ROLE OF ONCOLOGY REHABILITATION IN CANCER CARE

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ABSTRACT

Cancer is pervasive in the United States and worldwide. Early screening, diagnosis and treatment of cancer has led to a significant increase in survivorship over the last three decades. There are currently more than 18 million cancer survivors in the US. Treatment accelerates physiologic aging and functional decline toward frailty. Patients experience high levels of physical needs following medical treatment for cancer. This Ph.D. dissertation examines the role of oncology rehabilitation in cancer care.

If implementation of oncology rehabilitation is going to be adopted as a treatment option, it must first be appropriately evaluated. Having agreed-upon outcome measures is important. In a scoping review, we examined the heterogeneity in physical outcome measures used to evaluate the effects of cancer rehabilitation programs. Of the 2,550 abstracts screened, 41 met eligibility criteria and were included in the study. We found significant heterogeneity among the physical function outcome measures utilized to study outcomes among cancer survivors. There were 91 unique measures identified, and 27 unique physical side effects investigated.

We examined the impact of a 12-week supervised exercise oncology rehabilitation program on physical function among older breast cancer survivors. Our primary outcome measure was five times sit to stand (5TSTS) which is a validated indicator of fall risk among older individuals. Ninety-two participants met the inclusion criteria for this study. There was a significant difference in mean 5TSTS from baseline to follow-up. All secondary outcome measures also demonstrated significant improvement from baseline. The results of this study support current evidence for oncology rehabilitation as a component of care for older breast cancer patients to improve function and possibly reduce fall risk.

Oncology rehabilitation is not widely available. We conducted a survey of oncologists' knowledge, attitudes, and practices with respect to referrals to oncology rehabilitation. Oncologists were recruited from Florida Society of Clinical Oncology and Northern New England Clinical Oncology Society to complete a 32-question survey. Eighty-two surveys were collected. Oncologists reported referring 23.2% of patients to oncology rehabilitation over the last 12 months. Urban oncologists were less likely to refer to oncology rehabilitation compared to suburban oncologists and reported greater difficulty with the referral process. Our study adds to the limited research available identifying knowledge, attitudes, and practices of oncologists' use of oncology rehabilitation.

Oncology rehabilitation is a safe, feasible, and beneficial intervention for most cancer survivors. If oncology rehabilitation is going to be accepted as the standard of care for survivors of cancer and cancer treatment, we will need to expand the evidence base to more fully understand its benefits and potential risks, determine which patients are most likely to benefit, and improve access and availability.

DEDICATION

To Maria G, I am so thankful that our paths have crossed, you are an inspiration to me every day. Thank you for modeling strength, kindness, resiliency, and selfless acts in the most challenging of times.

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CHAPTER 1: A Scoping Review of Physical Outcome Measures Used to Evaluate the Impacts of Cancer and Oncology Rehabilitation

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Abbreviations: Oncology Rehabilitation (OR), Cardio-Oncology Rehabilitation (CORE), Evidence Database to Guide Effectiveness (EDGE), chemotherapy-induced peripheral neuropathy (CIPN), American Physical Therapy Association (APTA), clinical practice guideline (CPG), Piper Fatigue Scale (PFS), Brief Fatigue Inventory (BFI), Functional Assessment of Cancer Therapy (FACT), Multidimensional Fatigue Inventory (MFI-20), Disabilities of the Arm, Shoulder, and Hand (DASH), Numeric Pain Rating Scale (NPRS), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Pain Pressure Threshold (PPT), 30 Seconds Sit to Stand (30SSTS), 5 Times Sit to Stand (5TSTS), 6 Minute Walk Test (6MWT), Timed Up And Go (TUG), European Organization for Research and Treatment of Cancer – Quality of Life (EORTC-QLQ), Pittsburgh Sleep Quality Index (PSQI), high intensity interval training (HIIT), International Physical Activity Questionnaire (IPAQ), Cancer Fatigue Scale (CFS), Lymphedema Breast Cancer Questionnaire (LBCQ), Karnofsky Performance Scale (KPS), Godin Leisure-Time Exercise Questionnaire (GLTEQ), Patient-Reported Outcome Measurement Information System (PROMIS), Rate of Perceived Exertion (RPE), Fullerton Advance Balance (FAB)

ABSTRACT

Background: Exercise interventions have been shown to improve physical function before, during and after cancer treatment, but comparing the impacts of exercise interventions across studies is limited by the wide range of physical function outcome measures used. Having an agreed-upon common suite of measures would help cross-study comparisons.

Objective: Our primary purpose in this scoping review was to synthesize the published evidence regarding the physical function outcome measures that are used to assess changes associated with exercise and physical activity in cancer and cancer-related treatment. We also aimed to summarize the impact of physical activity interventions on the outcome measures utilized in this scoping review.

Methods: The lead author worked with a senior medical librarian to construct and refine a search strategy to identify studies with physical outcome measures related to exercise and cancer treatment between July 2018 and November 2024. The following databases were searched: Medline, PubMed, Cochrane Library, Web of Science. Abstracts were loaded into Covidence review software, deduplicated, and then screened by two authors to determine study eligibility based on title and abstract. Three hundred eighty-six studies underwent full-text review by two authors; the reviewers discussed differences for a final decision. Studies eligible included randomized controlled trials involving adult subjects diagnosed with cancer who underwent surgery, and/or chemotherapy, and/or radiation, physical function side effects, functional outcome measures, and exercise intervention. Studies that included subjects with metastatic cancer were excluded. Data were extracted by two authors including physical and mental function, side effects, outcome measures,

intervention, rehabilitation stage, cancer type and stage, results, adverse events, clinical implications, and study size. The study findings were reported by cancer and a detailed view of outcome measures by cancer type and frequency of measure use.

Results: A total of 2,550 references were retrieved. After deduplication and full-text review, 41 were included in this review. Twenty-three studies were specific to breast cancer and included 56 unique physical outcome measures. Six studies included a mix of breast, gynecologic, and prostate cancers with 22 physical outcome measures. There were 3 studies specific to prostate cancer and 3 studies that included a mix of prostate, colon, and colorectal cancer; both groups included 11 physical outcome measures. Two lung cancer studies were included with 14 physical outcome measures. One multiple myeloma study included 9 outcome measures. Three studies that included any cancer type included 8 physical outcome measures. In total, there were 41 articles reviewed that used 91 unique physical outcome measures to assess and monitor exercise impact on physical function.

Discussion: To our knowledge, this study is the first systematic scoping review on the heterogeneity of outcome measures used to assess physical function among cancer survivors undergoing exercise interventions. We observed substantial heterogeneity of outcome measures in the study populations. Findings from this review can inform future efforts to establish a common set of physical function measures that would be useful for cross-study comparisons and for subsequent systematic reviews.

INTRODUCTION

With early detection and diagnosis, improved cancer treatment options, and improvements in cancer prevention, patients are living longer following a cancer diagnosis. The National Cancer Institute estimates more than two million new cancer diagnoses in 2024. The current all cancer five-year survival rate is 74%, up from 50% in 1975. The median age at diagnosis for cancer of any site is 67 while the median age at death is 73.[1] Cancer and cancer treatment accelerate physiologic aging and functional decline.[2] Younger and older adults following cancer treatment report increased pain, chronic fatigue, peripheral neuropathy, lymphatic dysfunction, balance decline, decreased muscle strength and endurance, and decreased activity tolerance.[3] Acute, long term, and latent side effects associated with cancer and cancer treatment may present during treatment, persist long after treatment, or appear years after treatment completion. Physical side effects of cancer treatment impact function, activities of daily living, work responsibilities, family responsibilities, and mental health. Different types of cancer, various stages of cancer, multiple treatments used, comorbidities and precancer health status are factors in the heterogeneous list of common side effects.

Measurement of physical function is fundamental for the long-term management of cancer survivors. The scope of health outcomes utilized to assess physical function is broad. Improving our understanding of the scope and refining our selection of physical function outcome measures may be beneficial for program evaluation and clinical care. However, there is limited research to support a best practice approach. There is a need to determine the most suitable instruments for use in clinical practice, research, and program evaluation.

Cancer and Cancer Treatment Heterogeneity

Cancer care has changed substantially over the last 20 years; early diagnosis and treatment options have extended prognosis for many survivors. These advances have expanded the need for rehabilitation and a team-based approach to cancer care. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for a patient diagnosed with breast cancer is 260 pages long[4], providing myriad treatment pathways. Variables such as stage of breast cancer, hormone positivity, presence of the HER2 protein and the genetic makeup of the tumor are all factors that will aid the medical oncologist in the most effective treatment plan. Variability in treatment plans contributes to variability in short- and long-term adverse events that may negatively impact physical function and mental health.[5]

Rehabilitation clinicians cannot expect patients with the same cancer diagnosis to have received the same treatment protocols and thus cannot assume that these patients will present with similar impairments. Patients who receive anthracyclines may develop cardiac toxicity that results in fatigue and shortness of breath.[6] Taxane-based chemotherapy is a known neurotoxin which could present as chemotherapy-induced peripheral neuropathy (CIPN).[7] Vinca alkaloids may cause both a sensory and motor neuropathy.[8] With the increasing array of available cancer therapies, it is a challenge for rehabilitation clinicians to stay abreast of evidence-based treatments to mitigate side effects.

Heterogeneity of Rehabilitation Patient Care

The ability of rehabilitation clinicians to effectively assess and treat the multitude of side effects of cancer treatment continues to progress. The American Physical Therapy

Association's (APTA) Academy of Oncologic Physical Therapy has developed the Evidence Database to Guide Effectiveness (EDGE) Task Force comprehensive bibliography which makes recommendations regarding outcome measures to assess balance, pain, strength, and other outcomes for several of the more common cancers including breast, prostate and colorectal cancer. However, this bibliography has not been updated since 2019.[9] In addition, this guide does not address some of the more specific problems that may result from cancer treatment. In the example of chemotherapy-induced peripheral neuropathy (CIPN) there is emerging evidence for the use of vibration[10], strength training[11], endurance training[12], and blood flow restriction[13]; each of these approaches may require a unique array of outcome assessments.

The setting, structure and timing of initiation of rehabilitation interventions are other sources of heterogeneity in approach. Models may be hospital-based, community based, clinically integrated into the oncology clinical setting[14], or delivered virtually via telehealth[15] or phone intervention[16]. Determining which outcome measures are feasible and relevant across these settings is challenging.

Oncology Rehabilitation Guidelines

In 2017, the American Physical Therapy Association (APTA) published a clinical practice guideline (CPG) for exercise for cancer survivorship.[17] This CPG reinforces the general adult exercise guidelines and lacks detail specific to oncology patient needs. The APTA has developed CPGs for the diagnosis and treatment of breast cancer-related lymphedema[18,19], but has yet to develop similar guidelines for lymphedema as a consequence of treatment for head and neck cancers or gynecological cancers. The APTA also developed a CPG in 2022 for the Screening and Assessment of Cancer Related

Fatigue[20], and the associated CPG for the Treatment of Cancer Related Fatigue is forthcoming. APTA has yet to develop similar CPGs that address other treatment-induced side effects, leaving the rehabilitation clinician without a clear, evidence-based approach to treatment of a wide array of adverse effects.

In this study we sought to synthesize the published evidence regarding physical function outcome measures that are used to assess changes associated with exercise and physical activity in cancer and cancer-related treatment. We also aimed to summarize the impact of physical activity interventions on the outcome measures utilized in this scoping review. We are hopeful that this review will help guide future work to define a common set of physical function measures that would be useful for cross-study comparisons and future systematic reviews.

METHODS

A systematic scoping review was chosen to synthesize the most recent literature related to physical function for cancer survivors as it relates to the heterogeneity of outcome measures and exercise interventions. The principal investigator and one senior librarian performed a comprehensive search of multiple databases with a medical subject heading (MeSH) analysis of key articles provided by the research team. An iterative process was used to review and refine the searches. The formal search strategies used relevant controlled vocabulary terms, Boolean operators, and synonymous free-text word and phrases to systematically capture the concepts of *exercise intervention for cancer survivors* and the *heterogeneity of outcome measures*. Based on the research questions, a search strategy from the PICO framework was developed to identify research articles focusing on evidence related to physical function outcome measures, side effects,

(**O**utcome) and interventions (**I**nterest) associated with cancer survivorship (**P**opulation) before, during, and post-cancer treatment (**C**ontext).

The following databases were searched on October 16, 2024: CINAHL, PubMed, Cochrane Library (Wiley), and Web of Science. Peer-reviewed primary studies that were published in English between July 1, 2018, and October 16, 2024, were eligible for inclusion. Studies were included with cancer diagnosis, exercise intervention, physical function outcome measure, randomized controlled trial, and cancer stage I-III. Studies that included subjects with metastatic cancer were excluded (Appendix A). The starting date of mid-2018 was used because the American College of Sports Medicine released updated guidelines and recommendations on physical activity and exercise in cancer survivorship in 2019, and the American Physical Therapy Association released a summary of physical outcome measures associated with oncology rehabilitation in 2019.[21]

This scoping review was conducted using robust methodology that aligned with Arksey and O'Malley[22], utilizing Covidence to facilitate a systematic review process, and reported in accordance with PRISMA.

Data Extraction and Synthesis

The search results from each database were exported to a Zotero (Corporation for Digital Scholarship, Vienna, Virginia) library and deduplicated. This deduplicated set of references was then uploaded to Covidence (Covidence, Melbourne, AU) for review. Two authors (ROM and SOM) conducted a title and abstract review using a predetermined set of eligibility criteria. Since this study aimed to describe the heterogeneity of physical outcome measures used to guide exercise intervention for

cancer survivors, we deferred to the primary author for decision-making of appropriate outcome measures when there was uncertainty for inclusion. Both reviewers had to agree on the appropriateness of physical outcome measures to move on to the next step in the process. The reviewers met regularly via telephone and video conference to discuss and resolve any conflicts. The process was repeated for the full-text review stage.

After the eligible studies were identified, both reviewers extracted the following data into a Covidence data extraction template: Author, City, Country, Title, Journal, N (C:I), Mean Age (Age Range), Cancer Type, Cancer Stage, Study Arms, Outcome Measures, Collection Times, Rehab Stage, Results, Adverse Events/Feasibility, Research Opportunities and Clinical Implications. After the data were extracted, the authors arranged the findings by cancer type, outcome measures (see Table 1.1), and study findings (see Table 1.2 and 1.3).

RESULTS

The search produced 2,550 references. Following deduplication, 1,104 references were uploaded to Covidence, and another 12 duplicates were manually removed, leaving 1,092 references to screen. During the title and abstract review, 706 references were excluded. The remaining 386 references underwent full-text review by two reviewers, and 345 were removed, leaving 41 articles in the study. Randomized controlled trials were the only research designs included in this review. Our studies included 4,860 participants; the majority of participants were cancer stage I-III. The mean age for all studies ranged from 45 to 70 (see Figure 1.1 PRISMA Diagram).

Among the 41 studies reviewed, there were a total of 27 physical function related symptoms studied measured using 91 unique outcome measures. (Table 1.1). The

outcome measures studied most frequently were grip strength (11 studies), European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30/BR/GHB) (10 studies), 30 Second Sit To Stand (30SSTS) (8 studies), Numeric Pain Rating Scale (NPRS) (8 studies), 6 Minute Walk Test (6MWT) (7 studies), limb circumference (5 studies), Pittsburgh Sleep Quality Index (PSQI) (5 studies, all breast cancer), and Piper Fatigue Scale (PFS) (4 studies, all breast cancer). The heterogeneity of outcome measures selected for studies in this review will be further analyzed by cancer type.

Breast Cancer

There were 23 studies examining outcomes and interventions associated with breast cancer and related side effects and treatments. Twenty studies included cancer stage I-III (83%). There were a combined total of 2781 participants in the breast cancer studies. The mean age range for breast cancer studies was 46-59. The majority (11) of breast cancer studies were conducted during post-cancer treatment, 6 were conducted during active and post treatment, 4 were conducted during active treatment, and 2 were conducted during prehabilitation and active treatment time points. Symptoms assessed included fatigue, neuropathic pain, musculoskeletal pain, lymphedema, grip strength, leg strength, arm strength, function, active/passive range of motion, physical fitness series, cardiovascular, body composition, physical activity, sensation, and sleep.

Heterogeneity of Physical Function Outcome Measures

Unique outcome measures most common to breast cancer only studies were hand grip dynamometry (grip strength, 8 studies), 30 Second Sit to Stand (function, 8 studies), numeric pain rating scale (pain, 5 studies), Pittsburgh Sleep Quality Index (sleep, 5

studies), Piper Fatigue Scale (fatigue, 4 studies), and limb circumference (lymphedema, 4 studies). Twelve cancer-related side effects were included among breast cancer only studies with 50 unique physical function outcome measures. The side effects with the greatest heterogeneity and frequency of outcome measures selected for research among studies in this review were global function (13 outcome measures, 30 studies), strength (7 outcome measures, 15 studies), pain (6 outcome measures, 15 studies), lymphedema (7 outcome measures, 11 studies), and fatigue (4 outcome measures, 10 studies).

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Prehabilitation and Active Treatment

Lee et al. 2021[23] (HIIT intervention, 3 times per week for 8 weeks) demonstrated significant between group improvement in physical function (stair climb test and 6 MWT), and quality of life improvement (FACT-B). There were no between-group differences noted for fatigue (MFI-20), and physical function (TUG and 30SSTS).

Li et al. 2024[24] (aerobic and flexibility intervention, 3 days per week for 12 weeks) demonstrated significant improvement between groups in health-related physical fitness measures including body composition (waist circumference and waist to hip ratio), cardiovascular (VO2 peak), strength (grip strength), Physical Activity Energy Expenditure (IPAQ-SF), fatigue (CFS), and sleep improvement (PSQI). No between-group difference was noted for quality of life (FACT-B).

Active Treatment

Anandavadivelan et al. 2024[25] (HITT intervention, 16 weeks) demonstrated improvements in fatigue (PFS), cardiovascular (ARCET), strength (isometric mid-thigh

pull and grip strength), and pain (PPT). There was no between-group difference in fatigue and cardiovascular fitness.

Antunes 2024[26] (aerobic and resistance intervention, 3 times per week for 20 weeks) demonstrated improved physical function (EORTC QLQ-C30, 30SSTS, and grip strength).

Bruce et al. 2021[27] (aerobic, flexibility, and resistance with motivational interviewing intervention, 16 weeks) demonstrated improvement in function (DASH), acute pain (NRS), and quality of life (FACT-B). No differences were noted in neuropathic pain (NRS) and lymphedema (LBCQ).

Huo et al. 2024[28] (4 NJF shoulder patterns, 4 consecutive days or 4 physical therapy sessions including ROM, strength, stretch, manual, 4 consecutive days) demonstrated improvement in A/PROM (Goniometer), pain (VAS), and strength (grip strength). The NJF group showed greater improvements in the above-mentioned areas than the traditional physical therapy intervention and control group.

Active Treatment and Survivorship

Andersen Hammond et al. 2020[29] (4 sessions focused on nerve glides and neuropathic pain management) demonstrated improvements in pain (PPT) and strength (grip strength). There were no between-group differences noted with function (DASH and S-LANSS) and sensation (TSAII vibration).

Bruce et al. 2022[30] (aerobic, flexibility, and resistance, 16 weeks) demonstrated significant improvement in function (DASH), and improvement in pain (NRS). There were no between groups differences noted in lymphedema (LBCQ).

Huang et al. 2019[31] (brisk walk intervention, 12-week home-based starting first day of third chemotherapy cycle) demonstrated less fatigue (BFI) and sleep (PSQI) decline in intervention group and increased function (KPS and 6MWT).

Klein et al. 2021[32] (home-based exercise and instruction with ROM focus, 3 times per day until full function and no pain is demonstrated) demonstrated significant improvement in pain (NPRS), function (Quick DASH), and ROM (Goniometer).

Mavropalias et al. 2023[33] (aerobic and resistance home-based intervention, 5 consultations for support, 12 weeks) demonstrated significant improvement in fatigue (FACIT-F and BFI) and quality of life (FACT-B). There were no between-group differences noted with sleep (PSQI) and self-report of physical activity (GLTEQ).

Paskett et al. 2021[34] (patient education for lymphedema management including breathing, stretching, strengthening, and ROM with a compression sleeve, follow-up measurements for 18 months) demonstrated improvement in lymphedema (limb volume), and ROM (self-reported).

Survivorship

Bloomquist et al. 2021[35] (football fitness aerobic and strength intervention, 52 weeks, 2 times per week) demonstrated no difference between groups for lymphedema (L-Dex), function (DASH), and breast/arm symptoms (EORTC QLQ).

Esteban-Simon et al. 2024[36] (resistance and >10,000 steps per day intervention, 12 weeks, 2 times per week) demonstrated significant improvement in function (DASH) and strength (grip strength). There was no between-group difference in arm volume (circumferential measurement).

Guloglu et al. 2023[37] (proprioceptive neuromuscular facilitation or progressive resistance training or control intervention, 8 weeks, 2 times per week) demonstrated strength improvement (isokinetic dynamometer) in both intervention groups. Both groups demonstrated function (DASH) and pain (VAS) improvement with greater function improvement in the PNF group.

Han et al. 2023[38] (aerobic, strength, and social capital intervention, 6 weeks supervised plus 6 weeks unsupervised) demonstrated fatigue (PFS) improvement, but no difference in quality of life (FACT-B) were observed between groups.

Kim et al. 2020[39] (aerobic, strength, and social capital intervention, 6 weeks supervised plus 6 weeks unsupervised) demonstrated significant improvement in self-report of physical activity (GPAQ), improvements in fatigue (PFS), and sleep quality (PSQI).

Lee et al. 2022[40] (high intensity Circuit Resistance, 12 weeks, 2-3 times per week) demonstrated significant improvement in body composition (TKK-5401), reaction time (BS-FF), and balance (Y-Test). No differences were noted between groups for strength (grip and back strength TKK-5402, sit-up, sit and reach, and plank).

Ochi et al. 2022[41] (home-based HIIT with exercise counseling intervention, 12 weeks, 3 times per week) demonstrated significant improvement in cardiovascular (VO2 Peak) and strength (leg press). No between-group improvements observed in function (6MWT and chair stand) and strength (grip strength).

Qiao et al. 2022[42] (home-based exercise intervention, 6-14 weeks with goal of achieving >150 minutes of moderate to vigorous exercise per week) did not observe any differences between groups in fatigue (PFS and FACT-ES).

Rasmussen et al. 2023[43] (progressive resistance exercise intervention, 12 weeks, 2 sessions per week) demonstrated significant improvements in maximal strength (1RM bench press) and pain (PPT). No between-group differences were observed for AROM (Goniometer).

Sen et al. 2021[44] (complete decompression therapy with and without MLD compared, 15 sessions, 3 weeks) demonstrated significant improvement in arm volume (arm circumference), discomfort, heaviness, and swelling (VAS) in both groups, greater improvements were observed in MLD group. Both groups demonstrated improvements in function (Quick DASH and Lymph-ICF) with no between-group differences.

