

PAHFKB: A knowledge base to support personalized exercise prescription recommendations in prevention and intervention of heart failure

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Abstract

Background and Aims: Guidelines for exercise recommendations are typically designed for the population as a whole and do not account for individual differences, making it challenging to provide personalized exercise training for individuals with complex conditions. To address this issue, this study aimed to develop PAHFKB (Physical Activity-Heart Failure Knowledge Base), a knowledge-based system for personalized exercise prescription (EP) for heart failure (HF), by mining, analyzing, and organizing existing literature and data on the relationship between physical activity (PA) and HF.

Methods: Firstly, 3186 citations on PAHF were gathered from PubMed. Then, the data standards for personalized PAHF were defined with the entity-relationship model. Following data collection in accordance with these standards, PAHFKB was developed using MySQL and ASP.NET, integrating elaborate and diverse PAHF evidence, knowledge-based EP and visualization tools.

Results: PAHFKB (pahfkb.sysbio.org.cn) incorporated 357 studies published between 1989 and 2021, involving over 900,000 subjects from 43 countries. And 1010 PAHF items were extracted, encompassing 357 exercise training protocols, 333 outcomes, and 42 risk factors for HF prevention and intervention. Among all protocols, the most frequently employed regimen consisted of three 60-minute sessions of moderate-intensity aerobic exercise training on a weekly basis.

Conclusion: PAHFKB is an online system designed to support personalized EP in HF management. It incorporates diverse tools and visualization and will promote personalized decision support, establish data standards, and advance interpretable artificial intelligence in digital health. Ultimately, it will enhance clinical practice and digital therapy in the prevention and intervention of HF.

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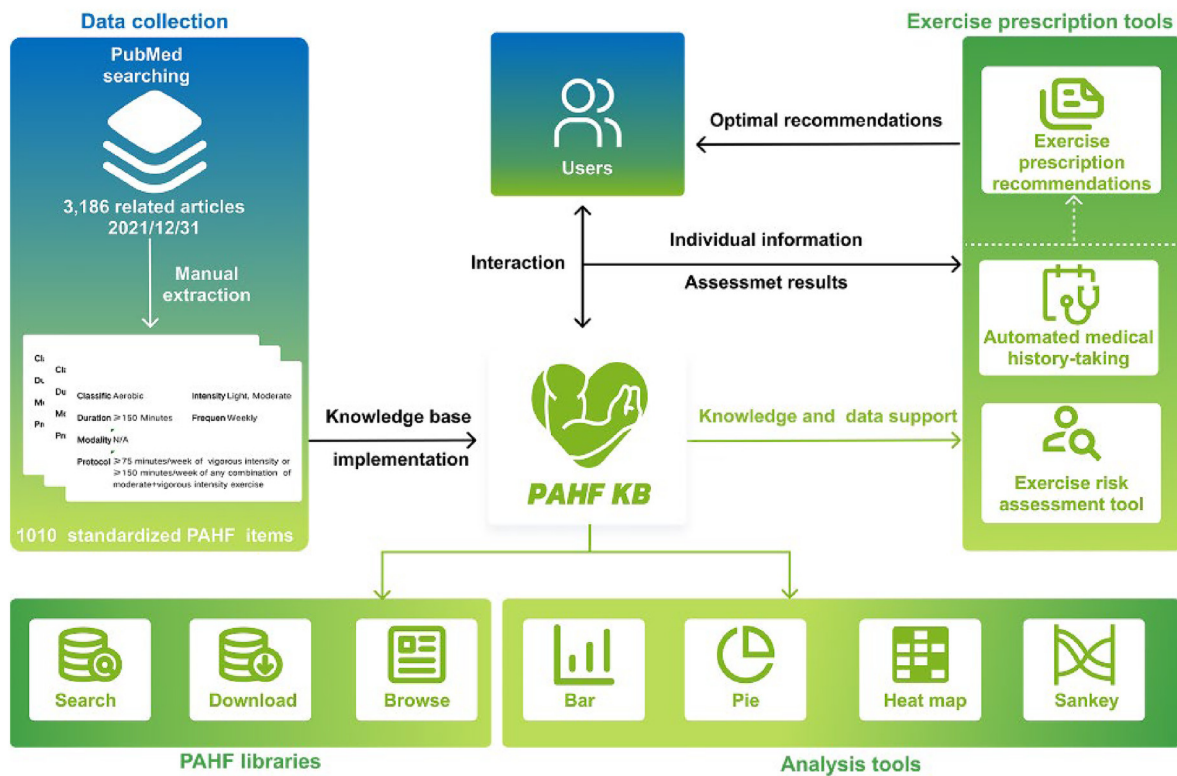
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Abstract

Graphical Abstract:



Keywords

Digital medicine, exercise prescription, heart failure, knowledge base, physical activity

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Introduction

Heart failure (HF) refers to a group of complex syndromes arising from ventricular dysfunction, characterized by exercise intolerance, fatigue, and dyspnea.^{1,2} Despite the evolution in medical treatments, the global incidence, burden, and cost of HF continue to persist unabated.^{3,4} From 1990 to 2017, both the prevalence and years lived with disability of HF have nearly doubled.³ In addition to population aging, the suboptimal implementation of pharmacological and device-based therapies contributes to the issue, particularly in developing countries. For example, in China, the utilization of beta-blockers and cardiac resynchronization therapy among patients with HF was a mere 25.6% and 0.3%, respectively.⁵

