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Systematic Review and Meta-Analysis

Gait and Balance Impairments in Breast Cancer Survivors: A Systematic Review and Meta-analysis of Observational Studies

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Breast neoplasms;
Mobility limitation;
Gait;
Postural balance;
Rehabilitation

Abstract
Objective: To systematically review and quantitatively synthesize gait and balance impairments in breast cancer survivors compared with age-matched controls or normative values for adults who never had breast cancer.
Data Sources: PubMed, Cumulative Index of Nursing and Allied Health, and Web of Science was searched using terms associated with *breast cancer*, *mobility*, and *adult* until November 2018.
Study Selection: Studies were included if they were randomized control trials, cross-sectional, prospective, pre-post, or case-control by design, included adult breast cancer survivors, reported gait and/or balance metrics as primary or secondary outcomes, were peer-reviewed publications, and were written in English. The search yielded 2117 results with 29 studies meeting the inclusion criteria.
Data Extraction: Two reviewers assessed study quality by the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies to determine the strength of evidence for each study that met the inclusion criteria. Basic descriptors of each study, study protocol, and balance and gait measures were extracted. Meta-analysis was performed for the single leg stance, functional reach, center of pressure velocity, gait speed, and timed up and go.
Data Synthesis: For quality assessment, 3 studies were rated good, 16 fair, and 10 poor. The meta-analysis indicated that there were no significant differences in single leg stance between breast cancer survivors and those who never had breast cancer ($P=.33$). Pooled values of the functional reach task (22.16cm; 95% CI, 8.98-35.33) and center of pressure velocity (1.2cm/s;

List of abbreviations: BCS, breast cancer survivor; BMI, body mass index; COP, center of pressure; RCT, randomized control trial; SOT, sensory organization test; TUG, timed Up and Go.
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95% CI, 0.87-1.55) suggest balance impairment in breast cancer survivors when compared with normative values. Breast cancer survivors also performed worse than those who never had breast cancer in challenging balance conditions that reduced sensory information or altered base of support. Pooled gait speed at a usual speed (0.91m/s; 95% CI, 0.2-1.6), fast speed across a short distance (1.2m/s; 95% CI, 0.31-2.1), and fast gait speed across a long distance (1.65m/s; 95% CI, 1.64-1.66) suggest gait impairments when compared with normative values. *Conclusions:* Breast cancer survivors may demonstrate gait and balance impairments compared with normative values. Clinicians should consider assessing changes in balance and gait in breast cancer survivors to improve functional independence and prevent fall-related injuries.

Breast cancer is the most commonly diagnosed cancer in women.[1] Approximately 1 in 9 women will be diagnosed as having breast cancer in the United States before the age of 85.[2] The current 5-year survival rate for breast cancer is 93%.[3] While breast cancer survivors (BCSs) have a high survival rate, they are still faced with acute and chronic adverse effects from cancer treatments. These adverse effects, such as fatigue, muscle weakness, and neuropathy, are associated with gait and balance impairments.[4] Neuropathy, for instance, affects up to 44% of BCSs at least 2 years post diagnosis and is associated with worse balance and greater risk of falls.[5,6] Gait and balance are fundamental for activities of daily living and maintaining functional independence,[7,8] and throughout clinical populations, impairments in gait and balance are associated with a high rate of falls.[9,10] Understanding gait and balance function in BCSs is critical to reduce their risk of fall-related injuries.

It is unclear how prevalent gait and balance impairments are in BCSs, which may be because of lack of understanding of these impairments. Past studies have focused primarily on clinical measures of balance and gait, such as the functional reach task or timed Up and Go (TUG).[11] More recently, studies have investigated changes in balance and gait function as they relate to impairment. For instance, Monfort et al[12] found gait speed and postural stability decreased after successive chemotherapy cycles. Winters-Stone et al[13] also found slower gait speed and shorter step length in BCSs with neuropathy, which was associated with an increased fall risk and greater disability. These studies suggest that not only is cancer treatment related to impairment, but impairment is also related to decreased quality of life. These novel studies further highlight growing concern of gait and balance impairment in BCSs and need to objectively measure these impairments.

Currently, there is a dearth of information about rehabilitating gait and balance impairments in cancer survivors. A pilot study (n = 4) found that tai chi is feasible, safe, and may improve balance in BCSs.[14] A more recent secondary analysis of a large randomized control trial (RCT) found that walking and resistance training improved symptoms of neuropathy in breast cancer patients, yet the researchers did not investigate the impact of the exercise program on gait or balance.[15] This may be because of a lack of information on the evidence and mechanisms of gait and balance impairments in cancer survivors. Quantifying and synthesizing these impairments may help inform the development of rehabilitation strategies aimed to improve gait and balance and enhance functional independence. Therefore, to our knowledge, this study is the first to systematically review and quantitatively synthesize the scientific evidence on gait and balance impairments in BCSs compared with those who never had breast cancer or normative values of healthy adults. We hypothesized that BCSs display worse gait and balance compared with age-matched persons who never had breast cancer or compared with normative values.

Methods

Study selection criteria

Studies that met the following criteria were included in the review: (1) had a study design of RCT, prospective, pre-post, case-control, or cross-sectional; (2) were of adults diagnosed as having breast cancer; (3) objectively measured gait and/or balance as primary or secondary measures; (4) were published peer-reviewed articles; and (5) were published in English. Studies were excluded if they were nonoriginal articles (ie, study protocols, reviews, or editorials).

Search strategy

The systematic review and meta-analysis was aligned to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses process.[16]

A keyword search was performed in PubMed, Cumulative Index to Nursing and Allied Health Literature, and Web of Science (table 1). Two reviewers (K.H. and T.W.) independently conducted title and abstract screening and jointly determined the list of articles for full-text review through discussion. Any disagreements or ties were resolved by a third independent reviewer (A.R.).

