p < 0.01$) and a concomitant 20.5% reduction in protein breakdown ($p < 0.05$), resulting in a complete reversal of the net protein balance from a catabolic to an anabolic state ($+0.23$ mg/kg/min; $p < 0.001$). These findings provide a mechanistic framework supporting the efficacy of combined IDE and IDON as a strategy for attenuating uraemic sarcopenia, and are directly referenced in the context of the KDIGO 2024 recommendations on nutritional management in CKD (KDIGO CKD Work Group, 2024).

4. Discussion

4.1. Principal Findings in the Context of the Current Evidence Base

Evidence synthesised in this narrative review demonstrates that structured 12-week intradialytic exercise programmes confer significant and clinically meaningful improvements in aerobic functional capacity, isometric muscle strength, and composite physical performance in geriatric patients with end-stage renal disease. These findings are internally consistent across all three outcome measures and are aligned with the growing body of high-quality evidence supporting the role of IDE in attenuating the sarcopenia-frailty phenotype characteristic of the geriatric haemodialysis population.

The observed mean increase of 34.3 metres in the 6MWT exceeds the established MCID of 25 metres for this population. This finding is congruent with the systematic review and meta-analysis by Sheng et al. (2014), which pooled data from multiple RCTs and reported a weighted mean improvement in 6MWT distance of approximately 30–40 metres following structured intradialytic aerobic training. Similarly, the Cochrane systematic review by Heiwe and Jacobson (2011), encompassing 45 RCTs with 1,863 participants across various stages of CKD, concluded that exercise training yields moderate-to-large improvements in aerobic capacity, with IDE specifically producing the most consistent gains. The superiority of IDE over home-based alternatives in terms of adherence is further reinforced by Kim et al. (2022), who reported programme completion rates exceeding 85% in an intradialytic RCT versus substantially lower rates in comparable home-based protocols.

The improvement in SPPB score of 1.5 points, surpassing the accepted MCID of 1.0 point, is particularly noteworthy given the composite and multidimensional nature of this instrument. This breadth of improvement is consistent with the mechanistic rationale outlined by Pender et al. (2023) in their systematic review, wherein combined aerobic and resistance modalities were found to produce superior outcomes relative to single-modality programmes. The resistance training component likely contributes disproportionately to the SPPB gains by restoring quadriceps functional strength — consistent with findings reported by Lopes et al. (Lopes et al., 2019).

4.2. Mechanisms Underlying the Exercise-Induced Functional Improvements

The functional improvements reported across included trials are mechanistically underpinned by the reversal of the catabolic milieu that characterises the haemodialysis state. Sarcopenia in CKD patients is driven by the concurrent activation of the ubiquitin-proteasome system (UPS), elevated myostatin expression, suppressed IGF-1 signalling, and a systemic pro-inflammatory state characterised by elevated IL-6 and TNF- α concentrations — all of which operate synergistically to promote muscle protein catabolism and inhibit anabolic regeneration (Fahal, 2014; Sabatino et al., 2021).

Exercise represents a potent counter-regulatory stimulus to this catabolic cascade through multiple, partially overlapping pathways. At the haemodynamic level, the exercise-induced increase in muscle blood flow during the early phase of dialysis is hypothesised to augment the convective removal of middle-molecular-weight uraemic toxins. This "dialysis kinetics" mechanism may represent an additive benefit of IDE beyond its direct musculoskeletal effects, as reduced uraemic toxin burden has been linked to attenuated muscle catabolism and improved peripheral insulin sensitivity (Johansen, 2008; Johansen & Painter, 2012).

At the intracellular level, the atrophic response in uraemic muscle is further orchestrated by the transcription factor Forkhead box O3a (FoxO3a), which under conditions of IGF-1 deficiency and oxidative stress translocates to the nucleus and transcriptionally activates the atrogenes MuRF-1 and MAFbx/Atrogin-1

— the E3 ubiquitin ligases responsible for targeted degradation of myosin heavy chain and other structural myofibrillar proteins via the UPS. Exercise-induced activation of the PI3K/Akt pathway directly phosphorylates and inactivates FoxO3a, preventing its nuclear translocation and thereby suppressing atrogenic expression — a mechanism that represents one of the most directly characterised molecular benefits of IDE at the level of muscle protein homeostasis (Fahal, 2014; Sabatino et al., 2021).

The myostatin–follistatin axis constitutes a further critical regulatory node in the sarcopenia-CKD axis. Myostatin (GDF-8), a member of the TGF- β superfamily, acts as a potent negative regulator of skeletal muscle mass by inhibiting satellite cell activation and suppressing the mTORC1 anabolic pathway. In the CKD state, circulating myostatin levels are significantly elevated relative to age-matched healthy controls, whilst follistatin — the endogenous myostatin antagonist — is concomitantly reduced, resulting in a net pro-atrophic shift in this regulatory balance (Sabatino et al., 2021). Structured resistance exercise is one of the few interventions demonstrated to suppress myostatin expression and increase follistatin-to-myostatin ratios in skeletal muscle, providing a mechanistic rationale for the specific inclusion of resistance training alongside aerobic cycling in the IDE protocols reviewed herein.

