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The Correlation Between Radiotherapy and Patients' Fear of Cancer Recurrence

A Systematic Review and Meta-analysis

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The purpose of this review was to explore the correlation between patients' fear of cancer recurrence (FCR) and radiotherapy. National Knowledge Infrastructure, Wanfang Database, China Science and Technology Journal Database, SinoMed, PubMed, Web of Science, EBSCO-CINAHL, Cochrane Library, and Ovid Embase were searched to identify relevant studies. Thirty-five eligible studies were included in the systematic review, and 22 of them were included in further meta-analysis. The results of the meta-analysis showed that the level of patients' FCR was positively correlated with radiotherapy, but the correlation was weak (overall $r = 0.075$; 95% confidence interval [CI], 0.046-0.103; $P = .000$). In terms of subgroup analysis based on cancer site (breast cancer vs other types of cancer), the breast cancer group ($r = 0.086$; 95% CI, 0.027-0.143; $P = .004$), the mixed-type group ($r = 0.073$; 95% CI, 0.033-0.112; $P = .000$), and the other-type group ($r = 0.071$; 95% CI, 0.015-0.126; $P = .013$) have a positive correlation with radiotherapy. Patients' FCR positively correlated with the receipt of radiotherapy. However, because of the variability among the studies, the results have limitations. Therefore, longitudinal studies are needed to verify the trajectory of FCR over radiation therapy.

KEY WORDS

fear of cancer recurrence, meta-analysis, radiotherapy

Cancer tumors has become one of the major diseases that threatens human health. According to the Global Cancer Agency, there have been approximately 19.3 million new cases of cancer in 2020 with 10 million deaths.[1] As one of the most common chronic diseases, tumors have characteristics such as high morbidity, high mortality, and high recurrence rate. At the same time, with the improvement of medical technology, the survival rate of patients with solid tumors is getting higher.[2]

Most cancer patients are receiving comprehensive treatment, including surgery, radiotherapy (RT), chemotherapy, targeted therapy, and immunotherapy.[3] One survey showed that approximately half of cancer patients with solid tumors need adjuvant RT.[4] The current RT technology mainly includes traditional photon and particle therapy, but compared with other treatment methods, RT technology will bring a series of toxic reactions to patients, including skin reactions, oral reactions, and fatigue,[5] which will not only increase the patient's physical burden but also severely increase the patient's psychological distress.[6] Therefore, many patients receiving RT generally experience negative emotions such as anxiety, worry, and fear.[7] Fear of cancer recurrence (FCR) is the most common negative emotion in cancer patients. Approximately 49% to 70% of patients experience FCR.[8]

Fear of cancer recurrence is defined as "a feeling caused by the recurrence or progression of cancer in the same organ or other part of the body."[9] Cancer survivors with high levels of FCR may experience psychological distress (eg, anxiety, depression, and posttraumatic stress symptoms)[10] and disorder of cognitive functions (eg, excessive checking behaviors and increased health service use),[11] even suicide.[10,12] A patient's FCR level is influenced by various factors.[13] Young

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The authors have no conflicts of interest to disclose.

DOI: 10.1097/NJH.0000000000000848

age, degree of education, severity of somatic symptoms, and course of disease have been reported to be correlated with higher FCR. However, the evidence for the relationship between the RT reception and the patient's FCR has been mixed. A study by Yang et al[14] reported a statistically significant association between treatment type (routine, routine + boost radiation treatment) and FCR (P = .006). However, Wroot et al[15] reported that RT was unrelated to cancer patients' FCR (odds ratio [OR], 0.88; P = .79).

Therefore, the purpose of this study was to explore the correlation between the patients' FCR and RT. This systematic review has been registered in PROSPERO with registration number CRD42021262135.

METHOD

Literature Search

National Knowledge Infrastructure, Wanfang Database, China Science and Technology Journal Database, SinoMed, PubMed, Web of Science, EBSCO-CINAHL, Cochrane Library, and Ovid Embase were searched from their inception to July 2021. The key search terms were neoplasm/tumor/cancer/malignancy, progression/exacerbation/recurrence/relapse, fear/worry/concern, radiotherapy/radiation treatment/radiotherapy, and/or targeted/radiation therapy.

Inclusion and Exclusion Criteria

The criteria to be included were as follows: (*a*) patients receiving RT; (*b*) prospective and retrospective study; (*c*) study variables—FCR and RT; (*d*) inclusion of complete information such as correlation coefficient (r), P value, and OR value; and (*e*) English or Chinese. Exclusion criteria included the following: (*a*) unpublished or duplicated studies, (*b*) studies without full text, and (*c*) studies using similar but inaccurate keywords such as "fear of death," "fear of the worst," or "chemoradiotherapy."