In comparison, exercise training offers a more cost-effective and efficient nonpharmacological intervention to

managing HF in most cases.⁶ Research increasingly shows that systematic and regular physical activity (PA) significantly enhances cardiorespiratory fitness while reducing HF-related morbidity and hospitalization rates.^{7,8} Given its numerous benefits, exercise training is recognized as a vital preventive and interventional strategy for HF.^{9–11} Numerous guidelines have been published to promote exercise training, yet, its clinical practice remains suboptimal. On the one hand, these guidelines or related reviews only provide general recommendations for all diseases.^{9,12} On the other hand, although they focused on the exercise medicine research status of cardiovascular disease (CVD), they only assessed and explained the effectiveness of exercise for patients and provide common knowledge (such as how to conduct exercise tests, and provide standardized exercise protocols), but lack personalized guidance based

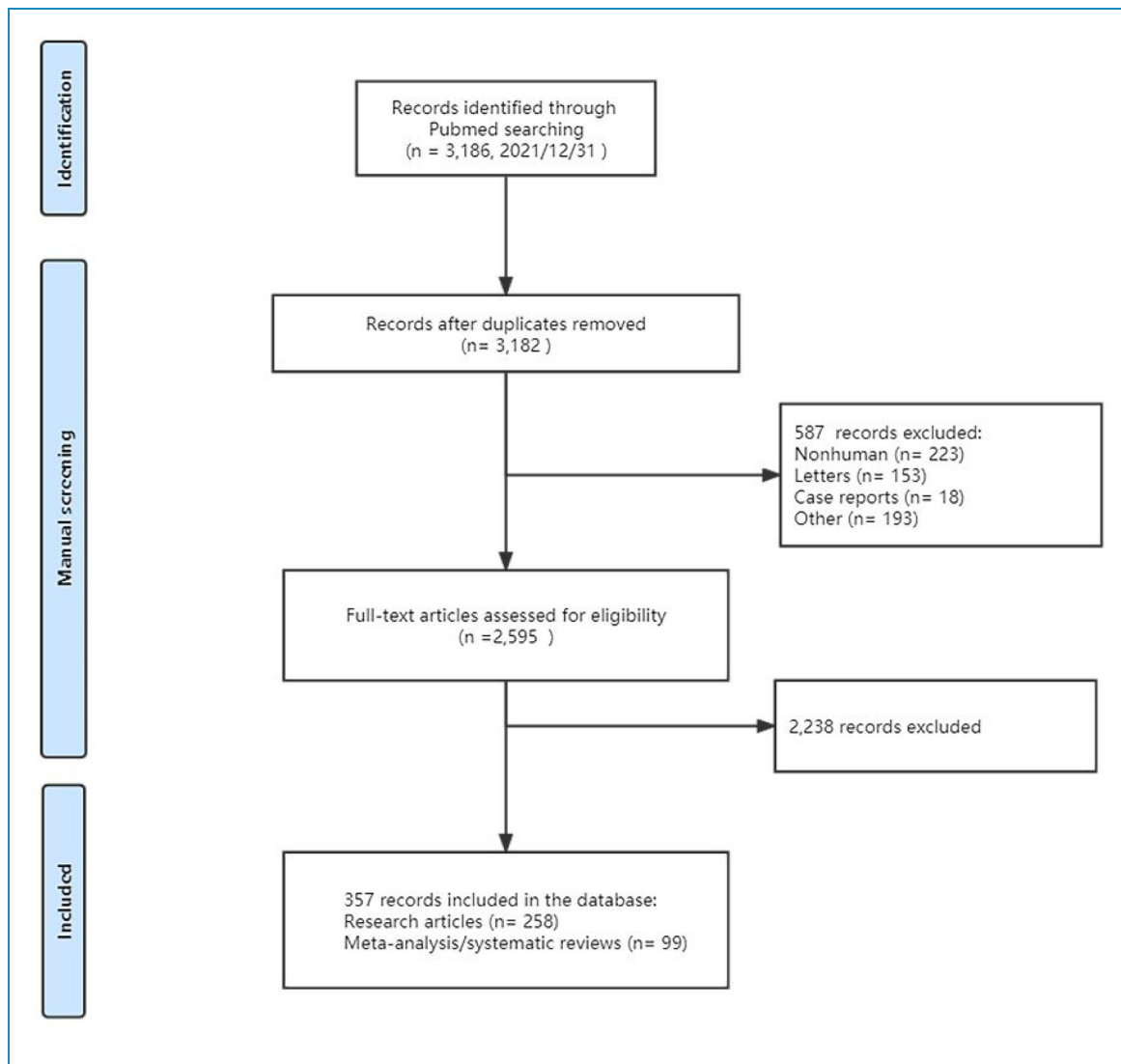


Figure 1. Flowchart for collection of PAHF studies. HF: heart failure; PA: physical activity.

