Original Article

Quality of Life, Fatigue, and Sleep Problems in Pancreatic Cancer Patients

A Randomized Trial on the Effects of Exercise

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Summary

Background: Improving quality of life (QoL) is an important treatment goal in pancreatic cancer patients. Although the beneficial effects of exercise on QoL are well understood, few studies have investigated more aggressive cancers such as pancreatic cancer.

Methods: Within a randomized trial, we assessed the efficacy of 6-month resistance training on physical functioning (primary outcome) and further QoL-related outcomes. 65 pancreatic cancer patients were assigned to home-based training, supervised training, or a usual care control group. Analysis-of-covariance models on changes from baseline to 6 and 3 months were applied.

Results: 47 patients completed the intervention period. After 6 months, no effects of resistance training were observed. However, after 3 months, explorative analyses showed significant between-group mean differences (MD) in favor for resistance training for physical functioning (pooled group: MD=11.0; p=0.016; effect size[ES]=0.31), as well as for global QoL (MD=12.1; p=0.016; effect size=0.56), and other outcomes, such as sleep problems and fatigue. Multiple imputation analyses yielded similar results. Home-based and supervised training performed similarly.

Conclusion: This first randomized resistance training trial in pancreatic cancer patients indicated clinically relevant improvements in QoL after 3 but not after 6 months. Given the severity of pancreatic cancer, exercise recommendations may already commence at surgery.

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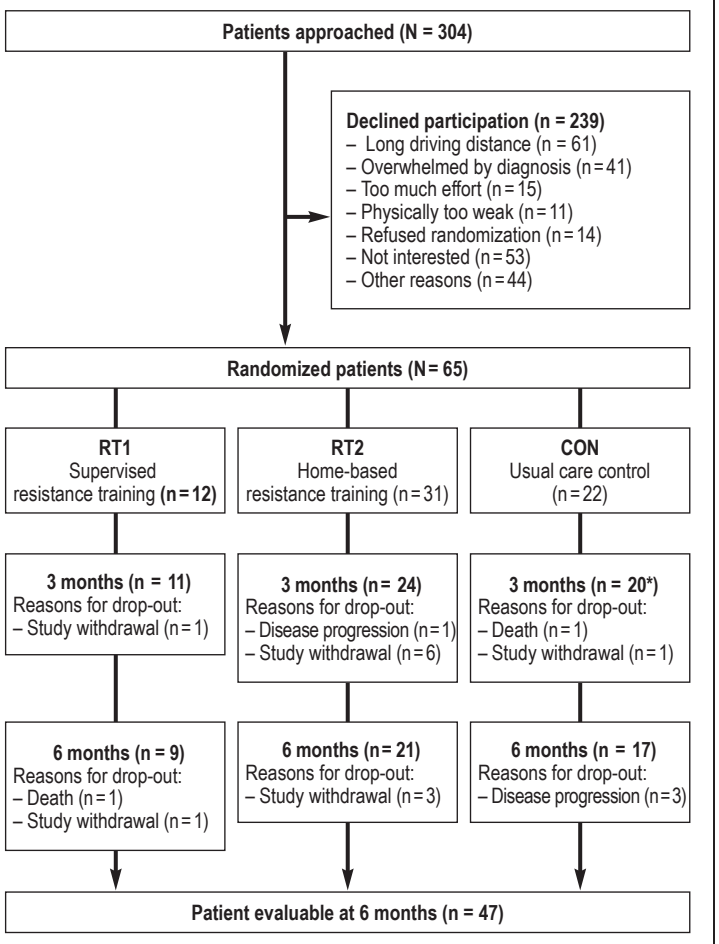
Pancreatic cancer is characterized by aggressive tumor growth with early metastases (1, 2). Further, cancer cachexia and sarcopenia are both ubiquitous characteristics which limit the ability to perform daily activities, compromise patients' quality of life (QoL), and have been associated with poor overall survival (3, 4). Therefore, preservation of physical functioning and health-related QoL are the main treatment goals of supportive cancer care.

Patient QoLvaries significantly depending on stage of disease and treatment phase. Thus, patients in a metastatic disease situation were found to have a lower QoL compared to surgically treated patients (5). Furthermore, patients shortly after surgery have a lower QoL than patients at two months after surgery (6). In the further course—three to six months postoperatively—the patients' QoL seems to stabilize (7, 8).

Physical activity plays an important role in supportive cancer care, as it has positive effects on physical and psychological well-being, both during and after cancer therapy (9). However, most studies on this topic investigated patients in an early stage of the disease, with less aggressive tumors and with a lower symptom burden. Studies including patients with more aggressive or advanced cancers are rare and most of them were conducted with small sample sizes and mixed entities (10, 11).

To date, only two randomized controlled trials (RCTs) have been published on exercise and QoL in

FIGURE 1



CONSORT flow diagram

* including 1 patient who did not complete a questionnaire at 3 months after the start of the study

pancreatic cancer patients (12, 13). A 6-week multimodal intervention (nutritional counseling, aerobic and resistance training, anti-inflammatory medication) in inoperable pancreatic cancer patients (n=20) observed no significant differences for fatigue and physical fitness (12). The second RCT conducted a 3-month home-based walking program among 102 pancreatic cancer patients (13). Although the intervention group improved with respect to fatigue, physical functioning, and QoL between-group comparisons did not reach significance.

The aim of the current study was to investigate the effects of a 6-month resistance training intervention on QoL and fatigue in pancreatic cancer patients. We hypothesized that patients who regularly perform resistance training experience better QoL, better physical functioning, fewer disease-related symptoms, and lower levels of fatigue.

Methods

Study design

Our study, the SUPPORT (Supervised Progressive Resistance Training for Pancreatic Cancer Patients) trial, is a three-arm exercise RCT comparing a supervised progressive resistance training group (RT1), a home-based progressive resistance training group (RT2), and a usual care control group (CON) over a 6-month intervention period. The primary outcome was the subscale physical functioning of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC) core module (C30) (14) at 6 months.

The study was approved by the Ethics Committee of the Medical Faculty of Heidelberg University (S-409/2013) and has been registered on Clinical Trials.gov (NCT01977066). Trials were conducted in accordance with the Declaration of Helsinki and International Council for Harmonization guidelines for good clinical practice. All patients provided written informed consent.

Participants were recruited between December 2013 and December 2015. The inclusion criteria were: resectable or non-resectable pancreatic cancer (stage I-IV); mostly treated at Heidelberg University Hospital or National Center for Tumor Diseases in Heidelberg; age ≥18 years and sufficient German language skills.

As they received identical treatment regimes, patients with adenocarcinoma of the distal bile duct (pancreatic biliary) and with ampullary ductal adenocarcinoma were also eligible. Patients were excluded from the study if they showed insufficient wound healing, impaired hematological capacity (either hemoglobin value <8g/dl or thrombocytes <50 000), heart failure or uncertain arrhythmia, uncontrolled hypertension, severe renal dysfunction (glomerular filtration rate <30%, creatinine >3mg/dl), reduced standing or walking ability, or any other comorbidities, that precluded their participation.

Patients living close to the study center (about <20 km) were randomized to RT1 or CON, while patients living further away were randomly assigned to RT2 or CON. A 2:1 block randomization, stratified by sex and age, with a random number generator and varying block sizes of 3 and 6 was used. Randomization of a patient was done by an independent biometrician according to the pre-specified allocation list.

Outcome measures were collected via self-reported questionnaires prior to the intervention (T0, baseline), at mid-intervention (T1, after 3 months) and post-intervention (T2, after 6 months). Baseline assessments took place at the earliest 3 months after surgical resection to allow for adequate wound healing. For practicability and safety reasons, parts of the study personnel were unblinded.

