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Exercise as an Intervention to Mitigate Decreased Cognitive Function From Cancer and Cancer Treatment

An Integrative Review

KEY WORDS
Cancer
Cognitive function
Exercise
Intervention

Background: Decreased cognitive function associated with non–central nervous system cancers and cancer treatment significantly affects cancer survivors' quality of life. Exercise may be an effective intervention to mitigate decreased cognitive function. **Objective:** The aim of this article is to conduct an integrative review to summarize and critique the available evidence related to the use of exercise as a potential intervention for decreased cognitive function from cancer and cancer treatment. **Methods:** We conducted an integrative review through January 2016 utilizing PubMed, CINAHL, and PsycINFO. Broad inclusion criteria included any quantitative study in which cognitive outcomes were reported in relationship to any type of exercise for adult cancer survivors. Effect sizes were calculated when possible based on available data. **Results:** Twenty-six studies were included for review. The majority of studies (including aerobic or resistance exercise as well as mindfulness-based exercise) were associated with some improved cognitive outcomes. However, studies varied significantly in levels of evidence, cognitive domains assessed, and types of cognitive measures. Less than half of the studies included objective measures of cognitive function. **Conclusions:** The evidence shows promising trends for the use of exercise as a potential intervention for improving cognitive function following cancer and cancer treatment, but questions remain concerning exercise type, timing of initiation, intensity, frequency, and duration.

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Implications for Practice: Additional research is warranted to understand how various types of exercise influence cognitive function in the cancer survivor population and to better understand the mechanisms driving these effects. Trial designs that include both objective and subjective measures of cognitive function are needed.

Decreased cognitive function associated with non–central nervous system cancers and cancer treatments is a challenging problem that is important to address for providing quality care and rehabilitation to cancer survivors. The most common cognitive sequelae can occur prior to, during, and after therapy and include difficulty within the cognitive domains of executive function, learning and memory, attention and concentration, information-processing speed, motor function, and spatial skills.[1–3] Estimates of cognitive impairment prior to the initiation of therapy are approximately 30% for breast cancers and other malignancies.[1] Incidence estimates during and shortly after chemotherapy range as high as 75%.[2,4] Approximately 30% of cancer survivors experience more long-lasting issues with cognitive function, which, in some cases, have been reported as late as 20 years following cessation of cancer treatment.[2,4,5] The impact of these cognitive problems on cancer survivors' quality of life is significant. Difficulty with executive function, word finding, and concentration impacts some survivors' work performance.[6] Likewise, survivors' comfort level in social situations and interactions with friends and family can be affected.[6] Survivors who experience decreased cognitive function express significant frustration with short-term memory issues, word finding, reading retention, and difficulty with sense of direction and response time when driving.[6] Thus, the development of appropriate interventions to prevent or mitigate these problems is of high importance.

Multiple mechanisms likely underlie the decreases in cognitive function experienced by cancer survivors.[7] The release of proinflammatory cytokines in response to both tissue invasion by the cancer and the administration of chemotherapy and direct injury to neural progenitor cells are postulated as 2 potential causal mechanisms.[8] Thus, interventions targeting a reduction in inflammation are of interest, as are interventions that enhance neuroplasticity, thereby facilitating recovery from neural progenitor cell injury.

Exercise may be an effective intervention to mitigate decreased cognitive function from cancer and cancer therapy. Exercise has been shown to decrease levels of markers of inflammation[9] and increase levels of brain-derived neurotrophic factor,[10] as well as increase hippocampal volume.[11] Exercise also has been shown to reduce the incidence of cognitive decline and improve cognition across several preclinical and clinical populations including the healthy elderly and those suffering from Alzheimer or Parkinson disease.[12–14]

Research is ongoing to investigate the potential for exercise to mitigate cancer-related decreases in cognitive function. Many types and combinations of exercise are under investigation, including aerobic, resistance, and mindfulness-based forms of exercise such as yoga, tai chi, and qigong. One common mechanistic thread postulated for components of all forms of exercise is the reduction of inflammation and proinflammatory markers.[9] Qualitative studies conducted primarily with survivors of breast cancer indicate that patients use a variety of forms of exercise as a strategy to attempt to regain mental clarity and enhance the ability to multitask and concentrate in the work environment.[6,15]

Despite the rather limited number of quantitative clinical research studies, the National Comprehensive Cancer Network has recommended exercise as a general strategy for managing cancer-related cognitive dysfunction.[16] However, other experts argue that the level of evidence does not yet support recommending exercise as a method for mitigating the cognitive effects of cancer and cancer treatment.[17] In an effort to determine whether existing evidence supports the use of exercise in the context of cancer-related cognitive dysfunction, we conducted an integrative review of the literature. The purpose of this integrative review is to summarize and critique the available quantitative clinical research evidence related to the use of exercise as a potential intervention for decreased cognitive function from cancer and cancer treatment. In addition, we briefly describe study results from interventional research to gain insight into reduction in inflammation as a potential mechanism underlying the effects of exercise on cognitive function.

■ Methods

An integrative review was conducted for this project because it is the only approach that allows diverse study methodologies to be synthesized, specifically a combination of experimental and nonexperimental studies.[18–20] The integrative review approach was selected because of the preliminary nature of the research in this area, consisting of experimental, quasi-experimental, and nonexperimental study designs, and the need to comprehensively capture and synthesize the work to date related to all types of exercise as potential intervention for cancer-related cognitive impairment. The wide variety of study designs and limited number of studies available for each form of exercise under investigation necessitated the establishment of very broad inclusion criteria, so as to facilitate determining the state of the knowledge in as much depth as possible. We conducted this integrative review using the scientific guidelines developed by Cooper[18,19] and refined by Whittemore and Knafl.[20] The process for conducting an integrative review includes problem identification, literature search, data evaluation, data analysis, and presentation.[20] Exercise was defined as any form of repetitive, structured, and intentional physical activity, including physical activity that was mindfulness based.[21,22] Physical activity was defined as any bodily movement produced by the contraction of skeletal muscle that increases energy above a basal level.[23,24]

Eligibility Criteria

Research considered eligible for inclusion met the following criteria: (1) full articles published prior to February 2016; (2) quantitative studies including experimental, quasi-experimental, and nonexperimental study designs, (3) primary or secondary cognitive outcomes reported; (4) cognitive outcomes assessed with objective or subjective measures; (5) adult cancer survivor population (>18 years of age); (6) exercise or physical activity self-reported, observed, prescribed (in terms of number/duration of sessions and/or home practice), device monitored, or supervised; and (7) exercise or physical activity consisted of aerobic, resistance, or mindfulness-based exercise, as well as combined modality interventions. Studies were excluded if not published in the English language.