on evidence.^{13–16} They neglected individual specificities, such as medication use, comorbidities, and surgical history.^{9,10} Comorbidities refer to the simultaneous presence of one or more diseases or conditions in a single individual. These diseases or conditions can interact with each other and may exacerbate the severity of a primary disease. For example, patients with HF often have other conditions such as diabetes, hypertension, or chronic kidney disease. These comorbidities can affect the treatment outcomes and prognosis of HF.^{17–19} When prescribing a personalized exercise regimen, the presence of comorbidities has a significant impact on the design and implementation of the prescription. First, comorbidities may limit the frequency, intensity, and types of exercise that the patient can perform. Second, comorbidities may also increase the risks associated with exercise. Therefore, when designing an exercise prescription (EP), a thorough health assessment

is essential to ensure the safety and effectiveness of the exercise program. While growing studies indicate that individual differences, such as genetic factors, physiological and physical characteristics, and lifestyle, can significantly affect the outcomes of exercise training.^{20,21} Therefore, when prescribing exercise for these individuals, physicians should consider multiple factors, such as age, health status, exercise habits, risk factors, and medical history. Currently, there have been several attempts to develop personalized EPs in the field of CVD.^{22,23} However, these attempts still have certain limitations. For instance, the exercise protocol is still limited to the FITT (frequency, intensity, time, type) principle; the tools lack public and reliable experimental evidence support; and the reasoning behind the exercise protocol lacks interpretability. Consequently, in clinical practice, prescribing safe and effective exercise regimens for specific patients remains challenging for

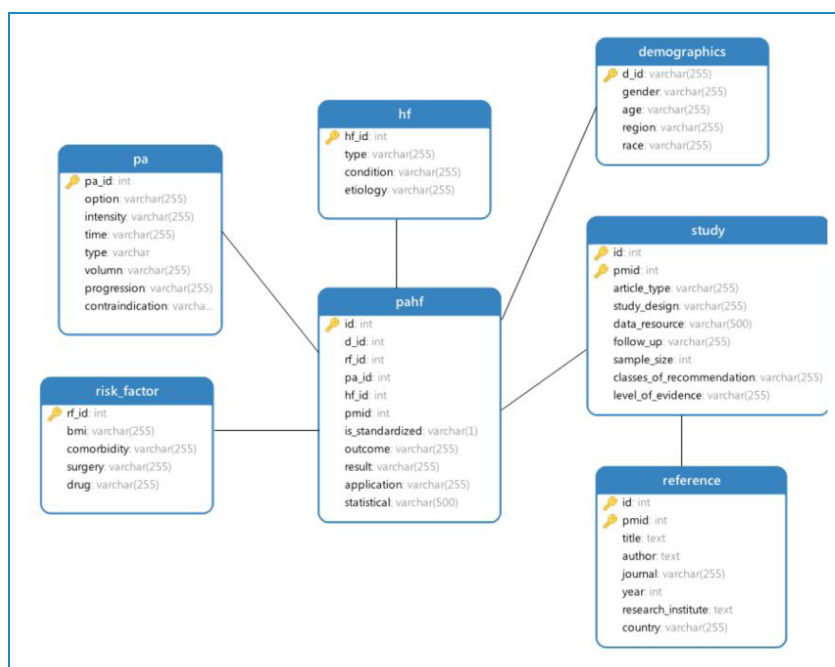


Figure 2. ER model for PAHF data. ER: entity-relationship; HF: heart failure; PA: physical activity.

physicians.^{24,25} Currently, there is no comprehensive investigation about existing literature on PAHF to support the development of personalized EPs system.²⁶

To address this issue and enhance clinical practice for exercise training, we developed the Physical Activity-Heart Failure Knowledge Base (PAHFKB) to provide comprehensive, evidence-based support for EP recommendations tailored to individuals with HF and associated risks. First, we summarized existing studies on PAHF and identified potential individual specificities that may influence EP generation. Then we established data standards to describe and collect the personalized PAHF dataset from literature. Finally, we developed a knowledge-based automated system for EP that considers individual specificities and designed a web-based user interface, providing clinicians and researchers with access to data resources, PA recommendation tools, and data analysis tools.

Methods

Data source

To ensure the rigor and validity of our findings, we utilized the PubMed database as our primary data source. PubMed is the preferred literature search tool in the field of medicine, biology, and life sciences, offering rigorously reviewed literature to ensure high-quality academic resources. We employed the search strategy “(Physical activity[ti] OR Exercise[ti] OR Sports[ti]) AND Heart failure[ti]”, which yielded 3186 publications until 31 December 2021 (Figure 1). Given the evidence quality,^{1,10} we excluded duplicates (2 results), nonhuman

studies (223 results), letters (153 results), case reports (18 results), and other unqualified studies (193 results), resulting in 2595 studies for full-text screening. After manual screening, we excluded 2238 articles that lacked conclusive data or conclusions, leaving with 258 original articles and 99 systematic reviews and meta-analyses for data collection.

Data extraction

Data extraction comprises data collection and standardization. Rational and consummate data standards are the prerequisite for both steps. Therefore, we developed structure and content standards to define and standardize PAHF data drawing upon related studies, state-of-the-art guidelines, professional expert opinions,^{9,10,27,28} and the functional requirements of PAHFKB.

We formed an entity-relationship model (Figure 2) to depict the main framework of relationships between PA and HF. In this model, a complete PAHF association included four main components: demographical characteristics, HF information, risk factors, PA protocol, and the effects of PA under the above conditions. To provide a more precise description of PA information, in addition to the traditional “FITT” concept,^{9,10,27} we added the latest parameters from ACSM EP, V(volume) and P(progression).²⁸ “Volume” refers to the capacity of exercise. For each exercise protocol, we calculated the exercise minutes required per week, in minutes. “Progression” refers to the process of gradually increasing exercise load or intensity in EP, which can ensure physical adaptation and gradual improvement of exercise performance. We documented details in the exercise protocol on

Table 1. Data content description criteria.

