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Physical activity and exercise during preoperative pancreatic cancer treatment

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Abstract

Purpose
Guidelines recommend exercise to cancer survivors, but limited data exists regarding exercise among patients undergoing preoperative cancer treatment. We examined differences in weekly self-reported exercise and accelerometer-measured physical activity among participants in a home-based exercise program administered during preoperative treatment for pancreatic cancer.

Methods
Participants were encouraged to perform at least 60 min/week of moderate-intensity aerobic exercise and at least 60 min/week of full-body strengthening exercises concurrent with chemotherapy, chemoradiation therapy or both sequentially and received resistance equipment, program instruction, and biweekly follow-up calls to encourage adherence. Self-reported aerobic and strengthening exercise minutes were measured using daily logs, and physical activity was measured objectively using accelerometers.

Results
Fifty participants (48% female, mean age 66 ± 8 years) participated for an average of 16 ± 9 preoperative weeks. Participants reported overall means of 126 ± 83 weekly minutes of aerobic exercise and 39 ± 33 weekly minutes of strengthening exercise in daily logs. Participants performed 158.7 ± 146.7 weekly minutes of accelerometer-measured moderate-to-vigorous physical activity. There were no significant differences in exercise or physical activity between treatment phases.

Conclusions
These findings suggest that it is feasible to target the entire preoperative course for exercise prescription. Although participants exceeded aerobic exercise recommendations on average, we observed low strengthening exercise adherence and wide variability in self-reported exercise and accelerometer physical activity variables. These findings suggest that additional support, including program adaptations, may be necessary to overcome barriers to exercise or improve motivation when prescribing exercise in this clinical scenario.

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Introduction

Guidelines published by the American Cancer Society (ACS) and the American College of Sports Medicine (ACSM) provide exercise recommendations to cancer survivors that generally mirror those for healthy adults [1, 2]. These guidelines recommend at least 150 min of moderate-intensity exercise or 75 min of vigorous-intensity exercise, or an equivalent combination, along with at least two strengthening sessions for major muscle groups each week. Although these guidelines are less concrete for people who are actively undergoing cancer treatment than for those who have completed therapy, they recommend that all people with cancer exercise and suggest that healthcare teams adapt exercise prescriptions on the basis of each individual's health status, anticipated disease trajectory, and treatments received [2].

People with pancreatic cancer are generally older and frequently present with age- and disease-associated conditions, including obesity, frailty, sarcopenia, and cachexia [3–6]. For some people with pancreatic cancer, a multimodality treatment strategy that includes surgery may be curative [7]. However, pancreatic operations are generally associated with a significant risk for postoperative complications, an arduous postoperative recovery, and long-term effects on normal physiology and quality of life [8–11]. Moreover, chemotherapy, chemoradiation therapy, or a sequence of both is increasingly administered prior to pancreatic cancer surgery [3, 5, 12, 13]. These treatments may be difficult for older adults with age- and disease-related comorbidities to tolerate, and may themselves be adversely associated with loss of skeletal muscle and physical fitness that further affect both treatment outcomes and survivorship [5, 14–16].

Interventions designed to optimize health and fitness prior to pancreatic cancer surgery therefore have a strong rationale. In the perioperative setting, the value of exercise has long been recognized, but enthusiasm has only recently shifted from the prioritization of exercise in the postoperative period (*rehabilitation*) to the preoperative period (*prehabilitation*) [17–19]. When prescribed prior to therapy, exercise has been suggested to reduce surgical complications, accelerate recovery, and facilitate the delivery of other necessary cancer treatments [18–20]. Prior studies that have evaluated the efficacy of exercise prescribed simultaneously with preoperative therapies for any cancer diagnosis are few [21, 22], however, and these have focused exclusively on people with breast, prostate, and colorectal cancer. Only one—a small pilot study we previously conducted—has evaluated exercise during preoperative therapy for pancreatic cancer [23]. A significant gap therefore exists in our understanding of the volume of exercise that can be realistically and safely prescribed among the generally older, more infirm group of patients with pancreatic cancer concurrent with the administration of potentially toxic therapies.

We aimed to measure both exercise (here defined as physical activity performed for training benefits, i.e., time spent intentionally performing aerobic or strengthening exercise) and physical activity (here defined as all bodily movement, i.e., including intentional exercise and as measured by a continuously worn accelerometer) in this context. Moreover, we have hypothesized that the levels of exercise and physical activity might vary during different types of cancer therapies due to differences in their toxicity profiles, schedules of delivery, and logistics of administration. To fill this knowledge gap and test our hypothesis, we employed both subjective and objective strategies to measure exercise and physical activity among patients with pancreatic cancer who participated in a home-based exercise program administered concurrent with preoperative chemotherapy and/or chemoradiation therapy.

Methods

Study setting and participants

Recruitment for this prospective, single-arm study (ClinicalTrials.gov identifier NCT02295956) took place at The University of Texas MD Anderson Cancer Center, a comprehensive cancer center in Houston, TX [24]. All study activities were approved by the MD Anderson Institutional Review Board under protocol #2014-0702. Informed consent was obtained from all individual participants included in the study. Participants were recruited as they presented for pancreatic cancer treatment planning between February 2015 and January 2017. Eligibility requirements were the following: biopsy-proven diagnosis of pancreatic adenocarcinoma; treatment plan including the administration of systemic chemotherapy, chemoradiation therapy, or both for at least 6 weeks prior to anticipated pancreatectomy; English fluency; telephone access; and willingness to participate in follow-up phone calls. Exclusion criteria were underlying and unstable cardiac or pulmonary disease or symptomatic cardiac disease (New York Heart Association functional class of III or IV), recent fracture or acute musculoskeletal injury that precluded ability to exercise using all four limbs, self-reported pain rating of at least 7 on a scale of 10, or myopathic or rheumatologic disease that limited physical function.