Intervention

The patients of the two resistance training groups RT1 and RT2 exercised twice a week for approximately 60

TABLE 1

Patient characteristics

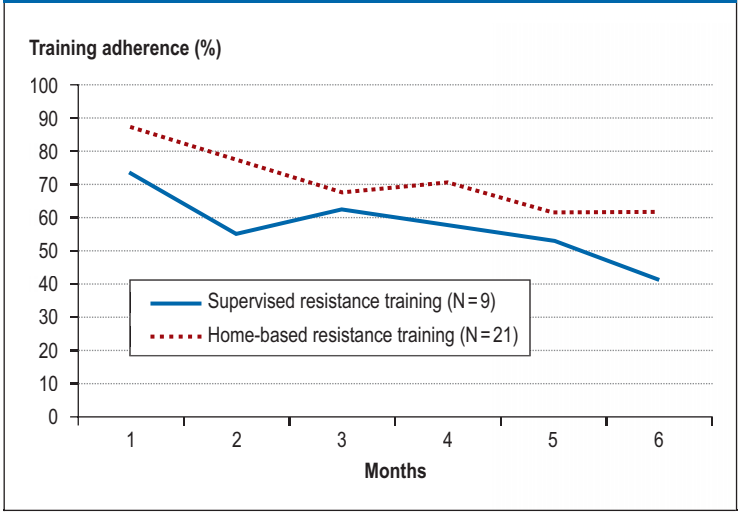
		Supervised resistance training (RT1)		Home-based resistance training (RT2)		Usual care control (CON)	
Total, N		9		21		17	
Men, n (%)		5	55.6%	12	57.1%	8	47.1%
Age, mean (SD)		62.8	(6.4)	61.0	(9.3)	58.7	(8.4)
BMI, mean (SD)		23.5	(3.1)	22.4	(2.9)	25.5	(5.6)
Days since surgery, mean (SD)		92.2	(23.4)	105.9	(41.8)	123.6	(88.9)
Days since first chemotherapy, mean (SD)		31.7	(26.0)	58.2	(46.2)	73.1	(95.6)
Type of adenocarcinoma, n (%)	pancreatic ductal	7	77.8%	20	95.2%	14	82.4%
	distal bile duct*	2	22.2%	1	4.8%	2	11.8%
	ampullary ductal	–	–	–	–	1	5.9%
Stage, n (%)	None	–	–	1	4.8%	–	–
	IA	–	–	1	4.8%	1	5.9%
	IB	2	22.2%	–	–	2	11.8%
	IIA	3	33.3%	3	14.3%	2	11.8%
	IIB	4	44.4%	15	71.4%	12	70.6%
	IV	–	–	1	4.8%	–	–
Management, n (%)	Surgery, adj. CT	8	88.9%	17	81.0%	17	100.0%
	neoadj. CT, surgery	–	–	2	9.5%	–	–
	neoadj. CT, surgery, adj. CT	1	11.1%	1	4.8%	–	–
	CT alone	–	–	1	4.8%	–	–
Operative procedure, n (%)	None	–	–	1	4.8%	–	–
	Total pancreatectomy	0	0.0%	4	19.0%	1	5.9%
	Distal pancreatectomy	2	22.2%	2	9.5%	3	17.6%
	Pancreatoduodenectomy	4	44.4%	7	33.3%	6	35.3%
	Partial PD, pylorus-preserving	3	33.3%	7	33.3%	7	41.2%
Exercise in the year before diagnosis, n (%)	None	2	22.2%	9	42.9%	8	47.1%
	0 – <9 MET×h/week	2	22.2%	2	9.5%	3	17.6%
	9 – <18 MET×h/week	2	22.2%	7	33.3%	4	23.5%
	≥ 18 MET×h/week	3	33.3%	3	14.3%	2	11.8%
Weight loss ≥ 10% during the last 6 months, n (%)		4	44.4%	13	61.9%	8	47.1%

* of pancreaticobiliary type
adj.,adjuvant; BMI, body mass index; CT, chemotherapy; MET, metabolic equivalent; neoadj., neoadjuvant; PD, pancreatoduodenectomy; SD, standard deviation

minutes for 6 months, according to the exercise guidelines of the American College of Sports Medicine for cancer survivors (15). Both resistance training interventions addressed major muscle groups of the upper and lower extremities. After a four-week adaptation phase, patients performed 8 exercises/session with 2–3 sets with 8–12 repetitions. Exercise intensities were of 60–80% One-Repetition Maximum in RT1 and 14–16 on the Borg Scale of Perceived Exertion (16) in RT2.

Detailed information and results on feasibility and efficacy of the resistance training on muscle strength are described elsewhere (17). Both interventions differed primarily by the mode of delivery (therapist-supervised at an exercise facility on weight machines vs. home-based with a training manual exercising at home supported by weekly phone calls). Patients of the control group received usual care in line with their cancer treatment and were advised not to change exercise behavior. Patients were called once a month and asked about possible treatment-related side effects.

FIGURE 2



Training adherence over the 6-month intervention period for supervised (RT1) and home-based (RT2) resistance training

Measurements

Changes in QoL were assessed using the EORTC C30 (14) and the pancreas-specific module (PAN26) (18). The C30 questionnaire covers a total of 30 items with 9 multi-item scales: 5 functional scales (physical, role, cognitive, emotional and social functioning) and 8 symptom scales (fatigue, pain, nausea/vomiting, dyspnea, sleep problems, appetite loss, constipation, and diarrhea), as well as a global health status and QoL scale. The PAN26 consists of 26 items covering 7 multi-item scales.

Cronbach's alpha ranged from 0.7 to 0.9 for all subscales in our study, except for diarrhea (Cronbach's alpha=0.5). After standard transformations, all scales ranged from 0–100. Higher scores indicated more symptoms and worse health-related QoL, with the exception of global health status, C30 functioning scales, and PAN26 satisfaction with health care scale with higher scores indicating better function and better QoL.

Fatigue was assessed using the German version of the Multidimensional Fatigue Inventory (MFI) (19). The validated 20-item questionnaire consists of 5 subscales (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue) ranging from 0 to 20, with higher scores indicating more fatigue (Cronbach's alpha=0.63–0.87).

Clinical data and patient characteristics were extracted and validated from the medical records or assessed by self-report of the patients. Weight and height were measured during the assessments. Additionally, patients reported their exercise behavior in the year before the pancreatic cancer diagnosis.

Statistical analyses

Sample size calculations were based on a two-sided F-test (significance level: $p<0.05$) comparing normal mean differences of 3 groups. Assuming effect sizes (ES) of 0.6 and 0.5 in RT1 and RT2, respectively, and a 25% drop-out rate, recruiting 67 patients per group corresponded to a power (probability of detecting an effect, given that the effect is really there) of 0.82.

Descriptive analyses were based on frequencies or mean values and standard deviations, depending on the scale of the variables. The primary dataset included all patients for which analyzable data were available after 6 months (complete–case analysis). Stability was investigated by comparing results from the complete-case dataset with those from multiple imputation methods (25 datasets). Data for patients who died or had disease progression, preventing further participation, within 6 months, were not substituted during the multiple imputation procedure.

For the primary endpoint (T2), an analysis of covariance (ANCOVA) was performed, with the changes since T0 as the dependent variable, group assignment (according to the intention-to-treat principle) as the independent variable, and the value of the variable at T0 as a covariable. In case of a significant difference between the three groups in the global F-test, paired t-tests were performed within the ANCOVA.

In addition, comparisons of the pooled resistance training group (RT), combining RT1 and RT2, with CON were conducted as exploratory analyses. The ES per training group was calculated by dividing the change from the pretest values to the posttest values by the pretest standard deviation (20, 21). Furthermore, the effects of an additional adjustment to age, sex, body mass index (BMI), time since first chemotherapy, and exercise behavior in the year prior to being diagnosed with pancreatic cancer were investigated. Similar exploratory analyses were performed for all secondary endpoints. The statistical software SAS 9.3 was used for all analyses.

Results

A total of 304 pancreatic cancer patients were approached *(Figure 1)*. Of these, 65 patients were randomized in the study and 47 completed the 6-month intervention phase. The drop-out rate was 22.7% in CON, 25% in RT1 and 32.3% in RT2.