Entity	Attributes	Standardized description
Demographics	Age	Children and youth (≤ 17 years), adult (18–64 years), elderly (≥ 65 years)
	Gender	Female, male
	Race	Aboriginal or Torres Strait Islander, African, African American, American, American Indian, Asian, Black, Hispanic, Latin, Pacific Islander, White, other
	Region	Country name (English short name in ISO 3166-1) ³⁹
Risk factor	BMI	Underweight ($< 18.5 \text{ kg/m}^2$), normal ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25.0\text{--}29.9 \text{ kg/m}^2$), obesity ($\geq 30 \text{ kg/m}^2$)
	Comorbidity	Anemia, angina, anxiety, arrhythmia, arthritis, atrial fibrillation, cancer, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, depression, diabetes, hypercholesterolemia, hyperlipidemia, hypertension, obesity, sleep disturbance, and sleep disordered breathing, dyslipidemia, myocardial infarction, valvular heart disease, stroke, dementia, other
	Surgery	Coronary bypass grafting, defibrillator with cardiac resynchronization therapy, implantable cardioverter defibrillator, pacemaker, percutaneous coronary intervention
	Drug	ACE-I, beta-blockers, ARBs, digitalis glycosides, diuretics, beta-blockers, MRAs, other
Heart failure	Type	Heart failure, heart failure with preserved ejection fraction, heart failure with reduced ejection fraction, ¹⁰ without
	Condition	NYHA class I, NYHA class II, NYHA class III, NYHA class IV, ¹⁰ other
	Etiology	Cardiomyopathic, Chagas, coronary artery disease, dilated cardiomyopathy, hypertensive, idiopathic, ischemic, valvular, other
Physical activity	Frequency	Sessions/week
	Intensity	Light (2–4 METs), moderate (4–6 METs), high (6–8 METs), vigorous (8–10 METs) ¹⁰
	Duration	Minute/session
	Classification	Aerobic, balance, endurance, flexibility, resistance, strength, ^{10,27} other

ACE-I: angiotensin-converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; BMI: body mass index; METs: metabolic equivalents; MRAs: mineralocorticoid receptor antagonist; NYHA: New York Heart Association.

how to progressively increase the exercise load or intensity. At the meantime, we incorporated “modality” and “protocol” to record specific exercise forms (e.g. walking, cycling, and jogging) and detailed exercise training strategies. In addition, we also supplemented information regarding contraindications. Informing about contraindications ensures that the exercise protocol fits to the individual’s health condition, avoiding potential worsening situations. To account for specific HF conditions, we used “type,” “stage,” and “etiology.” We also extracted possible factors from available medical evidence to describe demographic characteristics and risk factors. Except for the essential entities, we included study and reference entities to record research information for validation and future updates. As a knowledge base, we aimed to include a wide range of data sources to ensure the comprehensiveness

of PAHFKB. Consequently, the data quality might be uneven. Therefore, we used “recommendation classification” and “evidence level” based on the ESC quality criteria to differentiate the different levels of data quality.¹⁰

The attributes for specific PAHF information in the database were standardized for sharing and analysis, as illustrated in Table 1. Using the established criteria, PAHF data was manually extracted from the relevant literature and systematically stored in the database.

Knowledge base implementation

The Browser/Server architecture and the WIMA (Windows, IIS, MySQL, ASP.NET) web stack were adopted to construct the web-based platform. This architecture consisted

