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Original Research Article

The Effects of a Pre-Infusion And Home Exercise Program on Quality Of Life and Fatigue During Chemotherapy Treatment: a Case Study

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ABSTRACT

Introduction: The present study investigated the effects of a pre-infusion and home exercise program on QoL and cancer-related fatigue. Given the paucity of research examining effects of exercise during chemotherapy, research exploring exercise concomitant to infusion treatments is justified. **Methods:** The intervention took place over a period of eight weeks, with a functional assessment and a cancer-specific QoL questionnaire being administered at the start and end of the study. In addition, a general health-related QoL questionnaire was administered at the time of each supervised exercise session which occurred 72 hours prior to each infusion treatment. Lastly, exercise prescriptions were provided and adherence was tracked with the use of an accelerometer as well as follow up surveys between supervised exercise sessions. **Results:** Results revealed a substantial improvement in physical well-being from 4.85 to 0.57 following the exercise intervention. Consistent with these results, pain interference and pain intensity largely improved from the start of the study. Additionally, fatigue interfering with ADLs decreased from *moderate* to *not at all* at 9 days post-infusion and *moderate* to *slightly* at 5 days post-infusion by the end of the study. Psychological well-being measures went up from 5.44 to 6.89 after the treatment indicating that the patient's psychological well-being improved after the exercise intervention. The mean scores for distress and fear of recurrence also improved from 6.2 to 6 and 7.25 to 6, respectively, from pre to post infusion. There was a slight increase in social concerns from 6 to 6.63 indicating the participant had more concerns at the end than at the beginning of the study. Lastly, spiritual well-being improved modestly from 4.57 to 5.14 at the end of the intervention. **Conclusion:** It was found that this intervention had a positive impact on overall QoL, specifically with respect to physical well-being, fatigue, and pain interference and perception. Moreover, the infusion-based timing of this exercise intervention may have contributed to further gains in psychological well-being including a reduction in distress and fear of recurrence.

KEYWORDS: ADLs, Cancer-Related Fatigue, Exercise Oncology, Psychosocial Well-Being.

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Introduction

Cancer has become one of the largest growing epidemics in history continuing its rank as the second leading cause of death, following heart disease[1]. A surge in scientific research in oncology has improved cancer care, however, the specific cause is still unknown and a cure unidentified. The epidemiology of cancer reveals influences based on both internal and external factors such as; hormone and immune irregularities, diet, tobacco use, and physical inactivity[2]. Those fighting the disease are susceptible to and will most likely experience negative physiological and psychological effects. Cachexia is a hallmark symptom of cancer and is represented by extreme weight loss, skeletal muscle wasting, and an unhealthy depletion of adipose tissue[3]. This is one factor contributing to increased mortality rates across the population. In addition to the physical effects, there are significant psychological effects. With an increase in cancer-related fatigue and decreased stamina, many people lose the drive to fight. An inability to perform activities of daily living (ADLs) due to loss of muscle mass and stamina decreases quality of life (QoL) and further accentuates feelings of depression, anxiety, and self-worth[4].

Recent research has shown that safe and individualized exercise-based therapies, prescribed as part of cancer treatment, may help reduce many of the negative side effects associated with that treatment. The American College of Sports Medicine (ACSM) has focused on the effects of exercise in cancer survivors and declared that exercise is not only beneficial but also recommended. In fact, the ACSM along with the National Cancer Institute recommend daily physical activity mimicking that of healthy persons without disease. Consequently, with findings suggesting the numerous benefits of physical activity across the cancer continuum, the focus shifts to the specifics of exercise as it relates to the physical and mental well-being of the cancer population. Attention to time, intensity, and duration in relation to and in combination with routine, traditional treatments may reveal indispensable knowledge to continue improving overall cancer care[5].

The primary purpose of this study was to investigate the effects of a pre-infusion and home exercise program on the QoL and cancer-related fatigue of a cancer patient during chemotherapy. A secondary purpose of this study was to determine if providing the participant with a home exercise program including outreach from the study investigators along with a physical activity tracker would help the participant achieve the recommended goal of 150 minutes of physical activity per week.

We hypothesized that this program would provide positive mental health benefits including decreased anxiety and depression as well as a reduction in cancer-related fatigue. Additionally, we hypothesized that pre-infusion exercise therapy would help the patient maintain or increase ADLs following infusion therapy. Furthermore, the

convenience of not having to leave the house combined with the outreach may assist with adherence to an exercise program, thus potentially improving overall QoL for the patient.

