Nurse-led interventions on quality of life for patients with cancer
A meta-analysis

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Abstract

Background: To compare the quality of life outcome between nurse-led and non-nurse-led interventions for patients with cancer using a meta-analysis.

Methods: A systematic literature review was performed by searching randomized controlled trials about nurse-led interventions in PubMed, EMBASE, and Cochrane Library databases until June 2017. Pooled summary estimates for quality of life outcome was calculated as standardized mean difference (SMD) either on a fixed- or random-effect model via Stata 13.0 software.

Results: Seven literatures involving 1110 patients (554 in the nurse-led group and 556 in the control group) were included. Pooled analysis showed there were no differences in the global quality of life, cognitive, emotional, role, social and physical functions, appetite loss, diarrhea, and dyspnea scales of Quality of Life Questionnaire C30 version 3.0 core (QLQ-C30) questionnaires between the nurse-led and control groups. However, the nurse-led management program significantly decreased the occurrence of constipation (SMD = –0.36, 95% CI = –0.71 to –0.00; P = .001) and insomnia (SMD = –0.33, 95% CI = –0.99 to 0.32; P = .011) and reduced the financial difficulty (SMD = –0.34, 95% CI = –0.65 to –0.03; P = .033) for patients with cancer.

Conclusion: The nurse-led disease management strategy seemed to be effective to improve constipation, insomnia, and financial impacts for patients with cancer in quality of life assessment.

Abbreviations: CI = confidence intervals, EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 version 3.0 core questionnaire, PRISMA = Preferred Reporting Items for Systematic Review and Meta-analysis, QLQ-CRP29 = Quality of Life Questionnaire for colorectal cancer, QLQ-EN24 = Quality of Life Questionnaire for endometrial cancer, QLQ-ES18 = Quality of Life Questionnaire for oesophageal cancer, QLQ-OG25 = Quality of Life Questionnaire for gastric cancer, QoL = quality of life, RCTs = randomized controlled trials, SMD = standardized mean difference.

Keywords: cancer, constipation, financial difficulty, insomnia, nurse-led, Quality of Life Questionnaire C30 version 3.0 core questionnaire, quality of life

1. Introduction

Cancer is a major public health issue and is the leading cause of death worldwide, with an estimated 14,100,000, 1,688,780, 4,292,000, 217,057 new cancer cases and 8,200,000, 600,920, 2,814,000, 76,611 cancer deaths worldwide in 2012[1] or in the United States in 2017,[2] China in 2015,[3] and Korea in 2014,[4] respectively. Great advances have been achieved for cancer treatment, including surgery, chemotherapy, radiotherapy, or the combination of all 3 modalities. However, these treatments more or less induce some side effects (such as appetite loss, fatigue, and diarrhea) and cause feelings of depression, loneliness, hopelessness, worthlessness, or suicidal ideation, all which contribute to their reduced quality of life (QoL).[5,6] Several studies have demonstrated QoL is an excellent predictor for prognosis, where the reduced QoL is positively associated with shorter survival time.[7–9] Thus, how to improve the QoL has been one of the most important concerns for patients with cancer.

Recently, accumulating evidence suggests a nurse-led disease management program may provide more comprehensive care, including symptom management, psychological and/or social support, lifestyle changes, health education, support, tailored coaching, and follow-up.[10,11] Thus, a nurse-led strategy may be more effective for improving the QoL, which has been demonstrated by several studies.[12,13] However, controversial conclusions remain present among different studies. For example, Malmström et al[14] reported no significant difference between the nurse-led intervention group and the control regarding general quality of life for the function or symptom scales of the European Organization for Research and Treatment of Cancer
Quality of Life Questionnaire C30 version 3.0 core questionnaire (EORTC QLQ-C30) except for dyspnoea where the intervention group scored significantly higher compared with the control group. The study of Lin et al.\(^\text{11}\) revealed a significant difference in the 3 multi-item function scales (cognitive, emotional, and social), quality of life scale, and 5 symptom scales (fatigue, pain, insomnia, constipation, and financial impact) of QLQ-C30 between the nurse-led and control groups. This phenomenon may be attributed to the small sample size in each of the above-mentioned studies. Therefore, the aim of this study was to further comprehensively evaluate the efficacy of the nurse-led disease management programs in improving the QoL for patients with cancer using a statistical meta-analysis to synthesize all data on the nurse-led effects.

