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Types and Benefits of Intradialytic Exercise: A Narrative Review

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Abstract

This narrative review explores the types and benefits of intradialytic exercise (IDE) for patients undergoing hemodialysis (HD). IDE, which includes physical activities performed during HD sessions, aims to improve patients' strength, endurance, and overall health. The review highlights various forms of IDE, such as intradialytic aerobic exercise (IAE), intradialytic resistance exercise (IRE), stretching exercises, blood flow restriction exercise (BFRE), intradialytic inspiratory muscle training (IIMT), and intradialytic neuromuscular electrical stimulation (INES). IAE is noted for its accessibility and effectiveness in enhancing physical functions, reducing fatigue, and improving health-related quality of life (HRQoL). IRE is particularly beneficial for increasing muscle strength and mass. Stretching exercises help mitigate muscle cramps and restless legs syndrome. Although BFRE and combined exercise programs show promise, further research is necessary to consolidate their benefits. The review also addresses the safety, feasibility, and adherence of IDE, noting that IDE is safer and has higher adherence rates compared to exercises performed outside HD clinics, due to supervision by medical staff and regular scheduling. However, IDE faces challenges such as limited space, equipment, scheduling conflicts, and patient motivation. Despite these barriers, IDE is a potential intervention for improving the health outcomes of HD patients, advocating for its integration into routine HD care to optimize patient prognoses and enhance the standard of care.

Key Words: aerobic exercise; end-stage kidney disease; hemodialysis; intradialytic exercise; resistance exercise; outcome

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Introduction

In the past decades, medical development has revolutionized technological advancement, prolonging life expectancy and also increasing patients with chronic kidney disease (CKD) and end-stage kidney disease (ESKD), which is a severe irreversible condition with a profound impact on patients' outcomes[1]. Although considerable improvement has been achieved in the treatment of ESKD patients, including hemodialysis (HD) therapy, the population receiving HD still faces numerous challenges in many aspects, including physiological and psychological, such as protein-energy wasting syndrome, frailty syndrome, and sarcopenia. These challenges are attributed to the sedentary nature of the underlying diseases and the related treatment, such as HD, subsequently worsening physical ability, mental health, health-related quality of life (HRQoL), and even survival in HD patients[2-5].

Intradialytic exercise (IDE) has been proposed as a potential intervention to improve the health and well-being of HD patients. IDE involves physical activity during the HD session to enhance the patient's strength and endurance and target physiological and psychosocial parameters[6]. IDE presents a unique opportunity to integrate therapeutic exercises seamlessly into the treatment regimen. To date, existing studies outstand the effects of IDE on improving physical function, mitigating HD's physiological impacts, and preventing patients from being trapped in such a vicious circle brought by HD treatment. Specifically, IDE has been shown to have benefits on the potential improvements in muscle loss, 6-minute walking test (6MWT), and sit-to-stand test (STS). Besides, IDE has also been found to improve cardiopulmonary capacity[3,7], HRQoL[6,8-12], patient survival rate[13], and preserve cognitive function[14]. However, contraindications include unstable cardiovascular conditions, severe anemia, and active infections, which necessitate careful screening and monitoring by healthcare professionals[15]. Ensuring patient safety and optimizing exercise benefits require a multidisciplinary approach and adherence to clinical guidelines[16].

It is worth mentioning that IDE includes various modalities[17]. Common forms of IDE include intradialytic aerobic exercise (IAE), intradialytic resistance exercise (IRE), and combined IAE and IRE. These exercises have been extensively studied and are known to improve physical function, muscle strength, and cardiovascular fitness in HD patients. However, less common forms of IDE, such as stretching exercises, blood flow restriction exercise (BFRE), intradialytic inspiratory muscle training (IIMT), and intradialytic neuromuscular electrical stimulation (INES), have often been overlooked in the current body of literature despite their potential to offer unique and revolutionary therapeutic benefits.