Patients were on average 60.5 years (standard deviation [SD] = 8.4) old. Most patients had a normal weight (mean BMI = 23.7; *SD*=4.3) and were diagnosed with stage IIB cancer (67.4%) *(Table 1)*. More than half of the patients (53.2%) experienced a weight loss of >10% within 6 months before T0. Patients random^zed to the exercise groups performed on average 1.3 weekly training sessions (out of 2) which corresponds to an overall training adherence rate of 66.5%. Among the 47 patients who completed the 6-month intervention phase, training adherence dropped steadily over the 6 months in RT1 and RT2, from initially 73.6% and 87.5%, respectively, to 41.5% and 62.0% *(Figure 2)*. No adverse events occurred during exercise sessions.

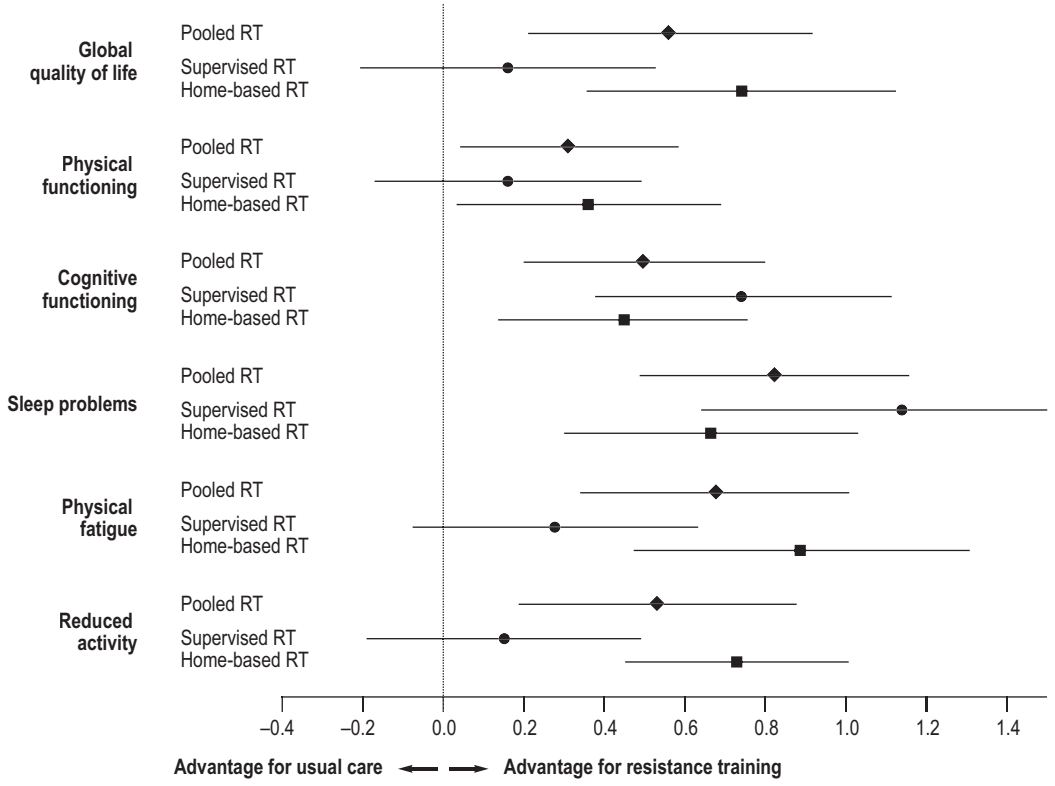
TABLE 2

Patient-reported quality-of-life variables, adjusted comparisons of means und group differences[*1]

Outcome	Group	N[*2]	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) MW (SD)	Baseline to T1			Baseline to T2		
						Adj.[*3] group differences [95% CI]	Comparison RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON; p (global)[*4]	Adj.[*3] group differences [95% CI]	Comparison RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON; p (global)[*4]
Quality-of-life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC)											
Global quality of life	RT	28	58.0 (18.2)	69.5 (18.0)	60.4 (25.0)	**12.1 [2.4; 21.8]**	**0.016**	**0.027**	–2.1 [–15.4; 11.2]	0.749	0.933
	CON	17	53.9 (13.5)	54.9 (19.6)	60.8 (17.1)						
Physical functioning	RT	30	72.8 (19.7)	84.7 (12.5)	79.9 (17.5)	**11.0 [2.2; 19.9]**	**0.016**	**0.050**	0.8 [–8.5; 10.1]	0.858	0.934
	CON	17	65.9 (14.5)	70.2 (22.5)	75.3 (18.2)						
Role functioning	RT	29	58.0 (32.3)	67.8 (25.9)	62.1 (28.8)	4.7 [–11.5; 20.8]	0.564	0.817	–12.4 [–27.2; 2.5]	0.100	0.092
	CON	16	36.5 (19.5)	53.9 (29.8)	63.5 (20.4)						
Cognitive functioning	RT	29	78.7 (19.9)	80.5 (22.3)	75.3 (23.8)	**13.7 [3.7; 23.7]**	**0.008**	**0.022**	4.5 [–7.9; 16.9]	0.465	0.765
	CON	16	77.1 (22.7)	62.7 (25.4)	69.8 (21.3)						
Fatigue	RT	30	50.6 (22.1)	42.1 (20.2)	46.1 (25.4)	-5.9 [–16.7; 4.9]	0.276	0.076	–0.3 [–13.6; 12.9]	0.958	0.857
	CON	17	53.6 (13.7)	50.0 (23.2)	48.7 (24.7)						
Pain	RT	30	31.7 (30.4)	23.9 (27.6)	25.0 (29.6)	–5.4 [–19.5; 8.8]	0.448	0.656	2.3 [–10.8; 15.3]	0.727	0.916
	CON	15	26.7 (30.7)	26.7 (25.8)	20.0 (16.9)						
Sleep problems	RT	30	40.0 (25.4)	31.1 (27.6)	30.0 (25.3)	**–18.9 [–34.0; –3.7]**	**0.016**	**0.022**	–11.9 [–26.7; 3.0]	0.115	0.140
	CON	17	35.3 (24.9)	47.1 (31.3)	39.2 (31.7)						
Multidimensional Fatigue Inventory (MFI)											
General fatigue	RT	30	13.0 (3.2)	11.8 (3.1)	11.6 (4.4)	–0.7 [–2.4; 0.9]	0.379	0.294	–0.7 [–2.9; 1.6]	0.542	0.816
	CON	16	12.4 (2.8)	12.1 (3.8)	11.8 (3.7)						
Physical fatigue	RT	30	13.3 (3.8)	10.0 (3.7)	10.7 (4.7)	**–2.5 [–4.6; –0.4]**	**0.019**	**0.034**	–1.9 [–4.4; 0.7]	0.147	0.222
	CON	16	12.6 (2.9)	12.1 (4.8)	12.1 (4.5)						
Reduced activity	RT	30	11.8 (4.1)	9.7 (3.7)	10.2 (4.5)	**–2.8 [–5.0; –0.5]**	**0.018**	**0.033**	–0.6 [–3.1; 1.8]	0.607	0.878
	CON	14	13.6 (2.4)	13.4 (4.5)	12.3 (5.0)						
Reduced motivation	RT	30	9.2 (3.6)	7.3 (3.0)	8.6 (3.8)	**–1.5 [–2.9; –0.2]**	**0.028**	0.076	–0.2 [–1.9; 1.4]	0.769	0.887
	CON	15	10.1 (4.1)	9.4 (3.6)	9.5 (3.5)						
Mental fatigue	RT	30	9.0 (3.3)	8.1 (3.3)	9.3 (4.6)	−1.0 [–2.7; 0.6]	0.210	0.448	−0.8 [–3.2; 1.6]	0.505	0.775
	CON	16	10.9 (3.8)	10.6 (4.2)	11.3 (4.0)						

*[1]Results of 7 of the altogether 15 subscales of the EORTC; results of all subscales see *eTable 3*; *[2]number of patients with complete information at T2; *[3]adjusted (adj.) on baseline; *[4]following a closed test; diff, difference; CI, confidence interval; CON, control group; RT, pooled resistance training group; RT1, supervised resistance training group; RT2, home-based resistance training group; SD, standard deviation; bold = significant group differences (p<0.05)

FIGURE 3



Effect sizes with 95% confidence intervals for selected quality-of-life variables with statistically significant global test. The figure shows the comparison of the pooled resistance training group (RT) as well as the pairwise comparison of supervised resistance training (RT1) and home-based resistance training (RT2) with the control group after 3 months (T1).