Santagnello et al. 2020[45] (resistance intervention, 12 weeks, 3 times per week) demonstrated significant improvement in function (10M UWT, 10M FWT, TUG, 5TSTS, and 30SSTS), and improvement in fatigue (BFI), body composition (DEXA).

Breast or Gynecologic Cancers

Two studies examined outcomes and interventions among patients with breast or gynecologic cancers. Both studies included cancer stage I-III, with combined total of 390 participants. The mean ages were 53 to 70. Both studies were conducted during the post cancer treatment phase of survivorship.

Heterogeneity of Physical Function Outcome Measures

Physical side effects assessed were function, exercise self-efficacy, and physical activity. Seven unique outcome measures were analyzed in the two breast and gynecologic cancer studies.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Survivorship

Gell et al. 2024[46] (tele-EF aerobic, strengthening, balance, and flexibility intervention, 16 weeks, 3 days per week) demonstrated significant improvement in function (PROMIS, 5TSTS, and 30SSTS). Self-report physical activity (PAL4) and self-efficacy (self-efficacy to regulate exercise) showed no differences between groups.

Seib et al. 2022[47] (website with educational podcasts and exercise planner supporting healthy lifestyle behaviors, 12 weeks) demonstrated improvements in quality of life (FACT-G), and function (SF-36). There was no between-group difference for pain (SF-36 bodily pain subscale).

Gynecologic Cancer

Four studies examined outcomes and interventions associated with gynecologic cancer and related side effects and treatments. Two studies included cancer stage I-III, one study included stage II-III, and one study included stage I-II. There was a combined total of 339 participants in the gynecologic cancer studies. The mean age range was 56 to 61. Two studies were conducted during post cancer treatment, one was conducted during active treatment, and one was conducted during prehabilitation into active treatment time points.

Heterogeneity of Physical Function Outcome Measures

Physical side effects assessed were function, body composition, lymphedema, fatigue, strength, and exercise self-efficacy. Twelve unique outcome measures were analyzed in the four gynecologic cancer studies.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Prehabilitation and Active Treatment

Shallwani et al. 2021[48] (bilateral lower limb compression, aerobic, and resistance intervention, >6 months, 12-16 hours per day) observed a delayed onset of lymphedema (circumferential measurements) with the intervention group.

Active Treatment

Wu et al. 2021[49] (CDT, rehabilitation exercise, and education intervention, once time per day for 20 days as a cycle, treatment contained two cycles for 40 days total) demonstrated significantly lower rate of lymphedema (circumferential measurements) with delayed onset. Fatigue (BFI) and quality of life (EORTC QLQ-C30/GHS/FS/SS) improved significantly.

Survivorship

Gorzelitz et al. 2022[50] (home-based strength intervention, 10 weeks, 2 times per week) demonstrated improvements in lean mass (DXA) in the intervention group. Improvements were also observed in strength (arm curls), flexibility (chair sit and reach), and function (30SSTS and 8ft up and go). There were no between-group difference observed in function (6MWT, PROMIS) and quality of life (FACT-EN).

Senisik et al. 2022[51] (exercise per ACSM guidelines, OMNIRES-Perceived Exertion Scale for Resistance intensity 3-6/10 with patient education about the benefits of regular exercise and healthy nutrition, 12 weeks) demonstrated significant improvement in function (FACT-G and FACT-F), strength (grip strength, leg and back extensor strength).

Prostate Cancer

Three studies examined outcomes and interventions associated with prostate cancer and related side effects and treatments. Two studies included cancer stage I-II, and one study included stage I-III. There was a combined total of 129 participants in the prostate cancer studies. The mean age range for prostate cancer studies was 62 to 65. Two studies were conducted during post cancer treatment, and one was conducted during active into post treatment time points.

Heterogeneity of Physical Function Outcome Measures

These studies assessed side effects of cardiovascular, strength, function, flexibility, and body composition. VO2 Peak was included in 3 out of 3 prostate cancer studies. There were 10 additional outcome measures in these studies.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment and Survivorship

Harrison et al. 2022[52] (resistance and aerobic intervention, 16 weeks, 3 times per week starting at 4 weeks prior to initiation of androgen deprivation therapy) demonstrated improvements in cardiovascular (VO2 peak), strength (1RM leg press), and function (6MWT).

Survivorship

Kang et al. 2021[53] (exercise intervention individualized on basis of participant, 12 weeks, 3 times per week) demonstrated significant improvements with cardiovascular fitness (VO2 peak), strength (arm curls), and flexibility (sit and reach).

Van Blarigan 2024[54] (progressive walking intervention, 16 weeks) demonstrated significant improvement in body composition (BMI) and improve in cardiovascular fitness (VO2 peak and RPE).

Prostate or Colorectal Cancers

One study examined outcomes and interventions among patients with prostate or colorectal cancer and related side effects and treatments. This study included cancer stage I-III. There were 478 participants were in this study, with a mean age of 66 and age range was 45 to 87.

Heterogeneity of Physical Function Outcome Measures

Side effects assessed were physical activity, function, and fatigue. Three unique outcome measures were included in this study.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment

Golsteijn et al. 2023[55] (OncoActive computer-tailored physical activity advice, 3 occasions) demonstrated significant improvements in fatigue (checklist). No between-group differences were observed for physical activity (MVPA from Actigraph) and physical function (EORTC-QLQ-C30).

Colon and Colorectal Cancers

Two studies examined outcomes and interventions associated with colon and colorectal cancers and related side effects and treatments. One study included cancer stage II-III; one study did not report the cancer stage included. There was a combined total of 220 participants in these studies. The mean ages were 55 to 62. Both studies were conducted during the active treatment phase.

Heterogeneity of Physical Function Outcome Measures

The side effects assessed were function, neuropathy, strength, pain, and falls. VO2 Peak was included in 3 out of 3 prostate cancer studies. The NPRS was included in both studies, and 8 additional outcome measures were included in these studies.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment

Brown et al. 2024[56] (home-based resistance intervention, progression consistent with ACSM guidelines, 4-6 sessions with a certified cancer exercise trainer) demonstrated gait speed improvements for participants greater than 60 years of age. There were no differences between groups observed for function (SPPB and sit to stand), strength (hand grip), and no change in self-report of physical function.

Eroglu et al. 2024[57] (hand-foot exercise intervention, 8 weeks, 3 days per week, 3 sessions per day) demonstrated significant improvement in peripheral neuropathy (CIPN) and quality of life (EORTC QLQ-C30). There were no between-group differences observed for falls (self-report).

Lung Cancer

Two studies examined outcomes and interventions associated with lung cancer and related side effects and treatments. One study included cancer stage I-III, and one study stage II-III. There was a combined total of 204 participants in these studies. The mean ages were 45 to 67. Both studies were conducted during the active treatment phase.

Heterogeneity of Physical Function Outcome Measures

The side effects assessed were lung function and Watson Theory of Caring. Both studies included the six-minute walk test and pulmonary function test.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment

Ji et al. 2023[58] (active cycle breathing intervention, 3 months, 2 times per day) demonstrated significant improvements with pulmonary function test (PEF, FEV1/FVC, VC), Watson Theory parameters, pain (VAS), quality of life (QLQ-C30) and improvements in function (6MWT, RPE and dyspnea). The intervention group experienced a significant reduction in post-surgical complications.

Tenconi et al. 2021[59] (therapeutic education, aerobic and resistance intervention, abdominal wall and Respiratory Muscle Training, 14 preoperative sessions and 39 postoperative session, 2-3 times per week plus 8 home-based sessions performed 3-4 times per week) demonstrated significant improvements for function (PFT and 6MWT). No differences between groups were observed for quality of life (SF-12).

Multiple Myeloma

One study examined outcomes and interventions associated with multiple myeloma and related side effects and treatments. This study included cancer stage R-ISS I-III. There were 86 participants in this study with a mean age of 67.

Heterogeneity of Physical Function Outcome Measures

Strength, function, pain, physical activity, and bone mineral density were assessed as side effects. This study included eight outcome measures.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment

Larsen et al. 2024[60] (modified weight-bearing home-based exercise and physical activity, 10-weeks, 8 times supervised) demonstrated less strength (knee extension

dynamometer and grip strength). Significant improvements were observed in function (6MWT and 30 SSTS), and quality of life (EORTC-QLQ-C30). There were no differences between groups observed in bone mineral density (DEXA) and physical activity (accelerometer).

Any Cancers

Three studies examined outcomes and interventions among patients with any types of cancer and related side effects and treatments. Two studies included cancer stage I-III; one study did not report the cancer stage included. A total of 233 participants were in these studies. The mean ages were 45 to 58. Two studies were conducted during the active treatment phase and one study was conducted post cancer treatment.

Heterogeneity of Physical Function Outcome Measures

The side effects assessed were neuropathy, balance, fatigue, function, pain, and fear of falls. Eight outcome measures were included in these studies.

Efficacy of Exercise Intervention on Physical Functional by Stage of Treatment

Active Treatment

Muller et al. 2021[11] (sensorimotor intervention or resistance intervention, 40 weeks, 3 days per week for 40 weeks vs. resistance training 2 days per week for 40 weeks) observed no between-group difference for TNS; however, all groups improved significantly. Quality of life (EORTC QLQ-C30) improved for both intervention groups. Fear of falling (FES-I) increased among participants of the control group.

Saraboon et al. 2021[61] (balance intervention, 6 weeks, 1 time per day) demonstrated less balance decline (FAB and SPPB). The intervention group's quality of life improved (FACT-Taxane).

Survivorship

Siebert et al. 2022[62] (moderate endurance and strengthening or vigorous endurance and strengthening, 4 weeks) demonstrated fatigue (MFI-20) and pain (NRS) improvements in both intervention groups, greater gains were observed in the vigorous intervention group.

Study Characteristics

A total of 41 studies were examined to conduct a scoping review of physical outcome measure examined in RCTs among oncology patients. Participants in the RCTs included in this study ranged from middle-aged to older adults. Over half of the studies reviewed patients with stage I-III breast cancer during active treatment and/or survivorship. This is not surprising given that breast cancer has the highest incidence rate among women in the US, and because of the success of modern treatment regimens, it also has the highest prevalence.[63] The studies included a wide range of physical outcome measures examining strength, endurance, pain, lymphedema, flexibility, range of motion, sensation, falls, balance, and sleep.

Only two studies reported adverse events with an exercise intervention. The complexity and variety of clinical presentations among cancer patients perhaps was a factor contributing to adverse events in combination with a continued need for evidence to support the myriad physical presentations.

DISCUSSION

Overview

The primary purpose of this scoping review was to synthesize the published evidence regarding physical function outcome measures that are used to assess changes

associated with exercise and physical activity interventions in cancer and cancer-related treatment. Consistent with previous reviews and professional summaries, we found a wide range of physical function outcome measures used in the assessment of exercise interventions in patients with cancer.[64] Function was measured with tests that assess physical strength (e.g. grip strength, leg press), more holistic measures that require a combination of balance, strength, coordination and endurance (e.g., 6 MWT, 5 STS), patient self-report questionnaires (e.g., DASH), self-reported pain, cardiovascular fitness (e.g., VO2 Peak), body composition, sleep, fatigue (e.g., FACIT-F), and more disease-specific measures such as lymphedema. The choice of outcome measures in any study is reflective of the specific goals of the study and a balance of ease of use, measurement burden, safety, cost, and other factors.

Global function is *inclusive* of strength, cardiovascular capacity, balance, sensation, mobility, pain status, and flexibility, and most efficiently represents multiple components of fitness within a dynamic movement system.[65,66] Consistent with the previous statement, the 2019 Academy of Oncologic Physical Therapy Task Force Cancer Evaluation Database to Guide Effectiveness (EDGE) provided holistic review of physical function outcome measures in the literature.[9] Mental health functioning is important to physical function, however, it is beyond the scope of this review.

After measures of more global function, the next most prevalent measures were those focused on assessment of strength followed by lymphedema, fatigue, and pain. The relative frequency of assessments of lymphedema is likely a reflection of the high proportion of studies focused on subjects living with breast cancer.

The American Cancer Society reports cancer-related side effects many of which align with those found in this scoping review. ACS physical function side effects that were not represented in our scoping review findings include bowel and bladder function.[67] Physical outcome measures and interventions to address bowel, bladder, and pelvic floor dysfunction are relatively limited research areas.

We aimed to report on efficacy of cancer-related exercise interventions based on outcome measures selected in this review. The authors sought updates to further define our understanding of physical function outcome measures utilized among cancer studies that target physical function and exercise intervention. We aimed to facilitate next steps in research to further define a common set of metrics used to assess and monitor physical function associated with cancer and cancer-related physical decline to support cancer survivors in maximizing their physical function.[81–83]

In an attempt to synthesize the results and add to the body of knowledge regarding measurement of physical function among cancer survivors we will discuss below the top five most frequent specific outcome measures examined in our 41 RCTs. The purpose of conducting a more detailed look at the measures is to raise awareness of current physical health outcome evidence, to support potential next steps in research, and to inform clinicians in patients care.

The top five most frequent outcome measures found in our study examining the impact of exercise intervention on physical function include: 1) EORTC-QLQ-30; 2) hand grip dynamometry; 3) numeric pain rating scale; 4) 30 Second Sit to Stand; and 5) 6 Minute Walk Test. Each of these measures has been validated and widely used. The **EORTC-QLQ-C30** is a questionnaire that assesses the quality of life of cancer patients

including physical, emotional, social functioning, pain, and fatigue; it demonstrates high evidence of content validity for assessing functional health, symptom burden, and health-related quality of life. The EORTC-QLQ-C30 has been shown to be a significant predictor of overall survival in patients with cancer.[68] Advantages of this measure are that is easily obtained by patient self-report, and that it assessed many domains, including quality of life, and emotional and social functioning. One disadvantage is that patient self-report may be influenced by many factors and may not be as reflective of physical function as a more objective measure. **Hand grip dynamometry** testing is a reliable and valid tool for measuring muscle strength. Hand grip strength has been associated with many health outcomes including all-cause, cancer, and cardiovascular mortality as well as morbidity, sarcopenia, and frailty.[69,70] Hand grip strength has also been shown to be an indicator of depression in older adults.[71] It is easily obtained with a low training burden. The **Numeric Pain Rating Scale** (0-10) assesses pain intensity in adults for a wide spectrum of conditions. It is a reliable, valid, and simple tool to administer. Pain intensity has been studied extensively over the last 30 years. Specifically, researchers and clinicians aim to better understand how pain intensity correlates with disability or daily function. Deimling et al. demonstrated that pain and fatigue are linked to functional difficulty among older breast cancer survivors.[72] Research shows that mild to moderate pain falls between 3 and 4, while moderate to severe pain falls between 6 and 8, and relates to physical function.[73] Given that the numeric pain scale is so widely used in both clinical and research settings, it offers the advantage of being able to compare patient experience across many conditions. The **30 Second Sit to Stand** test assesses leg strength, balance and endurance. This test has been shown to be a valid tool for

estimating peak oxygen uptake and 6-minute walk distance in women with breast cancer.[74] Diaz-Balboa et al. demonstrated that the 30 SSTS was an easy to use, low cost tool to estimate peak oxygen consumption and/or 6 MWT in women with early-stage breast cancer suggesting that it's use may facilitate stratification of functional capacity to most appropriately initiate therapeutic exercise.[74] The **6 Minute Walk** test originated as a tool to assess the functional status of patients with cardiopulmonary conditions. Over the last two decades the 6 MWT has been used as a valid, reliable, low-cost method of assessing functional ability in cardiac rehabilitation.[75] It has been shown to correlate with peak oxygen consumption. A recent meta-analysis showed that preoperative care, lifestyle management, and rehabilitation had a positive impact on 6 MWT among patients with colorectal cancer.[76] These last two measures (30 SSTS and 6 MWT) have an advantage of encompassing multiple domains of function, including strength, balance, and cardiovascular fitness. Future studies should consider the use of outcomes measures that encompass this holistic assessment of function.

Our secondary aim in this scoping review was to report on the effect of the interventions on outcome measures identified in this scoping review (Tables 1.2 and 1.3). For the purpose of this review, we have focused on the top five physical outcome measures. In 2023 Sturgeon and colleagues performed a systematic reviewed focused on the effects of exercise on understudied health outcomes in cancer survivors.[77] They found that function improved as measured by the EORTC-QLC-C30. Our scoping review was in agreement with Sturgeon et al[77] based on findings associated with use of EORTC-QLQ-C30. Consistency between our scoping review and Sturgeon et al. systematic

review suggest benefits of exercise as reported via EORTC-QLQ-C30, however, more research is needed to confirm the use of this outcome measure among cancer survivors.

Hand grip strength has high clinical value, is low cost to administer, and is correlated with functional status, and long-term outcomes. Silva et al. observed that cancer-related treatments are associated with decreased handgrip strength and subsequent decreased quality of life.[78] Our scoping review showed that hand grip strength is a common measurement, particularly among breast cancer studies, and is responsive to exercise interventions. These results support the use of hand grip strength as a physical outcome measure to assess and monitor changes associated with exercise intervention.

But-Hadzic et al. showed that the 6 MWT is a valid and reliable tool for discriminating between healthy women and breast cancer survivors.[79] Our scoping review showed that the 6 MWT was a commonly used physical outcome measure among a wide variety of cancer types. Our scoping review demonstrated variable 6 MWT results across cancer type and studies. 6 MWT is inclusive of several domains of function including strength, endurance, balance, and pain likely contributing to variability in results.

The numeric pain rating scale has been shown to have adequate validity, reliability, and responsiveness in patients with cancer pain.[80] It was a commonly used physical outcome measure among a wide variety of cancer types among studies of exercise interventions.

Findings from our study align with the current APTA EDGE summary with respect to physical outcome measures, and side effects assessed. Our study aligns with highly heterogenous physical outcome and findings associated with cancer-related treatment side effects. EDGE task force findings and our scoping review were consistent

in findings associated with 30-Second Sit to Stand. This was the only outcome measure in the top five most common from our scoping review also identified by the APTA EDGE task force as 'reasonable to use' and well-validated.[84] Dissimilar findings include use of the Pittsburgh Sleep Quality Index among breast cancer studies in our scoping review while it was not identified in the APTA summary. Findings from this study support continued development of oncology rehabilitation clinical practice guidelines.[64,85]

Limitations

Due to the heterogeneity of cancer and cancer care, there are low numbers of randomized controlled trials examining similar outcome measures and related impact of exercise intervention. Our study was limited to clinical trials and, therefore, may have omitted some important assessments of outcome measures that used other study designs. Studies published prior to July 2018 were not included in this review; however, authors relied on the EDGE task force summary for comparison of earlier studies. Lastly, a review of physical outcome measures and exercise intervention among all cancer types was a very broad topic. The authors are hopeful that a broader assessment of physical function will provide a larger scope of oncology rehabilitation and complement observations from studies with a narrower focus.

Future Directions

Oncology rehabilitation programs currently lack structure and recommendations partially due to heterogeneity of outcome measures and interventions to best support clinical practice.[86] In order for the field to continue to progress we need further development of rehabilitation clinical guidelines that take into account cancer type, stage, treatment, anticipated physical side effects, comorbidities, and other factors. These

guidelines would ideally be informed by high quality clinical trials that share some common outcome measure to allow for cross-study comparison and systematic review. Specific research is needed to evaluate which physical outcome measures might form a common core that is practical, feasible, and reflect outcomes that are important to patients and families.

Patients covered by Medicare may experience gaps in coverage as cancer is not a qualifying diagnosis for automatic referral. Research to support physical outcome measure as indicators for insurance reimbursement purposes may improve gaps experienced by cancer survivors.[87] There may be important lessons to be learned from the field of cardiac rehabilitation, which has been adopted as the standard care for patients following a qualifying cardiac event. The evidence to support cardiac rehabilitation has evolved to include standard interventions which include progression through phases, and common physical outcome measures that focus on physical function. There is an opportunity to learn from the evolution of cardiac rehabilitation starting with physical outcome measures that align between cancer and cardiac rehabilitation.

Outcome measure heterogeneity and lack of evidence to support physical function rehabilitation leaves clinicians uncertain, inconsistent, and perhaps less effective in their rehabilitation care.

CONCLUSION

This scoping review highlights the need for research to support oncology rehabilitation through the lens of physical outcome measures. In this study, we: 1) updated the evidence to support the state of heterogeneity of physical outcome measures, 2) identified the most common physical outcome measures being used in research to

provide guidance toward a common list of metrics to assess cancer-related physical decline, and 3) reported on efficacy on exercises intervention based on physical outcome measures.

