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Cost-effectiveness analysis of digital therapeutics for home-based cardiac rehabilitation for patients with atrial fibrillation after catheter ablation

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Abstract

Background: In recent years, numerous guidelines and expert consensuses have recommended that digital technologies and products, such as digital therapeutics (DTx), be incorporated into cardiac rehabilitation (CR).

Objective: The study aims to compare the cost-effectiveness of DTx for home-based CR (HBCR) with that of the conventional HBCR for patients with atrial fibrillation (AF) after catheter ablation in a real-world clinical setting.

Methods: Based on a single-center, prospective, blinded, randomized, parallel controlled trial of DTx-based HBCR for AF patients after catheter ablation, 100 AF patients undergoing catheter ablation were selected and randomized at a 1:1 ratio into a UC group (conventional HBCR) and DT group (DTx-based HBCR). The intervention lasted for 12 weeks. Medical cost data and clinical efficacy data (VO_2max) were acquired from trial data. Effect data (QALYs, anxiety and depression status, health beliefs related to cardiovascular disease, and exercise self-efficacy) were obtained from a patient questionnaire. The cost-effectiveness analysis was conducted to assess the economic benefits of DTx-based HBCR versus conventional HBCR, and the robustness of the results was verified by sensitivity analysis.

Results: In the DT group ($n = 49$), the mean QALYs increased 0.119 ± 0.09, VO_2max increased 9.3 ± 8.0 mL/(min*kg), anxiety, depression, health belief, and exercise self-efficacy had improved, and the total medical cost was $75{,}080.55 \pm 19{,}746.62$ CNY. In the UC group ($n = 48$), the mean QALYs increased 0.077 ± 0.06, VO_2max increased 4.9 ± 6.6 mL/(min*kg), anxiety, depression, health belief, and exercise self-efficacy had improved, and the total medical cost was $73{,}972.66 \pm 16{,}582.04$ CNY. The difference in the medical cost was 1107.89 CNY, and the incremental cost-effectiveness ratio was 33,572.42 CNY/QALY, which was lower than the willingness-to-pay threshold of 85,698 CNY (China's per capita GDP in 2022).

Conclusion: DTx-based HBCR is more effective and cost-effective than conventional HBCR.

Keywords

Atrial fibrillation, cardiac rehabilitation, home-based cardiac rehabilitation, digital therapeutics, cost-effectiveness analysis

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Introduction

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction, which is the most common sustained arrhythmia, with a prevalence of 2–4% in adults worldwide.[1] AF patients are prone to stroke, thromboembolism, heart failure, and myocardial infarction, seriously endangering their health.[2] There are approximately 59.7 million AF patients (including atrial flutter) worldwide and more than 10 million in China.[3–6] AF is a huge burden on patients, doctors, and healthcare systems globally, with annual management costs of 10,100–14,200 dollars/person in the United States and 450–3000 euros/person in Europe.[7] In China, the AF treatment cost is 3000 CNY/person, totaling 30 billion CNY.[2,8]

As proven by evidence-based medicine, catheter ablation is safe and effective in the treatment of AF, and it is far superior to drug therapy in maintaining sinus rhythm, reducing AF burden, ameliorating AF symptoms, and improving quality of life (QoL), making it one of the main treatments for AF.[9–19] However, the completion of catheter ablation does not mean the end of treatment, and patients often suffer from discomfort in the short term after surgery. Although catheter ablation can significantly improve the symptoms of AF patients, physical problems such as decreased exercise tolerance and low cardiopulmonary fitness still occur after surgery, and patients are often faced with psychological problems, such as poor sleep quality, anxiety, and depression.[20–24] These physical and psychological problems may raise the risk of recrudescence of AF, seriously affecting the patient's QoL and restricting their return to normal work and life. Therefore, professional cardiac rehabilitation (CR) is required for AF patients after catheter ablation.

CR is a medically supervised specialty field that utilizes a multidisciplinary approach to implement comprehensive secondary prevention programs for cardiovascular disease and has been listed as a level I recommendation for the treatment of cardiovascular disease.[1,25] CR is effective at controlling cardiovascular risk factors, reducing cardiovascular risk, improving patients' compliance with healthy lifestyle behaviors, raising QoL, and lowering the morbidity and mortality of cardiovascular events and the hospitalization rate of patients.[21,22,26–28] There is a U-shaped correlation between the incidence of AF and exercise, i.e., sedentary behavior or long-term high-intensity exercise could lead to an increase in the incidence of AF, while low- to moderate-intensity exercise can reduce the incidence of AF.[29–34] Therefore, the core of CR is to provide patients with individualized suggestions on exercise training and develop scientific exercise prescriptions so that their daily physical activity can be enhanced to improve cardiopulmonary function, reduce the risk of chronic diseases, and improve the long-term prognosis.[25,35–39]

CR can be classified into two modes: center- or hospital-based CR and home-based CR (HBCR), according to the scenarios of nursing care.[40] Center- or hospital-based CR is highly beneficial for implementing exercise prescription and monitoring feedback on exercise status, but it is expensive, and extra time and transportation costs are needed for patients to visit hospitals and rehabilitation centers. Due to some limitations in practical use, the popularization and patient participation of center- or hospital-based CR are low.[41–43] In HBCR, the patient exercises at home without a professional present according to the exercise prescription. Since it is not limited by time, traffic, site, and weather, HBCR reduces the difficulty of participating in CR and allows for better compliance, so it has been increasingly valued by medical personnel.[44,45] Many studies have provided evidence for the effectiveness and safety of HBCR interventions,[46–48] and HBCR not only is cheaper but also has similar outcomes to outpatient CR.[49–51] However, conventional HBCR also has some deficiencies: (a) The patient might be afraid of doing the exercises due to the worry that excessive physical activity could lead to the recrudescence of AF, cardiac discomfort, and accidents, so the patient might reduce or even avoid the exercise. (b) Due to lack of effective guidance on the exercise techniques, it is difficult for the patient to master them, resulting in a poor rehabilitation effect. (c) Due to the lack of exercise status monitoring and the inability to adjust the prescription according to patient feedback about the exercise, the patient has low compliance with self-guided exercise and fails to adhere to long-term exercise.

In recent years, numerous guidelines and expert consensuses have recommended that digital technologies and products be incorporated into CR, so that precise management of CR can be provided for patients through remote monitoring, rehabilitation guidance, and information feedback, thereby improving compliance and rehabilitation effect.[2,9,25,35] DTx is an evidence-based medicine modality that collects data and monitors indicators by digital means, helping clinicians' control and optimize the treatment, management, and prevention of diseases.[52] DTx devices are classified as new medical devices in several countries, and DTx and its related products must pass clinical testing before being approved by regulatory authorities. In 2017, the first prescription of DTx was approved by the US Food and Drug Administration. DTx has been applied to disease treatment, rehabilitation and prevention, and patient management in the fields of cardiovascular medicine, endocrinology, orthopedics, ophthalmology, neurology, and psychology.[53–62] As shown in several randomized controlled trials, patients undergoing DTx have better health improvement and symptom relief, and their

psychological status and QoL are significantly superior to those of controls. In addition, DTx enhances doctor–patient communication and disease risk factor management, reducing medical costs and enabling precision medicine.[44,45,63]

In 2019, the first randomized controlled trial of DTx-based HBCR for AF patients after catheter ablation in China was conducted in the First Affiliated Hospital of Nanjing Medical University.[64–66] Patients in the experimental group received DTx-based HBCR using the Recovery Plus app. The safety and effectiveness of DTx-based HBCR for AF patients after catheter ablation have been verified by a clinical trial. As shown in Figure 1, the procedure of DTx-based HBCR included the formulation of a personalized exercise prescription in the experimental group, remote monitoring by portable and wearable devices, exercise training guidance, and management by a rehabilitation team consisting of electrophysiologists, specialist nurses, and rehabilitative physicians. The Recovery Plus app has been approved for marketing by the National Medical Products Administration. Its user interfaces are shown in Figures 2 to 4, which display the personalized exercise prescription (including target heart rate, exercise action, and exercise duration), monitoring information (including exercise recording and physiological indicators during exercise), and exercise action guidance video for CR, respectively.

Building upon the RCT, we measured outcomes of physical health (quality-adjusted life years (QALYs) and maximal oxygen uptake (VO_2max)), mental health (anxiety and depression status, health beliefs related to cardiovascular disease, and exercise self-efficacy), and real-world data on medical costs to analyze the cost-effectiveness of the DTx-based HBCR for AF patients after catheter ablation using the evaluation methods and models of health economics. In this way, the economic and social benefits of DTx for CR were comprehensively assessed from the perspective of healthcare decision-makers (HCDMs), thereby providing decision support and reference information for the application and popularization of DTx.

