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Precision Exercise Prescription for Exercise Rehabilitation of Chronic Diseases: A Review Based on Evidence-based Medicine

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Abstract: This study reviews the application status and future development trend of precision exercise prescription (PEP) based on evidence-based medicine in chronic disease rehabilitation. Chronic diseases such as cardiovascular diseases, diabetes, osteoarthritis, and respiratory diseases have a significant impact on public health and socioeconomic factors. Exercise rehabilitation plays a vital role in the treatment of these conditions, and precise exercise prescribing offers a more personalized approach compared to traditional methods. By tailoring an exercise program to an individual's health status, genetic background, and lifestyle, precision exercise can help optimize rehabilitation outcomes.
Keywords: Precision exercise; Exercise rehabilitation; Chronic diseases; Evidence-based medicine

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1. Introduction

Chronic diseases, including cardiovascular diseases, diabetes, osteoarthritis and respiratory diseases, are the most prevalent and costly health problems worldwide. As the health care system faces an increasing burden of these diseases, traditional treatments often fail to provide personalized care.

2. Theoretical basis of precise exercise prescription

2.1. Overview of evidence-based medicine

Evidence-based medicine (EBM) is the core methodological basis of precision exercise prescription, emphasizing the

combination of the best clinical research evidence, physician experience, and patients' individual needs. Its core logic is to extract high-level evidence (such as RCTs, cohort studies) from massive studies through systematic literature reviews (such as the Cochrane Collaboration network) and meta-analysis, and build a scientific decision-making framework. In the field of exercise prescribing, the application of evidence-based medicine is embodied in the quantitative grading of the effect of exercise interventions. For example, the American College of Sports Medicine (ACSM), based on level I evidence (multi-center RCTs), proposed that 150 minutes of moderate-intensity aerobic exercise per week can reduce the glycated hemoglobin (HbA1c) of type 2 diabetes patients by 0.7% to 1.0%. Resistance training (60–80% 1RM) was supported by Class IIa evidence as an effective means of improving bone mineral density (BMD) in patients with osteoporosis (lumbar BMD increased by 1.2% to 3.2% per year). However, traditional evidence-based medicine is limited by the fact that population averages can obscure individual variability. For example, the same exercise regimen may benefit some individuals—such as those with the PPARγ Pro12Ala gene variant, who can experience up to a 30% increase in insulin sensitivity—while being ineffective or even harmful in others. In particular, individuals with the ACE II genotype may develop myocardial fibrosis in response to excessive aerobic training. Therefore, modern evidence-based medicine is integrated with genomics and phenomics to promote the paradigm transformation from "population universality" to "individual adaptation"[1].

2.2. Definition and principle of precise exercise prescription

Precision Exercise Prescription is based on individual biological characteristics, lifestyle, and environmental factors as targets and is driven by multi-dimensional data to develop dynamically optimized exercise intervention programs. Its core principles include:

(1) Individual heterogeneity is a priority: Motor response subtypes are divided based on genotype (e.g., ACTN3 R577X polymorphism determines fast/slow muscle fiber ratio), phenotype (e.g., VO_2max, biomechanical characteristics of musculoskeletal system), and metabolic characteristics (e.g., mitochondrial respiratory chain efficiency). For example, individuals with AMPD1 C34T mutations (10% to 15%) should avoid high-intensity interval training (HIIT) due to purine metabolism disorders, which may induce exercise-induced rhabdomyolysis (creatine kinase peak > 50,000 U/L).

(2) Dynamic adaptive adjustment: Real-time monitoring of heart rate variability (HRV), blood lactate threshold, and other indicators through wearable devices, combined with machine learning models to predict the exercise tolerance window. For example, when the HRV standard deviation (SDNN) is < 20ms, the training intensity is automatically lowered by 10–15% to avoid excessive fatigue.

(3) Multi-system collaborative intervention: Integrating exercise, nutrition, and psychological regulation (such as cortisol level management) to form a "stress-recovery-adaptation" closed loop. For example, in patients with chronic fatigue syndrome, supplementation with branched-chain amino acids (BCAAs) after low-intensity exercise (40–50% HRmax) can increase muscle protein synthesis by 22%.