A cited reference search (ie, forward reference search) and reference list search (ie, backward reference search) were conducted on the full-text articles that met the study eligibility criteria from the keyword search. Titles and abstracts of all articles were screened based on the eligibility criteria. Articles meeting the eligibility criteria were retrieved for full-text evaluation. Articles identified through a forward/backward search were further screened using the same selection criteria. The reference search was

Table 1 Search terms used for each database

Database	Search Terms
PubMed	("breast neoplasms" [MeSH]) AND ("gait" OR "walk*" OR "ambula*" OR "mobility" OR "locomotion" OR "balance" OR "posture") AND ("adult" [MeSH])
Cumulative Index to Nursing and Allied Health Literature	("breast cancer," "breast neoplasms," "breast tumor," or "breast carcinoma") AND ("gait," "walk*," "ambula*," "mobility," "locomotion," "balance," or "posture") AND ("adult," "aged," or "elderly")
Web of Science	("breast cancer." "breast neoplasms," "breast tumor," or "breast carcinoma") AND ("gait," "walk*," "ambula*," "mobility," "locomotion," "balance," or "posture") AND ("adult," "aged," or "elderly")

repeated on all newly identified articles until no additional relevant article was identified. Articles up to November 14, 2018, were identified.

Data extraction

A standardized data extraction form was used to collect the following methodological and outcome variables from each included study[17]: country of study, author(s), publication year, study design, sample size, participant characteristics (ie, age, body mass index [calculated as weight in kilograms divided by height in meters squared], education, race, cancer stage, treatment type, time since treatment, and adverse effects), and gait and/or balance measures. Gait measures included the 8-ft and 3-m TUG, usual and fast gait speeds, and the short physical performance battery gait score. To control for varying methodologies, fast gait speed was categorized into short distances ($\leq$10m) and long distances ($\geq$100m or $\geq$6min). Balance measures included single leg stance time, overall stability index, short physical performance balance battery score, functional reach, center of pressure (COP) displacement, velocity, root mean square, 95% confidence ellipse, and the sensory organization test (SOT). For pre-post and RCT studies, only pretest data were extracted in order to avoid the intervention effect on gait or balance measures. Two gait parameters (ie, gait speed and TUG) and 3 balance parameters (ie, single leg stance time, functional reach, and COP velocity) were included in the meta-analysis. These measures were selected during the review and were chosen because at least 2 studies reported these outcome measures.[17] Four studies were excluded from the meta-analysis. The gait and/or balance outcome measures reported in these 4 studies were overall stability index, COP displacement reported as median values, COP velocity reported as median values, and gait speed during backward walking. Because only 1 study reported 1 of these outcome measures, a meta-analysis could not be performed. Meta-analysis also could not be performed on measures that were reported as median values.

Data synthesis

Meta-analysis was performed on single leg stance time, functional reach distance, center of pressure (COP) velocity, usual gait speed, fast gait speed, 8-ft TUG time, and 3-m TUG time for BCSs. Meta-analysis was also performed to estimate the differential single leg stance time between BCSs and persons who never had breast cancer. Study heterogeneity was assessed using the I^2 index. The level of heterogeneity represented by the I^2 index was interpreted as modest ($I^2 \leq 25\%$), moderate ($25\% < I^2 \leq 50\%$), substantial ($50\% < I^2 \leq 75\%$), or considerable ($I^2 > 75\%$).[17] A fixed-effect model would be estimated when modest to moderate heterogeneity was present, and a random-effect model would be estimated when substantial to considerable heterogeneity was present.[17] All statistical analyses were conducted using the Stata, 14.2 SE version (StataCorp[a]). All analyses used 2-sided tests, and P values $>$.05 were considered statistically significant.

Study quality assessment

Study quality for all included studies was assessed by the National Institute for Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies because 19 of the studies are either cohort or cross-sectional. Study quality was assessed with 14 questions that were answered as "yes," "no," "cannot determine," "not applicable," or "not reported." All responses other than "yes" indicate risk of bias. Two reviewers assessed all articles, and any discrepancies were resolved by a third reviewer. Study quality scores helped measure the strength of evidence but were not used to determine the inclusion of studies.

Results

Study selection

Figure 1 shows the study selection flow chart. A total of 2117 articles were identified through the keyword search, with 3 articles identified from the forward/backward search. After removing duplicates, 2041 articles underwent title and abstract screening, and 1994 articles were excluded. The remaining 47 articles were read in full text, and 18 were excluded for not meeting the study selection criteria. Studies were excluded because they included multiple cancer types,[18-25] did not measure gait or balance parameters,[26-29] did not specify cancer type,[30-32] or were an inappropriate study design.[33,34] The remaining 29 articles were included in the review.[11,12,14,35-59]

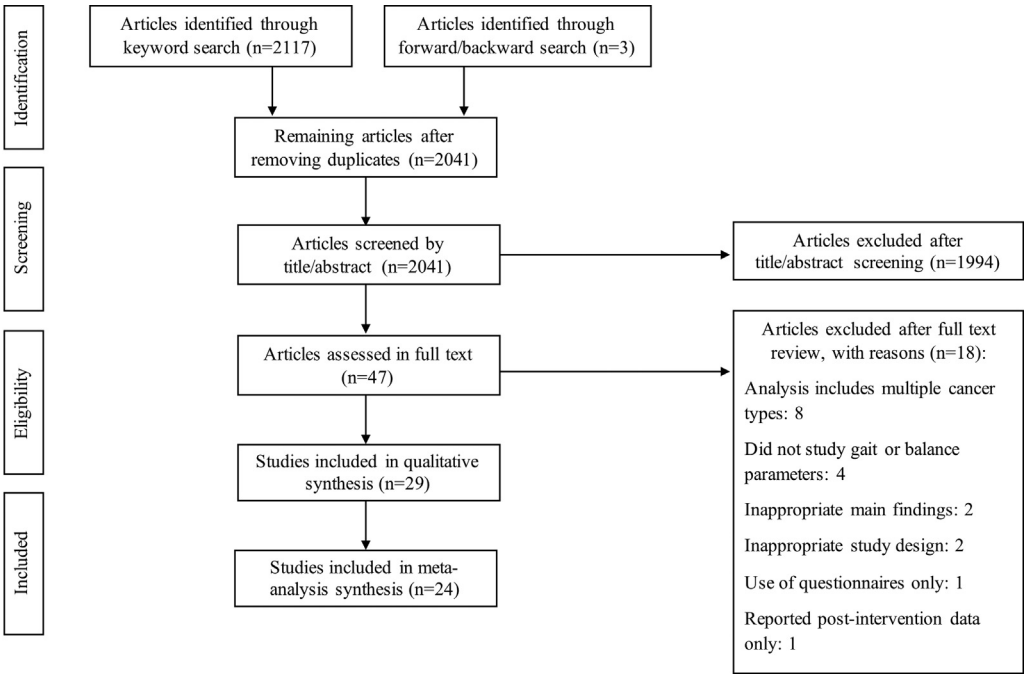

Fig 1 Study selection flow chart of studies in the systematic review and meta-analysis.

