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REVIEW

Global quality of life and mortality risk in patients with cancer: a systematic review and meta-analysis

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Abstract

Purpose This systematic review and meta-analysis aimed to examine the impact of global quality of life (QOL) on mortality risk in patients with cancer, considering cancer type and timepoint of QOL assessment.

Methods A systematic search was conducted using Cumulated Index to Nursing and Allied Health Literature, PubMed/MEDLINE, and Scopus databases from inception to December 2022. Observational studies that assessed QOL and examined mortality risk in patients with cancer were extracted. Subgroup analyses were performed for cancer types and timepoints of QOL assessment.

Results Overall, global QOL was significantly associated with mortality risk (hazard ratio: 1.06, 95% confidence interval: 1.05–1.07; $p < 0.00001$). A subgroup analysis based on cancer type demonstrated that lung, head and neck, breast, esophagus, colon, prostate, hematologic, liver, gynecologic, stomach, brain, bladder, bone and soft tissue, and mixed type cancers were significantly associated with mortality risk; however, melanoma and pancreatic cancer were not significantly associated with mortality risk. Additionally, global QOL was associated with mortality risk at all timepoints (pretreatment, posttreatment, and palliative phase); pretreatment QOL had the largest impact, followed by posttreatment QOL.

Conclusion These findings provide evidence that QOL is associated with mortality risk in patients with cancer at any timepoint. These results indicate the importance of evaluating the QOL and supportive interventions to improve QOL in any phase.

Keywords Quality of life · Cancer · Mortality risk · Systematic review · Meta-analysis

Introduction

In 2020, an estimated 19.3 million new cancer cases and approximately 10.0 million cancer deaths occurred globally. Cancer remains a crucial public health problem [1–3]; however, with the advances in treatment, the death rate has continued to decline [3]. It indicates that patients with cancer may spend their extended lives with physical and mental symptoms associated with cancer and its treatment; therefore, the need to consider the quality of life (QOL) in addition to the quantity of life is extremely important.

The World Health Organization defines QOL as an individual's perception of their position in life in the context of the culture and value systems where they live in relation to their goals, expectations, standards, and concerns [4]. This implies that there are multiple aspects to QOL and that global QOL is a particularly comprehensive and representative measure that reflects these multiple aspects. It has

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recently become clear that global QOL and quantity of life, including overall survival, are not independent outcomes but are related. In fact, a previous meta-analysis revealed that disease-specific QOL affects mortality in patients with heart failure [5]. In the field of cancer research, previous systematic reviews have demonstrated that QOL can be associated with mortality risk in patients with various types of cancer [6–8]; the challenge is that these studies have not yet been meta-analyzed.

Using a pooled analysis of individual patient data from clinical trials, Quinten et al. [9] showed that physical function QOL was associated with mortality risk, whereas other types of QOL, including global QOL, were not. However, previous studies have found that while global QOL is associated with mortality risk [10, 11], this does not apply to cancers such as melanoma, gynecologic cancers, and thyroid cancer [11]. Specifically, no consensus exists on the relationship between global QOL and mortality risk in patients with cancer. Additionally, these previous studies had the following challenges: only the European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) was used for the QOL measurement [9–11], only baseline QOL was assessed [9, 10], and categorization according to pre- and posttreatment perspectives was not performed [11]. To the best of our knowledge, there are no meta-analyses that comprehensively integrate all global QOL measures and examine the association with mortality risk in patients with cancer, nor are there any reports that examine cancer type or timing of QOL assessment as a subgroup.

It is hypothesized that once strong evidence of an association between global QOL and mortality risk is established and more relevant cancers and timepoints for QOL assessment are identified, the clinical indications for supportive care to improve QOL will become clearer. Hence, this study aimed to examine the impact of global QOL on mortality risk in patients with cancer, including cancer type and timepoint of QOL assessment.

Methods

This systematic review with meta-analyses was registered in the International Prospective Register of Systematic Reviews (registration number CRD 42023398206), and it followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines [12, 13].

