

Short Communication

Clinical practice guidelines for the care of psychologically distressed bereaved families who have lost members to physical illness including cancer

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Abstract

The Japanese Psycho-Oncology Society and the Japanese Association of Supportive Care in Cancer developed evidence-based clinical practice guidelines for the care of psychologically distressed bereaved families who have lost members to physical illness including cancer. The guideline development group formulated two clinical questions. A systematic literature review was conducted. The level of evidence and the strength of the recommendations were graded and recommendation statements validated using the modified Delphi method. The recommendations were as follows: non-pharmacological interventions were indicated for serious psychological distress (depression and grief); antidepressants were indicated for depression; however, psychotropic medications

including antidepressants were not recommended for 'complicated' grief. These guidelines will facilitate the provision of appropriate care to distressed bereaved family members and highlight areas where further research is needed.

Key words: bereavement, grief, depression, bereavement care, guideline, psycho-oncology

Introduction

Bereavement is the most distressing life event for human beings (1), and our previous studies demonstrated that 14.6% (95% confidence interval [CI]: 14.0–15.1), 11.6% (95% CI: 11.2–12.2) and 43.8% (95% CI: 40.6–47.4) of Japanese bereaved family members who had lost their members to cancer experienced depression, complicated grief and clinical psychological distress, respectively (2,3). In addition, bereavement is associated with increased suicide (4) and several serious physical diseases including cardiovascular disease (5,6) and stroke (7).

Currently, more than 370 000 Japanese people die of cancer (8). In addition, every year approximately 350 000, 100 000 and 95 000 die of cardiovascular disease, cerebrovascular disease and pneumonia, respectively. Therefore, there are more than a million people annually who experience the death of a loved one following a physical illness.

Considering the potentially serious negative impact of bereavement on health status, especially mental health, providing appropriate psychosocial care to bereaved family members is an essential health issue. However, there is very little evidence of appropriate interventions in, or standardized care strategies for, the psychological distress of bereaved family members (9). To the best of our knowledge, there are no evidence-based clinical practice guidelines for the optimal care of bereaved families in Japan.

This study initially began as part of a research study on the development of effective psychological care for bereaved family members of cancer patients and was supported by a Grant-in-Aid for Cancer Research from the Japanese Ministry of Labour, Health and Welfare, followed by academic support from the Japanese Psycho-Oncology Society (JPOS) and the Japanese Association of Supportive Care in Cancer. In this article, we describe the process involved in developing these guidelines and present a summary of the recommendations for the psychological care of bereaved families who have lost a member to a physical illness.

Methods

Procedure

This guideline focuses on optimizing care for psychologically distressed bereaved family members, especially those experiencing depression and complicated grief, who have lost a relative to physical illness including cancer. JPOS established a bereavement care guideline committee to develop the guideline. The guideline was developed by referring to the manual for the development of clinical practice guidelines by the Medical Information Networking Distribution Service (Minds ver. 7) (https://minds.jcqhc.or.jp/s/developer_guide). The guideline development group consisted of multidisciplinary members (six psychiatrists, six psychosomatic physicians, two psychologists, one pharmacist, one nurse, one physiotherapist, one grief professional and one representative of a cancer patient group). Initially, the guideline development group proposed several potential relevant clinical questions (CQs). Two CQs were finally chosen as clinical questions, while other clinical

questions were used as background questions. Using the two CQs, we conducted a systematic review of the literature and assessed the level of evidence and strength of recommendations made in previous studies.

Systematic review

The systematic review was conducted using the following four databases: PubMed, the Cochrane Central Register of Controlled Trials, PsychInfo and the Ichushi-Web of the Japan Medical Abstracts Society. The literature searched was limited to randomized controlled trials written in English or Japanese and published prior to 31 May 2020 for CQ1 and 15 September 2020 for CQ2. The search terms used to conduct this review are available on request. Due to the limited number of articles available that referred to cancer, additional searches were made of research on bereaved families of patients with a physical illness other than cancer (more than 70% of the subjects were bereaved families who lost their members to a physical illness including cancer). The relevant studies were identified in two stages. Firstly, two members of the guideline task force independently reviewed each abstract to select studies meeting the rough eligibility criteria for each CQ (stage 1; data not shown). Secondly, full-text articles of studies identified during stage 1 were screened according to strict eligibility criteria. Additional articles were identified by manual searching.