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Table 1.1 ***Physical Function Outcome Measures in Exercise Clinical Trials for Patients with Cancer (N=41)***

Cancer Type	Symptoms	Outcome Measure[a]	N Studies
Breast 23 Studies	Fatigue	PFS	4
		BFI	3
		FACIT-F	1
		MFI-20	1
		FACT-ES	1
	Pain	DASH	3
		NPRS	5
		S-LANSS	2
		PPT	3
		VAS	2
	Function	DASH	3
		Quick DASH	2
		30 SSTS	4
		5 TSTS	1
		6 MWT	3
		TUG	2
		EORTC-BR23	4
		FACT-B	5
		FACT-G	1
		PASE	1
		KPS	1
		Stair Climb Test	1
		10 M Walk	2
	Lymphedema	Limb circumference	4
		Limb volume	1
		L-Dex	1
		DXA	1
		Self-Report heaviness, discomfort w/VAS	1
		LBCQ	2
		Lymph-ICF	1
	Strength	Hand Grip Dynamometer	8
		Isometric Mid-Thigh Pull	1
		Leg Press	2
		Leg Extension	1
		Leg Curl	1
		Calf Raise	1
		Chest Press	1
	A/PROM	Goniometer	3
		Self-Report	1
	Physical Fitness Series	Grip strength, back strength, sit ups, plank, sit and reach, whole body reaction, balance	1
	Body Composition	DXA	2
	Cardiovascular	VO2 Peak	2
		ARCET	1
		Accelerometer	1
	Physical Activity	GPAQ	2
		IPAQ-SF	2
		GLTEQ	1

	Sensation	TSA II	1
	Sleep	PSQI	5
Breast and Gynecologic 2 Studies	Function	PROMIS	1
		FACT-G	1
		5 TSTS	1
		30 SSTS	1
		SF-36	1
	Exercise Self Efficacy	Self-Efficacy to Regulate Exercise	1
	Physical Activity	PAL4	1
Gynecologic 4 studies	Function	FACT-G	1
		FACT-F	1
		FACT-EN	1
		PROMIS	1
		EORTC QLQ C30 GHS	1
	Body Composition	DXA	1
	Lymphedema	Limb circumference	1
	Physical Fitness Series	Arm curls, 30 SSTS, chair sit and reach, back scratch, 6MWT, 8 ft up and go	
	Fatigue	BFI	1
	Strength	Hand Grip Dynamometer	1
		Leg Extension	1
		Back Extension	1
	Exercise Self Efficacy	Self-Efficacy to Regulate Exercise	1
Prostate 3 studies	Cardiovascular	VO2 Peak	3
		RPE	1
	Strength	Leg Press	1
		Chest Press	1
		Arm Curls	1
	Function	6 MWT	1
		TUG	1
		30 SSTS	1
		SF-12	1
	Flexibility	Sit and Reach	1
	Body Composition	BMI	1
Prostate and Colorectal 1 study	Physical Activity	MVPA Actigraph GT3X-BT	1
	Fatigue	Checklist	1
	Function	EORTC QLQ-C30	1
Colon and Colorectal 2 studies	Function	SPPB	1
		SF-36	1
		30 SSTS	1
		EORTC QLQ-C30	1
	Neuropathy	CIPNAT	1
	Strength	Hand Grip Dynamometer	1
	Pain	NPRS	2
		VAS	1
	Falls	Self-report	1
Lung 2 studies	Lung Function	PEF	2
		FEV1/FVC	2
		VC	2

		6 MWT	2
		RPE	1
		Dyspnea Scale	1
		EORTC QLQ-C30	1
		SF-12	1
	Watson Theory of Caring	Drainage tube time, total oxygen, supplementation time, time in bed, LOS, postop complications	
Multiple Myeloma 1 study	Strength	Knee Extension	1
		Hand Grip Dynamometer	1
	Function	6 MWT	1
		30 SSTS	1
		EORTC QLQ-C30	1
	Pain	BPI	1
	Physical Activity	Daily Diary	1
		Accelerometer	1
	Bone Mineral Density	DXA	1
All Cancer Types	Neuropathy	TNS	1
3 studies	Balance	FAB Scale	1
		Force Plates	1
	Fatigue	MFI-20	1
	Function	EORTC QLQ-C30	1
		SPPB	1
	Fear of Falls	FES-I	1
	Pain	NPRS	1

[a] See glossary on title page for list of abbreviation

Table 1.2 Design of Clinical Trials of Exercise Interventions Assessing Physical Function Outcomes for People with Cancer

Author Year City, Country	Title Journal	N (F,M) I: N C: N	Mean Age (Range)	Cancer Type and Stage	Study Arms
Anandavadivelan et al 2024 Stockholm, Sweden	Five-year follow-up of the OptiTrain trial on concurrent resistance and high-intensity interval training during chemotherapy for patients with breast cancer. Scientific Reports	N=179 RT: 79 AT: 80 UC:81	48 (18-70)	Breast I-III	C: Usual care I: 16 weeks HIIT
Andersen Hammond et al 2020 Manitoba, Canada	An Exploratory Randomized Trial of Physical Therapy for the Treatment of Chemotherapy-Induced Peripheral Neuropathy. Sage Journals	N=48 I:28 C:32	54(37-78)	Breast I-III	C: Usual care I: Four visits with PT for HEP and education focused on nerve glides 3 x daily and symptom management of neuropathic pain, cold intolerance, hyperalgesia
Antunes et al 2024 Portugal	Exercise Training Benefits Health-Related Quality of Life and Functional Capacity during Breast Cancer Chemotherapy: A Randomized Controlled Trial. Medicine and Science in Sports and Exercise	F=93 I: 47 UC:46	50(20-80)	Breast I-III	C: Usual care I: Aerobic and resistance training 3 times per week starting with chemo through 20 weeks of chemo

Bloomquist et al 2021 Copenhagen, Denmark	Effects of football fitness training on lymphedema and upper-extremity function in women after treatment for breast cancer: a randomized trial. ACTA Oncologica	N=68	48 (18-75)	Breast I-III	C: Usual activity I: Football fitness training, twice weekly for 52 weeks, supervised by exercise by physiologist or physical therapist, aerobic and strengthening
Bruce et al 2021 Coventry, UK	Exercise versus usual care after non-reconstructive breast cancer surgery (UK PROSPER): multicentre randomised controlled trial and economic evaluation. The BMJ	N=382 I: 132 C: 138	58(28-88)	Breast I-III	C: Usual care with written information leaflets recommending postoperative exercises and generic postoperative advice I: Supervised exercise program based on motivational interviewing techniques to improve ROM, strength, and increase PS, and written information leaflets; 3 months
Bruce et al 2022 Coventry, UK	Exercise to prevent shoulder problems after breast cancer surgery: the PROSPER RCT. Health Technology Assessment	N=350 I:175 C:175	58(22-88)	Breast I-III	C: Usual care plus information leaflet I: 7-10 days post-op ROM, stretch, behavioral change strategies, physical activity; 4 - 16 weeks progression of exercises
Esteban-Simon et al 2024 Almeria, Spain	Does a Resistance Training Program Affect Between-arms Volume Difference and Shoulder-arm Disabilities in Female Breast Cancer Survivors? The Role of Surgery Type and Treatments. Secondary Outcomes of the EFICAN Trial. Archives of Physical Medicine and Rehabilitation	N=58 I:30 C:28	52(28-76)	Breast Not reported	C: Usual care with >10,000 steps per day C: 12-week exercise group; 2 sessions per week resistance training protocol, divided into: 2 weeks of individual training sessions and 10 weeks of small-group training sessions plus >10,000 steps per day

Guloglu et al 2023 Istanbul, Turkey	Efficacy of proprioceptive neuromuscular facilitation in improving shoulder biomechanical parameters, functionality, and pain after axillary lymph node dissection for breast cancer: A randomized controlled study. Complementary Therapies in Clinical Practice	N=66 PNF: 22 PRT:22 C:22	46(30-65)	Breast II-III	C: Usual care I: PNF and PRT groups, exercises to affected extremity applied two days a week for 8 weeks, supervised by a physical therapist
Han et al 2023 Seoul, Korea	Long Term Effects of a Social Capital-Based Exercise Adherence Intervention for Breast Cancer Survivors With Moderate Fatigue: A Randomized Controlled Trial Integrative Cancer Therapies	N=30 I:24 C:26	49(20-69)	Breast I-III	C: Usual care with general written information on exercise given at the hospital I: 2-week social capital-based exercise adherence program with aerobic, strength training, and social capital activation strategy; once per week for 6 weeks with exercise expert, second 6 weeks home based unsupervised, 2 times per week with development of social capital
Huang et al 2019 Tao-Yuan, Taiwan	The effect of a 12-week home-based walking program on reducing fatigue in women with breast cancer undergoing chemotherapy: A randomized controlled study. International Journal of Nursing Studies	N=159 I:81 C:78	48(24-72)	Breast I-III	C: Usual care with weekly phone calls for input on managing chemotherapy-related side effect; no PA advice I: 12-week, home-based brisk walking program started on the first day of the third chemotherapy cycle, weekly phone calls to reinforce their motivation and adherence

Huo et al 2024 Shandong Province, China	Short-term effects of a new resistance exercise approach on physical function during chemotherapy after radical breast cancer surgery: a randomized controlled trial. BMC Women's Health	N=162 NJF:51 Convention Rehab:50 Control:61	50(20-80)	Breast I-III	C: Usual care with a self-training manual with suggestions and exercise methods for arms and shoulders NJF: Four physical therapy treatments using 4 NJF shoulder patterns for 4 consecutive days, one hour each session Conv Rehab: Four physical therapy sessions once per day for four consecutive days including ROM, stretch, strengthening, manual tx, one hour each session
Kim et al 2020 Seoul, Korea	Pre-post analysis of a social capital-based exercise adherence intervention for breast cancer survivors with moderate fatigue: a randomized controlled trial. Supportive Care in Cancer	N=48 I:23 C:25	48(20-69)	Breast I-III	C: Usual care with written information about exercise I: 12-week comprehensive physical exercise adherence program, aerobic and strength training exercises with social capital activation strategy; first 6 weeks, one time per week in small groups, second 6 weeks in home 2 times per week with social capital activity - leadership and trusting relationships
Klein et al 2021 Tel Aviv, Israel	A pilot study evaluating the effect of early physical therapy on pain and disabilities after breast cancer surgery: Prospective randomized control trail. The Breast	N=157 I: 73 C: 87	52(18-85)	Breast I-II	C: Standard care I: Exercises and instruction for home exercise in form of a booklet aimed at ROM; 3 times a day, 5 reps each until full function and no pain Arm 1: Small surgeries Arm 2: Large surgeries

Lee et al 2021 Duarte, CA	Effect of high-intensity interval training on patient-reported outcomes and physical function in women with breast cancer receiving anthracycline-based chemotherapy. Supportive Care in Cancer	N=30 I:15 C:15	47(20-74)	Breast I-III	C: Usual care I: HIIT for 8 weeks 3 times per week
Lee et al 2022 Cheongju, Korea	Impact of High-Intensity Circuit Resistance Exercise on Physical Fitness, Inflammation, and Immune Cells in Female Breast Cancer Survivors: A Randomized Control Trial. International Journal of Environment Research and Public Health	N=30 I:15 C:15	54(40-70)	Breast I-III	C: Usual care I: HCRE for 12 weeks 50 min a day 2-3 times a week
Li et al 2024 Hubei, China	Improving physical and mental health in women with breast cancer undergoing anthracycline-based chemotherapy through wearable device-based aerobic exercise: a randomized controlled trial. Frontiers in Public Health	N=40 I:21 UC:19	48(30-65)	Breast I-III	C: Usual care with health and oncology education I: Aerobics and flexibility training 3 days per week for 12 weeks during 4 cycles of chemotherapy

Mavropalias et al 2023 Joondalup, Australia	The effects of home-based exercise therapy for breast cancer-related fatigue induced by radical radiotherapy. Breast Cancer	N=106 I:51 C:55	52(32-78)	Breast I-III	C: Usual care I: 12-week home-based exercise program involving resistance and aerobic exercise supplemented by a 1-h face-to-face consultation, four 30-min telephone consultations, an exercise manual, and exercise equipment.
Ochi et al 2022 Tokyo, Japan	Cardiorespiratory fitness in breast cancer survivors: a randomized controlled trial of home-based smartphone supported high intensity interval training. BMJ Supportive & Palliative Care	N=50 I:25 C:25	(20-59)	Breast I-III	C: Usual care I: Home-based exercise for 12 weeks, three times per week, with counselling/ exercise guidance and support provided via personalized email and a newly developed smartphone app
Paskett et al 2021 Columbus, OH	A randomized study to prevent lymphedema in women treated for breast cancer: CALGB 70305 (Alliance). Cancer	N=554 I: 315 C:253	58(24-88)	Breast I-III	C: Lymphedema prevention education I: Lymphedema prevention education, breathing, stretching, strengthening, and personalize ROM exercises daily with hand weights and compression sleeve at home
Qiao et al 2022 Pittsburgh, PA	Perceived physical fatigability improves after an exercise intervention among breast cancer survivors: a randomized clinical trial. Breast Cancer	N=41 I:22 C:19	55(>18)	Breast I-III	C: Standard care I: 6-14 weeks personalized, home-based exercise program with a goal of achieving the recommended >150 min/week of moderate to vigorous exercise
Rasmussen et al 2023 Aalborg, Denmark	The Analgesic Effect of Resistance Training after Breast Cancer (ANTRAC): A Randomized Controlled Trial. Medicine & Science in Sports & Exercise	N=20 I:10 C:10	59(52-66)	Breast I-III	C: Usual care I: 12 week supervised progressive resistance training program, two sessions per week

Santagnello et al 2020 Minas Gerais, Brazil	Improvements in muscle strength, power, and size and self-reported fatigue as mediators of the effect of resistance exercise on physical performance breast cancer survivor women: a randomized controlled trial. Supportive Care in Cancer	N=26 I:13 C:13	55(40-75)	Breast I-III	C: Usual care with stretching 2 x per week I: Resistance training 3 x per week for 12 weeks, lower extremity
Sen et al 2021 Istanbul, Turkey	Manual Lymphatic Drainage May Not Have an Additional Effect on the Intensive Phase of Breast Cancer-Related Lymphedema: A Randomized Controlled Trial. Lymphatic Research and Biology	N=54 I:27 C:27	57(33-75)	Breast Not reported	C: 15-session program, weekday for 3 weeks, included compressive multilayer bandaging and exercise training, one-session educational program I: 15-session program, weekday for 3 weeks, included compressive multilayer bandaging and exercise training, 45 min to 1 hr MLD, then bandaging, one-session educational program
Gell et al 2024 Burlington, VT	Remotely delivered exercise to older rural cancer survivors: a randomized controlled pilot trial. Journal of Cancer Survivorship Burlington, VT	39(31,8) I:20 C: 19	70(61-84)	Breast, prostate, cervical, endome trial, other I-III	C: Usual care I: Tele-EF (enhanced fitness) group exercise program including aerobic, strengthening, balance and flexibility exercise, one hour class, 3 days per week

Seib et al 2022 Queensland, Australia	Improving health-related quality of life in women with breast, blood, and gynaecological Cancer with an eHealth-enabled 12-week lifestyle intervention: the women's wellness after Cancer program randomized controlled trial. BMC Cancer	N=351 I:175 C:176	53(26-80)	Breast, blood, gynecol I-III	C: Standard care I: 12-week website with educational podcasts and exercise planners; an interactive iBook with practical information to support adoption and maintenance of healthy lifestyle behaviors and tracking of health behavior changes; three virtual consultations to support development of goals
Gorzelitz et al 2022 Madison, WI	Improvements in strength and agility measures of functional fitness following a telehealth-delivered home-based exercise intervention in endometrial cancer survivors. Supportive Care in Cancer	N=40 I:20 C:20	61(18-74)	Endome trial I-III	C: Usual care I: Twice weekly home-based strength exercise, supervised for 10 weeks, 5 weeks of FU
Senisik et al 2022 Izmir, Turkey	The effect of resistance exercise on quality of life and fatigue in patients with gynecological cancer. Turkish Journal of Sports Medicine	N=160 I:80 UC:80	Not reported	Gynecol ogical I-II	C: Usual care advised of ACSM guidelines for exercise I: Exercise per ACSM guidelines, adjust intensity of sessions according to the validated OMNIRES-Perceived Exertion Scale for Resistance intensity 3-6/10, educated about the benefits of regular exercise and healthy nutrition; 12 weeks

Shallwani et al 2021 Montreal, Canada	Feasibility of a Pilot Randomized Controlled Trial Examining a Multidimensional Intervention in Women with Gynecological Cancer at Risk of Lymphedema. Current Oncology	N=30 I:15 C:15	47(20-74)	Gynecologic I-III	C: standard care, prescribed compression stockings if lymphedema developed over the course of the study I: Prescribed standard or custom-made compression class 1 stockings for bilateral lower limbs, wear stockings for 12 to 16 h daily for at least six months postoperatively; received individualized education from the certified lymphedema therapist on general aerobic and resistance exercise according to the Canadian Physical Activity Guidelines
Wu et al 2021 Nantong, China	Early prevention of complex decongestive therapy and rehabilitation exercise for prevention of lower extremity lymphedema after operation of gynecologic cancer. Asian Journal of Surgery	N=109 I:53 C:56	56(NR)	Gynecologic II-III	C: Usual care I: CDT, rehabilitation exercise, and education, 40 min, once a day for 20 d as a cycle, treatment contained two cycles for 40 d
Harrison et al 2022 Durham, NC	A randomized controlled trial comparing changes in fitness with or without supervised exercise in patients initiated on enzalutamide and androgen deprivation therapy for non-metastatic castration-sensitive prostate cancer (EXTEND). Prostate Cancer and Prostatic Diseases	M=26 I:13 C:13	65	Prostate I-III	C: Usual care I: Supervised resistance and aerobic exercise, 3 days per week x 16 weeks starting at 4 weeks before initiation of ADT; aerobic and resistance progressed

Kang et al 2021 Alberta, Canda	Effects of Exercise on Cardiorespiratory Fitness and Biochemical Progression in Men With Localized Prostate Cancer Under Active Surveillance: The ERASE Randomized Clinical Trial. JAMA Oncology	N=52 I:26 C:26	63(>18)	Prostate I-II	C: Usual care and continue typical level of exercise I: 12-week, 3 x weekly, supervised exercise program individualized on the basis of each participants baseline cardiopulmonary fitness, and the intensity and duration of exercise were increased over time
VanBlarigan et al 2024 San Francisco, CA	Effect of a Home-based Walking Intervention on Cardiopulmonary Fitness and Quality of Life Among Men with Prostate Cancer on Active Surveillance: The Active Surveillance Exercise Randomized Controlled Trial. European Association of Urology	N=51 I:26 C:25	62(42-80)	Prostate I-II	C: Usual care with printed PA recommendations I: 16-wk walking program was a nonlinear prescription designed to increase cardiorespiratory fitness; training sessions initially 3 d/wk, by week 5, 4d/wk, with increasing duration of each session, prioritizing duration of session and reducing prescribed intensity to the maximum % VO2peak that could be maintained
Golsteijn et al 2023 Heerlen, Netherlands	Long-term efficacy of a computer-tailored physical activity intervention for prostate and colorectal cancer patients and survivors: A randomized controlled trial. Journal of Sport and Health Science	478(62,416) I:249 C:229	66(45-87)	Prostate Colorectal I-III	C: Usual care I: OncoActive, computer tailored PA advice, provided on 3 occasions

Brown et al 2024 Baton Rouge, LA	Effect of resistance training on physical function during chemotherapy in colon cancer. Journal of the National Cancer Institute	181(86,95) I:92 UC:91	55(>18)	Colon II-III	C: Usual care advised to ask physician what exercise would be safe and effective I: Resistance training, home based weightlifting exercises, progression consistent with ACSM guidelines, 4-6 sessions with a certified cancer exercise training to learn each exercise
Eroglu et al 2024 Ankara, Turkey	The effect of hand-foot exercises on chemotherapy-induced peripheral neuropathy-related pain, falls, and quality of life in colorectal cancer: A randomized controlled trial. European Journal of Oncology Nursing	N=39 I:19 C:20	62(50-75)	Colorectal Not reported	C: Usual care I: Hand-foot exercise booklet and program; performed three sessions a day and three days a week fashion for 8 weeks at home
Ji et al 2023 Shandong, China	Effect of Using the Active Cycle of Breathing Technique Combined with Watson's Theory of Human Caring in Rapid Patient Rehabilitation Following Lung Cancer Surgery. Alternative Therapies	N=64(26,38) I:32 C:32	45(18-60)	Lung I-III	C: Usual care plus instruction to pay attention to nutritional intake and practice lip contraction and abdominal breathing I: Active cycle breathing technique training, twice per day, 3 months following surgery, patients cared for by Watson Theory of Human Caring Nursing Team, targeted health education, patient specific nutrition input, exercise with former patients, and WeChat to supervise outpatients ACBT

Tenconi 2021 Reggio Emilia, Ital	Rehabilitation for lung cancer patients undergoing surgery: results of the PUREAIR randomized trial. European Journal of Physical and Rehabilitation Medicine	140(54,86) I:70 C:70	67(NR)	Lung I-II	C: Standard care I: Received standard care plus intensive perioperative pulmonary rehabilitation, 14 preoperative sessions and 39 postoperative, preoperative sessions were divided into six outpatients, performed two to three times per week, plus eight homebased sessions performed three to four times per week, preoperative treatment 14 to 21 days; therapeutic education, aerobic training, resistance training for upper and lower limbs, abdominal wall and Respiratory Muscle Training (RMT)
Larsen et al. 2024 Roskilde, Denmark	Exercise in newly diagnosed patients with multiple myeloma: A randomized controlled trial of effects on physical function, physical activity, lean body mass, bone mineral density, pain, and quality of life. European Journal of Haematology	86(37,49) I: 44 C:42"	67(NR)	Multiple Myelom	C: Usual care I: Usual care plus 10-week structured exercise intervention including modified weight-bearing exercise; 8 physical therapist supervised exercise session and home-based exercise and physical activity
Muller 2021 Heidelberg, Germany	Preventive effect of sensorimotor exercise and resistance training on chemotherapy-induced peripheral neuropathy: a randomized-controlled trial. British Journal of Cancer	170(144,26) SMT: 52 RT: 60 C: 58	53(>18)	All I-III	C: Usual care without additional information about physical activity I: Sensorimotor training was, 3 days per week for 35 min, introductory one-to-one training session, a catalogue of exercises, 45 illustrated exercise cards, at home or in an open supervised training session I: Resistance training included machine-based 2 days per week for 45 min, and a 15 min home-based training once a week, machine-based RT and was performed in an experienced exercise oncology training facility

Saraboon et al 2021 Bangkok, Thailand	Effects of foam pad balance exercises on cancer patients undergoing chemotherapy: A randomized control trial. Journal of Bodywork & Movement Therapies	N=30 I:15 C:15	45(30-50)	All I-III	C: Usual care I: Balance exercise on a foam pad program consisted of 10 standing-position exercises, 40-minute program, once/day for six weeks
Siebert et al 2022 Cologne, Germany	A Randomized, Controlled Pilot Study to Evaluate the Immediate Effect of Targeted Exercise Therapy on Cancer-Related Fatigue in Cancer Survivors: The FatiGO Study. Oncology Research and Treatment	N=33 I End mod:7 I Str mod:5 I End vig:7 I Str vig:6 C:8	58(30-69)	All Not Reported	C: Usual care I: Subgroups included moderate endurance and strengthening, and vigorous endurance and strengthening, 4 weeks for 3 sessions per week

Table 1.3 Results of Clinical Trials of Exercise Interventions Assessing Physical Function Outcomes for People with Cancer

Author	Outcome Measures	Collection Times Rehab Stage	Results: relative to I group	Adverse Events, Feasibility	Research Opportunities & Clinical Implications
Anandavadivelan et al	Primary Outcome Fatigue: Piper Fatigue Scale (PFS) Secondary Outcome Cardio: astrand-rhyming fitness submaximal test, accelerometer Strength: isometric mid-thigh pull, grip strength Pain: Pressure pain threshold (PPT)	Baseline, 16 weeks, 1/2/5 years Active treatment	Fatigue and cardiovascular improvements, no between-group difference in fatigue and cardiorespiratory fitness, increase strength	Not reported	Develop enhanced strategies to assist survivors in maintaining their PAL and offering continuous motivational support and PA prescriptions
Andersen Hammond et al	Primary Outcome Neuropathic pain: NPRS, DASH, S-LANSS Secondary Outcome Sensation: TSAII vibration Pain: PPT Strength: hand dynamometry	Baseline 7-18 weeks 3 & 6 months post chemo Active treatment, survivorship	Pain decreased, hand strength improved DASH, S-LANSS and vibration no difference	Not reported	Future research to evaluate whether exercises might assist in minimizing dose reductions or treatment delay for the improvement of chemotherapy treatment delivery and general exercise benefit for sensory preservation

Antunes et al	Primary Outcome Function: EORTC QLQ-C30 Secondary Outcome Function: 30 second sit to stand Strength: hand grip	Baseline Weeks 8-12 of chemo End of chem week 20 Active treatment	Physical function improvements, less deterioration global health and emotional function	Not reported	Application of multidimensional tool such as Piper Fatigue Scale or QLQ-FA12 alongside QLQ-C30 could allow for a more comprehensive evaluation of cancer-related fatigue
Bloomquist et al	Primary Outcome Lymphedema: DXA, L-Dex Secondary Outcome Function: EORTC QLQ BR23, DASH	Baseline 6 & 12 months Survivorship	No difference in DEXA outcomes at 12 months no difference for EORTC QLQ BR23 or DASH	Participation in football training is feasible and suggests no negative effects on breast cancer-specific upper-body morbidity	Football training is a feasible evidence-based alternative to traditional exercise modalities that could potentially appeal to women who would not otherwise participate in exercise
Bruce et al 2021	Primary Outcome Function: DASH Secondary Outcome Function: DASH subscale pain, complications, health related quality of life, FACT-B+4 Pain: NPRS Lymphedema: Lymphoedema and Breast Cancer Questionnaire HR-QoL: SF-12, EQ-5D-5L	DASH Baseline, 6 weeks 6 & 12 months All other outcomes: 7-10 days postop 1, 3 & 12 months Active treatment	DASH improvement at 12 months; DASH subscales favoured Acute pain improved, neuropathic pain no difference; lymphoedema no difference; HR QoL scores improved	No increase in complications, lymphoedema, or adverse events was noted	Future research directions could evaluate application of preoperative screening criteria for the identification of women at higher risk of developing post-treatment limb related disability who could benefit from supervised exercise

Bruce et al 2022	Primary Outcome Function: DASH Secondary Outcome Pain: NRS, AL 17, I6, PR-5, self-reported, DN-4, FACT-B4 Lymphedema: LBCQ Function: PASE	Baseline 6 weeks 6 & 12 months Active treatment, survivorship	DASH improved Pain improvement, lymphedema no difference	Not reported	Need for private space for appointments identified, access to emotional support for PTs and integration of PT expertise within the multidisciplinary oncology team
Esteban-Simon et al	Primary Outcome Lymphedema: Circumferential Measurements Secondary Outcome Function: DASH Strength: Dynamometer	Baseline Week 12 Survivorship	Arm volume no difference; inverse association between changes in upper limb muscle strength and changes in perceived shoulder-arm disabilities Function and strength improved	Two adverse events occurred	Further research including diagnosis of lymphedema are needed and most efficient resistance training program in order to manage lymphedema and shoulder-arm disabilities through exercise.
Guloglu et al	Primary Outcome Strength: Isokinetic dynamometer Secondary Outcome Function: DASH Pain: VAS Patient perception: Global Rating of Change	Baseline Week 8 Survivorship	Strength improved PNF and PRT compared to control, no difference between PNF and PRT DASH improved both PNF and PRT, greater change in the PNF group; pain level in both groups improved, no difference between PNF and PRT; greater improvement in GRC among PNF	No exercise related side effects	The most important clinical result of this study is that PNF is an effective and improvable treatment option in the restoration of daily living activities of patients who have survived breast cancer.