Methods

Design

A single-center, prospective, blinded, randomized, parallel controlled trial of DTx-based HBCR for AF patients after catheter ablation was conducted from February 2019 to July 2019 in the First Affiliated Hospital of Nanjing Medical University, Jiangsu Province, China. The AF patients undergoing catheter ablation in the Cardiovascular Medicine Department of the First Affiliated Hospital of Nanjing Medical University were enrolled as subjects. The study protocol was approved by the Human Research Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (approval No.: 2020-SR-38) and registered in the US Clinical Trials Registry (Registration No.: NCT 04414007).

The inclusion criteria included (a) patients diagnosed with AF and scheduled to undergo catheter ablation, (b) those aged 18–75 years, (c) those who, or whose primary caregivers, could use smart phones, and (d) those who gave their informed consent and voluntarily participated in the study. The exclusion criteria included (a) history of

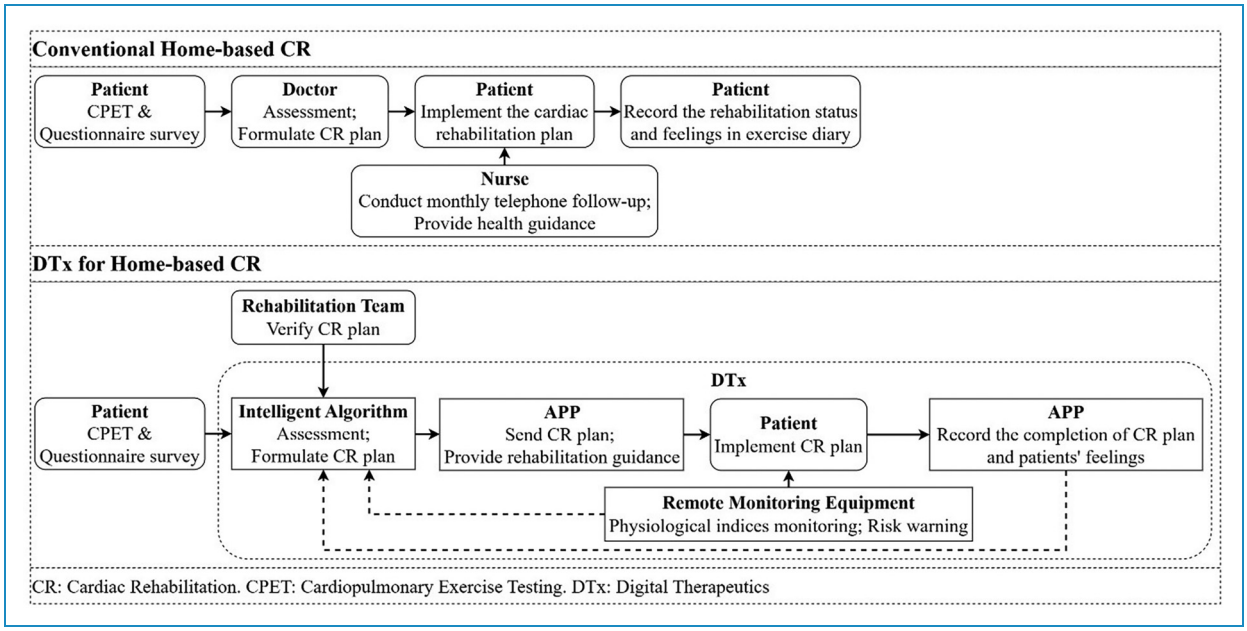

Figure 1. Procedure of DTx-based HBCR.

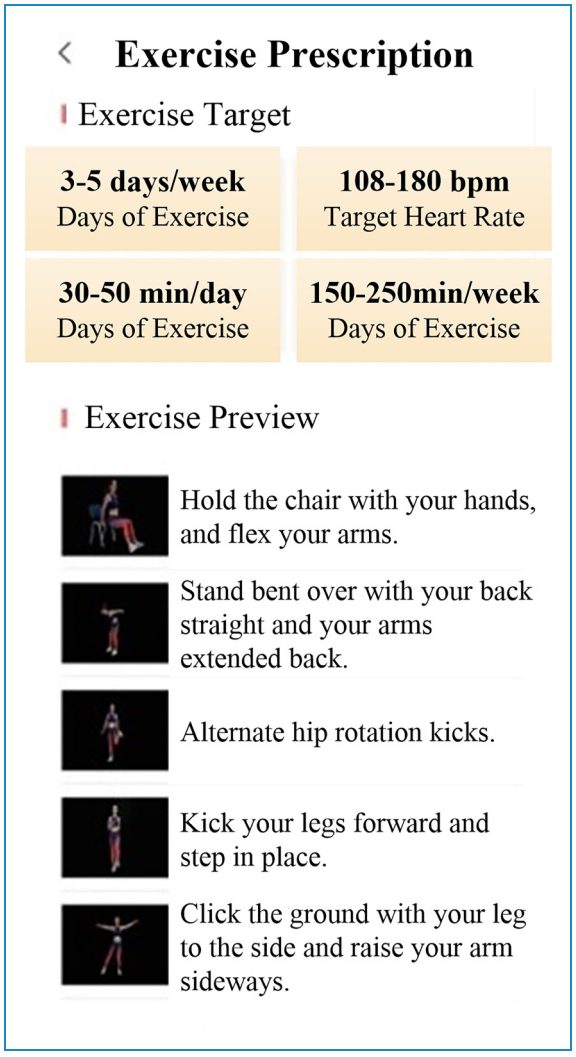

Figure 2. Exercise prescription.

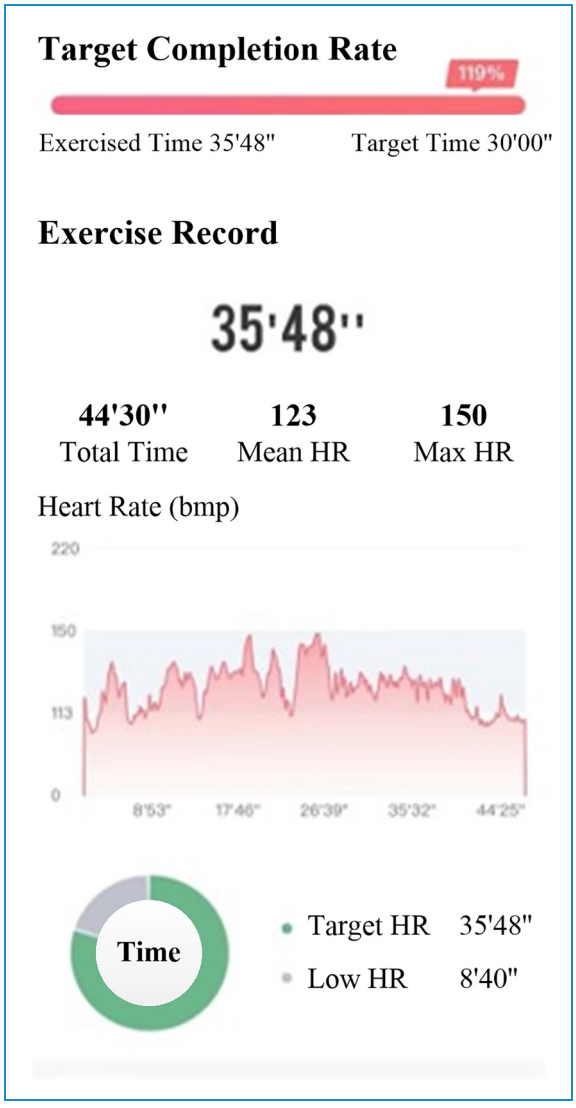

Figure 3. Exercise recording.

catheter ablation, (b) inability to complete the questionnaire due to expression and understanding problems, (c) history of mental illness, (d) severe physical disease or severe postoperative complications, and (e) acute heart failure or other contraindications to exercise. Patients who had to stop exercising due to receiving other treatments or being troubled by other diseases were eliminated from the study. All patients enrolled signed the informed consent form. They were randomized at a 1:1 ratio using a computer random number table into a UC group (n = 50) and a DT group (n = 50).

Interventions

In the UC group, routine postoperative nursing care was given, including in-hospital assessment and education and out-of-hospital exercise for 12 weeks. During hospitalization, routine health guidance, including postoperative drugs, diet, activities, and rest, as well as disease-related precautions, was provided by the nurses, and postoperative rehabilitation manuals were distributed. The patients were followed up by telephone weekly after surgery to find out their rehabilitation status. Moreover, re-examination was performed monthly after surgery, and exercise prescriptions were formulated according to the results of cardiopulmonary exercise testing (CPET) following the FITTVP principle (F: exercise frequency; I: exercise intensity; T: exercise time; T: exercise type; V: exercise volume; and P: exercise progression).[67] The specifics were as follows: (a) Aerobic exercise predominated. (b) Exercise of low to moderate intensity, reflected by the patient's heart rate during exercise, was prescribed. (c) Exercise was prescribed 3–5 times per week. (d) The cumulative time to reach the target heart rate in each exercise was ≥30 min, and the time of exercising was ≥150 min weekly. The target heart rate (heart $rate_{target}$) was defined as (heart $rate_{max}$–heart $rate_{rest}$)–(40–60)% + heart $rate_{rest}$, and the

alarm heart rate (heart $rate_{alarm}$) was heart $rate_{target}$ + 20 bpm.[68] The exercise rehabilitation status of patients in the UC group was recorded in their exercise diary. In addition, relevant supervision, including medication reminders and diet and lifestyle guidelines, was undertaken.

