BMC Medicine

RESEARCH

Open Access

Efficacy of digital therapeutics for perioperative management in patients with lung cancer: a randomized controlled trial

Jinming Xu[1,2†], Heng Ni[1,2†], Hanyu Zhan[1,2†], Hongfan Yu[3], Zhongjie Lu[1,2], Jieping Zhang[1,2], Hongbo Meng[4], Lin Hang[1,2], Lin Mao[4], Xiaoying Xu[1,2], Xiaojian Ma[4], Qiongyin Wu[1,2], Wen Xu[4], Danyu Xiang[1,2], Yufang Zeng[1,2], Di Meng[1,2], Xiao Teng[1,2], Li Yu[1,2], Liping Zeng[1,2], Pengzhi Ni[1,2], Huiwen Miao[1,2], Shaozi Fu[1,2], Luming Wang[1,2], Zhehao He[1,2], Chong Zhang[1,2], Xiayi Lv[1,2], Heyun Xu[1,2], Yihua Wu[5], Wang Lv[1,2], Qiuling Shi[3,6*] and Jian Hu[1,2,7*]

Abstract

Background Perioperative management and lung function recovery are vital for lung cancer patients. We conducted an open-label, single-center, noninferiority, randomized controlled trial in China to evaluate the efficacy of digital therapeutic (DTx)-assisted management vs. multidisciplinary management (MM) in the perioperative management of patients with lung cancer.

Methods From July 2022 to June 2023, 186 minimally invasive lung surgery patients were randomized, and 147 completed the study. The participants were randomly assigned a 1:1 ratio to receive DTx-assisted management ($n=72$) or traditional MM ($n=75$). The primary endpoint was the pulmonary function recovery rate measured by forced expiratory volume in the first second (FEV1%) 3 weeks after surgery, and the noninferiority margin was set to 4.8%. The secondary endpoints included hospital stay duration, 90-day unplanned readmission rate, symptom scores, patient management time, and patient satisfaction rate. Exploratory endpoints include factors influencing postoperative lung function recovery.

Results The lung function FEV1% recovery rate of the DTx group was not inferior to that of the MM group (87.18% ± 11.01% vs. 84.21% ± 11.75%). There were no significant differences between the two groups in terms of postoperative hospitalization duration or 90-day unplanned readmission rates. The patient management time in the DTx group was significantly shorter than that in the MM group (1.48 ± 3.22 min vs. 16.67 ± 6.41 min, $P<0.001$). Patient symptom scores tended to decrease over time after discharge, and the 5 target symptoms included pain, coughing, shortness of breath, disturbed sleep, and fatigue. On the 7th day after discharge, the DTx group had a lower occurrence rate of the 5 target symptoms triggering the alert threshold compared to the MM group ($P=0.002$). Patients with higher education levels achieved a better FEV1% recovery rate with DTx-assisted management ($P=0.021$).

†Jinming Xu, Heng Ni, and Hanyu Zhan contributed equally to this work.

*Correspondence:
Qiuling Shi
qshi@cqmu.edu.cn
Jian Hu
dr_hujian@zju.edu.cn
Full list of author information is available at the end of the article

Conclusions Compared with the MM group, the DTx group achieved noninferior results in all evaluated clinically meaningful endpoints but was significantly more efficient in perioperative management, providing an alternative digitalized management mode for patients with lung cancer surgery.

Trial registration ChiCTR2200064723.

Keywords Digital therapeutics, Lung cancer surgery, Perioperative management, FEV1% recovery, Minimally invasive surgery

Background

Lung cancer is one of the most prevalent and deadly types of tumors worldwide [1]. With the increasing popularity of chest CT screening, more early-stage lung cancers are being detected [2]. The widespread adoption of thoracoscopy techniques and the application of enhanced recovery after surgery (ERAS) concepts have brought hope for rapid recovery from minimally invasive surgery for lung cancer [3, 4], leading to a gradual reduction in hospitalization time for patients [5]. Nevertheless, surgical intervention for lung cancer inevitably results in complications and functional impairments, significantly impacting patients' lung function and quality of life [6], including issues such as pain, chronic cough, and breathing difficulties [7].

It has been reported that perioperative lung rehabilitation training and exercise training can benefit non-small cell lung cancer (NSCLC) patients who undergo surgical resection and improve their quality of life [8, 9]. However, as the hospitalization duration for patients with lung cancer decreases, guidance for rehabilitation and symptom management during hospitalization and after discharge becomes limited. Currently, most routine management methods for thoracic surgery patients after discharge lack effective intervention strategies [10, 11]. A multidisciplinary management (MM)-based ERAS approach might improve this situation [12, 13]; however, this approach imposes a significant workload on clinical staff and has deficiencies in timely intervention in patients' symptoms and rehabilitation guidance. Therefore, establishing an effective perioperative management mode for patients with lung cancer is of significant clinical importance.

The application of digital tools is effective for remote symptom monitoring and functional exercise guidance [14, 15]. Symptom assessment based on patient-reported outcomes (PROs) allows patients to provide direct quantitative feedback on the severity of symptoms [16], and it has been reported that the electronic PRO approach can improve short-term symptoms in patients with lung cancer [17]. The rapid rise of digital therapeutic (DTx), a software-based therapy, used independently or in conjunction with drugs, devices, or other therapies [18], has provided possibilities for disease prevention, intervention, and post-discharge patient recovery and management [19]. However, the application of DTx in the perioperative management of lung cancer remains limited, and evidence comparing the efficacy of DTx-assisted management and manual MM methods is still lacking.

We aimed to evaluate the efficacy of the DTx-assisted management mode, which empowers the MM team's work on patient education, exercise rehabilitation, and symptom monitoring and management, with a prospective randomized controlled trial (RCT) in China. We anticipate that the DTx mode will lead to noninferior lung function recovery compared with the traditional MM mode, providing a new convenient and high-efficacy alternative for the perioperative management of patients with lung cancer.

Methods

Study design

This RCT study was registered in the Chinese Clinical Trial Registry (ChiCTR2200064723). All patients were enrolled with written informed consent under institutional review board-approved protocols of the First Affiliated Hospital, Zhejiang University School of Medicine (IIT20220068C). This study was conducted in accordance with the Declaration of Helsinki and followed the CONSORT guidelines [20].