For the primary endpoint, physical functioning, the global test did not indicate an overall between-group difference at 6 months (p=0.93, *Table 2*). However, at month 3, explorative analyses revealed significant global between-group differences *(Table 2)*. Descriptively, physical functioning increased from baseline to the end of the 6-month intervention similarly in both training groups with reaching the maximum after 3 months *(eTable 1)*. In contrast, CON showed a steady increase during intervention. Mean differences (MD) were statistically significant at 3 months compared to CON for the pooled RT group (MD=11.0; p<0.05), as well as for RT2 (MD=11.8; p=0.02), with a similar but non-significant effect for RT1 (MD=9.1; p=0.14) *(Table 2, eTable 1)*. Sensitivity analyses based on further adjustments and multiple imputations yielded similar results *(eTable 2)*.

For secondary outcomes, all global tests were non-significant at 6 months. At 3 months, the global tests and the comparisons of RT with CON indicated significant differences for global QoL, cognitive functioning, sleep problems, physical fatigue, and reduced activity *(Table 2, eTable 3)*.

The subsequently performed pairwise-comparisons with CON showed similar effects for RT1 and RT2 *(eTable 1, Figure 3)*. The absolute values of effect sizes ranged from 0.16 to 1.14. RT2 showed significant between-group changes for all variables but sleep problems (MD=-14.9; p=0.07; ES=-0.66), RT1 for cognitive functioning (MD=17.9; p=0.01; ES=0.74), sleep problems (MD=-28.2; p=0.01; ES=-1.14), and the PAN26 hepatic (MD= –14.5; p=0.003; ES=-1.10). None of the other PAN26 scales indicated additional differences at any time *(eTable 4)*.

Sensitivity analyses yielded similar results *(eTable 2)*. Two variables with significant results in the complete-case analysis showed no significant differences in the imputed analyses (cognitive function and reduced activity), however, with p-values still between 0.05 and 0.1. Vice-versa, two variables had non-significant p-values ≤0.1 in the complete-case analyses with significant p-values after multiple imputation (role function and fatigue).

Discussion

This is the first RCT that investigated the effects of resistance training on QoL in pancreatic cancer patients. After the 6-month intervention period, there were no effects of resistance training on the primary endpoint physical functioning as well as on the other assessed QoL parameters. However, after 3 months, favorable effects of resistance training compared to usual care

were observed for physical functioning, as well as global QoL, cognitive functioning, sleep problems, physical fatigue, and reduced activity. Between-group differences and the corresponding absolute effect sizes of up to 1.14 after 3 months demonstrated the clinical and practical relevance of resistance training on QoL with moderate-to-large effect sizes (20). Both modes of delivery—supervised and home-based resistance training—showed similar effects.

We did not detect any between-group differences after 6 months. One explanation might be that mid-term training effects after 3 months were later cancelled out to some extent by disease progression. In addition, the adherence rate showed a continuous decline over the course of the intervention period.

Our results after 6 months were comparable with those of the previous exercise RCTs which also reported no between-group effects (12, 13). Our results at mid-intervention were in accordance with research regarding QoL and resistance training in cancer patients with other cancer entities (22–24). Meta-analyses, mainly based on breast and prostate cancer, demonstrated that resistance training held beneficial effects for QoL and physical functioning (25, 26). However, our study revealed higher effect sizes that are rather in line with a recent study on patients with colon cancer (27).

The 3-month results of our study on QoL indicate overall positive effects of resistance training. Here, the pairwise analyses for each parameter found comparable effects in the supervised and home-based resistance training groups. This result is highly relevant for the implementation of resistance training interventions in clinical practice, because not all cancer patients have easy access to training facilities, offering supervised training for patients living with cancer.

The present study has several strengths, especially the randomized controlled design, a good adherence rate to the standardized intervention, intention-to-treat analysis, and the use of a multidimensional assessment tool for QoL and fatigue.

A methodological limitation of this study is the limited sample size, resulting in a reduced generalizability. Recruitment difficulties resulted in lower numbers than originally planned (65 randomized patients instead of 201). Comparable recruitment experiences have been reported in a recent study on lung and pancreatic cancer patients (12). On the other hand, the observed effect sizes were partially higher and we applied more powerful statistical methods for the analyses than were used for the sample size calculations. Consequently, our study design was rather conservative. Nevertheless, the interpretation of the study, especially of non-significant results, need to be performed with caution. Another limitation is the monocentric study design. Further, both resistance training groups were not randomized to each other, resulting in unbalanced group sizes.

Key messages

- This is the first randomized controlled trial in patients with pancreatic cancer evaluating the effects of 6-months resistance training on multiple dimensions of quality of life.
- After the 6-month intervention period no between-group differences on QoL parameters were observed.
- After 3 months, clinically relevant improvements in physical functioning as well as global QoL, cognitive functioning, sleep problems, physical fatigue, and reduced activity with moderate-to-large effect sizes were observed.
- The resistance training was feasible in pancreatic cancer patients during and after cancer treatment with a mean training adherence rate of 66.5%. However, the adherence rate steadily decreased over the 6-month intervention period.
- Further measures are required to prolong the positive mid-term exercise effects.

Conclusion

This RCT was the first to show that resistance training may be a promising modality to relieve symptoms, improve physical functioning and QoL in pancreatic cancer patients. Given the high symptom burden and the limited survival time of these patients, we consider even the 3-month results as relevant, so that corresponding exercise recommendations should already be given at diagnosis. Future studies need to focus on prolonging the positive mid-term exercise effects, potentially by maintaining regular training.

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Data sharing
Upon completion of further analyses of the study, the authors are willing to share data with other researchers for scientific purposes. Please address your requests regarding the dataset to the corresponding author.

Conflict of interest
Prof. Steindorf received consultancy fees from Pfizer. She is co-author of the Breast Cancer and Sports brochure published by Pfizer. She received authorship/co-authorship fees for a publication related to the topic from Thieme-Verlag. She received reimbursement of travel expenses and lecture fees form BIC-Krankenkasse Dortmund, from Audi, Bosch, Adviva, and from Asklepios.

Dr. Wiskemann received reimbursement of congress fees and travel expenses as well as lecture fees from Pfizer, Celgene and MSD.

The remaining authors declare no conflict of interest.

