

Evidence-based Anticancer
Complementary and Alternative Medicine 4

William C.S. Cho *Editor*

Evidence-based Non-pharmacological Therapies for Palliative Cancer Care

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Evidence-based Non-pharmacological Therapies for Palliative Cancer Care

 Springer

Editor

William C.S. Cho
Department of Clinical Oncology
Queen Elizabeth Hospital
Kowloon
Hong Kong SAR

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Preface

Apart from being a life-threatening disease, cancer and its therapy are usually associated with a significant deterioration in the quality of life. Non-pharmacological therapies are increasingly gaining acceptance in the healthcare community as complementary to conventional cancer treatments. The medical and scientific communities are thrust for up-to-date and systematic sources of non-pharmacological therapies that are supported by concrete laboratory evidences and clinical trials. Subsequent to our previous volume entitled *Acupuncture and Moxibustion as an Evidence-based Therapy for Cancer*, this volume steps forward to gather leading oncologists, physicians, and scientists in the field to discuss the application of non-pharmacological therapies for the management of cancer. This book consists of 11 chapters presenting the research evidence relevant to the application of a range of commonly used non-pharmacological interventions in supportive cancer care, including massage, acupressure, Qigong, yoga, mind-body therapy, mindfulness-based intervention, and aromatherapy. An overview of the safety and side effects of non-pharmacological interventions for cancer care are also covered. In addition, the integration of non-pharmacological therapies with Western medicine in cancer treatment is included as well. This specialized volume delivers evidence-based information about non-pharmacological therapies for palliative cancer care that would be valuable for both medical professionals and cancer patients.

William C.S. Cho

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Contributors

Randal D. Beaton Department of Psychosocial and Community Health, University of Washington, Seattle, WA, USA

Michelle Bombacie Integrative Therapies Program, Division of Pediatric Oncology/Blood and Marrow Transplantation, Columbia University Medical Center, New York, NY, USA

Richard Bränström Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden

Caroline E. Bulsara Brightwater Care Group, Osborne Park, WA, Australia
Clinical Nursing and Midwifery Research Centre, Edith Cowan University, Joondalup, WA, Australia

Gulbeyaz Can Istanbul University Nursing Faculty, Abide-I Hurriyet Cad, Caglayan, Istanbul, Turkey

Gary Elkins Mind-Body Medicine Research Laboratory, Department of Psychology and Neuroscience, Baylor University, Waco, TX, USA

Edzard Ernst Complementary Medicines, Peninsula Medical School, University of Exeter, Exeter, UK

William Fisher Mind-Body Medicine Research Laboratory, Department of Psychology and Neuroscience, Baylor University, Waco, TX, USA

Jiro Imanishi MUIM Center for Integrative Medicine, Meiji University of Integrative Medicine, Nishikyo-ku, Kyoto, Japan

Sui-Whi Jane Department of Nursing and Graduate Institute of Nursing, Chang Gung University of Science and Technology, Kwei-Shan Hsiang, Tao-Yuan, Taiwan

Aimee Johnson Mind-Body Medicine Research Laboratory, Department of Psychology and Neuroscience, Baylor University, Waco, TX, USA

Kathy G. Kravits Department of Nursing Research, City of Hope, Duarte, CA, USA

Eun Jin Lee Nursing Department, Inha University, Namgu Incheon, South Korea

Myeong Soo Lee Division of Standard Research/Medical Research Division, Korea Institute of Oriental Medicine, Daejeon, South Korea

Complementary Medicines, Peninsula Medical School, University of Exeter, Exeter, UK

Mei-Nan Liao Administration Center of Medical Research Department, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan

Kuan-Yin Lin School and Graduate Institute of Physical Therapy, College of Medicine, National Taiwan University, Taipei, Taiwan

Yung-Chang Lin Division of Hematology/Oncology, Department of Internal Medicine, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan

Deborah H. Ndao Integrative Therapies Program, Division of Pediatric Oncology/Blood and Marrow Transplantation, Columbia University Medical Center, New York, NY, USA

Byeongsang Oh Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Anna S. Petterson SolarisCare Foundation, Nedlands, WA, Australia

Clinical Nursing and Midwifery Research Centre, Edith Cowan University, Joondalup, WA, Australia

Diane Rooney Integrative Therapies Program, Division of Pediatric Oncology/Blood and Marrow Transplantation, Columbia University Medical Center, New York, NY, USA

David Rosenthal Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Jim Sliwinski Mind-Body Medicine Research Laboratory, Department of Psychology and Neuroscience, Baylor University, Waco, TX, USA

Jau-Yih Tsao School and Graduate Institute of Physical Therapy, College of Medicine, National Taiwan University, Taipei, Taiwan

Sherry Warden Emeritus Faculty, University of Kentucky, Lexington, KY, USA

Diana J. Wilkie Department of Biobehavioral Health Science, College of Nursing, University of Illinois, Chicago, IL, USA

Anne M. Williams School of Nursing and Midwifery, Joondalup, WA, Australia

Clinical Nursing and Midwifery Research Centre, Edith Cowan University,
Joondalup, WA, Australia

SolarisCare Foundation, Nedlands, WA, Australia

Centre for Nursing Research, Innovation and Quality, Sir Charles Gairdner Hospital,
Nedlands, WA, Australia

Curtin Health Research Institute, Curtin University, Bentley, WA, Australia

Chapter 1

An Overview of Non-pharmacological Therapies for Palliative Cancer Care

Kathy G. Kravits

Abstract It is estimated that 1,596,670 new cancer cases were diagnosed in 2011. Symptoms commonly associated with cancer and cancer treatment include pain, nausea and vomiting, fatigue, insomnia, dyspnea, delirium, anxiety, depression and distress. An important aspect of cancer control is palliative care, which is guided by the principles of symptom relief, integration of psychological and spiritual care into the treatment plan, and promotion of quality of life (QoL). Palliative care is patient-focused, family-centered care delivered by a multidisciplinary team and is indicated early in the course of the illness. Palliative care has a broad mission to reduce symptom burden (in all domains of life), improve QoL, and as a result, reduce suffering. Palliative care provides a supportive environment in which there is collaboration between patients and health care providers to achieve the best possible results for the patient. This collaborative framework can incorporate the patient's use of non-pharmacological therapies such as relaxation and guided imagery to reduce stress and enhance QoL. Patients diagnosed with cancer are increasingly using non-pharmacologic strategies to address their illness concerns, including pain relief, desire to improve health, and desire to enhance QoL. Many of the non-pharmacological therapies used by patients do not have sufficient evidence to determine efficacy or safety. This chapter provides an overview of some of the most commonly used non-pharmacological therapies with a discussion of the evidence supporting their use and indications of risk of each therapy.

K.G. Kravits (✉)

Department of Nursing Research, City of Hope, Duarte, CA 91010, USA
e-mail: kkravits@coh.org

1.1 Cancer Incidence, Treatment, and Survival

As of 2007, approximately 11.7 million living Americans had been affected by cancer, and it is estimated that 1,596,670 new cases of cancer were diagnosed in 2011. Although a person may develop cancer at any age, those over the age of 50 are most at risk, and 78% of new diagnoses occur in individuals 55 or older. The overall survival rate associated with cancer between 1999 and 2006 is estimated to have been 68%, which is an increase of 18% from the 50% survival rate measured during 1975–1977 (ACS 2011). Thus, given newly diagnosed cases, increased survival rates, and an aging population, increasing numbers of patients, family members, and loved ones will be impacted by cancer in the coming years.

Multi-modal medical therapies, such as chemotherapy, radiation therapy, and surgery, are most often used to treat cancer today, and play a key role in the standard treatment and palliation of most cancers. A wide range of pharmacological agents are used in cancer treatment as well as in symptom management. However, the combination of therapies, especially if chemotherapy is included, increases the risk of side effects and associated symptoms (Kirkova et al. 2010). Cancer and cancer treatments are frequently associated with side effects that produce symptoms that negatively affect patients' quality of life (QoL) and well-being (Yennurajalingam et al. 2012). Some of the more commonly experienced symptoms include pain, dyspnea, delirium, nausea and vomiting, fatigue, insomnia, depression, and anxiety (Harrington et al. 2010).

Non-pharmacological therapies have a developing role in the management of cancer and cancer-related symptoms, and those that have established efficacy and safety provide new therapeutic strategies for professional health care providers, patients, survivors, and their family caregivers. In addition to the direct effects of the non-pharmacological therapies, involving patients and survivors in promoting their own well-being by participating in the management of their disease-related symptoms enhances their feelings of self-efficacy and QoL (Deng et al. 2009). Thus, integration of non-pharmacological therapies within traditional medical practice creates a comprehensive framework for managing symptoms, reducing suffering, and improving QoL (Fig. 1.1) (Deng et al. 2009).

1.2 Palliative Care

Palliative care is a method of health care founded with the express purpose of improving QoL and reducing suffering through the early management of illness-related symptoms (ICSI 2011). It incorporates the principles of patient-centered, family systems-oriented care. Palliative care may be provided to patients with catastrophic and/or chronic illnesses who are not necessarily at the end of life, and can be initiated as early as at the time of diagnosis.

The domains of care addressed by palliative care include physical, cultural, psychological, social, spiritual, legal, and ethical. This holistic approach supports inter-disciplinary practice within teams of highly qualified individuals of differing

Fig. 1.1 Cancer-related symptoms

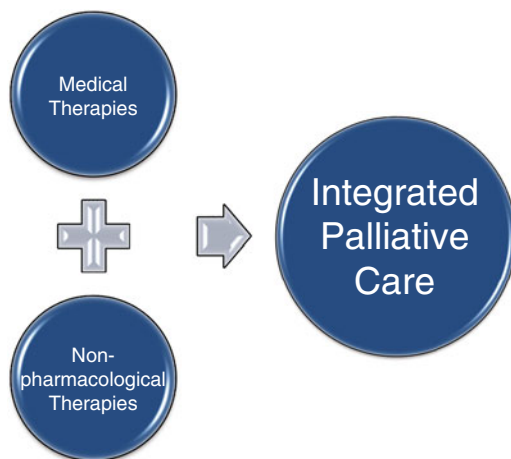
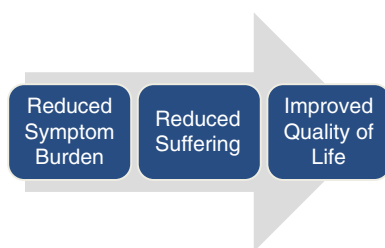


Fig. 1.2 Palliative care principles (ICSI 2011)



health care disciplines. It also provides a useful framework for assessing and managing symptoms for the purpose of reducing suffering and improving QoL (Fig. 1.2) (ICSI 2011).