Methods

Research Design

The study was approved by the Institutional Review Board at West Chester University. Descriptive statistics were used to investigate the effects of a pre-infusion and home exercise program on the physical and emotional QoL and cancer-related fatigue of a cancer patient during chemotherapy. The single participant completed a pre- and post-functional assessment and cancer-specific QoL questionnaires which included physical, psychological, and spiritual subscales. At the time of the initial functional assessment and questionnaire, the participant was provided with a fitness tracker (FitBit Versa, San Francisco, CA, USA) to wear throughout the duration of the study for a minimum of 12 hours per day. This provided data for the secondary aim of this study which was to determine if providing participants with a home exercise program, in addition to outreach from the study investigators and a physical activity tracker, would help to achieve the recommended goal of 150 minutes of physical activity per week.

Each supervised exercise session occurred within 72 hours prior to the participant's infusion treatment. Resting blood pressure (BP) and heart rate (HR) were recorded at the beginning and end of each session to ensure a full recovery to resting state. A supplemental QoL questionnaire was also completed at the start of each supervised session.

At-home exercises were prescribed via HEP2Go to the participant to improve the feasibility of achieving the 150 minutes of physical activity per week. Outreach to the participant occurred two times between supervised exercise sessions and incorporated questions regarding current QoL as well as adherence to the home exercise program.

Participant

To qualify as a participant in the current study, the candidate must have been at least 18 years of age at the start of the study, first time diagnosis of cancer regardless of type or stage (excluding hematological cancer), infusion treatment prescribed on a 14-21 day schedule, and must have ECOG Performance Status of 0-2.

The participant was held to the following exclusion criteria: current participation in an exercise program (accumulating more than 150 minutes of moderate intensity activity per week); presence of musculoskeletal diseases- fractures, tissue damage or evidence of bone metastasis; neurologic conditions - such as blurred vision or severe neuropathy; pulmonary conditions - including severe dyspnea or those who were oxygen dependent; mental health conditions – unmedicated depression, psychiatric disorders, substance abuse,

dementia; cardiovascular disease including irregular pulse/rhythm, chest pain, heart disease (including CHF), recent heart surgery (less than 1 year ago), demonstrated thromboembolism or deep vein thrombosis, use of blood thinning medication; comorbidities - uncontrolled diabetes, COPD, severe arthritis, lymphedema, uncontrolled thyroid disease, liver disease, peripheral vascular disease, renal disease, paralysis. No compensation or incentive was offered for participation.

Electronic medical records were reviewed in EPIC and the participant was identified as that who fit within the population characteristics and was not suffering from any of the conditions listed in the exclusion criteria. Once identified, an email was sent to the potential participant's physician to obtain clearance. If the physician agreed that the potential participant was an appropriate candidate for the study, the investigator contacted the potential participant at a treatment visit and discussed the study. The candidate interested in participating had the opportunity to review the informed consent with the primary investigator. Once all questions were addressed, the participant could decide to complete and sign the informed consent or choose to not participate in the study.

Exercise Therapy & Prescription

Baseline assessments collected at the start of the study included: a QoL survey (QoL-CSV), tests for aerobic capacity (6 minute walk test, 6MWT), muscular strength (grip strength), muscular endurance (30 second sit to stand), and flexibility (sit and reach). Prior to each supervised session, a questionnaire (PROMIS-29) was completed to assess QoL. Four supervised exercise sessions occurred over the period of 8 weeks specific to the patients' infusion schedule. Each supervised session was conducted within 72 hours prior to the patient's scheduled infusion therapy, resulting in one session every two weeks. These routines included all components of health-related fitness including a warm-up, a cool-down, aerobic conditioning, muscular strength, endurance training, and flexibility lasting approximately 60 minutes. All assessments and supervised exercise sessions occurred at a Center for Physical Rehabilitation.

A home exercise program was provided and completed between supervised exercise sessions. The home exercise prescriptions were designed and intended for the participant to obtain the Surgeon General's recommendation of 150 minutes of moderate intensity physical activity per week. Follow-up calls on days 5 and 9 after infusion treatments were made to assess QoL with a series of questions and to inquire on the status of completing the home exercise program. To further maintain adherence with the home exercise prescriptions, an accelerometer was distributed to the participant with the requirement of wearing the tracker for the duration of the study, a minimum of 12 hours per day. The tracker was provided not only to encourage the participant to comply

but to also provide necessary data of intensity, time, and type of physical activity throughout the study.