In the DT group, DTx-based HBCR management was offered for 12 weeks based on standard rehabilitation nursing care. The specifics were as follows: (a) In the outpatient re-examination 1 month after surgery, CPET was conducted and an exercise prescription was formulated, with the same content as that in the UC group. The exercise prescription was sent to the patient's mobile phone through the Shukang (Recovery Plus Inc., China) app, and both heart $rate_{target}$ and heart $rate_{alarm}$ were set. The heart rate of the patient during exercise was monitored in real time through the portable and wearable smart heart rate belt, and an alarm was raised in case of abnormality. (b) Through the portable and wearable smart heart rate belt, the heart rhythm and heart rate during daily life activities and during exercise were monitored, and abnormal electrocardiogram signals were captured in real time and transmitted to the monitoring center through the patient's mobile phone so that the rehabilitation team could make a judgment and promptly give its opinions on diagnosis and treatment. (c) The patient's total time of exercise, effective time (heart $rate_{target}$ maintained) of exercise, time to recover to resting heart rate, and subjective feeling about the exercise were recorded by the Recovery Plus app, based on which the professional rehabilitation team adjusted the exercise prescription and answered questions one to one online.

Outcome measurement

Primary outcomes were QALYs and VO_2max. Secondary outcomes were exercise self-efficacy, health beliefs related to cardiovascular disease, and anxiety and depression status. These outcomes reflected the patient's physical and psychological health status and QoL.

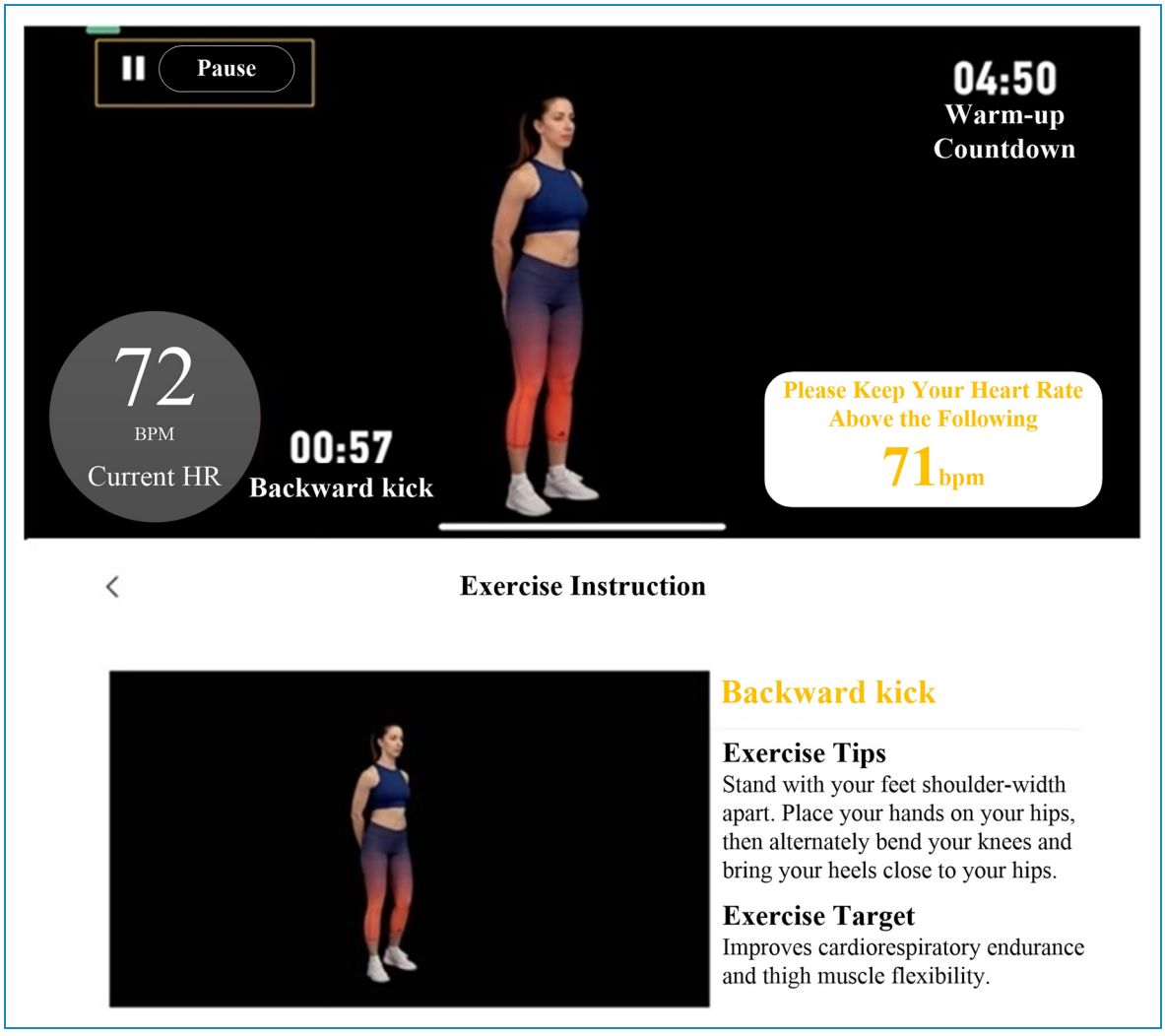

Figure 4. Guidance video for rehabilitation.

QALYs are a standardized universal indicator of health outcomes. This measure has been widely used in clinical trials and population studies, and its good reliability, validity, and sensitivity have been verified in many disease fields and populations. After a 12-week trial, the patient completed the Chinese version of EQ-5D-5L (developed by the EuroQol Group). Following the literature,[69] QALYs were calculated using the health utility value in line with China's real-world situation. Higher QALY values indicate better health status.

VO_2max refers to the maximum oxygen content taken in by the body during exercise with a respiratory exchange rate ≥1.10. Measured by CPET (Jaeger MS-CPX) and breath-by-breath analysis,[21] VO_2max is the gold standard for assessing cardiopulmonary function and exercise tolerance.[70] In this study, VO_2max was measured at baseline and 12 weeks later by the Bruce method using the professional exercise treadmill (h/p/cosmos, Germany) and MasterScreen CPX system (Jaeger, Germany).

The psychological condition of the patients was detected through their anxiety and depression statuses. Anxiety and depression statuses were assessed using the seven-item Generalized Anxiety Disorder Scale (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9), respectively, after 12 weeks. The lower the GAD-7 and PHQ-9 scores, the milder the anxiety and depression.[71,72]

Health beliefs were assessed using the Health Beliefs Related to Cardiovascular Disease Scale after 12 weeks. The scale consists of 25 items in such dimensions as cognitive sensitivity and severity of cardiovascular disease and the benefits and barriers of diet and exercise.[73] In this study, the Chinese version of the scale and the 4-point Likert scale (Cronbach's α: 0.932) were used.

Exercise self-efficacy was assessed at baseline and after 12 weeks through the International Physical Activity Questionnaire. The questionnaire consists of 10 items and reflects the confidence of the subject in undertaking regular physical activity and exercise.[74,75] In this study, the differences in exercise performance were compared by measuring the percentage of patients with moderate and high levels of activity. The International Physical Activity Questionnaire was translated into Chinese by the two-step method (bilingual translation and reverse translation), and it was then compared and validated by bilingual experts specialized in questionnaire design and cross-cultural validation (Cronbach's α: 0.84).

Cost-effectiveness analysis

The difference in cost-effectiveness was compared by the incremental cost-effectiveness ratio (ICER) between the DT group and UC group. ICER was calculated by the formula below:

$$\mathrm{ICER} = \frac{\mathrm{COST}_{\mathrm{DT\ Group}} - \mathrm{COST}_{\mathrm{UC\ Group}}}{\mathrm{EFFECT}_{\mathrm{DT\ Group}} - \mathrm{EFFECT}_{\mathrm{UC\ Group}}}$$

where EFFECT involved QALYs, VO_2max, exercise self-efficacy, health beliefs related to cardiovascular disease, and anxiety and depression status and COST represented medical costs during the trial, including examination fees, treatment fees, medicine fees, hospitalization fees, nursing care fees, and DTx fees. Cost data were acquired from the patient's electronic medical record. According to the recommendations of the World Health Organization and *China Guidelines for Pharmacoeconomic Evaluations*, the willingness-to-pay (WTP) threshold was set as 85,698 CNY/QALY (China's per capita GDP in 2022).[76,77]

The robustness of the model was tested by sensitivity analysis. In the one-way sensitivity analysis, two-way sensitivity analysis was performed on the input cost data to test the degree of influence of each parameter on the results, with the parameter change range of 80–120% of the baseline. In the probabilistic sensitivity analysis, assuming that the medical cost data were gamma-distributed, the QALY data were beta-distributed, and the state transition probability was lognormal-distributed. Simulations were performed 10,000 times using the Monte Carlo method to test the probability of cost-effectiveness in the DT group and UC group under different WTP thresholds.