Search Strategies

Two independent reviewers conducted literature searches in electronic medical databases including PubMed, CINAHL, and PsycINFO for research published through January 2016. The following search terms were systematically combined (see Table 1 for all permutations): *cancer*, *physical activity*, *exercise*, *aerobic exercise*, *resistance exercise*, *cognition*, *cognitive function*, *mindfulness*, *meditation*, *mindfulness-based exercise*, *qigong*, *yoga*, and *tai chi*. In addition, the National Comprehensive Cancer Network guidelines and reference lists from pertinent articles retrieved during the electronic database search were hand searched. The results of the independent literature reviews were examined for duplication, and the reviewers reached consensus on the documents meeting inclusion criteria for the integrative review.

Data Extraction and Analyses

Each article was reviewed and critiqued by both reviewers. Data related to study purpose, design, sample, intervention, measures, and results were extracted and summarized in Table 2. Data extraction for measures and results was restricted to cognitive outcomes and some potential mechanisms including biomarkers of inflammation. We did not extract data related to fitness measures unless these data specifically were investigated as predictors of cognitive function. We organized the evidence by type of exercise, that is, aerobic, resistance training, aerobic/resistance combination, and aerobic/other combination in which exercise was investigated as a component of a rehabilitation program or in conjunction with a neurostimulant. Mindfulness-based exercise was subdivided further into yoga, tai chi, and qigong. Two publications for different outcomes/time points of the same study are grouped into the same row in Table 2. Effect sizes (ESs) for cognitive outcomes were calculated where possible using the online calculator available from The Campbell Collaboration (David B. Wilson, PhD, George Washington University, http://campbellcollaboration.org/escalc/html/EffectSizeCalculator-Home.php). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) ranking system was used to evaluate the quality of evidence for study outcomes.[52] The GRADE levels of quality (high, moderate, low, very low) were adjusted (eg, upgraded or downgraded by 1 level) based on risk of bias related to sample size, cognitive function as a primary end point, specificity of instrumentation related to cognitive outcomes, and the inclusion of both objective and subjective measurements of cognitive function. The results of the data extraction were synthesized by both reviewers.

Results

The literature search yielded 363 citations. After removing duplicates (131 duplicates) and excluding citations not meeting eligibility criteria (205 citations), 26 full-text citations were included for the integrative review. The results of the literature

Table 1 • Search Term Permutations

Cancer	AND	Cognitive function	AND	Exercise		
				Physical activity		
				Mindfulness-based exercise		
				Mindfulness		
				Yoga		
				Tai chi		
				Qigong		
				Meditation	AND	Exercise
						Physical activity
Cancer	**AND**	**Cognition**	**AND**	**Exercise**		
				Physical activity		
				Mindfulness-based exercise		
				Mindfulness		
				Yoga		
				Tai chi		
				Qigong		
				Meditation	AND	Exercise
						Physical activity

Table 2 • Integrative Review Evidence

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Aerobic exercise studies							
Sprod et al[25] (2012)	Describe the prevalence of exercise during and after cancer treatment for older adults and to investigate relationships between exercise, symptoms, and self-rated health	Secondary analysis of prospective, observational study Assessment: baseline prior to chemo or XRT, 2 wk and 6 mo after Tx completion	N = 408 older adults (aged 65–92 y) with breast or genitourinary cancers during and following XRT and/or chemo	N/A	<u>Subjective CF (2°)</u> Memory loss and difficulty concentrating: 12-item URCC Symptom Inventory Self-reported exercise (single item)	Aged ≥80 y who exercised during Tx reported less memory loss ($P = .05$) and difficulty concentrating ($P = .01$). Those who exercised after Tx reported less memory loss ($P = .08$)	L
Knobf et al[26] (2013)	Evaluate the effect of a community-based exercise intervention on symptoms and QOL for breast cancer survivors	Prospective, quasi-experimental Assessment preintervention and 16 and 24 wk postintervention	N = 26 women with stage I or II breast cancer who were ≤36 out from completion of adjuvant chemo and either perimenopausal or postmenopausal at time of enrollment	Supervised exercise program delivered 3 times a week for 4-6 mo. Involved treadmill walking using a weight belt and heart rate monitor watch	<u>Subjective CF (2°)</u> Forgetfulness and concentration: BCPT Cognitive problems	Adherence: 88.2% mean attendance at all sessions over 24 wk. No significant cognitive improvements	L
Crowgey et al[27] (2014)	Test the hypothesis of a beneficial relationship between exercise behavior, cardiorespiratory fitness, and cognitive function in early breast cancer patients (ER^+, $HER2^-$) who received doxorubicin-based chemotherapy regimens	Cross-sectional, observational pilot	n = 37 breast cancer survivors (ER^+, $HER2^-$, stage I-III) previously treated with doxorubicin-containing chemo (≥6 mo postcompletion of chemo) n = 14 age-matched controls	N/A	<u>Objective CF (1°)</u> CNS Vital Signs software: psychomotor speed, reaction time, attention, cognitive flexibility, processing speed, executive function, verbal/visual/composite memory Godin Leisure Time Exercise Questionnaire LSI: Self-report of exercise frequency, duration, and intensity Cardiorespiratory fitness measured by 12-lead electrocardiogram and peak oxygen consumption (Vo_{2peak})	Survivors: Weak correlations between exercise behavior, Vo_{2peak}, and cognitive function Correlation between exercise behavior and visual memory ($r = 0.47$, $P = .004$)	L

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Myers et al[28] (2015)	Explore potential factors associated with PCI in breast cancer survivors	Cross-sectional, observational	N = 363 n = 317 women with breast cancer n = 46 controls	N/A	Self-report: Exercise type, frequency, and duration Ht/wt (BMI calculated) Subjective CF (1°) FACT-COG • PCI	Exercise frequency was associated with PCI for women exposed to chemo ($F_{3,135}$ = 3.78, P < .02) Exercise frequency moderated the relationship between BMI and PCI for women with breast cancer ($F_{3,198}$ = 2.4, P = .07). The moderation achieved significance for the women who received chemo ($F_{3,133}$ = 3.1, P = .02)	L
Resistance exercise studies							
Baumann et al[29] (2011)	Investigate the effect of a 12-wk resistance training program on the cognitive abilities of breast cancer survivors after chemo	Nonrandomized prospective intervention trial Assessment: survivors at preintervention and postintervention Controls only assessed at second time point	N = 17 n = 9 breast cancer survivors (stage I-III, receiving neoadjuvant chemotherapy) n = 8 controls	60 min of supervised resistance training twice a week for 12 wk	Objective CF (1°) MEMO–test-memory WIT–working memory d2–focused attention and concentration	Intervention group: pre and post d2 tests were lower than controls' posttest (pre: P = .040, post: P = .019) Improvement of error rates on d2 test (P = .017) Slight improvement in short-term verbal memory (P = .163) compared with controls (P = .048) Improved WIT scores (P = .049	L
Steindorf et al[30] (2014)	Investigate whether resistance exercise during XRT provides benefits on fatigue and QOL beyond potential psychosocial effects of group-based interventions	RCT Assessment: preintervention and postintervention (week 13)	N = 155 women with stage 0-III breast cancer scheduled for XRT n = 77 exercise n = 28 relaxation control	Supervised 12-wk resistance exercise program (60-min sessions twice weekly)	Subjective CF (2°) Fatigue assessment Questionnaire–cognitive fatigue Objective CF (2°) TMT–cognitive function	Adherence: 79% mean no. of sessions attended over 12 wk No improvement for the cognitive fatigue (P = .65, ES (d) = 0.07[b]) or cognitive function (P = .13)	M