Measures

Quality of Life/Cancer Survivor Version (QoL-CSV)

The QoL-CSV is a 41-item questionnaire developed by researchers from the City of Hope National Medical Center, designed to measure the overall QoL in patients with cancer. Used in both clinical practice and in research, this ordinal scale is administered with the intention of measuring a variety of cancer-specific side effects. Additionally, this questionnaire represents the four domains of QoL as it relates to patients with cancer including physical, psychological, social, and spiritual well-being. As such, these domains are represented through subscales within the questionnaire so that individual analysis can be conducted.

Patient-Reported Outcomes Measurement Information System (PROMIS)

PROMIS-29 is a generic health-related QoL questionnaire developed by PROMIS and designed to measure self-reported well-being across seven defined subscales including depression, anxiety, physical function, fatigue, pain interference, sleep disturbance, and social roles. Each subscale includes 4 questions plus a single pain intensity question for a total of 29 items. Based on a 5-point Likert Scale, this questionnaire was designed for frequent distribution to record patient's current feelings as well as tracking the changes over time.

RAND 36-Item Health Survey (RAND-36)

The RAND-36 questionnaire was modified to fit the needs of the current study by extracting one question from the five primary domains. These five areas of focus include general health perception, physical functioning and role limitations, bodily pain, social and emotional well-being, and fatigue. The questionnaire used in the current study was adapted into a 5-point Likert Scale for ease of use during the follow-up phone calls in which it was applied.

Statistical Analysis

Descriptive analyses were performed using IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp. to compare pre-intervention QoL to post-intervention QoL. Mean and standard deviation (mean $\pm$ SD) were found for each of the QoL-CSV questionnaire subscales including physical, psychological, social, and spiritual well-being. In addition, descriptive analyses were conducted for the PROMIS-29 and RAND-36 surveys.

Results

Participant Characteristics

The participant in this study was a 59 year old (60 y.o. at end of study) moderately active, white female, 1.57m tall, 61.24kg., 24.8 kg/m^2, who was diagnosed with breast cancer four months prior to the start of the study.

The participant did not suffer from any other conditions and was otherwise healthy. Clearance by the participant's oncologist was granted prior to the start of the study and informed consent was obtained from the participant.

Quality of Life/Cancer Survivor Version

Table 1 depicts the participant's progress in QoL-CSV results before and after the exercise intervention. These results indicate that the mean score of physical well-being items went down from 4.85 to 0.57 meaning that the patient's physical well-being scores largely improved following the exercise intervention.

Drawing upon Table 1, the mean score of the psychological well-being items went up from 5.44 to 6.89 after the treatment. These scores indicate that the patient's psychological well-being improved after the exercise intervention. The mean score of distress went down from 6.2 to 6 from pre to post intervention.

Additionally, the patient's level of fear for a second cancer diagnosis was reduced from almost *extreme* to *neutral* at post-intervention levels. Overall, the mean score of fear-related items went down from 7.25 to 6.

Furthermore, the results indicated an increase in patient's social concerns following the intervention. The mean score for items related to social concerns went up from 6 to 6.63 at post intervention levels.

Finally, the mean score of spiritual well-being items went up from 4.57 to 5.14 after the intervention. The participant reported somewhat higher scores related to their sense of purpose /mission and hopefulness after the intervention.

Table 1. Quality of Life- Cancer Specific Version Questionnaire.

	Before-Mean (SD)	After-Mean (SD)
Physical Well Being	4.85 (±2.6)	0.57 (±0.5) *
Psychological Well Being	5.44 (±1.74)	6.89 (±1.61)
How distressing were the following aspects of your illness or treatment	6.2 (±1.48)	6 (±1) *
To What Extent are you Fearful of	7.25 (±1.5)	6 (±1.15) *
Social Concerns	6 (±2.39)	6.63 (±1)
Spiritual Well Being	4.57 (±1.39)	5.14 (±1.46)

When scoring, all items in the Physical Well-Being Scale and some in the Psychological Well-Being Scale including "How Distressing were the following aspects of your illness or treatment", "To what extent are you fearful of diagnoses tests, reoccurrence, second cancer, and metastasis", as well as the items in the Social Concerns Scale were reverse coded. Therefore, lower post scores in these would indicate an improvement.

PROMIS-29 Profile v2.1

The PROMIS-29 questionnaire was administered at 3 time points. Each of these time points aligned with the days at which supervised exercise interventions occurred and were administered prior to the

beginning of each session. As shown in Figure 1, participant's physical functioning, depression, and fatigue remained stable during the study. Results also revealed the participant felt some anxiety at time 2 but it decreased at time 3. The participant's sleep disturbance was close to poor at time 1 and increased to fair time 2 and 3. Lastly, consistent with the results from the QoL-CSV, the participant reported large levels of decrease in pain interference and pain intensity from time 1- time 3.