All interested patients completed the Physical Activity Readiness Questionnaire (PAR-Q) [25]. Patients who reported chest pain, dizziness, loss of balance or loss of consciousness during physical activity, or chest pain at rest on the PAR-Q were ineligible for enrollment. Patients reporting cardiac or musculoskeletal concerns required clearance by appropriate physicians. Radiographic disease stage at presentation [26], pre-existing comorbidity [27], and performance status [28] were coded according to established guidelines by trained physicians and were extracted from participants' electronic medical records. Significant weight loss was noted for patients who reported ≥ 3 kg of weight loss in the previous 3 months at baseline and/or preoperative restaging [29].

Preoperative therapy

Participants were prescribed exercise concurrent with the administration of systemic chemotherapy, chemoradiation therapy, or a sequence of both (Fig. 1). The specific regimen and duration of therapy were individualized. Each regimen was followed by a break of 2–6 weeks off therapy prior to surgical consideration. Partial pancreatic resection was performed for selected participants who did not manifest clinical evidence of disease progression during therapy. Historically, approximately 50–75% of patients treated with this approach have proceeded with surgery [30].

Exercise program

As previously described, participants engaged in a multimodal, home-based exercise program that included both aerobic and strengthening exercise components [23]. Participants initiated exercise upon enrollment and were encouraged to continue for the duration of preoperative therapy (Fig. 1). The program was based on guidelines published by the ACS and ACSM for cancer survivors [1, 2], but with prescriptions attenuated to a minimum total of 120 weekly minutes of moderate-intensity exercise (60 min aerobic, 60 min strengthening) to accommodate exercise intervention concurrent with active therapy. Participants received comprehensive instruction from study staff explaining the exercise prescription and demonstrating proper form for strengthening exercises. Participants were called by research staff at least once every 2 weeks to encourage adherence, monitor for adverse events, and address questions.

Participants were encouraged to walk briskly or perform preferred aerobic exercise (e.g., stationary cycling or elliptical training) for at least 20 min per day on at least 3 days per week. Participants were encouraged to maintain moderate aerobic exercise intensity aerobic exercise, corresponding to ratings of 12–13 on the Borg Rating of Perceived Exertion scale [31]. Participants were encouraged to accumulate aerobic exercise in bouts of ≥ 10 consecutive minutes [32]. Participants

were also encouraged to perform strengthening exercises for at least 30 min per day at least 2 days per week. Prescribed strengthening exercises engaged most major muscle groups, including the proximal upper arms, shoulders, abdominals, back extensors, hips, and legs. Participants received graded resistance tube sets to perform all prescribed strengthening exercises; however, those who preferred to use other strengthening equipment (e.g., dumbbells and weight machines) were encouraged to do so. Participants were encouraged to maintain moderate exercise intensity while performing strengthening exercises and to perform 3 sets of 8–12 repetitions for each of 8 exercises targeting a variety of muscle groups for each strengthening session.
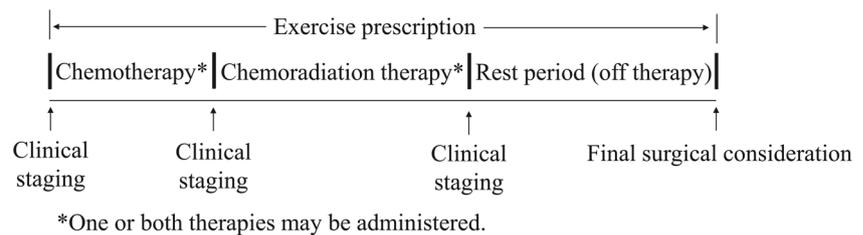
The exercise program duration was defined as the number of weeks (rounded to the nearest whole number) between the enrollment date and the date a final decision was made regarding surgery. Durations of each individual preoperative treatment modality were calculated as the number of full weeks between the day on which the specific treatment plan was finalized and the day on which the final treatment was received, or the day on which the treatment plan changed.

Subjective physical activity and exercise

Participants completed the International Physical Activity Questionnaire Short Form (IPAQ-SF) twice, to quantify total physical activity in the week prior to starting the exercise program and the final exercise program week. The IPAQ-SF has acceptable validity and reliability compared to other self-reported physical activity measures [33]. Per standard protocol, total energy expenditure from physical activity was estimated by multiplying average duration, weekly frequency, and metabolic equivalent task (MET) intensity for each activity domain (vigorous physical activity, moderate physical activity, and walking) and creating a sum across domains [33]. This data processing protocol produced estimates of total MET-minutes of physical activity per week.

Participants were instructed to record total minutes of moderate-intensity aerobic exercise and strengthening exercise in exercise logs each night at bedtime, either on paper or via automated email survey invitations sent through the Research Electronic Data Capture (REDCap) system (Vanderbilt University, 2015). Weekly total minutes were computed for aerobic and strengthening exercise for each 7-day period. Exercise duration was recorded as 0 min for blank fields and for days with incomplete logs. Average weekly aerobic, strengthening, and combined exercise minutes were then computed across each phase of therapy and across all exercise program weeks. Average weekly minutes of aerobic, strengthening, and combined exercise were compared to program recommendations to assess overall exercise adherence. Participants who did not complete any exercise logs were excluded from related analyses.

Fig. 1 Exercise prescription and treatment context

|◄─────── Exercise prescription ───────►|

| Chemotherapy* | Chemoradiation therapy* | Rest period (off therapy) |

↑ Clinical staging ↑ Clinical staging ↑ Clinical staging ↑ Final surgical consideration

*One or both therapies may be administered.