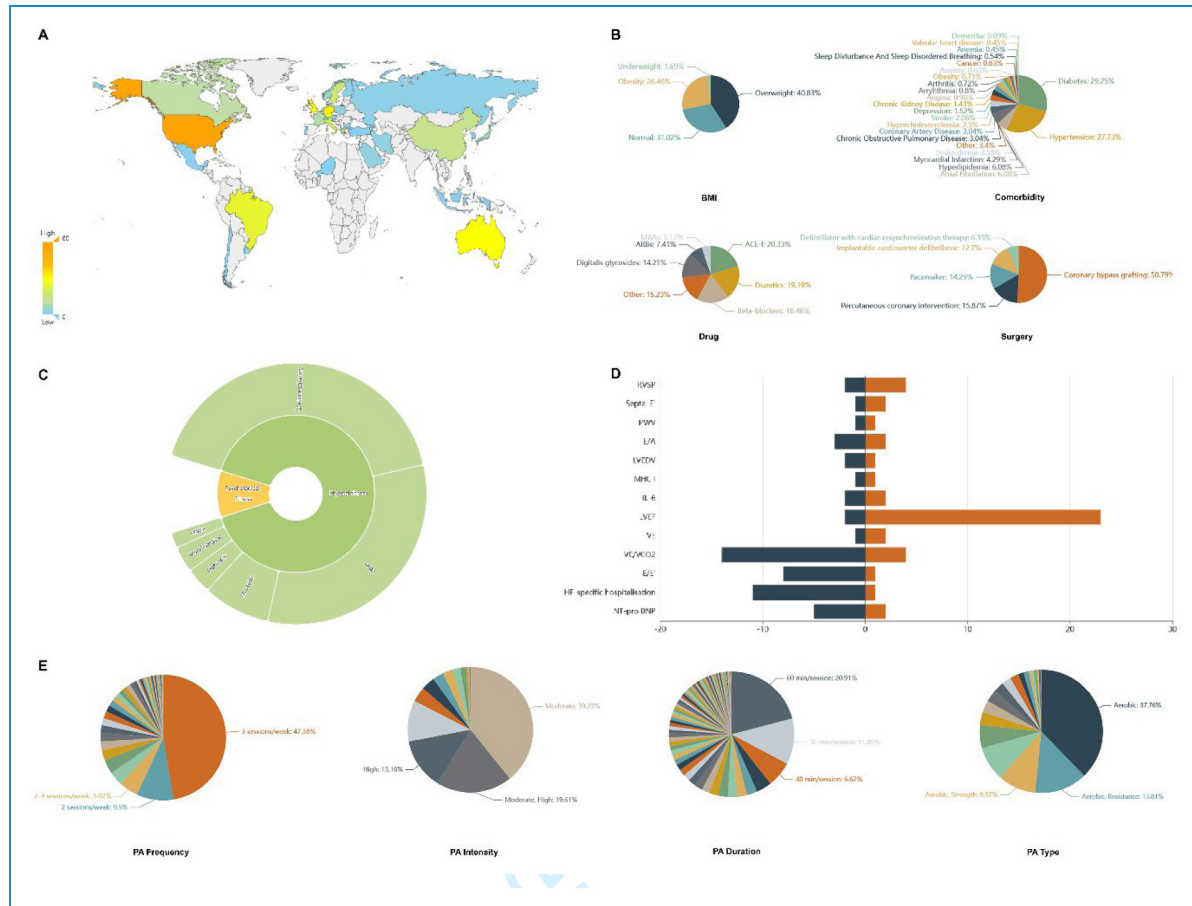


Figure 3. Data statistics for PAHFKB: (a) heat map of country distribution; (b) classification of risk factors; (c) classification of outcomes; (d) outcomes with conflict conclusions; (e) classification of FITT.

ACE-I: angiotensin-converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; BMI: body mass index; E/A: mean ratio of early to late mitral inflow velocities; E/E': the ratio of early diastolic transmitral velocity to early diastolic tissue velocity; FITT: frequency, intensity, time, type; HF: heart failure; IL-6: interleukin-6; LVEDV: left-ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; MHC I: myosin heavy chain class I; MRAs: mineralocorticoid receptor antagonist; NT-pro BNP: N-terminal pro-B-type natriuretic peptide; PA: physical activity; PAHFKB: Physical Activity-Heart Failure Knowledge Base; PWV: pulse wave velocity; ; RVSP: right ventricular systolic pressure; VE: minute ventilation; VE/VC02: the slope of the minute ventilation to carbon dioxide production.

of three layers: data, business, and presentation. In the data layer, the MySQL database management system was utilized to store and retrieve data. In the business layer, the ASP.NET MVC framework, coded in C#, was employed to develop the algorithms for all system functions (e.g. search engine, data visualization, and EP recommendation tools). Lastly, the presentation layer was implemented using the Bootstrap and Echarts frameworks, programmed with HTML and JavaScript, to provide a user-friendly interface.²⁹

Results

Data statistics

PAHFKB contains 357 studies published from 1989 to 2021 (Supplemental Figure 1), including 258 original articles and 99 systematic reviews/meta-analyses. Most of these studies

were conducted in developed countries, with the United States contributing 62, followed by Germany and Australia with 33 and 30, respectively (Figure 3(a)). These included more than 900,000 subjects aged 18 to 88, with 47% females and 53% males. Notably, New York Heart Association (NYHA) classification was the most frequently used in those studies. After standardizing other classifications according to the NYHA classification, HF subjects in classes I to IV were distributed as follows: 12%, 39%, 39%, and 5%, respectively.

From these studies, 1010 items were extracted, comprising 357 exercise training protocols, 333 outcomes, and 42 risk factors for PA in the prevention and intervention of HF. As illustrated in Figure 3(b), risk factors in PAHFKB are categorized into four types: body mass index, drug intake, comorbidity, and surgery history. Overweight (40%), diabetes (29%), angiotensin-converting enzyme inhibitor (ACE-I) (20%), and coronary bypass grafting (51%) represent the most prevalent



Figure 4. User interface of PAHFKB: (a) PAHF libraries; (b) exercise risk assessment tool; and (c) analysis tools. HF: heart failure; PA: physical activity; PAHFKB: Physical Activity-Heart Failure Knowledge Base.

risk factors for each type. Figure 3(c) displayed the outcomes which can be divided into physical fitness-related ($n=313$) and psychological fitness-related ($n=20$). Physical fitness-related outcomes can be further subdivided into cardiorespiratory fitness ($n=151$), metabolic fitness ($n=6$), morphological fitness ($n=6$), motor fitness ($n=2$), muscular fitness ($n=29$), and other physical fitness ($n=119$).³⁰ Among these, 13 PA outcomes were identified with conflicting conclusions (Figure 3(d)). Subsequent studies can use this statistical analysis to assess the consistency of conclusions regarding specific PA.

Furthermore, we summarized all the EPs according to the HF conditions and general risk factors (Figure 3(e) and Supplemental Table 1) and analyzed the data flow between different exercise FITT, and outcomes (Supplemental Figure 2). Overall, frequency ranges from daily to weekly, intensity varies from light to vigorous, duration spans from 1 to 240 minutes per session, and types include aerobic, balance, endurance, resistance, and strength. The most common features are 3 sessions per week (47%), moderate intensity (40%), 60 minutes per session (21%), and aerobic exercise (38%).