2. Methods

Ethical approval was waived for this meta-analysis because the data we extracted were open-access from individual studies that had obtained ethics approval. This review procedure was conducted according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) Guidelines.\(^\text{16}\)

2.1. Search strategy

All relevant articles were identified by systematical searches of electronic databases of PubMed, EMBASE, and Cochrane Library until June 2017. The used search strategies were: (“cancer” OR “carcinoma”) AND (“nurse-led” OR “nursing-led”). Furthermore, the reference lists of retrieved articles were also reviewed to manually obtain other potentially relevant articles.

2.2. Selection criteria

Articles eligible in this meta-analysis had to meet the following inclusion criteria: patients treated for cancer; prospective randomized controlled trials (RCTs) comparing the impact of the nurse-led with non-nurse-led disease management program; complete, detail research data for QoL outcomes assessed using any well validated QoL instrument or its derivatives preoperatively and postoperatively; only English publication languages; and original studies. Exclusion criteria were as follows: not RCT, such as case or cohort studies; studies unavailable to obtain a full-text form; studies not providing adequate data for QoL assessment; and studies using incompatible QoL instrument.

2.3. Data extraction and quality assessment

Two reviewers independently screened eligible studies from the databases and extracted the following data: authors, publication year, region of the study, research design, sample size, intervention and control details (description of intervention, intervention period, and follow-up time), and QoL outcomes (EORTC QLQ-C30, the most common, core questionnaire used to measure cancer-related QoL; and its cancer specific derivatives, including EORTC QLQ-OG25 for gastrointestinal cancer, etc.).\(^\text{17}\)

The quality of the RCTs was assessed by 2 reviewers independently according to the following 7 items:\(^\text{18}\) including a truly random allocation method used; the allocation concealment performed; comparable baselines between 2 groups; clear inclusion and exclusion criteria; blinding evaluation of the outcomes performed; the number and reason of withdrawals and dropouts in each group demonstrated; and the intention to treat analysis used. Each item with “yes” was scored 2, “partly yes” 1.5, “unclear” 1, and “no” 0. Studies with a total score >10 were regarded to have lower possibilities of biases. Any discrepancy during data extraction and quality assessment was resolved through discussion or consultation with a third researcher.

2.4. Statistical analysis

Meta-analysis was conducted by Stata 13.0 software (STATA Corporation, College Station, TX). Heterogeneity was assessed with the \(\chi^2\) based \(Q\) statistic and corresponding \(P\)-value to evaluate the dispersion of the true effect among the recruited studies.\(^\text{17}\) \(P < .1\) was considered statistically significant and then a random-effects model was used for meta-analysis; otherwise, a fixed-effects model was chosen to pool the study results. The \(I^2\) statistic was used to indicate the proportion of heterogeneity among study estimates.\(^\text{20}\) A standardized mean difference (SMD) and 95% confidence intervals (CIs) were calculated for effect size. Possible publication bias was estimated by using the Egger test.\(^\text{21}\) Sensitivity analysis was conducted using the trim and fill method and formalized as funnel plots to detect the effects of publication bias on the results.\(^\text{12}\) \(\text{SMD} < .05\) was considered to be statistically significant.

3. Results

3.1. Description of studies

The flow diagram of the literature search is shown in Fig. 1. Seven RCTs with a total of 1110 patients (554 in the nurse-led group and 556 in the control group) were ultimately considered to be eligible according to the inclusion and exclusion criteria.\(^\text{14,13,23-27}\) The characteristics of the included studies are presented in Table 1. Two studies included patients with esophageal cancer, 2 included patients with breast cancer,\(^\text{23,27}\) and the other included patients with endometrial cancer,\(^\text{23}\) acute lymphoblastic leukemia,\(^\text{13}\) and colon or rectal cancer,\(^\text{25}\) respectively. Five studies were performed in Europe\(^\text{14,24-27}\) and 2 in Asia.\(^\text{15,23}\) All studies applied the questionnaires of the QLQ-C30 to evaluate the QoL. Due to the difference in cancer type, the QLQ-C30 derivatives were different. The last follow up duration varied from 9 weeks to 18 months. According to the quality assessment score, all the included trials were of high quality (Table 2).

3.2. Main outcomes

QLQ-C30\(^\text{17}\) consists of 2-item global quality of life scale; 5 multi-item function scales, including cognitive, emotional, physical, role, and social; 6 single-item symptom scales for appetite loss, constipation, diarrhea, dyspnea, financial impact, and insomnia; and 3 multi-item symptom scales for fatigue, pain, nausea, and vomiting. Thus, they were respectively tested for meta-analysis.