Literature Screening and Data Extraction

At first, the Note Express software is used for the reduction. In the second phase, 2 researchers exclude inappropriate research by reading titles and abstracts, such as reviews and qualitative studies. In the third step, on the basis of the inclusion and exclusion criteria, documentation that could not obtain the complete text or data was excluded. Finally, 2 researchers (M.Z. and L.X.) extracted data from included studies, such as author, year, country, study type, cancer type, sample size, age, measurement tool, reliability and validity, and conclusions.

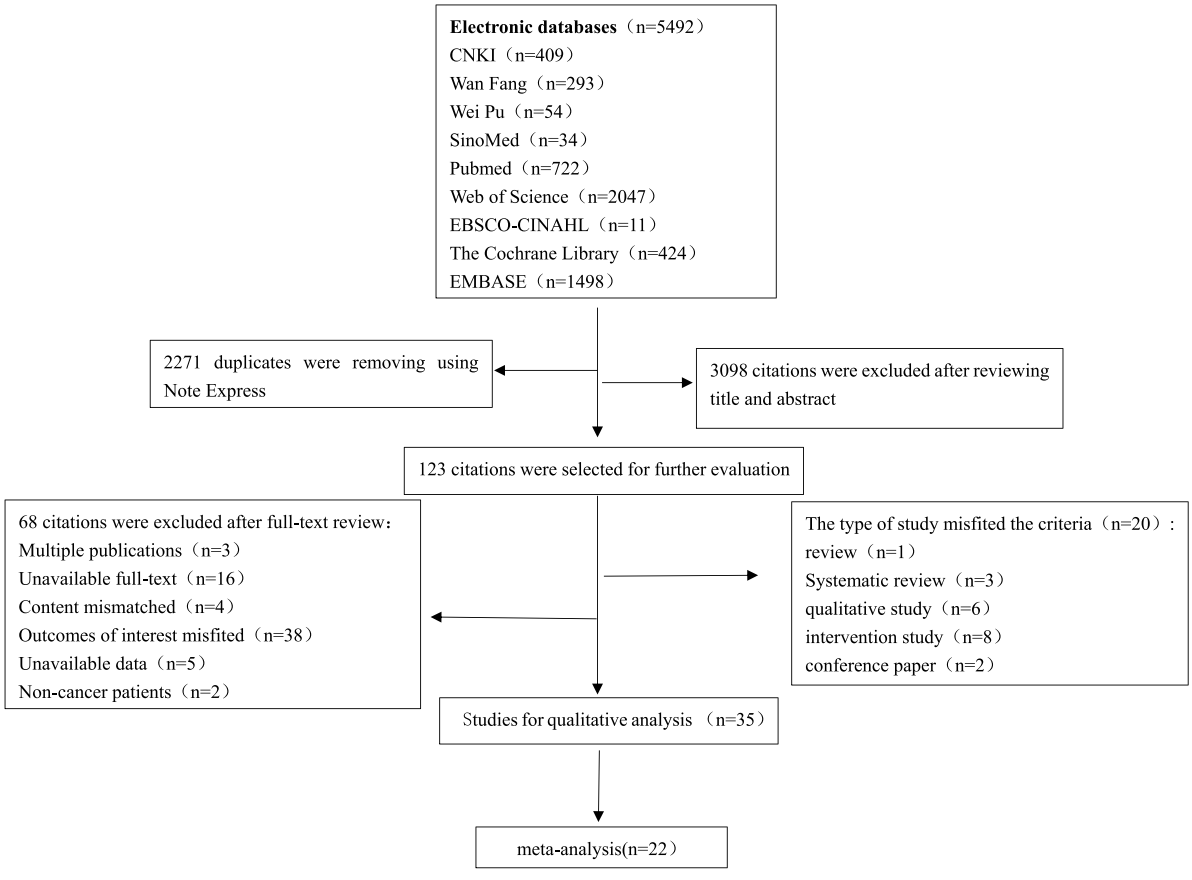

FIGURE 1. Flow diagram of the selection of the studies.

