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

Caner 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
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\textsuperscript{14} reported a statistically significant association between treatment type (routine, routine + boost radiation treatment) and FCR ($P = .006$). However, Wroot et al\textsuperscript{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.

![Flow diagram of the selection of the studies](https://example.com/flow_diagram.png)

**FIGURE 1.** Flow diagram of the selection of the 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 ($P = 0.75$). |
| Rabin, 2004, United States | Longitudinal | Breast | N = 69 | 48.4 (9.3) (range, 30-73) | Study-designed FoR scale | Cronbach $\alpha = 0.84$ | 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 $\alpha = 0.84$ | RT and cancer patients’ FCR ($r = 0.13$, $P \leq 0.05$). |
| 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 ($P = 0.85$). |
| 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 α = 0.95, test-retest r = 0.89 | There was a 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 α = 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 α = .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 α = 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 α = 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 α = 0.68 | There was no significant difference in FCR level between the RT group and the surgery group (Fisher Z = 1.290). |
| Koch, 2014, Germany | Cross-sectional | Breast | N = 2671 | 65 | FoP-Q Short Form (FoP-Q-SF, 12 items) | Cronbach α = 0.89 | Patients treated with radiation were less likely to experience moderate or high cancer recurrence fears (OR, 0.72 [0.55-0.94]). |
| 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-5F Cronbach $\alpha = 0.883$ | RT was unrelated to cancer patients’ FCR ($P = .449$). |

(continues)
| 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 $\alpha$ 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.
| Study                        | 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                                                           | Y                                                                                 | N                                           | N                                                                                | N                                             | N                                                                      | Y                                                                 | Y                                                               | N       | Medium |
| Leake et al, 2001           | Y                                           | Y                                                                                               | UN                                            | Y                                                           | N                                                                                 | N                                           | N                                                                                | N                                             | N                                                                      | Y                                                                 | N                                                               | Medium |
| Stanton et al, 2002         | Y                                           | UN                                                                                              | Y                                             | Y                                                           | N                                                                                 | Y                                           | Y                                                                                | N                                             | N                                                                      | Y                                                                 | N                                                               | High    |
| Humphris, 2019              | Y                                           | UN                                                                                              | Y                                             | Y                                                           | N                                                                                 | N                                           | 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                                           | N                                                                                | 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                                                                                | N                                             | Y                                                                      | Y                                                                 | Y                                                               | High    |
| Smard 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

| Study                                      | 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 Y N N N Y N Y Y                                           |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Liu et al, 2011                           | Y Y Y Y Y N N N Y Y Y                                             | Y N N N N Y Y Y Y                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | High     |
| McGinty et al, 2012                       | Y Y Y N N Y N N Y                                             | Y Y N N N Y N Y Y                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Ghazali et al, 2013                       | Y UN                                           | Y Y Y N N Y N Y Y                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Wiley et al, 2013                         | Y UN                                           | Y Y Y N N Y N Y Y                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Tewari and Chagpar, 2014                   | Y N Y Y N N N N N Y                                      | Y N N N N Y N N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Koch et al, 2014                          | Y UN                                           | Y Y Y N N UN N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Hong et al, 2015                          | Y Y Y Y N N Y N                                               | Y N N N N N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Perrucci et al, 2015                      | Y Y Y N N N N                                               | Y Y N Y Y N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | High     |
| Rogers et al, 2016                        | Y UN                                           | Y Y Y N N N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| van de Wal et al, 2016                    | Y Y Y Y N N Y N                                               | Y N N N N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | Medium   |
| Freeman-Gibb et al, 2017                  | Y Y Y Y N N N N                                               | Y N N N N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | High     |
| Starreveld et al, 2018                    | Y Y Y Y Y N N                                               | Y Y Y N N                                               |                                                   |                                                                |                                                                                                              |                                                      |                                                                                                                                  |                                                                                |                                                                                                                                  |                                                                                                                                             | High     |
| Study                  | 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   N   Y   Y   N   N   Y   Y   N   Y   Y   N   Y   Y | High                                                                                                           |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                                                                                   |         |
| Thewes et al, 2018    | Y   UN  Y   Y   N   N   UN  N   N   Y   Y   N   N   Y   Y | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Guimond et al, 2020   | Y   Y   Y   Y   N   N   Y   N   N   Y   Y   Y   Y   Y   Y | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Gotze et al, 2019     | Y   UN  Y   Y   N   N   UN  Y   N   Y   Y   Y   Y   N   Y | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Sun et al, 2019       | Y   Y   Y   Y   N   N   Y   N   N   Y   Y   Y   Y   N   N | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Wu et al, 2019        | Y   Y   Y   N   UN  UN  Y   N   N   Y   Y   Y   Y   Y   Y | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Wroot et al, 2020     | Y   N   Y   Y   N   N   N   N   N   N   N   N   Y   Y   Y | Medium                                                                                                          |                                              |                                              |                                                                                          |                                              |                                                                                   |                                                                                   |                                                                                   |                                                                                   |                      |
| Scannell et al, 2020  | Y   N   Y   Y   N   UN  UN  Y   Y   Y   N   Y   Y   N   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. 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, the heterogeneity was analyzed by $Q$ statistic, but not Hedges' $g$. 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 was 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. Thirteen studies were excluded from further meta-analysis (10 cross-sectional studies, 3 longitudinal studies).