Han et al	Primary Outcome Fatigue: Piper Fatigue Scale Secondary Outcome QoL: FACT-B Physical activity: GPAQ Depression and anxiety: K-HADS Sleep quality: PSQI Social capital: PSCS-8	Baseline, post-intervention, 1 and 6 months Survivorship	CRF improved all time points; QoL both groups improved; greater increase in activity; psychosocial factors favored improved all time points	Not reported	Future studies that expand the sample size and extend to BCS at longer survival periods may be helpful in better determining the effects of exercise adherence programs and their translatability to clinical practice
Huang et al	"Primary Outcome Fatigue: BFI Secondary Outcome Function: KPS, 6 MWT Sleep: PSQI Anxiety and depression: HADS-A"	First day of 2nd chemo cycle weekly logs 12 weeks Active treatment, survivorship	Fatigue increased overtime for both groups, less increase with intervention group Increased functional performance, lower sleep disturbance, and depression at a given time was associated with less fatigue at that time	Not reported	Positive effect of home-based brisk walking program on reducing fatigue during chemotherapy, this finding suggests that exercise interventions are possible during treatment and may be initiated early to help breast cancer survivors establish long-term healthy behaviors. Exercise is a cost-effective intervention in relieving fatigue and was shown to be more effective than pharmacological management; home-based brisk walking program is particularly appealing due to its low cost and less time restriction

Huo et al	Primary Outcome A/PROM: Goniometer Secondary Outcome Strength: Grip strength Pain: VAS	Baseline Post-intervention Active treatment	A/PROM improved; larger improvement noted with NJF compared to conventional Pain scores and grip improved in both groups, NJF had a larger improvement	Not reported	Long-term intervention study of NJF for more than 8 weeks in the future and follow-up the effect of the intervention to explore the long-term effect of NJF in improving shoulder dysfunction in patients with breast cancer
Kim et al	Primary Outcome CRF: Piper Fatigue Scale Secondary Outcome QoL: FACT-B, FACT-G PA: GPAQ Depression and Anxiety: K-HADS Sleep Quality: PSQI Social Capital: PSCS-8	Baseline, post intervention Survivorship	CRF improved; FACT-B and FACT-G improved; PA and sleep improved; depression, anxiety, social capital no difference	Not reported	Future research needs to evaluate whether the promising results on physical activity and behavioral fatigue observed in the short term will persist over time
Klein et al	Primary Outcome Pain: NPRS Secondary Outcome Function: Quick DASH ROM: Goniometer	Baseline preop 1, 3, & 6 months Active treatment Survivorship	Pain and disability reduced, function improved, ROM impact with large surgeries, ROM no change small surgeries	Not reported	Further research needed to examine extent of surgery and PT impact

Lee et al 2021	Primary Outcome QoL: FACT-B Secondary Outcome Fatigue: MFI-20 Mindfulness: FFMQ-15 Physical Function: TUG, stair climb test, 30SSTS, 6MWT	1 week before first session of chemotherapy, week 9 Prehabilitation, Active Treatment	FACT-B improved; stair climb test improved; 6MWT improved, MFI-20, FFMQ-15, TUG, and 30SSTS no difference	No adverse events were reported over the duration of the intervention	Future studies should extend the intervention period, allowing for training to overlap with consecutive chemotherapy regimens
Lee et al 2022	Primary Outcome Physical Fitness: Grip strength TKK-5401, back strength TKK-5402, sit ups BS-SU, plank, sit and reach, whole body reaction BS-FF, balance Y-Test	Baseline Week 12 Survivorship	Body composition improved; reaction time improved; Balance improved; grip and back strength, sit-up and plank, sit and reach, single leg stand EC no difference	Not reported	For future studies, large community-based trials should be conducted to evaluate the long-term health-related benefits of RE in FBCSs.
Li et al	Primary Outcome Health Related Physical Fitness: Body Composition, VO2 Peak, Grip Strength Secondary Outcome Physical Activity: IPAQ-SF Anxiety and Depression: SAS, SDS Fatigue: CFS Sleep Quality: PSQI QoL: FACT-B, V4.0	Baseline, after 4 cycles of chemotherapy Prehabilitation, Active Treatment	Waist circumference and waist to hip ratio improved; VO2 Peak improved; hand grip strength improved; PAEE improved; anxiety and depression improved; fatigue improved; sleep quality and QoL no difference	No serious exercise-related adverse events were observed during the exercise intervention. However, patients in the exercise group did experience non-serious events during exercise, including toe pain, knee pain, and weakness	Future research to explore the long-term effects of exercise in this population with precise equipment to monitor follow-up in real time

Mavropalias et al	Primary Outcome Fatigue: FACIT-F, BFI Secondary Outcome QoL: FACT-B+4 Sleep: PSQI Physical Activity: Godin Leisure-Time Exercise Questionnaire	Baseline Week 6 & 12 Month 6 & 12 Active treatment, survivorship	CRF improved throughout timepoints, usual care improved 6 weeks post-treatment and beyond; BFI improved 6 weeks and beyond, usual care 6 months and beyond improved QoL improved both groups 6 and 12 months; no difference in sleep; no difference in PA	No serious adverse events were reported during the study	The benefits observed in this study can occur even with unsupervised home-based exercise and minimal equipment cost; however, these benefits occur when exercise is conducted regularly and dissipate after cessation.
Ochi et al	Primary Outcome Cardio: VO2 Peak Secondary Outcome Strength: 1RM Leg Press, Grip Function: 6MWT, Chair Stand Test	Baseline Week 12 Survivorship	VO2Peak improved Leg Press improved; 6MWT, Grip, and Chair Stand no difference	No serious adverse events occurred	Findings support the incorporation of home-based and unsupervised exercise programs into breast cancer survivorship care plans
Paskett et al	Primary Outcome Lymphedema: Limb Volume Secondary Outcome Lymphedema: Circumference measurement Function: Self-reported ROM Adherence: Self-reported sleeve/gauntlet use and exercises	Baseline 6, 12, & 18 months Active Treatment Survivorship	Lymphedema improved severity of lymphedema no difference; ROM improved	Low adherence	Future research could test adherence enhancing strategies and assisted activities among woman at risk for developing breast cancer-related lymphedema

Qiao et al	Primary Outcome Physical Fatigue: PFS Secondary Outcome Global Fatigue: FACT-ES	Baseline Post-intervention Survivorship	Physical fatigue no difference Global fatigue no difference		Future work will also include examining perceived mental fatigability using the PFS in additional cancer survivorship groups
Rasmussen et al	Primary Outcome Pain: PPT, NRS Secondary Outcome Strength: 1RM Bench Press ROM: Goniometric Measurements Psychometrics: MRE, PRE	2 weeks before intervention 1 week before intervention 1 week after intervention 12 weeks after intervention Survivorship	PPT improved; Pain improved Maximal strength improved; Active ROM no difference	No adverse events reported for this intervention	Proximity to breast cancer treatment was approximately 80 months for participants, the results may not be applicable to BCS in earlier stages of recovery
Santagnello et al	Primary Outcome Fatigue: BFI Secondary Outcome Physical Activity: IPAQ-SF Body Composition: DEXA Function: 5TSTS, 30sec STS, TUG, 10M UWT, 10M FWT Strength: Leg Extension, Leg Curl, Leg Press, Calf Raise Muscle Power: Dynamometer	Baseline, post-intervention Survivorship	Fatigue improved; Lean body mass improved; All walking tests and TUG improved; 5TSTS and 30 SSTS improved	Not reported	LBM, MS, and self-reported fatigue seem to be possible therapeutic targets for improvements of physical performance in BC patients

Sen et al	Primary Outcome Lymphedema: Arm Circumference Discomfort, heaviness, and swelling: Self-reported VAS Secondary Outcome Function: Quick-DASH, Lymph-ICF	Baseline postintervention Survivorship	Arm volume decrease both groups; VAS discomfort, heaviness, and swelling decreased both groups, greater decrease in intervention group Quick-DASH and Lymph-ICF decreased both groups, no between-group differences	Not reported	Further studies are needed to determine whether compression bandaging is sufficient as a stand-alone treatment in managing BRCL
Gell et al	Primary Outcome Physical function: PROMIS Secondary Outcome Exercise Self Efficacy: Self-Efficacy to Regulate Exercise Function: 5TSTS, 30 SSTS Physical Activity: PAL4	Baseline Week 16 Survivorship	PROMIS improved 5TSTS and 30 SSTS improved; Self-Efficacy no difference; PAL4 no difference	Findings indicate that tele-EF is feasible in older, rural cancer survivors and results in positive changes in physical function and physical activity	Key to future implementation is the need for strategies to reach and recruit older rural cancer survivors who may not place a high value on exercise to participate in tele-exercise, particularly in situations where access is limited.
Seib et al	Primary Outcome: QoL: FACT-G Secondary Outcomes: Function: SF-36	Baseline Week 12 & 24 Survivorship	QoL improved Physical function improved; role limitations improved; bodily pain no difference; general health improved; vitality improved; social functioning and health improved	The program supported women to make incremental and feasible changes to less healthy lifestyle behaviours, enhancing their self-efficacy and developing and sustaining healthy lifestyle habits	Use of an interactive eHealth platform to deliver a real-time, dynamic, and technology-assisted intervention can enhance patient engagement and capacity for self-management while reducing accessibility barriers faced by many vulnerable populations

Gorzelitz et al	Primary Outcome Body Composition: DXA Secondary Outcome Function: Functional fitness test - arm curls, 30 sec chair sit to stand, chair sit and reach, back scratch, 6MWT, 8 ft up and go Patient Reported: PROMIS, FACT-EN, Self-efficacy for Exercise Scale	Baseline weeks 5 & 10 Survivorship	Body composition favored lean mass gain in intervention group, loss in control group FFT strength improved, flexibility 6 MWT no difference, 30 sec chair sit and 8 ft up and go improved, PROMIS, FACT-EN, and SEE no difference	No adverse events reported	Future work should consider a longer follow-up period to assess whether improvements are sustained and whether participants adhere to exercise protocols; results promise utility of resistance exercise to improve health and physical functioning in endometrial cancer survivors
Senisik et al	Primary Outcome Function: FACT-G, FACT-F Secondary Outcome Strength: Grip, Leg Extensors, Back Extensors	Baseline, week 12 Survivorship	FACT-G and FACT-F improved; Grip strength, leg and back extensor strength improved	No adverse events reported	In order to investigate the effects of physical activity on survival and prognosis in cancer, studies with larger populations are needed, where the effects of exercise and lifestyle interventions are observed for a longer period of time, comparing different types of exercise

Shallwani et al	Primary Outcome Lymphedema: Circumferential Measurement	Baseline Week 9 Prehabilitation, Active Treatment	Delayed onset of lymphedema	Two participants developed cellulitis	Future research efforts should carefully implement additional considerations to enhance the feasibility of conducting such studies and to support adherence to post-operative intervention strategies. Further research is warranted to establish the role of compression and exercise in reducing the risk of lymphedema in the gynecological cancer population.
Wu et al	Primary Outcome Lymphedema: Circumferential Measurements Secondary Outcome QoL: EORTC QLQ-C30/GHS/FS/SS Fatigue: BFI	Baseline 1 & 3 months 1 year Active Treatment	Lymphedema occurred at a lower rate and delayed onset; EORTC QLQ-C30/GHS/FS/SS improved; BFI improved	Not reported	Demonstrated that early treatment of CDT combined with rehabilitation exercise could reduce the incidence of lower limb extremity lymphedema, improve patients' quality of life and reduce cancer-related fatigue. This study might provide more clinical evidence for application of CDT and rehabilitation exercise in treatment of postoperative extremity lymphedema for cancer patients; more studies to confirm

Harrison et al	Primary Outcome Cardio: CPET VO2peak Secondary Outcome Strength: 1 RM Leg press and chest press Function: 6 MWT, TUG, Sit to Stand	Baseline Week 17 all, CPET week 5 Strength weeks 4 & 10 Active treatment, survivorship	Cardio improvements Leg strength, and 6MWT improvements	No grade 3-5 adverse events	Future trials examining the long-term effects of exercise training on CRF, drug tolerance, QoL, and overall survival
Kang et al	Primary Outcome Cardio: VO2 Peak Secondary Outcome Strength: Arm Curls Flexibility: Sit and Reach	Baseline Week 10 (due to covid) Survivorship	Cardio improved Strength and flexibility improved	Not reported	Demonstrated that HIIT increases cardiorespiratory fitness of prostate cancer in men on active surveillance - to support findings of this trial and to better determine whether the improvements can translate into better long-term clinical outcomes, larger randomized clinical trials are warranted.
VanBlarigan et al	Primary Outcome Cardio: VO2 Peak, RPE Secondary Outcome Body Composition: BMI Function: SF-12 Anxiety: MAX-PC	Baseline Week 16 Survivorship	Cardio improved BMI improved; Anxiety and fear decreased	There were no serious adverse events	Demonstrated that a 16-wk tailored home-based walking program increased cardiorespiratory fitness and reduced urinary obstruction/irritation and fear of cancer recurrence in men on active surveillance for prostate cancer.

Golsteijn et al	Primary Outcome Physical Activity: MVPA from Actigraph GT3X-BT Secondary Outcome Fatigue: Checklist Individual Strength Depression: Hospital anxiety and depression scale Physical Function: QLQ-C30	Baseline Months 6 & 12 Active treatment	PA no difference Fatigue improved; depression no difference; physical function no difference	No Reported	Surgery or brachytherapy are the primary treatments for prostate cancer and might be less invasive than external-beam radiotherapy
Brown et al	Primary Outcome Function: Short Physical Performance Battery Secondary Outcome Strength: Hand Grip Function: SF-36 PCS, sit to stand	Baseline, within 4 weeks after completing chemotherapy Active treatment	Composite SPPB no difference; gait speed improved for participants >60 and males; hand grip strength and sit to stand no difference; no change in self-reported physical function	Not reported	Additional well-designed trials are required to determine if exercise benefits patients vulnerable to declines in physical function during chemotherapy

Eroglu et al	Primary Outcome CIPN: CIPNAT Secondary Outcome Function: EORTC QLQ-C30 Pain: NRS Falls: Self-Report	Baseline, week 1-8 Active Treatment	Peripheral neuropathy and EORTC QLQ-C30 improved; Pain improved weeks 4-8; Falls no difference	Not reported	It is suggested to conduct research with larger samples to determine the effect of HFEP on falls, to monitor adherence with HFEP through home visits or using telehealth applications, conducting clinical trials in different patient populations with cancer experiencing CIPN-related symptoms, where HFEP is applied as an intervention, is recommended for the
Ji et al	Primary Outcome Lung function: PEF, FEV1/FVC, and VC: PF instrument Secondary Outcome Function: 6MWT, RPE, dyspnea scale Pain: VAS Watson Theory of Human Caring: drainage tube time, total oxygen supple-mentation time, time in bed, length of hospital stay; postoperative complications Function: EORTC QLQ-C30	Baseline Day 4 post-surgery 1-month post-intervention Active Treatment	PEF and FEV1/FVC and VC improved 6MWT both decreased post-surgery, ACBT group declined less, RPE and dyspnea lower; Watson Theory parameters improved; pain improved; postop complications lower; QoL improved	Not reported	ACBT combined with Watson Theory of Human Caring can better restore PF and ventilation function in patients following LC surgery and reduce the occurrence of postoperative complications; it can promote patient rehabilitation exercise, which will shorten postoperative hospital stays and improve QoL

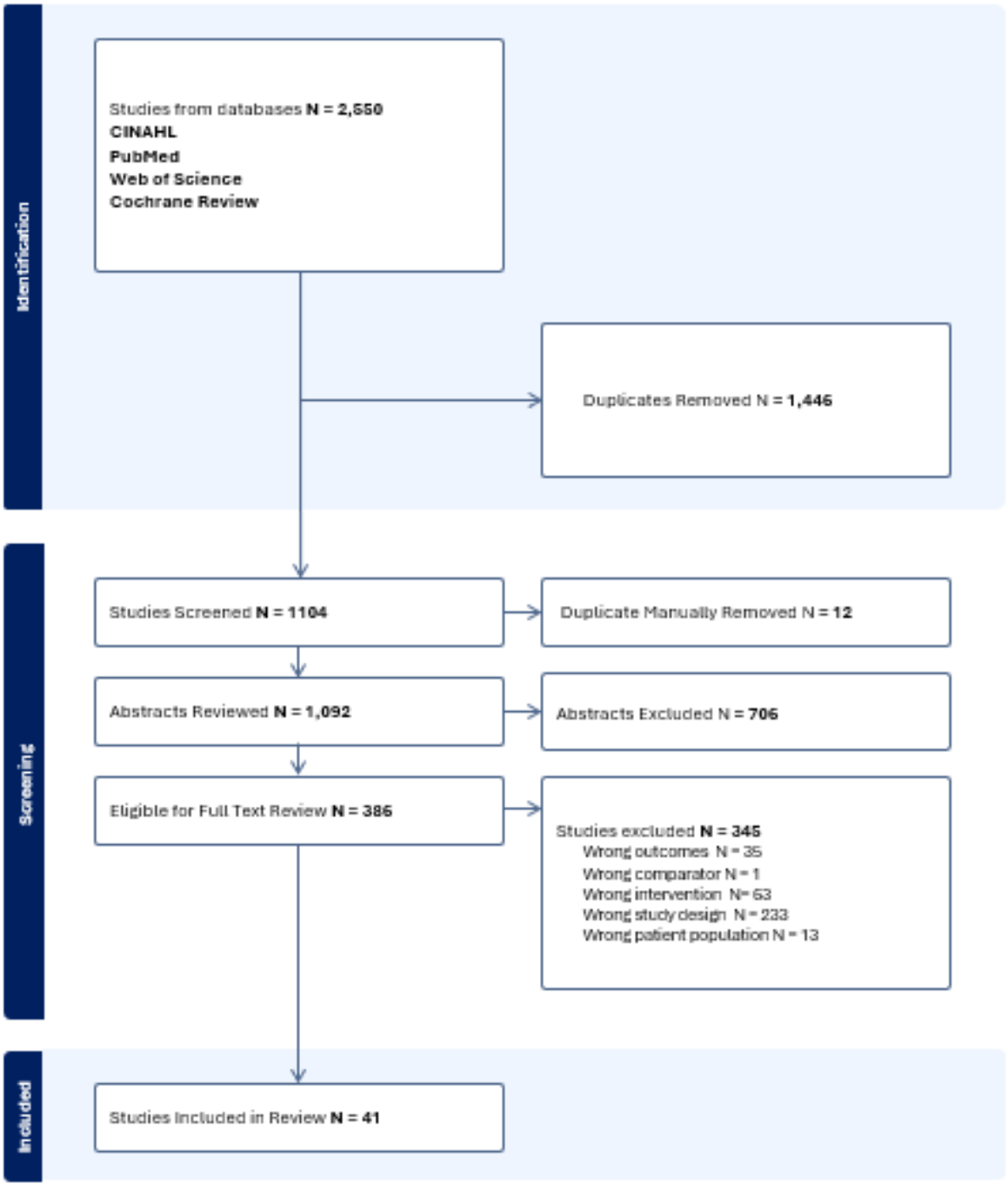
Tenconi et al	Primary Outcome Lung Function: PFT, 6MWT Secondary Outcome QoL: SF-12 Mood Disturbances: HADS Pain: NRS	Baseline 1 before surgery 1 month after surgery 6 months after surgery Active Treatment	PFT and 6MWT improved SF-12, pain, and HADS no difference	84 adverse events, 30 in the treatment group and 54 in the control group, 44 cases AE was related to the intervention, 22 cases AE was unrelated and in 18 cases a possible correlation, 2 cases effect of the AE on the treatment was temporarily suspension, out of all events 26 were severe adverse events required hospital admission and 1 event was considered to be life threatening	Pre and postoperative intensive pulmonary rehabilitation for NSCLC affected patients in early stage undergoing lung resection significantly improved exercise capacity at 6 months; rehabilitation administered in the preoperative phase also significantly reduced the decrease in exercise tolerance observed 1 month after surgery and could influence the incidence of postoperative complications.
Larsen et al.	Primary Outcome Strength: Knee Extension dynamometer Secondary Outcomes Function: 6 MWT, 30 SSTS Strength: Grip QoL: EORTC-QLQ-C30 Pain: BPI Physical Activity: Daily diary, accelerometers Bone Mineral Density: DEXA	Baseline 4 and 7 weeks 6 and 12 months Active Treatment	Knee extension strength declined in both groups first 6 months, both groups increased from 6 to 12 months, intervention group less decline Grip strength decline in both groups 30 SSTS improved both groups; 6MWT improved; accelerometer variable, no difference QoL improved both groups; Pain improved; BMD no difference	Hospitalizations due to infection, vertebral and non-vertebral fractures were not related to exercise, five non-serious adverse events were registered with only one being exercise-related, three resulted in discontinuation	It is important to note that our findings do not dismiss the potential benefits for selected patients. Importantly, we established that an individualized exercise program is feasible and safe. Exercise studies in MM are still warranted, particularly in older patients after completing primary treatment.