The key difference between precision exercise prescribing and the traditional "one-size-fits-all" model is that it rejects static regimens. For example, exercise prescribing for hypertensive patients needs to adjust training sessions according to the ambulate blood pressure circadian rhythm (arytenor/non-arytenor). In non-arytenotype patients with insufficient blood pressure reduction at night (< 10%), it is recommended to schedule the main exercise in the

morning to enhance blood pressure rhythm regulation (increase systolic blood pressure reduction by 8 mmHg) [2].

2.3. Biological basis of precise exercise prescription

The biological basis of precise exercise prescription is rooted in the differential regulation mechanism of individual molecular, cellular, and system-level heterogeneity on exercise adaptation:

(1) Gene polymorphism regulates exercise response: Gene variation determines the "dose-response" relationship of exercise benefit by affecting signaling pathways (e.g. AMPK, mTOR). For example, individuals with PGC-1α Gly482Ser polymorphism (rs8192678), whose mitochondrial biosynthesis capacity is 40% less sensitive to endurance training, would need to extend the training period (from 6 weeks to 10 weeks) to achieve the same VO_2max boost (+15%).

(2) Metabolic phenotyping: Based on metabolomics (such as plasma acylcarnitine profile), the population can be divided into "lipid metabolism-dominant" and "glucose metabolism-dominant". The former (35% of the population), due to the high oxidation efficiency of fatty acids, accounted for 70% of the fat supply in low intensity sustained exercise (LISS), while the latter required HIIT (85–90% HRmax) to maximize the glycogen consumption (muscle glycogen reduction > 60%) [3].

(3) Neuromuscular adaptation differences: Individuals with a higher proportion of fast muscle fibers (type II) (e.g. ACTN3 RR genotype) responded more significantly to explosive training (e.g., deep jumps, sprints) (22% higher vertical vertical jump height). The dominant slow muscle fiber (type I) (such as ACTN3 XX type) requires prolonged endurance training stimulation (> 8 weeks) to induce muscle fiber type conversion (type II increased by 5–8%).

(4) Dynamic response to epigenetic modification: Exercise regulates gene expression through DNA methylation (e.g., PPARδ gene promoter demethylation), histone acetylation, and other mechanisms. For example, 12 weeks of aerobic exercise reduced methylation levels of mitochondria-associated genes (such as TFAM) in fat tissue of obese patients by 30%, reversing insulin resistance. These biological mechanisms provide molecular targets and quantitative basis for the parameterization of precise exercise prescription (such as intensity, frequency, mode), and promote sports medicine from "experience-driven" to "data-driven".

3. Application of precise exercise prescription for exercise rehabilitation of chronic diseases

3.1. Rehabilitation of cardiovascular diseases (such as hypertension and coronary heart disease)

Exercise has become the core intervention for the rehabilitation of cardiovascular diseases by improving vascular endothelial function, reducing peripheral resistance, and enhancing myocardial efficiency. Precise exercise prescription should be personalized according to the patient's cardiopulmonary reserve (such as peak oxygen uptake VO_2peak), ambulate blood pressure pattern, and arteriosclerosis degree (such as carotid intimatomedia thickness IMT).

Table 1. Comparison of effects of different exercise modalities on cardiovascular diseases

Exercise type	Intensity parameters	Key physiological effects	Clinical effect data (12-week intervention)
Aerobic exercise	50–70% HRmax	Decrease in systolic blood pressure by 8-12 mmHg, increase in VO_2peak by 15%	40% reduction in angina frequency in coronary artery disease patients
Resistance exercise	60–80% 1RM	Improvement in arterial elasticity (PWV decreases by 1.2 m/s)	8% reduction in left ventricular mass index in hypertension patients
HIIT (High-Intensity Interval Training)	85–95% HRmax (1:1 work-rest ratio)	Increased myocardial mitochondrial density (+30%)	5%-7% increase in LVEF (Left Ventricular Ejection Fraction) in heart failure patients

Example of precision strategy include:

(1) Patients with arytenoid hypertension: HIIT is scheduled in the morning (peak systolic blood pressure), and circadian control of blood pressure can be enhanced by 4 × 4 minutes of high-intensity interval (85% HRmax) combined with 3 minutes of low-intensity recovery (10% increase in blood pressure reduction at night).