Objective physical activity

Physical activity was measured objectively using accelerometers (ActiGraph GT3X+, ActiGraph, LLC, 2011), which participants were instructed to wear over their right hip during all waking hours for two consecutive weeks at the approximate midpoint of each phase of therapy. For example, a patient who received chemotherapy followed by chemoradiation therapy and a treatment break prior to being considered for surgery participated in three unique 14-day accelerometer wear protocols. Two-week accelerometer wear protocols were selected to capture the potentially cyclical nature of fatigue and side effects from chemotherapy regimens, which are typically administered in cycles of 7–14 days [34]. Wear time was recorded in daily accelerometer logs.

Accelerometers recorded data at 60 Hz, with counts processed to measure physical activity in 1-min epochs [35]. A minimum of 10 h of daily wear time on a minimum of 7 days was required to compute physical activity for each wear period. Non-wear time, defined by at least 60 consecutive minutes of zero counts with allowance for up to 2 min with counts between 0 and 100 [36], was eliminated from accelerometer analyses. Raw accelerometer counts were processed according to standard cut points for adults to provide weekly estimates of light physical activity (LPA) and moderate-to-vigorous physical activity (MVPA) for each wear period [37]. MVPA accumulated in bouts of ≥ 10 consecutive minutes was also computed for each wear period [32]. Accelerometer physical activity was compiled by treatment phase and also averaged across all program weeks for each patient. Accelerometer data were processed using ActiLife Software, Version 6 (ActiGraph, LLC, 2016).

Statistical analyses

Descriptive statistics (frequencies and percentages or means and standard deviations) were used to quantify participants' sociodemographic, disease, and treatment characteristics and to quantify self-reported exercise and accelerometer physical activity across and within treatment phases. Due to the positively skewed distributions of self-reported energy expenditure from physical activity, Wilcoxon signed rank tests were used to compare changes in MET-minutes from baseline to preoperative restaging (paired observations) [38].

Additional nonparametric tests were used to examine differences in exercise and physical activity variables between men and women, between patients who underwent surgery and patients who did not undergo surgery, and between patients who reported significant weight loss at either time point and patients who did not. Spearman rank correlations were used to examine bivariate associations between age and BMI and exercise and physical activity variables. Nonparametric tests were used to determine whether mean change in self-reported physical activity (IPAQ-short form), self-reported exercise, or accelerometer physical activity differed among patients with various neoadjuvant treatment sequences. All aforementioned analyses were performed using SPSS Statistics Version 24 (IBM Corp., 2016).

Two-level, linear mixed models were used to compare self-reported exercise (weekly minutes of aerobic, strengthening, and combined exercise) and accelerometer physical activity (weekly minutes of LPA and MVPA) among the three neoadjuvant treatment phases. The first set of models included only treatment phase as a fixed effect and study ID as a random effect, and the second set of models included sex, age, surgery (yes/no), BMI, and treatment phase duration as covariates, based on evidence from bivariate analyses. Restricted maximum likelihood estimation with the Kenward-Roger approximation was used to adjust for small-sample bias and to account for differences in the numbers of participants with exercise and physical activity data within each treatment phase. Marginal mean estimations created means adjusted for sample size imbalance between phases and for sex, age, surgery (yes/no), and treatment phase duration. Linear mixed models were performed using SAS Version 9.4 (SAS Institute, 2013).

Results

Participants

Figure 2 illustrates the flow of participants through the study. Among the 56 patients who were offered potential enrollment, three (5.3%) declined to participate. Of the 53 patients screened for eligibility, one (1.9%) was ineligible for enrollment based on responses to the PAR-Q, and two (3.8%) were disqualified immediately following enrollment because of an early change to therapeutic plans. The intervention sample

included the remaining 50 participants. The participants' demographic and clinical characteristics and baseline physical activity are reported in Table 1. Participants were, on average, 66 years old, nearly half of participants were female, and 64% were overweight or obese at baseline. Sixty percent of patients had potentially resectable tumors, and 40% had borderline resectable tumors. The majority of patients had performance status of 0 or 1 and mild or moderate comorbidity scores. The majority of patients reported significant weight loss in the previous 3 months. Half of the participants underwent chemotherapy concurrent with exercise program participation, while the majority underwent chemoradiation and a "rest period" (off therapy) during participation. Participants were enrolled in the exercise program for a mean of 16 weeks.

Self-reported and objective measures of physical activity

Participants' weekly energy expenditure, self-reported using IPAQ-SF, was 1502.9 ± 1986.6 MET-minutes prior to enrollment and 2218.7 ± 2145.9 MET-minutes upon completion of the program ($p = .08$) (Table 1).

Forty-two (84%) participants submitted exercise logs for an average of $66 \pm 39\%$ of program days. There were no differences in daily exercise log completion by sex, age, baseline BMI, or treatment sequence, and there were no associations between log completion and accelerometer PA (all $p > .05$). Table 2 shows self-reported weekly volumes of aerobic and strengthening exercise. Protocol recommendations for aerobic and strengthening exercise in an average week were met by 34 (81%) and 9 (21%) of participants who submitted exercise logs, respectively (Table 2). Table 2 also reports weekly LPA and MVPA, measured by accelerometer and compiled across all treatment phases.

Over the entire course of the exercise period, men performed significantly more MVPA than women (197.1 ± 162.6 min/week vs. 123.7 ± 123.8 min/week, $p < .05$). There were significant positive correlations between baseline age and average weekly strengthening exercise ($B = .39$, $p = .01$) and a significant negative correlation between baseline BMI and average weekly MVPA in bouts of at least 10 min ($B = -.31$, $p = .04$). There were no significant differences in self-reported exercise or accelerometer PA between patients whose tumors were potentially resectable or borderline resectable at baseline or between patients who did and did not undergo surgery following treatment and exercise program participation (all $p > .05$). There were no differences in change in self-reported MET-minutes across treatment sequences ($p > .05$).