Patients

Patients planning to undergo minimally invasive pulmonary resection surgery staged I–IIIA and aged between 18 and 75 were enrolled in this study from July 2022 to June 2023. The FEV1 during preoperative lung function examination needs to be greater than or equal to 1.2 L and the FEV1% needs to be greater than or equal to 60% of the expected value. Patients should be able to use intelligent devices and fill out electronic questionnaires. The exclusion criteria were as follows: pre-surgery smoking cessation time less than 2 weeks; ECOG score greater than 1 point; receiving preoperative neoadjuvant therapy or thoracic surgery; unable to move due to organic changes such as trauma, illness, and severe arthritis; use of systemic corticosteroids within 1 month before surgery; previous history of major diseases, including a history of other malignant tumors within 5 years; a 6-month history of angina, myocardial infarction, and stroke; and

current existence of serious or uncontrollable systemic diseases, including thyroid disease, uncontrollable hypertension, coagulation dysfunction, or active infections, such as hepatitis B, hepatitis C, and human immunodeficiency virus (HIV).

Study endpoints

The primary endpoint was the recovery rate of FEV1% of lung function 3 weeks after surgery, and the recovery rate of FEV1% was defined via the following formula:

$$\text{Recovery rate} = \frac{\text{FEV1\% three weeks after surgey}}{\text{preoperative FEV1\%}}$$

The secondary endpoints included the postoperative length of hospital stay (LOS), 90-day unplanned readmission rate, symptom scores, patient satisfaction rate, and patient management time. The exploratory endpoints focused on identifying factors that influence postoperative lung function recovery. See details in Additional file 1: Trial protocol and statistical analysis [8, 9, 21–41].

The Perioperative Symptom Assessment for Lung Surgery (PSA-Lung) was used to assess symptom burden [42, 43], and detailed information on the PSA-Lung is provided in Additional file 1: Trial protocol and statistical analysis, Appendices, PSA-Lung Table. The symptom severity was rated from 0 to 10 for each item, and the symptom grade was defined as mild, moderate, or severe [44–48], as shown in Additional file 2: Table S1. The five predefined target symptoms included pain, cough shortness of breath, disturbed sleep, and fatigue. A symptom alert threshold event was defined as a target symptom score that reached the moderate or severe grade.

Study intervention

The study intervention methods, including the patient education module, exercise module, and symptom management module, are shown in Additional file 2: Table S2. The digital software Shu Yu app, designed by Shanghai CinoCore Health Technology Co., Ltd., is a class II medical device and approved by the National Medical Products Administration in China (Jiangsu Device Registration Approval No. 20232211057). It was used for perioperative management in the DTx group. All patients returned to the hospital for a comprehensive reexamination 3 weeks after surgery.

Education module

Preoperative stage: The DTx and MM groups received routine preoperative health education from thoracic doctors and nursing staff. The DTx group received an additional 10-min training session of the DTx software user guide and preoperative knowledge training courses on the software. The MM group received additional education from the rehabilitation department.

Postoperative stage: The DTx group patients received routine education 10 min per day before discharge, and they could obtain information from the software at any time before and after discharge. The MM group received routine education assisted by rehabilitation department physicians 30 min per day before discharge, and they received education via telephone follow-up after discharge.

Exercise module

Early ambulation is recommended for both the DTx group and MM group patients. There is no unified standard for exercise prescriptions yet, and the exercise module in this study adopted respiratory, aerobic, and resistance exercises [49–51].

Preoperative stage: The DTx and MM groups received 20 min of respiratory, aerobic, and resistance exercises. The DTx software collected baseline data to adjust the exercise intensity adaptively. The MM group patients received additional assistance from the rehabilitation department.

Postoperative stage: The DTx and MM groups received 20 min of respiratory exercise and 60 min of aerobic and resistance exercises per day. The DTx software automatically adjusted goals based on patients' exercise tolerance, exercise habits and preferences weekly. A rehabilitation therapist helped the MM group patients exercise before discharge, provided exercise prescriptions, and made dynamic adjustments via weekly telephone follow-up after discharge.

Symptom management module

The DTx group patients recorded symptoms through the software, which provided algorithm-based self-management advice and timely intervention instructions by doctors and nurses; if necessary, patients were informed to return to the hospital for further treatment.

The MM group patients recorded their symptoms via WeChat questionnaires, received routine management, and sought medical aid if necessary. If the patient does not fill out the report promptly, the healthcare team will retrospectively inquire about the patient's symptoms during the telephone guidance process and provide symptom intervention instructions.

Statistical analysis

The current study adopted a noninferiority method to assess the efficacy of DTx in perioperative lung cancer management [52]. This study assumes equivalent efficacy between the DTx group and the MM group. Based on preliminary trial data collected at our center, the

mean recovery rate of FEV1% at 3 weeks post-surgery is assumed to be 83.57% in both groups, with a standard deviation of 13%. The noninferiority margin is set at 5%. A one-sided significance level of 0.025 and a power of 90% are established. Sample size calculations via the specialized software PASS yield a requirement of 144 subjects per group (Additional file 2: Method S1 [53, 54]). Accounting for a dropout rate of no more than 20%, each group consists of 180 subjects, resulting in 360 participants. An independent statistical expert conducted a preplanned, interim noninferiority analysis. This analysis is expected to be conducted in the 12th month of the trial. When 108 events are observed among the randomized subjects (approximately 30% of the targeted lung function recovery events [55]), the external statistical expert will perform the interim analysis as scheduled. The O'Brien-Fleming α spending function approach is adopted, and the noninferiority margin is adjusted to 4.8% [56]. If the interim formal comparison for the clinical endpoint reaches the noninferiority margin, early termination of the study will be allowed to reduce the effort of medical and rehabilitation staff.