Data searches and sources

A systematic search was conducted using the Cumulated Index to Nursing and Allied Health Literature (CINAHL), PubMed/MEDLINE, and Scopus databases from inception to December 2022 (Fig. 1). The search strategy performed in each database included QOL, EORTC QLQ-C30 [14], Medical Outcomes Study Short-Form 36-Item Health [15], and Functional Assessment of Cancer Therapy-General (FACT-G) [16], along with keywords, such as cancer, neoplasm, tumor, sarcoma, hematological malignancy, lymphoma, carcinosarcoma, leukemia, mortality, survival, relapse, and recurrence (Appendix 1 [Online Resource 1]).

Study eligibility criteria and study selection

The study eligibility criteria were as follows: (1) observational studies, (2) original human studies published in English, (3) patients with any type of cancer in various settings, and (4) studies examining the association between QOL and mortality. Studies that investigated the relationship between symptoms and mortality were excluded. After removing duplicates, seven reviewers (TF, JN, SM, JI, TO, TT, and KS) independently evaluated study eligibility by reviewing the titles and abstracts of all potential citations according to the eligibility criteria. Full-text articles were retrieved for review when there was an indication that they met the eligibility criteria or when there was insufficient information in the abstract and title to decide. The final inclusion of eligible observational studies was determined in consensus meetings where all authors participated.

Data extraction

Two reviewers (TF and JN) extracted the data. The following data were extracted from each included study: (1) first author's last name, (2) publication year, (3) nationality, (4) cancer type, (5) number of patients, (6) sex, (7) age, (8) follow-up period, (9) number of deaths, (10) covariates adjusted in the multivariate analysis, and (11) risk estimates for mortality (hazard ratio [HR] and 95% confidence interval [CI]). When several different models of multivariate analyses were indicated, we used the results from the multivariate model with the most complete adjustment for potential confounders.

Quality assessment

The quality assessment of studies, including their risk of bias, was conducted using the Newcastle–Ottawa scale [17]. This tool includes the following eight domains: representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, demonstration that the outcome of interest was not present at the start of the study, comparability of cohorts based on the design or analysis, assessment of outcome, whether the follow-up was sufficiently long for outcomes to occur, and adequacy of cohort follow-up. Two trained reviewers (TF and JN) scored each item according to the criteria [17]. Potential disagreements