Follow Up Phone Survey (Modified RAND-36)

The follow up phone survey was used cyclically on days 5 and 9 post-infusion treatments for a total of 8 time points throughout the duration of the study. Figure 2 illustrates the participants general health as compared to the start of the study. Even though she felt about the same at Time 2, 5 days after the post-infusion treatment (PIT), she reported "feeling somewhat better now than at the beginning of the study" at all of follow-up points.

The participant believed that she did not have any problems completing her work or other regular daily activities as a result of her physical health regardless of 5 days or 9 days after PIT at follow-up points (Time 1-Time 3). In contrast, she did report having problems at Time 4, 9 days after PIT (see Figure 3).

Even though the participant believed that she had emotional problems (such as feeling depressed or anxious) that interfered with her normal social activities with family, friends, neighbors, or groups at Time 2 for 9 days after PIT, her emotions stayed stable and she reported no emotional problems for 5 days after PIT at all follow-up points and most of the 9 days after PIT (see Figure 4).

Figure 5 depicts the bodily pain following infusion treatments. The participant reported moderate body pain during the past 5 days. She didn't have as much pain during the past 9 days at the first three follow-up points. However, her body pain increased to moderate at time 4.

Fatigue that interfered with the ability to be active such as working, ADLs, and exercising decreased from *moderate* to *not at all* during four follow-up points for 9 days after PIT. For 5 days after PIT, it stayed stable at the first three follow-up points but later it went down to *slightly* at time 4.

Exercise Therapy & Prescription

To ensure the exercise intervention was consequential and the participant complied, baseline assessments were compared to post-assessment for functional changes. The participant's RHR increased from the start of the study as resting BP decreased (see Table 2). Cardiovascular fitness improved across all factors; distance traveled (267 meters pre-assessment, 308 meters post-assessment), ending HR (131 bpm pre, 125 bpm post), and the time for HR to return to rest (9 min pre, 5 min post). Muscular strength stayed relatively the same throughout the study, however, muscular endurance showed a

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slight improvement from 19 to 22 repetitions. Lastly, flexibility showed an increase of 3 cm from the start of the study.

Accelerometer Tracking

At-home exercises were measured using the accelerometer issued at the start of the study. Table 3 encapsulates the activity of the participant by distance (miles) covered as it relates to infusion treatments. *Days up to infusion* represent the mean of the 4 days leading to the next infusion day, for example, Time 2 for *days up to infusion* is the mean of the 4 days following *Day 9 post-infusion* for Time 1. Additionally, *Day 5 post-infusion* and *Day 9 post-infusion* are depicted in relation to the follow up phone surveys given on the same days. Although the mean for *days up to infusion* and *infusion day* remained relatively stable throughout the intervention, *day 5 post-infusion* and *day 9 post-infusion* improved when comparing Time 1 and 2 to Time 3 and 4.

Table 2: Functional Measurements.

	Pre-test	Post-test
Biometrics		
Resting heart rate	81 bpm	92 bpm
Resting blood pressure	118/78 mmHg	100/60 mmHg
Cardiovascular fitness (6 MWT)		
Distance	267 m	308 m
End HR	131	125
Time HR to return to rest	9 min	4 min
Muscular Strength (hand grip dynamometer)		
Right	22.8 kg	20.9 kg
Left (dominant)	25.4 kg	25.4 kg
Muscular Endurance (30 sec sit-to-stand)		
Repetitions	19	22
Flexibility (sit and reach box)		
Distance	22 cm	25 cm

Table 3: Accelerometer Distance (miles).

	Time 1	Time 2	Time 3	Time 4
Days up to infusion (mean)	4.5	6	3.5	4.75
Infusion day	3.75	4	4	3
Day 5 post-infusion	6	1	4	5
Day 9 post-infusion	2	4	5	4