Muller et al	Primary Outcome Neuropathy: Total Neuropathy Score Secondary Outcome Postural Control: Force Plates QoL: EORTC QLQ-C30 Fear Falls: FES-I	Baseline Post Chemotherapy, weeks 36 & 40 Active treatment	TNS all groups increased significantly; EORTC no difference during intervention, SMT and RT decrease during follow-up; COP no difference during intervention and follow-up; Fear of falling increased in UC	Twenty-three patients reported mild training associated adverse events without indication for medical treatment	SMT and/or RT might be effective strategies to prevent sensory CIPN symptoms in the feet during neurotoxic chemotherapy and enhance chemotherapy tolerance as well as QoL - future studies needed
Saraboon et al	Primary Outcome Balance: FAB Scale Secondary Outcome Function: SPPB, MDNS QoL: FACT-Taxane	Baseline, post-intervention Active Treatment	FAB and SPPB decreased in control; MDNS no difference; FACT-Taxane improved	Not reported	Foam pad balance exercise has a positive effect on balance, physical performance, and QoL in cancer patients undergoing chemotherapy. These results indicate that foam pad balance exercises can be used by patients during their chemotherapy treatment to prevent some chemotherapy-associated side effects.

Siebert et al	Primary Outcome Fatigue: MFI-20 Secondary Outcome Pain: NRS	Fatigue: NRS 3 x per day, MFI-20 weeks 1, 2, 3, & 4 Survivorship	Fatigue improved the most with vigorous intensity strength training, mental fatigue no difference; pain improved the most with vigorous intensity strength training	No adverse events were reported within this study, out of 300 planned exercise sessions 94.7% were completed	There is a lack of exact exercise recommendations for cancer survivors with fatigue. The intention of the main follow-up FatiGO study will be used to suggest a screening method for patients with fatigue and to give clear training instructions. The NRS assessment should give information about the immediate training effect with the intention to target the exercise training directly.

Figure 1.1

PRISMA Diagram



APPENDIX A

PubMed Search Strategy

cancer OR malignant OR neoplasm OR tumor OR neoplasia

AND

physical function OR fatigue OR cancer related fatigue OR muscle fatigue OR sarcopenia OR neuropathy OR pain OR lymph* OR balance OR gait

AND

exercise OR exercise therapy OR physical activity OR strengthening OR cardiovascular OR walk OR resistance OR aerobic OR endurance OR rehab OR oncology rehabilitation OR exercise program

AND

clinical trial OR meta-analysis OR randomized controlled trial OR systematic review

AND

Humans

AND

2018/07/01:2024/11/15

AND

English

CHAPTER 2: Fall Risk of Older Breast Cancer Survivors Participants of an Exercise-Based Oncology Rehabilitation Program

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Key Words: breast cancer, oncology, fall risk, function, strength, exercise, older cancer survivor

Financial Support: None

Abbreviations: Steps to Wellness (STW), Oncology Rehabilitation (OR), 5 Times Sit to Stand (5TSTS), 6 Minute Walk Test (6MWT), Short Form Physical Component Summary/Mental Component Summary (SF-36 PCS/MCS), Patient Health Questionnaire (PHQ-9), Activity of Daily Living (ADL)

ABSTRACT

Background: Cancer treatment diminishes physical function among older adults, placing them at higher risk for falls. Exercise has been shown to reduce falls in community-dwelling older adults and also to improve strength and physical function among individuals receiving and post cancer treatment. There is a gap in research regarding impact of exercise on fall risk of older for older breast cancer patients following cancer treatment.

Objective: The goal of this study was to analyze the impact of program-based exercise on fall risk for older breast cancer following breast cancer treatment.

Methods: Individuals aged 65 or older with a stage 0-III breast cancer were included. Participants (N=91) self-selected to attend Steps To Wellness Oncology Rehabilitation program, a 12-week supervised aerobic and resistance training intervention. Muscle strength, endurance, mental health, and physical function data was extracted from the program database. Data analysis was completed on baseline and follow-up for fall related physical function measures. The primary outcome measure was the five times sit to stand (5TSTS), a strong fall risk predictor.

Results: Clinically meaningful (3.0 seconds) and statistically significant (CI 2.4-3.5; P <0.0001) improvements were observed for 5 Times Sit to Stand following 12 weeks of supervised exercise. Secondarily, other outcome measures of physical function, strength, and endurance included leg press, chest press, 6 Minute Walk Test, and Short Form 36 physical and mental component scores improved significantly following 12 weeks of supervised exercise intervention.

Conclusion: Among older individuals following cancer treatment who self-selected to participate in an exercise-based rehabilitation program, measures of strength, endurance, and physical function improved. After 12-weeks of aerobic and resistance training, older breast cancer survivors demonstrated an improvement in the 5TSTS outcome measure. This study demonstrates that exercise intervention had a positive impact on common fall risk factors and the 5TSTS outcome measure which is an intermediary predictor of falls.

INTRODUCTION

Advancing age is a risk factor for cancer overall[1]. The median age of a cancer diagnosis from any site is 66 years[2] and 62 years for breast cancer[3]. Progress in cancer treatment has led to improved survival rates and a growing population of cancer survivors. More than 18 million individuals living in the US have a history of cancer[4]. Older adults, defined as 65 years or older, comprise the largest proportion (67%) of individuals with a cancer diagnosis. Breast cancer is the most common diagnosis among females (>4 million)[4]. Recent advances in early detection and cancer treatment require an expansion in cancer care to include the consequences of cancer as a chronic condition[3]. The 5-year survival rate is 99% for patients with stage I breast cancer, and 28% for patients with stage IV breast cancer[5]. More people are living longer with the side effects of cancer and cancer treatment. Breast cancer has a particularly high prevalence in part due to successful treatments but leaves survivors vulnerable to physical and physiologic decline.

Breast Cancer Treatment and Physical Decline

Breast cancer treatment combines different modalities dependent primarily on cancer type and stage and include surgery, radiation, chemotherapy, and hormonal therapies[6]. Acute and long-term effects of breast cancer neoadjuvant, main treatment, and adjuvant cancer treatment are well documented and include negative impacts on muscle strength, cardiovascular decline, peripheral neuropathy, cardiotoxicity, surgical and musculoskeletal pain, fatigue, muscle endurance, balance, pain, lymphatics, flexibility, gait, and health-related quality of life[7–18]. Chemotherapy, radiation, and surgery accelerate physiologic aging and decline toward frailty[19,20]. Patients experience high

levels of physical and psychological needs following breast cancer diagnosis and treatment. Maintaining function is of considerable importance in this vulnerable population as disability can threaten independence, impair quality of life, and lead to more significant healthcare costs. Functional decline due to aging and compounded by cancer treatment leads to an increased risk of falls in the older adult population[21].

It is well demonstrated in the literature that cancer medication and reduced physical activity, common during chemotherapy, radiation, and post-surgery, further contribute to neuromuscular decline and inactivity. Progressive decline in physical function and increased fall risk is determined not only by physical outcome measures[22–24], it is also influenced by one's own attitude and behavior toward exercise and the benefits of exercise.

Compared to age-matched non-cancer controls, cancer survivors have greater functional limitations as well as impaired mobility, which can interfere with activities of daily living[25,26]. The functional losses experienced by older breast cancer survivors are twice that of elderly women without breast cancer[25]. Physical function decline is less likely to recover in older cancer survivors compared to their younger counterparts[27]. Unfortunately, functional changes persist as older women continue to have higher odds of being unable to do heavy work, decreased functional status, and accelerated aging process[28–31]. Numerous studies on older adults have identified the physical burden of cancer and cancer treatment. Fitch et al. examined patient perspectives of over 3000 older cancer survivors – at three years post cancer treatment, 80% reported physical concerns, including function, cardiovascular, balance, mobility, and neuropathy[32]. In particular, lower limb physical function is a reliable indicator of functional status. Ezzatvar et al.

confirmed the "link between physical function and all-cause mortality, showing that cancer patients with reduced mobility are more prone to experience adverse outcomes and lower survival"[33]. Falls are associated with one or more identifiable risk factors including weakness, age, acute illness, and medication[34]. Loss of physical function, muscle strength, and muscle endurance associated with age and cancer treatment leads to increased fall risk, morbidity, and mortality[21]. Additionally, fall risk and falls have been associated with a wide variety of comorbidities and secondary health effects, including accumulation of medical issues, medications to address medial issues, decreased balance, pain, and depression[35]. Chen et al. reported an elevated risk of falls after breast cancer treatment compared to women never diagnosed with cancer[36].

Burden of Falls in Older Adults

Falls are the most common cause of injury in people 65 years of age and older. Over 30% of all 65 to 85-year-olds fall every year, while approximately 40% of individuals greater than 85 years fall each year[35]. Falls are an impactful problem for older cancer survivors that lead to injury, decreased independence, and increased healthcare costs[24]. Non-fatal older adult falls cost the U.S. healthcare system about $80 billion per year[37]. The older adult population is growing in the US; it is estimated that there will be 74 million older adults (age 65 and older) by 2030[38]. Falls among older adults are associated with significant morbidity, mortality, and healthcare costs. Advanced age, in combination with the consequences of cancer survivorship, leads to greater fall risk and subsequent physical and psychological decline[21].

Physical Decline and Exercise

Despite the known acceleration of functional decline with cancer and cancer treatment, there is limited research examining the integration of exercise into patient care services to maximize functional outcomes for patients following cancer treatment[39]. Sturgeon et al. acknowledge the heterogeneity in the effect of exercise on falls due to high variability across cancer, cancer treatment, and exercise interventions[39]. Min et al. conducted a randomized clinical trial investigating the impact of early exercise intervention following breast cancer treatment. This study found that function, muscle strength, and range of motion improved significantly in the exercise group compared to the control group. Researchers concluded that increased function and physical activity are associated with reduced healthcare costs, quicker return to ADLs and vocation, and improved prognosis[40]. A systematic review concluded that physical exercises can improve static and dynamic postural balance among patients treated for breast cancer. The authors of this study stated that more high-quality research is needed to determine the efficacy of exercise protocols and outcome measures[41].

Inactivity and sedentary lifestyles are associated with poorer health outcomes in general and specifically among breast cancer survivors[42]. There is limited research examining the impact of low activity on physical function and fall risk following cancer treatment. Philips et al. showed that breast cancer survivors are significantly more sedentary and less active than healthy age matched controls.[43]

The latest exercise recommendations for cancer survivors mirrors the ACSM exercise guidelines for all adults in the US to maximize health-related outcomes. Limited high-quality research has been conducted that examine the impact of physical activity and

exercise to meet the specific heterogeneity of cancer survivors experiencing functional decline. A recent systematic literature review of clinical practice guidelines on fall prevention and management for older adults noted that among 15 guidelines reviewed, *fall risk and exercise interventions* were the only two topics covered in all of the guidelines[44].

Exercise and Fall Risk

A 2019 Cochrane review on exercise and fall risk showed strong evidence of the positive impact of functional exercise and balance on reducing falls among community dwelling older people[45]. Additionally, a systematic review analyzing effectiveness of exercise interventions for preventing falls in community dwelling older adults was published in 2020, recapping well-established evidence indicating exercise *reduces falls* in older adults. The authors identified a gap in research to inform evidence based exercise recommendations to *maximize* fall risk benefits for community dwelling older adults[45].

A 2018 Cochrane review by Williams et al. concluded that more high-quality randomized controlled trials are required to increase evidence of the effects of exercise training on falls in patients following cancer treatment[47]. The evidence for programs based on prescription exercise as an intervention to reduce fall risk, improve strength, flexibility, and balance in cancer survivors is limited[47]. This review determined that no studies, to date, had been powered to detect a reduction in fall risk. Twiss et al. concluded that strength training over 24 months demonstrated meaningful gains in muscle strength and balance.[48]

There is scarce evidence that exercise training positively impacts fall risk among older cancer survivors[47]; available studies are low quality and underpowered. To the best

of our knowledge, no high-quality studies demonstrate the impact of strength, endurance, function, and balance on fall risk among *breast cancer survivors specifically* and broadly among all cancer survivors.

Benefits of Exercise and Recommendations

Exercise has the potential to reverse cancer-related declines in function[40,45,46]. Exercise can improve muscle mass and strength among a general aging population and can attenuate age related declines that increase risk for future disability[46]. Even among frail older adults, exercise can improve physical performance, including strength and mobility, and decrease self-reported disability[49]. The American College of Sports Medicine Exercise Guideline for Older Adults recommends a program of aerobic activity, strength training, flexibility, and balance exercises for community-dwelling older adults and for those with chronic conditions to be as physically active as their conditions and abilities allow[50]. While the American Cancer Society recommends exercise and a physically active lifestyle during and after treatment for cancer[51], cancer survivors fall well below recommended levels with 7% meeting recommendations[52,53]. Most recently, the American Society of Clinical Oncology (ASCO) released evidence-based exercise guidelines for oncologist and patients undergoing cancer treatment to preserve or improve health and wellness during cancer treatment. The recommendation states, "Oncology providers should recommend aerobic and resistance exercise during treatment of adults with curative intent to mitigate side effects of cancer treatment". Evidence to substantiate this recommendation was rated moderate to low. ASCO concluded that available evidence to develop more specific guidelines with respect to dosage was insufficient; additional high-quality research is needed to understand better the decision-

support tools to prescribe safe, feasible, and effective exercise intervention for this vulnerable population.[54]

Additionally, there is limited data evaluating the impact of exercise on functional decline and fall risk in an older cancer survivor population. Current evidence suggests that exercise is safe, reduces fatigue, increases endurance, mobility, and function[55]. Improving exercise guidelines and exercise prescription may significantly impact cancer-related side effects associated with function, safety, and quality of life. In a recent publication, Jensen-Battaglia et al. found that falls among older cancer survivors are more common than the general older adult population; a significant proportion of falls were associated with injury. This study found that patients experienced fewer falls after intervention guided by 'geriatric' assessment which included the domains of physical performance and functional status. The authors concluded a need for developing dedicated studies designed to evaluate fall risk and develop interventions to promote the management of falls among older adult cancer survivors[56]. Given the serious implication of loss of function and falls, high-quality evidence is needed to support cancer survivors and clinical guidelines to mitigate the impact of cancer treatment and improve safety and physical function outcomes for cancer survivors. This study sought to identify the impact of a 12-week supervised exercise program on fall risk for older breast cancer survivors. The authors hypothesize that supervised exercise will improve physical function outcomes and reduce fall risk in older breast cancer survivors.

METHODS

Study Design and Patient Population

This was a clinical intervention study of cancer patients referred to Steps to Wellness, an exercise-based oncology rehabilitation (OR) program at the University of Vermont Medical Center. The study population consisted of cancer survivors who self-selected to enroll in the STW Oncology program between January 1, 2012 and October 19, 2019.

A database repository of pre- and post-intervention objective and self-report measures physical activity, strength and function was utilized for this study. For the analysis, we included women aged 65 or older with a breast cancer diagnosis and the following criteria: completion of initial therapy at least two months prior, receipt of at least two modalities of therapy (surgery, radiation and/or chemotherapy), and a cancer stage of 0-IV. Individuals who were more than five years post diagnosis at the time of exercise initiation were excluded.

Measures of strength and function were obtained from individuals with a breast cancer diagnosis participating in an exercise-based OR program at the University of Vermont Medical Center. The program is an ongoing exercise intervention available to all cancer survivors and details are described elsewhere[57]. Before starting the OR program, participants are evaluated by a physician or advanced practice provider and a physical therapist (PT). If sufficient functional deficit or severe deconditioning is identified, patients are considered an evaluation fail and are unable to participate in the group exercise. For those who fail, one-on-one physical therapy is provided. If function

improves, they are reconsidered for the group exercise program. They repeat initial testing prior to program initiation.

The University of Vermont Institutional Review Board approved this study. All subjects underwent informed consent prior to participation.

Intervention

The OR program delivered a clinical exercise intervention at no cost to participants. The OR program was offered as a component of care to our institution's cancer survivors and guided by an interdisciplinary team of medical oncologists, physical therapists, and exercise physiologists. The program consisted of supervised aerobic and resistance training twice a week for 12 weeks or a total of 24 OR sessions. Aerobic activity generally included brisk walking for 20 minutes each OR session progressing to 40 minutes by week 8. Three additional days of aerobic training outside of the gym is encouraged. The resistance training includes 3 upper extremity and 5 lower extremity exercises with initial weight set at 60-70% of one repetition maximum. Two sets of 8-12 repetitions are completed for each exercise, allowing 1-2 minutes of rest between sets. When 12 repetitions can be completed, the resistance is advanced. While the core activities of aerobic and resistance exercises stay the same, each individual's specific activities are tailored to accommodate deficits as needed. Exercise trainers supervise for safety and help participants advance both aerobic and resistance training prescriptions. Participants were evaluated by a physician and a physical therapist prior to initiating the program for appropriateness of group setting exercise.

Outcome Measurements

Data was collected at baseline and upon completion of the 12 week exercise intervention. The subset of data analyzed for this study focuses on function, strength, endurance, and mental health.

Function was measured with a five time sit to stand (5TSTS)[58,59] and a 6-minute walk test (6MWT) test[60,61]. A 5TSTS measures lower extremity functional strength and endurance, and has significant predictive value for recurrent falls in community living older adults aged 65 and older independent of other risk factors for falling[62]. For the 5TSTS, patients cross their arms over their chest and are instructed to stand up from a standard-height chair and sit down five times. The time needed to complete the test is recorded. Patients requiring more than 15 seconds to complete the test have a 74% greater risk of recurrent falls[63]. Patients requiring more than 12 seconds to complete the tests predict risk of multiple falls and require further assessment[64]. A 5TSTS is an evidence-based fall risk measure, a time of 12 seconds or greater justifies initiation of a physical program to reduce risk.[65]

A 6MWT assesses submaximal aerobic capacity and whole-body functional capacity[60]. The test is performed in accordance with the published American Thoracic Society guidelines[66].

Strength is assessed with one-repetition maximum (1-RM) for the upper extremity (chest press) and the lower extremity (leg press). A 1-RM test is the greatest resistance that can be moved through a full range of motion in a controlled manner with appropriate technique. Testing procedures followed the recommendations outlined in the ACSM Guidelines for Exercise Testing & Prescription[67]. For all tests, a light weight is pressed

through the full range of the leg press motion two to three times to allow the participant to practice the movement. Subjects are asked to fully extend through the movement but to avoid locking joints and holding their breath. If participants do not reach their 1-RM within three tries, the test is stopped and performed on another day.

Self-report of functional health and well-being were collected using the Physical Component Summary (PCS) and Mental Component Summary (MCS) of the Medical Outcomes Study, Short Form Health Survey (SF-36) [68]. The PCS assesses a range of functional skills, including climbing stairs, lifting heavy items, and basic activities such as bathing, dressing, and roles related to physical function, bodily pain and general health. The MCS assesses a range of mental health factors, such as vitality, social function, and emotional status. The SF-36 includes 36 items that are scored (SF-36 Health Survey Manual, Version 2); raw scores for the PCS and MCS are transformed to a score with a range of 0–100, with higher scores indicating better functioning. Norm-based scoring is also presented for PCS and MCS, allowing for a comparison with the U.S. population scores. Norm-based scores have a mean of 50 and standard deviation of 10 in the general U.S. population.

Statistical Analysis

Descriptive statistics for demographic and baseline variables were calculated for all eligible participants ($n=91$). Results are presented as mean ± SD, median and range, or proportion depending on the variable. The continuous variables met the criteria for normal distribution and parametric testing. Participants were included in statistical analysis who had pre-and post- data for the 5 TSTS outcome measure. Statistical analysis included paired t-test and a repeated measures analysis of variance. Comparisons were

made between baseline and follow-up using paired t-tests for 5TSTS, leg press, chest press, 6MWT, PCS, MCS, and SF-36 general health question. In secondary analyses, we explored the effects of the intervention on the 5TSTS outcome in subgroupings of patients based on BMI, age, receipt of chemotherapy, receipt of radiation, STW attendance, and months since cancer diagnosis using paired t-tests or repeated measures analysis of variance (ANOVA). All statistical analysis was performed using STATA 16.0. The percentage of change in 5TSTS was calculated relative to age-matched normative values.

RESULTS

The study inclusion criteria were met for 91 older cancer survivors who completed a baseline and follow-up five times sit-to-stand (5TSTS) measure. Table 2.1 provides baseline characteristics for our study subjects and OR program. The mean age of the older cancer survivors at the start of the program was 72 ± 4.7 years (range 65-84). The time from cancer diagnosis until the start of the program was 13 $\pm$ 17.4 months. The mean BMI was 29 $\pm$ 5.8. Fifty-four percent of participants reported being married or living as married. Subject mean PCS and MCS were 44 $\pm$ 9.7 and 52 $\pm$ 9.0, respectively. One-third of subjects received chemotherapy, 82% received radiation, 100% received surgery, and 25% received all three treatment modalities. The median number of sessions attended was 19 out of 24. The majority (71%) attended >75% of sessions. The mean number of days to complete the program was 80 $\pm$ 10.2.

Change in functional measurements for primary and secondary outcome measures is represented in Table 2.2. 5TSTS was our primary objective measure. The mean 5TSTS baseline measure was 13.2 $\pm$ 3.7 seconds and 10.2 $\pm$ 3.8 seconds at follow-up with a

mean difference of 3.0 seconds. There was a significant difference in mean 5TSTS from baseline to follow-up (CI 2.4-3.5, (P <0.0001). At baseline, 60% of participants had a 5TSTS ≥ 12 seconds, while 22% of participants had a 5TSTS ≥12 seconds at follow-up. Other physical function, strength, and endurance measures collected were chest press, leg press, and 6MWT. Each of these outcomes improved from baseline measures to follow-up measures with 12-weeks of supervised exercise. Chest press and leg press measures improved from 44 ± 22.3 pounds to 56 ± 26.4 (CI 9-15; P <0.0001), and 123 ± 37.8 to 140 ± 41.9 (CI 10-24; P <0.0001) pounds respectively. The 6MWT improved from a mean distance of 451 ± 96.1 meters to 529 ± 120.0 meters (CI 55-101; P <0.0001). The mean 6MWT gain was 78 meters or 20% improvement. SF-36 physical component score (PCS) and mental component score (MCS), and PHQ-9 score improved from baseline to follow-up measures with 12-weeks of supervised exercise. SF-36 MCS and PCS scores improved from 53 ± 9.0 to 56 ± 6.7 (CI .4-4.3; P = 0.0192) and 45 ± 9.6 to 48 ± 8.2 (CI 2.4-4.9; P <0.0001) respectively. SF-36 'general health' question improved from 2.3 ± .85 at baseline to 2.6 ± .86 at follow up (CI .1-.4; P=0.0010). PHQ-9 improved from 3.7 ± 3.0 at baseline to 3.0 ± 3.0 at follow up (CI .1-1.3; P=0.0201). Statistically significant improvements were calculated for chest press, leg press, 6 MWT, SF-36 PCS, MCS, general health question, and PHQ-9.