Basic characteristics of the included studies

Table 2 reports the basic characteristics of the 29 articles included in the review. Fifteen studies were conducted in the United States,[11,12,14,36,37,39,41,44-48,50,57,60] 2 in Finland,[40,43] and 2 in Turkey.[35,51] For study design, 11 studies were cross-sectional,[35,37,38,40,42,43,45,47-49,52] 11 were RCTs,[14,39,44,46,50,51,54,55,57-59] and 3 were pre-post.[11,36,60] Six studies included a control group who had never had breast cancer.[35,38,42,45,47,52] Seventeen of the studies measured gait and/or balance as the primary outcome,[11,12,35-38,40-42,44-46,48,49,51,53,58] while 12 analyzed gait and/or balance as secondary outcomes.[14,39,43,47,50,52,54-57,59,60] The total sample size was 2025 BCSs and 138 persons who never had breast cancer. Average age was 53.8 years among BCSs and 52.3 years among those who never had breast cancer. The majority of BCSs were overweight, with a body mass index over 25. Most BCSs completed at least high school, and almost all were white. Cancer stage ranged from stage 0 to stage III, with most diagnosed as having stage II. Surgery and chemotherapy were the most common treatments. The most common adverse effects from treatment were lymphedema, neuropathy, and menopause. Six studies included participants with ongoing breast cancer treatment,[12,40,41,49,54,55] whereas 9 studies included participants 1 month following completion of cancer treatment.[35,36,42-44,46,47,56,60]

Table 3 reports gait and balance measures examined by the studies included in the review. Eleven studies analyzed only gait metrics,[36,39,43,49-51,53-55,57,59] 10 studies analyzed only balance metrics,[33,35,38,41,42,44,47,52,58,60] and 8 studies analyzed both gait and balance metrics.[11,14,34,37,40,45,46,48] Of the balance metrics studies, 5 reported the single leg stance task,[11,40,46,47,52] 4 reported the functional reach test,[11,14,33,60] 3 reported COP velocity,[41,42,45] 2 reported COP displacement,[38,42] 2 reported balance scores from the short form physical performance test,[34,37] 2 reported outcomes of the SOT,[45,47] 1 reported an overall stability score measure,[35] and 1 reported backward walking speed as a measure of dynamic balance.[44] Of the gait metrics studies, 16 reported gait speed[11,12,37,40,43,46,48-51,53-56,59] and 5 reported TUG.[11,14,36,45,49]

Table 4 compares the gait and balance analyzed between the breast cancer group and the control group who never had breast cancer. Six studies analyzed gait and balance measures including an overall stability index score,[35] single leg stance,[47,52] TUG,[45] COP displacement,[42,60] and COP velocity.[42,45]

Meta-analysis

Balance measures among BCSs are depicted in figure 2 for the single leg stance (fig 2A), functional reach (fig 2B), and COP velocity (fig 2C). The forest plot for single leg stance included studies that stopped the test after reaching 60 s. Meta-analysis estimated the duration of single leg stance time with eyes open on a firm surface to be 23.75 s (95% CI, 22.10-25.39) among BCSs, which is less than that of normative values (36±12s)[61,62] The estimated distance of the functional reach test was 22.16 cm (95% CI, 8.98-35.33), which is less than those of adults who never had breast cancer (38.08±0.53cm).[51] The estimated COP velocity was 1.2 cm/s (95% CI, 0.87-1.55), which is greater than values of individuals who never had breast cancer (0.72cm/s), suggesting worse postural control.[63,64]