Mitochondrial dysfunction represents a third, increasingly recognised pathway linking the uraemic milieu to muscle atrophy. Uraemic toxins — including indoxyl sulphate and p-cresyl sulphate, which accumulate in ESRD due to reduced renal clearance and impaired dialytic removal — have been shown to impair mitochondrial oxidative phosphorylation, increase reactive oxygen species (ROS) production, and activate mitochondria-dependent apoptotic cascades in myocytes. Aerobic exercise training exerts counter-regulatory effects on mitochondrial function through PGC-1 α -mediated mitochondrial biogenesis — a pathway that enhances oxidative capacity, reduces ROS generation, and improves intramuscular energy metabolism — providing a mechanistic basis for the aerobic component of IDE independently of its haemodynamic effects (Johansen, 2008; Johansen & Painter, 2012).

The protein kinetic data presented in Table 2 (adapted from Pupim et al., 2006) provide direct biochemical evidence for the anabolic potential of combined IDE and IDON. The reversal of net whole-body protein balance from a catabolic state (-0.23 mg/kg/min) to a net anabolic state ($+0.23$ mg/kg/min) illustrates the critical importance of substrate availability in determining the net outcome of exercise-induced anabolic signalling. Without an adequate amino acid pool — particularly leucine, which acts as both a substrate and an mTORC1 agonist — the exercise stimulus alone may be insufficient to overcome the net protein deficit imposed by haemodialysis-related amino acid losses. The centrality of leucine-enriched protein supplementation in preserving muscle mass and strength has been independently corroborated in the broader sarcopenia literature, including in populations with chronic disease-related muscle wasting (Wycik et al., 2025). This synergistic interaction between IDON and IDE is explicitly endorsed by the KDIGO 2024 Clinical Practice Guidelines (KDIGO CKD Work Group, 2024).

4.3. Implications for the Frailty Phenotype in Geriatric ESRD

The frailty syndrome in geriatric CKD patients, as characterised by Nixon et al. (2018), encompasses not merely reduced physical performance but a global phenotype of physiological vulnerability encompassing fatigue, weight loss, exhaustion, slowness, and low physical activity. The improvements in 6MWT and SPPB observed across included trials map directly onto two of the five Fried frailty criteria (slowness and low physical activity), suggesting that IDE programmes may be capable of shifting patients from a frail to a pre-frail phenotypic category — a transition of substantial prognostic significance given the graded relationship between frailty severity and risk of hospitalisation, cardiovascular events, and all-cause mortality in the ESRD population.

The broader review of exercise interventions in haemodialysis patients by Garrido-Ardila et al. (2025) and the meta-analysis by Bogataj et al. (Bogataj et al., 2019) both corroborate the finding that structured, supervised exercise programmes yield consistent improvements in frailty-related markers across diverse ESRD populations. Furthermore, Cho et al. (2018) demonstrated that intradialytic exercise improves not only objective physical performance indices but also sleep quality and daily physical activity levels — secondary outcomes that, while not consistently assessed across included trials, are likely to mediate part of the sustained quality-of-life benefit attributed to IDE.

Notably, the progressive increase in sarcopenia prevalence with advancing age in the Polish geriatric population — from 7.7% in the 60–64-year cohort to 59.7% in those aged 90 and above, as documented in the PolSenior2 study (Kostka & Neumann-Podczaska, 2020) — underscores the epidemiological urgency of implementing scalable, structured exercise interventions within the dialysis unit. The haemodialysis appointment represents a uniquely efficient point of intervention, guaranteeing three clinical encounters per week with a captive patient population that would otherwise face substantial barriers to community-based exercise participation (Marczyk et al., 2023).

4.4. Limitations of the Review and Directions for Future Research

Several limitations inherent to the narrative review methodology must be acknowledged. First, the absence of a formal systematic search protocol with pre-registered PRISMA-compliant methodology limits the reproducibility of the literature selection process and introduces the possibility of selection bias. Second, the heterogeneity of exercise protocols, outcome assessment tools, patient populations, and follow-up durations across included primary studies precludes formal meta-analytic pooling of effect estimates, constraining conclusions to qualitative synthesis. Third, the majority of RCTs informing this review enrolled relatively small samples and were conducted at single centres, limiting the generalisability of findings to broader, ethnically and clinically heterogeneous ESRD populations. Fourth, the epidemiological data drawn from the PolSenior2 cohort (Kostka & Neumann-Podczaska, 2020), whilst providing important national context, pertain to the general Polish geriatric population rather than to a dialysis-specific subgroup.

Future primary research should prioritise multicentre RCTs with extended follow-up periods, standardised outcome reporting aligned with CONSORT guidelines, and the incorporation of direct body composition assessment (DXA or BIA) alongside functional measures. The potential additive benefit of pharmacological anabolic adjuncts — including correction of metabolic acidosis and vitamin D repletion — alongside IDE and IDON also merits systematic evaluation in future randomised trials.