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Schmidt et al[31] (2015)	Investigate whether resistance exercise during chemo provides benefits on fatigue and QOL beyond potential psychosocial effects of group-based interventions	RCT Assessment: preintervention and postintervention (week 13)	N = 100 women with breast cancer beginning chemotherapy n = 49 exercise n = 46 relaxation control	Supervised 12-wk resistance exercise program (60-min sessions twice weekly)	Subjective CF (2°) Fatigue assessment Questionnaire–cognitive fatigue Objective CF (2°) TMT–cognitive function (concentration, cognitive flexibility)	Adherence: 79% mean no. of sessions attended over 12 wk Resistance exercise group demonstrated less fatigue ($P = .038$) and improvement on the cognitive measure ($P = .20$)	M
Aerobic/resistance exercise combination studies							
Hsieh et al[32] (2008)	Investigate the effects of supervised exercise training on cardiopulmonary function and fatigue in breast cancer survivors after completion of treatment	Prospective, quasi-experimental Assessment: baseline and after the 6-mo intervention	N = 96 breast cancer survivors referred for rehabilitation immediately after completing Tx n = 22 Sx n = 30 Sx/chemo n = 17 Sx/XRT n = 27 Sx/chemo/XRT	Individualized, supervised 60-min exercise sessions including aerobics and resistance training/ stretching	Subjective CF (2°) Revised Piper Fatigue Scale cognitive and mood fatigue subscale	Reduction in cognitive and mood fatigue ($P < .05$) for participants who received surgery in combination with other therapy. No change seen for the group receiving surgery alone	L
Schneider et al[33] (2007)	The authors also explored the impact of the intervention on the participants grouped by whether they received the intervention during (DTm) or after (FTm) treatment	Prospective, quasi-experimental Assessment: baseline and after the 6-mo intervention	N = 113 breast cancer survivors n = 96 FTm (see above study) n = 17 DTm	Same as above	Same as above	Reduction in cognitive/ mood fatigue was seen for participants receiving the intervention after completion of therapy (FTm) ($P < .05$)	L
Schneider et al[34] (2007)	Determine the cardiopulmonary function and fatigue alterations in male cancer survivors during (DTm) and after (FTm) treatment from individualized, prescriptive exercise interventions	Prospective, quasi-experimental Assessment: baseline and after the 6-mo intervention	N = 45 males (primarily prostate, colon, and lung) n = 37 FTm n = 8 DTm	Individualized, supervised 60-min exercise sessions including aerobics and resistance training/ stretching	Subjective CF (2°) Piper Fatigue Scale cognitive and mood fatigue subscale	The FTm group experienced reductions in cognitive/ mood fatigue ($P < .05$). No difference was seen in the DTm group	L
Galvao et al[35] (2010)	Examine the impact of a combined resistance and aerobic exercise program for androgen suppression therapy (AST) toxicities	RCT Assessment: baseline (at least 2 mo on AST) and after 12-wk intervention	N = 57 men with prostate cancer receiving AST n = 29 exercise n = 28 control	Resistance exercises and Aerobic exercises sessions held twice a week for 12 wk	Subjective CF (2°) EORTC QLQ-C30–cognitive function CRP levels–inflammation	Improvement for CF in the intervention group ($P = .007$) CRP decreased in intervention group ($P = .008$)	M

(continues)

Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Oechsle et al[36] (2014)	Evaluate the effects of multimodal aerobic and strength exercises on physical performance for hospitalized cancer patients receiving myeloablative chemotherapy	Secondary analysis of RCT pilot Assessment: baseline and end of hospitalization	N = 48 n = 24 exercise n = 24 control AML-18 NHL-9 MM-9 Germ cell-12	Supervised exercise program of warm-up, bicycle ergometer endurance training, and resistance exercises 5 times per week during hospitalization	Subjective CF (2°) EORTC QLQ-C30 MFIS–cognitive fatigue	No change in self-report of CF per EORTC. Cognitive fatigue more pronounced following chemo for control group ($P = .02$)	L
Marinac et al[37] (2015)	Explore the relationship between objectively measured PA and cognitive function for breast cancer survivors with a broad range of BMIs	Cross-sectional, observational	N = 136 PMP women with stage I-III breast cancer within 5 y of diagnosis and not currently receiving chemo n = 96 overweight/obese n = 40 lean	N/A	Objective CF (1°) Neurotrax Comprehensive Testing Suite: Staged information processing speed, verbal and nonverbal memory, Stroop Interference, Go–No-Go Response Inhibition, and Catch Game (executive function) PA assessed for 7 d by accelerometer	MVPA was positively associated with processing speed ($r = 0.20$, $P = .02$). A positive interaction was found between BMI and MVPA with processing speed ($P < .1$)	M
Leach et al[38] (2015)	Evaluate the effectiveness, safety, and satisfaction with a community exercise program for breast cancer survivors receiving or within 3 mo of completing chemo or XRT	Prospective, quasi-experimental Assessment: preintervention and at 12 wk	N = 80 breast cancer survivors receiving or within 3 mo of completing chemo or XRT	12-wk resistance, aerobic, and flexibility exercise program	Subjective CF (1°) FACT-COG • PCI • PCA	Adherence: 24.4% attended weekly sessions over 12 wk Cognitive function maintained from preintervention to 12-wk assessment	M
Aerobic exercise/other combination studies							
Schwartz et al[39] (2002)	Investigate the effect of exercise and methylphenidate on fatigue, functional ability, and cognitive function in patients with melanoma	Prospective, observational pilot Assessment: preintervention and 1 and 4 mo	N = 12 adults status postsurgery for melanoma resection and interferon naive. Two participants had history of regular exercise prior to the study	Methylphenidate 20 mg oral sustained release formulation daily in combination with a 4-mo aerobic exercise program (15–30 min/d, 4 d a week) prior to first interferon dose	12-min walk (functional ability) Objective CF (1°) TMT-A and TMT-B–general cognitive function	Adherence: 100% to exercise. 66% to methylphenidate past the first week TMT-B scores declined for "exercise only" group. An inverse correlation was seen with the 12-min walk and scores on both TMT-A ($r = -0.064$, $P = .04$) and TMT-B ($r = -0.67$, $P = .05$) suggesting a possible relationship between exercise and improvements in CF	L