Palliative care and hospice are not interchangeable (Table 1.1). Hospice care is initiated exclusively at end of life (six months or less), and has as its primary objective to achieve and maintain comfort. Through that effort, hospice care aims to reduce suffering and promote a peaceful death. Palliative care has a broader mission to reduce symptom burden (in all domains of life), improve QoL, and, as a result, reduce suffering.

1.3 Non-pharmacological Therapies

Non-pharmacological therapies, such as complementary and alternative medicine (CAM), are important approaches in palliative care. CAM therapies (excluding prayer) are used by approximately 50% of all adult patients (Barnes et al. 2004).

Table 1.1 Comparison of palliative care to hospice care (ICSI 2011)

Characteristics	Palliative care	Hospice
Life expectancy	Limited, no time constraints	Six months or less
Initiation of care	As early as at time of diagnosis	At the time of determination of six months or less to live, or thereafter
Primary goals of care	Reduce symptom burden Reduce suffering Improve quality of life	Achieve and maintain comfort Reduce suffering Promote a peaceful death

Table 1.2 Internationally used non-pharmacological therapies (Gage et al. 2009; Corbin et al. 2009; Shih et al. 2009)

United Kingdom	United States	Singapore
Percentage of participants using non-pharmacological therapies in an ambulatory cancer treatment setting (<i>n</i> = 358)	Percentage of participants using non-pharmacological therapies in a hospice setting (<i>n</i> = 344)	Percentage of participants using non-pharmacological therapies in an ambulatory cancer treatment setting (<i>n</i> = 227)
Reflexology (16%) Aromatherapy (10%)	Spiritual/religion (22%) Music therapy (16%)	Food supplements (59%) Traditional Chinese medicine (49%)
Massage (8%) Reiki (8%) Counseling (8%) Shiatsu massage (6%) Acupuncture (6%) Yoga (5%) Hypnosis (5%) Music (4%)	Pet therapy (14%) Aromatherapy (8%) Massage therapy (8%) Healing touch (7%) Herbs and supplements (4%) Relaxation therapy (3%) Acupuncture (3%) Biofeedback (2%)	Special diet (41%) Vitamins (40%) Others (31%) Minerals (21%) Aryveda (0.4%) – – –

In cancer patients, reports of use of CAM therapies ranges from 10 to 60% of patients (Mansky and Wallerstedt 2006; Cassileth and Gubili 2009; Wyatt et al. 2010). Individuals who use CAM therapies are typically younger, well-educated, and economically secure (Cassileth and Gubili 2009; Deng et al. 2009; Wyatt et al. 2010).

Patients may pursue the use of non-pharmacological therapies because of emotional reactions to their diagnosis, health care providers, and/or health care system; desire for more autonomy and control in the management of their care; and an uncompromising search for a cure that may not be possible under a formal medical system. Belief in forces that are outside the realm of scientific thought may provide a fertile ground for the use of alternative therapies, especially if peers support and promote the use of alternatives to traditional medical practice (Deng et al. 2009). Furthermore, the decision to use any specific medical system and/or therapy is informed by the health beliefs and cultural context of the individual (Table 1.2). Therefore, it is useful for providers to understand the preferences of the ethnic communities they support (Hsiao et al. 2006).

Palliative care approaches symptom management from a holistic framework. It is an inter-disciplinary form of care that integrates traditional Western medical practices with complementary therapies in a purposeful manner. Evidence-based non-pharmacological therapies, as discussed below, have a role in this form of integrative practice.

1.4 Evidenced-based Non-pharmacological Therapies

1.4.1 *Alternative Medical Systems*

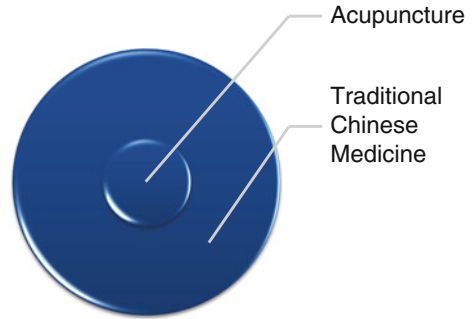
Acupuncture is part of a comprehensive system of traditional Chinese medicine (Fig. 1.3) (Deng et al. 2009), and involves the management of Qi (energy) through the use of precisely placed needles. It consists of replicable interventions, which makes evaluation of its effects possible across multiple studies. Evidence supports the use of acupuncture for adjunctive management of pain, as well as for poorly controlled nausea and vomiting, dyspnea, and xerostomia (Deng et al. 2009; Cassileth and Keefe 2010; Ernst 2011). It is safe when performed by a qualified practitioner (Deng et al. 2009).

A pilot study conducted by Dean-Clower and colleagues (2010) investigated the feasibility of acupuncture as an adjunct therapy for the management of cancer-related symptoms and QoL. This study used a single group design, and participants ($n=32$) were recruited from ambulatory breast and ovarian cancer populations. Participants were over the age of 21, had not received acupuncture in the preceding six months, had adequate platelets ($\geq 25,000$), and a Karnofsky performance scale score ≥ 60 .

The intervention consisted of 12 acupuncture sessions delivered over eight weeks (twice a week for four weeks and once a week for the following four weeks). Three well-trained, experienced acupuncturists provided the intervention using a manualized acupuncture protocol. In addition, participants who presented with symptoms of anxiety, nausea, pain, fatigue, depression, insomnia, constipation, or cough received additional acupuncture needle placement specific to the reported symptom. Electrical stimulation was not used.

Symptom data were collected using the Brief Pain Inventory, Rotterdam Symptom Checklist, and Profile of Mood States. Satisfaction with Life Domains Scale-Cancer and Cancer Coping Methods were also used. Measurements occurred at baseline and weekly thereafter. Initial analyses consisted of a two-sample Student's *t*-test using age, years since diagnosis, and symptom severity. A significance level of 0.05 was used. The results showed a significant decrease in anxiety, depression, fatigue, and pain, supporting the feasibility of acupuncture as an intervention for this patient population (Dean-Clower et al. 2010). The results also indicated an improvement in reported symptoms, although the small sample size limits the usefulness of these results. The authors endorsed the potential usefulness of acupuncture as an intervention for symptom management, but acknowledged that additional well-designed studies, including randomized controlled trials (RCTs), are needed before the developing evidence can be considered convincing.

Fig. 1.3 Alternative medical systems



1.4.2 Energy-based Therapies

Energy-based therapies currently being used as non-pharmacological therapies for symptom management include Reiki, healing touch and Qigong (Fig. 1.4). Evidence is unclear as to the benefit or risk of these therapies, as discussed below (Deng et al. 2009).

1.4.2.1 Reiki

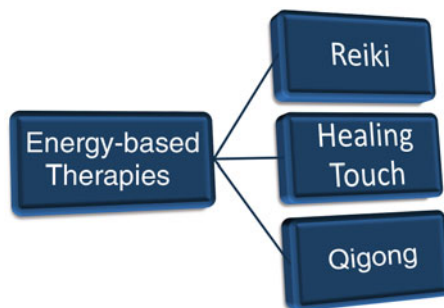
Reiki was developed in Japan in the early twentieth century by Mikao Usui. In Reiki, a practitioner uses his/her hands to direct a flow of healing energy to the recipient. It is thought that this energy work promotes relaxation (Baldwin et al. 2010).

In an RCT conducted by Beard and colleagues (2011), Reiki therapy was used as an intervention with 54 men who were receiving radiation therapy. Anxiety was reduced and relaxation increased in patients who received the intervention. However, the sample size limits the generalization of this study. In contrast, a double-blinded RCT, conducted by Catlin and Taylor-Ford (2011) and involving 189 participants receiving chemotherapy did not show a difference in effect between control and intervention groups, although there was improvement in comfort and well-being in both groups. The authors postulate that the presence of a registered nurse who gave one-on-one attention to both intervention and control participants may have produced the therapeutic effect. Thus, there is limited evidence from well-designed trials to support the use of Reiki, and additional study is needed (van der Vaart et al. 2009).

1.4.2.2 Healing Touch

Healing touch uses touch by a trained practitioner to restore the energy field of another and thus create an opportunity for the individual to heal themselves. This technique is non-invasive and non-manipulative. The therapeutic relationship is important for success (Hart et al. 2011).

Fig. 1.4 Energy-based therapies



Anderson and Taylor (2011) conducted a systematic review of healing touch RCTs. Inclusion criteria for the review included presence of a control group, randomization, and use of healing touch as single treatment or as adjunct therapy. They identified five RCTs that met their inclusion criteria, of which only two studies explored the use of healing touch with cancer patients. The first study conducted by Post-White and colleagues (2003) evaluated the use of healing touch in 164 breast cancer patients and used a cross-over design. The findings showed a significant decrease in pain, mood disturbance, and fatigue in patients who received healing touch. Therapeutic presence and massage were included in the study and showed improved mood disturbance. A limitation of this study was that the healing touch intervention was implemented while music was playing, thus making it difficult to identify the impact associated with healing touch.

The second study identified by Anderson and Taylor (2011) was an RCT with 62 patients that used a parallel design with a healing touch group and a mock healing touch group (Cook et al. 2004). Participants were blinded to their group assignment. Outcomes were measured using the SF-36, which assesses physical and mental health. Improvements in mental health and functional status were reported. One of the major limitations of this study was the lack of a usual care group, making it virtually impossible to draw conclusions about the impact of healing touch as compared to the usual standard of care.

The number of well-designed RCTs evaluating the effectiveness of healing touch is very limited. Therefore, although studies are improving, many more RCTs that are well-designed will be needed before the efficacy and safety of healing touch therapy can be established.

1.4.2.3 Qigong

Qigong is a system of healing and energy medicine from China that involves a practice using movement, breathing, and meditation to cleanse the body's life energy (Monti et al. 2008; Elkins et al. 2010). The number of well-designed studies



Fig. 1.5 Expressive arts therapies

evaluating the use of Qigong is limited. A recent RCT conducted by Oh and colleagues (2012) examined the effect of Qigong on cognitive function, QoL and a biomarker of inflammation (C-reactive protein) in cancer patients. The participants were 81 cancer patients who were randomized to a treatment and intervention group. The intervention consisted of a ten weeks Qigong program. Self-report measures were used, and the results supported an improvement in cognitive functioning and QoL in the treatment group. However, a significant limitation of this study was that it tested Qigong as a complete intervention required to produce benefit. Qigong includes breathing, movement, and meditation, each of which has been shown singly to have a positive effect on QoL. Therefore, a question remains as to whether all three components integrated into a practice of Qigong is necessary for effect, or if a comparable effect can be achieved by one of its component parts.