Global quality of life was evaluated in 6 studies. Obvious heterogeneity was found across these 6 trials (\(Q\) value = 20.19, \(df = 5\), \(P = .001\); \(I^2 = 75.2\)%; \(\tau^2 = 0.0908\)) and thus a random-effects model was performed. The pooled results suggested that there was no difference in the global quality of life (SMD = 0.17, 95% CI = −0.12 to 0.45; \(P = .255\)) between patients undergoing nurse-led management and not.

Six studies assessed the function status of the cognitive and social, but 7 for emotional and role. Obvious heterogeneity...
Figure 1. Flow diagram of literature screening process.

### Table 1
Characteristics of included studies.

| Study     | Year | Country | Cancer type                     | Intervention group                                                                 | Control group                  | Duration of intervention | QoL questionnaires | Time points of data collection |
|-----------|------|---------|---------------------------------|------------------------------------------------------------------------------------|--------------------------------|------------------------|---------------------|-------------------------------|
| Kim[23]   | 2017 | Korea   | Breast cancer                   | Education, behavioral training, stress management, cognitive therapy, emotional support (n = 30) | Routine discharge care (n = 30) | 7 weeks                | QLQ-C30             | Baseline; 6 w later; 9 w later |
| Beaver[24] | 2017 | England | Endometrial cancer              | Telephone supportive care (n = 129)                                                  | Conventional care (n = 130)   | 12 months             | QLQ-C30; QLQ-EN24     | Baseline; 3–6 m later         |
| Malmström[14] | 2016 | Sweden  | Oesophageal cancer              | Telephone supportive care (n = 41)                                                   | Conventional care (n = 41)   | 6 months              | QLQ-C30; QLQ-OG25; QLQ-INF025 | Baseline; 2 w later; 2 m later; 4 m later; 6 m later |
| Lin[15]   | 2016 | China   | Acute lymphoblastic leukemia    | Nurse-led (in-hospital care, follow-up support, and relatives and caregivers received training) (n = 40) | Traditional doctor-led (only in-hospital care) (n = 40) | 1.5 years             | QLQ-C30             | Baseline; 6 m later; 12 m later; 18 m later |
| Jefford[25] | 2016 | Australia | Colon or rectal cancer       | Survivor care (telephone follow-up, face-to-face end-of-treatment session, etc.) (n = 110) | Usual care (n = 111)         | 6 months              | QLQ-C30; QLQ-CR29     | Baseline; 8 w later; 6 m later |
| Kimman[27] | 2011 | Netherlands | Breast cancer                | Nurse-led follow-up (n = 150)                                                          | Hospital follow-up (n = 140) | 12 months             | QLQ C-30           | Baseline; 3 m later; 6 m later |
| Verschuur[26] | 2009 | Netherlands | Oesophageal or gastric cardia cancer | Nurse-led follow-up (home visit) (n = 54)                                              | Hospital follow-up (n = 140) | 12 months             | QLQ-C30; QLQ-OES18   | Baseline; 12 m later; Base line; 7 m later; 13 m later |

EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 version 3.0 core questionnaire, m = month, QLQ-CR29 = Quality of Life Questionnaire for colorectal cancer, QLQ-EN24 = Quality of Life Questionnaire for endometrial cancer, QLQ-OG25 = Quality of Life Questionnaire for oesophageal cancer, QLQ-OES18 = Quality of Life Questionnaire for gastric cancer, QoL = quality of life, w = week.
Dyspnea, the symptom scales of appetite loss, constipation, diarrhea, financial impact, and insomnia. No heterogeneity was detected across these 4 trials for appetite loss (Q value = 2.21, df = 3, P = .531; I² = 0.0%), diarrhea (Q value = 2.13, df = 3, P = .545; I² = 0.0%), but a significant heterogeneity was for constipation (Q value = 9.46, df = 3, P = .024; I² = 68.3%), dyspnea (Q value = 10.40, df = 3, P = .015; I² = 71.2%), financial impact (Q value = 7.34, df = 3, P = .062; I² = 59.1%), and insomnia (Q value = 31.65, df = 3, P = .000; I² = 90.3%). Therefore, a fixed or random-effects model was adopted, respectively.

The pooled analysis showed there was no difference in appetite loss (SMD = 0.07, 95% CI = -0.11 to 0.25; P = .452), diarrhea (SMD = 0.02, 95% CI = -0.20 to 0.16; P = .838), and dyspnea (SMD = 0.12, 95% CI = -0.24 to 0.49; P = .359) between patients undergoing nurse-led management and not, but the nurse-led management strategy significantly decreased the occurrence of constipation (SMD = -0.36, 95% CI = -0.71 to -0.00; P = .001) (Fig. 2) and insomnia (SMD = -0.33, 95% CI = -0.99 to 0.32; P = .011) (Fig. 3), and reduced the financial difficulty (SMD = -0.34, 95% CI = -0.65 to -0.03; P = .033) (Fig. 4).