Table 2 Study and participant characteristics

Author	Study ID	Country	Type of Study	Control Group Who Never Had Breast Cancer	Sample Size	Mean Age ± SD (y)	Stage (%)	Mean BMI± SD	Education, Level (%)	Race (%)	Treatment Type (No.)	Time Since Treatment ± SD	Adverse Effects
Anderson et al[50]	01	USA	RCT	No	104	40% between 50-65	I (49) II (38.5) III (11.5)	71%>25	High school or less (17) Some college (28) College graduate (51)	White (88.5) African American (11.5)	MAS (52) CT (62) RT (67)	NR	NR
Besar et al[35]	02	Turkey	Cross-sectional	Yes	24 BCSs 22 CON	BCSs 57.4±7.2 CON 55.1±6.6	NR	BCSs 28±3.9 CON 28.3±4.4	NR	NR	MAS (24)	>6 mo	LD (24)
Damush et al[36]	03	USA	Pre-post	No	29	59.6±6.6	I (45) II (55)	NR	High school (55)	White (91)	NR	3.1 y	NR
Eyigor et al[51]	04	Turkey	RCT	No	42	48.9±8	NR	NR	Primary (12) Secondary (33)	NR	MAS (41)	NR	NR
Extermann et al[37]	05	USA	Cross-sectional	No	56	70±3.9	I-III	NR	NR	White (92.8)	MAS (15), Breast conserving Sx (41)	NR	NR
Foley et al[11]	06	USA	Pre-post	No	52	59.7±10.4	NR	30.1±0.9	NR	NR	Sx (52), CT (44), RT (39), HT (20)	NR	NR
Fong et al[52]	07	China	Pre-post	Yes	17 BCSs 36 CON	BCSs 54±7 CON 56.9±8.3	NR	21.6±3.4	NR	NR	Sx (57), MAS (10), CT (8), RT (2)	NR	PostM (12), LD (8),
					57 BCSs 36 CON	BCSs 53.1±6.7 CON 56.9±8.3	NR	BCSs 21.5±3.7 CON 24±4.7	NR	NR	MAS (36) CT (23) RT (9)	NR	NR
Galantino et al[60]	08	USA	Pre-post	No	10	57±50-71	I (20) II (70) III (10)	NR	College (60%)	White (90) African American (10)	NR	>4 wk	PostM (10)
Galantino et al[14]	09	USA	Pre-post	No	12	59	I-III	NR	High school or less (8.3) Some college (58.33) College degree (8.33) Graduate (25)	White (91.6) African American (8.4%)	CT (8), RT (10), MAS (1), Lump (2)	NR	PostM (12),
Galiano-Castillo et al[53]	10	Spain	Cross-Sectional	No	87	48.3±8.5	I (36.8) II (42.5) III	NR	NR	NR	CT (4) RT (4)	NR	LD (10)
Haines et al[54]	11	Australia	RCT	No	81	55.1±10.9	NR	NR	NR	NR	CT (32) RT (82) HT (35)	Ongoing	NR
Husebo et al[55]	12	Norway	RCT	No	60	52.2±9.3	I (37.1) II (56.7) III (11.6)	NR	High school (17.9) College (34.3) University (46.3)	NR	MAS (45) CT (60)	Ongoing	NR
Kneis et al[38]	13	Germany	Cross-sectional	Yes	20 BCSs 16 CON	BCSs 48.8±4.5 CON 46.5±5.4	NR	BCSs 26.3 CON 27.0	NR	NR	CT (20)	NR	CIPN (20)
Kokkonen et al[40]	14	Finland	Cross-sectional	No	128	60	NR	27.2±5	NR	NR	CT (122)	Ongoing	NR
Montezuma et al[42]	15	Brazil	Cross-sectional	Yes	40 BCSs 40 CON	BCSs 51.5±6.5 CON 50.5±7.9	NR	BCSs 30.7±5.2 CON 30.5±5.8	NR	NR	MAS (40)	5.80±5.76 mo	NR
Mascherini et al[56]	16	Italy	Cohort	No	13	49.1±5.5	NR	26.5±3.6	NR	NR	NR	Between 3-5 mo	NR

(*continued on next page*)

Table 2 (*continued*)

Author	Study ID	Country	Type of Study	Control Group Who Never Had Breast Cancer	Sample Size	Mean Age ± SD (y)	Stage (%)	Mean BMI± SD	Education, Level (%)	Race (%)	Treatment Type (No.)	Time Since Treatment ± SD	Adverse Effects
Monfort et al[41]	17	USA	Prospective	No	32	47.6±11.2	II (50) III (50)	27.9±7.8	NR	NR	CT (32)	Ongoing	NR
Monfort et al[12]	18	USA	Prospective	No	33	47.8±11.2	II (52) III (16)	28.9±9.4	NR	NR	CT (33)	Ongoing	NR
Penttinen et al[43]	19	Finland	Cross-sectional	No	537	52.4	NR	>25 57%	13.9 (3.4)	NR	MAS (277), CT (492), RT (421) HT (445)	>4 mo	PostM (284)
Reis et al[57]	20	USA	RCT	No	41	56±11	I (51) II (29) III (32)	29±6.3	High school (29) Associate's (29) Bachelor's (27) Master's (12)	White (90) African American (7)	MAS (8) CT (19) HT (26)	NR	NR
Twiss et al[44]	21	USA	RCT	No	223	58.7±7.5	NR	26.77±4	NR	White (98.7) African American (0.87) American Indian (0.43%)	Sx (219), RT (101), CT (151)	5.95±6.1 y	LD (42) PostM (223)
Vollmers et al[58]	22	Germany	RCT	No	36	49.8±11.1	NR	NR	NR	NR	NR	NR	NR
Wampler et al[45]	23	USA	Cross-sectional	Yes	20 BCSs 20 CON	BCSs 50.4±9.3 CON 49.6±9.1	NR	BCSs 25.0 CON 25.61	NR	NR	CT (20)	NR	CIPN (20)
Wang et al[59]	24	Taiwan	RCT	No	72	50.4±9.6	I (22.2) II (77.8)	22.5	High school (35) College (36) Graduate (10)	NR	MAS (36) CT (72) RT (32)	NR	PostM (35)
Winters-Stone et al[47]	25	USA	Cross-sectional/ prospective	Yes	35 BCSs 26 CON	44.9±3.2	I (31.4) II (57.1) IIIa (2.8)	BCSs 26.6±5.4 CON 24.1±3.9	NR	NR	CT (35)	12.6±4.1 mo	Amenorrhea (35)
Winters-Stone et al[48]	26	USA	Case-control/ cross-sectional	No	59	58.5±9.7	0 (5) I (29) II (39) III (19)	28.3±7.2	NR	NR	CT only (17), ET (19), CT with estrogen inhibitor (23)	6-24 mo	NR
Winters-Stone et al[46]	27	USA	RCT	No	37	62.1±6.7	0 (5.6) I (39.6) II (41.5) III (5.7)	29.5±5.7	NR	NR	CT (32), RT (46), PostM (37)	>1 y	NR
Yuen and Sword[39]	28	USA	RCT	No	22	53.9±12.8	NR	NR	High school (13.5) Some college (86)	White (77) African American (23)	Sx (22) CT (18) RT (17)	NR	NR
Zak et al[49]	29	Poland	Cross-sectional	No	102	70.2±4.3	NR	27.3±4.3	Secondary (40.5) University (16.8)	NR	Sx (102), CT (7), RT (2) HT (27), RT + CT (23), HT + CT + RT (26)	Ongoing	NR

Abbreviations: CIPN, chemotherapy induced peripheral neuropathy; CON, controls (never had breast cancer); CT, chemotherapy; HT, hormone therapy; LD, lymphedema; MAS, mastectomy; NR, not reported; RT, radiation therapy; PreM, premenopause; PostM, postmenopause; Sx, surgery.