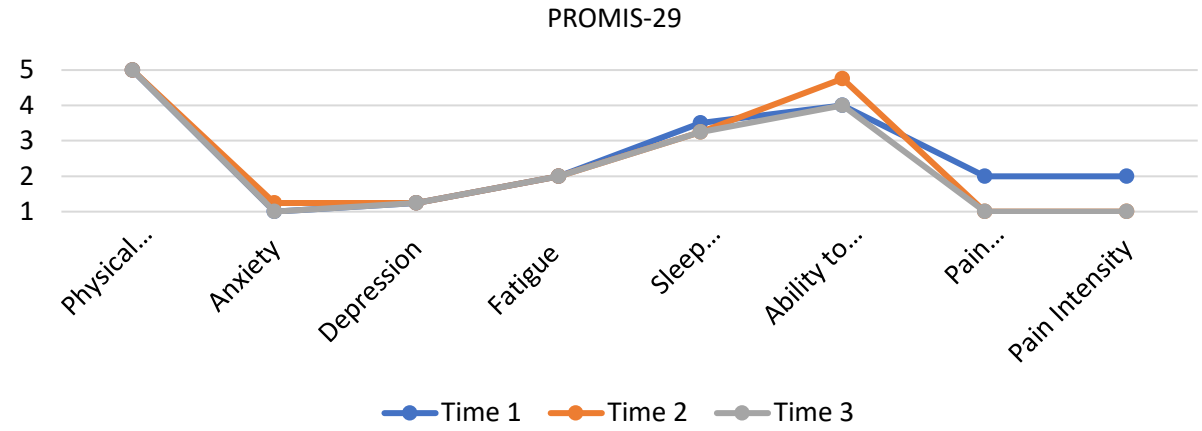

Figure 1. PROMIS-29 Questionnaire.

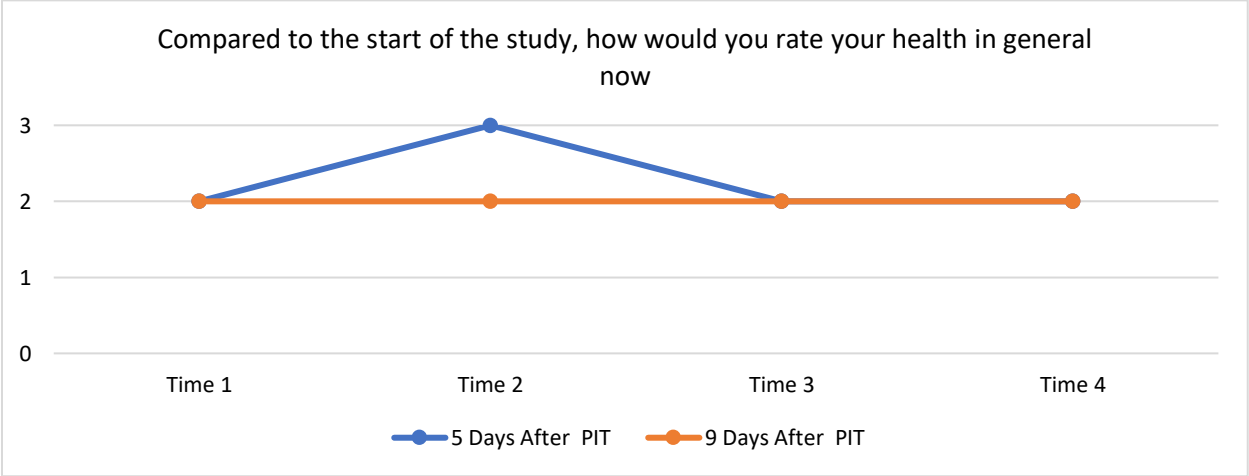

Figure 2. Follow Up- General Health.