A two-way ANOVA (3 or more groups) or paired t-test (2 groups) was performed to evaluate the effects of BMI, age, chemotherapy, radiation, months since diagnosis, and program session attendance on 5TSTS. The results indicated no significant effect on 5TSTS based on potential modifying variables listed above. Age categories (65-67, 67-

72, and >72) demonstrate the greatest impact (*p* value = .0674) on 5TSTS trending toward statistical significance (Table 2.3).

Baseline 5TSTS means were similar to age-matched normative values. A 5TSTS >12 seconds is indicative of increased fall risk. Pre-intervention increased fall risk by age categories was 51% (60-69 years), 64% (70-79 years), and 100% (80-89 years). Post-intervention increased fall risk by age categories was 14% (60-69 years), 29% (70-79 years), and 60% (80-89 years). At baseline, 54 participants were at higher risk for falls; upon completion of the program 21 participants were at higher risk for falls (Table 2.4).

DISCUSSION

In this study of an oncology rehabilitation program among women surviving breast cancer, we found that multiple measures of physical and functional status improved. Our 12-week supervised exercise oncology rehabilitation program, consisting of resistance training and aerobic training demonstrated improvement in 5TSTS measures among older breast cancer survivors. Functional status improvements were also demonstrated in other physical and mental health outcomes including leg press, chest press, 6MWT, SF-36 MCS/PCS/general health, and PHQ-9. This study sought to identify the impact of a 12-week supervised exercise program on fall risk for older breast cancer survivors.

The 12-week OR program improved 5TSTS, which reflects changes in muscle strength, endurance, balance, and fall risk. Our study found clinically meaningful improvements in 5TSTS among all older breast cancer participants; these findings were generally consistent across age, BMI, receipt of chemotherapy, receipt of radiation, attendance, and months since cancer diagnosis. Between-group differences were not

observed for 5TSTS. Our intervention was most impactful to the 67- to 72-year-old subgroup based on the greatest improvement in 5TSTS outcome as compared to the younger and older subgroups. Improvements in 5TSTS translates to increased function and independence, mitigation of events that cause injury and disability, and positive impact on survival and quality of life. Falls are a particular concern of older adults as they are a major cause of morbidity and mortality [21,34,65]. Older cancer survivors represent a high proportion of all cancer survivors[4]. The impacts of cancer therapy accelerate age-related physiologic declines, thus increasing their risk for falls, decreased function, and loss of independence[19,33,55]. Muscle strength and endurance are two physical components that are critical for maintaining function and minimizing fall risk in older adults[35,40,69]. We lack consensus on a clinical outcome measure that is most effective for evaluating fall risk for older adult breast cancer survivors. The 5TSTS is a cost-effective, feasible, validated functional outcome measure that may be an appropriate indicator to evaluate fall risk in our population.

In our cohort of older cancer survivors, over 60% are considered at risk for falls at baseline based on the time required to rise from a seated position five times (5TSTS $\geq$ 12 seconds)[64]. At follow-up, 22% of our cohort of participants were considered at risk for falls. Our 5TSTS findings were similar to previous studies completed in 2020 by Dittus et al. [27] and in 2021 by Blackwood and Rybicki[70] et al. All three studies observed lower than age and gender based normative values for baseline 5TSTS and improvements in fall risk factors following exercise intervention. Dittus et al. showed older cancer survivors had lower physical function and strength following cancer treatment than age and gender-matched older adults.[27] Older cancer patients experience greater functional decline than

the broader older adult population.[27] Dittus et al. demonstrated that a 12-week resistance and aerobic training intervention improved the physical function of older adult cancer survivors. Clinically meaningful change in 5TSTS was observed in the Dittus study across middle and older age breast cancer survivors. Our study aligned with these results and were specific to older breast cancer survivors.[71]

Our 5TSTS data for older cancer survivors is below the age-matched 5TSTS normative values of 11.4 seconds for 60 to 69 years, 12.6 seconds for 70 to 79 years, and 14.8 seconds for 80 to 89 years[72]. The oldest age subgroup, 80- to 89-year-olds, was perhaps the most impacted by cancer treatment, which is reflected in the largest negative deviation from age-matched normative values. 5TSTS was selected as the primary outcome measure due to fall risk predictive capacity, exercise capacity, safety, and ease of use in the clinical setting[73]. 5TSTS has been shown to be a reliable and valid tool for assessing function and fall risk for older long-term cancer survivors[70]. The authors acknowledge that there are many contributing factors associated with fall risk in older breast cancer patients. 5TSTS had been shown to be a valuable tool that can be used to inform an exercise plan to maximize function and minimize falls. To our knowledge, no high-quality randomized controlled trials have been conducted examining the effect of exercise intervention on function and fall risk of older breast cancer survivors. Broadly, exercise interventions examined in cancer survivors are efficacious for physical function outcomes[55]. Results from this study will further inform rehabilitation professionals in prescribing physical activity and exercise to meet the specific needs of functional decline and increased fall risk for older cancer survivors.

Secondary measures of function improved with 12-weeks of exercise intervention for older breast cancer survivors (6MWT, leg press, chest press, and SF-36 PCS/MCS, and PHQ-9). The 6MWT is a sub-maximal exercise test to assess aerobic capacity, function, and endurance. A mean improvement in 6MWT of 78 meters was a 20% gain for participants from baseline to follow-up testing. The minimally clinically important difference has been shown to be 50 meters.[74–76] Baseline 6MWT was comparable to normative values in 80 to 89 year-old community dwelling adults demonstrating the impact of cancer and cancer treatment[77]. Follow-up mean 6MWT was on par with normative values for 60 to 69 year-old community dwelling adults[74]. Upper and lower extremity strength, as measured by 1RM, improved from baseline to follow-up. Mean upper extremity strength improved by 12 pounds or 7%, while mean lower extremity strength improved by 17 pounds or 14%. A randomized controlled trial by Winters-Stone et al. compared the effect of resistance training, aerobic training, or stretching on functional outcomes. This study showed greater 1RM improvements among participants in the resistance treatment arm as compared to aerobic and stretching treatment arm. 6MWT results improved; however, changes were not statistically significant in any intervention arm[78].

Both the MCS and PCS scores improved by three points from baseline to follow-up. A change of five points has been demonstrated to be clinically meaningful among women diagnosed with stage 0-IIIa breast cancer.[79–82] Changes in both of these scores at follow-up are trending toward a clinically important difference.

PHQ-9 score improved by .7 points. A change of 3.7 has been shown to be a minimal clinically important difference; however, this study was not specific to older breast cancer survivors[83].

Our study adds evidence to the literature the older breast cancer survivors improved in measures of physical function and fall risk in response to an exercise-based oncology rehabilitation program. We also demonstrated that all older adult subgroups improved with an indication of difference in magnitude of improvement as a result of supervised exercise. Exercise is safe, effective, and beneficial for cancer survivors. Resistance training and aerobic exercise delivered via our OR program were beneficial across all subgroups analyzed in this study. This study expands on current knowledge regarding participation in aerobic and resistance training and the positive impact on physical function and fall risk among older breast cancer survivors. However, further investigation is needed to provide evidence to support the findings of this study. Research on function, fall risk, exercise, and older breast cancer survivors is extremely limited.

Supervised and unsupervised exercise has been well documented as an effective approach for reducing fall risk in the *general older adult population*[8,12,12,27]. Physical, functional, and mental health decline is associated with cancer and cancer treatment. Research has shown us that older adult cancer survivors have experienced accelerated aging and elevated fall risk as compared to age and gender-matched norms extrapolated from a non-cancer cohort. The benefit of aerobic and resistance exercise is well understood to impact muscle mass, strength, muscle endurance, balance, coordination, and cardiovascular fitness. Harnessing the principles of muscle, neurologic, and cardiovascular physiology to maximize functional outcomes is apparent; the intricacy of

cancer, cancer treatment, and physical decline to best fit a ‘prescription’ exercise program to a cancer survivor’s unique needs is less understood. Cancer type, cancer stage, and cancer treatments, in combination with individual circumstances, beliefs, and wellness, contribute to significant heterogeneity of this condition and patient population. This study demonstrates that an intervention of aerobic exercise and resistance training following cancer treatment is a promising intervention for improvements in muscle strength, endurance, and function which collectively have a positive impact fall risk for older adults. All subgroups (BMI, age, receipt of chemotherapy, receipt of radiation, months since diagnosis, and sessions attended) analyzed benefited from the intervention with positive trending functional gains (Table 2.3). Further work is needed to understand the impact of different components of an OR program for older breast cancer survivors. High-quality research is lacking to fully examine the exercise benefits on function and fall risk.

Study strengths include a well-organized OR program with strong ability to ascertain study outcomes. We were able to capture a relatively large sample of older adult breast cancer patients and demonstrated functional benefits across several outcome measures. We had a well-defined research question with clear analysis to appropriately answer our research question.

Limitations

There are a few limitations we must acknowledge with our study. Our OR program is located in one small, rural state at one medical center, generalizability to broader geographic locations may be limited. Our cohort self-selected to participate in this program; therefore, this population may be more active and higher functioning at

baseline as compared to the general cancer survivor population. This clinical study was available to all cancer survivors at our medical center, we did not include control groups of non-exercisers. Comorbidities may impact response to exercise training, these factors were not analyzed.

Future Directions

Future studies may consider the impact of the cohort effect of group exercise versus individual exercise vs one-on-one supervised rehabilitation for cancer patients. Our OR program attendance level was high (median 19 out of 24 sessions), and patients exercised in a common gym space with other cancer survivors. The social aspects associated with exercising have been shown to be an important factor for compliance among older adults.[84] Research shows that one-on-one physical therapy attendance post-surgery was 64%[85] compared to our mean attendance of 75%, suggesting benefits of group exercise, familiarity, and relationships. Additionally, research to support the development of clinical predication rules and clinical practice guidelines to better serve oncology rehabilitation care and maximize functional outcomes for cancer survivors.

CONCLUSION

Strength, function, and risk of falls improved with a 12-week exercise-based intervention for older adults following breast cancer treatment. Physical outcome measures of cancer survivors participating in our OR program were below normative values at baseline. Specifically, over 60% of our participants demonstrated a 5TSTS time that identified them as high fall risk, this number dropped to 20% at follow up. Other functional outcome measures showed that significant gains in strength and function can be achieved with a 12-week exercise intervention in an OR clinical setting. Subgroups of

breast cancer survivors, including age, BMI, receipt of chemotherapy and radiation, attendance, and months since diagnosis, all benefited from exercise intervention, there was clinically meaningful change across each group. Our results support current evidence for exercise as a component of care for cancer patients to improve functional outcomes, reduce fall risk, and further our understanding of exercise prescription based on patient and cancer factors.

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Table 2.1

Baseline Characteristics of Participants and Steps to Wellness Oncology Rehabilitation Program

Characteristics	N	Mean, Median, or Proportion
Age at start of Steps to Wellness, mean seconds (SD) (Range)	91	72 (4.7) (65-84)
Married or Living as Married (%)	90	54%
BMI, mean (SD) (Range)	88	29 (5.8) (19-48)
Normal/underweight (%)		28%
Overweight (%)		36%
Obese (%)		36%
SF-36, PCS mean (SD)	81	44 (9.7)
SF-36, MCS mean (SD)	81	52 (9.0)
PHQ9, mean (SD)	86	4 (3.3)
Months since diagnosis, mean (SD) (Range)	90	13 (17.4) (0-113)
Metastatic (%)	90	1%
Received Chemotherapy (%)	90	30%
Received Surgery (%)	91	100%
Received Radiation (%)	91	82%
Received Radiation	91	82%
Received Chemotherapy, radiation & surgery (%)	90	25%
Sessions Attended, median (range) % completing >75% of sessions	89	19 (1-24) 71%
STW Duration, span in days (SD) (Range)	88	80 (10.2) (54 - 128)

Table 2.2

Change in Functional Measures Before and After Participation in STW

Variable	**N**	**Baseline**	**Follow Up**	**Difference**	**95% CI**	***p* value[a]**
5 TSTS, mean sec (SD)	90	13.2 (3.7)	10.2 (3.8)	3.0	[2.4-3.5]	<0.0001
Chest Press, mean (SD)	63	44 (22.3)	56 (26.4)	12	[9-15]	<0.0001
Leg Press, mean (SD)	65	123 (37.8)	140 (41.9)	17	[10-24]	<0.0001
6 MWT, mean (SD)	80	451 (96.1)	529 (120.0)	78	[55-101]	<0.0001
SF-36, MCS mean (SD)	72	53 (9.0)	56 (6.7)	2.5	[.4-4.3]	0.0192
SF-36, PCS mean (SD)	72	45 (9.6)	48 (8.2)	3.6	[2.4-4.9]	<0.0001
SF-36 General Health, mean (SD)	74	2.3 (.85)	2.6 (.86)	.3	[.1 - .4]	0.0010
PHQ9, mean (SD)	78	3.7 (3.0)	3.0 (3.0)	.7	[.1-1.3]	0.0201

[a] Student's t-test

Table 2.3

Analysis of Variance 5TSTS

5 TSTS, mean (SD)	N	Baseline	Follow Up	Difference	*p* value[b]
Overall, mean sec (SD)	90	13.2 (3.7)	10.2 (3.8)	3.0	<0.0001
Normal/Underweight	25	12.5 (3.2)	8.9 (2.6)	3.6 (2.1)	0.4225
Overweight	31	13.3 (2.7)	10.3 (2.8)	3.0 (2.4)	
Obese	31	13.5 (4.2)	10.8 (4.6)	2.7 (3.3)	
<67 years	29	12.0 (2.6)	9.5 (2.5)	2.5 (2.2)	0.0674
67 - 72 years	35	13.2 (4.0)	9.5 (2.9)	3.8 (2.8)	
>72 year	26	14.4 (3.9)	12.1 (5.3)	2.3 (3.0)	
Chemotherapy: No	61	13.0 (3.6)	10.1 (3.9)	3.0 (2.7)	0.7800
Chemotherapy: Yes	27	13.5 (3.9)	10.4 (3.8)	3.1 (2.8)	
Radiation: No	16	13.4 (4.0)	10.7 (5.5)	2.7 (3.8)	0.6424
Radiation: Yes	73	13.2 (3.6)	10.1 (3.4)	3.1 (2.4)	
Months Since Dx <1 yr	67	12.7 (3.6)	9.8 (3.3)	2.9 (2.4)	0.5163
Months Since Dx ≥1 yr	21	14.8 (3.6)	11.4 (5.1)	3.4 (3.6)	
Attendance ≤ 18	30	13.9 (4.0)	11.5 (5.1)	2.4 (2.9)	0.2498
Attendance 19-20	29	13.0 (3.5)	9.5 (2.9)	3.4 (2.4)	
Attendance ≥ 21	29	12.9 (3.4)	9.5 (2.8)	3.3 (2.6)	

[b]ANOVA

Table 2.4.

STW Pre and Post 5TSTS Comparison to Age Matched Norms and 15 & 12 Second Fall Risk Predictive Value

5TSTS Normative Values, mean s (SD)	Age Range (STW N)	Pre 5TSTS, mean sec (range)	Pre N>12 s, (%Participants Fall Risk)	Post 5TSTS, mean sec (range)	Post N>12 s, (% Participants Fall Risk)
11.4 (1.8)	60-69 (49)	12.4 (7.2-24.5)	25 (51)	8.6 (5.5-17.0)	7 (14)
12.6 (4.8)	70-79 (37)	13.6 (8.0-25.4)	24 (64)	11.7 (6-25)	11 (29)
14.8 (5.5)	80-89 (5)	16.5 (12-24)	5 (100)	15.2 (10-30.35)	3 (60)

CHAPTER 3: Oncologists' Referral to Oncology Rehabilitation: Qualitative Analysis of Knowledge, Attitudes, and Practices

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Abbreviations: knowledge, attitudes, and practices (KAP), Florida Society of Clinical Oncology (FLASCO), Northern New England Clinical Oncology Society (NNECOS), American Society of Clinical Oncology (ASCO)

ABSTRACT

Background: Cancer survivorship is increasing across many different types of cancer resulting in increasing numbers of older adults with cancer treatment related morbidity that impacts participation in society, work related responsibilities, quality of life, and survival time. There is solid evidence to support the efficacy of inclusion of oncology rehabilitation as standard of care for the majority of cancer patients to improve pain, functioning, and overall quality of life throughout every stage of survivorship. Despite known benefits of exercise and oncology rehabilitation, referral and participation rates are low for oncology rehabilitation services. Knowledge, attitudes, and practices (KAP)

of oncologists with respect to oncology rehabilitation and referrals for integration of rehabilitation specialists are not well described in the literature.

Objective: The goal of this study was to analyze the knowledge, attitudes, and practices of oncologists with respect to referrals to oncology rehabilitation.

Methods: Participants were recruited from Florida Society of Clinical Oncology (FLASCO) and Northern New England Clinical Oncology Society (NNECOS) to complete a 32-question survey related to referral of patients to oncology rehabilitation. Data were analyzed based on geographic location, gender, years of practice, personal exercise habits, and perceived difficulty making an oncology rehabilitation referral.

Results: Eighty-two oncologists completed the survey. The mean oncology rehabilitation referral rate reported over the last 12 months of practice was 23%. There was relatively equivalent distribution of urban, suburban, and rural practitioners. There was a marginally statistically significant difference in referral rate between suburban and urban oncologists with suburban oncologists referring 30% of patients while urban oncologists referring 16% of patients (-5.6-24/7; P=0.017). Forty-seven oncologists reported that it is difficult to refer patients to oncology, 35 reported that it is not difficult to refer patients. Referral rates for these subgroups were 17% and 34% respectively (CI 8.8-25.1; P<0.0001).

Conclusion: Although oncologists have some knowledge of the benefits of exercise for their patients before, during, and after a cancer diagnosis, low referral rates persist. Oncologists were generally in agreement that exercise is safe and beneficial for cancer survivors. Referral rates remain low, and skills of medically trained exercise specialist are underutilized. Our study identified barriers to oncology rehabilitation referrals that

include organizational challenges, lack of referral mechanisms, lack of understanding of benefits of oncology rehabilitation, availability, time, and patient saturation.

INTRODUCTION

As of 2022, there were more than 18 million cancer survivors in the US[1–3]. It is estimated that there will be approximately 27 million cancer survivors by 2050 and that greater than 40% of those born today will develop cancer during their lifetime[4]. Breast cancer is the second most common cancer in women in the US while prostate cancer is the most common in men[5]. The incidence rate of breast cancer and prostate cancer have steadily increased over the last few decades. There are an estimated 300,000 new cases annually for breast and prostate cancers[6,7]. Due to early detection and advances in cancer treatment, overall cancer mortality rates are decreasing in the US over the last few decades[2]. Approximately two-thirds of cancer survivors are aged 65 years or older[8]. Physiologic decline due to aging and compounded by cancer treatment is associated with increased physical and functional challenges in the older adult population[9]. Medical treatment for cancer includes surgery, radiation, and systemic therapy including chemotherapy, immunotherapy, and hormonal therapy[5,10]. Acute and long-term effects of breast cancer neoadjuvant, main treatment, and adjuvant cancer treatment are well documented to result in a negative impact on muscle strength, muscle endurance, shoulder dysfunction, surgical/musculoskeletal dysfunction, chemotherapy-induced peripheral neuropathy, balance, pain, fatigue, lymphatics, flexibility, cardiotoxicity, autonomic imbalance, and health-related quality of life[11]. Patients experience high levels of physical, and psychological needs following cancer diagnosis and treatment. Cancer

has evolved to represent a new chronic disease that many individuals will experience with complex interdisciplinary medical management needs[12,13]. Maintaining function is of considerable importance in this vulnerable population, as disability can threaten independence, impair quality of life, and lead to increased healthcare costs[14–19].

Cancer survivorship is increasing across many different types of cancer resulting in growing numbers of older adults with cancer treatment-related morbidity that impacts participation in society, work-related responsibilities, quality of life, and life span. The five-year survival rate for breast cancer is 91% for all ages and stages[20]. The five-year survival rate for prostate cancer is 97% for all ages and stages[21]. It is estimated that 33% of patients not receiving therapy are experiencing three or more cancer-related symptoms[22]. A systematic review of the literature showed that for all cancer types, approximately 40% of patients experience one or more cancer-related symptom[23]. Research shows that breast cancer survivors demonstrate lower rates of working, work ability, and performance compared to the general population due to cancer-related fatigue, extremity, mobility, and function[24,25]. Cancer and cancer-related treatment symptoms develop and persist throughout the remainder of life. They can be physical, psychological, and emotional, and inflict financial burdens on the affected individuals, their families, and the healthcare system[26,27]. The healthcare costs for cancer care in 2019 was estimated to be more than 21 billion[28]. Physical disability is a leading cause of distress among cancer survivors[29].

In 2017, a National Cancer Policy Forum of the National Academies of Sciences called for coordination and communication among cancer survivors and their clinicians including post-treatment rehabilitation for managing physical needs due to cancer and

cancer treatment, and rehabilitation services are reimbursable as palliative oncology care[30]. There was a call for early inclusion of rehabilitation services for older adults, frail adults, and those undergoing surgery, radiation and/or chemotherapy. Post-treatment rehabilitation is recommended by this group for the management of physical needs experienced due to cancer and cancer treatment, and are reimbursable as palliative oncology care services[30].

Lack of care for cancer-related symptoms compounds the negative impact cancer and cancer treatment imparts on physical and cognitive function as well as the ability to reengage in society, recreation, and vocational activity. Prehabilitation and rehabilitation for cancer patients is a component of cancer care that has the potential to support patients to obtain, maintain, and maximize physical, cognitive, and vocational functional outcomes. There is evidence to support the use of oncology rehabilitation to address pain, functional decline, and quality of life throughout every stage of survivorship[26,31,32]. While survival rate is a critical focus for cancer care, identifying and supporting treatment-induced physical dysfunction is an integral part of cancer care. Oncology prehabilitation and rehabilitation are underutilized in the team-based approach to cancer care[32,33]. Despite the known benefits of exercise and oncology rehabilitation and strong data supporting the safety and efficacy of oncology rehabilitation, inclusion of services to address physical and functional needs is lacking in the current cancer patient care model[34]. Oncology rehabilitation is a facet of medical care for cancer patients that rehabilitation professionals should deliver as a component of standard practice for cancer patients. Challenges associated with cancer survivorship are stretching current models of cancer care to include strong partnerships between oncologists and rehabilitation

professionals to provide cancer care across the care continuum[12]. An interprofessional approach in comprehensive cancer rehabilitation allows healthcare providers to diagnose and treat a patient's physical, psychological, and cognitive impairments to maintain or restore function, reduce symptom burden, maximize independence, and improve quality of life[34]. By addressing the specific functional challenges and impairments faced by cancer patients, rehabilitation programs can make significant contributions to improving a patient's functional status, quality of life, overall sense of independence, and health[31,35,36].