(2) Patients with coronary heart disease: Determine the anaerobic threshold (AT) based on cardiopulmonary exercise test (CPET), and control the prescription intensity below 5–10% AT (60–75% of heart rate reserve) to avoid the risk of myocardial ischemia.

3.2. Rehabilitation of diabetes and metabolic syndrome

Exercise improves skeletal muscle glucose uptake efficiency by activating the AMPK-GLUT4 pathway and improves adipose tissue inflammation (IL-6 decreases by 30% to 50%). Precise prescription requires a combination of insulin secretion pattern (C-peptide level) and body composition (visceral fat area VFA) [4].

Table 2. Effects of exercise types on metabolic improvement in diabetic patients

Exercise type	Parameters	Biological mechanism	Effect data (HbA1c changes)
Aerobic exercise	60% VO_2max, 30 minutes/day	Increased muscle capillary density (+20%)	HbA1c reduction by 0.5–1.2% (Type 2 Diabetes)
Resistance training	70% 1RM, 3 sets × 10 reps	Enhanced insulin receptor sensitivity in muscle cells	Fasting blood glucose decrease by 1.3–2.1 mmol/L
Flexibility training	Static stretching, 30 seconds per muscle group	Improved microcirculation (blood flow velocity +15%)	25% reduction in postprandial blood glucose fluctuations

Examples of individual cases includes:

(1) Insulin-resistant patients (HOMA-IR > 3.0): The combination of resistance and aerobic (2:1 time ratio) preferentially activates GLUT4 transport in type II muscle fibers, which can increase insulin sensitivity by 35%.
(2) β-cell function decline (C-peptide < 0.8ng/mL): Avoid long-term aerobic exercise (> 60 minutes/time), and change to short-term multiple exercise (3 × 10 minutes/day) to reduce the damage of oxidative stress on islet cells.

3.3. Rehabilitation of bone and joint diseases (such as osteoarthritis, low back pain)

The repair effect of exercise on bone and joint is reflected in subchondral bone remodeling induced by mechanical stimulation and regulation of synovial fluid metabolism. Low intensity pulse loading (such as water stepping) can increase the hydrostatic pressure in the knee cartilage compression area, promote proteoglycan synthesis (25% increase in content), inhibit MMP-13 enzyme activity (40% decrease), and delay cartilage degradation. For patients with lumbar degeneration, core stability training effectively reduces the L4-L5 shear force (from 1200N to 850N) by enhancing the synergistic contraction of the transverse abdominis and multifidus muscles (60% increase in myoelectric activity synchronization), and reduces the recurrence rate of disc herniation [5].

Table 3. Effects of personalized exercise programs for osteoarthritis

Intervention goal	Exercise type	Biomechanical parameter	Effect data (6 months)
Knee OA	Water stepping (depth 1.2m)	60% reduction in joint load	WOMAC pain score decreased by 45%
Lumbar Degeneration	Core stability training	Abdominal muscle activation rate >80%	Reduced recurrence of low back pain by 55%
Hip OA	Closed-chain exercises (pedaling angle 30°)	35% reduction in hip joint contact pressure	Gait symmetry index improved to 0.92

Personalized programs need to be stratified based on imaging progress and pain tolerance. In patients with early osteoarthritis (Kellgren-Lawrence grade II), vibration training (frequency 25Hz, amplitude 2mm) stimulated subchondral bone microstructure repair, increased trabecular thickness by 8%, and decreased pain VAS score by 4 points (on a 10-point scale). In patients with chronic low back pain with limited hip mobility (flexion < 115°), priority should be given to dynamic joint loosening combined with stretching of the hip flexor muscles to reduce the phase difference of the lumbar-pelvic rhythm from 20° to 8°, thereby reducing the compensatory lumbar torsional moment by 30%. For postoperative rehabilitation (such as ACL reconstruction), closed-chain exercises (such as squatting against a wall) control the knee flexion Angle to 0–60° within 6 weeks after surgery, ensuring that the graft stress is < 50N and avoiding early relaxation caused by excessive load [6].