TABLE 1 Characteristics of the 35 Included Studies

First Author, Year, Country	Study Design	Cancer Type	Sample Size	Age at Survey, Mean (SD), y	FoR Instruments	Reliability	Main Findings
Northouse, 1981, United States	Cross-sectional	Breast	N = 30	54 (10.5)	Fear of Cancer Recurrence Questionnaire	72% of the items having correlations greater than 0.6	RT was not significantly related to cancer patients' FCR.
Leake, 2001, Australia	Cross-sectional	Gynecological malignant tumor (cervical, endometrial, ovarian, etc)	N = 202	?	Rate your fear of your cancer coming back	?	RT was not significantly related to cancer patients' FoR.
Stanton, 2002, United States	Cross-sectional	Breast	N = 70	52.63 (11.94) (range, 30-80)	6 items from the 22-item Fear of Recurrence Questionnaire (FRQ)	?	There was no relationship between RT and cancer patients' FCR.
Mehta, 2003, United States	Cross-sectional	Prostate	N = 53	71.6	Fear of Recurrence Scale (5-item)	?	FCR was more severe before RT and improved after RT, but there was no significant change in the following 2 y.
Humphris, 2019, United Kingdom	Longitudinal	Oral and oropharyngeal malignancy	N = 87	58.3 (11.3)	Worry of Cancer Scale	?	Radiation therapy was weakly associated with fear about cancer recurrence (r = –0.08).
Härtl, 2003, Germany	Cross-sectional	Breast	N = 274	55.8 (11.5) (range, 27.5-99.5)	QLQ-C30 questionnaire version 2.0	?	No relationship between RT and cancer patients' FCR (P = .75).
Rabin, 2004, United States	Longitudinal	Breast	N = 69	48.4 (9.3) (range, 30-73)	Study-designed FoR scale	Cronbach α = 0.84	RT (received vs did not receive) was unrelated to FCR.
Deimling, 2006, United States	Cross-sectional	Breast, colorectal, prostate	N = 321	72.3 (7.5)	Cancer-related Health Worries Scale (4-item)	Cronbach α = 0.84	RT and cancer patients' FCR (r = 0.13, $P \leq .05$).
Mellon, 2007, United States	Cross-sectional	Breast, colon, uterine, prostate	N = 123	65 (6.2) (range, 52-75)	FRQ (22-item)	Reliability coefficients = 0.92	RT was unrelated to patients' and caregivers' FCR.
Skaali, 2009, Norway	Cross-sectional	Testicular	N = 1336	44.8 (10.1)	Single question of FoR	?	RT was unrelated to FCR (P = .85).

(continues)

TABLE 1 Characteristics of the 35 Included Studies, Continued

First Author, Year, Country	Study Design	Cancer Type	Sample Size	Age at Survey, Mean (SD), y	FoR Instruments	Reliability	Main Findings
Simard, 2009, Canada	Cross-sectional	Breast, prostate, lung, colorectal	N = 600	Breast, 59.0 (0.6); prostate, 69.1 (0.5); lung, 62.0 (1.5); colorectal, 61.6 (1.3)	FCR inventory (42-item)	Cronbach $\alpha = 0.95$, test-retest $r = 0.89$	There was relationship between RT and cancer patients' higher FCR ($P = .005$).
Bergman, 2009, United States	Longitudinal	Prostate	N = 78	63 (8)	The Memorial Anxiety Scale (5-item)	?	There was no significant association between having had RT with higher FoR ($P = .97$).
Rogers, 2010, United Kingdom	Cross-sectional	Head and neck	N = 123	?	7-item FRQ	Cronbach $\alpha = 0.90$	RT was not associated with FoR ($P = .86$).
Janz, 2011, United States	Cross-sectional	Breast	N = 1837	56.8 (11.4)	Worry About Recurrence Scale (3-item)	Cronbach $\alpha = .88$	There was a significant association between having had RT with higher FoR ($P < .001$).
Liu, 2011, United States	Longitudinal	Breast	N = 506	58 (10)	First 4 items of Concern About Recurrence Scale (CARS)	Cronbach $\alpha = 0.87$	There was no relationship between RT and cancer patients' FCR ($P = .87$).
Sung, 2011, Korea	Cross-sectional	Thyroid	N = 357	43.9 (11.3)	Fear of Progression Questionnaire (FoP-Q)	?	Postoperative RT had no significant effect on FCR in cancer patients ($P = .414$).
McGinty, 2012, United States	Cross-sectional	Breast	N = 155	58.8 (11.83)	Modified Cancer Worry Scale (CWS) (4-item)	Cronbach $\alpha = 0.87$	RT was not related to cancer survivors' FCR (6.70 [2.62]).
Ghazali, 2013, United Kingdom	Longitudinal	Head and neck	N = 189	62 (12) (range, 24-87)	7-item FoR questionnaire	?	Radiation (received vs not received) was not associated with FCR (mean [SD], 19.20 [9.40] vs 17.2 [8.10]).
Wiley, 2013, United States	Cross-sectional	Choroidal, melanoma	N = 98	63.71 (range, 24-88)	Concern of Recurrence Scale	Cronbach $\alpha = 0.68$	There was no significant difference in FCR level between the RT group and the surgery group (Fisher $Z = 1.280$).
Koch, 2014, Germany	Cross-sectional	Breast	N = 2671	65	FoP-Q Short Form (FoP-Q-SF, 12 items)	Cronbach $\alpha = 0.89$	Patients treated with radiation were less likely to experience moderate or high cancer recurrence fears (OR, 0.72 [0.55-0.94]).