The process of making recommendations

Each four- and two-member teams drawn from the task force drafted the recommendation statements for CQs 1 and 2. The modified Delphi method was used to validate the draft recommendation statements. The draft versions for the Delphi rounds were initially developed by the multidisciplinary guideline development group mentioned above. Subsequently, the Delphi rounds were conducted by 17 representatives of other specialties (i.e. six palliative care physicians, one medical oncologist, one home care physician, one internist, one surgeon, one psychiatrist, two psychosomatic physicians, one nurse, two psychologists and one representative of a cancer patient group). After two Delphi rounds and an external review conducted by four external reviewers (i.e. one palliative care physician, one oncologist, one nurse and one psychologist), the final versions of the recommendation statements were approved.

Strength of recommendations and level of evidence

The strength of recommendations and the level of evidence were graded using the system developed by the Medical Information Networking Distribution Service, following the concepts of the grading of the recommendations, assessment, development and evaluation system. Briefly, the strength of each recommendation was graded as 1 (strong) or 2 (weak), and the level of evidence was graded using four different classes [A (high); B (moderate); C (low) and D (very low)].

Management of conflicts of interest for the guideline

The JPOS ethics and conflicts of interest committee reviewed and checked the conflicts of interest status of each of the guideline development committee members.

Results

CQ1. Are non-pharmacological interventions recommended to ameliorate clinical psychological distress experienced by bereaved family members?

Recommendation (2C): non-pharmacological interventions are indicated for serious psychological distress (depression and grief) experienced by bereaved adults (≥ 18 years) who 'lost their' significant others to physical illness including cancer.

The systematic review finally identified 25 papers (the studies identified are listed in [Supplementary Table 1](#)). Of these, 11 studies focused on the bereaved families of cancer patients, 2 on AIDS patients, 1 on dementia patients and 11 on patients with other physical diseases. The types of interventions used included cognitive behavioral therapy, grief therapy and palliative care including psychological support.

Depression

Twenty-two studies included depression as a study outcome and 12 of these included depression outcomes that were suitable for inclusion in a meta-analysis. The meta-analysis demonstrated that non-pharmacological interventions significantly reduced depression in bereaved family members (standardized mean difference -0.56 [95% CI: $-1.00, -0.11$]). Heterogeneity was high, as study participants, the timing of depression measures, the intervention duration and the type of interventions used all differed. One of the studies found that depression in bereaved family members worsened.

We decided upon recommendation 2C according to these findings.

Grief

Nineteen studies included grief as a study outcome and 12 of these included grief outcomes that were suitable for inclusion in a meta-analysis. The meta-analysis demonstrated that non-pharmacological interventions significantly reduced distress or duration of the grieving process in bereaved family members (standardized mean difference -0.79 [95% CI: $-1.20, -0.38$]). Heterogeneity was high, as study participants, the timing of outcome measures, intervention duration and the types of interventions used all differed. There was no study indicating an increase in the distress or duration of the grieving process in grief.

Anxiety, quality of life and post-traumatic growth

Thirteen studies included anxiety as a study outcome and nine of these were suitable for inclusion in a meta-analysis. The meta-analysis demonstrated that non-pharmacological interventions did not significantly reduce anxiety in bereaved family members (standardized mean difference -0.49 [95% CI: $-1.15, 0.16$]).

The meta-analysis included six studies that assessed the quality of life as a study outcome and three studies included quality of life outcomes that were suitable for inclusion in a meta-analysis. The meta-analysis demonstrated that non-pharmacological interventions did not significantly improve the quality of life of bereaved family members (standardized mean difference 0.19 [95% CI: $-0.06, 0.44$]).