A review of the literature conducted by Oh and colleagues (2012) examined the evidence supporting the effect of Qigong on QoL, immune function, and survival in cancer patients. The inclusion criteria used to select the studies were RCT design, controlled clinical trial design, published in English, a minimum of ten cancer patient participants, and measures of QoL, immune function, and survival. Eight articles were evaluated, and the results were unconvincing for Qigong having an effect on QoL. However, results on immune function and survival were more promising. Limitations of the studies included in the review included insufficient sample sizes to achieve necessary power to detect changes in effect, lack of RCT design, limited description of the Qigong intervention, and lack of description of the stage of disease of the study participants.

Overall, the quality of the studies of Qigong has been highly variable, with many having significant and numerous design flaws. Therefore, the evidence cannot be accurately evaluated until additional well-designed studies are reported (Monti et al. 2008; Lee et al. 2007; Oh et al. 2012).

1.4.3 Expressive Arts Therapies

Expressive arts therapies use the creative arts to promote well-being, enhance QoL, and reduce symptom burden in cancer patients. Therapies commonly identified as expressive arts therapies are music therapy, art therapy, dance therapy, and creative writing (Stuckey and Nobel 2010). Of these, music and art therapy have substantial emerging evidence to support their use (Fig. 1.5).

1.4.3.1 Music Therapy

Music therapy is the use of music (passive listening and active participation) by a trained music therapist to reduce symptoms of suffering and improve QoL (Magill and Luzzato 2002). Symptoms that have been reported to be reduced by listening to music include anxiety, pain, fatigue, and nausea. Improved QoL has also been reported (Deng et al. 2009).

Several well-designed RCTs have been conducted in recent years to evaluate the effect of music therapy. In a small RCT of 25 terminal patients receiving hospice care conducted by Horne-Thompson and Grocke (2008), music therapy was shown to reduce patient anxiety at end of life. A secondary analysis of the data indicated that there were significant reductions in pain, fatigue, and drowsiness as well. Results from another RCT, which also looked at music therapy and anxiety, in 60 ambulatory patients with stage II breast cancer indicated a significant reduction in anxiety in the intervention group (Bulfone et al. 2009). In 2011, Li and colleagues (2012) conducted an RCT with 120 breast cancer patients to examine the effect of music therapy on anxiety. Their results supported the use of music therapy for anxiety reduction. Taken together, despite the variation in patient populations, all three studies suggest that music therapy is effective in reducing disease-related anxiety.

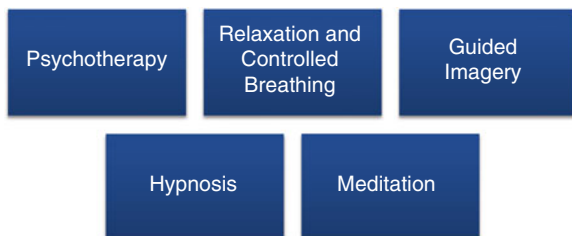
The effect of music therapy on pain has also been studied. Huang and colleagues (2010) conducted an RCT exploring the effect of music therapy on pain in which 126 hospitalized cancer patients were randomized to experimental and control groups. The experimental group listened to music for 30 min. Measurements of pre- and post-intervention pain levels were made using visual analog scales, and showed a significant decrease in pain ratings for the experimental group. In 2011, Li and colleagues (2011) conducted a RCT of the effectiveness of music therapy on pain in 120 mastectomy patients randomized into intervention and control groups. Pain ratings were significantly reduced in the intervention group after a twice a day 30 min music intervention.

Evidence is growing to support the use of music therapy for palliation of symptoms associated with cancer and other chronic illnesses. No risks have been associated with listening to music in the literature. Therefore, in the absence of associated risks and with the development of affirmative evidence, use of music therapy by cancer patients can reasonably be supported.

1.4.3.2 Art Therapy

Art therapy is a form of psychotherapy that occurs between a client and an art therapist that uses visual art making to promote self-regulation and well-being (Wood 1998). However, there are limited numbers of well-designed RCTs in the art therapy literature. Barriers that have inhibited the development of well-designed art therapy RCTs include the orientation of art therapists who embrace, as a core value, creativity. Many art therapists who view the creative process as an essential element of successful art therapy are biased against the use of reductionist scientific methods to evaluate art interventions, believing that these methods diminish the role of the

Fig. 1.6 Mind-body therapies



creative process (Grulke et al. 2006). In addition, unique and individualized art interventions that lack standardization across clients, therapists, and settings are products of the valuation of the creative process and are difficult to study.

Although several articles reviewing art therapy investigations concluded that art therapy efficacy research is early in its development, some RCTs were identified as well-designed inquiries (Metzl 2008; Geue et al. 2010; Wood et al. 2011). For example, a small RCT of a weekly individualized art therapy intervention was conducted with 41 breast cancer patients who received radiation therapy. The results showed that patients who received art therapy had better QoL scores than did those assigned to the control group (Svensk et al. 2009). Although the small sample limits the ability to generalize the findings to a larger population, the results are suggestive and warrant a follow-up study with a larger sample.

Another small RCT conducted by Thyme and colleagues (2009) examined the impact of brief art therapy on depression, anxiety, and somatic symptoms in 41 breast cancer patients between the ages of 37 and 69 years. The intervention consisted of five sessions of art therapy that encouraged emotional expression. This study showed a significant decrease in anxiety, depression and somatic symptoms in the art therapy intervention group. Thus, although there is limited data available to support the use of art therapy for cancer patients, individual studies suggest that art therapy may enhance well-being and reduce pain, anxiety, depression, and fatigue. However, further research is required (Gabriel et al. 2001; Bar-Sela et al. 2007). Very few, if any risks, have been identified as being associated with art therapy (Deng et al. 2009). Therefore, although evidence that convincingly supports the use of art therapy is lacking, the absence of risk associated with the intervention makes it reasonable to allow its use with patients.

1.4.4 Mind-Body Therapies

Mind-body therapies, which include psychotherapy, relaxation and controlled breathing, guided imagery, hypnosis, and meditation, are recommended for use in managing anxiety, mood disturbance, and pain and in improving health-related QoL in cancer patients (Fig. 1.6). The research is of moderate quality and convincing, with benefits outweighing risks (Deng et al. 2009).

1.4.4.1 Psychotherapy

Psychotherapy can be defined as a wide variety of interventions arising from different philosophical and theoretical orientations that are useful in the reduction and/or prevention of psychological distress. The interventions are interactional and are delivered by a health care professional (Akechi et al. 2008). In a 2011 meta-analysis, Hodges and colleagues (2011) found that the definitions of “psychological interventions” used in psychotherapy research were highly variable and lacked consistent descriptions. The variability of the definitions makes it difficult to compare results across studies and to determine if evidence of efficacy was present.

Supportive/Expressive Groups

Supportive/expressive psychotherapy groups are common interventions used with cancer patients. The use of supportive forms of group psychotherapy has been well-studied, and several studies confirm the acceptability of the group format to patients (Montazeri et al. 2001; Schnur and Montgomery 2010; Ledesma et al. 2011). The effectiveness of supportive group psychotherapy in the treatment of cancer-related distress in general is unclear (Jacobsen and Jim 2008; Hodges et al. 2011). However, some studies that measured the effect of group psychotherapy interventions on selected symptoms do reflect a positive effect such as improvements in depressive symptoms, anxiety, fatigue, or QoL (Akechi et al. 2008; Jacobsen and Jim 2008; Bookbinder and McHugh 2010).

In contrast, a supportive/expressive group psychotherapy study of 353 women with breast cancer failed to demonstrate any reduction in distress (Classen et al. 2008). The intervention in this study developed social support and emotional expression through fluid and spontaneous interactions with health care professionals. Another RCT of 382 women with breast cancer who received supportive group psychotherapy consisting of psycho-education, exercise, and supportive counseling reported a significant reduction in anxiety but no effect on depression (Bjornekleit et al. 2012). The interventions in each of these studies were unique and may have contributed to the differences in the findings of these studies.

A comparative effectiveness RCT conducted by Breitbart and colleagues (2010) used a structured, manualized meaning centered group psychotherapy intervention *vs* a manualized supportive group psychotherapy intervention that focused on themes emerging from the group dynamics. Participants included 90 individuals diagnosed with stage III or IV solid tumor cancers who were randomized to one of the groups. The results indicated significant improvements in sense of meaning, anxiety, and desire for death in the meaning centered group, but no improvements were noted in the supportive group psychotherapy group.

Together, these findings suggest that structured group processes that balance information with support may be effective strategies for using group psychotherapy to reduce symptom burden in the cancer patient population.

Individual Therapy

There are limited reports in the literature of individual psychotherapy for the management of cancer-related symptoms. Nissim and colleagues (2011) conducted a qualitative study of a brief psychotherapy intervention for patients with cancer. This small study of ten patients conducted at a large cancer center evaluated the use of a manualized intervention consisting of three to six sessions. Reports from participants supported the idea that the intervention was acceptable, comfortable, and useful.

Ramsay and colleagues (2007) evaluated the effects of group peer counseling and individual counseling on cancer-related anxiety and depression. Using a comparative effectiveness perspective, participants were randomized to either the group ($n=9$) or individual counseling ($n=9$) arms of the study. There was no difference in the results between either treatment arms. Although a positive effect was found with both types of interventions, further study is recommended. Investigation of use of counseling throughout the cancer trajectory may provide evidence of the most beneficial timing for the use of each of these interventions.

Research on psychotherapy for the treatment of psychological distress is generally robust and supports its effectiveness for many issues. On the other hand, research on the use of psychotherapy in cancer patient populations and for cancer-related distress is less robust, and there is ambiguity in the results, indicating the need for additional study.