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Korstjens et al[40] (2006)	Investigation of a 12-wk rehabilitation group on QOL for cancer survivors	Prospective, quasi-experimental Assessment: preintervention, week 6 (T1), and week 12 (T2)	N = 658 adults diagnosed with any type of cancer who completed Tx at least 2 mo prior to consent and who reported issues with physical or psychosocial functioning Sample included primarily breast (50%), blood/lymphoma (11.4%) patients who received surgery (83.3%) combined with chemo and/or XRT (68.9%)	Physical training—supervised small-group sessions held twice a week; 60 min devoted to bicycle ergometers alternating with fitness apparatus and group sports/games; 30 min devoted to indoor aqua aerobics Seven 2-h psychoeducation sessions	Subjective CF (2°) EORTC QLQ-C30 CF scale	Improvement in the CF scale was reported at T2 ($P < .01$)	M
Rogers et al[41] (2009)	Determine feasibility and preliminary effectiveness of a 12-wk PA behavior change intervention for breast cancer survivors receiving antiestrogen therapy	RCT feasibility pilot Assessment preintervention and postintervention	N = 41 sedentary women receiving estrogen modulators or aromatase inhibitors for stages I, II, IIIA breast cancer n = 21 exercise n = 20 control	Individualized 12-wk PA behavior change intervention (BEAT [Better Adherence after Treatment for Cancer]) including 12 individual supervised exercise sessions	PA—7-day monitoring with accelerometer Body composition and anthropometrics (BMI, waist/hip circumference, percent body fat) Subjective CF (2°) FACT-COG	Adherence: 100% to individual exercise sessions. 99% to all intervention sessions The intervention group did demonstrate increases in total PA ($P = .004$) and decline in waist/hip ratio ($P = .02$). No change was noted for BMI or percent body fat No change in self-reported CF ($P = .22$, ES[b] (d) = −0.41)	M
Miki et al[42] (2014)	Investigate the feasibility and efficacy of speed-feedback therapy with a bicycle ergometer on cognitive function in elderly cancer survivors	RCT Assessment: preintervention and 4 wk	N = 78 adults ≥65 y of age diagnosed with breast or prostate cancer n = 38 exercise n = 40 control	Physical exercise task involving sustained attention: 5 min of bicycle ergometer pedaling to match computerized continuously varying target speed, weekly for 4 wk	Objective CF (1°) Frontal Assessment Battery Conceptualization, mental flexibility, programing, sensitivity to interference, inhibitory control, and environmental autonomy	Improvement in objective CF at 4 wk for the intervention group ($P = .003$, ES[c] (d) = 0.69). Younger age associated with improved CF ($P = .018$)	M

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Mindfulness-based exercise studies							
Yoga							
Culos-Reed et al[43] (2006)	Examine the physical and psychological benefits from a 7-wk yoga program for cancer survivors	RCT Assessment: preintervention and postintervention	N = 38 adults a minimum of 3 mo posttreatment (95% women, 85% breast cancer) n = 20 exercise n = 20 control	7 wk of 75-min yoga sessions	Subjective CF (2°) POMS confusion-bewilderment dimension. SOSI cognitive disorganization subscale EORTC QLQ-C30 cognitive function items	Intervention group demonstrated trend toward improved confusion ($F = 3.29$, $P < .10$) and cognitive disorientation ($F = 3.27$, $P < .10$) No change in CF	M
Vadiraja et al[44] (2009)	Compare the effects of an integrated yoga program with brief supportive care for breast cancer survivors receiving adjuvant radiation therapy	RCT Assessment: preintervention and postintervention	N = 88 (aged 30–70 y, stage I-III disease, Zubrod score of 0–2, minimum of high school education) n = 44 exercise n = 44 control	Attendance at three 60-min in-person yoga sessions/wk for 6 wk and home practice on nontreatment days Brief supportive care: 15-min counseling by trained social worker 3–4 times over 6-wk study period	Subjective CF (2°) EORTC QLQ-C30 cognitive subscale	Adherence: 56.7% attended majority of sessions over 6 wk Improvement in CF for the yoga group (9.8 ± 4.35, $P = .03$, ES[b] (d) = 0.48)	M
Galantino et al[45] (2012)	Investigate effects of yoga on cognitive function for women with early stage breast cancer	Case series: Recruited prior to initiation of chemo and followed for 6 mo Assessment: prechemo and 1 and 3 mo following completion of chemo	N = 4 stage II breast cancer survivors prior to receiving chemo	Iyengar-inspired, 70-min, twice-weekly small-group yoga sessions over 6 wk Followed by 6 wk of abbreviated home-based yoga (15 min 3 times a week)	Subjective CF (1°) PCQ–self-report of CF Objective CF (1°) CogState (computerized measure of cognition)—attention, memory, executive function, language, social-emotional cognition	Trends noted for improvement of speed, accuracy, and error reduction on CF assessments No appreciable change in participants' perceptions of cognitive abilities	VL