No study included post-traumatic growth as a study outcome.

CQ2. Are pharmacological treatments using psychotropic medication recommended to ameliorate psychological distress experienced by bereaved family members? This CQ was further divided to assess two different types of distress.

CQ2a. Are pharmacological treatments using psychotropic medication recommended to ameliorate depression experienced by bereaved family members?

Recommendation (2C): Antidepressants are recommended for depression experienced by bereaved adults (≥ 18 years) who 'lost their' significant other to physical illness including cancer.

The systematic review identified two randomized controlled trials and three pre-post comparative studies that included depression as a study outcome (the studies identified are listed in [Supplementary Table 1](#)). A meta-analysis was not conducted because of study heterogeneity.

Reynolds *et al.* (10) conducted a randomized controlled trial demonstrating that the tricyclic antidepressant nortriptyline was superior to placebo at alleviating bereavement-related major depression. Pasternak *et al.* (11) conducted an open trial to examine the efficacy of nortriptyline for bereavement-related major depression which resulted in the significant symptomatic improvement of depression. Three other studies also suggested the effectiveness of antidepressants.

CQ2b. Are pharmacological treatments using psychotropic medication recommended to ameliorate complicated grief experienced by bereaved family members?

Recommendation (2C): Psychotropic medications, including antidepressants, are not recommended for complicated grief experienced by bereaved adults (≥ 18 years) who 'lost their' significant other to physical illness including cancer.

The systematic review identified one randomized controlled trial and two pre-post comparative studies.

Shear *et al.* (12) conducted a randomized controlled trial to investigate the efficacy of citalopram (antidepressant, serotonin reuptake inhibitor, not available in Japan) that failed to demonstrate a significant effect on complicated grief. Two other studies each demonstrated the ineffectiveness of nortriptyline and the effectiveness of bupropion, respectively.

Discussion

To the best of our knowledge, this is the first evidence-based clinical practice guideline that has used the formal guideline development method to optimize psychological care for bereaved families who have lost a member to physical illness including cancer. Considering the huge number of bereaved family members worldwide suffering from profound psychological distress, this guideline could facilitate the provision of appropriate care to many in need.

The guideline committee concluded that non-pharmacological interventions should be recommended for serious psychological distress including depression and grief, although the types of interventions varied. With regard to pharmacotherapies, the pharmacological interventions recommended included antidepressants for symptoms of major depressive disorders; however, psychotropic medications, including antidepressants, were not recommended for complicated grief. We hope that these findings will help medical staff to improve their clinical practice.

After developing these guidelines, we noticed that there were very few empirical studies investigating the efficacy of non-pharmacological and/or pharmacological interventions to ameliorate

psychological distress in bereaved family members. In addition, there were no Japanese studies of non-pharmacological interventions or psychosocial interventions included in the systematic review results. Considering the potential cultural differences affecting the medical system and preferred interventions (13), more Japanese studies should be encouraged.

Good cancer care must include care for family members, and the Cancer Control Act emphasizes the care needs of the whole family (14). However, one Japanese study has shown that very few relatives or bereaved family members are provided with psychosocial support or treatment in Japan (15). There is no doubt that support for family members including the bereaved is essential; therefore, the development of a comprehensive support system for caregivers of patients with serious illness remains an urgent clinical issue in Japan.

In the future, we would like to include new CQs in these guidelines, such as whether prophylactic interventions can prevent the development of depression and complicated grief.

In conclusion, these guidelines will contribute to the optimization of care and treatment for psychological distress in bereaved family members. However, additional clinical studies are warranted to investigate the needs of bereaved family members more appropriately.

Supplementary Material

Supplementary material is available at *Japanese Journal of Clinical Oncology* online.

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Conflict of interest statement

The authors have no conflicts of interests to declare that may be affected by the publication of the manuscript. T.A. has received

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