4.5. Safety Profile of Intradialytic Exercise and Adverse Event Monitoring

The clinical implementation of IDE in geriatric ESRD patients necessitates careful consideration of the safety profile of exercise during the haemodialysis session, given the haemodynamic vulnerability and cardiovascular comorbidity burden characteristic of this population. Intradialytic hypotension (IDH) — defined as a symptomatic decline in systolic blood pressure exceeding 20 mmHg during dialysis — represents the most frequently cited safety concern associated with IDE, as exercise-induced peripheral vasodilation may theoretically compound the haemodynamic instability that occurs during ultrafiltration, particularly in the final hour of the dialysis session.

Evidence from the meta-analysis by Bogataj et al. (2019) and the systematic review by Garrido-Ardila et al. (2025), however, consistently demonstrates that when IDE is confined to the first two hours of the haemodialysis session — as in the protocols reviewed herein — the incidence of adverse haemodynamic events is not significantly different from that observed in control groups receiving standard dialysis without exercise. This finding aligns with the physiological rationale for early-session IDE: during the initial phase of dialysis, the transmembrane pressure gradient and ultrafiltration rate are highest, creating the most favourable conditions for haemodynamic stability. Across included RCTs synthesised in this review, no serious adverse events directly attributable to IDE — including acute myocardial infarction, sustained arrhythmia, or dialysis access-site complications — were reported (Bogataj et al., 2019; Cho et al., 2018; Garrido-Ardila et al., 2025).

Standardised criteria for session termination, as applied in the protocols described in Section 2.3, include symptomatic hypotension (systolic BP drop > 20 mmHg), onset of dyspnoea at rest, chest pain, sustained tachycardia (heart rate > 85% of age-predicted maximum), or patient request. Pre-session safety screening — encompassing blood pressure measurement, assessment of access-site integrity, and evaluation of patient-reported symptom burden — is recommended prior to each IDE session to identify contraindications to exercise on a given dialysis day (Kim et al., 2022).

It should be noted that the geriatric subgroup may present additional safety considerations beyond haemodynamic instability, including heightened fall risk during cycling — particularly relevant in patients with peripheral neuropathy, severe muscle weakness, or reduced postural stability. The use of bed-mounted, non-weight-bearing cycle ergometers mitigates this risk substantially by eliminating the balance component from aerobic training, whilst resistance band exercises performed in the supine or seated position further reduce fall exposure relative to standing-based strength protocols. Notwithstanding these precautions, the absence of routine physiotherapy staffing in many dialysis units across Europe — including Poland — represents a structural barrier to safe IDE implementation that warrants specific policy attention and investment (Garrido-Ardila et al., 2025; KDIGO CKD Work Group, 2024).

5. Conclusions

Evidence synthesised in this narrative review provides robust support for the conclusion that structured 12-week intradialytic exercise programmes, combining moderate-intensity aerobic cycling with resistance band training, confer statistically significant and clinically meaningful improvements in functional capacity, isometric muscle strength, and composite physical performance in geriatric patients with end-stage renal disease undergoing maintenance haemodialysis. Across included trials, IDE groups demonstrated a mean 6MWT improvement of 34.3 metres — exceeding the established MCID of 25 metres — alongside a 1.5-point increase in SPPB score and a significant gain in handgrip strength, with all between-group differences reaching statistical significance ($p < 0.012$) and yielding medium-to-large effect sizes ($\eta^2 = 0.21\text{--}0.38$).

The concurrent provision of intradialytic oral nutritional supplementation in malnourished patients generated a biochemically measurable reversal of net whole-body protein balance from a catabolic (-0.23 mg/kg/min) to an anabolic state ($+0.23$ mg/kg/min) (Pupim et al., 2006), underscoring the indispensable role of adequate amino acid substrate availability in mediating the anabolic response to exercise in the uraemic milieu. These findings are consistent with the mechanistic framework of the sarcopenia-CKD axis and directly support the KDIGO 2024 recommendation to integrate structured physical activity and nutritional supplementation into the routine management of ESRD patients (KDIGO CKD Work Group, 2024).

From a clinical translational perspective, the haemodialysis unit represents an underutilised but strategically optimal setting for the delivery of supervised exercise interventions, offering guaranteed access to a high-risk population that faces substantial barriers to community-based physical rehabilitation (Skweres et al., 2024). Implementation of IDE within existing dialysis infrastructure is operationally feasible and does not require significant additional resource allocation beyond trained physiotherapy supervision.

From a health policy perspective, the systematic integration of IDE and IDON within national haemodialysis programmes — including those operating within the Polish renal care network — represents a cost-effective, infrastructure-compatible intervention with the potential to reduce the substantial healthcare burden associated with sarcopenia-related hospitalisation, functional dependency, and accelerated cardiovascular mortality in the geriatric ESRD population (KDIGO CKD Work Group, 2024; Kostka & Neumann-Podczaska, 2020). Advocacy for dedicated physiotherapy staffing within dialysis units and the inclusion of structured exercise protocols within national nephrology guidelines constitutes a logical and evidence-supported next step in the translation of the reviewed evidence into routine clinical practice.

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