Therefore, this narrative review seeks to fill this gap by comparing these common and less common IDE, synthesizing current knowledge on their types and benefits, and identifying barriers to implementation. By evaluating the impact of different IDE regimens, we aim to advocate for integrating IDE into routine HD care, ultimately optimizing patient outcomes and enhancing the standard of care for HD patients.

Types and Merits of IDE

We illustrate the types and benefits of IDE for HD patients in Figures 1 and 2 and summarize the features and benefits of various types of IDE in Table 1.

2.1 IAE

IAE involves activities that increase heart rate and breathing, which can be implemented through cycling, walking, or jogging on a treadmill during HD treatment[17,18]. The protocols and regimens used in various studies to implement IDEs vary widely.

Table 1. Summary of key features and benefits of various types of IDE

Types	Key features	Benefits
IAE	- Activities include cycling, walking, or using the treadmill during HD. - Typically being applied for 30 minutes, 2-3 times weekly. - Economical and accessible due to its simplicity and safety.	- Improving 6MWD, STS5, and STS30. - Enhancing cardiopulmonary fitness. - Improving HRQoL - Reducing fatigue and depression symptoms. - IAE with cognitive training preserving cognitive ability
IRE	- Activities utilizing weights, elastic bands, or body weight. - Focusing on improving strength, endurance, and muscle mass. - Typically, with mid-to-low intensity, performed twice weekly.	- Improving 6MWT, and STS30 - Enhancing lean leg muscle mass - Improving cardiopulmonary fitness - Improving HRQoL - Improving dialysis adequacy
IAE+IRE	- Activities combine IAE and IRE	- Improving walking - Improving cardiopulmonary fitness - Improving HRQoL - Improving dialysis adequacy
Stretching IDE	- Activities generally used as a warm-up or cool-down exercise. - Simple, non-invasive, and easy to perform.	- Maintaining physical flexibility - Reducing muscle cramps and restless legs syndrome
BFRE	- Using cuffs to restrict venous blood flow while maintaining arterial flow. - Providing muscle-building benefits with lower weight loads. - Suitable for HD patients who cannot perform high-intensity resistance training.	- Improving walking capacity - Improving muscle strength, - Improving dialysis adequacy.
IIMT	- Using a breathing device to strengthen respiratory muscles. - Typically being performed thrice weekly during HD sessions.	- Improving 6MWT - Improving pulmonary function (e.g., PEmax, FEV1%) and inspiratory muscle strength
INES	- Using electrical stimuli on muscles to induce contractions. - Suitable for HD patients unable to perform physical exercises.	- Improving walking capacity and general physical function (e.g., 6WMT) - Preventing muscle loss and improves lower limb strength

Abbreviation: 6MWD, 6-minute walk distance; **BFRE**, Blood flow restriction exercise; **HD**, Hemodialysis; **HRQoL**, Health-related quality of life; **IAE,** Intradialytic aerobic exercise; **IDE,** intradialytic exercise; **IIMT**, Intradialytic inspiratory muscle training; **INES**, Intradialytic neuromuscular electrical stimulation; **IRE**, Intradialytic resistance exercise; **STS30,** thirty times sit to stand test; **STS5,** 5 times sit to stand test

For example, intradialytic cycling programs have been implemented at different intensities and durations. However, an IAE taken for 30 minutes or more during an HD session, two to three times weekly, is a commonly applied model[7,17,18]. Unlike the general concept that the application of IDE is complex and costly, necessitating staff and facilities to approach the treatment[19], IAE is more favorable for its aerobic, economical, and safe attributes, which highlight its accessibility and have predominantly been applied in IDE programs, with cycling facilities such as ergometers being widely accepted[18].