Using SAS 9.4 statistical software and the central randomization system, a randomization table for study participants with consecutive numbering was generated at a 1:1 ratio between the DTx and MM groups. Each participant is assigned a unique random number during the study period. The chi-square test, *t*-test, linear model, linear mixed effect model, and analysis of covariance were used for statistical analysis. If the data were not normally distributed, a nonparametric test was adopted. A linear mixed-effect model was adopted to adjust for each symptom of concern. Given the symmetrical correlation between various response time points of PRO, which also tends to diminish over time, the covariate structure employs a first-order autoregressive model [57]. Statistical analyses were conducted via SPSS 22.0 software (IBM SPSS Inc., USA) and R software version 4.3.1 (The R Foundation for Statistical Computing).

Results

Patients

When 147 events were observed among the randomized subjects (40.83% of the targeted lung function recovery events), the interim analysis was performed, the primary endpoint reached the noninferiority margin, and the study was terminated. A total of 252 patients were screened, and 186 patients were randomly allocated to each group. Thirty-five patients (18.8%) met the exit criteria due to hospital stays longer than 7 days, did not receive surgery, had benign pathology, or were lost to follow-up. A total of 72 patients were ultimately included in the intervention group (DTx group), and 75 patients were included in the control group (MM group), as shown in Fig. 1. There was no significant difference in the baseline characteristics between the two groups, as shown in Table 1.

Primary and secondary endpoints

The primary endpoint was the recovery rate of FEV1% of lung function 3 weeks after surgery. The FEV1% recovery rate of the DTx group was not inferior to that of the MM group (87.18% ± 11.01% vs. 84.21% ± 11.75%), with a mean difference of 3.05% (−0.61%, 6.71%), and the lower limit was greater than −Δ (−4.8%), as shown in Additional file 2: Fig. S1.

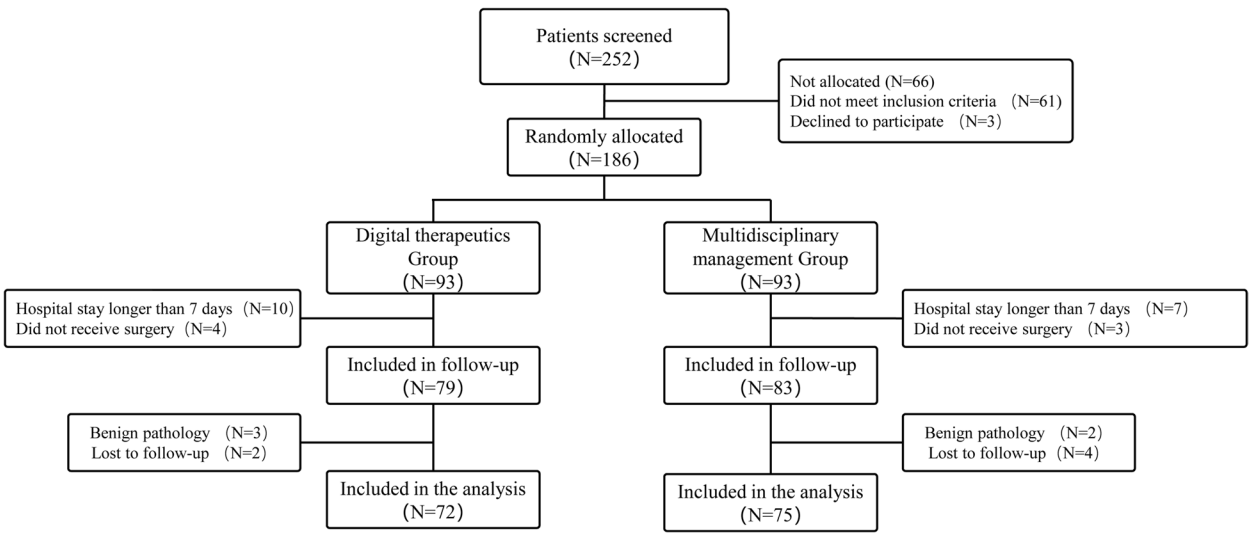

Fig. 1 Flow diagram of the patient selection process

Table 1 Baseline characteristics of the included patients

Characteristics	No. (%)		*P*value
	DTx group ($n=72$)	MM group ($n=75$)	
Sex			
Male	13 (18.06)	16 (21.33)	0.770
Female	59 (81.94)	59 (78.67)	
Age	48.19 ± 11.80	48.07 ± 11.39	0.947
Charlson score			0.902
0	57 (79.17)	61 (81.33)	
> 0	15 (20.83)	14 (18.67)	
Presurgery FEV1%	99.74 ± 12.64	99.22 ± 14.12	0.813
BMI	26.22 ± 2.47	22.84 ± 2.79	0.157
Smoking history			0.495
Never	69 (95.83)	69 (92.00)	
Currently or ever	3 (4.17)	6 (8.00)	
Education level			0.156
Junior high school or lower	29 (40.28)	40 (53.33)	
Senior high school or above	43 (59.72)	35 (46.67)	
Surgical approach			0.389
Wedge resection	45 (62.50)	42 (56.00)	
Segmentectomy	17 (23.61)	16 (21.33)	
Lobectomy	10 (13.89)	17 (22.67)	
Stage			0.527
I	71 (98.61)	72 (96.00)	
II	1 (1.39)	2 (2.67)	
IIIA	0	1 (1.33)	
Histology			0.379
Minimally invasive adenocarcinoma	36 (50.00)	45 (60.00)	
Invasive adenocarcinoma	34 (47.22)	27 (36.00)	
Others	2 (2.78)	3 (4.00)	
Surgical site			0.924
Right upper lobe	24 (33.33)	28 (37.33)	
Right lower lobe	17 (23.61)	14 (18.67)	
Right middle lobe	1 (1.39)	2 (2.67)	
Left upper lobe	19 (26.39)	19 (25.33)	
Left lower lobe	11 (15.28)	12 (16.00)	

The secondary endpoints included postoperative LOS, 90-day unplanned readmission rate, symptom scores, patient satisfaction rate, and patient management time. There was no significant difference between the DTx and MM groups, with a mean postoperative LOS of 3.85 vs. 3.84 days ($P=0.966$) and a 90-day readmission rate of 6.94% vs. 6.67% ($P=1.000$), as shown in Table 2. Notably, the patient management time in the DTx group was significantly shorter than that in the MM group (1.48 ± 3.22 min vs. 16.67 ± 6.41 min, $P<0.001$), suggesting greater efficacy of DTx management. The patient satisfaction survey results of the DTx group are shown in Table 3. A total of 91.67% of patients in the DTx group believed that software operations had slight or no difficulty, and the percentages of patients who believed that education, exercise, and symptom management modules were highly effective were 90.28%, 90.28%, and 94.44%, respectively.