Figure 3 illustrates average self-reported weekly minutes of aerobic and strengthening exercise and average weekly MVPA during each preoperative phase. No significant associations were observed between phase and weekly exercise or physical activity in either unadjusted or adjusted models (all $p > .05$).

Discussion

In this study, we sought to evaluate the extent to which patients with pancreatic cancer engage in physical activity prescribed during preoperative chemotherapy and/or chemoradiation therapy. We identified considerable variance in participants' weekly self-reported exercise and objectively measured MPVA. However, weekly MPVA was consistent with exercise recommendations for healthy adults and cancer survivors. Exercise and physical activity volumes were similar during the administration of chemotherapy and chemoradiation therapy and during a treatment break within which no additional cancer treatment was administered. These findings suggest that the exercise recommendations for healthy adults and cancer survivors are realistic targets for patients receiving preoperative chemotherapy and chemoradiation prior to pancreatic cancer surgery, but that further efforts are needed to improve compliance and to reduce barriers to participation.

ACS and ACSM guidelines recommend that all people with cancer, like healthy adults, participate in physical activity. Guidelines advocate an overall volume of 150 min of moderate-intensity exercise or 75 min of vigorous-intensity exercise, or an equivalent combination, along with at least two strengthening sessions for major muscle groups each week [1, 2]. They also note that exercise prescriptions should be adapted on the basis of each cancer survivor's health status, anticipated disease trajectory, and treatment course. We attenuated the exercise prescription in the intervention described herein as we anticipated that the generally elderly and infirm population with pancreatic cancer would find it difficult to achieve the volume of activity achieved by healthy adults, particularly concurrent with the administration of toxic therapies. Nevertheless, participants' mean volumes of aerobic exercise and MPVA were actually far closer to the general physical activity recommendation than to the intentionally attenuated program recommendation. On the other hand, few participants consistently met the weekly strengthening recommendation. Because resistance exercise may increase both lean body mass and strength [21], future studies must consider and address possible explanations for this discordance.

It is difficult to draw comparisons regarding adherence with similar studies conducted in the oncology setting, because prior studies evaluating activity prescribed concurrently with preoperative treatment are limited. We recently demonstrated feasibility of home-based exercise in a separate group of 15 patients undergoing preoperative treatment of pancreatic cancer, with participants, on average, exceeding the weekly aerobic exercise prescription based on self-reported data from daily logs [23]. A recent systematic review of preoperative

Fig. 2 Flow of participants
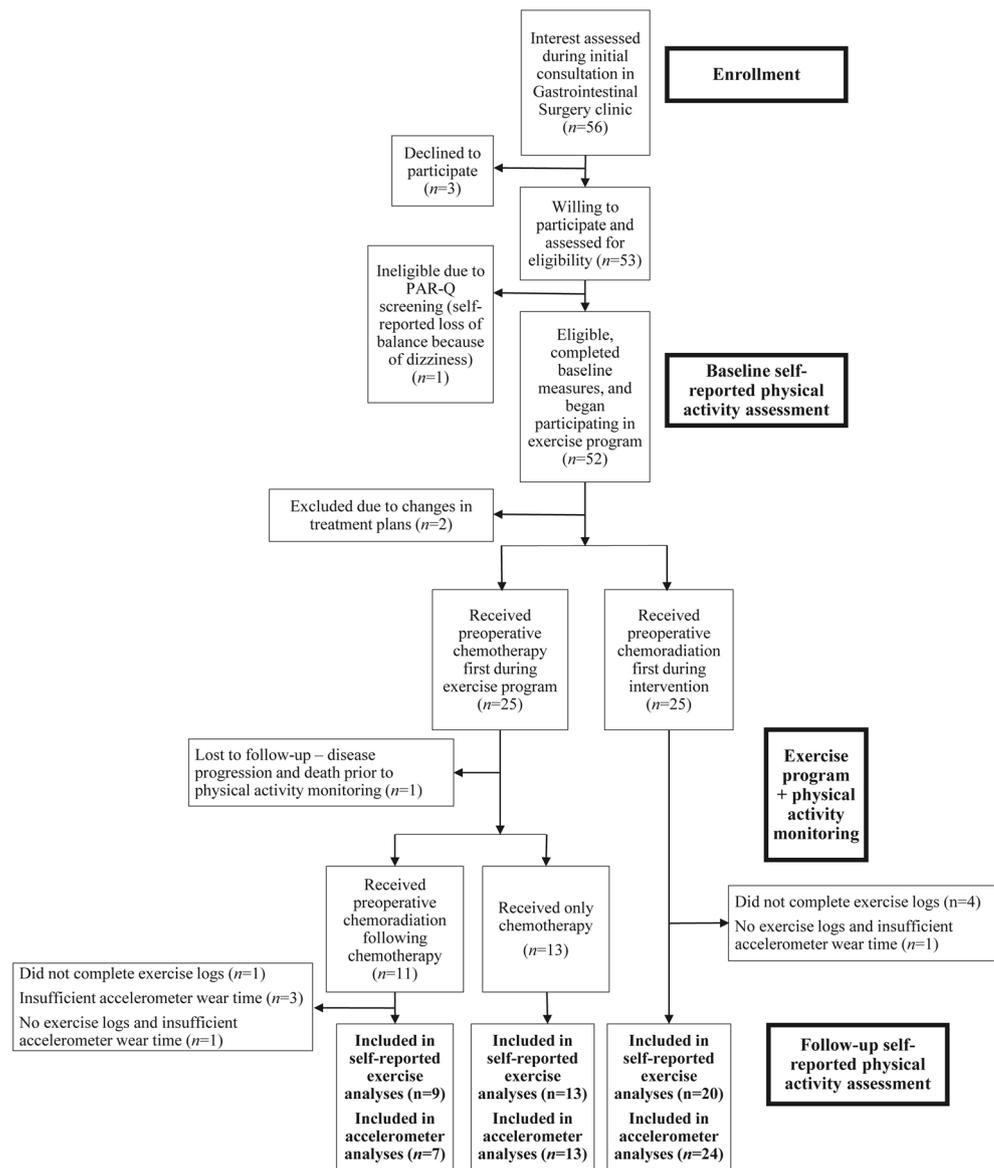
exercise in people with cancer undergoing preoperative therapy evaluated only four studies, the largest of which reported 35 participants, and three of which included only participants with breast cancer [22]. However, notwithstanding differences between the exercise volumes prescribed in these studies, it is notable that the proportion of participants who met the prescribed weekly recommendation for aerobic exercise (81%) in the intervention described here were comparable to those reported by that systematic review (66–96%). It was also similar to the adherence of participants who participated in an exercise program prior to colorectal cancer surgery (78%) [39], even though the exercise program reported here was longer (16 weeks vs. 4 weeks) and was administered during active treatment with chemotherapy and/or chemoradiation, while participants in the colorectal cancer study did not receive therapy concurrent with exercise. Although preoperative exercise