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Derry et al[46] (2015)	Compare impact of 12 wk of Hatha yoga classes to wait-list control on self-report of cognitive problems	Secondary analysis of RCT Assessment: baseline, immediately postintervention and at 3 mo	N = 200 breast cancer survivors within 2 mo to 3 y of completing all treatment except antiestrogen therapy n = 100 exercise n = 100 wait list control	90-min small-group yoga sessions twice a week for 12 wk	Subjective CF (1°) BCPT Cognitive problems scale (forgetfulness, difficulty concentrating, and ease of distraction) Markers of inflammation: LPS-stimulated production of IL-6, IL-1B, TNF-α	Adherence: 75.4% attended majority of sessions over 12 wk 23% less cognitive problems for yoga group than controls at the 3-mo assessment ($P = .003$) Frequency of yoga practice was associated with less cognitive problems at 3 mo ($P < .001$). High yoga practice frequency associated with cognitive improvement between 1- and 3-mo assessments ($P = .011$) Markers of inflammation did not predict cognitive complaints	M
Komatsu et al[47] (2016)	Test the feasibility of a self-directed home yoga program for breast cancer survivors receiving chemo	Prospective, quasi-experimental Assessment: preintervention and postintervention	N = 18 breast cancer survivors receiving chemo	4-wk yoga program included 30-min orientation and a 90-min group class followed by participant's choice of three 15-min home-yoga courses (low- or high-intensity options)	Subjective CF (1°) Japanese version of CFQ CFS cognitive fatigue subscale	Adherence: 94.4% reported home practice >2 times/wk over 4 wk Improvement for cognitive fatigue ($P = .01$) No change demonstrated for CF ($P = .21$)	L
Janelsins et al[48] (2016)	Assess the effects of the YOCAS yoga program on memory and identify relationships between memory and sleep for cancer survivors	Secondary analysis of an RCT Assessment: preintervention and postintervention	N = 328 cancer survivors between 2 and 24 mo from completion of surgery, chemo, and/or XRT and with persistent sleep disturbance n = 168 exercise n = 160 control	YOCAS program: eight 75-min group sessions twice a week at community based sites)	Subjective CF (1°) MDASI–memory item Pittsburgh Sleep Quality Index	Reduction in memory difficulty for intervention group (mean change = −0.60, $P < .05$, ES[b] (d) = −0.24). Baseline sleep quality moderated effects of postintervention memory difficulty ($P < .05$). Changes in sleep quality mediated reduction in memory difficulty in the intervention group ($P < .05$)	M

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Table 2 • Integrative Review Evidence, Continued

Reference	Study Purpose	Study Design	Sample Size	Intervention	Measures	Results	Q[a]
Tai chi							
Reid-Arndt et al[49] (2012)	Investigate the effects of a 10-wk tai chi program on the neuropsychological, psychological, and physical health of female cancer survivors	Prospective, quasi-experimental Assessment: preintervention and within 1 mo following completion of the intervention	N = 23 women a minimum of 12 mo after completion of cancer treatment Sample included breast (n = 16), ovarian (n = 3), endometrial (n = 1), NHL (n = 2), and CLL (n = 1); 100% had received chemo, 65.2% surgery, and/or 60.9% XRT. Less than half received antiestrogen therapy (47.8%)	Modified classic yang style tai chi (Tai Chi Fundamentals): twice-weekly 60-min sessions	Objective CF (1°) RAVLT (memory) TMT-B, Stroop Test (executive function) COWA (language) WAIS-III Digit Span and Digit Symbol, TMTA (attention) Subjective CF (1°) MASQ–verbal and visual subscales	Improvement noted for all neuropsychological test scores ($P<.05$), 2 MASQ subscales for verbal ($P=.01$) and visual ($P<.05$) memory	M
Qigong							
Oh et al[50] (2012)	Compare the effect of a 10-wk medical qigong intervention to standard of care on cognitive function for cancer patients	RCT Assessment: preintervention and postintervention	89 Participants enrolled in a parent trial to investigate qigong impact on QOL, fatigue, mood, and inflammation n = 37 exercise n = 44 control Breast (n = 25), colorectal (n-19), other (n = 45) Receiving (or completed) chemo; qigong naive, with >12-mo survival expectancy 54 completed the study: intervention group (n = 23), standard of care (n = 31)	Attendance of at least one of two 90-min supervised qigong sessions weekly and at least 30 min a week of home practice	Subjective CF (1°) EORTC QLQ–cognitive function version 3 FACT-COG version 3 PCI, PCA, QOL subscales Serum levels of CRP	Adherence: 70% attended majority of sessions over 10 wk The qigong group demonstrated improvements in self-reported CF on the EORTC ($P<.05$, ES[c] (d) = 0.6968) and FACT-COG ($P<.05$, ES[c] (d) = 0.6203) ($P<.001$) after adjustment for age, gender, diagnosis, treatment status, and baseline data. Lower levels of CRP also were noted ($P=.042$). No association was noted between CRP levels preintervention and postintervention with self-reported CF	M

Abbreviations: 1°, primary outcome; 2°, secondary outcome; BCPT, Breast Cancer Prevention Trial Symptom Index; BMI, body mass index; CFQ, Cognitive Failures Questionnaire; CFS, Cognitive Fatigue Scale; chemo, chemotherapy; CI, cognitive impairment; CLL, Chronic Lymphocytic Leukemia; CNS, central nervous system; COWA, Controlled Oral Word Association; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; CRP, C-reactive protein; ER, estrogen receptor; ES, effect size; FACT-COG, Functional Assessment of Cancer Therapy–Cognition; HER, human epidermal growth factor receptor; Ht, height; IES-R, Impact of Event Scale–Revised; IL, interleukin; LPS, lipopolysaccharide; LOE, level of evidence; LSI, leisure score index; MASQ, Multiple Abilities Self-report Questionnaire; MDASI, MD Anderson Symptom Inventory; MFIS, Modified Fatigue Impact Scale; MVPA, moderate to vigorous physical activity; NHL, Non Hodgkin Lymphoma; PA, physical activity; PANAS, Positive and Negative Affect Schedule; PCA, perceived cognitive abilities; PCI, perceived cognitive impairment; PCQ, Perceived Cognition Questionnaire; PMP, post menopausal; POMS SF, Profile of Mood States–Short Form; QOL, quality of life; RAVLT, Rey's Auditory Verbal Learning Test; RCT, randomized controlled trial; SOSI, Symptoms of Stress Inventory; TMT, Trail-Making Test; TNF-α, tumor necrosis factor α; Tx, treatment; URCC, University of Rochester Cancer Center; WAIS, Wechsler Adult Intelligence Scale; WIT, Wilde Intelligence Test; wt, weight; XRT, radiation therapy; YOCAS, Yoga for Cancer Survivors.

[a]Quality of evidence based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) ranking system. The GRADE system offers 4 levels of evidence: high (H), moderate (M), low (L), and very low (VL).[51]

[b]Effect size published for study.