3.4. Rehabilitation of respiratory diseases (such as chronic obstructive pulmonary disease, asthma)

Exercise rehabilitation improves lung function by enhancing the mechanical efficiency of respiratory muscles and optimizing the ventilation/blood flow ratio (V/Q). Inspiratory muscle training (IMT), using progressive loading

(initial intensity 30% MIP, weekly increase of 5%), increased diaphragm thickness from 2.3mm to 2.8mm, increased maximum inspiratory pressure (MIP) by 35%, and increased 6-minute walking distance by 90m in COPD patients. Upper limb endurance training (e.g., stretch band rowing) reduces the perception of dyspnea (Borg scale score from 5 to 3) by reducing compensatory overactivation of auxiliary respiratory muscles (scalenes, sternocleidomastoid) (40% reduction in EMG amplitude).

Precise intervention should be combined with pulmonary function classification and acute attack risk. In patients with severe COPD (GOLD III grade), intermittent aerobic regimen (1 minute high-intensity + 2 minutes low-intensity alternating), combined with oxygen inhalation during exercise (flow rate 2–4L/min), can maintain SpO_2 above 92%, and improve training compliance by 50%. For exercise-induced asthma, the use of progressively increasing intensity (10% load increase every 3 minutes) during the preheating phase, combined with ambient humidity control (> 50%), can reduce the incidence of bronchoconstriction from 25% to 8%. In addition, the use of a Heat-and-Moisture device (HME) during exercise in a low temperature environment (< 10℃) can reduce the moisture loss of the airway by 50% and significantly relieve the cough after exercise.

3.5. Cancer rehabilitation

Exercise plays a multi-dimensional rehabilitation role by regulating tumor microenvironment and neuroendocrine network. Aerobic exercise (e.g., cycling) enhances radiotherapy sensitivity (local control rate increased by 15%) by increasing the tumor perfusion oxygen partial pressure (pO_2 from 10 to 25mmHg). Resistance training (60% 1RM) reduced serum IL-6 levels by 45% and improved fatigue (FACIT-F score) by 30% in breast cancer patients by inhibiting the NF-κB pathway. For chemotherapy-induced peripheral neuropathy (CIPN), proprioceptive training (such as balance board exercises) increased the vibration perception threshold (from 15μm to 8μm) and reduced the risk of falls by 60%.

Individualized prescription should integrate tumor type, treatment stage, and functional status. In patients with breast cancer lymphedema, progressive resistance training (initial load 30% 1RM, weekly increase of 5%), combined with intermittent pressure therapy, can reduce the affected limb volume by 18%, and no risk of worsening edema. After hematopoietic stem cell transplantation, low-intensity cycle training (40% HRmax) during granulocyte recovery period (ANC > 0.5×10^9/L) can shorten the length of hospital stay by 3.5 days and reduce the incidence of infection by 25%. For advanced cancer patients, the “pre-rehabilitation” strategy was adopted, and respiratory muscle training and nutritional strengthening were performed 4 weeks before surgery, which reduced the risk of postoperative lung complications by 40% and the length of ICU stay by 2 days [7].

4. Challenges and future development direction

4.1. Challenges of individualized exercise prescription

The central challenge of individualized exercise prescribing lies in the highly heterogeneous nature of human biology. At the physiological level, gene polymorphisms (such as ACTN3 R577X) lead to significant differences in exercise adaptability: the effect of muscle hypertrophy after resistance training can reach 12–15% in RR genotype carriers, while only 5–7% in XX genotype carriers. Metabolic phenotypes (such as the difference in mitochondrial respiratory chain efficiency > 30%) further affect energy use patterns, for example, the lipid burning efficiency of low-intensity exercise in patients with lipid metabolism is 1.8 times that of those with glucose metabolism.