The patients' symptoms were assessed via PRO measures. There was no significant difference in the patient completion rate between the DTx and MM groups, as shown in Additional file 2: Table S3 and Additional file 2: Fig. S2. The 5 target symptoms showed a decreasing trend over time after discharge. There was no significant difference in the mean value of the 5 target symptoms between the DTx and MM groups ($P=0.162$), as shown in Fig. 2A

Table 2 Perioperative assessment of secondary endpoints of the included patients

Outcomes	DTx group ($n=72$)	MM group ($n=75$)	*P* value
Postoperative length of stay, day	3.85 ± 0.99	3.84 ± 1.07	0.966
90-day unplanned readmission[a]			1.000
No	67	70	
Yes	5	5	
Patient management time, min	1.48 ± 3.22	16.67 ± 6.41	< 0.001

[a] In addition to readmission due to adverse events, another patient in the DTx group returned to the hospital due to COVID-19

Table 3 Patient satisfaction survey of the DTx group

Index	Grade[a]				
	A: highest	B: high	C: moderate	D: low	E: lowest
Operational difficulty	0	4 (5.56%)	2 (2.78%)	5 (6.94%)	61 (84.72%)
Efficacy of patient education module	47 (65.28%)	18 (25.00%)	5 (6.94%)	0	2 (2.78%)
Efficacy of exercise module	52 (72.22%)	13 (18.06%)	5 (6.94%)	2 (2.78%)	0
Efficacy of symptom management module	51 (70.83%)	17 (23.61%)	4 (5.56%)	0	0

[a] Grade A indicates that the operational difficulty and effectiveness of different modules were the highest, and the degree gradually decreased from A to E

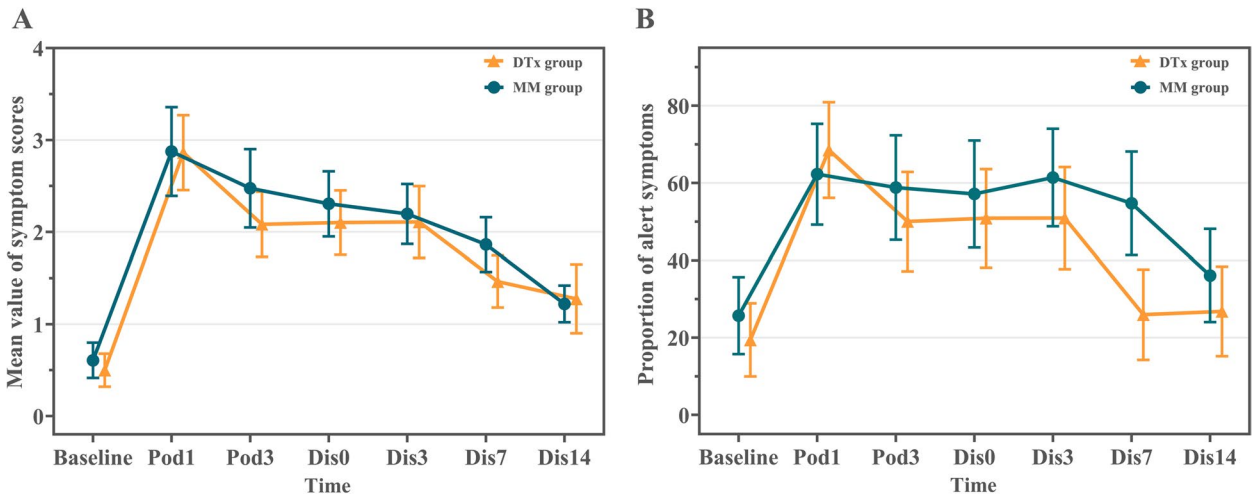

Fig. 2 Comparison of 5 target symptoms between the DTx group and MM group. **A** Comparison of the mean values of the 5 target symptoms. **B** Comparison of the alert event ratios for 5 target symptoms. Pod postoperative day, Dis discharge

and Additional file 2: Tables S4 and S5. Furthermore, whether the 5 target symptoms trigger an alert threshold should receive increased attention. A comparison of the alert event ratios of the 5 target symptoms between the DTx and MM groups is shown in Fig. 2B and Additional file 2: Tables S6 and S7. These findings suggested that the DTx group exhibited a comparable ability to the MM group in terms of patient alerts to symptom events ($P=0.780$). A significant difference in the number of alert events triggered by the 5 target symptoms was observed on the 7th day after discharge ($P=0.002$), with the MM group manifesting a greater number of alert symptoms than the DTx group.

Exploratory endpoints

The exploratory endpoints focused on identifying factors that influence postoperative lung function recovery. Subgroup analyses were conducted to explore potential factors, and we found that among individuals with lower educational levels, there was no significant difference in

the FEV1% recovery rate between the DTx group and the MM group ($P=0.914$). However, among those with higher educational levels, those in the DTx group had a significantly better FEV1% recovery rate than those in the MM group ($P=0.021$), as shown in Additional file 2: Table S8. The results indicated that patients with higher levels of education were more likely to benefit from DTx-assisted management.

Discussion

We conducted a RCT to evaluate the efficacy of DTx in perioperative management in patients receiving minimally invasive lung cancer surgery. The DTx product used in this study was developed by Shanghai CinoCore Health Technology Co., Ltd.. It is a class II medical device approved by the National Medical Products Administration in China (Registration No. 20232211057, Jiangsu, China). To align with the ERAS protocol, the DTx product was customized by incorporating the following features: [1] A symptom management module tailored to address five core symptoms specific to lung cancer patients who have undergone surgical interventions. (2) Educational materials curated by our hospital, integrated into the underlying education module. These customizations aim to enhance patient care and outcomes throughout the treatment journey. A detail visual representation of the product's architecture and key features is represented in Additional file 2: DTx product description.