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► **Supplementary material**
eTables:
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Supplementary material to:

Quality of Life, Fatigue, and Sleep Problems in Pancreatic Cancer Patients

A Randomized Trial on the Effects of Exercise

by Karen Steindorf*, Dorothea Clauss*, Christine Tjaden, Thilo Hackert, Florian Herbolsheimer, Thomas Bruckner, Lutz Schneider, Cornelia M. Ulrich, and Joachim Wiskemann

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eTABLE 1

Pairwise comparisons and effect sizes for quality-of-life variables with significant global test for the 3-group comparison (see eTable 3)

Outcome	Group	N*1	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)		Baseline to T1			Baseline to T2		
							Adjusted*2 group differences [95% CI]	p (diff)	Effect size	Adjusted*2 group differences [95% CI]	p (diff)	Effect size
Quality-of-life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC)												
Global quality of life	RT1	9	67.6 (12.1)	70.4 (23.2)	63.9 (30.6)	RT1-CON	6.3 [–7.3; 19.9]	0.357	0.16	–3.4 [–22.2; 15.4]	0.720	–0.81
	RT2	19	53.1 (19.3)	69.2 (15.8)	58.8 (22.6)	RT2-CON	**14.4 [4.0; 24.8]**	**0.008**	**0.74**	–1.6 [–16.1; 12.9]	0.824	–0.21
	CON	17	53.9 (13.5)	54.9 (19.6)	60.8 (17.1)							
Physical functioning	RT1	9	75.9 (18.7)	84.4 (16.7)	83.0 (22.9)	RT1-CON	9.1 [–3.0; 21.3]	0.137	0.16	2.2 [–10.6; 15.0]	0.728	–0.27
	RT2	21	71.4 (20.5)	84.8 (10.7)	78.6 (15.1)	RT2-CON	**11.8 [2.3; 21.3]**	**0.016**	**0.36**	0.3 [–9.7; 10.3]	0.957	–0.30
	CON	17	65.9 (14.5)	70.2 (22.5)	75.3 (18.2)							
Cognitive functioning	RT1	9	87.0 (11.1)	90.7 (12.1)	79.6 (28.6)	RT1-CON	**17.9 [4.1; 31.7]**	**0.012**	**0.74**	4.0 [–13.0; 21.1]	0.637	–0.35
	RT2	20	75.0 (22.0)	75.8 (24.5)	73.3 (21.9)	RT2-CON	**12.0 [1.2; 22.8]**	**0.030**	**0.45**	4.8 [–8.8; 18.3]	0.482	0.25
	CON	17	77.1 (22.7)	62.7 (25.4)	69.8 (21.3)							
Sleep problems	RT1	9	40.7 (27.8)	22.2 (23.6)	22.2 (23.6)	RT1-CON	**–28.2 [–48.6; –7.9]**	**0.008**	**–1.14**	–20.1 [–40.1; –0.0]	0.050	–0.82
	RT2	21	39.7 (25.0)	34.9 (28.8)	33.3 (25.8)	RT2-CON	–14.9 [–31.0; 1.2]	0.069	–0.66	–8.4 [–24.2; 7.5]	0.294	–0.41
	CON	17	35.3 (24.9)	47.1 (31.3)	39.2 (31.7)							
Multidimensional Fatigue Inventory (MFI)												
Physical fatigue	RT1	9	12.8 (4.4)	10.7 (4.7)	9.2 (5.6)	RT1-CON	–1.5 [-4.3; 1.3]	0.290	–0.28	–3.0 [–6.4; 0.5]	0.088	–0.62
	RT2	20	13.5 (3.5)	9.7 (3.3)	11.3 (4.2)	RT2-CON	**–3.0 [–5.3; –0.8]**	**0.010**	**–0.89**	–1.4 [–4.1; 1.4]	0.319	–0.47
	CON	17	12.6 (2.9)	12.1 (4.8)	12.1 (4.5)							
Reduced activity	RT1	9	10.9 (4.7)	10.3 (5.4)	9.6 (5.7)	RT1-CON	–1.6 [–4.7; 1.4]	0.291	–0.15	–0.6 [–4.0; 2.7]	0.701	0.27
	RT2	21	12.1 (3.8)	9.5 (2.8)	10.5 (3.9)	RT2-CON	**–3.2 [–5.6; –0.8]**	**0.010**	**–0.73**	–0.6 [–3.3; 2.0]	0.633	0.13
	CON	15	13.6 (2.4)	13.4 (4.5)	12.3 (5.0)							

*1 Number of patients with complete information at T2
*2 adjusted on baseline
diff, difference; CI, confidence interval; CON, control group; RT1, supervised resistance training group; RT2, home-based resistance training group; SD, standard deviation;
bold = significant group differences (p<0.05)

eTABLE 2

Patient-reported quality-of-life variables (all subscales) of the imputed dataset (N = 59 patients*[1]), adjusted pairwise group comparisons and global tests

Outcome	Group	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)		Baseline to T1			Baseline to T2		
						Adjusted*[2] group difference [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*[3]	Adjusted*[2] group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*[3]
Quality-of-life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC)											
Global quality of life	RT1	66.7 (11.2)	67.7 (22.8)	60.9 (32.0)	RT1-CON	3.6 [–9.1; 16.3]	0.572	**0.007**	–6.0 [–26.4; 14.3]	0.553	0.759
	RT2	55.8 (17.5)	71.2 (18.3)	56.8 (28.6)	RT2-CON	**14.7 [4.7; 24.6]**	**0.005**		–5.3 [–20.8; 10.2]	0.495	
	RT	58.7 (16.7)	70.4 (19.9)	58.3 (28.6)	RT-CON	**12.0 [2.5; 21.5]**	**0.015**		–5.7 [–19.9; 8.6]	0.427	
	CON	55.6 (14.9)	56.4 (20.8)	61.9 (20.6)							
Physical functioning	RT1	76.7 (19.0)	84.8 (17.9)	82.4 (24.5)	RT1-CON	8.7 [–3.1; 20.6]	0.146	**0.038**	1.5 [–12.1; 15.1]	0.821	0.951
	RT2	72.7 (18.9)	85.8 (14.3)	78.3 (19.5)	RT2-CON	**11.7 [2.6; 22.9]**	**0.013**		–0.4 [—10.8; 10.0]	0.937	
	RT	73.7 (18.8)	85.2 (15.1)	78.8 (20.6)	RT-CON	**10.9 [2.3; 19.4]**	**0.014**		–0.7 [–10.6; 9.2]	0.889	
	CON	65.2 (14.4)	70.2 (22.5)	74.7 (18.8)							
Role functioning	RT1	66.7 (33.3)	75.0 (33.0)	75.2 (35.9)	RT1-CON	6.4 [–15.9; 28.8]	0.564	0.829	–4.4 [–25.1; 16.3]	0.670	**0.037**
	RT2	52.9 (31.6)	63.2 (28.9)	54.5 (28.6)	RT2-CON	1.3 [–14.8; 17.4]	0.872		**–18.4 [–33.2; –3.5]**	**0.017**	
	RT	56.5 (32.1)	67.0 (31.0)	60.3 (30.8)	RT-CON	3.5 [–12.5; 19.6]	0.662		**–15.8 [–30.5; –1.1]**	**0.036**	
	CON	38.9 (19.8)	55.1 (30.3)	66.1 (23.1)							
Emotional functioning	RT1	76.8 (20.0)	76.3 (21.3)	75.8 (23.4)	RT1-CON	8.8 [–8.2; 25.9]	0.302	0.403	1.8 [–16.6; 20.1]	0.847	0.972
	RT2	51.5 (28.5)	58.3 (28.9)	55.4 (30.7)	RT2-CON	7.9 [–4.9; 20.7]	0.219		1.4 [–11.3; 14.1]	0.827	
	RT	58.3 (28.6)	63.4 (27.6)	60.2 (29.5)	RT-CON	8.5 [–3.1; 20.1]	0.149		1.1 [–10.7; 12.9]	0.854	
	CON	57.9 (25.3)	54.7 (29.3)	59.1 (33.5)							
Cognitive functioning	RT1	83.3 (19.7)	86.0 (22.0)	75.5 (32.1)	RT1-CON	**15.1 [1.3; 29.0]**	**0.033**	0.087	1.7 [–15.7; 19.2]	0.845	0.959
	RT2	75.7 (20.6)	73.0 (26.6)	70.7 (25.2)	RT2-CON	8.3 [–2.9; 19.4]	0.143		1.9 [–11.3; 15.0]	0.777	
	RT	77.7 (20.4)	76.6 (26.3)	71.5 (28.1)	RT-CON	10.0 [–0.5; 20.6]	0.062		1.5 [–11.2; 14.2]	0.814	
	CON	75.0 (26.4)	64.2 (26.1)	68.3 (24.5)							
Social functioning	RT1	62.1 (30.8)	76.8 (26.5)	74.3 (33.1)	RT1-CON	10.0 [–9.8; 29.8]	0.314	0.490	5.6 [–17.5; 28.7]	0.626	0.217
	RT2	46.2 (27.5)	55.5 (34.4)	49.0 (34.1)	RT2-CON	–0.7 [–16.2; 14.7]	0.923		–11.4 [–28.9; 6.2]	0.199	
	RT	50.3 (28.8)	61.4 (34.5)	56.0 (35.9)	RT-CON	2.9 [–11.9; 17.6]	0.697		–6.8 [–23.4; 9.8]	0.415	
	CON	53.6 (30.6)	61.1 (30.2)	64.2 (32.3)							