Table 3 Gait and balance outcome measures for studies included in this review for BCS

Study ID	Gait Measures	Mean Outcome ± SD	Balance Measures	Mean Outcome ± SD
01	Fast gait speed—long (m/s)	1.49±0.28		
02			Overall Stability Index EO	0.47±0.32
			Overall Stability Index EC	2.64±0.93
03	8-ft TUG (s)	5.17±1.7		
04	Fast gait speed—long (m/s)	1.39±0.13		
05	Usual gait speed (m/s) (400m)	1.23±0.48	Short Physical Performance Balance	3.82±0.49
	Short Physical Performance Battery Gait Score	3.75±0.48	Battery Score	
06	TUG (s)	8.05±2.39	Single leg stance time (s)	26.8±20.9
	Fast gait speed—long (m/s)	1.16±0.23	Functional reach (cm)	29.7±7.4
07			Single leg stance time EO firm (s)	17.27±5.15
			Single leg stance time EO foam (s)	12.35±5.39
08			Functional reach (cm)	24.36±16.37
09	TUG (s)	8.90±3.67	Functional reach (cm)	12.63±6.10
			Berg Balance Scale	53.58±4.32
10	Median fast gait speed—long (m/s)	0.80		
11	Fast gait speed—long (m/s)	1.47±0.24		
12	Fast gait speed—long (m/s)	1.77±0.17		
13			Median COP displacement (cm)	63.1
14	Fast gait speed—short (m/s)	1.64±0.4	Single leg balance, UKK (s)	37.3±23
	Fast gait speed—long (m/s)	1.18±0.54	Single leg balance, TOIMIVA (s)	17.74 ±9.73
15	Fast gait speed—long (m/s)	1.24±0.47		
16			Median COP displacement (cm)	106.5
			Median COP velocity EO (cm/s)	1.8
			Median COP velocity EC (cm/s)	2.0
17			COP velocity (cm/s)	1.05±0.06
			COP root mean square (cm)	0.48±0.03
			COP 95% confidence ellipse area	2.113±0.305
18	Fast gait speed—short (m/s)	1.5±0.2	COP medial-lateral root mean square	0.33±0.11
	Step length (m)	0.69±0.07	(cm)	
19	Fast gait speed—long (m/s)	1.79±0.17		
20	Fast gait speed—long (m/s)	1.1±0.24		
21			Backward walking velocity (m/s)	0.43
22	TUG (s)	6.69±0.994	COP velocity EO (cm/s)	1.4±0.5
			COP velocity EC (cm/s)	2.1±1
			Sensory Organization Test —Composite	69±10
23			Single leg stance EO sway area (cm^2)	21.03±5.9
24	Fast gait speed—long (m/s)	1.36±0.17		
25			Single leg stance time EO (s)	60.6±46.5
			Single leg stance time EC (s)	15.7±16.4
26	Usual gait speed (m/s)	0.31±0.05	Sensory Organization Test—Visual	80.35±14.61
	Fast gait speed—short (m/s)	0.45±0.07		
27	Usual Gait Speed (m/s)	1.2±0.2	Single leg stance time (s)	23.52±9.60
28	Fast gait speed—long (m/s)	1.51±0.21		
29	8-ft TUG (s)	9.12±3.38		
	Usual gait speed (m/s)	NR		

NOTE. Values are mean ± SD or as otherwise indicated.
Abbreviations: EC, eyes closed; EO, eyes open; NR, not reported.

Gait measures among BCSs for usual gait speed, fast gait speed at a short distance, and fast gait speed at long distance are shown in figure 3. Meta-analysis estimated the usual gait speed to be 0.91 m/s (95% CI, 0.2-1.6), fast gait speed at a short distance to be 1.2 m/s (95% CI, 0.31-2.1), and fast gait speed at a long distance to be 1.65 m/s (95% CI, 1.64-1.66), which are slower than normative values (usual gait speed=1.1±0.09m/s; fast gait speed short-=2.01±0.26m/s; fast gait speed long=1.71±0.15m/s). For the TUG, 2 studies used an 8-ft course[36,49] while 3

Table 4 Gait and balance outcome measures for studies that included a breast cancer survivor group and control group who never had breast cancer

Study ID	Gait and/or Balance Measure	Breast Cancer Group	Control Group
02	Overall Stability Index EO	0.47±0.32	0.51±0.32
	Overall Stability Index EC	2.64±0.93	1.29±0.53
07	Single leg stance EO firm (s)	17.27±5.15	18.45±4.15
	Single leg stance EO foam (s)	12.35±5.39	15.94±4.94
13	Median COP displacement (cm)	63.1	63.3
16	Median COP displacement (cm)	106.5	70.8
	Median COP velocity EO (cm/s)	1.8	1.2
	Median COP velocity EC (cm/s)	2.0	1.5
22	COP velocity EO (cm/s)	1.4±0.5	0.9±0.2
	COP velocity EC (cm/s)	2.1±1	1.1±0.2
	Sensory Organization Test—Composite	69±10	80±5
	TUG (s)	6.69±0.994	5.85±0.86
25	Single leg stance EO (s)	60.6±46.5	115±67.2
	Single leg stance time EC (s)	15.7±16.4	24±28.9

NOTE. Values are mean ± SD or as otherwise indicated.
Abbreviations: EC, eyes closed; EO, eyes open.

studies used a 3-m course.[11,14,45] The estimated 8-ft course time was 7.14 s (95% CI, 3.27-11.01; fig 4), and the estimated 3-m course time was 7.65 s (95% CI, 6.25-8.87; see fig 4), which is greater than normative reported values (6.44±0.17s).[63]

There were no differences for the single leg stance time between BCSs and those who never had breast cancer (P=.33; fig 5).

Study quality assessment

Study quality assessment using the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies is provided for each study in supplemental table S1. Overall, 3 studies were rated good, 16 were rated fair, and 10 were rated poor. Because most studies are cross-sectional studies, breast cancer and gait and/or balance outcomes were assessed at the same time point, providing weak evidence as to whether breast cancer and its treatment cause gait and balance impairments or if gait and balance impairments precede cancer diagnosis. Therefore, it is possible that gait and balance impairments in BCSs may be influenced by factors apart from breast cancer. Additionally, 8 studies provided justification for their sample size,[44,46,47,52,54,55,58,59] and no studies reported assessors blinded to breast cancer diagnosis.