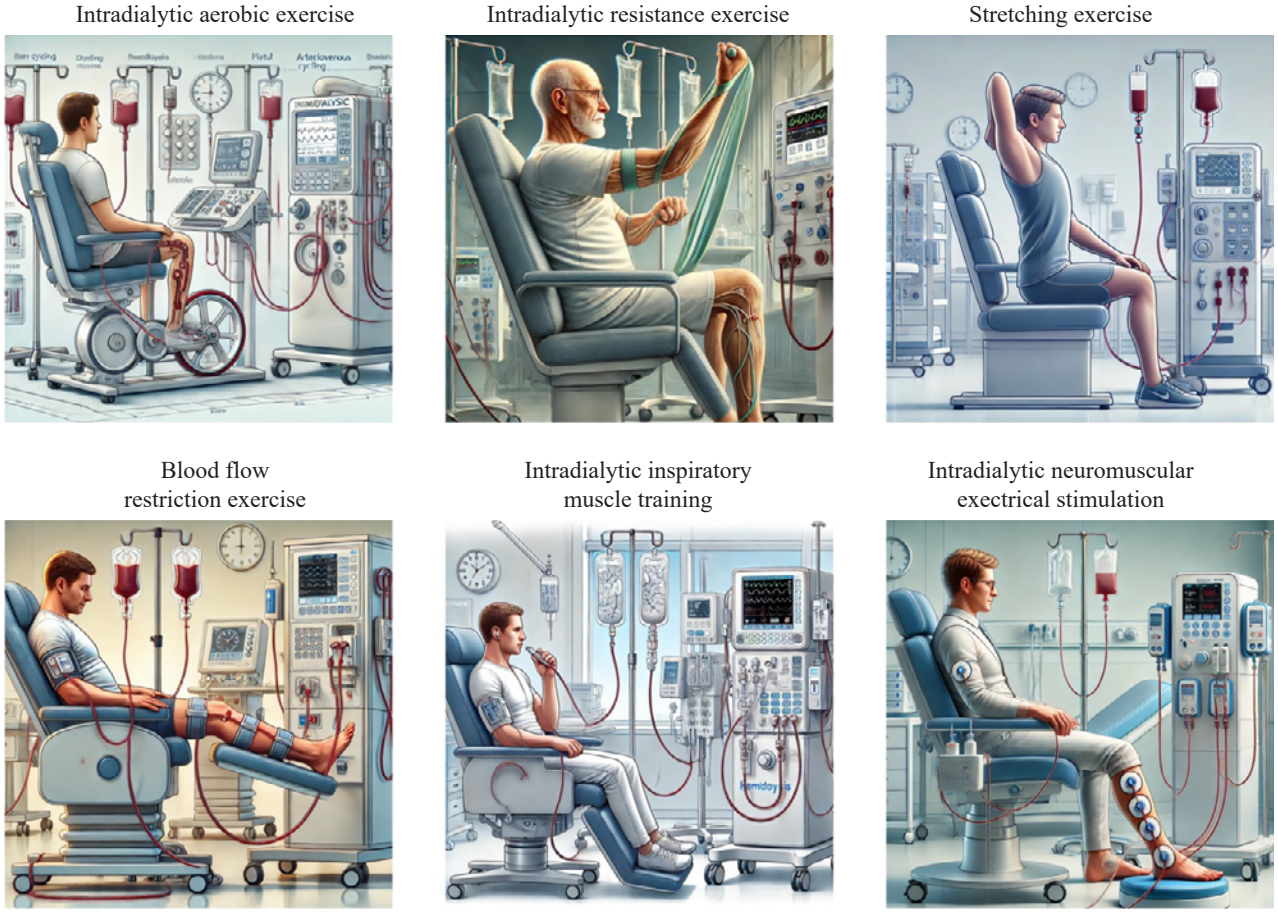
The most significant benefits of IAE is the enhancement of physical functions, including 6WMD, five times sit to stand test (STS5), and thirty times sit to stand test (STS30), which is generally agreed upon in the current literature[20-24]. Additionally, it is reported to benefit muscle strength, power, fatigability, and cardiopulmonary fitness[25]. Further, Krase et al. (2022) found in their seven-month study that HD patients receiving IAE training reflected a significant muscle thickness retention compared to the control group ($p = 0.02$) [26].