1.4.4.2 Hypnosis

Hypnosis can be defined as focused attention experienced by a receptive individual in response to an experience either facilitated by a hypnotist or self-guided. Suggestions are offered during the experience for changes in sensation, perception, cognition, affect, mood, or behavior (Green et al. 2005). With the advent of systematic exploration of hypnosis by RCTs, a new understanding of its role in the management of disease symptoms has been achieved. There is significant evidence that hypnosis is effective at reducing cancer-related symptoms such as pain, nausea and vomiting, fatigue and anxiety (Elkins et al. 2007; Richardson et al. 2007; Jensen 2009; Mendoza and Capafons 2009; Montgomery et al. 2010). The National Institutes of Health support the use of hypnosis as an adjunct therapy for the management of cancer pain.

It has been determined by the National Institute of Health Technology Assessment Panel that hypnosis is effective in alleviating chronic pain, including cancer pain, procedural pain, nausea and vomiting (NIH 1996). There is substantial evidence for the ability of hypnosis to reduce pain, decrease chemotherapy-induced nausea and vomiting, decrease anxiety, and enhance health-related QoL (Deng et al. 2009). Hypnosis should not be used with patients who have a history of psychosis, a cognitive impairment that leads to an inability to concentrate, or personality disorders, particularly if psychotic features are attached (Deng et al. 2009). There are minimal to no side effects of hypnosis reported in the research literature.

1.4.4.3 Relaxation Training with Controlled Breathing

Relaxation is a state prompted by enhanced parasympathetic tone and reduced sympathetic tone. When individuals are in a relaxed state, their heart and respiratory rates slow, and feelings of calm predominate (Schaffer and Yucha 2004). Controlled breathing, progressive muscle relaxation, and guided imagery are some of the techniques that may be used to elicit a state of relaxation (Elkins et al. 2010).

Kondo and colleagues (2009) examined the difficulty cancer patients may have learning relaxation. Study participants reported that mastering abdominal breathing was difficult and that fatigue interfered with their ability to continue relaxation practice. These findings suggest that it is useful to identify functional status prior to beginning relaxation training.

Evidence indicates that relaxation training decreases pain, anxiety, and distress, and improves mood, sleep quality, and fatigue (Kwekkeboom et al. 2008; Lolak et al. 2008; Deng et al. 2009; Rabin et al. 2009; Yang et al. 2010; Chan et al. 2011). Ongoing relaxation practice produces a better effect than a brief relaxation experience (Deng et al. 2009). The safety of relaxation has also been investigated, and evidence suggests that relaxation training is tolerated by cancer patients, even those with advanced disease (Demiralp et al. 2010; Adamsen et al. 2012). As a whole, the evidence supporting the use of relaxation training with cancer patients is robust.

1.4.4.4 Guided Imagery

Guided imagery is an interaction between a facilitator and receiver that uses the imagination to create images that promote and support feelings of relaxation (King 2010). Although guided imagery may be used as a component of hypnotic induction, it is not the same as hypnosis (Green et al. 2005).

Studies of guided imagery suggest that it decreases anxiety, depression, pain, and body discomfort (Leon-Pizarro et al. 2007; King 2010). A study by Menzies and colleagues (2006) demonstrated that guided imagery improved self-efficacy. Another study, using a three session intervention of combined guided imagery, relaxation, and controlled breathing, involving 11 highly stressed couples ($n=22$) showed a significant drop in perceived stress post-intervention (Rogers et al. 2011). Lai and colleagues (2010) conducted a pilot study with 53 cancer patients who were experiencing cancer-related dyspnea. The study used a one-group, repeated measures design, and a highly structured intervention that combined music and guided imagery. During the 20 min intervention period, guided imagery was used for 4 min. The remainder of the intervention period consisted of silence (6 min) or music (10 min). The results of this study supported the premise that music and guided imagery can promote relief from cancer-related dyspnea. However, the study was limited by lack of a control group and use of a combined intervention. Finally, a recent review of the effects of guided imagery on cancer pain reported that three out of five studies included in the review showed that patients experienced a decrease in pain and pain-related distress (King 2010).

Thus, preliminary evidence supports the use of guided imagery for cancer-related distress, pain, and anxiety. This is further supported by the fact that no reports of adverse effects are noted in the literature. However, research in guided imagery suffers from a lack of consistency in the quality of the individual trials, and additional research with more rigorous designs and larger sample sizes is needed.

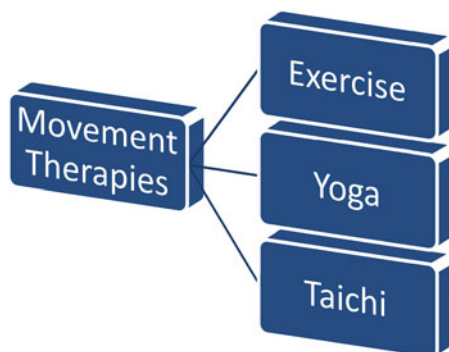
1.4.4.5 Meditation

Meditation is an attentional state reached through intentional focusing of attention on a repetitive behavior and/or thought (e.g. reciting repetitively a specific word or phrase). Meditation may also be practiced by noticing in the moment all thoughts, feelings, and sensations without judgment or attempts to direct those thoughts, feelings and sensations. Mindfulness meditation is the form of meditation most often studied in the cancer patient population (Deng et al. 2009).

Lerman and colleagues (2012) conducted an RCT of 68 female cancer patients (average age of 57 years) who had completed active treatment and were clinically stable. Participants were randomized to an intervention group or a wait list group based upon the overall scores obtained at baseline on the study measures. Of all the participants, 70% were breast cancer patients. Measures used in this study included the Symptoms Checklist, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, and the Symptoms Stress Inventory. Breast cancer patients received an additional questionnaire, EORTC QIQ-30 BR23. All of these instruments have established reliability and validity, and data were collected pre- and post-intervention.

The intervention consisted of weekly 2 h sessions for eight weeks augmented by a single 4 h weekend retreat during week 6, with mindfulness as a core principle. Program content included disease education, yoga, meditation, communication skills and mindful breast self-exams. The wait list group was specifically prohibited from practicing meditation and yoga. Statistically significant improvements in QoL scores, depression, and anger were found in members of the treatment group (Lerman et al. 2012).

In another RCT of 84 women with breast cancer, an six weeks mindfulness-based program was evaluated using pre- and post-intervention measures. Participants were 21 years or older, had a history of stage 0, I, II, or III breast cancer, had been treated with a combination of surgery, radiation and/or chemotherapy, and had completed treatment at least 18 months prior to participation in the study. Participants were randomized to the intervention group or a wait list control group. Those in the wait list control group received the usual standard of care. The Mindfulness Based Stress Reduction-Breast Cancer (MBSR-BC) program, which consisted of 6, 2 h weekly sessions conducted by a licensed clinical psychologist, was the intervention used in this study. The content focused on emotional responses, group support, and physical symptoms. The MD Anderson Symptom Inventory was used to measure patient symptoms was. It has established reliability and validity and measures symptom intensity and impact on functional status. Data were collected at baseline and within

Fig. 1.7 Movement therapies

two weeks of completing the intervention. Symptoms improved for both the intervention and control groups. Statistically significant improvement in fatigue and sleep quality was found in the treatment arm (Lengacher et al. 2012).

In summary, mindfulness meditation has been investigated using a wide range of study designs, although sample sizes tend to be smaller and there are few RCTs. Results suggest that mindfulness meditation may improve QoL, feelings of well-being, fatigue levels, anxiety and depression. No risk factors were identified in any of the studies.

1.4.5 Movement Therapies

Movement therapies involve the use of physical activity to improve physical conditioning, reduce fatigue, promote relaxation, and enhance QoL. Examples of movement therapies used with and by cancer patients include structured exercise programs (aerobic and resistance training), Taichi, and yoga (Fig. 1.7).

1.4.5.1 Exercise

Exercise used for management of cancer-related symptoms in research studies includes aerobic exercise, resistance training, and combined aerobic exercise and resistance training interventions. Many of these interventions are conducted in 30–45 min sessions three to four times per week over several weeks (Speck et al. 2010). The challenge in understanding the effect of exercise on cancer-related symptoms as represented in the current body of literature is that the interventions are variable between studies.

For example, an exercise RCT involving 121 men receiving radiation therapy for prostate cancer was conducted by Segal and colleagues (2009). The intervention consisted of aerobic exercise and resistance training offered over 24 weeks. The results showed a significant decrease in fatigue scores in both the resistance and

aerobic groups. However, one serious adverse event of acute myocardial infarction occurred in the aerobic exercise group. The participant reported a negative cardiac history. The authors hypothesized that the adverse event was most likely related to the aerobic exercise performed by an individual with pre-existing occult cardiovascular disease. The authors acknowledged that pre-intervention evaluation using symptom-limited exercise stress testing in individuals over the age of 45 and with a sedentary history would be a prudent precaution to take.

In another RCT, Midtgaard and colleagues (2011) investigated the impact of exercise on depression in 209 male and female cancer patients. The intervention consisted of aerobic exercise, resistance training, relaxation practice, and massage over six weeks. The HADS-A (anxiety) and HADS-D (depression) measures were used to assess anxiety and depression in the participants pre- and post-intervention. The results indicated a significant improvement in depression but no significant effect on anxiety.

In 2008, Courneya and colleagues (2008) conducted an RCT of an exercise intervention that consisted of aerobic and resistance exercise training. The RCT involved 242 breast cancer patients, and it was found that the participants' exercise preference influenced the QoL outcomes. Satisfaction with the type of assigned exercise was associated with positive QoL outcomes.

Exercise is recommended for improving emotional well-being and health-related QoL and reducing fatigue (Deng et al. 2009). In addition, exercise has been shown to improve depression but not anxiety (Midtgaard et al. 2011). Exercise is considered safe if implemented with input from the supervising physician and monitored by health care professionals in a supervised setting.

1.4.5.2 Yoga

Yoga is a 5,000 years old spiritual practice that uses body postures, controlled breathing, and meditation to achieve improved physical, emotional, and spiritual well-being (Galantino et al. 2012). There are many forms of yoga, which emphasize differing aspects of practice. However, all forms include some combination of body postures (asana), controlled breathing (pranayama), and meditation (Elkins et al. 2010). Yoga may be practiced as a solo practice or a group practice, and is frequently led by a yoga instructor.