Discussion

This study systematically reviewed and quantitatively synthesized existing scientific evidence on gait and balance characteristics of individuals diagnosed as having breast cancer. A total of 21 out of 29 studies provide evidence that BCSs display gait and balance impairments. Specifically, there is some form of gait or balance impairment as measured by the functional reach task, COP velocity, gait speed, or TUG.

Maintaining standing balance involves the complex interplay of multiple physiological components, and deficits in any processes will lead to balance impairment.[65] Balance impairments in BCSs may result from reduced muscle strength and loss in proprioception from neuropathy, which are common adverse effects from breast cancer treatment.[66] One study that found BCSs with functional reach impairments also found worse leg strength than normative values.[11] Additionally, proprioceptive deficits may also contribute to poor balance. Proprioception involves the somatosensory systems sending and receiving information about the body's orientation to keep the center of mass stabilized.[67] Four studies included in the review found balance impairments in BCSs treated with neurotoxic chemotherapy, which is associated with peripheral neuropathy that may lead to proprioceptive loss.[34,38,41,45] Recent evidence suggests walking and resistance exercise many reduce neuropathy symptoms, suggesting that future work should explore the impact of exercise on gait and balance in BCSs receiving neurotoxic chemotherapy.[15] Additionally, because taxane- and platinum-based chemotherapy are common treatments for BCSs, clinicians should assess gait and balance with tests such as the functional reach or standing balance with a force plate.[68]

From the 3 different balance tasks analyzed in the meta-analysis, BCSs display balance impairment when compared with normative values of adults who never had breast cancer. Additionally, BCSs appear to have worse balance in the absence of visual feedback and when proprioception is challenged. For instance, 2 studies[42,45] found greater COP velocity in BCSs than those who never had breast cancer when without visual feedback during a standing balance task. Furthermore, Besar et al[35] found that BCSs have worse overall postural stability when visual information was not present compared with those who never had breast cancer. Wampler et al[45] also found worse balance performance during the no-visual component of the SOT. Moreover, BCSs also demonstrated worse balance than those who never had

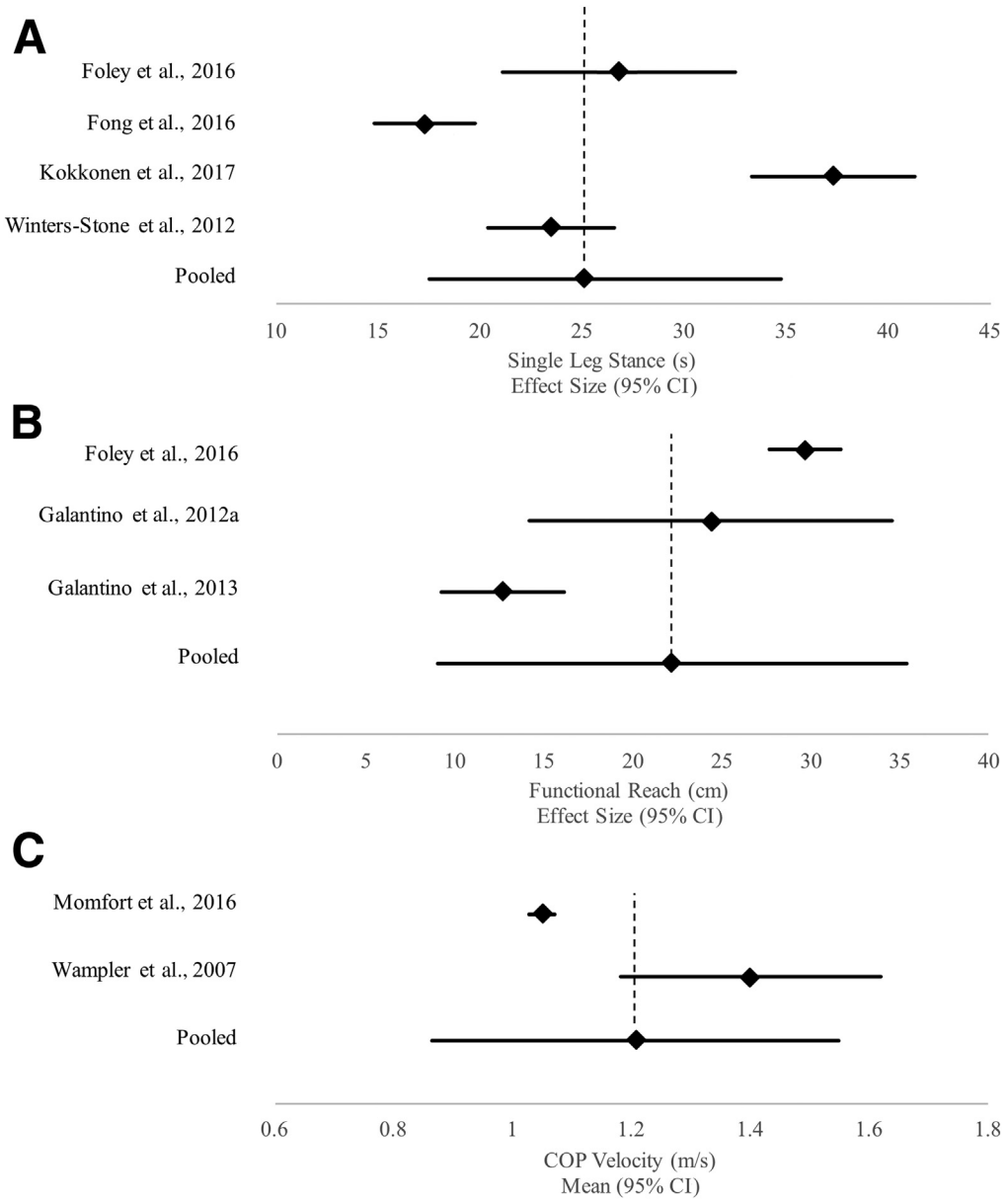

Fig 2 Forest plot of weighted mean (95% CI) for single leg stance (A), functional reach (B), and center of pressure velocity (C).

breast cancer when standing on a foam surface[52] and worse balance when standing on a compliant surface without visual feedback.[45] Collectively, these investigations suggest BCSs heavily rely on visual feedback to maintain upright posture, which may be because of the loss of proprioception commonly displayed after cancer treatment. When assessing balance, clinicians should rely on tests that challenge balance through the absence of visual feedback or with challenging proprioceptive conditions. Furthermore, clinicians should use caution using the single leg stance test because there are mixed results when comparing with those who never had breast cancer and normative values.