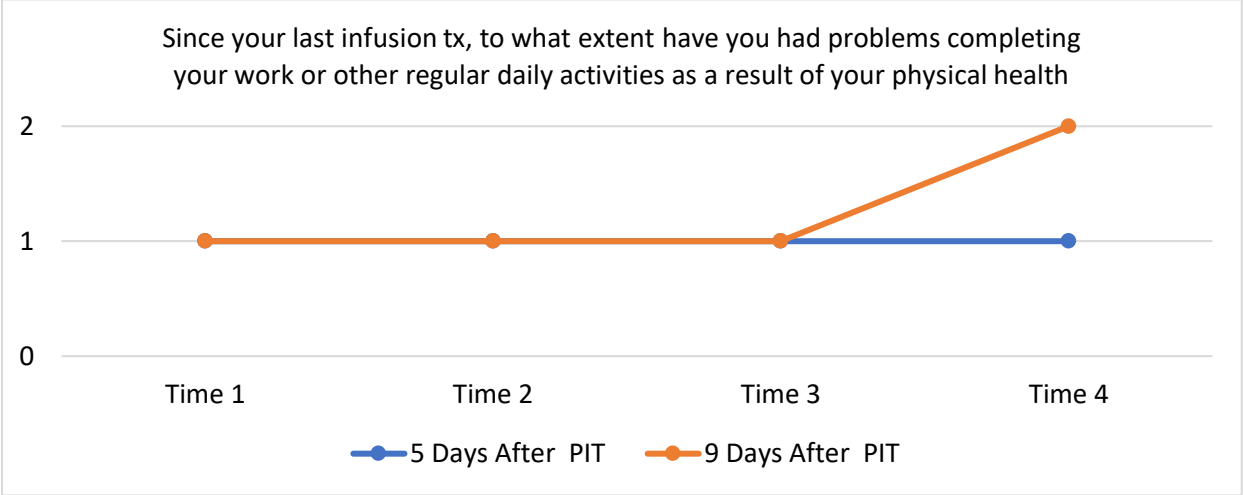

Figure 3. Follow Up- Daily Activities.

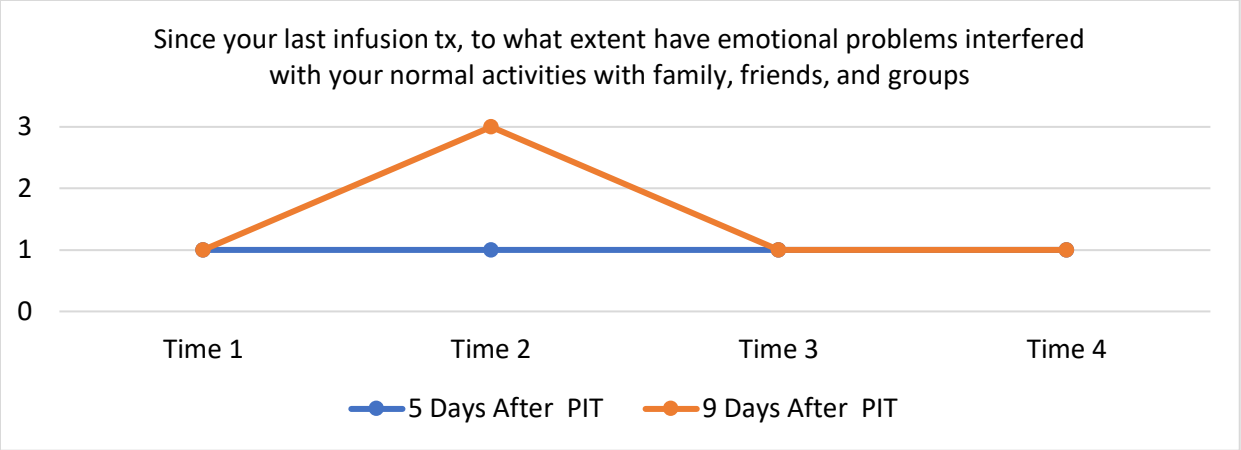

Figure 4: Follow Up- Emotional Interference.

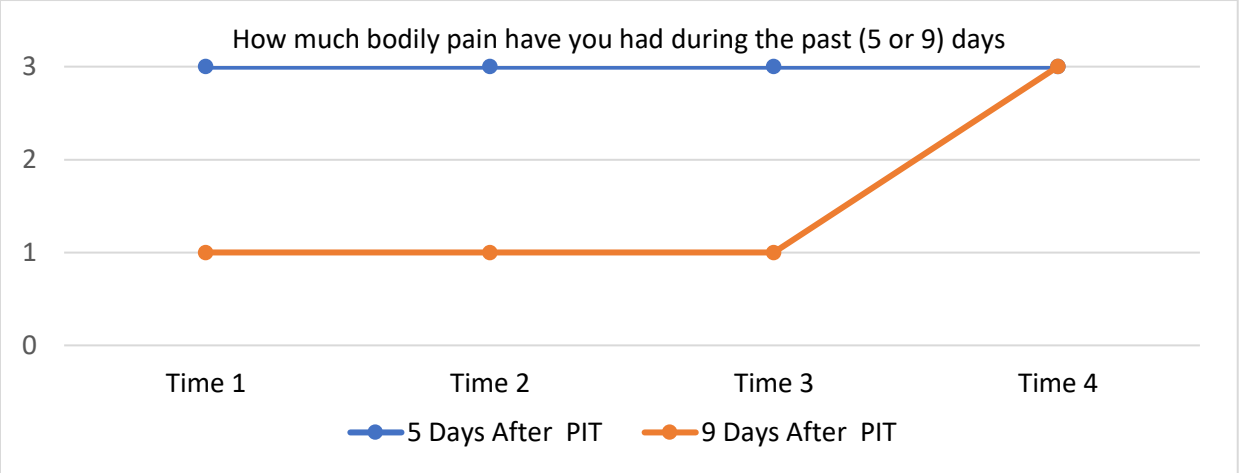

Figure 5: Follow Up- Pain.