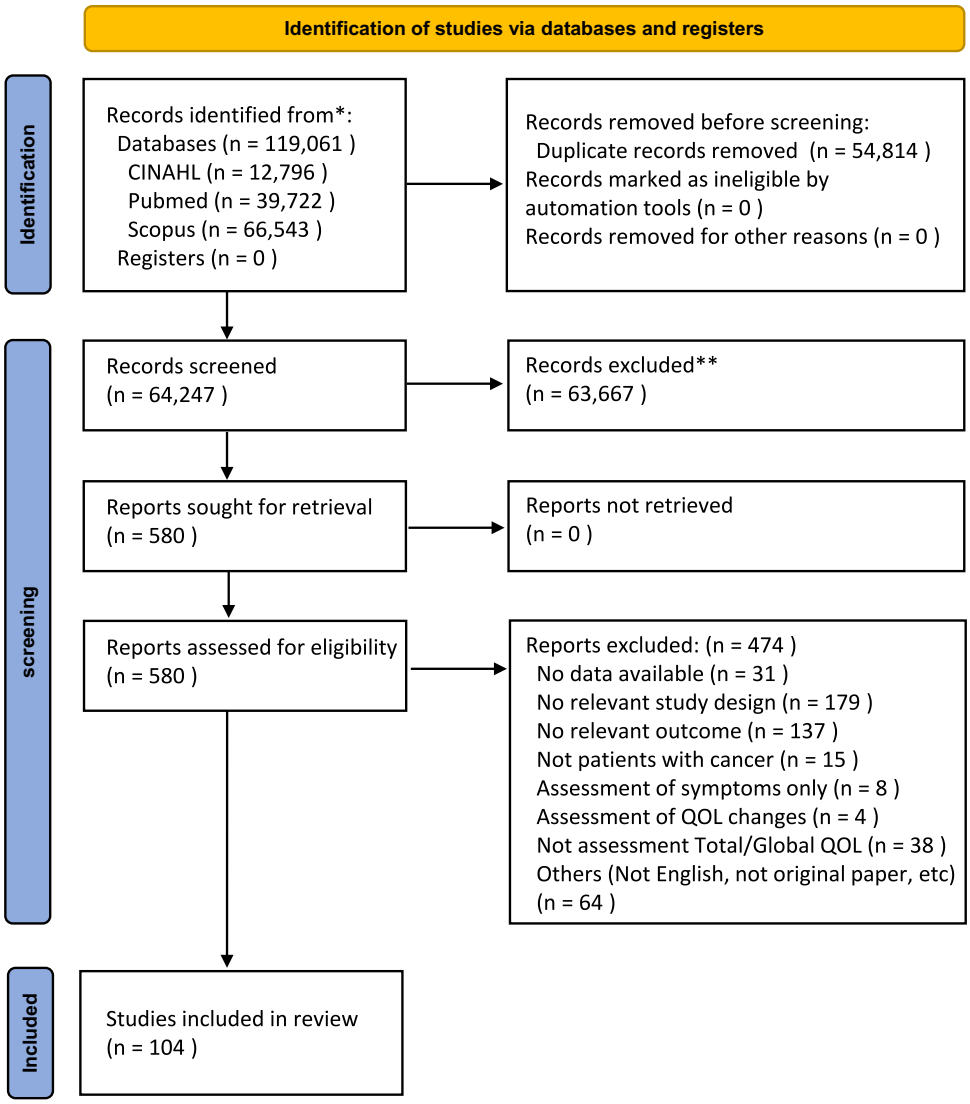

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses study flow diagram of the selection process

were resolved during consensus meetings attended by all authors.

Data analysis

Risk estimates of total mortality related to global QOL were analyzed for each type of cancer (lung, head and neck, breast, liver, esophagus, prostate, hematologic, colon, gynecologic, stomach, brain, melanoma, bladder, pancreas, and bone and soft tissue, and mixed type), and all types of cancer were subsequently pooled. In an additional analysis, we investigated the association between global QOL and total mortality during QOL evaluation (pretreatment, posttreatment, and palliative phase). In this study, posttreatment was defined as both during and after treatment. We used adjusted HRs and 95% CIs in multivariate analysis as a measure of the effect size for all studies. The univariate HR was only used if it was reported, rather than the multivariate HR. Inverse variance-weighted averages used the natural logarithmic HR, and the standard error was calculated using a random-effects model. Moreover, we assessed the heterogeneity using the I^2 statistic. All statistical analyses were performed using Review Manager version 5.1 (RevMan; The Cochrane Collaboration, London, UK).

Results

The literature search yielded 119,061 articles; this was reduced to 64,247 articles after excluding duplicates. Based on the screening of titles and abstracts, 580 articles were deemed eligible and underwent full-text review. Overall, 104 articles were identified and determined to be suitable for meta-analysis after review (Fig. 1).

Study characteristics

Characteristics of included studies are summarized in Appendix 2 [Online Resource 1]. This meta-analysis included any type of cancer, such as lung [18–38], head and neck [39–49], breast [50–60], liver [22, 61–66], esophagus [67–73], prostate [23, 74–79], hematologic [80–86], colon [87–95], gynecologic [96–98], stomach [99–101], brain [102–104], melanoma [60, 105, 106], bladder [107, 108], pancreas [109, 110], bone and soft tissue [111], and mixed type cancers [112–121]. QOL was evaluated using the EORTC QLQ-C30 [14, 18, 19, 21, 26–30, 32, 36, 37, 41, 42, 45, 47–53, 55, 58, 61, 63, 65–67, 69–74, 76, 79–81, 84, 85, 87, 88, 90, 91, 94, 95, 97–99, 102, 106–111, 113, 118, 121, 38], FACT-G [16, 20, 22, 23, 57, 62, 77, 82, 83, 92, 93, 96, 103, 104, 114, 117], EuroQOL Five Dimensions [43, 86, 100, 112, 122], Lung Cancer Symptom Scale [24, 25, 31, 34, 35, 123], Rotterdam Symptom Checklist [68, 105, 120, 124], Spitzer Quality of Life Index [33, 44, 60, 64, 125], Quality of Life Index [56, 75, 89, 110], European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care [115, 116, 126], QOL for Cancer Patients Treated with Anti-Cancer Drugs [59, 127], self-rated health [78, 119], Auckland Quality of Life Questionnaire [40, 128], General Quality of Life Inventory-74 [54], General Health Questionnaire with Health versus Disease scoring [46], QOL-20 [101], and Neck Radiotherapy Questionnaire [44, 129]. The follow-up period ranged from 1 month to 8.5 years.