This review also found evidence of gait impairments in BCSs, as indicated by impairments in usual and fast gait speeds and TUG performance. Pamoukdijan et al[69] found that usual gait speed under 0.8 m/s was an independent predictor of death in older cancer survivors. While the population in this review is well below the age of older adults, this highlights the importance of maintaining gait function with age after cancer treatment. While more studies used longer walking tests to assess endurance, our results suggest that walking tests at shorter distances will also capture changes in gait. There was large variability in gait speed between studies that may result from varying sampling methods and cancer treatment. Further work should identify which factors contribute to slow gait speed because exercise interventions may only benefit a subgroup of BCSs.

Gait impairments may result from fatigue and proprioceptive deficits. Fatigue is the most common adverse effect following breast cancer treatment.[70] In older adults, greater fatigue has found to be significantly associated with slower

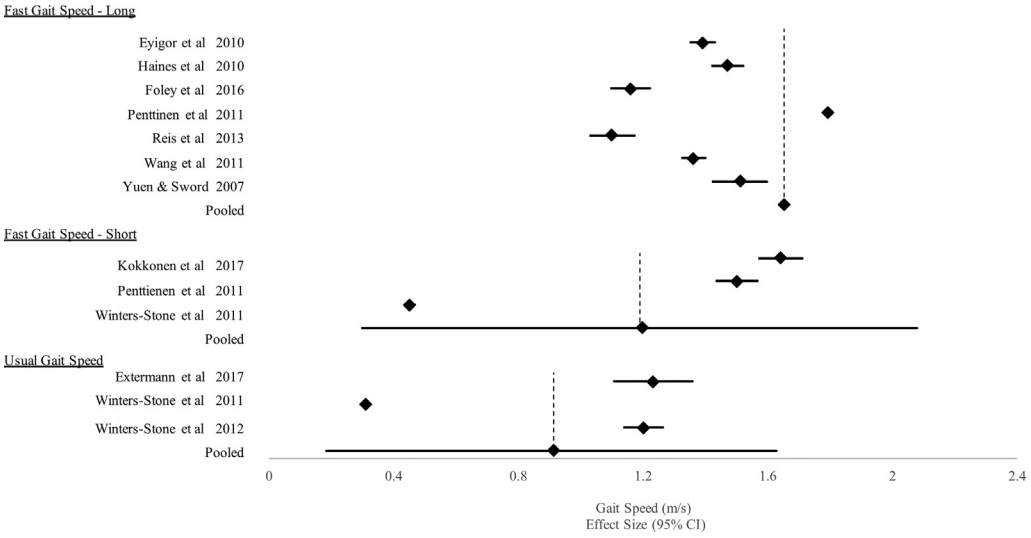

Fig 3 Forest plot of weighted mean (95% CI) for usual gait speed, fast gait speed at a short distance, and fast gait speed at a long distance (m/s).

walking speed.[71] Therefore, it may also be possible that cancer-related fatigue contributes to slowed walking. While 2 of the studies[40,46] that measured gait speed also measured fatigue, neither of the studies explored the possibility of an association. Furthermore, proprioceptive deficits due to neuropathy may also influence gait speed because they inhibit information reaching the central nervous system to coordinate gait and maintain a constant speed.[72] Three studies in the review that analyzed gait included BCSs with neuropathy, suggesting that symptoms of neuropathy may impair normal walking patterns.[12,38,45] Future work should continue to identify which factors contribute to slow gait speed and explore whether exercise improves these factors and, consequently, gait function in BCSs.

The timescale of mobility impairment recovery following breast cancer treatment is poorly understood. While 3 of the studies tested BCSs during treatment, no overall conclusion could be determined if mobility is worse during or after treatment because of inconsistent findings.[40,41,49] Conversely, 2 studies followed BCSs over consecutive treatments and found impaired postural stability and gait speed over time, indicating that postural stability and gait worsened with continuous chemotherapy.[12,41] It is also evident that gait and balance impairments persist up to 5 years post treatment. Further work should determine when gait and balance impairments first appear with cancer treatment and if they resolve over time. This may help determine when an intervention is most effective to improve mobility.

For the studies included in the review, heterogeneity was substantial, indicating large variations between studies. This may be a result of differences in age range and cancer severity between studies. For instance, some studies included older women with breast cancer, and mobility has shown to decline with advanced age.[73] Some studies recruited postmenopausal women, and loss of estrogen has been associated with declines in balance function.[74] Furthermore, treatment types differed across studies and adverse-effects differences related to

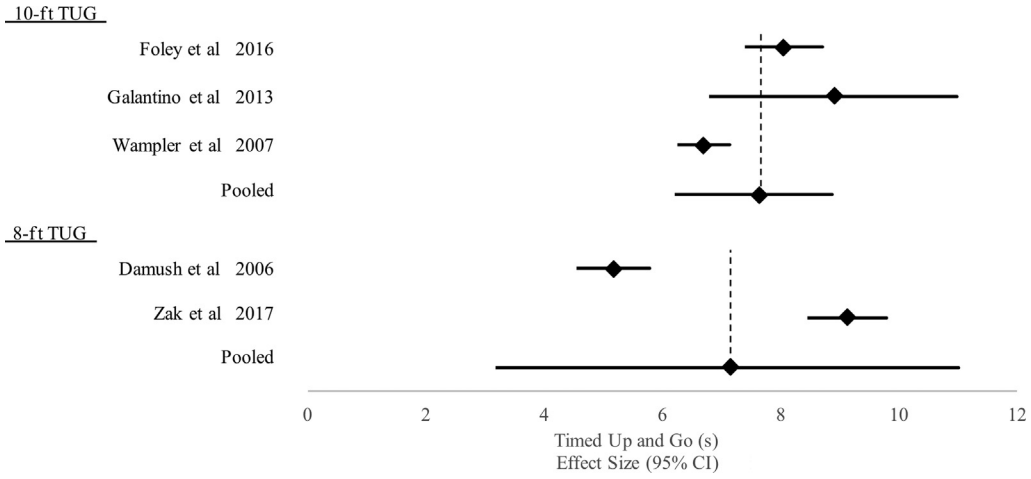

Fig 4 Forest plot of weighted mean (95% CI) for the TUG test (s) for an 8-ft distance and 3-m distance.