Compared with the traditional manual MM mode involving thoracic surgeons, nursing staff, and rehabilitation practitioners, the innovative mode based on DTx has achieved noninferior results in terms of the recovery of patients' pulmonary function, comparable postoperative LOS, and 90-day readmission rates. Postoperative symptoms were controlled and managed properly in both groups, as presented by a consistent decreasing trend in the 5 target symptom scores. The number of alert events of the 5 target symptoms in the DTx group was significantly lower than that in the MM group on the 7th day after discharge, indicating the benefits of proactive remote monitoring and timely intervention. On the other hand, the DTx group allows care teams to largely reduce their workload and improve work efficiency during the patient recovery stage, and patients achieve high levels of satisfaction with this innovative model.

The study, to the best of our knowledge, is the first RCT in the field of thoracic surgery that evaluated the efficacy of postoperative pulmonary functional recovery and symptom alleviation using MM mode as a control arm [4, 5, 12]. The recovery rate of FEV1% was selected as the primary endpoint, given its established use as a standard measure of lung function recovery [58–60] and its strong correlation with health-related quality of life (HRQoL) [61, 62]. Previous studies have demonstrated a peak decline in FEV1 functionality typically occurring between 2 and 4 weeks post-surgery, highlighting its sensitivity to airway obstruction and responsiveness to short-term interventions, such as postoperative rehabilitation exercises [60, 63]. On this basis, we have demonstrated the noninferiority of DTx, highlighting its efficacy in perioperative care for patients with lung cancer. Owing to the increasing volume of surgeries and the overwhelming workload for both care teams and rehabilitation therapists, it has become challenging to implement standardized rehabilitation training extensively among patients and extend it beyond the hospital stay. Moreover, variations in patients' cognitive levels and compliance result in inconsistent outcomes. Compared with the MM group, the DTx group required less time to manage patients, which can greatly improve management efficiency, save medical resources, and may play a pivotal role in increasing the fairness of healthcare access [64]. Therefore, the portability and scalability of DTx offer promising prospects for advancing the management of lung cancer patients during the perioperative period.

The current study innovatively integrates DTx with PRO to fully utilize the software for managing perioperative care for patients with lung cancer. Patient symptom management in PRO mode allows healthcare providers to offer timely interventions, significantly improving management efficiency, cost-effectiveness, and patient satisfaction [17, 65–67]. The DTx-assisted management method in the study was carefully designed with a patient education module, exercise module, and symptom management module. Based on timely bidirectional communication between doctors and patients through software, the DTx method effectively transcends geographical and time barriers [68]. Altering patients' beliefs and behavior patterns deepens their understanding of the disease and engages them more actively in self-management. Prior studies have shown that patients with greater involvement have better outcomes [12, 69, 70].

The implementation of the DTx-assisted management mode requires several key elements. First, it heavily relies on initial DTx product training provided by the care team. Once patients are aware of and thereafter engaged in this innovative management pattern, the efficiency of ongoing remote management will be significantly improved. The care team also needs training and dedication to this initial DTx introductory setup before the innovative model delivers its anticipated result. Second, the implementation of DTx is contingent on patients' ability to use smartphones. It has been reported that educational level is associated with decreased lung function [71]. In this study, we observed that patients with higher educational levels achieved better lung function

recovery from DTx management. Third, prompt intervention for alerted symptoms during the patient recovery period increases compliance with the management plan. DTx is highly beneficial for physicians with respect to mild symptom management and mild-to-severe symptom monitoring. However, it cannot replace physicians in providing medical advice. Once patients receive prompt feedback from their care team, they perceive the product to be a bidirectional communication hub, which is a critical component in establishing a therapeutic alliance. If there is no guidance from health care professionals, relying solely on self-management by patients may lead to a discount in effectiveness [72].

Limitations

This study has several limitations. (1) Trials lack blinding of patients and investigators due to the nature of the intervention. (2) As this was a single-site trial, most of the patients included in the study were in stage I, with a relatively small proportion of stage II and III patients. This finding aligns with patient segmentation in patients treated in our hospital, and more evidence is needed to determine whether DTx can benefit populations with late-stage disease. (3) As the trial was conducted only in China, the efficacy of the DTx-assisted management mode needs more evidence in other countries where cultures and clinical practices are different. A regional or an international multicenter trial is needed for further validation. (4) The trial focused on a specific cohort and excluded patients who experienced severe postoperative complications, which may have limited our ability to fully capture the range of complications observed in real-world clinical settings. For readers interested in the analysis of patients with prolonged hospitalization, detailed results are presented in Additional File 3. To address this potential limitation and enhance the applicability of our findings to a broader patient population, further research will be valuable in exploring the impact of more severe complications on patient outcomes.

Conclusions

In conclusion, the DTx-assisted management demonstrated noninferior efficacy in lung function recovery (FEV1%) compared to traditional multidisciplinary management for lung cancer surgery patients. Additionally, DTx significantly reduced patient management time and improved symptom control, offering a more efficient digitalized alternative for perioperative care.

Abbreviations

DTx	Digital therapeutic
ECOG	Eastern Cooperative Oncology Group
ERAS	Enhanced recovery after surgery
FEV1%	Forced expiratory volume in the first second
HIV	Human immunodeficiency virus
HRQoL	Health-related quality of life
LOS	Length of hospital stay
MM	Multidisciplinary management
NSCLC	Non-small cell lung cancer
PROs	Patient-reported outcomes
PSA-Lung	Perioperative Symptom Assessment for Lung Surgery
RCT	Randomized controlled trial

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04012-2.

Additional file 1. Trial protocol and statistical analysis.

Additional file 2: Method S1. Two-sample *t*-tests for noninferiority assuming equal variance. Tables S1–S8. Table S1. Symptom grading by symptom score. Table S2. Study interventions in the DTx group and MM group. Table S3. Patient compliance rate during the perioperative period. Table S4. Comparison of the mean values of the 5 target symptoms between the DTx and MM groups. Table S5. Comparison of the mean values of the 5 target symptoms between the DTx and MM groups via the linear mixed effect model. Table S6. The alert event ratio comparison of 5 target symptoms between the DTx and MM groups. Table S7. Comparison of the alert event ratios of the 5 target symptoms between the DTx and MM groups via the linear mixed effect model. Table S8. Subgroup analysis of factors influencing postoperative lung function recovery. Figures S1–S2. Fig. S1. Noninferiority comparison of FEV1% between the DTx group and MM group. Fig. S2. Patient compliance rate during the perioperative period. DTx product description.