Risk of *bias* assessment

The risk of bias was assessed using the Newcastle–Ottawa scale. Of the included studies, 61, 41, and 2 were considered high (8–9 points), moderate (6–7 points), and low quality, respectively (Appendix 3 [Online Resource 1]).

Impact of global QOL on mortality risk

Overall, 124 datasets from 104 studies were included in a random-effects meta-analysis. The effect of global QOL on mortality risk was estimated using a forest plot of inverse HR and 95% CI. Ultimately, global QOL was significantly associated with mortality risk (HR: 1.06, 95% CI 1.05–1.07, $p < 0.00001$, $I^2 = 86\%$; Fig. 2). A subgroup analysis based on cancer type demonstrated that lung (HR: 1.10, 95% CI 1.07–1.13, $p < 0.00001$, $I^2 = 88\%$), head and neck (HR: 1.09, 95% CI 1.06–1.12, $p < 0.00001$, $I^2 = 81\%$), breast (HR: 1.03, 95% CI 1.01–1.04, $p = 0.001$, $I^2 = 79\%$), esophagus (HR: 1.03, 95% CI 1.01–1.04, $p = 0.0002$, $I^2 = 76\%$), colon (HR: 1.12, 95% CI 1.06–1.17, $p < 0.00001$, $I^2 = 94\%$), prostate (HR: 1.10, 95% CI 1.04–1.17, $p = 0.002$, $I^2 = 82\%$), hematologic (HR: 1.05, 95% CI 1.01–1.10, $p = 0.02$, $I^2 = 68\%$), liver (HR: 1.20, 95% CI 1.08–1.35, $p = 0.001$, $I^2 = 89\%$), gynecologic (HR: 1.15, 95% CI 1.01–1.31, $p = 0.03$, $I^2 = 81\%$), stomach (HR: 1.79, 95% CI 1.34–2.38, $p < 0.0001$, $I^2 = 0\%$), brain (HR: 1.05, 95% CI 1.02–1.08, $p = 0.003$, $I^2 = 0\%$), bladder (HR: 1.98, 95% CI 1.57–2.50, $p < 0.00001$, $I^2 = 0\%$), bone and soft tissue (HR: 8.29, 95% CI 3.13–21.98, $p < 0.0001$), and mixed type cancers (HR: 1.03, 95% CI