Data collection and analysis

The general demographic data and medical data were collected from all enrolled patients during hospitalization. CPET was performed in the outpatient re-examination 1 month after surgery and after the 12-week intervention. After the 12-week intervention, the exercise diary of patients in the UC group was recycled, and the implementation situation of exercise prescription in the DT group was directly found through the background of Recovery Plus app. The data were statistically analyzed by SPSS 22.0 and compared by the two-independent-samples-*t*-test between two groups and by paired *t*-test within each group before vs. after intervention. The rank sum test and the χ^2 test were used for ordered categorical variables. The test level was $\alpha = 0.05$ (two-sided), and $P < 0.05$ was considered statistically significant.

Results

In total, 138 AF patients undergoing catheter ablation were preliminarily screened, and a total of 100 patients were enrolled. The test procedure is shown in Figure 5. During the 12-week intervention period, three patients withdrew from the study (one in the DT group and two in the UC group), so 49 patients in the DT group and 48 patients in

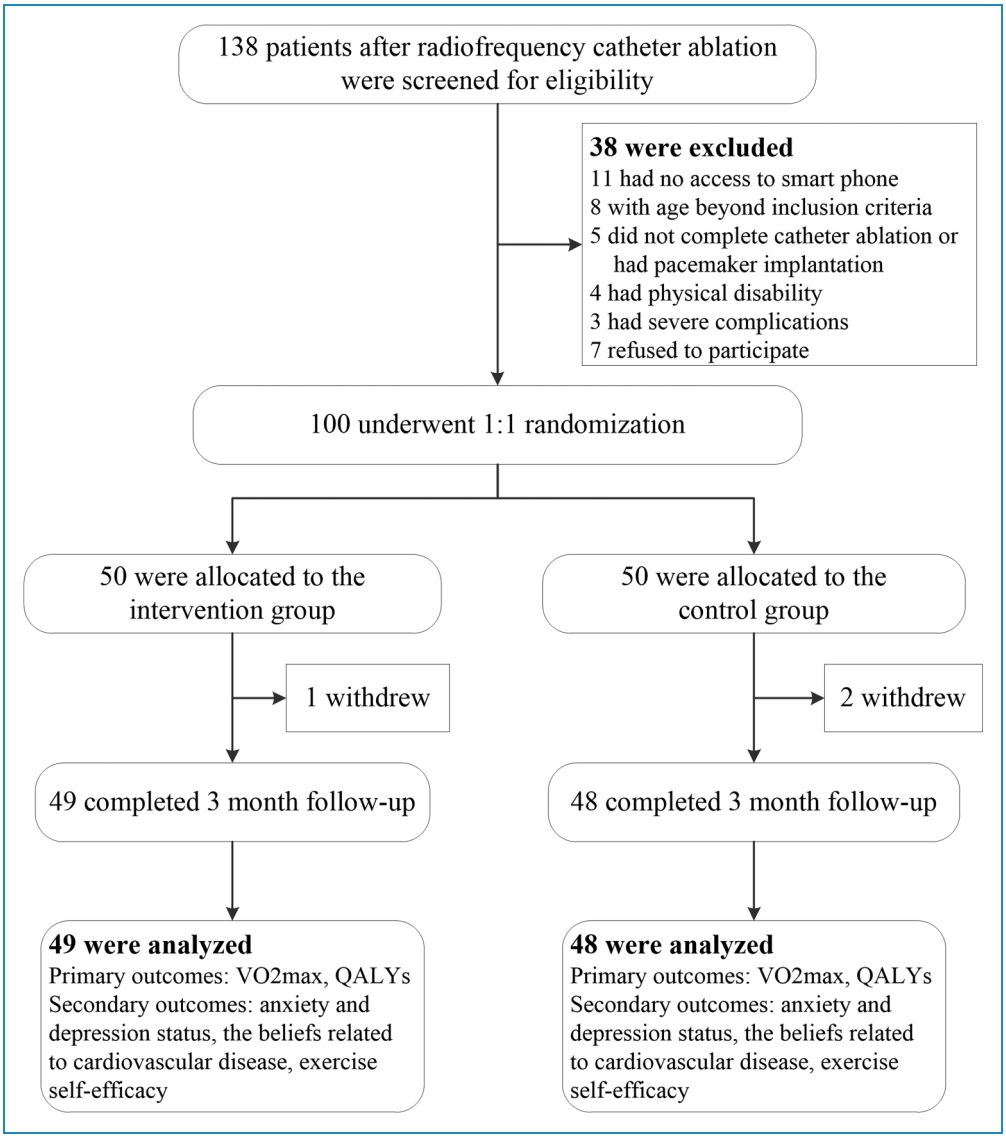

Figure 5. Study procedure.

the UC group were finally included in the analysis.[64] There were no cardiovascular-related adverse events caused by exercise. The demographic data of patients and trial-related clinical indicators were investigated at baseline. The data were acquired from the electronic medical record database of the First Affiliated Hospital of Nanjing Medical University (Table 1).

Table 2 shows the outcome measures of patients in the DT group and UC group pre- and postintervention. At baseline, there were no significant differences between the two groups in QALYs ($P=0.538$), VO_2max ($P=0.462$), anxiety status ($P=0.752$), depression status ($P=0.957$), health beliefs ($P=0.047$), and exercise self-efficacy ($P=0.646$).

Table 3 presents the changes in outcome measures after the intervention. After 12 weeks of interventions, both groups had significant improvements in primary and secondary outcomes compared to baseline. In the DT group, the mean QALYs were 0.909 ± 0.073, which increased by 0.119 ± 0.09; VO_2max was 27.3 ± 5.6 mL/(min*kg), which increased by 9.3 ± 8.0 mL/(min*kg); the GAD-7 score was 3.8 ± 2.8 points, which decreased by 3.3 ± 3.1 points; the PHQ-9 score was 5.1 ± 3.5 points, which decreased by 5.1 ± 3.6 points; the health belief score was 79.7 ± 8.4 points, which increased by 11.1 ± 10.5 points; and the exercise self-efficacy score was 61.7 ± 15.6 points, which increased by 8.3 ± 4.8 points. In the UC group, the mean QALYs were 0.876 ± 0.092, which increased by 0.077 ± 0.058; VO_2max was 22.9 ± 6.3 mL/(min*kg), which increased by 4.9 ± 6.6 mL/(min*kg); the GAD-7 score was 5.1 ± 2.4 points, which decreased by 2.7 ± 3.2 points; the PHQ-9 score was 7.0 ± 3.5 points, which decreased by 3.1 ± 2.9 points; the health belief score was

Table 1. Baseline data of patients.

	DT group (n = 49)	UC group (n = 48)	P value
Sex			0.726
Male	31 (63.3%)	32 (66.7%)	
Female	18 (36.7%)	16 (33.3%)	
Age	57 ± 9	57 ± 11	0.744
Educational level			0.953
Primary school or below	7 (14.3%)	7 (14.5%)	
Junior high school	11 (22.3%)	9 (18.8%)	
Senior high school	22 (44.9%)	24 (50.0%)	
Bachelor degree or above	9 (18.4%)	8 (16.7%)	
Preoperative New York Heart Association (NYHA) grade			0.964
I	17 (34.7%)	17 (35.4%)	
II	23 (46.9%)	21 (43.8%)	
III	7 (14.3%)	7 (14.6%)	
IV	2 (4.1%)	3 (6.2%)	
Type of AF			0.181
Paroxysmal	34 (69.4%)	22 (56.3%)	
Persistent	15 (30.6%)	26 (43.7%)	
Course of AF			0.708
≤1 year	15 (30.6%)	11 (22.9%)	
1–5 years	18 (36.7%)	22 (45.8%)	
5–10 years	7 (14.3%)	5 (10.4%)	
≥10 years	9 (18.4%)	10 (20.9%)	
Times of ablation			0.509
First	36 (73.5%)	38 (79.2%)	
Repeated	13 (26.5%)	10 (20.8%)	
Complications			
Hypertension	22 (44.9%)	26 (54.2%)	0.361

(continued)

Table 1. Continued.

	DT group (n = 49)	UC group (n = 48)	P value
Diabetes mellitus	5 (10.2%)	3 (6.2%)	0.497
Coronary heart disease	7 (14.3%)	7 (8.3%)	0.355
Health status within 1 year of the end of the intervention			
Stable	44 (89.80%)	41 (85.42%)	0.453
Recrudesce	5 (10.20%)	7 (14.58%)	0.513
Death	0 (0%)	0 (0%)	0.621

Table 2. Outcome measures pre- and postintervention (Data are shown as mean ± SD).