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**Table 2**

Methodologic quality of included randomized controlled trial studies.

| Study     | Year | Truly random | Concealed allocation | Baseline features | Eligibility criteria | Blinding assessment | Loss to follow-up | Intention to treat | Study quality scores |
|-----------|------|--------------|----------------------|-------------------|----------------------|---------------------|-------------------|-------------------|---------------------|
| Kim[23]   | 2017 | Yes          | Yes                  | Yes               | Yes                  | Yes                 | Yes               | Yes               | 14                  |
| Beaver[24]| 2017 | Yes          | Yes                  | Yes               | Clear               | Yes                 | Yes               | No                | 10                  |
| Malmström[14] | 2016 | Yes          | Unclear             | Yes               | Yes                  | Unclear             | Yes               | No                | 10                  |
| Lin[15]   | 2016 | Yes          | Unclear             | Unclear           | Yes                  | Yes                 | Yes               | Yes               | 14                  |
| Jefford[25] | 2016 | Yes          | Yes                  | Yes               | Yes                  | Yes                 | Yes               | No                | 11                  |
| Verschuur[26] | 2017 | Yes          | Unclear             | Yes               | Yes                  | Clear               | Yes               | Yes               | 11.5                 |

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Figure 2. Forest plots for constipation between the nurse-led and non-nurse-led groups. CI = confidence intervals, SMD = standardized mean difference.
Figure 3. Forest plots for insomnia between the nurse-led and non-nurse-led groups. CIs = confidence intervals, SMD = standardized mean difference.

Figure 4. Forest plots for financial impact between the nurse-led and non-nurse-led groups. CIs = confidence intervals, SMD = standardized mean difference.
Six RCT trials were included in the meta-analysis to evaluate the symptom scales of fatigue, pain, nausea, and vomiting. A significant heterogeneity was observed for fatigue (Q value = 23.41, df = 5, P = .000; I² = 78.6%) and pain (Q value = 11.15, df = 5, P = .048; I² = 55.2%), but no heterogeneity for nausea and vomiting (Q value = 7.47, df = 5, P = .188; I² = 33.0%). Hereby, a random-effects or fixed model was utilized, respectively. The combined results indicated the nurse-led management strategy had no significant influence on the fatigue (SMD = −0.03, 95% CI = −0.35 to 0.28; P = .841), pain (SMD = 0.05, 95% CI = −0.16 to 0.27; P = .624), nausea and vomiting (SMD = −0.08, 95% CI = −0.22 to 0.06; P = .264) of patients with cancer.

3.3. Publication bias and sensitivity analysis

Egger test (Fig. 5) indicated no publication bias in the global quality of life (P = .219), cognitive (P = .887), emotional (P = .521), physical (P = .524), role (P = .337), social (P = .466), appetite loss (P = .694), constipation (P = .673), diarrhea (P = .350), dyspnea (P = .859), insomnia (P = .715), financial impact (P = .997), fatigue (P = .344), pain (P = .715), nausea, and vomiting (P = .813). When we reperformed the meta-analyses using a trim and fill method in sensitivity analyses (Fig. 6), the results remained the same as the primary analyses, further indicating our results were statistically stable and reliable.

4. Discussion

Although there have been systematic review studies to investigate the effects of nurse-led management programs for patients with cancer, 6,10–14,28–29 few of them explored the influence on the patients’ QoL. 11,31 In the study of Lewis et al, 11,2 studies 13,30 were included, but they were excluded in our study because no efficient data could be obtained in them, for example, data were expressed as median (interquartile ranges) 13 or min–max, not standard deviation. 30 While the study of Suh et al 10 included the RCT and non-RCT literatures 31 by February 2016 and the assessment criterions of them were inconsistent (Functional Assessment of Cancer Therapy—Colorectal 32; Functional Assessment of Cancer Therapy Scale—General 33). In this study, we, for the first time, focused only on the RCT to perform a meta-analysis in order to survey the effects of nurse-led management programs on the QoL for patients with cancer. All our included RCT articles evaluated the QoL using the common, core questionnaire EORTC QLQ-C30. Our study indicated that the nurse-led management programs significantly decreased the occurrence of constipation (P = .001) and insomnia (P = .011) and reduced the financial difficulty (P = .033) for patients with cancer, but had no effects on other scales of QLQ-C30.