User interface and applications

PAHFKB consists of six parts: “Home”, “PAHF Libraries”, “Exercise Prescription Tools”, “Analysis Tools”, “Contact Us”, and “Help”. The “Home”, “Contact Us”, and “Help” pages give a general introduction to the system, including basic information, data and tools portals, links to related guidelines, a user’s manual, as well as contact information.

PAHF libraries

PAHF libraries (Figure 4(a)) provide users with a multifunctional search engine including keyword retrieve, datasets download, and detailed browse functions. By inputting keywords in the search box, users will get results from the database with matched parts highlighted. Then, by clicking the download button, users are allowed to save the results in multiple formats: JSON, XML, CSV, TXT, SQL, and MS Excel. Card and full-screen views, as well as customizable column choices, are available in the right-side toolbar for users to flexibly adjust the datasets table. The detail button also provides users with more information about specific PAHF items, such as the primary data and study design.

Exercise risk assessment tools

Health screening before exercise is crucial to avoid adverse events, especially for patients and individuals with CVD risk factors.³¹ Therefore, in accordance with the American College of Sports Medicine’s (ACSM) guidelines, PAHFKB provides exercise risk assessment tools (Figure 4(b)) that consist of the PA level assessment questionnaire (PAL-Q) and the PA readiness questionnaire (PAR-Q).^{9,32} These questionnaires should be completed and used under the guidance of a doctor. Firstly, through the PAL-Q, users can obtain optimal exercise intensity recommendations based on their daily exercise activity under a doctor’s supervision. Subsequently, by completing the PAR-Q, users can assess their exercise risk under a doctor’s supervision to determine whether

Please choose a category of **HEART FAILURE TYPE** based on your physical condition.

1 **Heart Failure**

Heart Failure With Preserved Ejection Fraction
Heart Failure With Reduced Ejection Fraction
Without
None of above / Unknown

Please choose a category of **HEART FAILURE CONDITION** based on your physical condition.

2 **NYHA Class II**

NYHA Class I
NYHA Class II
NYHA Class III
NYHA Class IV
None of above / Unknown

Please choose a category of **COMORBIDITY** based on your physical condition.

Anemia
Angina
Anxiety
Arrhythmia
Arthritis
Atrial Fibrillation
Cancer
Chronic Kidney Disease
Chronic Obstructive Pulmonary Disease
Coronary Artery Disease
Depression
Diabetes
Dyslipidemia
Hypercholesterolemia
Hypertension
Myocardial Infarction
Obesity
Sleep Disturbance And Sleep Disordered Breathing
Stroke
Valvular Heart Disease
None of above / Unknown

Please choose a category of **SURGERY** based on your physical condition.

Coronary Bypass Grafting

Defibrillator With Cardiac Resynchronization Therapy
Implantable Cardioverter Defibrillator
Pacemaker
Percutaneous Coronary Intervention
None of above / Unknown

Please choose a category of **DRUG** based on your physical condition.

ACE-I

Arbs
Beta-Blockers
Digitalis Glycosides
Diuretics
Mas
None of above / Unknown

Please choose a category of **AGE** based on your physical condition.

Adult
Elderly

Physical Activity Recommendations

PA No. 1
Classification Aerobic, Resistance
Frequency 2-5 sessions/week
Intensity Moderate
Time 30-60 min/session
Type Cycling, Tai Chi, Walking
Protocol NA
Statistical SDNN and RMSD (15.46 and 17.56 ms, resp., $P < 0.05$)
Recommendation lb
Reference 18221

PA No. 2
Classification NA
Frequency 2 sessions/week
Intensity Moderate
Time 50 min/session
Type Cycling, Step-board, Treadmill
Protocol Patients underwent a standard cardiac rehabilitation program including a 15-min warm-up period followed by 35 min of exercise on a treadmill, a stair machine and a bicycle at 60-70% of maximal heart rate. Compliance was monitored, and the exercise prescription was adjusted if maximal exercise capacity has improved. Exercise was performed twice a week for a total of 18 weeks.
Statistical 6-min walk test 308 ± 87 to 423 ± 91 m, $p < 0.001$; modified Bruce exercise test 5.6 ± 3.6 to 9.8 ± 3.4 min, $p < 0.001$
Recommendation lb
Reference 18951

PA No. 3
Classification NA
Frequency 2 sessions/week
Intensity Moderate
Time 60 min/session
Type Cycling, Step-board, Treadmill
Protocol Each training session included a 15-minute warm-up period, followed by 45 min of exercise on a treadmill, a stair machine, and a bicycle targeting 60-70% of the heart rate reserve (Karvonen equation), which was typically between 90 and 95 bpm.
Statistical +11%
Recommendation lb
Reference 19069

PA No. 4
Classification NA
Frequency 2 sessions/week
Intensity High
Time 25 min/session
Type NA
Protocol Patients in HIIT started with intervals of 2-min duration at 80-85% PHR, separated by 2 min of recovery at 50% of PHR to achieve a total "on-time" of 16 min of high-intensity exercise. They were progressed by the start of the second week of training to completing four, 4-min intervals at 85-90% PHR, separated by 3 min at 50% PHR. Each training session began with a 10-min warm-up at 50% of PHR and ended with a 5-min cool down at the same intensity
Statistical pre = 2.1 ± 0.3 ; post = 1.3 ± 0.7 ; $P = 0.02$
Recommendation lb
Reference 19743