Outcome	Group	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)		Baseline to T1			Baseline to T2		
						Adjusted*2 group difference [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3	Adjusted*2 group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3
Fatigue	RT1	39.4 (21.9)	43.6 (22.5)	36.8 (32.6)	RT1-CON	4.9 [–8.8; 18.6]	0.473	**0.015**	–2.1 [–21.6; 17.4]	0.831	0.883
	RT2	54.5 (21.1)	39.2 (24.6)	51.7 (29.5)	RT2-CON	**–11.5 [–21.9; –1.0]**	**0.032**		2.2 [–12.4; 16.8]	0.761	
	RT	50.4 (22.0)	40.6 (24.3)	47.6 (29.3)	RT-CON	–7.7 [–18.3; 3.0]	0.155		1.6 [–11.9; 15.1]	0.812	
	CON	53.1 (13.5)	49.6 (23.3)	48.5 (25.4)							
Nausea, vomiting	RT1	3.0 (10.1)	2.1 (11.8)	1.2 (12.2)	RT1-CON	–10.1 [–25.4; 5.3]	0.193	0.389	–1.8 [–15.2; 11.6]	0.790	0.373
	RT2	14.5 (18.7)	9.1 (22.1)	9.8 (21.1)	RT2-CON	–5.8 [–17.5; 5.9]	0.327		5.5 [–4.5; 15.4]	0.275	
	RT	11.6 (17.4)	6.8 (20.8)	7.1 (19.6)	RT-CON	–8.0 [–19.6; 3.6]	0.171		3.2 [–6.4; 12.7]	0.514	
	CON	14.8 (17.0)	15.0 (21.8)	4.4 (10.8)							
Pain	RT1	19.7 (29.6)	20.6 (29.9)	19.8 (30.2)	RT1-CON	–2.6 [–21.1; 15.9]	0.779	0.658	–0.4 [–19.6; 18.8]	0.967	0.927
	RT2	35.7 (28.6)	25.0 (31.3)	25.2 (34.0)	RT2-CON	–6.7 [–21.8; 8.4]	0.380		–2.8 [–18.1; 12.6]	0.720	
	RT	31.7 (29.9)	24.3 (30.6)	24.1 (31.1)	RT-CON	–5.5 [–19.9; 9.0]	0.451		–2.3 [–16.2; 11.6]	0.739	
	CON	25.4 (33.9)	26.2 (24.6)	23.1 (20.7)							
Dyspnea	RT1	18.2 (22.9)	20.0 (26.3)	4.3 (23.8)	RT1-CON	–5.1 [–28.0; 17.7]	0.653	0.848	–22.6 [–46.1; 0.9]	0.060	0.140
	RT2	32.4 (31.0)	25.3 (34.9)	25.3 (32.5)	RT2-CON	–4.8 [–23.1; 13.5]	0.598		–4.6 [–22.5; 13.4]	0.612	
	RT	28.8 (30.1)	23.3 (29.5)	19.0 (34.6)	RT-CON	–5.9 [–21.6; 9.8]	0.453		–10.0 [–27.9; 7.9]	0.267	
	CON	27.8 (26.2)	28.5 (30.5)	28.9 (35.9)							
Sleep problems	RT1	36.4 (27.7)	19.8 (27.7)	18.3 (30.2)	RT1-CON	**–28.3 [–48.8; –7.8]**	**0.008**	**0.020**	–20.9 [–41.8; 0.1]	0.051	0.139
	RT2	34.4 (28.3)	31.5 (36.2)	30.4 (33.1)	RT2-CON	–15.4 [–31.5; 0.7]	0.061		–7.6 [–23.5; 8.3]	0.340	
	RT	35.0 (27.8)	27.6 (34.1)	26.0 (34.2)	RT-CON	**–19.8 [–34.9; –4.8]**	**0.011**		–12.4 [–28.6; 3.8]	0.130	
	CON	35.2 (24.2)	47.3 (31.4)	38.4 (32.0)							
Appetite loss	RT1	24.2 (33.6)	12.9 (32.9)	1.8 (24.7)	RT1-CON	–2.7 [–23.3; 17.9]	0.792	0.960	–10.4 [–35.1; 14.3]	0.400	0.397
	RT2	36.1 (38.6)	19.5 (30.5)	19.6 (37.2)	RT2-CON	–0.2 [–17.2; 16.7]	0.978		5.2 [–14.2; 24.6]	0.591	
	RT	33.4 (36.4)	17.2 (31.7)	14.1 (33.6)	RT-CON	–2.0 [–18.3; 14.2]	0.801		–0.5 [–17.8; 16.9]	0.956	
	CON	18.5 (28.5)	13.6 (27.3)	11.2 (29.6)							
Constipation	RT1	3.0 (10.1)	16.4 (32.0)	14.4 (34.4)	RT1-CON	10.4 [–6.5; 27.4]	0.223	0.345	3.9 [–15.5; 23.4]	0.685	0.384
	RT2	26.7 (32.0)	20.4 (31.4)	9.9 (26.8)	RT2-CON	–1.2 [–15.3; 12.9]	0.865		–8.1 [–24.4; 8.1]	0.318	
	RT	20.3 (29.7)	19.4 (32.4)	11.4 (27.7)	RT-CON	2.0 [–11.4; 15.3]	0.770		–3.6 [–17.9; 10.6]	0.611	
	CON	7.4 (18.3)	8.9 (20.4)	11.9 (24.1)							