Recent research has shown that IAE can potentially enhance peak oxygen consumption (VO_2peak) in ESKD patients[7]. ESKD patients who underwent 2 to 6 months of IAE observed an approximate 17% increase in VO_2peak[7]. Pu et al. (2019) also support this stance, reporting a significant increase in VO_2peak[3]. However, some researchers argue that the causal relationship between VO_2peak and IDE remains unclear, and the research might not be methodologically robust due to limited samples, thus questioning the significance of the results[18,27-29].

Few studies have also revealed the clinical significance of IAE on fatigue symptoms [30] and depression[24], yet the discussion on these topics might be limited in conclusion. IAE was found to have no significant impact on increasing muscular mass[20,31], mental component summary (MCS) of HRQoL[29], or cardiopulmonary capacity[18,27-29], though this remains widely debated[3,7,25].

Previous studies have depicted the significance of IAE and IRE schemes on the physical com-

Figure 1. Illustration of the types of IDE in HD patients



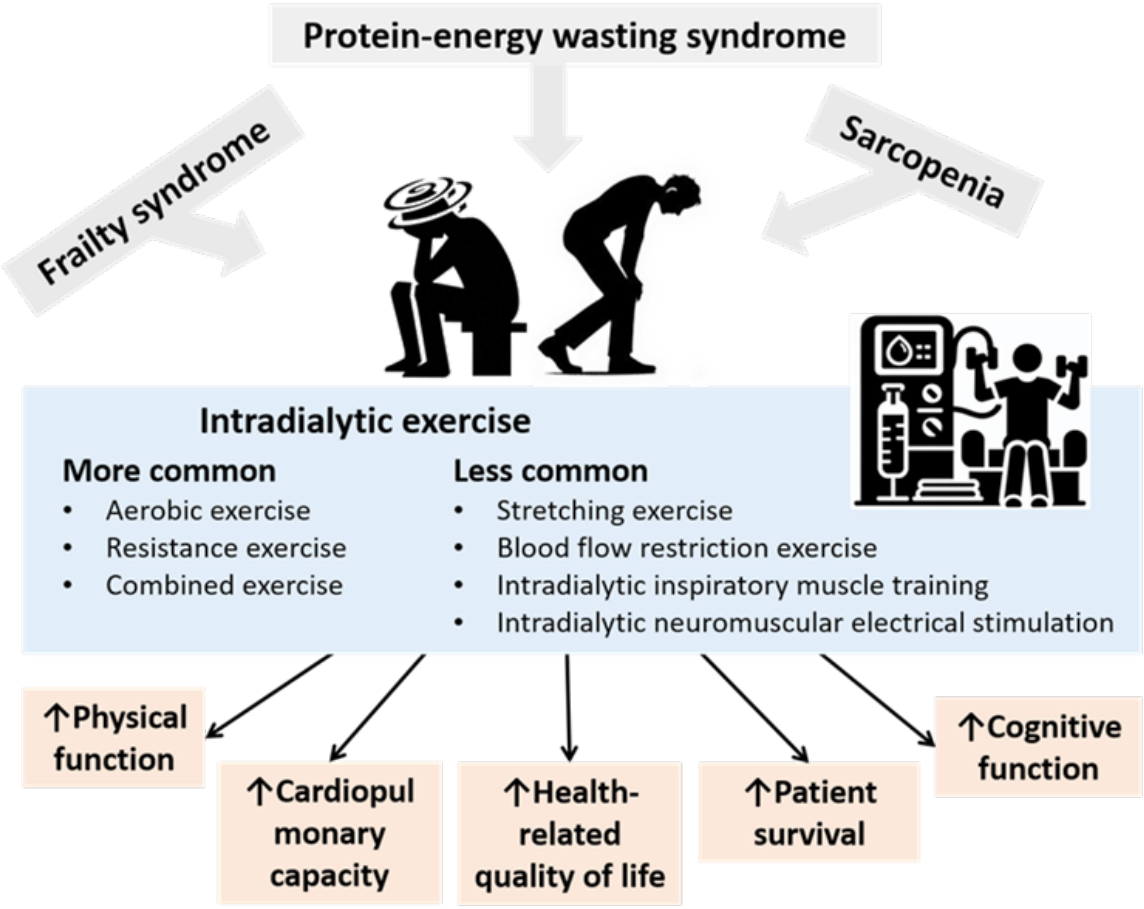
Note: The pictures were drawn by GPT-4o by OpenAI.