	DT group (n = 49)			UC group (n = 48)		
Outcome	Pre	Post	P value	Pre	Post	P value
Primary outcomes						
QALYs	0.789 ± 0.095	0.909 ± 0.073	0.007	0.799 ± 0.091	0.876 ± 0.092	0.03
VO_2max (mL/(min*kg))	19.1 ± 4.7	27.3 ± 5.6	<0.001	18.7 ± 4.9	22.9 ± 6.3	<0.001
Secondary outcomes						
Anxiety	7.2 ± 3.6	3.8 ± 2.8	0.037	7.1 ± 3.5	5.1 ± 2.4	0.018
Depression	10.2 ± 3.1	5.1 ± 3.5	0.192	10.1 ± 3.3	7.0 ± 3.5	0.549
Health belief	70.4 ± 2.5	79.7 ± 8.4	<0.001	69.9 ± 2.1	74.7 ± 6.6	<0.001
Exercise self-efficacy	50.6 ± 15.2	61.7 ± 15.6	<0.001	50.3 ± 14.5	52.8 ± 17.4	0.417

74.7 ± 6.6 points, which increased by 2.5 ± 15.2 points; and the exercise self-efficacy score was 52.8 ± 17.4 points, which increased by 4.2 ± 5.3 points. This indicates that HBCR can improve patients' cardiopulmonary function, while the effectiveness of DTx-based HBCR was also verified. This is consistent with the findings of previous studies.[21,22,26,27] In addition, patients in the DT group had a lower GAD-7 score and PHQ-9 score than the UC group indicating lower levels of anxiety and depression in the DT group, which provides the evidence that the patients in the DT group had better psychological health than the UC group.

The medical cost data in the two groups were acquired from the electronic medical record database of the First Affiliated Hospital of Nanjing Medical University, as shown in Table 4. The total medical cost was 75,080.55 ± 19746.62 CNY in the DT group and 73,972.66 ± 16582.04 CNY in the UC group, a difference of 1107.89 CNY.

Cost-effectiveness analysis

Table 5 shows the cost-effectiveness ratio in the DT group and UC group. Compared with those in the UC group, the mean annual QALYs increased by 0.0324, VO_2max increased by 4.5 mL/(min*kg), the GAD-7 score decreased by 0.6 points, the PHQ-9 score decreased by 1.9 points, the health belief score increased by 5.0 points, and the exercise self-efficacy score increased by 8.8 points in the DT group. The results showed that patients in the DT group had significantly higher VO_2max improvement than the UC group, indicating that patients had improved cardiopulmonary capacity.

The ICERs were 33,572.42 CNY/QALY, 246.20 CNY/(mL/(min*kg)) of VO_2max, 852.22 CNY/GAD-7 score, 583.10 CNY/PHQ-9 score, 221.58 CNY/health belief score, and 125.90 CNY/exercise self-efficacy score. The

Table 3. Changes in outcome measures. (Data are shown as mean ± SD).

Outcome	DT group (n = 49)	UC group (n = 48)	P value
Primary outcomes			
QALYs	0.119 ± 0.09	0.077 ± 0.058	<0.001
VO_2max (mL/(min*kg))	9.3 ± 8.0	4.9 ± 6.6	0.003
Secondary outcomes			
Anxiety	−3.3 ± 3.1	−2.7 ± 3.2	0.762
Depression	−5.1 ± 3.6	−3.1 ± 2.9	0.207
Health belief	11.1 ± 10.5	2.5 ± 15.2	0.002
Exercise self-efficacy	8.3 ± 4.8	4.2 ± 5.3	<0.001

Table 4. Medical costs in the DT group and UC group (data are shown as mean ± SD).

Medical costs (CNY)	DT group (n = 49)	UC group (n = 48)	P value
Examination	4944.06 ± 2879.13	4649.13 ± 1090.36	0.133
Treatment	65,424.39 ± 17014.3	67,153.91 ± 16244.74	0.447
Medicine	3000.89 ± 6193.89	1365.17 ± 485.36	0.001
Hospitalization	557.29 ± 336.66	480.41 ± 161.13	0.002
Nursing care	354.92 ± 259.61	324.04 ± 293.86	0.251
DTx	799	0	-
Total	75,080.55 ± 19,746.62	73,972.66 ± 16,582.04	0.343

ICER of 33,572.42 CNY/QALY was lower than the WTP threshold of 85,698 CNY (China's per capita GDP in 2022). The above results demonstrate that DTx-based HBCR is highly cost-effective for AF patients after catheter ablation.

Sensitivity analysis

The tornado diagram of the one-way sensitivity analysis is shown in Figure 6. The results showed that the treatment fees had the greatest impact on ICER, followed by examination fees, medicine fees, DTx fees, hospitalization fees, and nursing care fees. Regardless of the changes in parameters within their ranges, ICER remained below the WTP threshold (China's per capita GDP in 2022).

Probabilistic sensitivity analysis was performed through Monte Carlo simulation according to the parameter distribution of relevant items input into the model. The ICER scatter plot and cost-effectiveness acceptability curve are shown in Figures 7 and 8, respectively. In the DT group, 63.7% of the scatter points fell below the WTP threshold of 85,698 CNY (China's per capita GDP in 2022), while 92.4% of the scatter points fell below the WTP threshold of 257,094 CNY (three times China's per capita GDP in 2022). Therefore, the probability of cost-effectiveness in the DT group was higher than that in the UC group. In the DT group, the probability of cost-effectiveness was 85.2% under the WTP threshold of 85,698 CNY (China's per capita GDP in 2022), and it was 98.7% under the WTP threshold of 257,094 CNY (three times China's per capita GDP in 2022). Moreover, the probability of cost-

effectiveness increased with the increase in the WTP threshold in the DT group.

Discussion

This study is the first randomized controlled trial of DTx-based HBCR for AF patients after catheter ablation in China. The results showed that DT was superior to UC in physical outcomes (cardiopulmonary endurance and health status) and psychological outcomes (anxiety and depression status, health beliefs related to cardiovascular disease, and exercise self-efficacy), suggesting that AF patients receiving DTx-based HBCR after catheter ablation would have better rehabilitation outcomes than those receiving conventional HBCR. Multiple randomized controlled trials have shown that DTx-based HBCR achieves better health improvement and symptom relief, and the patients' psychological status and QoL are significantly better than those of controls.[53–62] The above findings are similar to the conclusion in this study, further demonstrating the safety and effectiveness of DTx in CR.

Furthermore, cost-effectiveness analysis on DTx-based HBCR for AF patients after catheter ablation was conducted with real-world data using the evaluation methods of health economics. The results showed that the ICER was 33,572.42 CNY/QALY between the DT group and the UC group, far below the WTP threshold of 85,698 CNY (China's per capita GDP in 2022), suggesting that DTx-based HBCR is highly cost-effective. When we tested the robustness of the model by sensitivity analysis, the model passed both one-way sensitivity analysis and probabilistic sensitivity analysis, and the results were valid and reliable. The cost of DTx refers to the management fees of DTx, which had a small impact on the

Table 5. ICER in the DT group and UC group.

Outcome	Difference	ICER
Primary indicators		
QALYs	0.033	33,572.42
VO_2max (mL/(min*kg))	4.5	246.20
Secondary indicators		
Anxiety	−1.3	852.22
Depression	−1.9	583.10
Health belief	5.0	221.58
Exercise self-efficacy	8.8	125.90