Outcome	Group	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)		Baseline to T1			Baseline to T2		
						Adjusted*2 group difference [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3	Adjusted*2 group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3
Diarrhea	RT1	21.2 (22.5)	31.1 (42.4)	22.8 (41.5)	RT1-CON	3.0 [–18.0; 23.9]	0.778	0.905	–3.2 [–27.6; 21.1]	0.791	0.720
	RT2	34.9 (34.3)	36.3 (38.0)	40.7 (42.8)	RT2-CON	–1.5 [–18.7; 15.7]	0.864		5.5 [–13.9; 24.8]	0.571	
	RT	31.1 (32.0)	34.9 (37.1)	35.6 (48.1)	RT-CON	–0.5 [–15.8; 14.8]	0.949		2.9 [–17.0; 22.7]	0.771	
	CON	22.2 (32.3)	28.8 (28.1)	26.7 (31.5)							
Financial difficulties	RT1	18.2 (27.3)	18.1 (29.6)	13.5 (37.5)	RT1-CON	–8.9 [–28.2; 10.5]	0.362	0.363	–9.7 [–31.9; 12.4]	0.381	0.572
	RT2	28.9 (33.6)	24.6 (38.3)	32.3 (39.6)	RT2-CON	–10.9 [–27.2; 5.5]	0.185		1.0 [–17.2; 19.2]	0.912	
	RT	26.0 (32.1)	22.7 (34.4)	26.1 (39.3)	RT-CON	–9.5 [–23.4; 4.4]	0.174		–3.2 [–19.2; 12.7]	0.686	
	CON	18.5 (30.7)	27.3 (36.2)	23.5 (35.5)							
Multidimensional Fatigue Inventory (MFI)											
General fatigue	RT1	11.8 (3.5)	11.8 (3.5)	10.6 (5.6)	RT1-CON	0.1 [–2.1; 2.3]	0.917	0.144	–0.7 [–3.8; 2.4]	0.648	0.884
	RT2	13.4 (3.0)	11.4 (3.7)	11.9 (4.7)	RT2-CON	–1.5 [–3.2; 0.3]	0.099		–0.5 [–3.0; 2.1]	0.699	
	RT	13.0 (3.2)	11.5 (3.7)	11.5 (4.8)	RT-CON	–1.0 [–2.7; 0.7]	0.234		–0.5 [–2.8; 1.8]	0.657	
	CON	12.4 (2.7)	12.1 (3.8)	11.7 (3.8)							
Physical fatigue	RT1	13.3 (4.1)	11.1 (4.5)	9.5 (5.6)	RT1-CON	–1.4 [–4.1; 1.2]	0.282	**0.006**	–2.9 [–6.3; 0.5]	0.096	0.261
	RT2	13.7 (3.7)	9.5 (4.3)	11.2 (5.5)	RT2-CON	**–3.4 [–5.5; –1.2]**	**0.003**		–1.5 [–4.4; 1.4]	0.312	
	RT	13.6 (3.8)	10.0 (4.2)	10.8 (5.3)	RT-CON	**–2.8 [–4.8; –0.7]**	**0.010**		–1.8 [–4.4; 0.8]	0.169	
	CON	12.7 (2.9)	12.1 (4.8)	12.1 (4.6)							
Reduced activity	RT1	11.4 (4.5)	10.4 (5.3)	9.6 (5.7)	RT1-CON	–1.3 [–4.3; 1.8]	0.411	0.065	–1.2 [–4.6; 2.2]	0.481	0.675
	RT2	12.3 (3.8)	9.5 (3.9)	10.4 (4.9)	RT2-CON	**–2.7 [–4.9; –0.4]**	**0.022**		–1.1 [–3.7; 1.6]	0.421	
	RT	12.0 (4.0)	9.7 (4.1)	10.2 (5.1)	RT-CON	**–2.5 [–4.6; –0.3]**	**0.029**		–0.9 [–3.3; 1.5]	0.457	
	CON	13.5 (2.2)	12.9 (4.5)	12.4 (5.0)							
Reduced motivation	RT1	9.2 (3.4)	7.3 (3.4)	8.0 (4.3)	RT1-CON	–1.5 [–3.4; 0.4]	0.119	0.106	–0.8 [–3.0; 1.4]	0.465	0.701
	RT2	9.5 (3.9)	7.5 (3.5)	9.0 (4.1)	RT2-CON	**–1.5 [–2.9; –0.0]**	**0.048**		0.0 [–1.7; 1.7]	0.980	
	RT	9.4 (3.7)	7.5 (3.3)	8.7 (4.1)	RT-CON	**–1.5 [–2.9; –0.1]**	**0.035**		–0.1 [–1.8; 1.5]	0.855	
	CON	9.9 (4.0)	9.3 (3.6)	9.3 (3.5)							
Mental fatigue	RT1	7.3 (2.5)	6.6 (2.5)	7.7 (4.8)	RT1-CON	–1.5 [–3.7; 0.8]	0.191	0.372	–1.2 [–4.6; 2.3]	0.506	0.801
	RT2	10.1 (4.0)	9.1 (4.0)	10.1 (5.3)	RT2-CON	–1.0 [–2.7; 0.8]	0.272		–0.5 [–3.1; 2.0]	0.682	
	RT	9.3 (3.9)	8.5 (3.8)	9.4 (5.0)	RT-CON	–1.0 [–2.6; 0.6]	0.210		–0.7 [–3.1; 1.7]	0.546	
	CON	10.9 (3.7)	10.6 (4.2)	11.1 (4.1)							

*1 n = 11 in RT1; n = 30 in RT2; n = 18 in CON
*2 adjusted on baseline
*3 following a closed test
diff, difference; CI, confidence interval; CON, control group; RT, pooled resistance training group; RT1, supervised resistance training group; RT2, home-based resistance training group; SD, standard deviation; bold = significant group differences (p<0.05)

eTABLE 3

Patient-reported quality-of-life variables (all subscales), adjusted comparisons of means and group differences

Outcome	Group	N*[1]	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)	Baseline to T1			Baseline to T2		
						Adjusted*[2] group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*[3]	Adjusted*[2] group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*[3]
Quality-of-life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC)											
Global quality of life	RT	28	58.0 (18.2)	69.5 (18.0)	60.4 (25.0)	**12.1 [2.4; 21.8]**	**0.016**	**0.027**	–2.1 [–15.4; 11.2]	0.749	0.933
	CON	17	53.9 (13.5)	54.9 (19.6)	60.8 (17.1)						
Physical functioning	RT	30	72.8 (19.7)	84.7 (12.5)	79.9 (17.5)	**11.0 [2.2; 19.9]**	**0.016**	**0.050**	0.8 [–8.5; 10.1]	0.858	0.934
	CON	17	65.9 (14.5)	70.2 (22.5)	75.3 (18.2)						
Role functioning	RT	29	58.0 (32.3)	67.8 (25.9)	62.1 (28.8)	4.7 [–11.5; 20.8]	0.564	0.817	–12.4 [–27.2; 2.5]	0.100	0.092
	CON	16	36.5 (19.5)	53.9 (29.8)	63.5 (20.4)						
Emotional functioning	RT	30	60.8 (30.3)	64.8 (26.2)	62.5 (26.3)	8.9 [–3.3; 21.1]	0.150	0.319	0.5 [–10.8; 11.7]	0.933	0.962
	CON	16	57.3 (23.1)	52.5 (27.4)	59.9 (28.7)						
Cognitive functioning	RT	29	78.7 (19.9)	80.5 (22.3)	75.3 (23.8)	**13.7 [3.7; 23.7]**	**0.008**	**0.022**	4.5 [–7.9; 16.9]	0.465	0.765
	CON	16	77.1 (22.7)	62.7 (25.4)	69.8 (21.3)						
Social functioning	RT	29	47.7 (29.8)	57.5 (32.3)	55.7 (33.1)	1.6 [–12.5; 15.7]	0.820	0.668	–2.9 [–19.5; 13.6]	0.724	0.375
	CON	16	51.0 (29.5)	58.3 (28.5)	60.4 (30.4)						
Fatigue	RT	30	50.6 (22.1)	42.1 (20.2)	46.1 (25.4)	–5.9 [–16.7; 4.9]	0.276	0.076	–0.3 [–13.6; 12.9]	0.958	0.857
	CON	17	53.6 (13.7)	50.0 (23.2)	48.7 (24.7)						
Nausea, vomiting	RT	30	10.9 (17.4)	7.5 (16.4)	8.3 (17.4)	–7.3 [–18.6; 4.0]	0.198	0.404	4.0 [–5.3; 13.3]	0.386	0.284
	CON	17	14.7 (17.6)	15.7 (21.6)	4.9 (9.8)						
Pain	RT	30	31.7 (30.4)	23.9 (27.6)	25.0 (29.6)	–5.4 [–19.5; 8.8]	0.448	0.656	2.3 [–10.8; 15.3]	0.727	0.916
	CON	15	26.7 (30.7)	26.7 (25.8)	20.0 (16.9)						
Dyspnea	RT	30	31.1 (28.9)	25.6 (25.8)	20.0 (20.7)	–4.4 [–20.0; 11.2]	0.572	0.782	–9.7 [–26.0; 6.5]	0.233	0.180
	CON	17	29.4 (26.0)	29.4 (28.6)	29.4 (35.1)						
Sleep problems	RT	30	40.0 (25.4)	31.1 (27.6)	30.0 (25.3)	**–18.9 [–34.0; –3.7]**	**0.016**	**0.022**	–11.9 [–26.7; 3.0]	0.115	0.140
	CON	17	35.3 (24.9)	47.1 (31.3)	39.2 (31.7)						
Appetite loss	RT	30	33.3 (39.1)	18.9 (28.6)	15.6 (27.3)	–0.1 [–15.4; 15.2]	0.992	1.000	0.8 [–16.0; 17.6]	0.927	0.448
	CON	17	19.6 (29.0)	13.7 (26.5)	11.8 (28.7)						
Constipation	RT	30	18.9 (29.9)	21.1 (29.7)	10.0 (23.4)	4.7 [–8.7; 18.1]	0.486	0.411	–5.5 [–19.1; 8.2]	0.426	0.418
	CON	17	7.8 (18.7)	9.8 (19.6)	11.8 (23.4)						