Rosario-Concepcion[37] reported low utilization despite some perceived benefits among study participants. This study acknowledged that there is a gap in knowledge among oncologists about the benefits of rehabilitation in cancer patient care and identified factors such as lack of information and awareness about cancer rehabilitation and poor access as being perceived barriers. Stubblefield[34] reported similar underutilized oncology rehabilitation referral patterns for reasons associated with a lack of knowledge about cancer rehabilitation on the part of patients and clinicians, and limited access to services. A scoping review by Kennedy et al. reported on organizational barriers as the central issue related to referrals to oncology rehabilitation and that "cancer care is hindered by a web of interrelated barriers across all levels of the healthcare system".[38] Kennedy et al. called for clinical trials to understand and develop new comprehensive interdisciplinary cancer care models that provide an integrated approach to a broader scope of health outcomes for cancer patients.

Oncology clinicians largely agree with the need for exercise to be addressed during cancer care. However, there are barriers to this care since exercise oncology

programs in the US are not systematically integrated into medical models of care[38,39]. There is limited high-quality research available examining the reason for the lack of referrals to oncology rehabilitation and/or prescription exercise for cancer survivors. Knowledge, attitudes, and practices of oncologists with respect to oncology rehabilitation and referrals for integration of rehabilitation specialists are not well described in the literature. The aim of this project is to investigate oncology providers' knowledge, attitudes, and practices (KAP) associated with prescription exercise and oncology rehabilitation referrals.

METHODS

The study design was a cross-sectional questionnaire on oncologist's knowledge, attitudes, and practices associated with referral patterns to oncology rehabilitation. (Appendix B)

Survey and Data Collection

A focus group consisting of an oncologist, a hematologist, and a physical medicine and rehabilitation physician provided feedback on the survey used for this study which was developed from a previously published survey[37]. The survey questions included demographic information including age, sex, cancer specialty, type of practice, years of practice, weekly patient panel, self-reported geographic location, and exercise habits. Qualitative and quantitative survey data consisted of knowledge of exercise impact on numerous health outcomes, attitude towards exercise during various stages of treatment, practice patterns associated with referrals to exercise specialists, and challenges with referrals to exercise specialists. The survey included 15 demographic questions, and 32 oncology rehabilitation knowledge, attitudes, and practice (KAP)

questions. The survey data was collected electronically via REDCap or in person at participating oncology society's annual conference.

Participants and Data Collection

Information about the survey was provided and participants gave informed consent to participate. Permission was granted by the Florida Society of Clinical Oncology (FLASCO) and the Northern New England Clinical Oncology Society (NNECOS) to recruit participants for this study. Participants were recruited to voluntarily participate from FLASCO and NNECOS via email distribution containing the survey link and in person at the annual oncology society conferences. Data was collected electronically to a Red Cap survey instrument or via paper and manually added to Red Cap. A study information sheet was provided to all participants. All survey data were coded, a unique number was given to every participant, and stored in Red Cap.

Statistical Analysis

Microsoft Excel was used for statistical analysis. Descriptive statistics were used to characterize participants, and participant oncology rehabilitation knowledge, attitudes, and practices. A stratified analysis was completed to examine subgroup referral rate differences.

RESULTS

Eighty-two participants responded to the 32-question survey from the NNECOS Spring 2023 conference in person (N=40) and FLASCO Fall 2022 conference in person (N=42), or electronically (N=7). Membership information was not available for both oncology societies. The total number of oncologists in northern New England and Florida was estimated to be 300 and 1,200 respectively. The mean age (SD) of

participants was 50 (11.7), 66% of participants were male, 34% were female. The majority of participants identified as white (60%), Asian (23%), or Hispanic/Latino (9%). The mean years practicing in their oncology specialty was 20 (10.9), the mean number of cancer patients treated per week was 43 (27.4) with a mean referral rate to oncology rehabilitation of 23%. Practice settings included private practice (22%), hospital-based (12%), medical centers (26%), and academic medical centers (40%). Geographic areas of practice included urban (32%), suburban (38%), and rural (34%). The self-reported weekly exercise consisted of >150 minutes (48%), 75-150 minutes (35%), and less than 75 minutes (18%). Most participants reported exercising at a moderate intensity (62%) (Table 3.1).

The impact of prescription exercises following cancer treatment was rated on a 7-point Likert Scale (1-7, 1=strongly disagree, 4=neutral, 7=strongly agree). Participants generally 'agree' that prescription exercise can have a positive impact on lymphedema (6.4), ADLs (6.3), QoL (6.3), fall risk (6.3), fatigue (6.2), anxiety and depression (6.1), pain (6.0), sleep (5.9), bone health (5.8), cognitive function (5.8), reduce negative effects of cancer treatment (5.5), cardiotoxicity (5.2), and neuropathy (5.1) (Table 3.2). Overall, participants generally disagreed that there were risks for cancer survivors participating in exercise (3.4). Exercise was viewed as beneficial during treatment (5.7), necessary during treatment (5.0), and generally safe during treatment (5.5). Participants rated patients as capable of exercise during treatment (5.1), capable upon completion of treatment (5.8), and oncology rehabilitation referral would be well received by patients (5.4). Oncologists in this study feel very neutral about giving general exercise advice (5.0), discussing exercise as part of their role in treatment (4.8), and confidence in referring to oncology

rehabilitation (5.8). Oncologists responded weak to moderate to the statement 'rate your level of knowledge about prescription exercise and oncology rehabilitation'. Participants reported a *23% referral rate* to oncology rehabilitation over the last 12 months, while 57% of participants stated that it is *difficult to refer* patients to an oncology rehabilitation. The top referral reasons included lymphedema (77%), weakness (71%), and balance issues (67%) (Table 3.7).

Overall self-reported referral rate to oncology rehabilitation was 23%. Referrals to oncology rehabilitation varied by location with physicians from suburban areas reporting 30% referral rate, rural physicians reporting a 21%, and urban physicians reporting a 16% referral rate (Table 3.3). A one-way ANOVA was performed to compare the effect of geographic location on referral rate to oncology rehabilitation. A one-way ANOVA revealed that there was a statistically significant difference in referral rate between at least two of the geographic locations (p=0.0308) (Table 3.4). Stratified analysis of the difference of means between groups revealed a marginally statistically significant difference in referral rate between urban and suburban (p=0.0169). The Bonferroni adjusted p-value <0.0167 indicated a meaningful difference in referral patterns of urban vs suburban (Table 3.5). Referral percentages of suburban vs rural was p-value=0.1508, and urban vs rural was p-value=0.2509.

Providers reporting 'not difficult to refer to oncology rehabilitation' (33.6%) had a higher self-report referral rate as compared to providers reporting 'difficult to refer' (16.6%; $P = <0.0001$). Female referring providers reported higher rates of referral to oncology rehabilitation (29.6%) compared to male referring providers (20.7%; P = 0.09). Older referring providers (27.0%) are more likely to refer patients to oncology

rehabilitation compared to younger referring providers (20.5%), however, lack statistical significance (P = 0.0642). There was no effect from self-reported exercise habits (P = 0.7153) and geographic location (P = 0.3408) on self-reported referral rates to oncology rehabilitation (Table 3.6).

The top five reasons oncologists reported for referral to oncology rehabilitation included lymphedema, weakness, ADLs, balance, pain, and fatigue. The top five factors impacting referral frequency included treatment side effects, age, stage, comorbidities, and physical activity risk. The top five barriers to referral for oncology rehabilitation include knowledge of services, information about cancer rehabilitation among patients, knowledge about the benefits of oncology rehabilitation, time during a medical oncology office visit, and patient saturated with information (Table 3.7).

DISCUSSION

This study consisted of a questionnaire distributed to oncologists of FLASCO and NNECOS to examine factors influencing referral patterns to oncology rehabilitation from the referring provider's perspective. The key finding was that overall, oncologists refer to oncology rehabilitation at a disproportionate rate of 23% as compared to physical and functional decline associated with cancer and cancer treatment[23]. This study sought to describe the knowledge, attitudes, and practices of oncologists with respect to oncology rehabilitation and referrals to oncology rehabilitation. There are currently no standardized guidelines for the implementation of oncology rehabilitation, access to oncology rehabilitation remains low[34], and referrals to rehabilitation specialists during and post cancer treatment are underutilized[37].

The impact of cancer and cancer treatment are well documented and include a negative impact on muscle strength, cardiovascular decline, peripheral neuropathy, cardiotoxicity, surgical and musculoskeletal pain, fatigue, muscle endurance, balance, pain, lymphatics, flexibility, gait, and health-related quality of life[14,15,17–19,40–45]. Patients often experience significant symptom burdens associated with physical and mental domains which is a strong predicator of physical decline and mortality[46]. The benefits of exercise associated with oncology rehabilitation are well documented in the literature to prevent, maintain, and even reverse cancer-related declines in function[31,47,48]. Exercise assists in the management of cancer and the consequences of debilitating treatments. Exercise can improve physical performance, including strength and mobility, and decrease self-reported disability[49]. While the American Cancer Society recommends exercise and a physically active lifestyle during and after treatment for cancer, cancer survivors fall well below recommended levels at an estimated 7%[50]. Fitch et al. examined the patient perspectives of over 3000 older cancer survivors. At three years post-cancer treatment, 80% reported physical concerns including function, cardiovascular, balance, mobility, and neuropathy[51]. A systematic review examining the effects of exercise rehabilitation on physical function in adult cancer survivors found that moderate to vigorous exercise improved physical function, muscle strength, cardiovascular fitness when performed at smaller doses than recommended in general exercise guidelines for no less than three times per week[52]. Meeting general physical activity guidelines has been shown to maximize health and quality of life and minimize chronic conditions among cancer survivors[53]. Despite research evidence to support utilization of exercise in cancer care and the known benefits of oncology rehabilitation, there are factors that are

negatively influencing the clinical translation and implementation of this service, therefore, likely impacting long term consequences for cancer survivors. Rosario-Concepcion found that less than 15% of oncologists refer their patients to rehabilitation services[37] in a questionnaire study of oncologists. Hardcastle et al. found that 46% of oncologists reported regularly promoting physical activity to patients, 20% provided written information about physical activity, and 23% referred to oncology rehabilitation[54]. An additional systematic literature review by Alderman et al. reported that 18% of healthcare professionals referred patients to receive physical activity programming and advice from exercise professionals. The oncologists of our study were in alignment with past studies demonstrating low referral rates of 23%.

This study confirmed that the low oncology rehabilitation referral rate phenomenon persists and aligns with previous studies. Critical to this study, we aimed to demonstrate specifics of the underutilized aspect of this issue, and the associated facilitators and barriers to referrals for oncology rehabilitation within the broader standard of care for cancer survivors. Our study found statistically significant referral differences between self-reported geographic location, and difficulty to refer (yes/no). There was an association between lower referral rates and participants reporting 'difficult to refer'. Suburban providers report referring at the highest rate while urban providers report at the lowest rate among FLASCO and NNECOS members. A higher number of urban providers reported difficulty referring while a lower proportion of suburban providers reported difficulty referring. The combination of these findings suggests potential organizational, and referral mechanism challenges (Table 3.3). To the best of our knowledge, there are no prior studies specifically examining oncology rehabilitation

referral rate by geographic location and/or declaration of difficulty referring. There is very limited research identifying factors that may influence an oncologist's referral patterns to oncology rehabilitation. However, Agoriwo et al. looked at factors that influence the utilization and delivery of rehabilitation services among persons with Parkinson's disease and cited lack of referrals ordered and nonavailability of exercise professionals as barriers to access. More specifically, patients with Parkinson's disease in urban, suburban, and rural settings use of rehabilitation services varied widely from 14% to 62%[55]. Borg et al. identified factors associated with non-attendance at exercise-based cardiac rehabilitation include distance to rehabilitation facility greater than 16km, smoking, a higher burden of comorbidities, and male sex[56]; they concluded that individual and structural factors likely contribute to attendance rate. The cardiac study *did not mention referral rate as a barrier*; distance and personal factors were identified, suggesting integration of cardiac rehabilitation referral to standard of care for patients with heart conditions.

Older providers (>50 years) reported referring at a higher rate than younger providers (≤50 years) trending in the direction of statistical significance (Table 3.6). Previous research has shown that an increased level of exercise awareness with their patients is associated with the following: professionals practicing for more than 10 years; a belief that physical activity reduces side effects of treatment; a higher confidence level; and disagreement that physical activity has associated risks[57]. We feel that this difference by age subgroup is notable, in combination with previously stated geographic location and difficult referring findings, perhaps the age findings suggest structural and organization challenges with referring to oncology rehabilitation. Perhaps these results

are a reflection of organizational familiarity, mechanisms to refer, increased time management burden felt with younger providers, and ease of including exercise referrals with oncology care. A 2021 study identified lack of time, lack of exercise specialists to consult, and exercise promotion outside the area of competence as a barrier to promoting exercise and activity among cancer patients[58]. More research is needed to better understand the referral rate differences represented in our data.

Previous research by Spellman et al. examined practices of oncology clinicians toward promoting of physical activity. This study, published in 2013, reported that 55% of oncology clinicians felt that advising patients on physical activity was not part of their role, 93% were in agreement that physical activity can improve quality of life of cancer survivors, 49% agreed that regular physical activity reduced effects of treatment, and 25% agreed that some risks are associated with participating in regular physical activity. The last decade has brought some changes in these areas. Our study shows that oncologists are neutral with respect to their role in advising patients on physical activity. We continue to be in agreement with regard to improvement in quality of life and reduce treatment effects. Importantly, our study found that oncologists feel that there are decreased risks associated with engaging in prescription exercise as a cancer survivor. This demonstrates increased knowledge and benefits of exercise during and post-cancer treatment among our study participants.

Oncologists from all geographic locations identified knowledge of a referral mechanism, knowledge about the benefits of rehabilitation, and information about oncology rehabilitation among patients as barriers to referrals. Providers from urban locations felt that time during office visits and patient interest were larger contributors to

challenges with referrals compared to providers from rural and suburban locations. These findings may be a factor in this subgroup of providers that influenced a higher rate of 'difficult to refer'. Our results show that urban providers are more challenged than suburban providers to refer to oncology rehabilitation and have provided some insight into the time and perceived patient interest as the components that weigh more heavily in lower referral patterns. These results indicate that urban providers may see a higher number of patients per day at more frequent intervals; therefore, compressed daily schedules negatively impact referral rates compared to suburban and rural providers. Suburban and rural providers indicated that their patients are saturated with information; perhaps this is an opportunity to increase awareness among providers regarding potential contributions to patient care from rehabilitation specialists. Broadly for all subgroups, referral mechanisms, knowledge, awareness of organization access to oncology rehabilitation, and information about the benefits oncology rehabilitation may indicate challenges from an organization and structure perspective; these barriers also suggest need for provider and patient education regarding oncology rehabilitation (Table 3.7). The barriers identified in our study are similar to other reported barriers in the literature which describe poor rehabilitation access, lack of time, lack of knowledge and resources, lack of motivation and interest, and poor recognition of the correlation between physical dysfunction and oncology rehabilitation in the cancer population[34,37,59,60].

Also unique to our study, we examined the association between sex on referral rate. Females reported referring at a slightly higher rate than males; there was a mean difference of 8.9% between females and males. In a systematic review and meta-analysis, Jefferson et al. concluded that female physicians may reflect a more patient-centered

approach.[61] Previous studies have shown that greater patient participation and decision making has been associated with improved outcomes and quality of life among cancer patients[61]. Referring provider's exercise habits do not seem to be a factor in referral rate to oncology rehabilitation given the small difference in referral rate found in this study (Table 3.6). Similarly, Alderman et al. found that healthcare professionals' personal physical activity levels did not seem to be associated with whether they discussed physical activity with their patients.

Our findings show that oncologists view oncology rehabilitation as generally favorable during treatment from a beneficial and safety perspective; providers are neutral on their opinion of necessity during treatment. Alderman et al. systematic literature review findings stated that 55% to 64% of oncologists understand that physical activity is beneficial and important to cancer care while a larger proportion of providers were unsure of the safety of physical activity thus took a conservative approach to incorporating exercise discussions[57]. Referring provider awareness of the safety of physical activity/oncology rehabilitation has improved in recent years; most oncologists agree that rehabilitation is beneficial but there is a significant gap between understanding the benefits of exercise for cancer survivors and referral rate. We acknowledge that the 'safe during treatment' question requires additional research; cancer and cancer treatment is highly heterogeneous with a broad spectrum of physical, medical, and cognitive impacts on the patient.

Our study was a first to explore oncologists' attitudes regarding capacity of cancer survivors to engage in exercise during and after treatment, both of which were viewed as slightly favorable upon completion of treatment with a neutral opinion of their capacity

during treatment. Providers felt mildly agreeable that a referral would be well received by patients; these results are similar to a study showing that late stage lung cancer patients report an interest in receiving rehabilitation services despite high levels of disability and related distress[60]. Providers were neutral about confidence giving general advice about exercise and confidence referring to oncology rehabilitation. Oncologists did not feel that exercise intervention or exercise educations was their role in treatment of cancer patients. Past research has shown that confidence regarding exercise for cancer patients correlates with an increased rate of promoting exercise for this patient population[54]. As stated previously, gains in confidence, capacity, and attitude will likely continue to impact referral rates in a positive direction. However, the responsibility of exercise advice and exercise planning has been identified by this study, and previous studies to be ideally suited for medically trained exercise professionals. This cluster of findings suggests that there is a critical need for standard care of cancer patients to include a referral from the medical/surgical oncology team to oncology rehabilitation where a medically trained exercise professional can access each patient, create a plan of care, and triage one-on-one care, group exercise, or community based depending on individual needs. The Hardcastle study concluded that patient's physical activity promotion may be improved through strategies that increase oncologists' perceived behavioral control[54]. One-third of oncologists know the recommended exercise guidelines for cancer patients[57]. The majority rated weak to moderate knowledge of oncology rehabilitation; however, the vast majority of oncologist in this study reported agreement/strong agreement that prescription exercise is beneficial for physical and mental health function decline associated with cancer and cancer treatment. There is a disconnect between these aspects, knowledge of

oncology rehabilitation and benefits of exercise for cancer patients. Perhaps the most appropriate path to achieving increased oncologists' promotion of oncology rehabilitation is through integration of exercise professionals to the oncology team. Integration of oncology rehabilitation to cancer standard of care moves function and physical decline from low priority or not addressed to formally acknowledging cancer and its related functional deficits as a chronic condition that may be best served by a professional exercise specialist[12,13] (Table 3.7).

Rehabilitation for cancer patients has historically been associated with lymphedema management[62] and/or orthopedic type deficits, most commonly a musculoskeletal impairment[63]. Our study confirmed that the top five reasons for referral to oncology rehabilitation were solidly aligned with a very orthopedic diagnosis code driven approach to oncology rehabilitation versus a holistic team-based approach to cancer care. (Table 3.7). Oncologists felt that Doctor of Physical Therapy and Physical Medicine and Rehabilitation Doctors are the most appropriate medically trained exercise professionals for oncology rehabilitation referrals. Our study is the only study that we are aware of that specifies provider perspective on the benefits of oncology rehabilitation for the most common cancer symptoms. This study found that oncologists perceive exercise intervention to be most beneficial for lymphedema, ADLs, QoL, fall risk, fatigue, anxiety, depression, and pain. Sleep, bone health, cognitive function, cardiotoxicity, and peripheral neuropathy were less favorable regarding improvement associated with exercise (Table 3.2). High quality research is needed to better understand the impact of exercise on all cancer related physical symptoms. All of the cancer treatment related symptoms listed in our survey are highly relevant and fall within the scope of practice of

a medically trained exercise professional, however, individually they lack the essence of a holistic oncology rehabilitation program. In 2022, the American Society of Clinical Oncology (ASCO) published guidelines recommending regular aerobic and resistance exercise for people receiving cancer treatment with curative intent. ASCO guidelines recommend prehabilitation exercise for patients scheduled for surgery. The ASCO guidelines emphasize the critical need for research in active cancer, treatment, and exercise.[64]

Based on the findings from our study, we support Stout et al. in their systematic literature review call for oncology rehabilitation as a reimbursable programmatic service integrated into standard of care for cancer survivors thus mitigating organization and structural barriers, relieving time constraints for oncologists, providing education opportunities for patients and an interprofessional connection for oncology providers to confidently utilize rehabilitation services for acute and long term benefit of function and quality of life[31]. A critical shift in the paradigm of cancer treatment includes not only survival but also preventing functional loss during treatment and improving strength, endurance, and function following treatment. The heterogeneity of cancer and cancer care aligns well with the concept of inclusion of oncology rehabilitation as the standard of care to maximize patient outcomes, safety, and overall quality of care. The largest challenges in integration of oncology rehabilitation to cancer care are proving to be organizational and availability, the referral process, and provider and patient education regarding oncology rehabilitation. The National Cancer Institute has designated 62 comprehensive cancer centers in the US. More than 90% of NCI Cancer Centers do not include oncology rehabilitation services on their websites.[65] High-quality research is

needed to determine best practices for cancer care from a system and team perspective, outcomes, patient experience, and provider perspective. For these reasons, it is imperative that we better understand the current challenges associated with underutilization of oncology rehabilitation care.

Strengths and Limitations

Strengths of our study include the following: study methodology and a questionnaire designed to address the proposed research question and broaden the breadth and depth of information on the 'low referral rate' for oncology rehabilitation. There are limits to the generalizability of the results from this study due to regional recruitment of participants and relatively small sample size opting to participate and potential selection bias related to the convenience sampling approach. Finally, we were not able to calculate a response rate because we did not have an estimate of the size of the target population.

CONCLUSION

Oncologists' knowledge, attitude, and practice associated with oncology rehabilitation referrals must be further examined by researchers and translated into action by providers and our healthcare system. Cancer survivors are surviving in high numbers and living longer with function and physical impairments associated with chronic cancer. Oncologists were generally in agreement that exercise is safe and beneficial for cancer survivors. Referral rates remain low, and the skills of medically trained exercise specialists are underutilized. Our study identified barriers to oncology rehabilitation referrals that include organizational challenges, lack of referral mechanisms, lack of

understanding of benefits of oncology rehabilitation, availability, time, and patient saturation.

Clinical Implications

Cancer survivors would benefit from integration of oncology rehabilitation as standard care for cancer patients. Benefits of oncology rehabilitation for cancer survivors would include physical function restoration, and improvement in overall health and quality of life for cancer survivors. Integration into standard care requires systems level, referral process, availability and access, insurance reimbursement, and provider and patient education.