PA No. 5
Classification Endurance
Frequency 3 sessions/week
Intensity Light, Moderate
Time NA
Type Cycling
Protocol Outpatient ICD group performed loaded cycling on ergometer divided into intervals and the conditioning exercises with elements of resistance training three times a week. Intensity of endurance training was based on the maximum heart rate achieved by the patient during an exercise test. Maximal training heart rate was calculated according to the Karvonen formula. The training program consisted of 3 min of warm-up (10 W), 2 min of loaded cycling up to 120 W, 2 min of low intensity exercise (10 W load), and 2 min of rest. Every patient had individual values of maximum workload. Cycle ergometer sessions lasted 30 min during which patients were cycling with the cadence of 55 to 64 rpm. Resistance trainings lasted from 5 to 10 min. Exercises involving a single muscle group of one limb alternately with a load of up to 50% of muscle strength were performed. There were 10-12 repetitions in one cycle during 1 min working phase. Patients exercised until their fatigue level reached 11-12 points, according to the original 21-point Borg scale.
Statistical $p = 0.001$
Recommendation lb
Reference 20055

PA No. 6
Classification NA
Frequency 2 sessions/week, 23 sessions/week
Intensity NA
Time 60 min/session, 35 min/session
Type Tai chi
Protocol The protocol included traditional warm-up exercises and 5 subsequent simplified tai chi movements. Each cohort was taught by 1 or 2 certified and experienced instructors (6 total study instructors with average experience of 19 years). Warm-up exercises included weight shifting; arm swinging; gentle stretches of the neck, shoulders, spine, arms, and legs; visualization techniques; and traditional breathing methods. These exercises focus on releasing tension in the body, incorporating mindfulness and imagery into movement, increasing awareness of breathing, and promoting overall relaxation of body and mind. The core tai chi movements were adapted from Master Cheng Man-Ching's Yang-style short form and performed repetitively. Chairs were provided for resting, and patients were allowed to progress at their own comfort and pace
Statistical -19 [-23, -3] vs 1 [-16, 3], $P = .02$
Recommendation lb
Reference 20137

Click to switch to card view

Click to filter results

Special cautions

References for ACTH Guidelines for Exercise Testing and Prescription

Contraindications:

- Unstable angina
- Uncontrolled hypertension/resting systolic blood pressure > 180 mm Hg and/or resting)
- diastolic blood pressure > 110 mm Hg
- Orthostatic blood pressure drop of > 20 mm Hg with symptoms
- Significant aortic stenosis (aortic valve area < 1 cm²)
- Uncontrolled atrial or ventricular arrhythmias
- Uncontrolled sinus tachycardia (> 120 beats/min)
- Uncompensated heart failure
- Third-degree atrioventricular block without pacemaker
- Active pericarditis or myocarditis

Figure 5. Physical activity recommendation tool of PAHFKB.
PAHFKB: Physical Activity-Heart Failure Knowledge Base.

medical clearance is needed before initiating exercise. Before using PA recommendation tool, we have emphasized the importance of conducting exercise tests and provided the detail link. Additionally, The Borg Rating of Perceived Exertion (RPE)³³ is provided for individuals to self-report their perceived exertion during physical activities. Using these exercise risk assessment tools under the guidance of a doctor is important in ensuring the safety of patient exercise and monitoring the effectiveness of exercise training.

Analysis tools

This module offers five visualization tools to assist users to analyze PAHF data: publication years, country distribution, classification of risk factors, outcomes, and the data flow between outcomes and PA FITT (Figure 4(c)). Each tool consists of two parts: data selection and result visualization. In the first part, users are prompted to select the data for analysis. The results are subsequently generated and displayed in the second part. The view toggle and result download functions can be accessed through the right toolbar.

Physical activity recommendation tool

The PA recommendation tool consists of two parts (Figure 5):

1. automated medical history-taking module and
2. PA recommendations module.

Initially, users are required to answer questions in the first module. Based on the user's responses, this module predicts potential PA protocols in the PAHF libraries. Then, considering feedback from the libraries and the prioritization of EP decision factors (HF condition, risk factors, and demographic characteristics), the module automatically generates the next question and relevant options. To ensure accurate and personalized recommendations, this automated medical history-taking process continues looping to collect the user's physical conditions until the knowledge base infers the optimal PA recommendations.

Subsequently, the second module presents the final recommendations. Each recommendation is extracted from an evidence-based study and includes basic information along with the standardized PA protocol (statistical results, classification of recommendations, and reference information). Additionally, this module offers a view toggle, data filter, customizable columns, and recommendation download functions to assist users in comparing and analyzing recommendations flexibly.

Figure 5 illustrates the process of PA recommendation. First, the automated medical history-taking module sequentially generates six questions to collect information about the user's HF type, status, comorbidities, surgery history,

drug intake, and age. Then, based on the answers ("heart failure", "NYHA class II", "diabetes", "coronary bypass grafting", "ACE-I", and "elderly"), the second module recommends six optimal PA protocols and relevant special cautions. In this case, the most frequently recommended FITT for PA is "2 times/week", "moderate", "60 minutes/session", and "aerobic".