In a review of studies comparing exercise to yoga, Ross and Thomas (2010) found that yoga was superior to exercise in all outcome measures other than fitness. Symptoms in chronically ill patients found to be improved by yoga included fatigue, mood, pain, and QoL. Yoga can also decrease patient anxiety, as shown in a 2009 RCT involving 98 early breast cancer patients undergoing treatment (Rao et al. 2009). Participants were recruited prior to primary treatment (surgery) and received an intervention of 60-min daily sessions of yoga. Members of the intervention group had a decrease in anxiety as compared to controls. In addition to these benefits, yoga has been found to improve sleep quality, health-related QoL, anxiety, and depression (Deng et al. 2009; Elkins et al. 2010). It is a safe intervention if led by a qualified yoga instructor.

1.4.5.3 Taichi

Taichi, a Chinese martial art, uses slow motion movement, breath control and active relaxation for promotion of well-being and health. Embedded in the practice of Taichi are some of the principles associated with mindfulness meditation as well (Reid-Arndt et al. 2012).

Reid-Arndt and colleagues (2012) conducted a small ($n=23$) pilot study with female cancer survivors whose treatment had been completed a minimum of 12 months earlier. Measures of cognitive functioning, psychological distress, and physical functioning were administered at baseline and within one month of completing the intervention. The intervention consisted of a 10-week Taichi course taught by a trained Taichi instructor who was blinded to all data. The course was adapted from training methods established for Yang style Taichi. The results of the study revealed improvements in balance, cognitive functioning, and stress levels none of which reached statistically significant levels.

The limitations of this study include the small sample and lack of control group. A larger sample with sufficient power to detect change would be important to include in a randomized controlled trial design of this intervention. However, the results do indicate areas of study that may be important to consider especially in the area of cognitive functioning.

Although the data is limited, there is some evidence that Taichi can improve health-related QoL (Monti et al. 2008; Sprod et al. 2012). A systematic review of controlled clinical trials of the effect of Taichi identified three RCTs that assessed the effects of Taichi within the breast cancer patient population (Lee et al. 2007). The results of these trials suggested that Taichi practiced over time resulted in reduced fatigue and improved depression scores, health-related QoL, and mood. However, the limited numbers of well-designed trials and small numbers of participants studied makes it difficult to evaluate the effect of Taichi. Preliminary evidence is suggestive, but no recommendations can be made at this time.

1.4.6 Touch Therapies

Touch therapies consist of those therapies that use physical contact to create a result. Examples of touch therapies presented here include massage therapy and reflexology (Fig. 1.8).

1.4.6.1 Massage Therapy

Massage can be defined as the manipulation through touch of the soft tissues of the body for the purpose of promoting well-being and relaxation, as well as relief of symptom distress (Wilkinson et al. 2008). Massage includes many different forms of touch, ranging from light touch to deep tissue massage.

Fig. 1.8 Touch therapies

The literature evaluating the use of massage with cancer patients who are receiving palliative care is growing. Prior to 2008, systematic reviews observed that the evidence was positive but not convincing (Wilkinson et al. 2008; Ernst 2009). Multiple RCTs have since been published and provide additional evidence for the benefit of massage in the cancer patient population. Examples of such trials are described below.

Kutner and colleagues (2008) published a report of a large RCT of massage and light touch. Participants ($n=380$) were randomized to one of three groups: a massage group, a light touch group, and a control group. The number of participants included in the immediate analysis was 298; and the total included in the long term analysis was 348. Massage had the greatest effect on reducing pain and improving mood, while simple touch also improved mood and reduced pain. These results provide preliminary support for the use of massage and simple touch for management of pain and mood. However, the therapists were not blinded to the data collection and bias may have been introduced (Kutner et al. 2008).

In a study to test the effect of a Swedish massage intervention on mood, Listing and colleagues (2009) conducted an RCT with 86 participants diagnosed with breast cancer. Significant reductions in discomfort, fatigue, and mood disturbance were found in the intervention group. However, a confounding variable was the role of inter-personal interaction of the masseuse and client, and some questions exist about its impact on the findings. Findings that massage has a positive effect on patients were also supported by a study of 34 breast cancer patients (Krohn et al. 2011). This study examined classical massage and found that depression and anxious depression were reduced in the intervention group as compared to the control group.

Massage is recommended for the management of pain and/or anxiety, and there are indications that it may be useful for nausea prevention and management. It is important to note that deep tissue massage is contraindicated in individuals who have cancer or those who have bleeding tendencies (Deng et al. 2009). It is critical that appropriately trained and certified individuals are employed to provide therapeutic massage in the clinical setting.

1.4.6.2 Reflexology

Reflexology is an intervention arising out of the Chinese and Indian health systems. The underlying principle of reflexology is that the body is represented on the sole of the foot; internal organs may be influenced by pressure exerted upon corresponding areas of the foot (Ernst 2009).

A 2011 review conducted by Ernst of RCTs that investigated the effect of reflexology identified 23 RCTs that met the criteria for inclusion in the review. Of those trials, 14 did not support use of reflexology, eight suggested positive effects, and one was ambiguous. Of the eight that suggested a positive effect, two were conducted with a cancer patient population (Ernst et al. 2011). One of those, an RCT led by Sharp, investigated the psychological effects of reflexology in breast cancer patients. A three group design of self-selected support alone, self-selected support and reflexology, and self-selected support and scalp massage was employed with 183 female participants. The results failed to demonstrate a difference between groups (Sharp et al. 2010). Because there are limited numbers of well-designed studies investigating reflexology and results have been inconclusive, further research is required before any conclusions can be drawn about the efficacy and/or safety of this intervention.

1.5 Uses of Non-pharmacological Therapies for Cancer Symptom Management in Palliative Care

Symptoms commonly associated with cancer and cancer treatment include pain, nausea and vomiting, fatigue, insomnia, dyspnea, delirium, anxiety, depression and distress. Symptoms may present early in treatment and may persist for five years or longer after the termination of treatment (Harrington et al. 2010). A systematic review of the literature found that in patients treated for breast, prostate, colorectal, and gynecological cancer, fatigue, sleep disturbances, depression, anxiety, and pain persisted five years post-treatment at rates ranging between 14 and 41% (Harrington et al. 2010). Fatigue is one of, if not the most, commonly cited symptoms associated with cancer and its treatment (Walsh et al. 2000).

Complicating the successful management of symptoms is the occurrence of multiple symptoms simultaneously. Clusters of symptoms that commonly occur together have been identified, and are defined as concurrent and related symptoms that may or may not have a common etiology (Dodd et al. 2001). Examples of symptom clusters include fatigue, nausea, weakness, appetite, altered taste, and vomiting (Gift et al. 2004); fatigue, anxiety, insomnia, and depression (Redeker et al. 2000); and pain, nausea, and fatigue (Kurtz et al. 2007). The presence of symptom clusters that may or may not be related requires a comprehensive assessment and treatment plan that integrates pharmacological and non-pharmacological therapies delivered by an interdisciplinary team.

1.5.1 Pain

Pain is an unpleasant subjective sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (Pasero and McCaffery 2011). The NCCN (2011d) emphasize the need for health care professionals who are skillful at assessing, identifying, and treating cancer pain as it is one of the

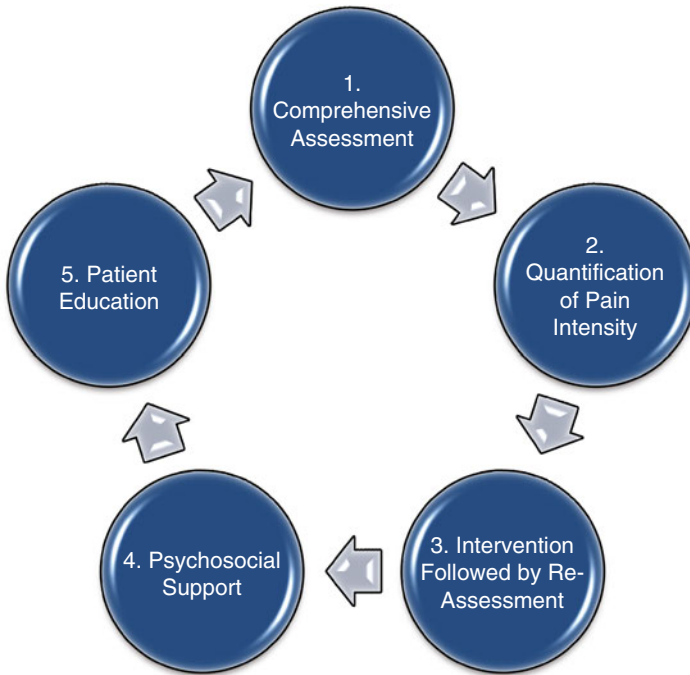


Fig. 1.9 Required elements of adult cancer pain practice guidelines (NCCN 2011d)

most common symptoms associated with cancer treatment. The required components of the practice guideline are (Fig. 1.9):

1. A comprehensive assessment
2. Quantification of pain intensity by the patient
3. Re-assessment of pain intensity at specified intervals following intervention
4. Psychosocial support
5. Patient education

The guidelines recommend that non-pharmacological therapies (Table 1.3) be considered in situations where there is reason to believe that the pain will be relieved or function improved. However, availability of a qualified health care provider to provide non-pharmacological therapy may limit access to that therapy. Non-pharmacological therapies can be considered early in the pain management process if it is apparent that pain relief may be improved by the use of the therapies and functionality enhanced, and patient use of non-pharmacological therapies should be assessed (NCCN 2011d). It is incumbent upon the health care provider to inquire about the use of non-pharmacological therapies and their effects. Non-pharmacological therapies in use that may pose a risk can be discussed and evaluated in a collaborative and thoughtful manner by provider and patient.

Table 1.3 Non-pharmacological interventions for adult cancer pain (NCCN 2011d)

Therapy	Evidence	Cautions
Hypnosis	Convincing evidence supports use for pain management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Evidence supports use for pain management	Safe when performed by a qualified provider
Relaxation training	Evidence supports use for pain management	Safe when performed by a qualified provider
Psychotherapy (cognitivebehavioral therapy, coping training)	Evidence supports use for distress related to pain management	Safe when performed by a qualified and licensed health care practitioner
Acupuncture	Preliminary evidence supports use for pain management	Safe when performed by a qualified practitioner
Massage	Preliminary evidence supports use for pain management	Massage should not be used in those with tendencies towards bleeding or over the tumor bed or surgical wound, deep massage should not be used

1.5.2 Nausea and Vomiting

Nausea is a subjective symptom involving an unpleasant sensation experienced in the back of the throat and the epigastrium, which may or may not result in vomiting. Acute nausea occurs within minutes or hours after events such as chemotherapy. Delayed nausea generally occurs at least 24 h after events such as chemotherapy and may last for several days. Anticipatory nausea occurs before the actual stimulus and develops only after an individual has had a previous bad experience with an event such as chemotherapy that resulted in nausea or vomiting (King and Tarcatu 2010).