(continues)

TABLE 1 Characteristics of the 35 Included Studies, Continued

First Author, Year, Country	Study Design	Cancer Type	Sample Size	Age at Survey, Mean (SD), y	FoR Instruments	Reliability	Main Findings
Tewari, 2014, United States	Cross-sectional	Breast	N = 392	?	"How often do you worry that your cancer may come back or get worse?"	?	RT was related to cancer patients' increased FCR ($P = .04$).
Hong, 2015, China	Cross-sectional	Nasopharynx	N = 216	47.81 (10.75)	Quality of life questionnaire (QLQ-C30 V2.0)	?	FCR is a psychological distress caused by radiation therapy. (FCR incidence rate is 18.52%.)
Perrucci, 2015, Italy	Longitudinal	Breast	N = 117	?	Quality of Life Questionnaire	?	FoR was unchanged at a median of 20 and 80 mo after partial ($P = .483$) or whole breast irradiation ($P = .417$).
van de Wal, 2016, Netherlands	Cross-sectional	Prostate	N = 283	70.0 (range, 54-89)	CWS (8-item)	Cronbach $\alpha = 0.88$	There was a significant association between having had RT with higher FCR ($t = –2.033$, $P = .043$).
Rogers, 2016, United Kingdom	Cross-sectional	Head and neck	N = 513	65 (range, 58-72)	Single-item FoR and 7-item FRQ	?	RT was related to cancer survivors' FCR ($P = .001$).
Freeman-Gibb, 2017, United States	Cross-sectional	Breast	N = 117	Range, 46-55	FRQ (22-item)	Cronbach $\alpha = 0.90$	RT was related to cancer survivors' FCR ($r = 0.3$).
Starreveld, 2018, Belgium	Longitudinal	Breast	N = 267	54.31 (10.09)	CARS	Cronbach $\alpha = 0.94$	RT was unrelated to cancer patients' FCR ($P = .8$).
Thewes, 2018, Netherlands	Cross-sectional	Testicular, breast, sarcoma	N = 73	Range, 18-35	CWS (8-item)	Cronbach $\alpha = 0.89$	RT was significantly associated with higher FCR ($P = .15$).
Yang, 2018, United Kingdom	Longitudinal	Breast	N = 94	57.9 (11.5) (range, 28-85)	Fear of Recurrence Scale (FCR7)	Cronbach $\alpha = 0.92$	Patients who received additional enhanced radiation had higher levels of FCR ($P = .006$).
Sun, 2019, China	Cross-sectional	Breast, leukemia, colorectal, nasopharynx cancer	N = 249	33.12 (4.82)	FoP-Q-SF	Cronbach $\alpha = 0.883$	RT was unrelated to cancer patients' FCR ($P = .449$).

(continues)

TABLE 1 Characteristics of the 35 Included Studies, Continued

First Author, Year, Country	Study Design	Cancer Type	Sample Size	Age at Survey, Mean (SD), y	FoR Instruments	Reliability	Main Findings
Gotze, 2019, Germany	Longitudinal	Prostate, breast	N = 1002	Mean age, 68	FoP-Q-SF	Cronbach $\alpha = 0.87$	RT was not significantly related to patients' FCR ($P = .194$).
Wu, 2019, United States	Longitudinal	Prostate	N = 69	64.5 (8.1)	"How worried are you about a recurrence of your prostate cancer?" and "How worried are you about that your prostate cancer has spread?"	Cronbach α were 0.85, 0.79, and 0.78 for baseline, 6-mo, and 12-mo time points.	There was a significant effect of radiation on patient FCR at 12 mo ($P < .05$).
Wroot, 2020, Canada	Longitudinal	Leukemia, solid, lymphoma, central nervous system tumors	N = 228	Range, 4.7-21	"Are you concerned about the following health issues: fear of cancer coming back?"	?	RT was unrelated to cancer patients' FCR (OR, 0.88; $P = .79$).
Guimond, 2020, Canada	Longitudinal	Breast	N = 81	Range, 31-75	Fear of Cancer Recurrence Inventory (9-item)	Cronbach $\alpha = 0.74$	There was a significant association between having had RT with higher FCR ($P = .39$).
Scannell, 2020, Germany	Cross-sectional	Uveal melanoma	N = 138	?	EORTC QOL questionnaire QLQ-C30/OPT30 (30-item)	?	There was no statistically significant difference between the 2 groups with regard to worry about recurrent disease (Enucleation, 42.0 [29.8]; brachytherapy, 38.5 [26.9]).