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. The scale had items ranging from 1 to 42, and some studies measured FCR with self-written questions. 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. 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. Two studies showed that receiving RT was a protective factor of FCR. Twelve studies showed that higher levels of FCR were associated with RT.

TABLE 1. Characteristics of the included studies

| Author and Year | Study Type | FCR Measure | Sample Size | Age Range | Site |
|-----------------|------------|-------------|-------------|-----------|------|
| Belinda 2018    | Mixed      | Questionnaire | 120         | 18-73     | Breast |
| Bergman2009     | Other      | Questionnaire | 180         | 18-73     | Breast |
| Danilo2018      | Breast     | Questionnaire | 180         | 18-73     | Breast |
| Deming 2006     | Mixed      | Questionnaire | 150         | 18-73     | Breast |
| Guimond 2019    | Breast     | Questionnaire | 120         | 18-73     | Breast |
| Hall 2003       | Breast     | Questionnaire | 180         | 18-73     | Breast |
| Hasey 2022      | Mixed      | Questionnaire | 180         | 18-73     | Breast |
| Heide 2019      | Mixed      | Questionnaire | 150         | 18-73     | Breast |
| Hengen 2013     | Breast     | Questionnaire | 120         | 18-73     | Breast |
| Humphreys2003   | Other      | Questionnaire | 180         | 18-73     | Breast |
| Jan2011         | Breast     | Questionnaire | 120         | 18-73     | Breast |
| Laurie 2017     | Breast     | Questionnaire | 180         | 18-73     | Breast |
| Lisa 2009       | Other      | Questionnaire | 180         | 18-73     | Breast |
| Liou 2011       | Breast     | Questionnaire | 180         | 18-73     | Breast |
| Rogers2010      | Other      | Questionnaire | 180         | 18-73     | Breast |
| Rogers2016      | Other      | Questionnaire | 180         | 18-73     | Breast |
| Smanid2009      | Mixed      | Questionnaire | 180         | 18-73     | Breast |
| Skakel 2010     | Other      | Questionnaire | 180         | 18-73     | Breast |
| Sung2011        | Other      | Questionnaire | 180         | 18-73     | Breast |
| Tewar 2014      | Breast     | Questionnaire | 180         | 18-73     | Breast |
| Vanc 2013       | Other      | Questionnaire | 180         | 18-73     | Breast |
| Yang2015        | Breast     | Questionnaire | 180         | 18-73     | Breast |

TABLE 2. Quality assessment of the studies

| Study | Quality |
|-------|---------|
| Belinda 2018    | Medium  |
| Bergman2009     | Medium  |
| Danilo2018      | Medium  |
| Deming 2006     | Medium  |
| Guimond 2019    | Medium  |
| Hall 2003       | Medium  |
| Hasey 2022      | Medium  |
| Heide 2019      | Medium  |
| Hengen 2013     | Medium  |
| Humphreys2003   | Medium  |
| Jan2011         | Medium  |
| Laurie 2017     | Medium  |
| Lisa 2009       | Medium  |
| Liou 2011       | Medium  |
| Rogers2010      | Medium  |
| Rogers2016      | Medium  |
| Smanid2009      | Medium  |
| Skakel 2010     | Medium  |
| Sung2011        | Medium  |
| Tewar 2014      | Medium  |
| Vanc 2013       | Medium  |
| Yang2015        | Medium  |

FIGURE 2. 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 \( (I^2 = 33.861, P = .062, Q \text{ value} = 31.751) \). 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 \( (r = 0.086; 95\% \text{ CI}, 0.027-0.143; P = .004) \), whereas results of the mixed-type group \( (r = 0.075; 95\% \text{ CI}, 0.033-0.112; P = .000) \) and the other-type group \( (r = 0.071; 95\% \text{ CI}, 0.015-0.126; P = .013) \) 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 \( (\text{intercept} = 0.98995, SE = 0.54072, T = 1.83080, P = .08207) \), 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 \( (r = 0.075, P = .000) \). The study by Yang et al20 included 15 studies for meta-analysis and showed that there was no statistically significant correlation between FCR and RT in the breast cancer group \( (P = .588) \). This systematic review showed that there was a positive correlation between FCR and RT in the breast cancer group according to 22 studies \( (r = 0.086, P = .004) \).

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**FIGURE 3.** Subgroup meta-analysis of the relationship between radiotherapy and fear of cancer recurrence.
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. The theoretical model of the FCR of Lee-Jones et al. 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). 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 6% (4/52) of the patients were willing to express their feelings and thoughts about FCR. 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. 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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