Vomiting is a self-protective mechanism by which the body attempts to expel toxic substances and involves the expulsion of gastric contents through the mouth, caused by forceful contraction of the abdominal muscles (King and Tarcatu 2010).

Nausea and vomiting are sometimes associated with cancer and its treatment. Cancer therapies that are often associated with nausea and vomiting as side effects include chemotherapy, radiation therapy, and treatment with other medications (NCCN 2011c). Medications for the treatment of cancer-related nausea and vomiting have become more effective in recent years. However, despite treatment with these medications, some patients continue to experience nausea and vomiting.

Anticipatory nausea and vomiting (ANV), which is thought to be a conditioned response to noxious stimuli, is a form of nausea and vomiting that is very difficult to treat. Figure 1.10 illustrates the cycle that supports the development of ANV. In cancer patients, chemotherapy is usually the trigger for development of ANV. Risk factors for ANV are age less than 50, nausea and vomiting with the last chemotherapy session,

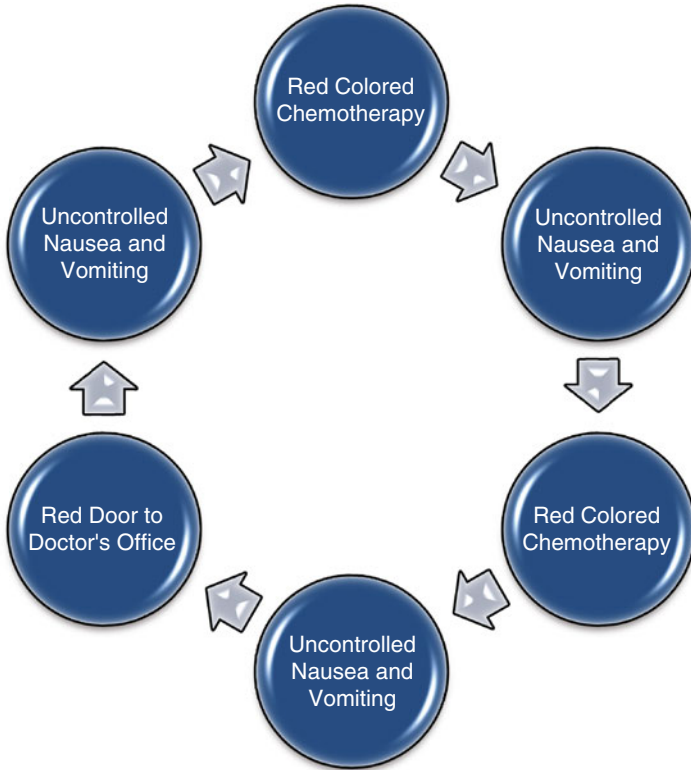


Fig. 1.10 Conditioned response in chemotherapy-induced anticipatory nausea and vomiting (Roscoe et al. 2011)

expectations of nausea, anxiety, susceptibility to motion sickness, and feeling warm at the last chemotherapy session (Roscoe et al. 2011).

Non-pharmacological therapies have been shown to be very effective in the management of ANV (Table 1.4) (Mundy et al. 2003). In particular, interventions such as hypnosis, yoga, relaxation training, and guided imagery have been shown to be very beneficial (Roscoe et al. 2011).

1.5.3 *Dyspnea*

Dyspnea or breathlessness is defined as a subjective experience of breathing discomfort that consists of qualitatively distinct sensation that varies in intensity (American Thoracic Society 1999).

Dyspnea is a common symptom experienced by cancer patients. It has been reported that as many as 70% of patients experience dyspnea towards the end of life. There are some indications that anxiety and distress contribute to dyspnea, but it is

Table 1.4 Non-pharmacological interventions for cancer-related anticipatory nausea and vomiting (ANV) (Roscoe et al. 2011)

Therapy	Evidence	Cautions
Hypnosis	Convincing evidence supporting use for ANV management	Safe when performed by a qualified and licensed health care practitioner
Relaxation training	Evidence supports use for ANV management	Safe when performed by a qualified provider
Guided imagery	Developing evidence supporting use for ANV management	Safe when performed by a qualified provider
Acupuncture	Preliminary evidence to supports use for relief of ANV	Safe when performed by a qualified practitioner

Table 1.5 Non-pharmacological interventions for cancer-related dyspnea (Booth et al. 2008)

Therapy	Evidence	Cautions
Music therapy	Convincing evidence supports use for distress related to dyspnea management	Safe for use with this patient population
Relaxation training	Evidence supports use for dyspnea management	Safe when performed by a qualified provider
Psychotherapy (cognitivebehavioral therapy, coping training)	Evidence supports use for distress related to dyspnea management	Safe when performed by a qualified and licensed health care practitioner
Hypnosis	Developing evidence supporting use for dyspnea management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Developing evidence supporting use for dyspnea management	Safe when performed by a qualified provider
Acupuncture	Limited evidence to support use for relief of anxiety in the context of dyspnea	Safe when performed by a qualified practitioner

unclear whether they are etiological factors or contribute to exacerbating a process already present (Booth et al. 2008).

Non-pharmacological therapies have a role in managing the distress associated with dyspnea. Cancer-related dyspnea is a chronic, progressive symptom that may occur throughout the illness trajectory. Preparing patients to use non-pharmacological therapies for the management of dyspnea early in the disease process maximizes the opportunity for a successful remedy of the symptom. Non-pharmacological therapies recommended for use with dyspnea include hypnosis, self-hypnosis, guided imagery, relaxation, controlled breathing, music therapy, and acupuncture (Table 1.5) (Bausewein et al. 2008). Inter-disciplinary care teams can contribute to managing this symptom by using the full range of therapeutic modalities available.

Table 1.6 Non-pharmacological interventions for cancer-related fatigue (Sood and Barton 2010)

Therapy	Evidence	Cautions
Exercise	Convincing evidence of benefit for the management of fatigue	Safe if implemented with input from the supervising physician
Yoga	Convincing evidence of benefit for the management of fatigue	Safe if supervised by a qualified yoga instructor
Hypnosis	Developing evidence supporting use for fatigue management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Developing evidence supporting use for fatigue management	Safe when performed by a qualified provider
Relaxation training	Developing evidence supporting use for fatigue management	Safe when performed by a qualified provider
Controlled breathing	Developing evidence supporting use for fatigue management	Safe when performed by a qualified provider
Mindfulness meditation-based stress reduction	Developing evidence supporting use for fatigue management	Safe when led by a qualified provider

1.5.4 Fatigue

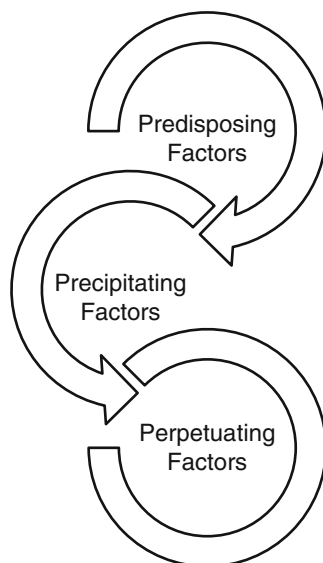
The National Comprehensive Cancer Network defines fatigue as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and cancer treatment that is not related to recent activity and that interferes with usual functioning (NCCN 2011a). Fatigue is one of most common symptoms associated with cancer and its treatment. Approximately 84% of patients with cancer experience fatigue (Walsh et al. 2000), and patients who receive chemotherapy and radiation have very high rates of fatigue (59–100%) (Sood and Barton 2010). The mechanism of cancer fatigue is not well understood, and standard therapy for cancer-related fatigue is treatment of the underlying conditions (Sood and Barton 2010).

Among the non-pharmacological therapies, exercise and yoga have the strongest evidence supporting an effect in treating cancer-related fatigue (Deng et al. 2009). Other therapies that have preliminary evidence of benefit include hypnosis, mindfulness-based stress reduction, relaxation training, and controlled breathing (Table 1.6) (Sood and Barton 2010).

1.5.5 Insomnia

Insomnia is characterized by ineffective sleep patterns that result in poor sleep. One model of insomnia is the three P Model (Fig. 1.11) in which predisposing, precipitating, and perpetuating factors promote the development of insomnia. Predisposing

Fig. 1.11 Three P model of insomnia (Ebben and Spielman 2009)



factors include those qualities of the individual that might prevent restful sleep, such as genetics or anxiety. Precipitating factors include stressful life circumstances or over indulgence in caffeine, while perpetuating factors, such as poor sleep hygiene, entrench the poor quality of sleep (Ebben and Spielman 2009). Treatment of insomnia largely involves behavioral interventions that focus on promoting consistent and restful sleep routines (Fig. 1.11).

There is convincing evidence to support the use of progressive muscle relaxation, guided imagery, meditation, and hypnosis in the treatment of insomnia (Deng et al. 2009; Ebben and Spielman 2009). There is also preliminary evidence that yoga and exercise may be useful in the management of insomnia (Table 1.7) (Deng et al. 2009).

1.5.6 Cancer-related Anxiety and Distress

Cancer- and cancer treatment-related anxiety is a normal response to the experience of a chronic and potentially life threatening illness. Anxiety is often associated with restlessness, irritability, loss of appetite, and feelings of apprehension (Pasacreta et al. 2010). Anxiety associated with adjustment to cancer and cancer-related treatment may be differentiated from an anxiety disorder by the length and severity of symptoms as described in the DSM-IV-TR:

Distress is a multi-factorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis (NCCN 2011b).

Table 1.7 Non-pharmacological interventions for cancer-related insomnia (Deng et al. 2009; Ebben and Spielman 2009)

Therapy	Evidence	Cautions
Hypnosis	Convincing evidence supporting use for insomnia management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Convincing evidence supporting use for insomnia management	Safe when performed by a qualified provider
Relaxation training	Convincing evidence supporting use for insomnia management	Safe when performed by a qualified provider
Mindfulness meditation-based stress reduction	Convincing evidence supporting use for insomnia management	Safe when led by a qualified provider
Exercise	Developing evidence supporting use for insomnia management	Safe if implemented with input from the supervising physician
Yoga	Developing evidence supporting use for insomnia management	Safe if supervised by a qualified yoga instructor

Convincing evidence supports the use of psychotherapy, music therapy, hypnosis, guided imagery, controlled breathing, relaxation training, exercise, yoga, acupuncture, and meditation in the management of cancer-related distress and anxiety (Deng et al. 2009). Reiki, healing touch, and art therapy have preliminary evidence that is supportive but not convincing (Table 1.8).