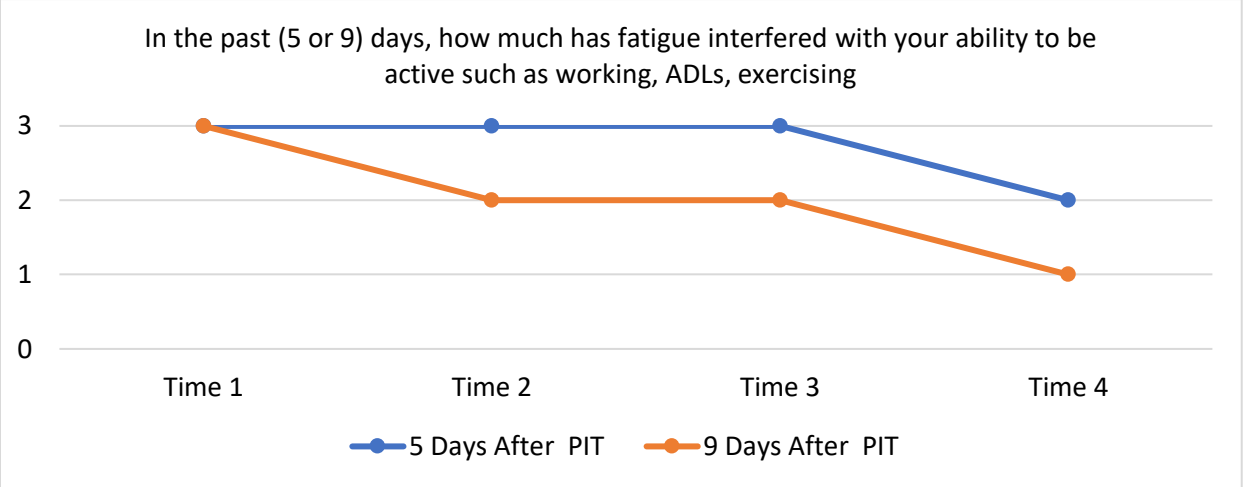

Figure 6: Follow Up- Fatigue.

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Discussion

Given that the majority of research is focused on the use of exercise therapy throughout the cancer continuum with little to no focus on infusion-based timing of exercise, the present study investigated the effects of a pre-infusion and home exercise program on QoL and cancer-related fatigue. Although the original design of this study was for meant to include multiple participants, only one consented. As anticipated, the acute timing of exercise interventions to infusion treatments yielded measurable improvements in the participants' psychological well-being including decreased anxiety and fear. Specifically, the QoL-CSV revealed that the participant reported greater ease in coping with the disease, greater sense of control, increased concentration, and improved memory following the intervention. This is consistent with similar studies observing improved mental health through exercise interventions[6-7]. This is also in accordance with PROMIS-29 presenting some anxiety at Time 2 but a decrease at Time 3 which occurred near the end of the intervention. It is possible that the slight elevation in anxiety at Time 2 could in part be due to work-related issues the participant expressed to the investigator around this same time. In addition, the intervention seemed to help the participant reduce personal fear related to other similar diagnosis, reoccurrence and metastasis from almost extreme to more neutral levels. This is a notable finding as cancer survivors' psychological well-being is often threatened due to the fear of recurrence[8].

This said, the participant's level of distress did not show a large difference before and after the intervention. Additionally, the PROMIS-29 revealed stable values for depression throughout the study. According to recent research, it is possible that feelings of depression and distress require extended periods of exercise in order to see change[9]. The limited duration of the present study, 8 weeks, may not have been sufficient for meaningful change in these areas of mental health. The latter should also be considered for the slight increase observed in social concerns. Moreover, these items may be less contingent upon exercise participation, regardless of time, and more a factor of burdens outside the realm of control, i.e. the financial burden associated with the disease and the influx of debt that occurs throughout the treatment[10].