has been shown to improve clinical outcomes in several cancer contexts [17–20], the extent to which these improvements occur among patients receiving preoperative treatment concurrent with exercise prescription is not yet clear. Previous studies involving individuals undergoing preoperative cancer treatment have shown that exercise improves physical fitness [22], but have not yet shown improvements in other important clinical outcomes (e.g., tolerance and completion of therapy, reducing surgical complications, and accelerating postoperative recovery). We aim to elucidate the efficacy of exercise prescription concurrent with preoperative pancreatic cancer treatment in a currently accruing clinical trial (ClinicalTrials.gov Identifier: NCT03187951) [24].

We hypothesized that despite a consistent exercise prescription, participants' activity would vary depending upon the treatment that they were simultaneously receiving, owing

Table 1 Characteristics of study sample (N = 50)

	Value
Mean age at enrollment, years ± SD	66 ± 8
Sex, n (%)	
Female	24 (48)
Male	26 (52)
Mean BMI at baseline, kg/m^2 ± SD	27.6 ± 5.3
Normal weight (18.5 ≤ BMI < 25), n (%)	18 (36)
Overweight (25 ≤ BMI < 30), n (%)	18 (36)
Obese (BMI ≥ 30), n (%)	14 (28)
Radiographic disease stage at baseline, n (%)[a]	
Potentially resectable	30 (60)
Borderline resectable	20 (40)
Performance status at baseline, n (%)[b]	
0	14 (28)
1	32 (64)
2	4 (8)
Comorbidity score at baseline, n (%)[c]	
None	7 (14)
Mild	17 (34)
Moderate	21 (42)
Severe	5 (10)
Weight loss ≥ 3 kg in the previous 3 months at baseline, n (%)	37 (74)
Energy expenditure from physical activity, weekly MET-minutes ± SD	1502.9 ± 1986.6
Preoperative phases with concurrent exercise prescription, n (%)[d]	
Systemic chemotherapy	25 (50)
Chemoradiation therapy	36 (72)
Off therapy	41 (82)
Mean exercise program duration, weeks ± SD	16 (9)
During chemotherapy	17 (8)
During chemoradiation	4 (2)
During preoperative period off therapy	6 (2)
Outcome following preoperative chemotherapy and/or chemoradiation, n (%)	
Surgical resection	24 (48)
No surgical resection	26 (52)

[a] Katz et al. (2008) (see reference [25])

[b] ECOG performance status

[c] ACE-27 comorbidity score

[d] Percentages exceed 100% because patients participated during multiple preoperative phases

to differences in side effects, treatment schedules, and other exercise barriers. For example, systemic chemotherapy is more commonly associated with fatigue than chemoradiation therapy, and fatigue might be expected to reduce exercise motivation and ability. On the other hand, cycles of systemic chemotherapy for pancreatic cancer are typically administered over 1–3 days every 1–2 weeks, a schedule that may provide patients with ample opportunity for recovery between cycles,

permitting them to compensate by exercising more when the cycle's worst side effects have passed. Chemoradiation therapy, in contrast, is generally well tolerated but is associated with a more intensive treatment schedule, as fractions are typically delivered 5 days per week. Although we detected no difference between activity achieved during each of these treatment phases and a break period during which no active therapies were administered, high inter-individual variability across exercise and physical activity measures observed may represent sequelae of these differences, including participant-to-participant differences in treatment toxicities.

In unadjusted bivariate analyses, we observed significant differences in physical activity by sex, with men performing significantly higher MVPA than women, which is consistent with findings from previous research in cancer survivorship [40]. We also observed a significant negative correlation between BMI and physical activity, which is consistent with findings from previous research in older adults [41]. Although these demographic and anthropometric variables contributed to the high degree of variability observed in exercise and physical activity in each treatment phase, there were no significant differences between phases after adjusting for these variables. We are currently evaluating other intra- and interpersonal factors that may influence physical activity adoption and maintenance, including motivation, self-efficacy, and social and environmental supports and barriers [24].