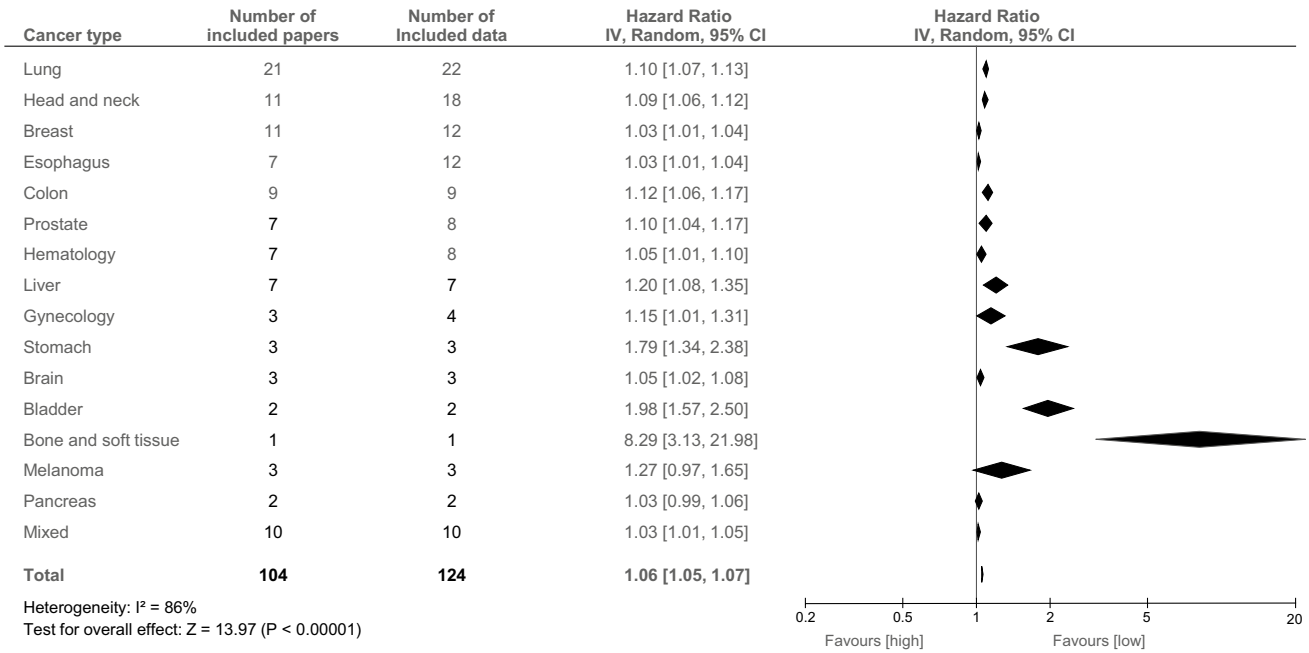

Fig. 2 Meta-analysis of the impact of global quality of life on mortality risk in patients with cancer

1.01–1.05, p = 0.009, I^2 = 94%) were significantly associated with mortality risk; conversely melanoma (HR: 1.27, 95% CI 0.97–1.65, p = 0.08, I^2 = 89%) and pancreatic cancer (HR: 1.03, 95% CI 0.99–1.06, p = 0.11, I^2 = 18%) were not significantly associated with mortality risk (Appendix 4 [Online Resource 1]).

Impact of global QOL on mortality risk classified based on the time of evaluation

Pretreatment global QOL

A meta-analysis of 80 datasets from 74 studies showed that pretreatment global QOL was significantly associated with mortality risk (HR: 1.06, 95% CI 1.05–1.07, p < 0.0001, I^2 = 84%; Fig. 3).

Posttreatment global QOL

A meta-analysis of 30 datasets from 24 studies showed that posttreatment global QOL was significantly associated with mortality risk (HR: 1.06, 95% CI 1.04–1.08, p < 0.00001, I^2 = 85%; Fig. 3).

Palliative phase global QOL

A meta-analysis of five datasets from five studies revealed that palliative phase global QOL was significantly associated with mortality risk (HR: 1.04, 95% CI 1.01–1.06, p = 0.009, I^2 = 89%; Fig. 3).

Global QOL was associated with mortality risk at all timepoints (pretreatment, posttreatment, and palliative phase). The largest effect size was for pretreatment QOL (Z = 2.61), followed by posttreatment QOL (Z = 6.28). Although palliative phase QOL was significantly associated with mortality risk, the effect size was relatively small (Z = 2.61; Fig. 3).

Discussion

To the best of our knowledge, this is the first study to reveal the impact of global QOL on mortality risk in patients with cancer, including cancer type and timepoint of QOL assessment. Insufficient evidence exists regarding the relationship between QOL and prognosis in patients with cancer, presenting an issue worth consideration. The main findings of this study were as follows: global QOL is significantly associated with mortality risk in patients with cancer; the relationship between global QOL and mortality risk varies according to cancer type; global QOL is associated with mortality risk at all timepoints (pretreatment, posttreatment, and palliative phase); and pretreatment QOL had the largest impact, followed by posttreatment QOL.

In addition to survival, QOL is one of the most crucial outcomes, particularly in the setting of advanced disease [10]. Therefore, the relationship between QOL and prognosis has attracted increasing attention. A previous pooled analysis study reported the association between QOL and survival in patients with cancer [10]. Although results on the relationship between QOL and prognosis varied among the included studies, and heterogeneity was found after pooling, our meta-analysis revealed that global QOL is significantly associated with mortality risk for any type of cancer, similar to previous research. While the association between QOL and prognosis may be influenced by various factors, including the progression of occult disease and the gradual deterioration of the biological/physiological status of the patients studied, more than 90% of the articles in this meta-analysis controlled for confounding factors, and more than 80% had a sufficient follow-up period. These observations suggest the importance of focusing on QOL when confronting patients with cancer. However, the mechanism of the association between QOL and mortality remains unclear. Previous studies have demonstrated that age [130–132], clinical stage [130–132], symptoms [130], psychosocial problems [130, 132], physical activity [130], and nutritional status [130] were factors associated with QOL in patients with cancer. Global QOL is an indicator that includes these factors and is reported to be associated with prognosis; however, it remains unclear as to which of these concepts related to global QOL may be acting as confounding variables; therefore, identifying these factors acting as confounders warrants further study.