It was posited that pre-infusion exercise therapy would help maintain or increase ADLs following infusion therapy. Exceeding predictions, the participant's physical well-being scores largely improved following the exercise intervention. Specifically, concerns related to fatigue, aches or pain, sleep changes, constipation, and nausea nearly faded after the intervention while they were reported as severe problems by the participant prior to intervention. Also, at a post-intervention level, the participant rated her overall physical health close to excellent. The latter is consistent with the improvements noted in the scoring of this scale. In accordance with previous research

as even short bouts of exercise interventions have been shown to reduce fatigue and lessen the perception of pain[11]. Congruent results were observed from PROMIS-29 as the participant rated a decrease in pain interference and pain intensity from Time 1-Time 3. The opposing value of increased pain at Time 4, 9 days post-infusion of the follow up survey should be considered an acute rating relative to that specific day rather than the overall perception of pain. In fact, research has shown that chronic pain is unpredictable on a daily basis[12] and therefore does not represent the overall perception of pain in the long-term.

As the secondary purpose of the current study was to determine adherence to the intervention, the use of a home exercise program, activity tracker, and outreach program proved beneficial. It was anticipated that the convenience of home-based exercises combined with the outreach would assist with adherence to the exercise intervention. Adherence was evident with data gathered from the Fitbit displaying a general trend in increased activity, specifically when comparing day 5 and day 9 post-infusion from Time 3-4 to Time 1-2. The participant averaged greater distance (miles) on days following infusion in the latter part of the intervention. This is consistent with the decreased fatigue, pain, and pain perception observed in the latter half of the intervention.

Although consistent HR and daily activities were difficult to track due to syncing malfunctions with the accelerometer, a general trend of increased RHR was observed. This was also apparent when comparing functional post-assessments to baseline. An overlooked side-effect of many chemotherapy medications is heart palpitations with an elevated HR[13,14] therefore this was not a marked concern. Incidentally, the participant's resting BP decreased by the end of the intervention.

As a by-product to the intervention and augment the attestation of compliance, physical strength gains were anticipated and achieved. The functional post-assessment revealed the participant's cardiovascular fitness improved with a faster return to rest HR following aerobic exercise. Furthermore, at the end of the study, the participant performed longer bouts and additional repetitions of the same exercises than at the start of the study resulting in increased muscular endurance. Lastly, improved flexibility was measured further attesting to the fulfillment of the exercise prescriptions.

Limitations & Future Research

This present study was not without limitations. Although every attempt was made during recruitment, a high non-participation rate led to a sample size of one, thereby decreasing the power of the study. Further, reliability, validity, and generalizability are weakened due to the case-study nature of this present study. Of nearly thirty qualifying candidates interviewed, the primary reasons for non-participation were largely the same; "too busy/ not enough time to dedicate",

"overwhelmed with other appointments and procedures", "concerned about the effects of exercise", and "not interested". This information could be explored further to increase patient accessibility and understanding, thereby improving patient participation. Future research would benefit from a larger number of participants which may be accomplished with longer recruitment periods. In addition, exercise prescription adherence was of vital importance to the overall efficacy of this study. In spite of prudent consideration taken to objectively measure adherence to at-home exercise prescriptions through the utilization of an accelerometer (Fitbit Versa), there were periods of missing data likely due to loss of battery life or malfunction which further challenged validity and reliability. Future research may want to consider a more rigorous tracking method either with the use of an alternative accelerometer or daily monitoring of activity and proper functioning of the Fitbit. Lastly, specific factors of psychological well-being (depression, distress) were difficult to observe due to the limited duration of the intervention. Considering that longevity of exercise is needed to see change in these areas, future research should attempt to prolong the length of the exercise intervention in order to accurately measure effects on mental health.

Implications & Recommendations

This investigational case study provides meaningful findings that can be applied to the current process of care as well as offer new and purposeful directions for future research in cancer treatment. The current standard of care for this patient population does not include an exercise prescription nor does it provide consultation of potential benefits. According to Sturgeon et al. (2017), patients predominantly would like to learn about exercise interventions available and would prefer to hear them prior to the start of treatment from an expert in the field such as an exercise physiologist. This said, practitioners are the first line of contact that have the ability to bridge this gap. It is important that practitioners become knowledgeable on these current findings to better serve and provide care for their patients. The physical and psychological well-being of participation in an exercise program would not only improve patient outcomes but their success would also facilitate improving the standard of care.

There remains a paucity of research investigating benefits of exercise and physical activity throughout the cancer continuum. Although this present study attempted to advance the understanding and awareness of these benefits acutely around infusions, continued research is essential in delineating alternative timing and the effects on pain perception and fatigue on an individual level. Further, providing needs assessments and monitoring daily pain levels throughout an exercise intervention may unveil insights into a more individualized and patient-specific cancer care.

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