ponent summary (PCS) of HRQoL[9,12]. However, a meta-analysis by Salhab et al. (2019) investigating 22 studies concluded that both the physical and mental component scales of HRQoL are positively affected by aerobic IDE, indicating that aerobic and resistance IDE do not show statistical significance on the mental component scale of HRQoL[6]. Hu et al. (2022) also found a similar result, concluding that IDE can considerably enhance most of the PCS of HRQoL, primarily through aerobic exercise intervention alone[10]. Besides, research indicates that IAE significantly improves overall cognitive function, and suggests that incorporating IAE during HD sessions is a beneficial strategy for enhancing cognitive health in HD patients[14].

2.2 IRE

Typically, resistance exercise programs utilize various types of equipment, such as dumbbells, elastic bands, body weight, or training machines, and vary in the number of sets and repetitions performed to improve muscle strength and endurance[17,32]. Although traditional resistance programs are the most common method to enhance muscle strength, function, and mass, they are too complex to be applied during HD sessions for HD patients[33]. Therefore, IRE is usually adopted as a mid-to-low-intensity strength training and undertaken during HD sessions at least twice weekly[17,34]. Since the differences between IRE training methods regarding the resistance source do not show statistical signifi-

Figure 2. Illustration of the benefits of IDE in HD patients



Abbreviation: HD, Hemodialysis; **IDE,** intradialytic exercise

cance, clinicians and HD patients have the flexibility to choose methods.[33]

Clinically, IRE has been found to benefit muscle mass and physical functions. For an IDE intervention of 12 weeks, researchers observed muscle growth in the quadriceps (cross-sectional area)[35], increased skeletal muscle quality[36], and enhanced self-reflected physical functioning[35,36]. Pender et al. (2023) reviewed seven studies and concluded that a 12-week moderate-high intensity progressive resistance training can prevent muscle loss in HD patients and further increase muscle mass, with a 5% increase in legs and a 4.2% increase in the body[37]. This result was further confirmed in a randomized control trial[38]. IRE has also been found to benefit physical indicators of HD patients, including physical functions[38,39], STS30[40], HRQoL[39], PCS[9,12], and dialysis efficacy[39]. However, opposite results existed that a study argued that IRE does not significantly improve 6MWD (6-minute walk distance)[39].

2.3 Combined IAE and IRE

Combined exercise programs may depend on individuals, yet IAE and IRE are widely applied to provide a comprehensive workout regimen[17]. These programs have varied in their specific protocols, with some studies incorporating both IAE and IRE in the same session, while others alternate between the two types of exercises on different days[41].

As the most accessible IDE, IAE is usually the core component in combined IDE. Hu et al. (2023) revealed that combined IAE and IRE improves walking capacity, cardiorespiratory fitness, dialysis adequacy, and HRQoL in HD patients[17]. Similarly, Giannaki et al. (2023) support this perspective, claiming that aerobic-combined hybrid IDE could be comparable to traditional aerobic exercises, providing cardio-protective properties for HD patients participating in IDE intervention[42]. However, its potential to increase muscular mass is doubted[20,31].