This study aimed to examine the association between global QOL and prognosis based on cancer type; lung, head and neck, breast, esophagus, colon, prostate, hematologic, liver, gynecologic, stomach, brain, bladder, and bone and soft tissue cancers were significantly associated with mortality risk. In addition to cancers that were significant in previous studies (colorectal, rectal, prostate, and hematological malignancies) [11], global QOL in this study was associated with mortality risk for several cancers. Additionally, although not significant in a previous study [11], this association was found to be significant for gynecological cancer in our study, adding to the body of evidence. Nevertheless, this association was not significant for melanoma or pancreatic cancer. Similar to our results, the aforementioned previous study also reported that melanoma was not significant [11]. Determining why only melanoma and pancreatic cancer were not predictors of mortality risk is challenging. This may be because survival rates for these cancers are low. Additionally, fewer original articles exist for this type of cancer; therefore, the relationship between QOL and prognosis may not have been adequately examined.

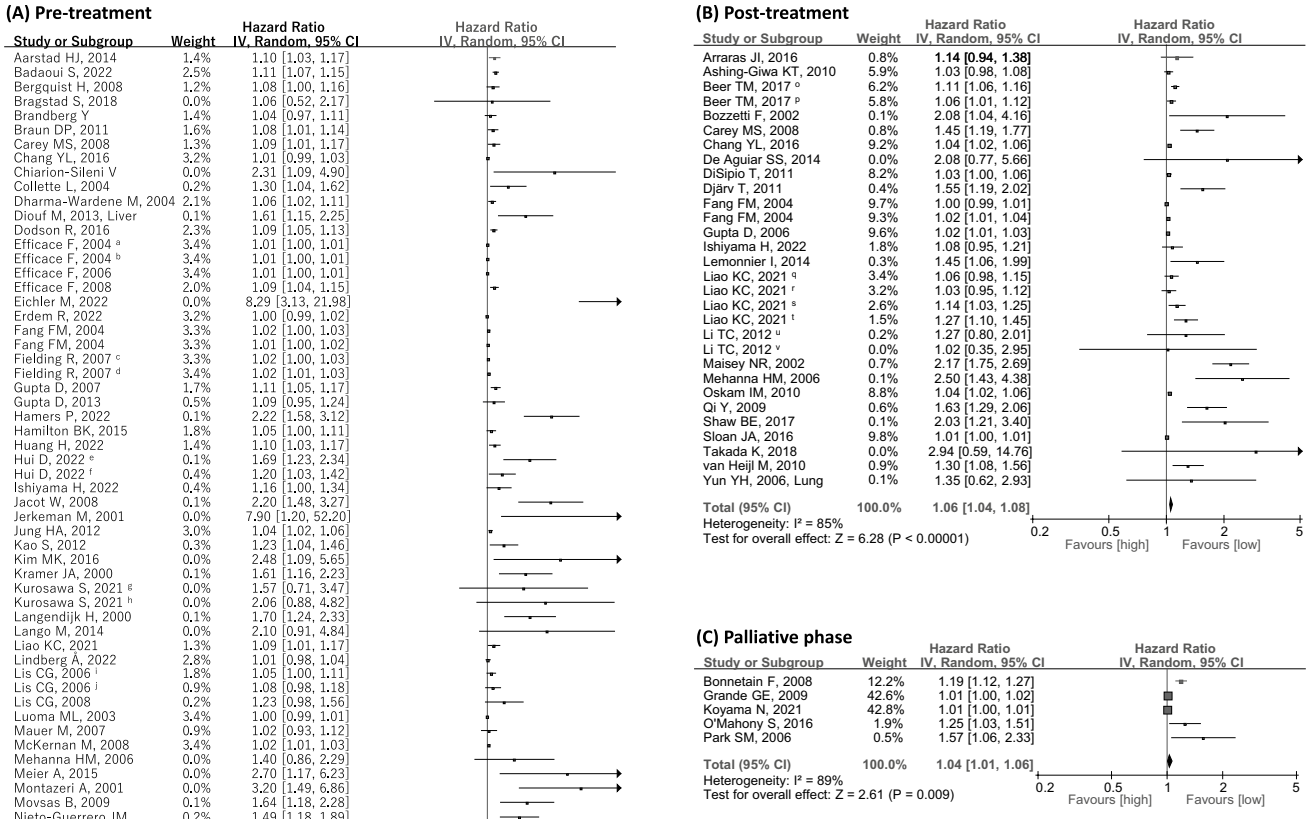

Fig. 3 Meta-analysis of the impact of global quality of life on mortality risk classified according to the time of evaluation. [a]Baseline health-related quality-of-life data as prognostic factors in a phase III multicenter study of women with metastatic breast cancer [52], [b]health-related quality of life parameters as prognostic factors in a nonmetastatic breast cancer population: an international multicenter study [53], [c]liver, [d]lung, [e]lung, [f]prostate, [g]EuroQol 5 Dimension (index), [h]EuroQol 5 Dimension (visual analog scale), [i]colon, [j]pancreas, [k]advanced, [l]curable, [m]Head and Neck Radiotherapy Questionnaire, [n]Spitzer Quality of Life Index, [o]AFFIRM study, [p]PREVAIL study, [q]during treatment, [r]3 months posttreatment, [s]1 year posttreatment, [t]2 years posttreatment, [u]nonsurgery, and [v]surgery

By focusing on the timepoints of QOL assessment, global QOL was found to be associated with mortality risk at all timepoints (pretreatment, posttreatment, and palliative phase). Although the relationship between baseline QOL and prognosis has been investigated, no reports have examined the relationship by timepoint, including the pretreatment, posttreatment, and palliative phases, which we believe to be of interest. Given that global QOL is associated with mortality risk at all timepoints, the importance of evaluating the QOL for any phase of cancer is supported. Furthermore, the effect size by timepoint showed that pretreatment QOL had the highest effect size. Therefore, improving QOL before treatment is important and should be addressed.