Finally, although we did not detect any significant differences between preoperative phases in MVPA that occurred in bouts, it is important to note that participants accumulated a mean of only 55 min of MVPA weekly in bouts lasting at least 10 min. Several points are worthy of emphasis in this regard. First, the pattern of MVPA accumulation observed among participants in this study may be another reflection of significant barriers faced by older adults undergoing cancer therapy. Nonetheless, the importance of MVPA in continuous bouts compared to simply accumulating MVPA is unclear [42], and future studies employing continuous monitoring strategies among cancer survivors should examine differences in health-related outcomes across different patterns of physical activity accumulation. Second, we processed accelerometer data with commonly used cut points that were generated from data from the general adult population [37]. Other accelerometer cut points for older adults apply a more liberal definition of LPA and MVPA, but these have not been used as widely [43]. For this reason, both total and MVPA in bouts may be underreported in this study in relation to actual energy expenditure. Future studies should examine energy expenditure during physical activity among participants undergoing cancer therapy and identify ideal cut points.

This study has several important strengths. First, we utilized both self-reported and objective measures to examine exercise and physical activity during different preoperative treatment phases. Tools measuring self-reported exercise have

**Table 2** Volume of exercise and physical activity

	Mean (SD) or n (%)
Aerobic exercise (logs)	$n = 42$
Minutes/week	126 (83)
Achieved weekly recommendation[a]	34 (81)
Strengthening exercise (logs)	$n = 42$
Minutes/week	39 (33)
Achieved weekly recommendation[a]	9 (21)
Physical activity (accelerometer)	$n = 44$
LPA (minutes/week)	923.8 (294.5)
MVPA (minutes/week)	158.7 (146.7)
Bouted MVPA (minutes/week)[b]	55.1 (92.9)

Abbreviations: *LPA*, light physical activity; *MVPA*, moderate-to-vigorous physical activity

[a] Weekly recommendations were ≥ 60 min/week of aerobic exercise and ≥ 60 min/week of strengthening exercise

[b] MVPA accumulated in continuous intervals ≥ 10 min

demonstrated modest validity and reliability, but they are subject to recall issues and reporting and favorability biases [44]. Physical activity measurement with accelerometers is important to corroborate and validate self-reported data. Second, this simple, home-based exercise program administered to patients with pancreatic cancer should be generalizable to various contexts in cancer survivorship. Patients with pancreatic cancer tend to be elderly and may experience both debilitating disease symptoms and treatment side effects; their ability to perform considerable volumes of exercise during treatment suggests that patients in other cancer contexts should be able to do the same. Third, our use of home-based exercise is of particular importance as it may be a critical strategy to increase physical activity across the wide range of cancer survivorship contexts [45].
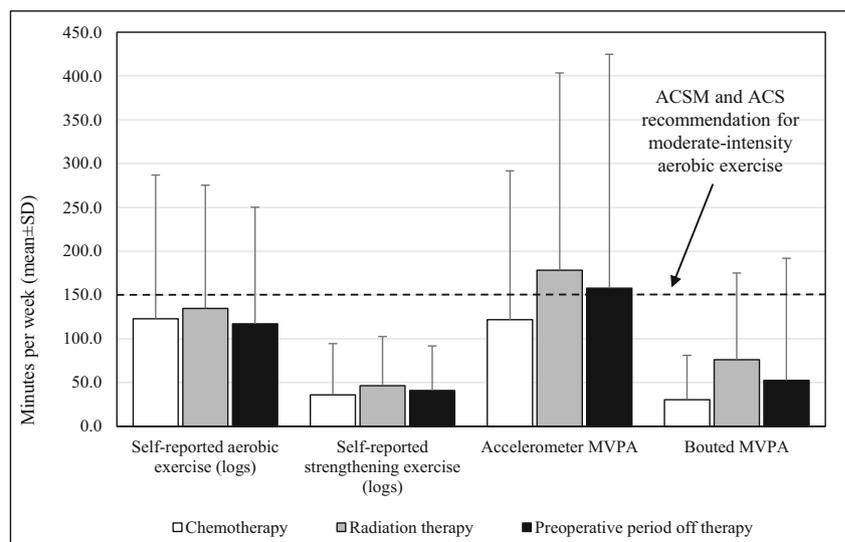
Several limitations are also notable. The wide variability in treatment courses and durations (reflecting the true nature of cancer care) created statistical limitations that future studies should attempt to control using stratification or matching suitable controls. The rate at which daily exercise logs were completed varied among participants, and this may have introduced bias in the summation of self-reported aerobic and strengthening exercise. We addressed this potential bias conservatively by recording exercise minutes as zero on days missing reports and adding objective measurement of activity with accelerometers. Nonetheless, future studies should prioritize or incentivize exercise log completion to more accurately understand adherence. Although we could detect no significant difference between volumes of exercise and physical activity by type of treatment, this investigation was not powered to detect such differences between treatment phases. Future exercise programs for patients undergoing preoperative treatment for pancreatic cancer should continue to target the entire course of therapy, but they should also measure potential differences in adherence, motivation, and barriers within each treatment phase. Given the lower adherence to strengthening exercise compared to aerobic exercise components, it will be particularly important for future exercise programs to explore barriers and motivation involving this modality. Finally, although frequent contact between study personnel and participants likely contributed to exercise motivation and was an intervention strength, other clinical teams may be unable to offer the same degree of support.

This is the first study to employ objective physical activity measurement among patients undergoing preoperative chemotherapy and/or chemoradiation therapy for pancreatic cancer. Future studies should randomize larger groups of patients, stratified by expected treatment course and anticipated treatment duration, in order to assess the efficacy of preoperative exercise for improving perioperative well-being and treatment among people with cancer.