Abbreviations: EORTC, European Organisation for the Research and Treatment of Cancer; FCR, fear of cancer recurrence; FoR, fear of recurrence; OR, odds ratio; QLQ-C30, The quality of life C30 questionnaire; RT, radiotherapy.

TABLE 2 Quality Assessment of Included Studies

	Identify Sources (Survey, Literature Review)	Inclusion and Exclusion Criteria for the Exposed and Nonexposed Groups Are Listed or Reference to Previous Publications	Give a Time Frame for Identifying the Patient	If Not Population Origin, Whether the Subjects Are Continuous	Whether the Evaluator's Subjective Factors Obscure Other Aspects of the Research Object	Describes Any Assessment to Ensure Quality	Explained the Reasons for Excluding Any Patients From the Analysis	Describe Measures to Evaluate and/or Control Confounders	If Possible, Explain How Missing Data Are Handled in the Analysis	Patient Response Rates and Data Collection Integrity Were Summarized	If There Is Follow-up, Identify the Expected Percentage of Patients With Incomplete Data or Follow-up Results	Quality
Northouse, 1981	Y	Y	Y	Y	N	N	N	N	N	Y	N	Medium
Leake et al, 2001	Y	Y	UN	Y	N	N	Y	N	N	Y	N	Medium
Stanton et al, 2002	Y	UN	Y	Y	N	Y	Y	Y	N	Y	Y	High
Humphris, 2019	Y	UN	Y	Y	N	UN	N	N	N	Y	Y	Medium
Mehta et al, 2003	Y	Y	Y	Y	N	UN	UN	N	N	Y	UN	Medium
Härtl et al, 2003	Y	Y	Y	Y	N	N	Y	N	N	N	N	Medium
Rabin et al, 2004	Y	UN	Y	Y	N	N	N	N	UN	Y	Y	Medium
Deimling et al, 2006	Y	Y	Y	Y	N	Y	Y	N	N	Y	N	Medium
Mellon et al, 2007	Y	Y	Y	Y	N	UN	Y	N	N	UN	N	Medium
Bergman et al, 2009	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	High
Simard and Savard, 2009	Y	Y	Y	Y	N	N	Y	N	N	Y	N	Medium
Skaali, 2009	Y	UN	Y	Y	N	N	Y	N	N	N	N	Medium
Rogers et al, 2010	Y	Y	Y	Y	N	UN	Y	N	N	Y	N	Medium
Janz et al, 2011	Y	UN	Y	Y	N	UN	Y	N	N	Y	N	Medium

(continues)

TABLE 2 Quality Assessment of Included Studies, Continued

	Identify Sources (Survey, Literature Review)	Inclusion and Exclusion Criteria for the Exposed and Nonexposed Groups Are Listed or Reference to Previous Publications	Give a Time Frame for Identifying the Patient	If Not Population Origin, Whether the Subjects Are Continuous	Whether the Evaluator's Subjective Factors Obscure Other Aspects of the Research Object	Describes Any Assessment to Ensure Quality	Explained the Reasons for Excluding Any Patients From the Analysis	Describe Measures to Evaluate and/or Control Confounders	If Possible, Explain How Missing Data Are Handled in the Analysis	Patient Response Rates and Data Collection Integrity Were Summarized	If There Is Follow-up, Identify the Expected Percentage of Patients With Incomplete Data or Follow-up Results	Quality
Sung et al, 2011	Y	UN	Y	Y	N	N	Y	N	Y	Y	N	Medium
Liu et al, 2011	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	High
McGinty et al, 2012	Y	Y	Y	Y	N	Y	UN	N	N	Y	N	Medium
Ghazali et al, 2013	Y	UN	Y	Y	N	N	Y	N	N	Y	UN	Medium
Wiley et al, 2013	Y	UN	Y	Y	N	N	Y	N	N	Y	N	Medium
Tewari and Chagpar, 2014	Y	N	Y	Y	N	N	N	N	N	Y	N	Medium
Koch et al, 2014	Y	UN	Y	Y	N	UN	N	N	UN	Y	N	Medium
Hong et al, 2015	Y	Y	Y	Y	N	N	Y	N	N	N	N	Medium
Perrucci et al, 2015	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	High
Rogers et al, 2016	Y	UN	Y	Y	N	N	Y	N	N	Y	N	Medium
van de Wal et al, 2016	Y	Y	Y	Y	N	N	Y	N	Y	Y	N	Medium
Freeman-Gibb et al, 2017	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	High
Starreveld et al, 2018	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High