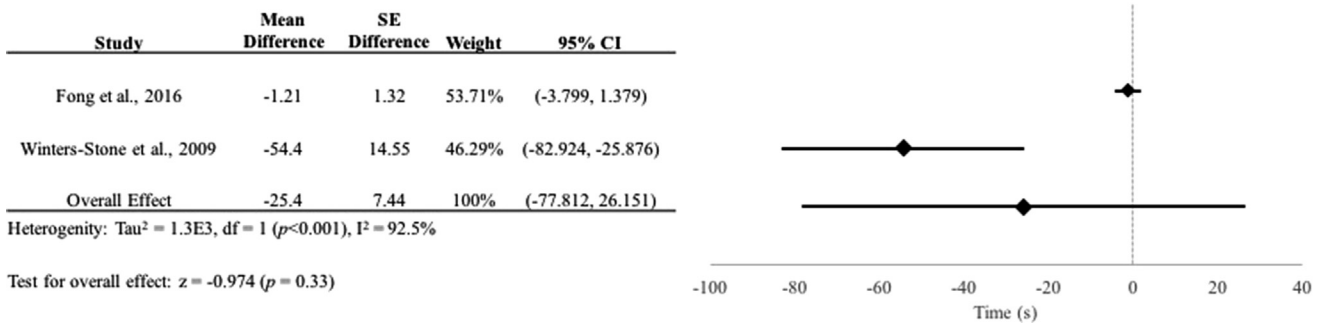

Fig 5 Forest plot of effect size (95% CI) for single leg stance (s) comparing breast cancer survivors to those who never had breast cancer.

particular treatments may influence mobility outcomes. Collectively, these variations may confound the pooled effect and effect size results.

This study provides evidence of gait and balance impairments in BCSs. While current exercise interventions in BCSs have shown to improve quality of life and decrease fatigue and pain,[75,76] few studies have examined whether exercise can improve gait and balance in this population. Because aerobic and resistance training can improve leg strength, fatigue, and proprioception in cancer survivors, it is possible that exercise can improve gait and balance.[77] Feasibility studies have found improvements in balance with yoga and tai chi,[14,33,60] but future steps should implement RCTs to determine if exercise interventions will improve gait and balance impairment. Because poor gait and balance are linked to a greater risk of falls and worse quality of life,[7,78] successful interventions have potential to enhance functional independence, improve gait and balance impairment, and prevent falls and fall-related injuries.

This review provides important information for BCSs and clinicians. BCSs should report any noticeable changes in their gait or balance to clinicians because early detection may prevent long-term impairment. Clinicians should also assess gait and balance at the clinic both during and following treatment. Assessing balance with a force plate will better detect changes in stability, but the functional reach test can also be quickly administered and detect balance impairments. To assess gait speed, clinicians should assess usual and fast gait speed over 10 m or use TUG because a shorter distance appears to be able to detect changes in gait. Assessing and tracking their gait and balance can help identify BCSs in need of rehabilitation to improve their mobility. Improving gait and balance may reduce fall risk and prevent fall-related injuries such as hip fractures.[79] Future research is also needed to help clinicians identify the type, intensity, and frequency of exercises that may improve gait and balance and reduce fall risk tailored for BCSs.

Study limitations

While this is the first study to systematically review mobility impairments in BCSs, it is not without limitations. The single leg balance was the only task that studies used to compare BCSs and those who never had breast cancer. Given the numerous measures of balance, overall conclusions about balance cannot be drawn from a single measure. Additionally, only 7 of the studies included a control group who never had breast cancer. Therefore, most of the findings among BCSs were compared with normative values. Furthermore, because of the high risk of bias from the included studies, the identified gait and balance impairments should be interpreted with caution. Many of the studies did not aim to understand balance or gait in BCSs as their primary purpose, which limits findings compared with those who never had breast cancer or over multiple time points. The high number of fair and poor quality studies also suggest that many of these studies are not suited to understand gait and balance impairments in BCSs. While some RCTs may be well-designed and lack study bias, these exercise interventions were not designed to understand mobility and, therefore, may not have a representative sample. There is a need for future work to better understand gait and balance impairments in BCSs. Moreover, the small number of studies included in the meta-analysis prevented an assessment of publication bias.[17]

Of the balance tests in the review, the majority were static balance tests. Although important, adverse events related to poor balance such as falls typically occur during dynamic movements.[80] Therefore, future studies should analyze both dynamic and static stability. For gait measures, studies reported gait speed and TUG times, but no studies reported spatial-temporal measures of gait (ie, step time, width, and length). Gait speed is an important component of gait, but characterizing spatiotemporal parameters of individual steps provides additional information about overall mobility.[81] Future studies should further understand gait function.

Conclusion

This study systematically reviewed and quantitatively synthesized gait and balance measures in BCSs. The results suggest that BCSs have balance impairment and declines in gait speed. The pooled estimates for functional reach scores, COP velocity, gait speed, and TUG times based on the meta-analysis were all lower than their respective normative values, indicating potential balance and gait impairments in BCSs. Specifically, it was found that BCSs demonstrated worse stability in the static balance tasks

when the visual and proprioceptive systems were challenged. Both usual and fast gait speed at short and long distances were also slower than adults who never had breast cancer. Clinicians should consider assessing changes in gait and balance in BCSs to identify those at risk for falls. Future interventions should target walking and balance exercises to improve mobility in BCSs.

Supplier

a. Stata, version 14.2 SE; StataCorp.

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