Additional File 3: Analysis including patients with prolonged hospitalization. Table S1-S3. Table S1. Baseline characteristics of the patients (including patients with prolonged hospitalization). Table S2. Perioperative assessment of secondary endpoints of the included patients. Table S3. Subgroup analysis of factors influencing postoperative lung function recovery. Figure S1. Noninferiority comparison of FEV1% between the DTx group and MM group.

Acknowledgements

We are grateful for the efforts and software support of Shanghai CinoCore Health Technology Co., Ltd., especially for Mr. Kaishen Chen, Ms. Jing Gao, Dr. Kun Wang, Mr. Qi Yang and Mr. Qihua Xu.

Authors' contributions

Concept and design: J.H., Q.S., J.X., Z.L., W.L., J.Z. and H.M. Acquisition, analysis, or interpretation of data: J.X., H.N. and H.Z. Drafting the manuscript: J.X. and H.N. Statistical analysis: H.Z., H.Y, and Y.W. Nursing team: J.Z., L.H., X.X., Q.W., D.X., and Y.Z. Rehabilitation team: H.M., L.M., X.M., and W.X. Thoracic surgeon team: D.M., X.T., L.Y., L.Z., P.N., H.M., S.F., L.W., Z.H., C.Z., X.L. and H.X. All authors read and approved the final manuscript.

Funding

This study was funded by the Key R&D Program of Zhejiang (2023C03172), the Major Science and Technology Projects of Zhejiang Province (2022C04030, 2020C03058), the National Key Research and Development Program of China (2022YFC2407303), and the Research Center for Lung Tumor Diagnosis and Treatment of Zhejiang Province (JBZX-202007).

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This RCT study was registered in the Chinese Clinical Trial Registry (ChiCTR2200064723). All patients were enrolled with written informed

consent under institutional review board-approved protocols of the First Affiliated Hospital, Zhejiang University School of Medicine (IIT20220068C).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Thoracic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China. [2]Enhanced Recovery After Surgery (ERAS) Center of Thoracic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China. [3]State Key Laboratory of Ultrasound in Medicine and Engineering, College of Biomedical Engineering, Chongqing Medical University, Chongqing, China. [4]Department of Rehabilitation Medicine, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China. [5]Department of Toxicology of School of Public Health, Zhejiang University School of Medicine, Hangzhou, China. [6]School of Public Health, Chongqing Medical University, Chongqing, China. [7]Key Laboratory of Clinical Evaluation Technology for Medical Device of Zhejiang Province, Hangzhou, China.