Fig. 3 Weekly exercise and physical activity during preoperative phases

Compliance with ethical standards

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Brown JK, Byers T, Doyle C, Coumeya KS, Demark-Wahnefried W, Kushi LH, McTieman A, Rock CL, Aziz N, Bloch AS, Eldridge B, Hamilton K, Katzin C, Koonce A, Main J, Mobley C, Morra ME, Pierce MS, Sawyer KA (2003) Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. CA Cancer J Clin 53(5):268–291

2. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL (2010) American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 42(7):1409–1426. https://doi.org/10.1249/MSS.0b013e3181e0c112

3. Cooper AB, Holmes HM, des Bordes JK, Fogelman D, Parker NH, Lee JE, Aloia TA, Vauthey JN, Fleming JB, Katz MH (2014) Role of neoadjuvant therapy in the multimodality treatment of older patients with pancreatic cancer. J Am Coll Surg 219(1):111–120. https://doi.org/10.1016/j.jamcollsurg.2014.02.023

4. Antoun S, Borget I, Lanoy E (2013) Impact of sarcopenia on the prognosis and treatment toxicities in patients diagnosed with cancer. Curr Opin Support Palliat Care 7(4):383–389. https://doi.org/10.1097/spc.0000000000000011

5. Cooper AB, Slack R, Fogelman D, Holmes HM, Petzel M, Parker N, Balachandran A, Garg N, Ngo-Huang A, Varadhachary G, Evans DB, Lee JE, Conrad C, Vauthey JN, Fleming JB, Katz MH (2014) Characterization of anthropometric changes that occur during neoadjuvant therapy for potentially resectable pancreatic cancer. Ann Surg Oncol 22(7):2416–2423. https://doi.org/10.1245/s10434-014-4285-2

6. Fleming JB, Gonzalez RJ, Petzel MQ, Lin E, Morris JS, Gomez H, Lee JE, Crane CH, Pisters PW, Evans DB (2009) Influence of obesity on cancer-related outcomes after pancreatectomy to treat pancreatic adenocarcinoma. Arch Surg (Chicago, Ill : 1960) 144(3):216–221. https://doi.org/10.1001/archsurg.2008.580

7. National Cancer Institute (2015) Pancreatic cancer treatment. http://www.cancer.gov/cancertopics/pdq/treatment/pancreatic/HealthProfessional/page5. Accessed March 16 2015

8. Bachmann J, Michalski CW, Martignoni ME, Buchler MW, Friess H (2006) Pancreatic resection for pancreatic cancer. HPB 8(5):346–351. https://doi.org/10.1080/13651820600803981

9. Huang JJ, Yeo CJ, Sohn TA, Lillemoe KD, Sauter PK, Coleman J, Hruban RH, Cameron JL (2000) Quality of life and outcomes after pancreaticoduodenectomy. Ann Surg 231(6):890–898

10. Park JW, Jang JY, Kim EJ, Kang MJ, Kwon W, Chang YR, Han IW, Kim SW (2013) Effects of pancreatectomy on nutritional state, pancreatic function and quality of life. Br J Surg 100(8):1064–1070. https://doi.org/10.1002/bjs.9146

11. Cloyd JM, Tran Cao HS, Petzel MQ, Denbo JW, Parker NH, Nogueras-Gonzalez GM, Liles JS, Kim MP, Lee JE, Vauthey JN, Aloia TA, Fleming JB, Katz MH (2017) Impact of pancreatectomy on long-term patient-reported symptoms and quality of life in recurrence-free survivors of pancreatic and periampullary neoplasms. J Surg Oncol 115(2):144–150. https://doi.org/10.1002/jso.24499

12. Cooper AB, Tzeng CW, Katz MH (2013) Treatment of borderline resectable pancreatic cancer. Curr Treat Options in Oncol 14(3):293–310. https://doi.org/10.1007/s11864-013-0244-6

13. Tempero MA, Malafa MP, Behrman SW, Benson AB 3rd, Casper ES, Chiorean EG, Chung V, Cohen SJ, Czito B, Engebretson A, Feng M, Hawkins WG, Herman J, Hoffman JP, Ko A, Komanduri S, Koong A, Lowy AM, Ma WW, Merchant NB, Mulvihill SJ, Muscarella P 2nd, Nakakura EK, Obando J, Pitman MB, Reddy S, Sasson AR, Thayer SP, Weekes CD, Wolff RA, Wolpin BM, Burns JL, Freedman-Cass DA (2014) Pancreatic adenocarcinoma, version 2.2014: featured updates to the NCCN guidelines. J Natl Compr Cancer Netw 12(8):1083–1093

14. Katz MH, Pisters PW, Evans DB, Sun CC, Lee JE, Fleming JB, Vauthey JN, Abdalla EK, Crane CH, Wolff RA (2008) Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. J Am Coll Surg 206(5):833–846

15. West MA, Loughney L, Barben CP, Sripadam R, Kemp GJ, Grocott MP, Jack S (2014) The effects of neoadjuvant chemoradiotherapy on physical fitness and morbidity in rectal cancer surgery patients. Eur J Surg Oncol 40(11):1421–1428. https://doi.org/10.1016/j.ejso.2014.03.021

16. Sahai SK, Ismail H (2015) Perioperative implications of neoadjuvant therapies and optimization strategies for cancer surgery. Curr Anesthesiol Rep 5(3):305–317

17. Silver JK (2015) Cancer prehabilitation and its role in improving health outcomes and reducing health care costs. Semin Oncol Nurs 31(1):13–30. https://doi.org/10.1016/j.soncn.2014.11.003

18. Silver JK, Baima J (2013) Cancer prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. Am J Phys Med Rehabil 92(8):715–727. https://doi.org/10.1097/PHM.0b013e31829b4afe

19. Carli F, Scheede-Bergdahl C (2015) Prehabilitation to enhance perioperative care. Anesthesiol Clin 33(1):17–33. https://doi.org/10.1016/j.anclin.2014.11.002