(continues)

TABLE 2 Quality Assessment of Included Studies, Continued

	Identify Sources (Survey, Literature Review)	Inclusion and Exclusion Criteria for the Exposed and Nonexposed Groups Are Listed or Reference to Previous Publications	Give a Time Frame for Identifying the Patient	If Not Population Origin, Whether the Subjects Are Continuous	Whether the Evaluator's Subjective Factors Obscure Other Aspects of the Research Object	Describes Any Assessment to Ensure Quality	Explained the Reasons for Excluding Any Patients From the Analysis	Describe Measures to Evaluate and/or Control Confounders	If Possible, Explain How Missing Data Are Handled in the Analysis	Patient Response Rates and Data Collection Integrity Were Summarized	If There Is Follow-up, Identify the Expected Percentage of Patients With Incomplete Data or Follow-up Results	Quality
Yang et al, 2018	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	High
Thewes et al, 2018	Y	UN	Y	Y	N	N	UN	N	N	Y	N	Medium
Guimond et al, 2020	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	Medium
Gotze et al, 2019	Y	UN	Y	Y	N	UN	Y	N	Y	Y	N	Medium
Sun et al, 2019	Y	Y	Y	Y	N	N	Y	N	N	Y	N	Medium
Wu et al, 2019	Y	Y	Y	Y	N	UN	UN	Y	N	Y	Y	Medium
Wroot et al, 2020	Y	N	Y	Y	N	N	N	N	N	Y	Y	Medium
Scannell et al, 2020	Y	N	Y	Y	N	UN	UN	Y	UN	Y	N	Medium

Abbreviations: N, no; UN, unclear; Y, yes.

Literature Quality Evaluation

Two researchers independently evaluated the quality of researches by the criteria of observational studies designed by the Agency for Healthcare Research and Quality including 11 items, such as data sources, study settings, study participants, variables, result data, bias, sample size, quantitative variables, and statistical methods.[16] Items were scored on those specific criteria (yes = 1, no = 0, unclear = 0). Scores of 0 to 3, 4 to 7, and 8 to 11 points were defined as low, medium, and high quality, respectively. If there was disagreement, we discussed it with a third investigator to reach a consensus.

Statistical Analysis

The effect size was to derive the correlation (r) and the accompanying 95% confidence interval (CI) by applying the Comprehensive Meta-analysis software. Because of the large sample size of some included studies,[17–19] the heterogeneity was analyzed by Q statistic, but not Hedges' g.[20] When $P < .1$ or $I^2 > 50\%$, the heterogeneity between studies was large, and the random-effects model was adopted. Otherwise, the fixed-effects model is adopted. When $\alpha = .05$, $P < .05$ was considered statistically significant. Funnel plots and Egger's regression intercept test were used to assess publication bias. Because more than half of the patients in the included studies were given a diagnosis of breast cancer, this study performed a subgroup analysis based on cancer site, such as breast cancer group, mixed-type group (including but not limited to breast cancer), and other-type group.

RESULTS

Literature Search Results

The specific screening process is shown in Figure 1. Searching 9 databases identified 5492 studies. Duplicates were excluded, revealing 2271 samples of literature, and 3098 were clearly not relevant after examination of titles and abstracts. After retrieval of full texts and further evaluation, 123 studies were excluded. Finally, 35 studies were identified and retained, in which 22 studies were included in the meta-analysis.[14,15,17–19,21–37] Thirteen studies were excluded from further meta-analysis (10 cross-sectional studies,[38–47] 3 longitudinal studies[48–50]).