Psychological factors (such as self-efficacy) are also critical: patients with a depression scale (PHQ-9) score of > 10 experienced a 40% reduction in exercise compliance, and cognitive behavioral interventions were needed to increase participation. Environmental variables (such as air pollution PM2.5 > 50μg/m³) offset the cardiovascular benefits of exercise, reducing the carotid IMT improvement rate from 8% to 3%. In terms of dynamic adjustment, the existing technology is difficult to capture changes at the molecular level in real time (such as IL-6 fluctuations of 200% within 24 hours after exercise), resulting in delayed prescription update. In the future, multimodal biosensor networks need to be developed to integrate epigenetic (DNA methylation), metabolome (lactate/pyruvate ratio) and neuroimage data (fMRI brain region activation patterns) to achieve "hour-level" prescription iteration [8].

4.2. Obstacles to the implementation of precise exercise prescription

Globally, the density of sports medicine specialists is only 0.7 per 100,000 people, and 75% are concentrated in high-income countries. The imbalance in resource allocation results in less than 15% of diabetes patients in developing countries receiving individualized exercise guidance. Patient engagement is constrained by multiple factors: low-income groups forgo community exercise programs due to transportation costs (8–12% of monthly income), while older patients have difficulty accessing remote monitoring systems due to the digital divide (only 30% use smart devices). There are structural barriers to clinical integration: only 28% of healthcare systems cover exercise prescription costs, and electronic medical record systems lack standardized fields for exercise parameters (e.g., anaerobic threshold AT, muscle strength symmetry). An international survey showed that only 13% of general practitioners prescribed exercise, mainly due to lack of training (65%), lack of time (42%), and lack of effectiveness assessment tools (58%).

4.3. Combination of emerging technology and precise exercise prescription

Smart wearable devices are moving from single parameter monitoring to multi-physical field fusion sensing: the new electronic skin synchronously detects muscle strain (accuracy 0.1%), skin temperature (± 0.1 °C) and sweat metabolites (such as lactate concentration, error < 5%), and alerts the risk of rhabdomyolysis in real time through edge computing (automatic suspension of training when the predicted value of creatine kinase is > 5000U/L). AI algorithms achieve cross-population generalization through transfer learning: A neural network trained on 100,000 + motor response databases can generate effective prescriptions (RMSE < 0.8MET) for new diseases such as long COVID syndrome with only 50 samples. VR technology breaks through the limitations of traditional scenarios: Parkinson's patients can reduce the frequency of frozen gait attacks by 55% through customized virtual environments (such as dynamic balance beam training), and the mechanism involves the functional recombination of the cerebellar-basal ganglia circuit (fMRI shows a 40% enhancement of dentate nucleus activation) [9].

4.4. Future research direction

Future research needs to break through the complex interaction network of "gene-environment-behavior". Millions of cohorts based Mendelian randomization analysis identified motion sensitivity causal genes (e.g. PPARδ rs2016520) and established a polygenic risk score (PRS) model to predict the risk threshold for HIIT-induced arrhythmias (a three-fold increase in risk with PRS > 0.7). Metabolomic-driven dynamic prescription: Automatic adjustment of carbohydrate intake during exercise by real-time monitoring of plasma acylcarnitine profiles (detection delay < 10 minutes) (supplementation of 0.8g/kg/h when 60g of carbohydrate is lost per litre of sweat). Cross-scale modeling is another focus: from molecular dynamics simulations (e.g., myosin ATPase conformational changes) to organ-level

finite element analyses (knee joint contact stress cloud maps), the construction of digital twins to guide postoperative rehabilitation load (error < 5N).

5. Conclusion

In conclusion, precision exercise prescription offers a promising approach to chronic disease rehabilitation, providing a personalized, evidence-based approach to optimize rehabilitation and improve quality of life. As the demand for customized healthcare solutions grows, there is a need to develop more sophisticated models that incorporate individual differences such as genetics, lifestyle, and disease progression.

Disclosure statement

The author declares no conflict of interest.

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