Constipation is a common problem following chemotherapy (such as opioid, vincristine), with an estimated incidence of approximately 50% in patients with cancer. 15,35 It is speculated that this may be related with the alteration in the composition of the microflora in the stomach and duodenum (e.g., decreased quantity of Lactobacillus, Bifidobacterium, Bacteroides, but increased quantity of different pathogenic microorganisms), 36 the pH of the intestinal environment, and the damage to the gastrointestinal tract propulsion. 37 Thereby, prevention of constipation is one of important goals when designing the nurse-led management program to enhance QoL in cancer patients. As expected, our study showed the nurse-led strategy significantly decreased the mean constipation score compared with the control group, which was in accordance with previous studies. 15,38,39

Insomnia is also a common complaint among cancer patients, affecting 30% of the population. 39 Insomnia activates the inflammation at the systemic (i.e., circulating levels of C-reactive protein), cellular (i.e., toll-like receptor 4), and genomic levels (i.e., nuclear factor-kB, signal transducer, and activator of transcription family protein). 40–41 Elevated C-reactive protein levels are reported to be associated with increased cancer symptom burden and decreased survival rate. 42 In addition, it is reported that every 10-unit increase in insomnia is significantly associated with 0.86, 0.21, 0.48, 0.27, and 0.53 unit decrease in
health, social, psychological, family, and overall QoL, respectively. Therefore, the anti-insomnia regimen also should be performed to enhance QoL. In our study, the mean insomnia score was significantly lower in the nurse-led group compared with the control group, indicating the nurse-led strategy may be more effective for alleviating sleep disturbances. This conclusion was in line with the previous studies.

Financial difficulty is a significant problem in patients undergoing cancer-related therapies. It is reported that the mean monthly out-of-pocket and lost income costs are $1455 and this costs of care have increased substantially in recent years. Patients who report "a lot" of financial burden are more likely to rate their physical health, mental health, and satisfaction with social activities and relationships as poor compared with those with no financial hardship, resulting in worse QoL score.

How to resolve financial distress and the related mental stress is a routine cancer care. In our study, the financial difficulty was significantly reduced in the nurse-led group for patients with cancer, indicating the nurse-led strategy may be more effective for alleviating the financial burden. This conclusion was in consistent with the previous study.

There are several limitations of our meta-analysis that should be taken into account when interpreting our meta-analysis results. First, some of included studies may not be blinded due to lack of description. Although all included studies were in high quality, non-blinded studies may introduce unavoidable bias. Second, the design of nurse-led intervention programs varied among different studies, which may also introduce some biases. Third, a significant heterogeneity was present for analysis of the significant variables (constipation, financial impact, and insomnia). However, the statistical results were not affected after omitting each study by sensitivity analysis, indicating our conclusion may be credible. Fourthly, most of the studies assessed the short-term effectiveness (within 6 months) and the follow up time was different among studies. Fifth, the articles included in this meta-analysis were limited to those published to June 2017, thus some relevant unpublished studies may be missed. This led to a relatively small sample size which may be the contributor to cause the non-significance in other scales of QoL (such as chemotherapy related diarrhea, nausea, and vomiting when comparing the nurse-led with the control group.

5. Conclusion

The nurse-led disease management strategy seemed to be effective to improve constipation, insomnia, and financial impacts for patients with cancer in QoL assessment.

Author contributions

Conceptualization: Xiuju Cheng.
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References

[1] Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.
[2] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017;67:7–30.
[3] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–35.

[18] Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365–76.

[21] Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias in meta-analysis. Biometrics 2004;60:150–60.

[28] Zweers D, De GE, Teunissen SC. Non-pharmacological nurse-led interventions to manage anxiety in patients with advanced cancer: a systematic literature review. Int J Nurs Stud 2015;56:102–13.

[24] Kim YH, Choi KS, Han K, et al. A psychological intervention program to complement the treatment of adolescent acute lymphoblastic leukemia patients. Appl Nurs Res 2016;32:e1–5.

[16] Brown L, Payne S, Royle G. Patient initiated follow up of breast cancer. Int J Nurs Stud 2017;63:307–16.

[22] Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:453–63.

[3] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–35.

[5] Brown SR, Mathew R, Keding A, et al. The impact of postoperative complications on long-term quality of life after curative colorectal cancer surgery. Ann Surg 2014;259:916–23.

[23] Kim YH, Choi KS, Han K, et al. A psychological intervention program to complement the treatment of adolescent acute lymphoblastic leukemia patients. Appl Nurs Res 2016;32:e1–5.