Characteristics of Included Studies

The total sample size of 35 studies was 13018 (ranging from 30 to 2671), and the age of study subjects ranged from 14 to 73 years. Five studies did not report the age of study subjects.[27,30,39,47,49] With regard to FCR measurement tools, 14 studies did not report reliability and validity.[15,18,24,26,29,30,32,39–41,46–49,51] The scale had items ranging from 1 to 42, and some studies measured FCR with self-written questions.[15,18,30,37,39] The main characteristics of the included research studies are shown in Table 1. On the basis of evaluation criteria of observational studies, the number of items evaluated as "yes" was higher, indicating that the quality of the study was higher. In 4 studies, the number of "yes" was less than 5.[30,34,45,52] However, no study was excluded from the systematic review because of limited quality. Table 2 shows the quality assessment of the studies in this systematic review.

Systematic Review

A total of 35 studies were included in this systematic review. The finding of studies did not reach a consistent conclusion about the correlation between FCR and RT. Twenty studies showed that no statistical significance existed between FCR and RT.[15,18,19,24,26–29,33,36,38–40,42–44,47–50] Two studies showed that receiving RT was a protective factor of FCR.[21,45] Twelve studies showed that higher levels of FCR were associated with RT.[14,17,23,25,30–32,34,35,37,46,50]

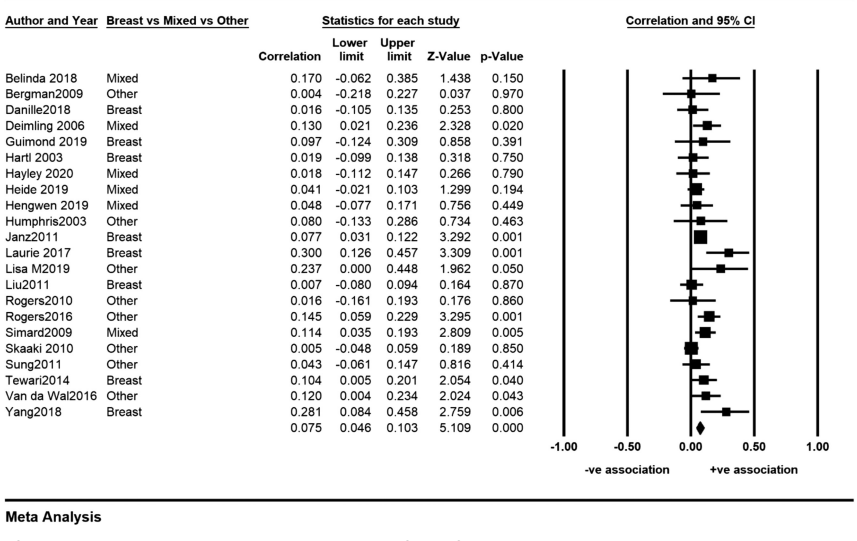

FIGURE 2. Meta-analysis of the relationship between radiotherapy and fear of cancer recurrence.

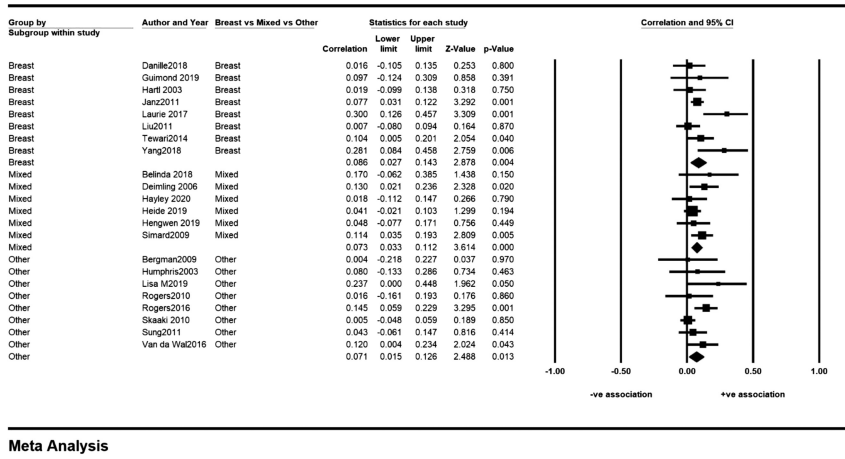

FIGURE 3. Subgroup meta-analysis of the relationship between radiotherapy and fear of cancer recurrence.