Discussion

To facilitate the clinical translation and scientific investigation of exercise training for the prevention and intervention of HF, we developed the automated knowledge-based system on EP in HF, termed the PAHFKB. In contrast to the prevailing clinical and health practice guidelines, this work provides comprehensive, diverse, and informative collection of PAHF resources, rather than relying on "averaged" evidence. Additionally, the PAHFKB system incorporates search engines, EP recommendation tools, and visualized analysis tools. Driven by data, facts, and knowledge, these tools deliver timely and up-to-date PAHF support for future research in personalized and digital health management.³⁴ During data extraction, we established the primary framework to characterize PAHF data, marking an initial step towards standardizing personalized EP for HF rehabilitation.

Specifically, existing guidelines offer exercise recommendations for patients with a single disease but fail to address exercise training for those with multiple conditions. Capitalizing on its benefits, the PAHFKB can assist healthcare professionals in offering more personalized and diverse EPs tailored to the unique needs of each patient. As depicted in Figure 5, the PA recommendation tool provided 6 evidence-based exercise training recommendations for an individual with both HF and diabetes after fully considering HF conditions, the main comorbidity, and important risk factors ("heart failure", "NYHA class II", "diabetes", "coronary bypass grafting", "ACE-I", and "Elderly"), rather than only one broad recommendation for all patients with HF. These evidence-based recommendations not only aid healthcare professionals in making informed decisions about EPs but also offer individuals a broader range of options to enhance the efficiency and adherence to their exercise programs. Although previous efforts have been made to develop relevant health guidelines or EP systems in CVDs, such as Life's Simple 7 of AHA, the P3-EX, and the EPAC EXPERT tool, their underlying logic remains reliant on guidelines or non-evidence-based prescription recommendation processes.^{23,35–37} Comparatively, our manually curated and standardized PAHF resources can provide more robust data support and knowledge-driven foundations for the development of personalized clinical decision support system in the future. Table 2 provides a detailed comparison of these guidelines or tools in various aspects, demonstrating the advantages of PAHFKB.

Table 2. The comparison of current CVD health guidelines/exercise prescription tools.

	AHA	The P3-EX	The EAPC expert tool from Hansen	PAHFKB
Applicable fields	CVD	CVD	CVD	Designed for heart failure, with standardized information of disease conditions, etiology, comorbidities, surgical details, and other relevant data
Aims	Evaluate health status and provide guidelines for health improvement	Recommend exercise prescriptions	Recommend exercise prescriptions	Recommend exercise prescriptions
Exercise protocol principle	/	FITT	FITT	From FITT to FITT-VP with contraindications
Source of evidence	The data or experimental evidence lacks transparency. No exercise protocol recommendations are provided	The knowledge is sourced from the guidelines of the AHA and the American College of Sports Medicine. No explainable exercise prescription recommendation process	The data or experimental evidence lacks transparency. No explainable exercise prescription recommendation process	Each exercise protocol has undergone experimental validation documented in publicly published literature, along with relevant exercise outcomes

AHA: American Heart Association; CVD: cardiovascular disease; FITT-VP: frequency, intensity, time, type, volume and progression; PAHFKB: Physical Activity-Heart Failure Knowledge Base; The EAPC expert tool: The European Association of Preventive Cardiology Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool; P3-EX: Prioritize Personalize and Prescribe Exercise.

Despite being the first PAHFKB, this study has some limitations. First, the process of literature reading and data entry is carried out manually, which ensures higher accuracy but results in a low efficiency. To address the increased workload brought by the expansion of data sources, we plan to use natural language processing algorithms for data filtering and preliminary extraction in the next version, thereby improving efficiency. Second, the existing PAHF data standards are relatively simplistic, only considering the primary decision parameters. In the next version, a more systematic and comprehensive data standard (e.g. ontology) will be developed for PAHF, covering as many relevant influencing factors as possible. Third, although the datasets and recommendations in PAHFKB are evidence-based, external validation is necessary to assess the potential medical and economic benefits of this system. Future research will involve prospective studies evaluating the system's impact on clinical practice. Lastly, while the basic PA recommendation tool offers good interpretability and transparency, its capabilities are limited by the data sources. It can only provide answers based on existing evidence and is unable to predict or address complex questions. In subsequent work, deep learning algorithms will be combined to create a more powerful

decision support model, while maintaining the overall interpretability of the model.^{26,38}

Conclusion

PAHFKB holds profound significance in advancing the management of HF through personalized EPs. By synthesizing data from a vast array of studies, PAHFKB transcends traditional, one-size-fits-all guidelines, offering a user-friendly tool that tailors exercise recommendations to the unique needs of individual patients. This system not only bridges the gap between research and clinical practice but also sets a new standard for integrating data-driven insights into personalized healthcare. Its ability to accommodate the complexities of comorbid conditions and varying patient profiles ensures that clinicians can make informed decisions that enhance patient outcomes and adherence to exercise regimens. PAHFKB is a transformative platform that has the potential to revolutionize PA management for HF, ultimately leading to more precise, effective, and patient-centered care.

Contributorship: BS and KZ designed the research; BS, KZ, SR, and TB designed the data extraction and standardization criteria;

KZ, SR, XL, CZ, EW, and JW conducted data collection, extraction, and standardization; KZ, EW, XL, RW, and LS designed and developed users' interface; KZ, TB, SR, RW, DL, and EW drafted the edited manuscript; and BS supervised the study and revised the manuscript.

Data availability statement: The raw data and tools are available at pahfkb.sysbio.org.cn.

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