Received: 3 March 2024 Accepted: 14 March 2025
Published online: 28 March 2025

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17–48.
2. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395–409.
3. Boffa DJ, Kosinski AS, Furnary AP, Kim S, Onaitis MW, Tong BC, et al. Minimally invasive lung cancer surgery performed by thoracic surgeons as effective as thoracotomy. J Clin Oncol. 2018;36(23):2378–85.
4. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalez M, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardio-Thoracic Surg : Off J Eur Assoc Cardio-Thoracic Surg. 2019;55(1):91–115.
5. Haro GJ, Sheu B, Marcus SG, Sarin A, Campbell L, Jablons DM, et al. Perioperative lung resection outcomes after implementation of a multidisciplinary, evidence-based thoracic ERAS program. Ann Surg. 2021;274(6):e1008–13.
6. Altorki N, Wang X, Kozono D, Watt C, Landrenau R, Wigle D, et al. Lobar or sublobar resection for peripheral stage IA non-small-cell lung cancer. N Engl J Med. 2023;388(6):489–98.
7. Rice D, Rodriguez-Restrepo A, Mena G, Cata J, Thall P, Milton D, et al. Matched pairs comparison of an enhanced recovery pathway versus conventional management on opioid exposure and pain control in patients undergoing lung surgery. Ann Surg. 2021;274(6):1099–106.
8. Arbane G, Tropman D, Jackson D, Garrod R. Evaluation of an early exercise intervention after thoracotomy for non-small cell lung cancer (NSCLC), effects on quality of life, muscle strength and exercise tolerance: randomised controlled trial. Lung Cancer (Amsterdam, Netherlands). 2011;71(2):229–34.
9. Stigt JA, Uil SM, van Riesen SJ, Simons FJ, Denekamp M, Shahin GM, et al. A randomized controlled trial of postthoracotomy pulmonary rehabilitation in patients with resectable lung cancer. J Thoracic Oncol : Off Publ Int Assoc Study Lung Cancer. 2013;8(2):214–21.
10. Dai W, Zhang Y, Feng W, Liao X, Mu Y, Zhang R, et al. Using patient-reported outcomes to manage postoperative symptoms in patients with lung cancer: protocol for a multicentre, randomised controlled trial. BMJ Open. 2019;9(8): e030041.
11. Du J, Wu C, Li A, Chen J, Li Q, Wu X. Effectiveness of enhanced recovery after surgery-based respiratory function exercise in elderly patients with lung cancer and its effect on postoperative functional recovery. Altern Ther Health Med. 2023;29(6):56–61.
12. Cassidy MR, Rosenkranz P, McCabe K, Rosen JE, McAneny D. I COUGH: reducing postoperative pulmonary complications with a multidisciplinary patient care program. JAMA Surg. 2013;148(8):740–5.
13. Tahiri M, Goudie E, Jouquan A, Martin J, Ferraro P, Liberman M. Enhanced recovery after video-assisted thoracoscopic surgery lobectomy: a prospective, historically controlled, propensity-matched clinical study. Can J Surg J Can Chirurgie. 2020;63(3):E233–40.
14. Basch E. Digital therapeutics for remote symptom monitoring and management in cancer care: the current and future state. Ann Oncol. 2023;34(8):635–7.
15. Basch E, Schrag D, Henson S, Jansen J, Ginos B, Stover AM, et al. Effect of electronic symptom monitoring on patient-reported outcomes among patients with metastatic cancer: a randomized clinical trial. JAMA. 2022;327(24):2413–22.
16. Weinfurt KP, Reeve BB. Patient-reported outcome measures in clinical research. JAMA. 2022;328(5):472–3.
17. Dai WFW, Zhang Y, Wang XS, Liu Y, Pompili C, Xu W, Xie S, Wang Y, Liao J, Wei X, Xiang R, Hu B, Tian B, Yang X, Wang X, Xiao P, Lai Q, Wang X, Cao B, Wang Q, Liu F, Liu X, Xie T, Yang X, Zhuang X, Wu Z, Che G, Li Q, Shi Q. Patient-reported outcome-based symptom management versus usual care after lung cancer surgery: a multicenter randomized controlled trial. J Clin Oncol. 2022;40(9):988–96.
18. Hong JS, Wasden C, Han DH. Introduction of digital therapeutics. Comput Methods Programs Biomed. 2021;209: 106319.
19. Wang C, Lee C, Shin H. Digital therapeutics from bench to bedside. NPJ digital medicine. 2023;6(1):38.
20. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Int J Surg (London, England). 2011;9(8):672–7.
21. Crandall K, Maguire R, Campbell A, Kearney N. Exercise intervention for patients surgically treated for non-small cell lung cancer (NSCLC): a systematic review. Surg Oncol. 2014;23(1):17–30.
22. Shannon VR. Role of pulmonary rehabilitation in the management of patients with lung cancer. Curr Opin Pulm Med. 2010;16(4):334–9.
23. Kenny PM, King MT, Viney RC, Boyer MJ, Pollicino CA, McLean JM, et al. Quality of life and survival in the 2 years after surgery for non small-cell lung cancer. J Clin Oncol. 2008;26(2):233–41.
24. Cavalheri V, Burtin C, Formico VR, Nonoyama ML, Jenkins S, Spruit MA, et al. Exercise training undertaken by people within 12 months of lung resection for non-small cell lung cancer. Cochrane Database Syst Rev. 2019;6(6):CD009955.
25. Loganathan RS, Stover DE, Shi W, Venkatraman E. Prevalence of COPD in women compared to men around the time of diagnosis of primary lung cancer. Chest. 2006;129(5):1305–12.
26. Schroedl C, Kalhan R. Incidence, treatment options, and outcomes of lung cancer in patients with chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2012;18(2):131–7.
27. Divisi D, Di Francesco C, Di Leonardo G, Crisci R. Preoperative pulmonary rehabilitation in patients with lung cancer and chronic obstructive pulmonary disease. Eur J Cardio-Thoracic Surg : Off J Eur Assoc Cardio-Thoracic Surg. 2013;43(2):293–6.
28. Lowery AE, Krebs P, Coups EJ, Feinstein MB, Burkhalter JE, Park BJ, et al. Impact of symptom burden in post-surgical non-small cell lung cancer survivors. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2014;22(1):173–80.
29. Cesario A, Ferri L, Galetta D, Pasqua F, Bonassi S, Clini E, et al. Post-operative respiratory rehabilitation after lung resection for non-small cell lung cancer. Lung cancer (Amsterdam, Netherlands). 2007;57(2):175–80.
30. Bradley A, Marshall A, Stonehewer L, Reaper L, Parker K, Bevan-Smith E, et al. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2013;44(4):e266–71.
31. Messaggi-Sartor M, Marco E, Martinez-Tellez E, Rodriguez-Fuster A, Palomares C, Chiarella S, et al. Combined aerobic exercise and high-intensity respiratory muscle training in patients surgically treated for non-small cell lung cancer: a pilot randomized clinical trial. Eur J Phys Rehabil Med. 2019;55(1):113–22.
32. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg. 2017;152(3):292–8.