20. Kim BJ, Caudle AS, Gottumukkala V, Aloia TA (2016) The impact of postoperative complications on a timely return to intended oncologic therapy (RIOT): the role of enhanced recovery in the cancer journey. Int Anesthesiol Clin 54(4):e33–e46. https://doi.org/10.1097/aia.0000000000000113

21. Padilha CS, Marinello PC, Galvao DA, Newton RU, Borges FH, Frajacomo F, Deminice R (2017) Evaluation of resistance training to improve muscular strength and body composition in cancer patients undergoing neoadjuvant and adjuvant therapy: a meta-analysis. J Cancer Surviv 11(3):339–349. https://doi.org/10.1007/s11764-016-0592-x

22. Loughney L, West MA, Kemp GJ, Grocott MP, Jack S (2016) Exercise intervention in people with cancer undergoing neoadjuvant cancer treatment and surgery: a systematic review. Eur J Surg Oncol 42(1):28–38. https://doi.org/10.1016/j.ejso.2015.09.027

23. Ngo-Huang A, Parker NH, Wang X, Petzel MQB, Fogelman D, Schadler KL, Bruera E, Fleming JB, Lee JE, Katz MHG (2017) Home-based exercise during preoperative therapy for pancreatic cancer. Langenbeck's Arch Surg 402:1175–1185. https://doi.org/10.1007/s00423-017-1599-0

24. PancFit: multimodal exercise during preoperative therapy for pancreatic cancer. (2017). https://clinicaltrials.gov (Identification No. NCT02295956)

25. British Columbia Ministry of Health (1992) Physical activity readiness questionnaire. British Columbia, Canada

26. Katz MHG, Pisters PWT, Evans DB, Sun CC, Lee JE, Fleming JB, Vauthey JN, Abdalla EK, Crane CH, Wolff RA, Varadhachary GR, Hwang RF (2008) Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. J Am Coll Surg 206(5): 833–846. https://doi.org/10.1016/j.jamcollsurg.2007.12.020

27. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr (2004) Prognostic importance of comorbidity in a hospital-based cancer registry. JAMA 291(20):2441–2447. https://doi.org/10.1001/jama.291.20.2441

28. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP (1982) Toxicity and response criteria of the eastern cooperative oncology group. Am J Clin Oncol 5(6): 649–655

29. Huffman GB (2002) Evaluating and treating unintentional weight loss in the elderly. Am Fam Physician 65(4):640–650

30. Lim KH, Chung E, Khan A, Cao D, Linehan D, Ben-Josef E, Wang-Gillam A (2012) Neoadjuvant therapy of pancreatic cancer: the emerging paradigm? Oncologist 17(2):192–200. https://doi.org/10.1634/theoncologist.2011-0268

31. Borg G (1970) Perceived exertion as an indicator of somatic stress. Scand J Rehabil Med 2(2):92–98

32. US Dept. of Health and Human Services (2008) Physical activity guidelines for Americans. US Dept. of Health and Human Sercies, Centers for Disease Control and Prevention, National Center for Disease Prevention and Health Promotion. http://www.health.gov/paguidelines/guidelines/. Accessed 9 April 2018

33. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35(8):1381–1395. https://doi.org/10.1249/01.mss.0000078924.61453.fb

34. Conroy T, Desseigne F, Ychou M, Ducreux M, Bouche O, Guimbaud R, Becouarn Y, Montoto-Grillot C, Gourgou-Bourgade S, Adenis A (2010) Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O]) versus gemcitabine (G) as first-line treatment for metastatic pancreatic adenocarcinoma (MPA): preplanned interim analysis results of the PRODIGE 4/ACCORD 11 trial. J Clin Oncol 28(15_suppl):4010–4010

35. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP (2005) Accelerometer use in physical activity: best practices and research recommendations. Med Sci Sports Exerc 37(11 Suppl): S582–S588

36. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M (2008) Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 40(1):181–188. https://doi.org/10.1249/mss.0b013e31815a51b3

37. Freedson PS, Melanson E, Sirard J (1998) Calibration of the computer science and applications, Inc. accelerometer. Med Sci Sports Exerc 30(5):777–781

38. Whitley E, Ball J (2002) Statistics review 6: nonparametric methods. Crit Care 6(6):509–513

39. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, Liberman AS, Stein B, Charlebois P, Feldman LS, Carli F (2014) Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. Anesthesiology 121(5):937–947. https://doi.org/10.1097/aln.0000000000000393

40. LeMasters TJ, Madhavan SS, Sambamoorthi U, Kurian S (2014) Health behaviors among breast, prostate, and colorectal cancer survivors: a US population-based case-control study, with comparisons by cancer type and gender. J Cancer Surviv 8(3):336–348. https://doi.org/10.1007/s11764-014-0347-5

41. Riebe D, Blissmer BJ, Greaney ML, Garber CE, Lees FD, Clark PG (2009) The relationship between obesity, physical activity, and physical function in older adults. J Aging Health 21(8):1159–1178. https://doi.org/10.1177/0898264309350076

42. Loprinzi PD, Davis RE (2016) Bouted and non-bouted moderate-to-vigorous physical activity with health-related quality of life. Prev Med Rep 3:46–48. https://doi.org/10.1016/j.pmedr.2015.12.005

43. Copeland JL, Esliger DW (2009) Accelerometer assessment of physical activity in active, healthy older adults. J Aging Phys Act 17(1):17–30

44. Trost SG, O'Neil M (2014) Clinical use of objective measures of physical activity. Br J Sports Med 48(3):178–181. https://doi.org/10.1136/bjsports-2013-093173

45. Hardcastle SJ, Cohen PA (2017) Effective physical activity promotion to survivors of cancer is likely to be home based and to require oncologist participation. J Clin Oncol 35(32):3635–3637. https://doi.org/10.1200/jco.2017.74.6032