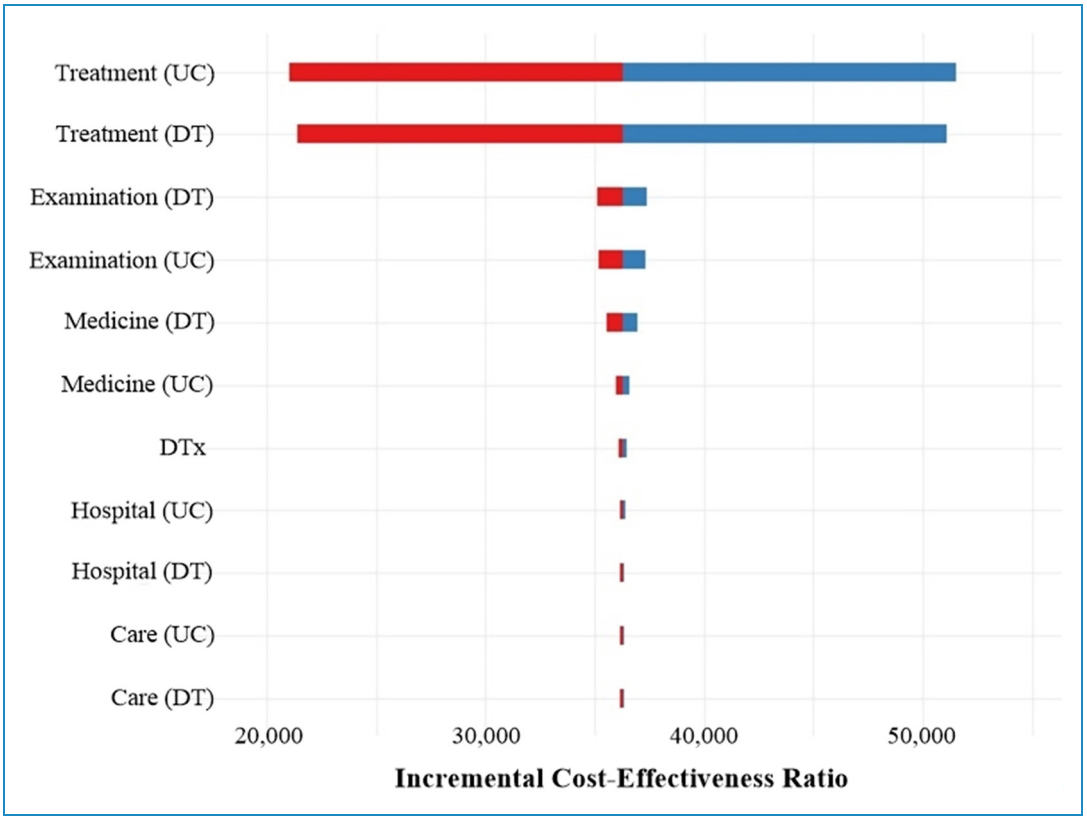

Figure 6. Results of one-way sensitivity analysis.

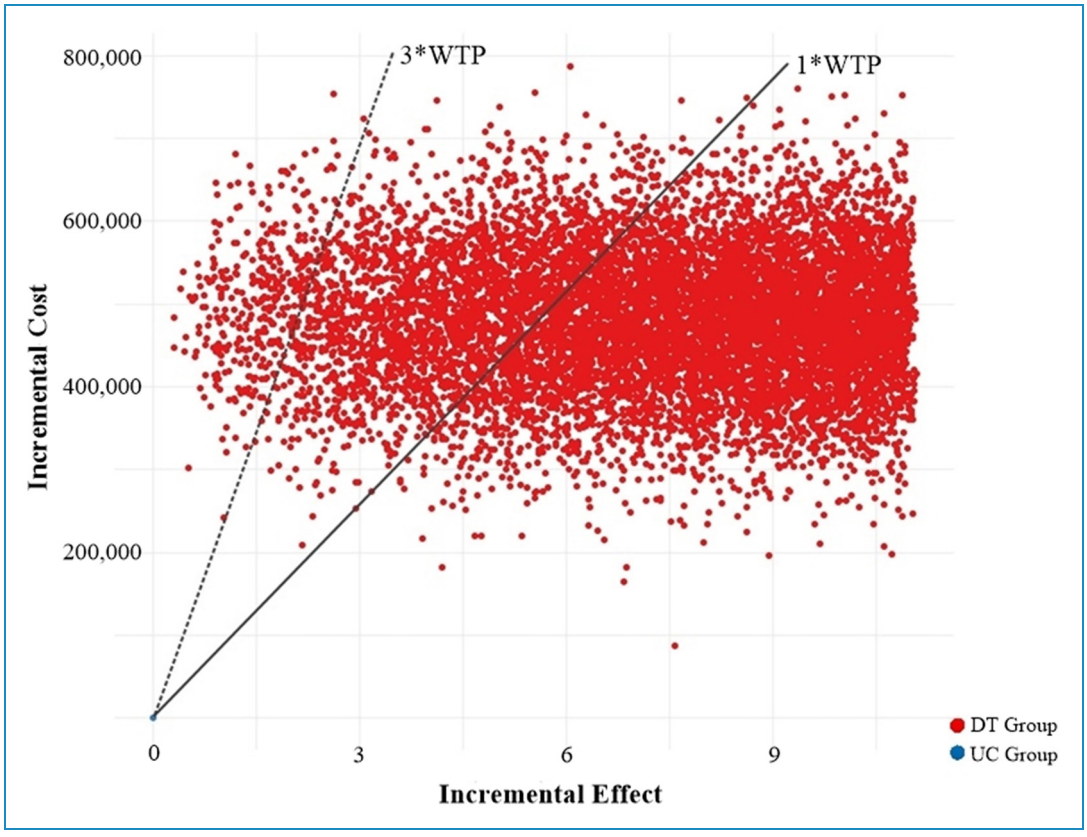

Figure 7. Scatter plot of ICER for the DT group versus the UC group.

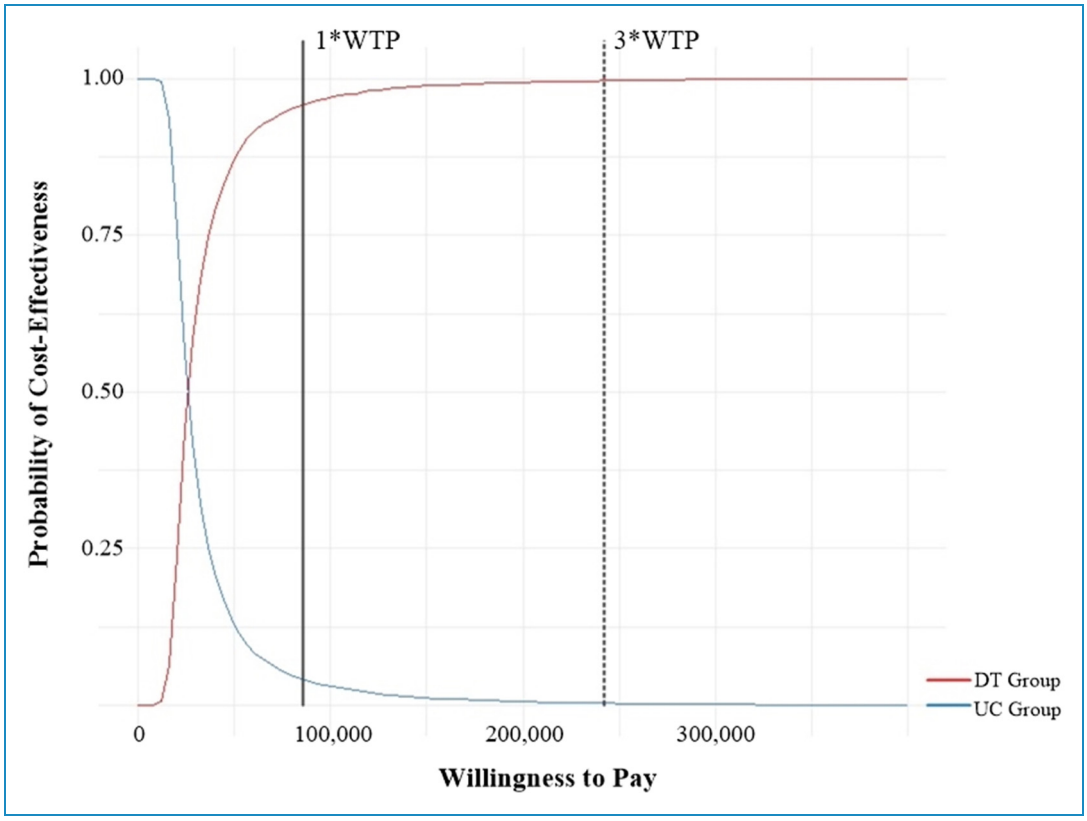

Figure 8. Cost-effectiveness acceptability curve.

results, indicating that most patients will accept the cost of DTx within a reasonable range. The ICER of DTx-based HBCR is lower than the WTP threshold, and DTx-based HBCR can reduce the fatigue of patients from visiting the hospital and traveling due to their difficulty moving, so DTx-based HBCR is more cost-effective.[78–80] Telehealth CR is cost-effective, and third-party payer funding for telehealth CR promotes patient engagement, which will increase overall CR utilization.[81] The above findings are consistent with the conclusions of this study, strongly suggesting that DTx can not only provide more precise disease management but also help save on medical costs.

In addition to the improvement of physiological outcomes in AF patients, the outcomes of psychological health (anxiety and depression status, health beliefs related to cardiovascular disease, and exercise self-efficacy) were also measured in this study to perform cost-effectiveness analysis on DTx-based HBCR from multiple perspectives. The results showed that the DT group had better psychological health status than the UC group, both their anxiety and their depression were relieved, and the health beliefs related to cardiovascular disease and exercise self-efficacy were noticeably better. CR is the comprehensive management of patients with cardiovascular diseases that aims to reduce physiological and psychological risk factors for cardiovascular diseases, improve QoL, and help patients return to normal work and life as soon as possible. The results of this study and the conclusions of relevant guidelines, consensuses, and studies corroborate each other, further confirming the value of CR. As real-world evidence, the research data in this paper supplement the theoretical foundation of CR.