33. Rollins KE, Lobo DN, Joshi GP. Enhanced recovery after surgery: current status and future progress. Best Pract Res Clin Anaesthesiol. 2021;35(4):479–89.
34. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. Clin Nutr. 2010;29(4):434–40.
35. Chinese Reserch Hospital Association sfHs. Expert consensus on enhanced recovery after hepatobiliary & pancreatic surgery (2015 editon). Zhonghua Xiao Hua Wai Ke Za Zhi. 2016;15(1):1–6.
36. Che GWLL. Enhanced lung recovery after surgery, is it a necessary for precision therapy. Zhongguo Fei Ai Za Zhi. 2017;20(8):549–54.
37. Degenhardt THN, Fasching PA, et al. Documentation patterns and impact on observed side effects of the CANKADO ehealth application: an exploratory analysis of the PreCycle trial. J Clin Oncol. 2020;38(15):2083–2083.
38. Galiano-Castillo N, Cantarero-Villanueva I, Fernandez-Lao C, Ariza-Garcia A, Diaz-Rodriguez L, Del-Moral-Avila R, et al. Telehealth system: a randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. Cancer. 2016;122(20):3166–74.
39. Glattki GP, Manika K, Sichletidis L, Alexe G, Brenke R, Spyratos D. Pulmonary rehabilitation in non-small cell lung cancer patients after completion of treatment. Am J Clin Oncol. 2012;35(2):120–5.
40. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev. 2012;2012(8):CD008465.
41. Dennett AM, Peiris CL, Shields N, Prendergast LA, Taylor NF. Moderate-intensity exercise reduces fatigue and improves mobility in cancer survivors: a systematic review and meta-regression. J Physiother. 2016;62(2):68–82.
42. Yu H, Yu Q, Tang L, Dai W, Wei X, Wang Y, et al. Measuring the symptom burden of lung surgery patients: the validity and utility of the Perioperative Symptom Assessment for Lung Surgery (PSA-Lung). 28th Annual Conference of the International Society for Quality of Life Research. Qual Life Res. 2021;30(S1):1–177.
43. Yu H, Lei C, Wei X, Wang Y, Xu W, Tang L, et al. Electronic symptom monitoring after lung cancer surgery: establishing a core set of patient-reported outcomes for surgical oncology care in a longitudinal cohort study. Int J Surg. 2024;110(10):6591–600.
44. National Comprehensive Cancer Network. Adult cancer pain (version 2.2023). 2023. https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf.
45. National Comprehensive Cancer Network. Cancer-related fatigue (version 2.2023). 2023. https://www.nccn.org/professionals/physician_gls/pdf/fatigue.pdf.
46. Zhang J, Su X, Xu W, Yu Q, Dai W, Wang Y, et al. Identifying patients who suffered from post-discharge cough after lung cancer surgery. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2022;30(9):7705–13.
47. Yu Q, Yu H, Xu W, Pu Y, Nie Y, Dai W, et al. Shortness of breath on day 1 after surgery alerting the presence of early respiratory complications after surgery in lung cancer patients. Patient Prefer Adherence. 2022;16:709–22.
48. National Comprehensive Cancer Network. Distress management (version 2.2023). 2023. https://www.nccn.org/professionals/physician_gls/pdf/distress.pdf.
49. Voorn MJJ, Franssen RFW, Hoogeboom TJ, van Kampen-van den Boogaart VEM, Bootsma GP, Bongers BC, et al. Evidence base for exercise prehabilitation suggests favourable outcomes for patients undergoing surgery for non-small cell lung cancer despite being of low therapeutic quality: a systematic review and meta-analysis. Eur J Surg Oncol. 2023;49(5):879-94.
50. Voorn MJJ, Driessen EJM, Reinders R, van Kampen-van den Boogaart VEM, Bongers BC, Janssen-Heijnen MLG. Effects of exercise prehabilitation and/or rehabilitation on health-related quality of life and fatigue in patients with non-small cell lung cancer undergoing surgery: a systematic review. Eur J Surg Oncol. 2023;49(10):106909.
51. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):e13-64.
52. Piaggio G, Elbourne DR, Pocock SJ, Evans SJ, Altman DG. Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. JAMA. 2012;308(24):2594–604.
53. Chow SC, Shao J, Wang H, Lokhnygina Y. Sample size calculations in clinical research. 3rd ed. Boca Raton, Florida: Taylor, Francis/CRC; 2018.
54. Julious SA. Sample sizes for clinical trials with normal data. Stat Med. 2004;23(12):1921–86.
55. Genge A, van den Berg LH, Frick G, Han S, Abikoff C, Simmons A, et al. Efficacy and safety of ravulizumab, a complement c5 inhibitor, in adults with amyotrophic lateral sclerosis: a randomized clinical trial. JAMA Neurol. 2023;80(10):1089–97.
56. DeMets DL, Lan KK. Interim analysis: the alpha spending function approach. Stat Med. 1994;13(13–14):1341–52 discussion 53–6.
57. Cnaan A, Laird NM, Slasor P. Using the general linear mixed model to analyse unbalanced repeated measures and longitudinal data. Stat Med. 1997;16(20):2349–80.
58. Shin S, Kong S, Kang D, Lee G, Cho JH, Shim YM, et al. Longitudinal changes in pulmonary function and patient-reported outcomes after lung cancer surgery. Respir Res. 2022;23(1):224.
59. Yokoba M, Ichikawa T, Harada S, Naito M, Sato Y, Katagiri M. Postoperative pulmonary function changes according to the resected lobe: a 1-year follow-up study of lobectomized patients. J Thorac Dis. 2018;10(12):6891–902.
60. Kim SK, Ahn YH, Yoon JA, Shin MJ, Chang JH, Cho JS, et al. Efficacy of systemic postoperative pulmonary rehabilitation after lung resection surgery. Ann Rehabil Med. 2015;39(3):366–73.
61. Spinou A, Lee AL, O'Neil B, Oliveira A, Shteinberg M, Herrero-Cortina B. Patient-managed interventions for adults with bronchiectasis: evidence, challenges and prospects. Eur Respir Rev. 2024;33(174):240087.
62. Omata M, Wakabayashi R, Kudoh S, Kida K. Correlation between bronchodilator responsiveness and quality of life in chronic obstructive pulmonary disease. Allergology international : official journal of the Japanese Society of Allergology. 2007;56(1):15–22.
63. Brocki BC, Andreasen JJ, Langer D, Souza DS, Westerdahl E. Postoperative inspiratory muscle training in addition to breathing exercises and early mobilization improves oxygenation in high-risk patients after lung cancer surgery: a randomized controlled trial. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2016;49(5):1483–91.
64. Cui D, Janela D, Costa F, Molinos M, Areias AC, Moulder RG, et al. Randomized-controlled trial assessing a digital care program versus conventional physiotherapy for chronic low back pain. NPJ digital medicine. 2023;6(1):121.
65. Lizée T, Basch E, Trémolières P, Voog E, Domont J, Peyraga G, et al. Cost-effectiveness of web-based patient-reported outcome surveillance in patients with lung cancer. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2019;14(6):1012–20.
66. Howell D, Harth T, Brown J, Bennett C, Boyko S. Self-management education interventions for patients with cancer: a systematic review. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2017;25(4):1323–55.
67. Berry DL, Hong F, Halpenny B, Partridge AH, Fann JR, Wolpin S, et al. Electronic self-report assessment for cancer and self-care support: results of a multicenter randomized trial. J Clin Oncol. 2014;32(3):199–205.
68. Lehne M, Sass J, Essenwanger A, Schepers J, Thun S. Why digital medicine depends on interoperability. NPJ digital medicine. 2019;2:79.
69. Skolarus TA, Metreger T, Wittmann D, Hwang S, Kim HM, Grubb RL 3rd, et al. Self-management in long-term prostate cancer survivors: a randomized, controlled trial. J Clin Oncol. 2019;37(15):1326–35.
70. Denis F, Basch E, Septans AL, Bennouna J, Urban T, Dueck AC, et al. Two-year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. JAMA. 2019;321(3):306–7.
71. Tabak C, Spijkerman AM, Verschuren WM, Smit HA. Does educational level influence lung function decline (Doetinchem Cohort Study)? Eur Respir J. 2009;34(4):940–7.
72. van der Hout A, van Uden-Kraan CF, Holtmaat K, Jansen F, Lissenberg-Witte BI, Nieuwenhuijzen GAP, et al. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. Lancet Oncol. 2020;21(1):80–94.

Publisher's Note