[c]Effect size calculated for this review.

search are depicted in a Preferred Reporting Items for Systematic Reviews and Meta-analyses diagram (Figure).[51]

Study Characteristics

Results from the data extraction are summarized in Table 2. Study designs included 11 randomized controlled trials (RCTs),[30,31,35,36,41–44,46,48,50,53] 11 quasi-experimental trials,[26,27,29,32–34,37,38,40,47,49] 3 observational studies,[25,28,39] and 1 case series.[45] Twelve of the studies were designed to measure cognitive function as a primary end point.[27–29,37–39,42,45–48,50,54] Nine studies included objective measures of cognitive function,[27,29–31,37,39,42,45,49] 21 studies included subjective measures of cognitive function,[25,26,28,30–36,38,40–49,54,55] and 4 studies included both objective and subjective cognitive function measures.[30,31,45,49] Sample sizes ranged from as few as 4 (for the case series) to 658. Ten studies involved patient populations other than breast cancer survivors.[25,34–36,39,40,42,48,49,56]

The majority of the exercise intervention research published to date (n = 19) has involved aerobic exercise (n = 4),[25–28] resistance training (n = 3),[29–31] and a combination of both aerobic exercise and resistance training (n = 11)[32–36,38] with or without other intervention components such as cognitive rehabilitation training (n = 2),[40,41] sustained attention task (n = 1),[42] or neurostimulants (n = 1).[39] Less research has been conducted in the arena of mindfulness-based exercise (n = 8). Most of the mindfulness-based exercise studies have involved the investigation of yoga (n = 6)[43–48] as compared with tai chi (n = 1)[49] and qigong (n = 1).[56] Significant variation was noted for the specific instruments used and the cognitive domains assessed across studies.

The majority of the studies involving either aerobic or resistance training exercise or both (15 of 19) were associated with improved cognitive function[25,27–29,31,35,37,38,40,42,54] or demonstrated mixed results[32–34,36] in which cognitive function outcomes for some domains were improved and cognitive function for other domains were not. All of the 8 mindfulness-based exercise studies were associated with some improved cognitive function outcomes, although 2 demonstrated mixed results.[43,47]

Twelve of the studies were designed to investigate cognitive function as a primary outcome. Of these, 11 demonstrated some significant positive results for cognitive function with exercise.[27–29,37–39,42,46–48,50] One insufficiently powered study, involving a series of only 4 case studies, showed trends for positive outcomes in objective measures of cognitive function without appreciable change in subjective measures.[45] Six of the studies were designed to measure objective cognitive function across multiple cognitive domains.[27,29,37,42,45,49] Of the 12 studies with significant findings, 6 included objective cognitive

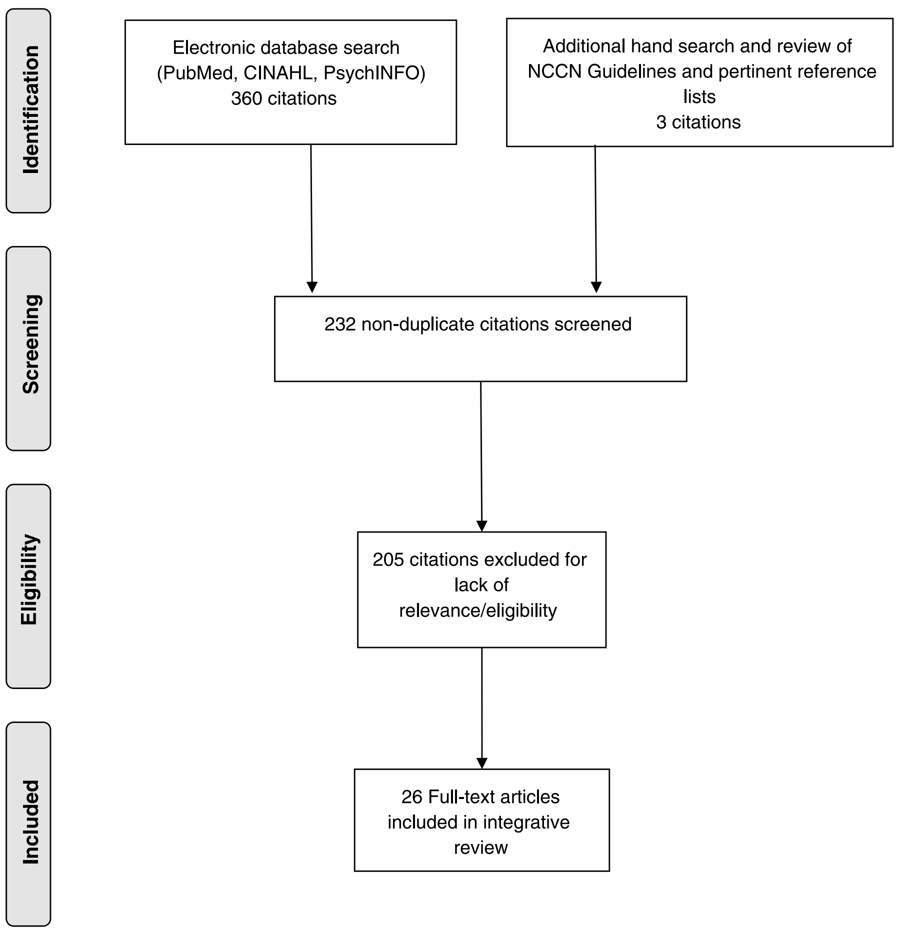

Figure ■ Preferred Reporting Items for Systematic Reviews and Meta-analyses diagram of systematic search.

measures,[27,29,31,37,39,42,49] and 6 included subjective cognitive measures.[28,48–50,54]

Levels of Evidence

Significant variability in the levels of evidence was noted across studies. Three of the 11 RCTs were reports of secondary analyses of existing data,[36,46,48] and 2 were small pilot studies.[36,41] Only 5 of the RCTs were designed to investigate cognitive function as a primary outcome.[42,46,50,53] Of these, only 3 included objective measures of cognitive function,[46,50,53] Only 8 of the 15 non-RCT studies were designed with cognitive function measures as primary outcomes,[27–29,37–39,45,47] 6 of which included objective measures.[27,29,37,39,45,49] Based on the GRADE system, none of the studies met criteria for a high ranking of quality of evidence. Fourteen studies were ranked as moderate, including 2 resistance exercise studies,[30,31] 6 of the aerobic/resistance/other combination studies,[35,37,38,40,42,57] and 6 of the mindfulness-based exercise studies.[43,44,46,48,49,55] The rest of the studies were ranked low[25–29,32–34,36,39,47] or very low for the case series.[45]

Randomized Controlled Trials

Restricting the examination of the evidence to the 11 RCTs, we found that results from 7 studies indicated improved cognitive function with some form of exercise. The significant positive outcomes on cognitive function were noted for resistance exercise (n = 1),[31] aerobic/resistance exercise combination (n = 1),[35] aerobic exercise/other combination (n = 1),[42] and mindfulness-based exercise (n = 4).[44,46,48,50] Two of these studies were designed to investigate objectively measured cognitive function. Resistance exercise was associated with improvement in the domains of concentration and cognitive flexibility.[31] Speed feedback therapy (aerobic exercise/other combination involving sustained attention) was associated with improvements in cognitive flexibility and inhibitory control, 2 domains important to executive function.[42] One study trended toward positive subjective cognitive outcomes (mindfulness-based exercise),[43] and another study demonstrated mixed results (aerobic/resistance exercise combination) for 2 measures of subjective cognitive function.[36] Two of the studies' results were not significant for changes in cognitive outcomes. These included resistance exercise (n = 1)[30] and aerobic exercise/other combination (12-week physical activity behavior change intervention) (n = 1).[41]