For HCDMs, DTx achieves the migration of treatment scenarios and the transformation of intervention subjects, expands the ability of patients to obtain active clinical nursing within and outside the traditional scenarios (e.g., home-based nursing, remote nursing, and digital healthcare), provides an optional innovative therapeutic regimen for special patient groups (e.g., low-income, rural, and urban groups), and effectively improves medical accessibility. DTx provides technical support services for patients, nursing staff, and other end-users, mitigating the differences in economic and social factors, such as regional and medical resource allocation.

Conclusion

In conclusion, DTx-based HBCR for AF patients after catheter ablation is more effective and achieves better health status than conventional HBCR. DTx-based HBCR has a lower ICER than the WTP threshold, so it is highly cost-effective.

Limitation

First, the sample was small in this single-center trial. Therefore, the findings may vary in other areas. Second, only patients who had smart phones and could operate relevant software were enrolled, but these are younger and more educated than the average population with AF, resulting in an analysis bias. Finally, the follow-up period was short, so a longer-term follow-up study is required to determine all the effects of DTx-based HBCR.

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References

1. Hindricks G, Potpara T, Dagres N, et al. ESC Scientific Document Group. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association For Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; 42: 373–498.
2. Chinese Society of Pacing and Electrophysiology, Committee of Heart Rhythm, China Medical Doctor Association & Expert Committee of Atrial Fibrillation Prevention and Treatment of Atrial Fibrillation Center Union of China.

Current knowledge and management of atrial fibrillation: consensus of Chinese experts 2021. *Chinese Journal of Cardiac Arrhythmias* 2022; 26: 74.
3. Roth GA, Mensah GA, Johnson CO, et al. GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol* 2020; 76: 2982–3021.
4. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* 2006; 27: 949–953.
5. Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham heart study. *Circulation* 2004; 110: 1042–1046.
6. Hu SS, Gao RL, Liu LS, et al. Summary of the 2018 report on cardiovascular diseases in China. *Chinese Circ J* 2019; 34: 209–220.
7. Wolowacz SE, Samuel M, Brennan VK, et al. The cost of illness of atrial fibrillation: a systematic review of the recent literature. *Europace : Eur Pacing, Arrhythmias, And Card Electrophysiol : J Working Groups on Card Pacing, Arrhythmias. And Cardiac Cellul Electrophysiology Eur Soc Cardiol* 2011; 13: 1375–1385.
8. Hu ZC, Jiang C, Zheng LH, et al. 2019 Clinical performance and quality measures for atrial fibrillation in China. *Chinese Circ J* 2020; 35: 427–437.
9. Professional Committee of Cardiovascular Disease Prevention and Rehabilitation, Chinese Association of Rehabilitation Medicine, Hu DY, Chen GY, Meng XP, et al. Chinese Expert consensus on cardiac rehabilitation in patients with atrial fibrillation. *Chinese J Intern Med* 2021; 60, 11.
10. Verma A, Macle L, Cox J, et al. & CCS Atrial Fibrillation Guidelines Committee. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: catheter ablation for atrial fibrillation/atrial flutter. *Can J Cardiol* 2011; 27, 60–66.
11. Society of Cardiac Pacing and Electrophysiology, Chinese Society of Biomedical Engineering & Chinese Society of Pacing and Electrophysiology. Radiofrequency catheter ablation for tachyarrhythmia: a revised guideline. *Chinese J Card Pacing Electrophysiol* 2002; 16: 15.
12. Latchamsetty R and Morady F. Catheter ablation of atrial fibrillation. *Heart Fail Clin* 2016; 12: 223–233.
13. Parameswaran R, Al-Kaisey AM and Kalman JM. Catheter ablation for atrial fibrillation: current indications and evolving technologies. *Nat Rev Cardiol* 2021; 18: 210–225.
14. Haegeli LM and Calkins H. Catheter ablation of atrial fibrillation: an update. *Eur Heart J* 2014; 35: 2454–2459.
15. Skelly A, Hashimoto R, Al-Khatib S, et al. *Catheter ablation for treatment of atrial fibrillation*. Technology assessment. (prepared by the pacific northwest evidence-based practice center under contract no. HHSA 290-2012-00014-I.) AHRQ Publication. Rockville, MD: Agency for Healthcare Research and Quality, 2015.
16. Ganesan AN, Shipp NJ, Brooks AG, et al. Long-term outcomes of catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *J Am Heart Assoc* 2013; 2: e004549.
17. Wazni O, Wilkoff B and Saliba W. Catheter ablation for atrial fibrillation. *N Engl J Med* 2011; 365: 2296–2304.
18. Yap YG and Camm AJ. *Essentials of atrial fibrillation*. London, Greater London: Springer healthcare limited, 2014.
19. Atrial Fibrillation Association. Catheter ablation for atrial fibrillation. 2013.
20. Shi S, Shi J, Jia Q, et al. Efficacy of physical exercise on the QoL, exercise ability, and cardiopulmonary fitness of patients with atrial fibrillation: a systematic review and meta-analysis. *Front Physiol* 2020; 11: 740.
21. Risom SS, Zwisler AD, Rasmussen TB, et al. Cardiac rehabilitation versus usual care for patients treated with catheter ablation for atrial fibrillation: results of the randomized CopenHeartRFA trial. *Am Heart J* 2016; 181: 120–129.
22. Suaya JA, Stason WB, Ades PA, et al. Cardiac rehabilitation and survival in older coronary patients. *J Am Coll Cardiol* 2009; 54: 25–33.
23. Takano N, Amiya E, Oguri G, et al. Influence of atrial fibrillation on oxygen uptake and exercise tolerance in cardiovascular patients; close association with heart rate response. *Int J Cardiol Heart & Vasculature* 2019; 22: 84–91.
24. Bao ZP, Sun GZ, Wang J, et al. Effects of multi-modality home care based on digital platform on sleep quality in patients with atrial fibrillation after radiofrequency ablation. *J Nurses Train* 2021; 36: 1468–1471.
25. AACVPR. *Guidelines for cardiac rehabilitation programs*. 6th Ed. Champaign: Human Kinetics, 2021.
26. Bjarnason-Wehrens B, McGee H, Zwisler AD, et al. & Cardiac Rehabilitation Section European Association of Cardiovascular Prevention and Rehabilitation. Cardiac rehabilitation in Europe: results from the European Cardiac Rehabilitation Inventory Survey. *Eur J Cardiovascular Prevention Rehabil: Off J Eur Soc Cardiol, Working Groups Epidemiol Prevention Card Rehabili Exercise Physiol* 2010; 17, 410–418.
27. Reed JL, Terada T, Chirico D, et al. The effects of cardiac rehabilitation in patients with atrial fibrillation: a systematic review. *Can J Cardiol* 2018; 34: S284–S295.
28. Hammill BG, Curtis LH, Schulman KA, et al. Relationship between cardiac rehabilitation and long-term risks of death and myocardial infarction among elderly Medicare beneficiaries. *Circulation* 2010; 121: 63–70.
29. Merghani A, Malhotra A and Sharma S. The U-shaped relationship between exercise and cardiac morbidity. *Trends Cardiovasc Med* 2016; 26: 232–240.
30. Ricci C, Gervasi F, Gaeta M, et al. Physical activity volume in relation to risk of atrial fibrillation. A non-linear meta-regression analysis. *Eur J Prev Cardiol* 2018; 25: 857–866.
31. Morseth B, Løchen ML, Ariansen I, et al. The ambiguity of physical activity, exercise and atrial fibrillation. *Eur J Prev Cardiol* 2018; 25: 624–636.
32. Liu CS, Qiu J and Liu QM. Research progress on the relationship between exercise and atrial fibrillation. *Chinese J Interv Cardiol* 2015; 23: 409–411.
33. Myrstad M, Aarønæs M, Graff-Iversen S, et al. Physical activity, symptoms, medication and subjective health among veteran endurance athletes with atrial fibrillation. *Clin Res Cardiol : Off J German Card Soc* 2016; 105: 154–161.
34. Sanchis-Gomar F, Perez-Quilis C, Lippi G, et al. Atrial fibrillation in highly trained endurance athletes - description of a syndrome. *Int J Cardiol* 2017; 226: 11–20.