One study showed that patients' FCR correlated with RT, but there was no change of FCR in 2 years of follow-up.[41]

Meta-analysis

The meta-analysis of 22 studies was based on *P* and *r*. Heterogeneity test showed that I^2 was less than 50%, *P* = .062 was less than .1, and *Q* value was 31.751; therefore, the random-effects model was used for analysis (I^2 = 33.861, *P* = .062, *Q* value = 31.751). The total estimated correlation was 0.075 with a 95% CI of 0.046 to 0.103. The *Z* value was 5.109, and the *P* value was .000 (2-tailed). The forest map is shown in Figure 2.

The results of the subgroup meta-analysis showed that the cancer type was related to the degree of correlation. Twenty-two studies were divided into the "breast cancer group," "mixed-type group," and "other-type group" on the basis of cancer site. Results of the breast cancer group showed a stronger correlation between FCR and RT (*r* = 0.086; 95% CI, 0.027-0.143; *P* = .004), whereas results of the mixed-type group (*r* = 0.073; 95% CI, 0.033-0.112; *P* = .000) and the other-type group (*r* = 0.071; 95% CI, 0.015-0.126; *P* = .013) showed a statistically significant correlation. The forest map is shown in Figure 3. Figure 4 shows that the 22 studies were symmetrically distributed in a funnel shape. Egger's regression intercept test showed no statistically significant *P* value (intercept = 0.98995, SE = 0.54072, *T* = 1.83080, *P* = .08207), so we assume that no significant publication bias exists.

DISCUSSION

The results of the meta-analysis showed that the correlation between FCR and RT was significantly positive but weak (overall *r* = 0.075, *P* = .000). The study by Yang et al[20] included 15 studies for meta-analysis and showed that there was no statistically significant correlation between FCR and RT in the breast cancer group (*P* = .538). This systematic review showed that there was a positive correlation between FCR and RT in the breast cancer group according to 22 studies (*r* = 0.086, *P* = .004).

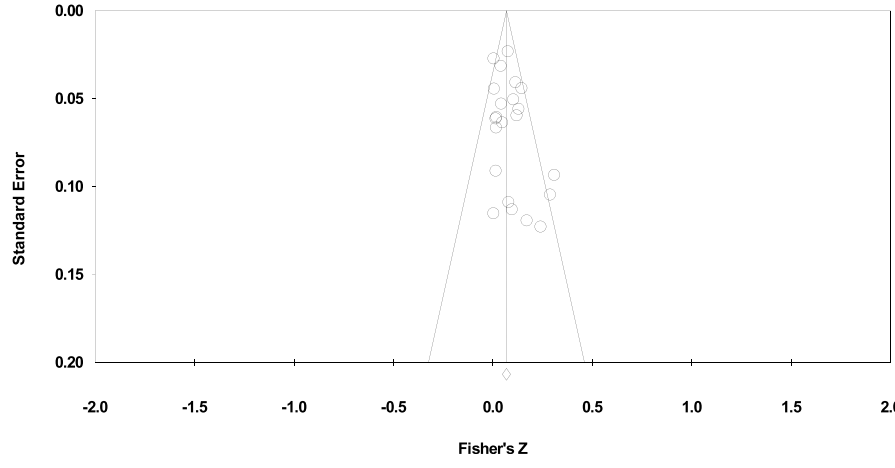

FIGURE 4. Funnel plot.

Radiotherapy is one of the important treatments for cancer patients. When shrinking the tumor, it also damages the normal tissues around the tumor, causing a series of toxic reactions, including damaged skin, oral mucositis, fatigue, and pain.[53] The theoretical model of the FCR of Lee-Jones et al[54] shows that physical symptoms are an important predisposing factor for the FCR.

Patients undergoing RT may experience a higher level of FCR, because the skin reaction caused by treatment may impair their appearance and often remind them that they have cancer ($P < .001$).[17] In addition, some patients even overinterpret common physical symptoms and regard those as signs of cancer metastasis, such as headache and sore throat. Overinterpreting symptoms will make patients worry about tumor recurrence and progression, but only 8% (4/52) of the patients were willing to express their feelings and thoughts about FCR.[27] The FCR aggravates the patient's distress and further increases physical burden, which not only damages the patient's mental health but also affects the quality of life and even shortens their survival time.[12] Therefore, we should develop targeted intervention programs, relieve patients' FCR and improve their quality of life during RT.

The results of this systematic review are limited. Because only English or Chinese literature is retrieved, nearly half of the studies do not report the reliability and validity of FCR measurement tools. Moreover, the subjects are mainly composed of White and elderly cancer patients. Therefore, the interpretation of the results should be done with caution. High-quality longitudinal investigation is still needed to explore the correlation between FCR and RT to provide a basis for clinical medical staff to construct scientific intervention programs and reduce the level of FCR.

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