Effect sizes (as Cohen *d*) were published for 4 of the 11 RCTs included in this review.[30,41,44,48] We calculated the ES (Cohen *d*) for 2 additional RCTs based on available data.[42,50] Effect sizes ranged from 0.0700 to 0.6968 and are reported in Table 2. A medium ES ($d = 0.6203$-0.6969) was demonstrated for 89 women with breast cancer participating in an RCT to evaluate the effect of a 10-week medical qigong intervention. In this study, subjective measures of cognitive function were primary study outcomes.[50] A medium ES also was demonstrated for the use of speed feedback therapy (described above) ($d = 0.69$).[42] The remaining ESs were small, $d < 0.05$.

Non–Randomized Controlled Trials

Three of the non-RCT studies involved self-reported exercise,[25,27,28] and 1 study used accelerometer measurement of 7 days of usual activity.[37] The remaining 4 studies involved observation of nonrandomized prescribed study-specific exercise interventions. All but 1 of the 15 non-RCT studies[26] reported a positive association between exercise and subjective measures of cognitive function. Results of 2 cross-sectional observational studies suggested a relationship between higher body mass index (BMI) and reports of decreased cognitive function.[28,37] Myers et al[28] found that higher frequency of aerobic exercise was associated with decreased negative impact of higher BMI on self-reported cognitive function for women with breast cancer exposed to chemotherapy. Marinac et al[37] found a significant positive interaction between BMI and moderate to vigorous physical activity on measures of processing speed for women with breast cancer within 5 years of diagnosis (not currently receiving chemotherapy). Leach et al[38] conducted a quasi-experimental study to evaluate an aerobics/resistance combination exercise program delivered during and within 3 months of completing chemotherapy or radiation therapy and found no significant decline in subjective cognitive function between baseline and the postintervention assessment (at 12 weeks). The perceived cognitive impairment subscale of the Functional Assessment of Cancer Therapy–Cognition did drop by 2.4 points. The authors reported this as an improvement; however, lower perceived cognitive impairment scores actually indicate worse perceived cognitive function per the instrument scoring guidelines.[58] Improvement in visual memory was demonstrated with aerobic exercise.[27] Resistance exercise was associated with improvements in working memory, attention, and concentration.[29] Mindfulness-based exercise (specifically tai chi) was associated with improvements in memory, attention, verbal fluency, and executive function.[49]

Prescribed Exercise

The studies with prescribed study-specific exercise interventions (22 of 26) also varied by the types of cancer treatment, timing of initiation of the intervention, frequency, and duration of the intervention. Nine of the studies[26,32,40,42,43,45,46,48,49] were designed to investigate cognitive outcomes for patients who had completed surgery, chemotherapy, and/or radiation therapy. Results from all but 1 of these studies demonstrated positive cognitive outcomes.[26] Four studies were designed to evaluate exercise interventions during and after cancer therapy.[33,34,38,50] Results from 2 of these studies conducted for breast or prostate cancer survivors indicated positive cognitive outcomes after, but not during, cancer treatment.[33,34] Mixed results were demonstrated for cognitive outcomes for studies designed to evaluate cognitive function during radiation (n = 2),[30,44] chemotherapy (n = 4),[29,31,36,47] or antihormonal therapy (n = 2).[35,41] Only 1 small study was conducted to evaluate cognitive outcomes for patients with melanoma receiving immunotherapy with interferon, and this study showed no significant associations between exercise and cognitive function.[39] Adherence rates were reported for 10 of the studies and ranged from 24.4% to 100%.

The frequency of exercise was associated with cognitive outcomes in 1 mindfulness-based exercise study.[46] Women with higher yoga practice frequency (75th percentile, 29 min/d) reported less problems with cognitive function from immediately following the intervention to the 3-month follow-up ($M = 0.97$; $t_{175} = -2.58$; $P = .011$).

The duration of prescribed study-specific exercise interventions ranged from 4 weeks to 6 months, with weekly frequencies ranging from twice to 5 times per week. Only 1 study addressed the intensity of exercise.[37] Marinac et al[37] reported that moderate to vigorous physical activity was positively associated with processing speed performance compared with light physical activity or sedentary lifestyle (as measured by metabolic equivalents per day for aerobic/resistance combination exercise intervention).

Inflammation

Randomized controlled trials designed to investigate biomarkers of inflammation in conjunction with cognitive function yielded mixed results. C-reactive protein levels were measured in 2 studies.[35,50] C-reactive protein levels decreased for men with prostate cancer participating in a combined resistance and aerobic exercise program[35] but were not associated with preintervention or postintervention self-reported cognitive function for those survivors of breast, colorectal, and other cancers participating in a 10-week program of medical qigong.[50] Markers of inflammation (interleukin 6, interleukin 1B, tumor necrosis factor α) did not predict self-reported cognitive function for breast cancer survivors participating in a 12-week yoga program.[46] None of the studies investigating biomarkers included objective measures of cognitive function.

■ Discussion

We examined the existing evidence for the use of exercise as an intervention for cancer- and cancer treatment–related cognitive dysfunction. As noted previously, 11 RCTs have been published to date, and these did not consistently measure cognitive function as a primary outcome, nor did they consistently measure cognitive function in both a subjective and objective manner. Of all the studies reviewed, only 9 studies used objective measures of cognitive function. Experts in the field have argued that subjective cognitive function is the most clinically relevant measure and that self-report should be considered the primary outcome for research in this field.[59] However, objective measures of cognitive function are crucial to answering questions related to the efficacy of interventions for performance in specific cognitive domains. Ideally, study designs should include both measures as research is conducted to understand more about the mechanism of cancer- and cancer treatment–related cognitive impairment.