2.4 Stretching IDE

As distinct from aerobic and resistance exercise, stretching is usually applied as a cool-down procedure after IDEs[13]. Stretching exercise is essential for maintaining physical ability[23], serving as a warm-up before dialysis[43], and a method employed in control group[23,39].

Stretching IDE has been shown to improve neurological phenomena such as muscle cramps and restless legs syndrome. Dhudum (2020) investigated 15 papers, all concluding that stretching IDE is statistically significant in mitigating muscle cramps[44]. Chavda and Singh (2018) supported this stance, revealing that stretching IDE could reduce intradialytic fluid-loss-induced muscle cramps[45]. Specifically, two sampled groups observed severe muscle cramps (66.7% and 33.3%), which decreased to 1.7% of severe conditions, 8.3% of moderate muscle cramps, and 1.7% of healed conditions post-stretching IDE intervention. In India, muscle cramps can be witnessed in up to 86% of ESKD patients undergoing HD treatment[44]; thus, the effectiveness of stretching IDE in alleviating this symptom is noteworthy. Despite limited research on stretching exercise, current literature has confirmed its significance in reducing muscle cramps[44-46] and restless legs syndrome[43,47].

2.5 BFRE

BFRE incorporates external compression by cuffs or bands around a proximal limb during exercise. This procedure restricts venous blood flow while still permitting arterial blood flow and increases blood pooling in the capillary beds of the exercising muscle. Following the elevation of metabolic stress and cellular swelling and increase of growth hormone production, the BFRE achieves muscle-building benefits with lower weight loads than traditional training[48-51].

The concept of BFRE is relatively recent; thus, there might be limited trials based on this type of IDE on HD patients. However, research from Dias et al. (2019) found that compared to other IDE, moderate-intensity BFRE can improve HD adequacy[51]. It was also found that introducing BFRE can improve walking capacity, muscle strength, and dialysis efficacy, yet the sources of relevant aspects lack more papers to consolidate the results[16,28].

2.6 IIMT

IIMT uses a breathing training device to strengthen inspiratory muscles[52]. The training is conducted during HD sessions using an electronic device with a linear pressure load of respiratory incentives; a nose clip is applied on patients to breathe through a mouthpiece with resistance in the inspiratory branch, using the corresponding maximum inspiratory pressure, typically performed three times per week[52].

The application of IIMT is suitable for improving pulmonary functions and expiratory and inspiratory muscle strength for HD patients[53,54]. Specifically, the research found that PEmax, FVC%, PEF%, FEV1%, and PImax were significantly improved[55], suggesting a potential intervention for improving cardiopulmonary capacity. Further, an 8-week IIMT intervention was not found to have complications, yet the improvement in HRQoL was insignificant[54].

2.7 INES

Since some HD patients cannot perform physical IDE intervention, INES is employed as an alternative[56]. Intermittent electrical stimuli on muscles or peripheral nerves cause involuntary muscle contractions and prevent central or peripheral muscle paralysis-induced muscle atrophy[57,58]. During the HD session, electrical stimulation is applied to the bilateral femoral quadriceps muscles for 20-40 minutes[17].

Recent research has confirmed the effectiveness of INES in preventing muscle loss and increasing muscle strength in the lower limbs[59,60], suggesting that stimulation intervention can be applied to HD patients suffering from muscle sarcopenia, muscle weakness, or wasting[60]. This relationship has been echoed by Brüggemann et al. (2017), who indicated that significant muscle strength improvement only occurs with high-frequency INES[61].