1.5.7 *Cancer-related Depression*

Cancer- and cancer treatment-related depression is a normal response to the experience of a chronic and potentially life threatening illness. Depression often presents with fatigue, weight loss, sleep problems, concentration difficulties, irritability, and apprehension (Pasacreta et al. 2010). Depression associated with adjustment to cancer and cancer-related treatment may be differentiated from a depressive disorder by the length and severity of symptoms. There is evidence supporting the use of psychotherapy, art therapy, massage, exercise, yoga, meditation, relaxation, and guided imagery with depression (Table 1.9) (Deng et al. 2009).

1.6 Conclusion

Non-pharmacologic therapies for the management of cancer-related symptoms are being embraced by patients and their caregivers, and by health care specialties such as palliative and supportive care. Evidence that supports the safety and efficacy

Table 1.8 Non-pharmacological interventions for cancer-related anxiety and distress (Deng et al. 2009)

Therapy	Evidence	Cautions
Psychotherapy	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when performed by a qualified and licensed health care practitioner
Music Therapy	Convincing evidence supporting use for cancer related anxiety and distress management	No evidence of risk reported
Acupuncture	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when performed by a qualified provider
Hypnosis	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when performed by a qualified provider
Relaxation training	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when performed by a qualified provider
Controlled breathing	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when led by a qualified provider
Mindfulness meditation-based stress reduction	Convincing evidence supporting use for cancer related anxiety and distress management	Safe when led by a qualified provider
Exercise	Convincing evidence supporting use for cancer related anxiety and distress management	Safe if implemented with input from the supervising physician
Yoga	Convincing evidence supporting use for cancer related anxiety and distress management	Safe if supervised by a qualified yoga instructor
Reiki	Preliminary, but not convincing evidence	No evidence of risk reported
Healing touch	Preliminary, but not convincing evidence	No evidence of risk reported
Art therapy	Preliminary, but not convincing evidence	Safe when performed by a qualified and licensed health care practitioner

of these therapies is required in order to move forward with the integration of non-pharmacologic therapies into the standard of care for symptom management. Evidence that supports individual therapies is growing, and some therapies, such as hypnosis, have significant and convincing evidence to support their use. Continued efforts to construct well-designed studies that investigate non-pharmacological therapies are necessary for the continued development and acceptance of these therapies into the standard of care.

Table 1.9 Non-pharmacological interventions for cancer-related depression (Deng et al. 2009)

Therapy	Evidence	Cautions
Art therapy	Convincing evidence supporting use for cancer depression management	Safe when performed by a qualified and licensed health care practitioner
Guided imagery	Convincing evidence supporting use for cancer depression management	Safe when performed by a qualified provider
Relaxation training	Convincing evidence supporting use for cancer depression management	Safe when performed by a qualified provider
Mindfulness meditation-based stress reduction	Convincing evidence supporting use for cancer depression management	Safe when led by a qualified provider
Exercise	Convincing evidence supporting use for cancer depression management	Safe if implemented with input from the supervising physician
Yoga	Convincing evidence supporting use for cancer depression management	Safe if supervised by a qualified yoga instructor
Massage	Convincing evidence supporting use for cancer depression management	Massage should not be used in those with tendencies towards bleeding or over the tumor bed or surgical wound, deep massage should not be used
Psychotherapy	Preliminary evidence supporting use for cancer depression management	Safe when performed by a qualified and licensed health care practitioner

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Chapter 2

Effect of Massage Therapy on Anxiety and Depression in Cancer Patients

Jiro Imanishi

Abstract Massage therapy has many kinds of effects on the physical and psychological conditions of healthy people and patients. Since it is well known that massage therapy can reduce anxiety, depression, and stress, it is given to patients with cancer. Many researchers examined the effects of massage therapy including aromatherapy massage and observed a reduced state and trait anxiety, and improved mood, depression, and quality of life (QoL) in healthy people. It was found that massage therapy including aromatherapy massage can decrease the scores of State-Trait Anxiety Inventory and psychological confusion of Profile of Mood State in healthy volunteers. Furthermore, it was recognized that patients with mild depression was ameliorated by aromatherapy massage. There are many studies on the effect of massage therapy including aromatherapy massage on anxiety, depression, stress, and QoL in patients with cancer. It appears that massage therapy can reduce anxiety and stress and improved QoL. In conclusion, massage therapy including aromatherapy massage in cancer patients would be beneficial for the reduction of anxiety, depression, and stress as well as pain, and is generally safe. However, further studies, especially randomized clinical trials, should be performed.

J. Imanishi (✉)

MUIM Center for Integrative Medicine, Meiji University of Integrative Medicine,
Kyoto Eminence 6th floor, 2-4 Higashi-Sakaidani-cho, Ooharano,
Nishikyo-ku, Kyoto 610-1143, Japan
e-mail: imanishi-micro@nifty.com

2.1 Introduction

Therapies for cancer including surgery, chemotherapy, radiation therapy, and immunotherapy have become highly sophisticated, and the curing, remission, and survival rates of patients have been greatly improved. However, psychological approaches for treating cancer patients have not yet been successfully developed and a number of cancer patients suffer from psychological issues such as anxiety, depression, and hopelessness. Therefore, psycho-oncological care is essential for cancer patients.

In addition, surgery, chemotherapy, and radiation therapy causes physical discomfort such as nausea, vomiting, constipation, diarrhea, hematological disturbances, neurological symptoms including numbness, pain, and dizziness, and psychological symptoms. Naturally, cancer itself induces various kinds of physical and mental discomfort such as pain, anxiety, depression, fatigue, and symptoms specific for the kinds and loci of cancer.

Complementary and alternative medicine (CAM) is defined by the National Center for Complementary and Alternative Medicine in the United States as a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.

Many CAM therapies are used as adjuncts to relieve the physical and psychological discomfort caused by cancer itself and chemotherapy, surgery, and radiation. Therefore, the combination of modern medicine with CAM therapies, namely integrative medicine, is very important for cancer treatment, although different interventions are needed for different cancer stages, such as new diagnosis, period of remission, recurrence, long-term survival, and/or end of life.

In this chapter, the author reviewed studies on the effect of massage therapies including aromatherapy massage in the treatment of cancer.

2.2 Effect of Massage Therapy on Anxiety and Depression

2.2.1 *Effect of Commonly Used Massage Therapy*

Massage therapy has a long history and is one of the oldest forms of medical treatment in the world. It was first described in China in the second century B.C. and soon after in India and Egypt. Ever since then, massage therapy has been used for various medical conditions (Field 1998). However, after the development of new modern medical drugs in the 1940s, massage therapy was forgotten and ignored in mainstream medicine.

The recent boom in CAM is attracting attention to massage therapy. Generally, massage therapy is considered to improve circulation, facilitate the elimination of waste, reduce swelling, and soothe the function of peripheral and central nervous systems.

Table 2.1 Psychological changes with State-Trait Anxiety Inventory (STAI) by massage therapy in healthy people

	Pre-test		Post-test		<i>p</i> -value
	Mean	SD	Mean	SD	
State-anxiety	39.59	7.96	29.03	6.15	<0.001
Trait-anxiety	45.12	12.3	42.18	12.12	<0.001

Eleven healthy adult subjects were recruited and the scores of the STAI were measured before and after a 30-min aromatherapy massage or control massage. Results showed that state anxiety scores from the STAI decreased significantly ($p < 0.001$) after both aromatherapy and control massage, which suggest that both aromatherapy massage and control massage were effective in inducing relaxation in terms of decreasing state anxiety levels

One of the most common applications of massage therapy is reducing pain. Quinn et al. (2002) showed that massage therapy reduced chronic tension headaches in four subjects, comparing with baseline measures. However, the use of massage for relaxation and reducing levels of anxiety is also becoming popular. For example, massage therapy has been reported to reduce levels of anxiety and stress hormones and improve the clinical course in children under various medical conditions (Field 1995). The psychiatric effects of massage therapy, reductions in anxiety and hostility, and diminished depression have all been documented. Diego et al. (2002) randomly assigned 17 aggressive adolescents to a massage therapy group or relaxation therapy group to receive 20-min therapy sessions, twice a week for five weeks. The massaged adolescents had lower anxiety after the first and last sessions. By the end of the study, they also reported feeling less hostile and they were perceived by their parents as being less aggressive. Significant differences were not found for the adolescents who were assigned to the relaxation group.

The effect of massage on psychological relaxation was examined in normal subjects in a non-controlled trial with 32 subjects, aged from 18 to 56 years (10 males; 22 females) (Kuriyama et al. 2005a). A 25-min whole body massage was performed and the scores of State-Trait Anxiety Inventory (STAI) were determined as psychological measures. Results showed that both state and trait anxiety scores decreased significantly ($p < 0.001$) (Table 2.1).

Field et al. (1996) also reported similar results. Twenty-two depressed adolescent mothers received ten 30-min sessions of massage therapy or relaxation therapy over a 5-week period. Subjects were randomly assigned to each group. In the massage therapy group, both trait and state anxiety scores were significantly reduced, with the latter more so, which is reasonable because the “state anxiety” score represents a temporary condition that changes every moment, while the “trait anxiety” score represents a more general and long-standing quality of anxiety.

In addition, because subjects with high initial anxiety levels tended to have more decreased anxiety scores after massage therapy in our study, massage may be useful for reducing anxiety in patients with high anxiety levels such as psychosomatic and neurotic patients due to cancer. It is rather unusual that trait anxiety was also reduced in our study, which is thought to be due to large changes in state anxiety and partly due to a social desirability bias.

Furthermore, there have been reports on the effect of massage on the immune functions. Namely, Birk et al. (2000) reported that in a randomized prospective controlled trial with 42 subjects randomly assigned to one of three treatment groups or a control group receiving standard care and 45-min overall body massage therapy over a 12-week period, no significant changes were found in any enumerative immune measure (CD4⁺ lymphocytes, CD8⁺ lymphocytes, CD4⁺/CD8⁺ lymphocyte ratio and natural killer cells).