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Table 3.1

Participant Demographics

Characteristics ***N=82***	***Mean or Proportion***	**Median (Range)**	**IQR**	**95% CI**
Age, Mean (SD)	50 (11.7)	50 (31-70)	41-60	[47.4 - 52.6]
Years as a physician, years (SD)	20 (10.9)	18 (4-42)	10-30	[17.2 - 22.0]
Number of cancer patient treated/week, Mean (SD)	43 (27.4)	40 (3-150)	25-50	[36.3 - 49.3]
% patients referred to Oncology Rehab Mean (SD)	23 (19.8)	20 (0-85)	10-30	[19.2 - 28.0]
Male, N (%)	55 (66.3)			
Female, N (%)	27 (33.7)			
Race, N (%)				
White	49 (59.8)			
Asian	19 (23.2)			
Hispanic/Latino	7 (8.5)			
Multiracial	4 (4.9)			
Black	2 (2.4)			
Hawaiian/Pacific Islander	1 (1.2)			
Practice Setting, N (%)				
Private	17 (21.7)			
Hospital Based	10 (12.0)			
Medical Center	22 (26.5)			
Academic Medical Center	33 (39.8)			
Geographic Area of Practice, N (%)				
Urban	26 (31.7)			
Suburban	31 (37.8)			
Rural	25 (34.1)			
Self-report exercise/week, N (%)				
>150 min	36 (47.6)			
75-150 min	29 (35.4)			
<75 min	15 (18.3)			
No exercise	2 (2.4)			
Self-report exercise intensity, N (%)				
Mild	15 (18.3)			
Moderate	51 (62.2)			
Vigorous	16 (19.5)			

Table 3.2

Questionnaire Descriptive Statistics

Prescription Exercise Can Improve: *	**Urban N=26 Mean(SD) (Range) Median (IQR) 95% CI**	**Suburban N=31 Mean(SD) (Range) Median (IQR) 95% CI**	**Rural N=25 Mean(SD) (Range) Median (IQR) 95% CI**	**Total N=82 Mean(SD) (Range) Median (IQR) 95% CI**	**% Agree (5) or Strongly Agree (6)**
Lymphedema	6.4 (.86) (4-7) 7 (6.0-7.0) 6.1 - 6.8	6.5 (.62) (5-7) 7 (6.0-7.0) 6.3 - 6.8	6.3 (.94) (3-7) 7 (6.0-7.0) 5.9 - 6.7	6.4 (.80) (3-7) 7 (6.0-7.0) 6.3 - 6.6	96.3
Ability to Perform ADLs	6.4 (.80) (5-7) 7 (6.0-7.0) 6.1 - 6.7	6.7 (.76) (5-7) 7 (6.0-7.0) 6.4 - 6.9	6.3 (.91) (4-7) 7 (6.0-7.0) 5.9 - 6.7	6.3 (.82) (4-7) 7 (6.0-7.0) 6.2 - 6.5	93.7
Quality of Life	6.6 (.69) (5-7) 7 (6.2-7.0) 6.3 - 6.9	6.3 (.90) (5-7) 7 (5.0-7.0) 6.0 - 6.6	6.0 (1.21) (3-7) 6 (5.0-8.0) 5.5 - 6.5	6.3 (1.00) (3-7) 7 (5.0-7.0) 6.0 - 6.5	93.9
Reduce Risk of Falls	6.4 (.76) (4-7) 7 (6.0-7.0) 6.1 - 6.7	6.3 (.69) (5-7) 6 (6.0-7.0) 6.0 - 6.5	6.2 (.91) (4-7) 6 (6.0-7.0) 5.8 - 6.6	6.3 (.79) (4-7) 6 (6.0-7.0) 6.5 - 6.5	91.5
Reduce Fatigue	6.5 (.71) (5-7) 7 (6.0-7.0) 6.2 - 6.8	6.1 (.96) (5-7) 7 (5.0-7.0) 5.8 - 6.5	6.0 (1.04) (4-7) 6 (5.0-7.0) 5.6 - 6.4	6.2 (.95) (4-7) 7 (6.0-7.0) 6.0 - 6.4	90.2
Anxiety and Depression	6.3 (.72) (5-7) 6 (6.0-7.0) 6.0 - 6.6	6.0 (1.00) (4-7) 6 (5.0-7.0) 5.6 - 6.3	6.1 (.88) (5-7) 6 (5.0-7.0) 5.7 - 6.4	6.1 (.88) (4-7) 6 (5.0-7.0) 5.9 - 6.3	83.9
Pain	6.0 (1.02) (4-7) 6 (5.2-7.0) 5.6 - 6.4	6.2 (.75) (5-7) 6 (6.0-7.0) 5.9 - 6.5	5.9 (1.05) (4-7) 6 (5.0-7.0) 5.4 - 6.3	6.0 (.94) (3-7) 6 (5.0-7.0) 5.8 - 6.2	85.3
Sleep	6.0 (.96) (4-7) 5 (4.2-7.0) 5.6 - 6.4	6.0 (.89) (5-7) 6 (5.0-7.0) 5.7 - 6.3	5.8 (1.16) (3-7) 6 (5.0-7.0) 5.3 - 5.2	5.9 (1.02) (3-7) 6 (5.0-7.0) 5.7 - 6.2	77.8
Bone Health	6.1 (.97) (4-7) 6 (7.0-5.0) 5.8 - 6.5	5.7 (1.29) (4-7) 6 (4.0-7.0) 5.2 - 6.2	6.4 (1.36) (3-7) 6 (4.0-7.0) 5.9 - 6.9	5.8 (1.23) (3-7) 6 (5.0-7.0) 5.5 - 6.1	75.6
Cognitive Function	6.0 (1.00) (4-7) 6 (5.0-7.0) 5.6 - 6.4	5.8 (.98) (4-7) 6 (5.0-7.0) 5.5 - 6.2	5.5 (1.06) (4-7) 5 (5.0-6.2) 5.1 – 6.0	5.8 (1.02) (4-7) 6 (5.0-7.0) 5.5 – 6.0	70.1
Reduce Effects of Cancer Treatment	5.3 (1.57) (1-7) 5 (5.0-6.0) 4.7 – 6.0	5.4 (1.73) (1-7) 5 (5.0-7.0) 4.7 - 6.1	5.7 (1.00) (4-7) 5 (5.0-7.0) 5.3 - 6.1	5.5 (1.48) (1-7) 5 (5.0-7.0) 5.1 - 5.8	67.1
Cardio-toxicity	5.3 (1.31) (3-7) 5 (4.0-6.8) 4.7 - 5.8	5.2 (1.34) (4-7) 5 (4.0-7.0) 4.7 - 5.7	5.0 (1.35) (2-7) 5 (4.0-6.0) 4.4 - 5.6	5.2 (1.33) (2-7) 5 (4.0-6.2) 4.9 - 5.5	57.3
Peripheral Neuropathy	4.9 (1.37) (2-7) 5 (4.0-6.0)	5.3 (1.32) (4-7) 5 (4.0-7.0)	4.8 (1.34) (2-7) 4 (4.0-6.0)	5.1 (1.35) (2-7) 5 (5.0-6.0)	56.1

	4.4 - 5.5	4.8 - 5.8	4.3 - 5.4	4.8 - 5.4	
Risks for Cancer Survivors with prescription exercise	3.1 (1.71) (1-6) 3 (2.0-4.8) 2.5 - 3.8	4.1 (1.92) (1-7) 4 (2.0-5.0) 3.4 - 4.8	2.7 (1.65) (1-6) 2 (1.0 - 3.2) 1.5 – 2.8	3.4 (1.85) (1-7) 3 (2.0-5.0) 2.9 - 3.8	15.8
In my opinion prescription exercise is:					
Beneficial during treatment	5.8 (1.67) (3-7) 6 (5.0-7.0) 5.3 - 6.3	5.7 (1.29) (3-7) 6 (5.0-7.0) 5.2 - 6.2	5.7 (1.18) (5-7) 6 (5.0-7.0) 5.2 - 6.2	5.7 (1.20) (3-7) 6 (5.0-7.0) 5.5 - 6.0	74.2
Necessary during treatment	5.0 (1.37) (2-7) 5 (4.0-6.0) 4.5 - 5.6	4.9 (1.45) (2-7) 5 (4.0-6.0) 4.4 - 5.4	5.3 (1.46) (3-7) 5 (4-7) 4.7 - 5.9	5.0 (1.41) (2-7) 5 (4-7) 4.7 - 5.4	54.1
Generally safe during treatment	5.5 (1.24) (3-7) 6 (5.0-6.0) 4.9 - 5.9	5.4 (1.19) (3-7) 5 (4.0-6.0) 5.0 - 5.8	5.6 (1.10) (4-7) 6 (5.0-6.2) 5.1 - 6.0	5.5 (1.16) (3-7) 5 (5.0-6.0) 5.2 - 5.7	63.4
Most of my patients are capable of exercising during treatment	4.9 (1.03) (3-7) 5 (4.0-5.8) 4.5 - 5.3	5.3 (.97) (4-7) 5 (5.0-5.8) 4.9 - 5.6	5.2 (1.00) (3-7) 5 (5.0-6.0) 4.8 - 5.6	5.1 (1.01) (3-7) 5 (5.0-6.0) 4.9 - 5.4	57.6
Most of my patients are capable of exercising upon completion of treatment	5.7 (.93) (3-7) 6 (5.2-6.0) 5.3 - 6.1	5.8 (.92) (3-7) 6 (5.0-6.0) 5.5 - 6.1	5.8 (.97) (4-7) 6 (5.0-6.0) 5.4 - 6.2	5.8 (.93) (3-7) 6 (5.0-6.0) 5.6 – 6.0	69.2
Oncology rehabilitation referrals would be well received by patients	5.5 (1.33) (1-7) 5 (5.0-6.0) 4.9 - 6.0	5.6 (1.18) (4-7) 5 (4.2-7.0) 5.2 - 6.0	5.2 (1.03) (3-7) 5 (4.0-6.0) 4.7 - 5.6	5.4 (1.18) (1-7) 5 (5.0-6.0) 5.1 - 5.7	63.4
Confident giving general advice	5.1 (1.26) (2-7) 5 (5.0-6.0) 4.6 - 5.6	4.9 (1.41) (3-7) 5 (4.0-5.0) 4.3 - 5.4	5.0 (1.34) (2-7) 5 (4.0-6.0) 4.8 - 5.6	5.0 (1.35) (2-7) 5 (4.0-6.0) 4.7 - 5.3	54.1

about exercise to patients					
Discussing exercise with patients is part of my role in treatment	5.8 (1.47) (1-7) 5 (4.0-6.0) 5.2 - 6.4	5.0 (1.50) (2-7) 5 (4.0-6.0) 5.4 - 6.6	5.2 (1.41) (3-7) 5 (4.0-7.0) 4.6 - 5.8	5.1 (1.45) (1-7) 5 (4.0-6.0) 4.8 - 5.4	55.8
Confident referring patients to an oncology rehabilitation program	5.5 (1.48) (2-7) 6 (4.2-7.0) 4.9 - 6.1	6.0 (1.07) (3-7) 6 (5.0-7.0) 5.6 - 6.4	5.8 (1.16) (4-7) 6 (5.0-7.0) 5.3 - 6.2	5.8 (1.24) (2-7) 6 (5.0-7.0) 5.5 - 6.0	67.9
Self-report Knowledge of Oncology Rehabilitation*	2.4 (.58) (1-3) 2 (2.0-3.0) 2.2 - 2.6	2.5 (.74) (1-4) 2 (2.0-3.0) 2.2 - 2.8	2.5 (.98) (1-4) 2 (2.0-4.0) 1.8 - 3.2	2.5 (.76) (1-4) 2 (2.0-4.0) 2.3 - 2.7	0

1-7 Likert Scale: 1= Strongly Disagree, 7=Strongly Agree * 0-3 Scale: 0=Absent, 3=Strong

Table 3.3

Self-Reported Referral Rate to Oncology Rehabilitation and Difficulty Referring

Mean Referral (SD)(Range) Median (IQR) 95% CI	**Urban**	**Suburban**	**Rural**	**Overall**
Percent patient referred over last 12 months	**16.4 (14.50) (0-60) 15 (9.5-20.0) [10.3 - 22.5]**	**30.1 (23.18) (0-85) 30 (20.0-37.2) [21.4 - 38.7]**	**21.7 (17.26) (0-75) 20 (10.0-27.0) [14.6 - 28.8]**	**23.2 (19.75) (0-85) 20 (10.0-30.0) [18.8 - 27.6]**
Difficult to refer patients to oncology rehabilitation	Y=17 N=9	Y=14 N=17	Y=16 N=9	Y=47 (57.3%) N=35 (42.7%)

Table 3.4

One Way ANOVA: Self-Report Referral Percentage by Geographic Location

Variables	**N**	**Mean Referral (SD)(Range) Median (IQR) 95% CI**	***p-value***
Overall Referral Rate to Oncology Rehabilitation	82	23.2 (19.75) (0-85) 20 (10.0-30.0) [18.8 - 27.6]	
Urban referral	26	16.4 (14.50) (0-60) 15 (9.5-20.0) [10.3 - 22.5]	***0.0308***
Suburban referral	31	30.1 (23.18) (0-85) 30 (20.0-37.2) [21.4 - 38.7]	
Rural referral	25	21.7 (17.26) (0-75) 20 (10.0-27.0) [14.6 - 28.8]	

Table 3.5

Pairwise Comparison of Self-Report Referral Percentage by Geographic Location

Geographic Location	**N**	**Mean Referral %**	**Difference**	**95% CI**	***p-value***
Urban	26	16.6	13.5	-5.562 – 24.707	***0.0169***
Suburban	31	30.1			
Suburban	31	30.1	*8.4*	-3.130 – 19.770	*0.1508*
Rural	25	21.7			
Urban	26	16.6	*5.1*	-3.875-14.485	*0.2509*
Rural	25	21.7			
Bonferroni Adjustment P-value <0.0167					

Table 3.6

Bivariate Analysis of Referral Percentage by Age, Sex, Exercise Habits, Location, Difficulty Referring

Variables	N	Mean Referral %	Difference	95% CI	*p-value*
Referral Percentage					
>50 years	40	27.0	6.5	-1.93 – 14.90	0.0642
≤50 years	43	20.5			
Referral Percentage					
Male	52	20.7	8.9	5.40 – 12.45	0.0901
Female	27	29.6			
Referral Percentage					
≥150 minutes per week	36	22.6	1.4	-7.36 – 10.12	0.7153
<150 minutes per week	46	24.0			
Geographic Location				-4.18 - 11.93	0.3408
FLASCO	42	20.3	3.9		
NNECOS	40	24.2			
Difficult to Refer					
Yes	49	16.6	*17.0*	**8.82 – 25.11**	**<0.0001**
No	32	33.6			

Table 3.7

Additional Characteristics, Facilitators and Barriers Describing Referrals to Oncology Rehabilitation

	Urban N=26	**Suburban N=31**	**Rural N=25**	**Total N=82**
Rank *most suitable to least suitable* provider to deliver exercise intervention	Doctor of Physical Therapist Physical Medicine and Rehabilitation Doctor Exercise Specialist Oncology Nurse Athletic Trainer	Doctor of Physical Therapist Physical Medicine and Rehabilitation Doctor Oncology Nurse Exercise Specialist Athletic Trainer	Doctor of Physical Therapist Physical Medicine and Rehabilitation Doctor Exercise Specialist Oncology Nurse Athletic Trainer	Doctor of Physical Therapist Physical Medicine and Rehabilitation Doctor Exercise Specialist Oncology Nurse Athletic Trainer
Regarding prognosis, at what point would you decide not to refer a patient for oncology rehabilitation	4.5 months	4.5 months	6 months	5 months
Top 5 reasons for oncology rehabilitation referral	Lymphedema ADLs Weakness Balance Msk/surgery pain	Lymphedema Balance ADLs Fatigue Msk/surgery pain	Lymphedema Weakness ADLs Balance Msk/surgery pain	Lymphedema 77% Weakness 71% ADLs 67% Balance 67% Msk/surgery pain & Fatigue (tie) 43%

Top 5 factors impacting referral frequency	Age Tx side effects Stage Comorbidities Type	Tx side effects Age Comorbidities PA Risks Type	Tx side effects Age Stage Comorbidities PA Risks	Tx side effects 53% Age 49% Stage 45% Comorbidities 45% PA Risks 38%
Top 5 barriers to referral for oncology rehabilitation	Knowledge of services or referral mechanism Time during office visit Knowledge about benefits of rehabilitation services Information about cancer rehabilitation among patients Patient interest	Knowledge of services or referral mechanism Knowledge about benefits of rehabilitation services Information about cancer rehabilitation among patients Patient saturated with information Time during office visit	Knowledge of services or referral mechanism Information about cancer rehabilitation among patients Time during office visit Knowledge about benefits of rehabilitation services Patient saturated with information	Knowledge of services or referral mechanism 64% Information about cancer rehabilitation among patients 46% Knowledge about benefits of rehabilitation services 45% Time during office visit 39% Patient saturated with information 33%

Appendix B. Knowledge, Attitudes, and Practices Questionnaire

Mayo Clinic
Physical Medicine & Rehabilitation
Jacksonville, Florida

University of Vermont
Larner College of Medicine
Burlington, Vermont

Knowledge, Attitude, and Practice Survey of Oncology Providers Regarding Referrals to Oncology Rehabilitation for oncology patients during and after cancer treatment

Please respond to the following questions/statements.

1. Following cancer treatment:

Prescription exercise can improve the **quality of life** of cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise is associated with **reduced fatigue** in cancer survivors.

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can reduce the **risk of falls** in cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve cancer related **pain** in cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve **lymphedema** in cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve **bone health** in cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise is associated with improved **sleep** in cancer survivors

1————2————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can reduce **cardiotoxicity** in cancer survivors

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can reduce **peripheral neuropathy** in cancer survivors

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve **cognitive function** in cancer survivors

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve the **ability to perform daily tasks** in cancer survivors.

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise can improve **anxiety and depression** in cancer survivors

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

Prescription exercise is associated with **reduced effects** of cancer treatment

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

There are some **risks** for cancer survivors participating in prescription exercise.

1————————2————————3———— 4 ————5———— 6 ————7
Strongly Disagree — Neutral — Strong Agree

2. Who would you consider *most suitable* to deliver a prescription exercise intervention to cancer survivors? Rank the following disciplines from 1 - 5.
   1 being the '*most suitable*' and 5 being the '*least suitable*'

Athletic Trainer____
Exercise specialist _____
Oncology nurse _____
PM&R Physiatrist_____
Physical Therapist_____

3. **Rate your level of knowledge** about prescription exercise and oncology rehabilitation.

Strong Moderate Weak Absent

4. List the multidisciplinary components of an oncology rehabilitation program.
Please list:

5. In my opinion prescription exercise/oncology rehabilitation is:

beneficial during *treatment*

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

necessary during *treatment*

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

generally safe during *treatment*

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

*6. Most of my patients with a cancer diagnosis are capable of exercising **during** cancer treatment*

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

*7. Most of my cancer survivors are capable of exercising **upon completion** of cancer treatment*

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

*8. Providing exercise prescription or oncology rehabilitation referrals **would be well received by patients***

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

9. I feel confident giving **general advice** about exercise to cancer survivors.

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

10. Discussing exercise with cancer survivors is **part of my role** in cancer treatment and care

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

11. I would be confident in **referring** cancer survivors to an exercise specialist or oncology rehabilitation program

1————2————3———— 4 ————5———— 6 ————7
Strongly Neutral Strong
Disagree Agree

12. What **percentage** of ALL of your patients with cancer have you **referred for prescription** exercise/oncology rehabilitation in the past 12 months? (percentage of patients) _____

13. Is it **difficult to refer cancer survivors** to an exercise specialist or oncology rehabilitation at your facility?

Yes No

14. With regard to an estimated prognosis, at what point would you decide not to refer a patient for rehabilitation? "I would **not** refer a patient for rehabilitation if their life expectancy was:

a. <1 month
b. <3 months
c. <6 months
d. <12 months
e. "I would refer a patient for rehabilitation regardless of their estimated prognosis"

15. What cancer related patient problems do you refer for *Oncology Rehabilitation*?

Select your top 5 reasons for referral to Oncology Rehabilitation

Lymphedema	Muscular/Surgical Pain	Contractures
Disability in Activities of Daily Living	Gait	Nutrition
Dysphagia	Fatigue	Orthosis
Weakness	Endurance	Mental Health
Balance	Prolonged immobilization	Pelvic Floor Dysfunction
Neuropathic pain	Nociceptive pain	Amputation
Weight control	Osteoarthritis	I don't refer oncology pts for rehab
Body image	Sexual dysfunction	

16. What **factors impact your frequency of referral** to exercise prescription/oncology rehabilitation? Select all that apply

Age
Cancer treatment side effects
Risks associated with physical activity
Stage of Cancer
Type of Cancer
Comorbidities
Other:_____

17. What **barriers do you identify in your** referral and delivery mechanism of rehabilitation services? (select all that apply)

a. Lack of knowledge of services or referral mechanism
b. Lack of knowledge about benefits of rehabilitation services
c. Lack of information about cancer rehabilitation among cancer patients
d. Perceiving a lack of importance of cancer rehabilitation by oncologists
e. Lack of governmental support such as subsidized medical cost
f. Lack of financial support and reimbursement for counseling on exercise
g. Lack of medical equipment

h. Lack of time during office visit
i. Concerns about the safety of exercise
j. Concerns about the effectiveness of exercise
k. Lack of patient interest
l. Patient saturated with information and recommendations
m. Other: _____

Demographic Information

1. **Age:** _____

2. **Sex:** male female

3. **Race/Ethnicity:**
   American Indian/Alaska Native (non-Hispanic)
   Asian (non-Hispanic)
   Black (non-Hispanic)
   Hispanic/Latino
   Multiracial (non-Hispanic)
   Native Hawaiian and Other Pacific Islander (non-Hispanic)
   White (non-Hispanic)

4. **Number of years as a physician**:_____

5. **Select stage of medical practice**:
   Medical School
   Residency
   Fellowship
   Attending

6. H**ave you had any prior training in prescription exercise or oncology rehabilitation?**
   Medical school
   Residency
   Fellowship
   Continuing Medical Education
   Other
   No prior training received

7. Number of years since completing exercise prescription or ***oncology rehabilitation training***:_____

8. How would you rate the extent of your training in ***oncology rehabilitation***?
   Substantial
   Moderate
   Minimal
   None

9. **Your practice setting**:
   - Private or single specialty group clinic
   - Hospital based
   - Multispecialty
   - Medical center
   - Academic medical center

10. **Approximate number of cancer patients you treat per week**:_____

11. **Select the top 5 types of cancer diagnoses you treat.**

Breast	Gynecological
Lung	Head & Neck
Spine	Brain
Gastroenterology	Prostate
Lymphomas	Leukemia
Bone	Endocrine
Other	

12. **What is your area of Specialty**:
    - Surgical Oncology
    - Medical Oncology
    - Radiation Oncology
    - Rehabilitation Oncology
    - Pediatric Oncology
    - Other:_____

13. How do you describe the **general area in which you treat oncology patients**?
    Urban Suburban Rural

14. How much **exercise do *you* engage** in each week:
    - ≥150 minutes of exercise each week
    - 75 - 150 minutes of exercise each week
    - < 75 minutes of exercise each week
    - Minimal to no exercise each week

15. What is **typically *your* exercise intensity**?
    - Mild
    - Moderate
    - Vigorous

Are you willing to be contacted in the future to provide more information about your attitudes toward rehabilitation in patients with advanced cancer?

Yes No

If so, how can we contact you?

Telephone:
e-mail:

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