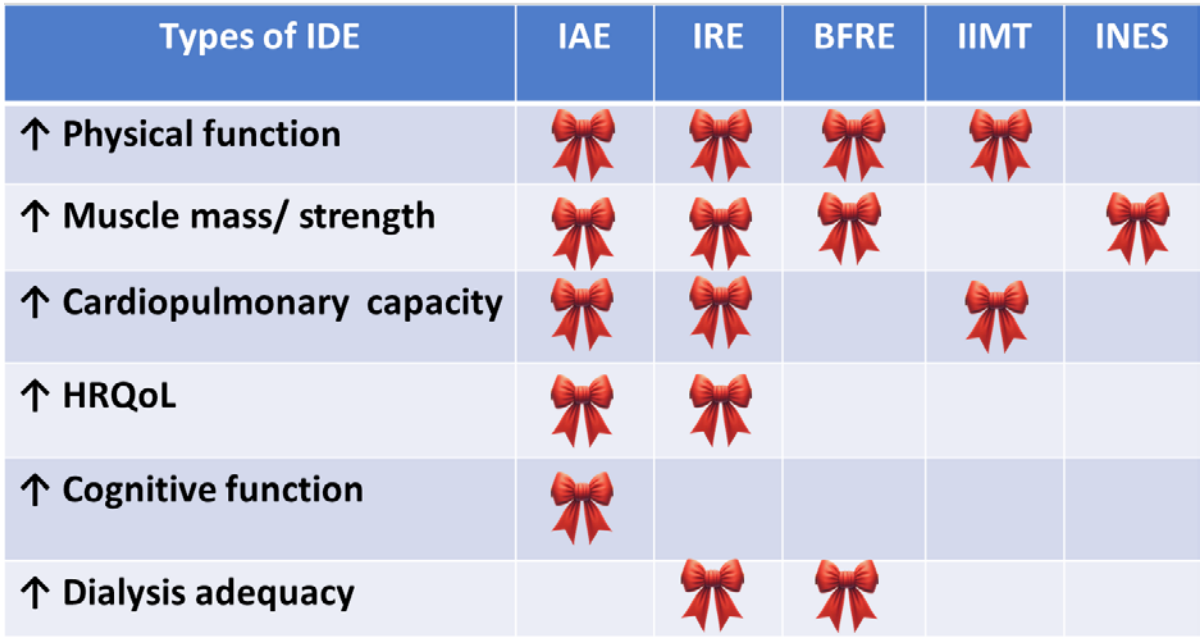
Additionally, a 10% improvement in 6WMT was found between the INES and control groups, suggesting that INES can improve walking capacity[30] and general physical functions[62,63]. On the other hand, this kind of muscle stimulation improved all components of Short Form-8; however, the results were insignificant[60].

Clinical benefits, safety, feasibility, and adherence

Figure 3 illustrates the clinical benefits of various types of IDE on HD patients. IAE, IRE, BFRE, and IIMT are all found to improve patients' physical function. IAE, IRE, BFRE and INES enhance muscle mass and strength, while IAE, IRE, and IIMT boost cardiopulmonary capacity. Both IAE and IRE have been shown to improve HRQoL. Additionally, combining IAE with cognitive training enhances cognitive function, and both IRE and BFRE improve dialysis adequacy. (Figure 3)

Regarding safety, feasibility, and adherence, IDE is safer and has a higher adherence rate than exercise performed outside HD clinics. This is due to the supervision by physicians or nursing staff and the regular exercise schedule that coincides with HD sessions. However, IDE is less feasible than its counterpart because of limited space, equipment, scheduling conflicts, and patient motivation[64]. However, current literature is insufficient to draw firm conclusions regarding the comparisons of safety, feasibility, and adherence of various types of IDE, highlighting the need for further studies.

Figure 3. Summary of clinical benefits of various types of IDE



Note: Red bows denote beneficial in the type of clinical benefits
Abbreviation: BFRE, Blood flow restriction exercise; **HRQoL**, Health-related quality of life; **IAE,** Intradialytic aerobic exercise; **IDE,** intradialytic exercise; **IIMT**, Intradialytic inspiratory muscle training; **INES**, Intradialytic neuromuscular electrical stimulation; **IRE**, Intradialytic resistance exercise

Barriers to promoting IDE application

Despite the benefits mentioned above, the adherence rate of IDE varied significantly from 18% to 90%[11,65]. The barriers affecting the adherence rate of IDE are summarized below.