Outcome	Group	N*1	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)	Baseline to T1			Baseline to T2		
						Adjusted*2 group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3	Adjusted*2 group differences [95% CI]	Comparison between RT and CON p (diff)	Global test for the differences between RT1, RT2 and CON p (global)*3
Diarrhea	RT	28	32.2 (32.7)	35.6 (35.6)	38.1 (37.1)	–0.0 [–15.9; 15.8]	0.997	0.994	5.0 [–12.3; 22.4]	0.561	0.503
	CON	17	19.6 (31.3)	27.5 (27.0)	25.5 (30.1)						
Financial difficulties	RT	29	27.8 (34.0)	23.3 (32.9)	27.6 (34.6)	–6.8 [–18.6; 4.9]	0.249	0.485	–4.3 [–19.5; 10.8]	0.569	0.565
	CON	17	17.6 (31.4)	22.9 (31.5)	23.5 (34.9)						
Multidimensional Fatigue Inventory (MFI)											
General fatigue	RT	30	13.0 (3.2)	11.8 (3.1)	11.6 (4.4)	–0.7 [–2.4; 0.9]	0.379	0.294	–0.7 [–2.9; 1.6]	0.542	0.816
	CON	16	12.4 (2.8)	12.1 (3.8)	11.8 (3.7)						
Physical fatigue	RT	30	13.3 (3.8)	10.0 (3.7)	10.7 (4.7)	**–2.5 [–4.6; –0.4]**	**0.019**	**0.034**	–1.9 [–4.4; 0.7]	0.147	0.222
	CON	16	12.6 (2.9)	12.1 (4.8)	12.1 (4.5)						
Reduced activity	RT	30	11.8 (4.1)	9.7 (3.7)	10.2 (4.5)	**–2.8 [–5.0; –0.5]**	**0.018**	**0.033**	–0.6 [–3.1; 1.8]	0.607	0.878
	CON	14	13.6 (2.4)	13.4 (4.5)	12.3 (5.0)						
Reduced motivation	RT	30	9.2 (3.6)	7.3 (3.0)	8.6 (3.8)	**–1.5 [–2.9; –0.2]**	**0.028**	0.076	–0.2 [–1.9; 1.4]	0.769	0.887
	CON	15	10.1 (4.1)	9.4 (3.6)	9.5 (3.5)						
Mental fatigue	RT	30	9.0 (3.3)	8.1 (3.3)	9.3 (4.6)	–1.0 [–2.7; 0.6]	0.210	0.448	–0.8 [–3.2; 1.6]	0.505	0.775
	CON	16	10.9 (3.8)	10.6 (4.2)	11.3 (4.0)						

*1 Number of patients with complete information at T2
*2 adjusted on baseline
*3 following a closed test
diff, difference; RT, pooled resistance training group; CI, confidence interval; CON, control group; RT1, supervised resistance training group; RT2, home-based resistance training group; SD, standard deviation; bold = significant group differences (p<0.05)

eTABLE 4

Patient-reported quality-of-life variables of the EORTC QLQ-PAN26 Pancreatic-specific Module, adjusted comparisons of means and group differences

PAN26 subscales	Group	N*[1]	Start of intervention Baseline (T0) Mean (SD)	Middle of intervention after 3 months (T1) Mean (SD)	End of intervention after 6 months (T2) Mean (SD)		Baseline to T1			Baseline to T2		
							Adjusted*[2] group differences [95% CI]	p (diff)	Global test for the differences between RT1, RT2 and CON p (global)	Adjusted*[2] group differences [95% CI]	p (diff)	Global test for the differences between RT1, RT2 and CON p (global)
Pancreatic pain	RT1	9	22.2 (19.1)	19.8 (20.8)	17.6 (19.3)	RT1-CON	–6.8 [–23.4; 9.8]	0.412	0.655	–10.4 [–27.5; 6.8]	0.229	0.467
	RT2	21	36.5 (25.9)	26.2 (21.8)	28.2 (24.8)	RT2-CON	–4.8 [–18.4; 8.7]	0.474		–5.1 [–19.1; 8.9]	0.467	
	CON	17	23.5 (21.9)	27.0 (20.1)	28.4 (19.8)							
Digestion	RT1	30	27.8 (31.2)	18.5 (24.2)	11.1 (16.7)	RT1-CON	–12.8 [–35.7; 10.1]	0.264	0.521	–16.8 [–39.5; 5.9]	0.143	0.195
	RT2	16	33.3 (25.8)	33.3 (27.9)	38.1 (29.9)	RT2-CON	–6.1 [–25.7; 13.4]	0.529		3.9 [–15.4; 23.2]	0.685	
	CON	16	33.3 (25.8)	33.3 (27.9)	29.2 (28.2)							
Altered bowel habits	RT1	30	37.0 (26.1)	37.0 (30.9)	42.6 (38.3)	RT1-CON	–9.9 [–31.6; 11.8]	0.363	0.438	3.5 [–14.4; 21.5]	0.692	0.562
	RT2	20	56.7 (33.1)	47.5 (31.2)	49.2 (30.5)	RT2-CON	–10.9 [–29.0; 7.2]	0.232		–5.5 [–20.4; 9.4]	0.459	
	CON	17	37.3 (28.0)	47.1 (31.3)	39.2 (28.8)							
Hepatic symptoms	RT1	29	18.5 (19.4)	1.9 (5.6)	7.4 (8.8)	RT1-CON	**–14.5 [–23.7; –5.3]**	**0.003**	**0.008**	–2.8 [–12.1; 6.6]	0.554	0.697
	RT2	21	11.9 (21.2)	10.3 (19.3)	9.2 (12.7)	RT2-CON	–2.1 [–9.3; 5.1]	0.559		1.0 [–6.3; 8.3]	0.783	
	CON	17	5.9 (11.7)	8.8 (12.0)	6.9 (11.9)							
Body image	RT1	28	18.5 (21.2)	20.4 (18.2)	24.1 (20.6)	RT1-CON	–3.3 [–24.0; 17.4]	0.750	0.947	4.4 [–17.8; 26.6]	0.692	0.903
	RT2	20	55.8 (27.2)	45.0 (27.6)	43.9 (35.2)	RT2-CON	–0.3 [–16.7; 16.2]	0.974		–0.7 [–18.2; 16.9]	0.939	
	CON	16	40.6 (25.8)	36.5 (31.2)	35.3 (28.2)							
Health care satisfaction	RT1	8	68.8 (27.4)	77.1 (36.7)	75.0 (46.3)	RT1-CON	7.1 [–21.0; 35.2]	0.610	0.864	3.6 [–25.1; 32.4]	0.798	0.897
	RT2	18	74.1 (19.2)	72.2 (26.2)	69.6 (25.8)	RT2-CON	1.1 [–21.5; 23.6]	0.924		–2.4 [–26.1; 21.2]	0.834	
	CON	13	76.9 (25.0)	71.8 (32.2)	73.6 (24.1)							
Sexuality	RT1	7	42.9 (30.2)	33.3 (25.5)	38.1 (24.9)	RT1-CON	–3.6 [–31.8; 24.7]	0.798	0.358	11.2 [–15.9; 38.3]	0.405	0.169
	RT2	13	48.7 (34.3)	50.0 (30.4)	48.8 (31.7)	RT2-CON	13.6 [–10.8; 38.1]	0.263		21.7 [–1.2; 44.5]	0.062	
	CON	11	31.8 (27.3)	37.9 (25.9)	25.8 (20.2)							

*[1] Number of patients with complete information at T2; *[2] adjusted on baseline

diff. difference; EORTC, European Organization for Research and Treatment of Cancer; SD, standard deviation; CI, confidence interval; CON, control group; RT1, supervised resistance training group RT2, home-based resistance training group; bold = significant group differences (p<0.05)