Previous studies have demonstrated that supportive care improves QOL in patients with cancer [133–136]. Rehabilitation, which is a form of supportive care, is also considered important before treatment (prehabilitation), and its effectiveness on QOL has been examined [137]. Furthermore, our results demonstrate that posttreatment QOL had the second highest effect size on mortality risk. This suggests that supportive care aimed at improving QOL should be seamless from pretreatment to posttreatment. Although QOL is an important outcome measure, this study is meaningful as it clarifies that global QOL is both an outcome and a prognostic factor in the palliative phase. A previous study showed that palliative care led to significant improvements in QOL and survival [138]. During this phase, patients and their families can benefit from an extended period of high QOL. Considering the above, it is important to periodically conduct a global QOL assessment throughout the pretreatment, posttreatment, and palliative phases, as well as provide supportive care to improve global QOL based on the results of these assessments.

This review has some limitations. First, we used the CINAHL, PubMed/MEDLINE, and Scopus databases for the search. Although this appears to have yielded a sufficient number of articles, the possibility that more articles could have been extracted using additional databases cannot be ruled out. Second, this review was limited to studies published in English; relevant studies published in other languages may offer other findings. Finally, the papers included in this study were varied, and QOL assessment methods were mixed; therefore, heterogeneity was observed.

Conclusions

Global QOL is significantly associated with mortality risk in patients with cancer. Regardless of the phase, a significant relationship was observed between global QOL and mortality risk. These results indicate the importance of periodically evaluating the global QOL at all phases of treatment, as well as supportive care to improve global QOL. Further studies are needed to understand the mechanisms and association between QOL and prognosis in patients with cancer.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11136-024-03691-3.

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Author contributions TF and JN made substantial contributions to the conception and design. TF and JN were accountable for the collection and assembly of data. TF, JN, SM, JI, TO, TT, and KS performed the literature search and data analysis. TF and JN were major contributors in drafting and writing the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests The authors declare that they have no competing interests.

Ethical approval Not applicable.

Consent for publication Not applicable.

Data availability The datasets used and/or analyzed during this study are available from the corresponding author upon reasonable request.

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