The studies varied widely with the selection of instruments and the cognitive domains measured. In many cases, cognitive outcomes were measured solely by subscales of instruments that were not designed with a cognitive focus and were composed of very few items (such as the 2 items addressing forgetfulness and concentration on the Breast Cancer Prevention Trial Symptom Index, the 2 items addressing concentration and memory of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, or the single memory item on the MD Anderson Symptom Inventory). Instruments such as the Functional Assessment of Cancer Therapy–Cognition and the Patient-Reported Outcomes Measurement Information System scales for applied cognition (cognitive concerns, cognitive abilities) have been validated in the cancer survivor population and specifically designed to assess cancer survivors' perceived cognitive impairment.[58,60]

The International Cognition and Cancer Task Force (ICCTF) has recommended a core set of instruments to be used prospectively to measure the specific cognitive domains typically affected by cancer and cancer therapy.[1] Only 6 of the studies reviewed were designed to measure multiple cognitive domains.[27,29,37,42,45,49] None of these studies addressed all of the domains specified by the ICCTF. Improvements were seen in the cognitive domains of working and visual memory, attention and concentration, cognitive flexibility and inhibitory control, and verbal fluency. The small numbers of studies conducted for each of the various types of exercise makes drawing conclusions about the type(s) of exercise that may have the most positive impact on a particular cognitive domain difficult.

Of the 26 studies reviewed, sample sizes ranged from as few as 4 (for the case series) to 658. Of the 11 RCTs, only 5 had sample sizes of 100 or more, and these varied for the types of exercise interventions studied. Effect sizes were published for only 4 of the RCTs, and appropriate data were available to calculate ES for only 2 additional studies. Medium ESs were noted for 2 of these studies, one involving mindfulness-based exercise (qigong) and the other a form of aerobic/combination exercise (speed feedback therapy). All other ESs were small. Additional comprehensive, longitudinal, randomized controlled studies are needed to ascertain the ESs of the various types of exercise on both subjective and objective cognitive function across multiple and standardized domains.

Very few studies addressed issues related to timing of initiating exercise interventions, duration of the intervention, intensity and frequency of exercise, or adherence and compliance. Given the fact that approximately 30% of cancer survivors demonstrate some cognitive impairment prior to the initiation of cancer therapy, early initiation of exercise intervention may be warranted.[1] Aerobic/resistance exercise may vary in intensity compared with the gentle exercise used in mindfulness-based exercise such as yoga and qigong. However, some preliminary evidence indicates that yoga meets the criteria for moderate-intensity physical activity.[61]

Both aerobic/resistance and mindfulness-based exercises have been shown to reduce markers of inflammation.[9] However, some evidence suggests that mindfulness-based exercise may affect cognitive function by different mechanisms than non–mindfulness-based exercises.[46] The mindfulness component may provide additional benefit via stress-reduction pathways in addition to the reduction of inflammatory markers and other neurotrophic pathway mechanisms associated with non–mindfulness-based exercise. Additional research is needed because of the limited evidence available from the studies conducted to date.

The majority of the studies addressed the issues of decreased cognitive function in the breast cancer population. Expanding the work to other types of malignancies and designing studies to answer the questions surrounding timing, duration, and frequency are needed to advance the state of the knowledge and provide the evidence necessary for practice change.

Limitations

Exploration of the use of exercise as an intervention for cancer- and cancer treatment–related decreases in cognitive function remains a nascent field of research. As such, we conducted this integrative review using very broad inclusion criteria in order to capture as much of the available evidence as possible relating to this area of inquiry. As a result, the literature selected for inclusion in the review varied widely in terms of levels of evidence, design limitations, and homogeneity of patient populations, cancer treatment regimens, types of exercise, primary end points, and instrumentation.

Although several studies examining the influence of exercise on cognitive function have been reported, the science in this area is limited primarily because of issues with study design and the limited number of studies conducted for each type of exercise. Thus, a great deal of work remains to be done to advance the state of the knowledge about the use of exercise as a potential intervention for cancer- and cancer treatment–related decreased cognitive function. However, despite variations in study design and low to moderate quality of evidence per the GRADE ranking system, most of the studies reviewed indicated that aerobic, resistance, and mindfulness-based exercises may be beneficial in mitigating the cognitive dysfunction experienced by cancer survivors.

Implications for Future Research

Additional RCTs are warranted to understand how various types of exercise influence cognitive function in the cancer survivor population and to better understand the mechanisms driving these effects. A multitude of questions remain unanswered. Does the type of exercise matter? Do the intensity, frequency, and duration of exercise make a difference in cognitive outcomes? What is the best timing for initiating an exercise intervention? Does the type of cancer treatment influence the efficacy of various types of exercise interventions? Which cognitive domains are most sensitive to exercise interventions? What role do patient preferences play in adherence to exercise interventions? Do certain patient characteristics drive exercise intervention preferences (such as gender, age, performance status)?

A direct comparison of aerobic and/or resistance training exercise to mindfulness-based exercise would be of benefit for determining differences in the mechanisms for these different types of activities. Trial designs that include both objective and subjective measures of cognitive function still are preferred, although some experts in the field have argued the case for self-report being the most clinically meaningful for this patient population.[62] The ICCTF recommends greater consistency in the selection of core objective cognitive measures in order to facilitate comparisons across studies.[1] In future studies, controlling for comorbidities such as hypermetabolic syndrome, obesity, diabetes, and cardiovascular disease will be important, as well as the assessment of markers of inflammation, neurotrophic factors, and cardiovascular fitness. Potential relationships with markers of inflammation should be explored for both subjective and objective cognitive function. Much of the work to date has involved breast cancer survivors. Expansion to survivors of malignancies beyond breast cancer also is needed. Given the significant impact that decreased cognitive function has on survivors' quality of life, continuing research is of key importance to determine the effectiveness of interventions, such as exercise, for improving cognitive function.

Conclusions

The methodological variability and the limited number of studies conducted for each type of exercise make it difficult to make confident conclusions about the efficacy of exercise for improving cognitive function in cancer survivors. However, given that 21 of the 26 studies reviewed demonstrated positive results and the improvements noted in the cognitive domains of working and visual memory, attention and concentration, cognitive flexibility and inhibitory control, and verbal fluency, we conclude that the evidence shows promising trends for the use of exercise as a potential intervention for improving cognitive function following cancer and cancer treatment and provides support for the conduct of additional research.

Implications for Oncology Nursing Practice

Oncology nurses are key to providing quality cancer care including, but not limited to, the identification and management of disease and treatment-related sequelae. Educating cancer survivors and their families about the current evidence for the use of exercise as a potential intervention for cancer- and cancer treatment–related decreased cognitive function is an important component of survivorship care. Oncology nurses also are well positioned to question patients about cognitive concerns, as well as to assess eligibility and inform cancer survivors about available studies investigating exercise as an intervention for this very troubling adverse effect. The evidence for exercise interventions continues to grow, but much work remains to be done to form clear recommendations. Oncology nurse researchers are encouraged to design and conduct studies to answer these important questions necessary to inform clinical practice.

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