4.1 Physical aspects of patients

ESKD patients undergoing HD are subject to fatigue symptoms because of the disease's nature and the HD therapy. For example, a drop in intravenous adenosine triphosphate (ATP) levels occurs during the intradialytic phase, attributing to clinical intolerance and fatigue [66]. The fatigue symptoms prohibit patients from completing the IDE. Therefore, some researchers suggest starting with low to moderate-intensity IDE to ensure safety and prevent patient intolerance. Gradually, the intensity can be increased to higher levels, which are more effective in alleviating fatigue symptoms and maximizing the benefits of IDE[41,67].

4.2 Psychosocial aspects of patients

ESKD patients often have minimal regular physical activity in the past, remaining inactive throughout their lives. Psychosocial attitudes hinder IDE initiation, including frustration, passive negativism, shame, introversion, social isolation, closure personality, self-pity, "self-abandonment," and resignation. Additionally, some patients are profoundly depressed and lack self-initiative for behavior change related to exercise. A lack of motivation and guidance for patients is a crucial barrier.

4.3 Financial and care-providing team's support

IDE equipment is expensive and complicated[33]. Thus, financial considerations play a significant role in implementing IDE programs[68-70]. Additionally, care-providing teams for IDE, whether nursing staff

or additional personnel, are costly for training and daily practice[19,71]. At the same time, lack of knowledge, non-adherence, and fatigue might increase staff's workload[65]. Furthermore, low accessibility to IDE-related information for caregivers and families is a barrier[68-70].

Conclusion

IDE presents a promising intervention for enhancing the health outcomes of HD patients. IAE is particularly effective in improving physical functions, reducing fatigue, and enhancing HRQoL. IRE significantly benefits muscle strength and mass. Stretching exercises alleviate muscle cramps and restless legs syndrome. While BFRE and combined exercise programs show potential, further research is needed to confirm their benefits. Overall, IDE is a valuable addition to routine HD care, offering substantial improvements in patient well-being.

Declaration of Generative AI and AI-assisted technologies

During the preparation of this work, the authors used GPT-4o by OpenAI to improve readability and make illustrations. After using this tool, the authors reviewed and redesign the contents as needed and take full responsibility for the content of the publication.

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透析中運動的種類和益處：一個敘述性文獻回顧

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摘要

本敘述性文獻回顧探討了透析中運動（intradialytic exercise）的類型和對接受血液透析（HD）患者的臨床益處。透析中運動包括在血液透析過程中進行的體力活動，旨在改善患者的力量、耐力和整體健康。回顧強調了各種形式的透析中運動，例如透析中有氧運動（intradialytic aerobic exercise）、透析中阻力運動（intradialytic resistance exercise）、伸展運動、血流限制運動（BFRE）、透析中吸氣肌訓練（intradialytic inspiratory muscle training）和透析中神經肌肉電刺激（intradialytic neuromuscular electrical stimulation）。透析中有氧運動因其可及性和在增強身體功能、減少疲勞和改善與健康相關的生活品質（health-related quality of life）方面的有效性而備受關注。透析中阻力運動對增加肌肉力量和質量特別有益。伸展運動有助於減輕肌肉痙攣和不寧腿症候群。儘管血流限制運動和組合運動計劃顯示出潛力，但需要進一步的研究來確定其益處。回顧還討論了透析中運動的安全性、可行性和依從性，指出由於醫療人員的監督和定期安排，透析中運動比在血液透析診所外進行的運動更安全且依從率更高。然而，透析中運動面臨空間有限、設備不足、時間安排衝突和患者動機不足等挑戰。儘管存在這些障礙，透析中運動是一種潛在的干預措施，可改善血液透析患者的健康結果，倡導將其納入常規血液透析護理，以優化患者的預後並提高護理標準。