35. Professional Committee of Cardiovascular Disease, Chinese Association of Rehabilitation Medicine. Guidelines for cardiovascular rehabilitation and secondary prevention in China 2018 simplified edition. *Chinese J Intern Med* 2018; 57: 9.
36. Reed JL, Mark AE, Reid RD, et al. The effects of chronic exercise training in individuals with permanent atrial fibrillation: a systematic review. *Can J Cardiol* 2013; 29: 1721–1728.
37. Smart NA, King N, Lambert JD, et al. Exercise-based cardiac rehabilitation improves exercise capacity and health-related QoL in people with atrial fibrillation: a systematic review and meta-analysis of randomised and non-randomised trials. *Open Heart* 2018; 5: e000880.
38. Myrstad M, Malmo V, Ulimoen SR, et al. Exercise in individuals with atrial fibrillation. *Clin Res Cardiol : Off J German Card Soc* 2019; 108: 347–354.
39. Malmo V, Nes BM, Amundsen BH, et al. Aerobic interval training reduces the burden of atrial fibrillation in the short term: a randomized trial. *Circulation* 2016; 133: 466–473.
40. Thomas RJ, Beatty AL, Beckie TM, et al. Home-based cardiac rehabilitation: a scientific statement from the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology. *Circulation* 2019; 140: e69–e89.
41. Beatty AL, Truong M, Schopfer DW, et al. Geographic variation in cardiac rehabilitation participation in Medicare and Veterans Affairs populations: opportunity for improvement. *Circulation* 2018; 137: 1899–1908.
42. Arena R, Williams M, Forman DE, et al. & American Heart Association Exercise, Cardiac Rehabilitation and Prevention Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity and Metabolism. Increasing referral and participation rates to outpatient cardiac rehabilitation: the valuable role of healthcare professionals in the inpatient and home health settings: a science advisory from the American Heart Association. *Circulation* 2012; 125, 1321–1329.
43. Balady GJ, Ades PA, Bittner VA, et al. American Heart Association Science Advisory and Coordinating Committee. Referral, enrollment, and delivery of cardiac rehabilitation/secondary prevention programs at clinical centers and beyond: a presidential advisory from the American Heart Association. *Circulation* 2011; 124, 2951–2960.
44. Scalvini S, Zanelli E, Comini L, et al. Home-based exercise rehabilitation with telemedicine following cardiac surgery. *J Telemed Telecare* 2009; 15: 297–301.
45. Piotrowicz E, Korzeniowska-Kubacka I, Chrapowicka A, et al. Feasibility of home-based cardiac telerehabilitation: results of TeleInterMed study. *Cardiol J* 2014; 21: 539–546.
46. Stefanakis M, Batalik L, Antoniou V, et al. Safety of home-based cardiac rehabilitation: a systematic review. *Heart & Lung : The J Crit Care* 2022; 55: 117–126.
47. Anderson L, Sharp GA, Norton RJ, et al. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2017; 6: CD007130.
48. Antoniou V, Davos CH, Kapreli E, et al. Effectiveness of home-based cardiac rehabilitation, using wearable sensors, as a multicomponent, cutting-edge intervention: a systematic review and meta-analysis. *J Clin Med* 2022; 11: 3772.
49. Dalal HM, Zawada A, Jolly K, et al. Home based versus centre based cardiac rehabilitation: Cochrane systematic review and meta-analysis. *BMJ (Clin Res ed.)* 2010; 340: b5631.
50. Higgins RO, Rogerson M, Murphy BM, et al. Cardiac rehabilitation online pilot: extending reach of cardiac rehabilitation. *J Cardiovasc Nurs* 2017; 32: 7–13.
51. Lee AJ, Strickler GK and Shepard DS. The economics of cardiac rehabilitation and lifestyle modification: a review of literature. *J Cardiopulm Rehabil Prev* 2007; 27: 135–142.
52. Digital Therapeutics Alliance. DTx Value Assessment & Integration Guide (Version 2022; 2.0).
53. Moravcová K, Karbanová M, Bretschneider MP, et al. Comparing digital therapeutic intervention with an intensive obesity management program: randomized controlled trial. *Nutrients* 2022; 14: 2005.
54. Kim M and Choi HJ. Digital therapeutics for obesity and eating-related problems. *Endocrinol Metabolism (Seoul, Korea)* 2021; 36: 220–228.
55. Ritterband LM, Thorndike FP, Morin CM, et al. Real-world evidence from users of a behavioral digital therapeutic for chronic insomnia. *Behav Res Ther* 2022; 153: 104084.
56. Lewkowicz D, Wohlbrandt AM and Bottinger E. Digital therapeutic care apps with decision-support interventions for people with low back pain in Germany: cost-effectiveness analysis. *JMIR Mhealth Uhealth* 2022; 10: e35042.
57. Xiao S, Angjeli E, Wu HC, et al. Luminopia Pivotal Trial Group. Randomized controlled trial of a dichoptic digital therapeutic for amblyopia. *Ophthalmology* 2022; 129, 77–85.
58. Gilson A, Gassman M, Dodds D, et al. Refining a digital therapeutic platform for home care agencies in dementia care to elicit stakeholder feedback: focus group study with stakeholders. *JMIR Aging* 2022; 5: e32516.
59. Fortune DG, Ravnkilde V, Ryan S, et al. A digital therapeutic for management of psychosocial aspects of psoriasis: a pre–post proof of concept study. *Skin Health and Disease* 2022; 2: e103.
60. Kario K, Harada N and Okura A. Digital therapeutics in hypertension: evidence and perspectives. *Hypertension (Dallas, Tex 1979)* 2022; 79: 2148–2158.
61. Li Y, Gong Y, Zheng B, et al. Effects on adherence to a mobile app-based self-management digital therapeutics among patients with coronary heart disease: pilot randomized controlled trial. *JMIR Mhealth Uhealth* 2022; 10: e32251.
62. Kawasaki S, Mills-Huffnagle S, Aydinoglo N, et al. Patient- and provider-reported experiences of a mobile novel digital therapeutic in people with opioid use disorder (reSET-O): feasibility and acceptability study. *JMIR Formative Res* 2022; 6: e33073.
63. Lear SA. The delivery of cardiac rehabilitation using communications technologies: the "virtual" cardiac rehabilitation program. *Can J Cardiol* 2018; 34: S278–S283.
64. Cai C, Bao Z, Wu N, et al. A novel model of home-based, patient-tailored and mobile application-guided cardiac telerehabilitation in patients with atrial fibrillation: a randomised controlled trial. *Clin Rehabil* 2022; 36: 40–50.
65. Wang J, Sun GZ, Bao YG, et al. Dynamic trajectory of exercise rehabilitation adherence of patients with atrial fibrillation after radiofrequency ablation in the internet+ home cardiac rehabilitation mode. *Chinese Gen Pract* 2021; 24: 4074.

66. Bao ZP, Sun GZ, Yang G, et al. Effects of Internet+ home exercise rehabilitation on exercise tolerance and exercise compliance in patients with atrial fibrillation after radiofrequency ablation. *Chinese J Rehabil Med* 2021; 36: 4.
67. Ehrman RD, Liguori JK and Magal M. *ACSM's guidelines for exercise testing and pre-scription*. 10th ed. Alphen aan den Rijn: Wolters Kluwer, 2018.
68. Thompson PD, Arena R, Riebe D, et al. American College of Sports Medicine. ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition. *Curr Sports Med Rep* 2013; 12, 215–217.
69. Luo N, Liu G, Li M, et al. Estimating an EQ-5D-5L value set for China. *Value in Health : The J Int Soc Pharmacoeconomics Outcomes Res* 2017; 20: 662–669.
70. Herdy AH, Ritt LE, Stein R, et al. Cardiopulmonary exercise test: background. Applicability and interpretation. *Arq Bras Cardiol* 2016; 107: 467–481.
71. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; 166: 1092–1097.
72. Spitzer RL, Kroenke K and Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient health questionnaire. *JAMA* 1999; 282: 1737–1744.
73. Tovar EG, Rayens MK, Clark M, et al. Development and psychometric testing of the health beliefs related to cardiovascular disease scale: preliminary findings. *J Adv Nurs* 2010; 66: 2772–2784.
74. Bandura A. Guide for constructing self-efficacy scales. *Self-Efficacy Beliefs Adolescents* 2006; 5: 307–337.
75. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exercise* 2003; 35: 1381–1395.
76. Edejer TTT, Baltussen R and Tan-Torres Tetal (eds) *Making choices in health: WHO guide to cost-effectiveness analysis*. Vol. 1. Geneva: World Health Organization, 2003.
77. Liu GE, Hu SL and Wu JH. China guidelines for pharmacoeconomic evaluations. *China J Pharm Econ* 2011; 3: 6–9.
78. Jiang X, Yao J and You JH. Cost-effectiveness of a telemonitoring program for patients with heart failure during the COVID-19 pandemic in Hong Kong: model development and data analysis. *J Med Internet Res* 2021; 23: e26516.
79. Grustam AS, Severens JL, De Massari D, et al. Cost-effectiveness analysis in telehealth: a comparison between home telemonitoring, nurse telephone support, and usual care in chronic heart failure management. *Value in Health : The J Int Soc Pharm Outcomes Res* 2018; 21: 772–782.
80. Yun JE, Park JE, Park HY, et al. Comparative effectiveness of telemonitoring versus usual care for heart failure: a systematic review and meta-analysis. *J Card Fail* 2018; 24: 19–28.
81. Batalik L, Filakova K, Sladeckova M, et al. The cost-effectiveness of exercise-based cardiac telerehabilitation intervention: a systematic review. *Eur J Phys Rehabil Med* 2023; 59: 248–258.