Diego et al. (2001) recruited HIV⁺ adolescents (mean CD4⁺ cells = 466 mm³) from a large urban university hospital's outpatient clinic and randomly assigned to receive massage therapy ($n = 12$) or progressive muscle relaxation ($n = 12$) two-times per week for 12 weeks. Adolescents who received massage therapy vs those who experienced relaxation therapy showed enhanced immune function by the end of the 12 weeks study. Immune changes included increased natural killer cell number (CD56) and CD56⁺CD3⁻. In addition, the HIV disease progression markers CD4/CD8 ratio and CD4 number showed an increase for the massage therapy group only.

Miller and Cohen (2001) reviewed evidence for the hypothesis that psychological interventions can modulate the immune response in humans, and concluded that although the reviewed data provide only modest evidence of successful immune modulation, it would be premature to conclude that the immune system is unresponsive to psychological interventions.

The mechanisms of the mode of action of massage therapy are recognized as follows: massage therapy induces pain reduction by increasing serotonin and endorphins, improving blood flow, improving lymphatic circulation, and interpersonal attention (Corbin 2009).

The hypothalamic-pituitary adrenal axis is known to play an important role in the mind-immune interaction. Positive correlations between plasma cortisol levels and neutrophil numbers have been observed in a group of hospitalized depressed patients (Kronfol and House 1989). Ironson and Field (1996) reported that 29 gay men (20 HIV-positive, 9 HIV-negative) received daily massage for one month, and massage therapy decreased cortisol in 24-h urine collections. And they suggested that decreased neutrophil counts after massage therapy were probably the result of a relaxation-induced down-regulation of the sympathetic nervous system and reduced stress hormone levels.

Thus, massage therapy is an effective relaxation/stress management technique that could reduce anxiety, downregulate the sympathetic nervous system, and reduce stress hormone levels.

2.2.2 Effect of Aromatherapy Massage on Anxiety and Depression

In general, aromatherapy is the use of essential oils, the pure volatile portion of aromatic plant products, for therapeutic or medical purposes. As is the case with other CAM therapies, use of aromatherapy has increased in recent years. Essential

oils have many kinds of pharmacological actions including anti-microbial, sedative, analgesic, spasmolytic, and estrogen or steroid hormone-like effects. Since various kinds of essential oils such as true lavender, rose, mandarin, sweet orange, sandalwood, and geranium have anxiolytic activities, aromatherapy has been used for the relief of depression and anxiety.

Like classical massages, aromatherapy massage also acts on the central nervous system, relieving depression and anxiety, reducing stress, relaxing, sedating or stimulating, and restoring both physical and emotional wellbeing (Buckle 1997).

Although there are few published clinical trials examining the effectiveness of aromatherapy, the number of trials has been increasing in recent years. Cooke and Ernst (2000) reviewed six randomized clinical trials to study the effect of aromatherapy massage, and concluded that aromatherapy appeared to have at least a transient effect in the reduction of anxiety, but there was no evidence of a lasting benefit.

The effect of aromatherapy massage on psychological measures in comparison with control massage was examined using an open controlled study (Kuriyama et al. 2005b). Data were compared in a repeated measures design immediately before and after aromatherapy massage in the same subjects. They were also compared in the measures design between aromatherapy massage and control massage in the same subjects. Eleven healthy adult subjects were recruited and the scores of the STAI and self-rating depression scale were measured before and after a 30-min aromatherapy massage or control massage (Table 2.1). Results showed that in psychological measures, state anxiety scores from the STAI decreased significantly ($p < 0.001$) after both aromatherapy and control massage. Our results suggest that both aromatherapy massage and control massage were effective in inducing relaxation in terms of decreasing state anxiety levels. State anxiety scores were significantly reduced, although trait anxiety scores did not change. Although a difference in effect between aromatherapy massage and control massage was not observed, massage and aromatherapy massage are suggested, from the results of our study, to be an effective relaxation/stress management technique to reduce anxiety.

Hongratanaworakit (2011) examined the effects of blended essential oil on autonomic parameters and on emotional responses in humans following transdermal absorption. Blended essential oil consisted of lavender and bergamot oils. Human autonomic parameters, such as blood pressure, pulse rate, breathing rate, and skin temperature, were recorded. In addition, subjects had to rate their emotional condition in terms of relaxation, vigor, calmness, attentiveness, mood, and alertness in order to assess subjective behavioral arousal. Forty healthy volunteers participated in the experiments. Blended essential oil was applied topically to the skin of the abdomen of each subject. Compared with the placebo, blended essential oil caused significant decreases in pulse rate and systolic and diastolic blood pressure, which indicated a decrease in autonomic arousal. At the emotional level, subjects in the blended essential oil group rated themselves as 'more calm' and 'more relaxed' than subjects in the control group. From the results of this and our studies, it was concluded that aromatherapy causes relaxation.

Next, we examined the effects of aromatherapy massage on cognition using a neuropsychological test designed for patients with depression (Okamoto et al. 2005).

Table 2.2 Effect of aromatherapy massage on Hamilton Depression Rating Scale (HAM) and Profile of Mood State (POMS) in patients with mild depression

	Pre-test		Post-test		<i>p</i> -value
	Mean	SD	Mean	SD	
HAM	14.8	2.39	8.8	3.63	0.039
POMS					
Tension-anxiety	57	9.25	51.4	8.88	0.144
Depression-dejection	58.6	14.36	54.2	10.33	0.144
Anger-hostility	56	13.17	50.6	11.72	0.144
Vigor	40.4	25.24	52.2	10.47	0.223
Fatigue	60.2	12.95	52.6	8.38	0.068
Confusion	62.2	13.07	51.6	8.05	0.043

Five patients aged 31–59 years, with Diagnostic and Statistical Manual of Mental Disorders-IV mild unipolar major depression, received a 30-min aromatherapy massage twice a week for four weeks, using essential oils of sweet orange, geranium, and basil. Patients were submitted to the 17-item HAM and POMS one week before the first session and one week after the last session. Results showed that HAM scores and “confusion” of POMS significantly improved, which suggests that improvements in depressive states were gained subjectively and objectively

This study was carried out with five patients aged 31–59 years, with the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV mild unipolar major depression (not including psychotic features). None of the patients had a lifetime history of electroconvulsive therapy, head injury, or substance dependence. None of the patients used anti-depressants or received psychotherapy. Each received a 30-min aromatherapy massage twice a week for four weeks, using essential oils of sweet orange, geranium, and basil. In order to examine the response to treatment, patients were submitted to the 17-item Hamilton Depression Rating Scale (HAM) and Profile of Mood State (POMS) one week before the first session and one week after the last session. Cognitive function was evaluated using the Wisconsin Card Sorting Test (WCST). Results showed that HAM scores and “confusion” of POMS were significantly improved, suggesting that improvements in depressive states were gained subjectively and objectively. “Confusion”, one of the subscales of POMS, indicated subjective disturbances of cognition and thought (Table 2.2). Errors, perseverative errors, and perseverative responses of the WCST significantly decreased (Table 2.3), meaning an improvement in prefrontal dysfunction, because WCST assessed rule conceptualization and modification of strategies for responses to verbal feedback, and is particularly sensitive to damage in the prefrontal cortex. Because of the 4-week interval, improvements in WCST scores may be due to a learning effect. However, Moreaud et al. (1996) reported a study where WCST was administered before and 21 days after treatment for major depressive patients. Results of this study suggested that improvements in WCST scores did not always depend on the intervals of the first and second administration of WCST.

Many types of depressive conditions can be involved in decreases in metabolism and low blood flow in the frontal lobe. Hirata et al. (2002) reported that olfactory stimulation increased blood flow to the prefrontal cortex. Komori et al. (1995) gave

Table 2.3 Effect of aromatherapy massage on Wisconsin Card Sorting Test (WCST) in patients with mild depression

	Pre-test		Post-test		<i>p</i> -value
	Mean	SD	Mean	SD	
WCST					
Total number of errors	24.4	3.97	17.2	3.19	0.042
Non-perseverative errors	8.8	2.28	7	3.08	0.144
Perseverative errors	15.6	5.03	10.2	2.17	0.043
Perseverative responses	16.8	5.81	10.4	2.51	0.042
Conceptual level responses	62	1.87	61.8	2.49	1
Number of categories completed	5.8	0.45	6	0	0.317
Trials to complete first category	12.4	3.05	14	2.92	0.465
Failure to maintain set	1	1.73	0.4	0.55	0.414
Learning to learn	-3.13	4.08	2.62	3.31	0.138

Five patients aged 31–59 years, with Diagnostic and Statistical Manual of Mental Disorders-IV mild unipolar major depression, received a 30-min aromatherapy massage twice a week for four weeks, using essential oils of sweet orange, geranium, and basil. Cognitive function was evaluated using the WCST. Errors, Perseverative Errors, and Perseverative Responses of the WCST significantly decreased, which means an improvement in prefrontal dysfunction because WCST assesses rule conceptualization and modification of strategies for responses to verbal feedback and is particularly sensitive to damage in the prefrontal cortex

the citrus fragrances to 12 depressive subjects and the results indicated that the doses of anti-depressants necessary for the treatment of depression could be markedly reduced. The treatment with citrus fragrance normalized neuroendocrine hormone levels and immune function and was rather more effective than anti-depressant. Thus, aromatherapy is possibly useful as a complementary therapy for depression.

2.2.3 *Effects of Aromatherapy, Except for Anxiety and Depression*

In addition to reductions in anxiety and improvements in the depressive state, the sedative effect of essential oils is well-known, as well as their sleep-promoting effects (Perry and Perry 2006). Therefore, aromatherapy may help to improve sleep disturbance in the elderly. Due to behavioral disturbances, patients with dementia often have marked difficulties in sleeping, and so aromatherapy may be particularly useful for them. In fact, aromatherapy has been previously used for people with dementia to reduce disturbed behavior (Henry et al. 1994; Ballard et al. 2002; Holmes et al. 2002; Snow et al. 2004), promote sleep (Wolfe 1996), stimulate motivational behavior (MacMahon and Kermod 1998), and improve cognitive function (Kennedy and Scholey 2006).

Ballard et al. (2002) conducted a placebo-controlled trial to determine the value of aromatherapy with essential oil of *Melissa officinalis* (lemon balm) for agitation in 72 people with severe dementia. They were randomly assigned to aromatherapy with melissa essential oil ($n=36$) or placebo (sunflower oil) ($n=36$). Seventy-one patients completed the trials. Sixty percent (21/35) of the active treatment group and 14% (5/36) of the placebo-treated group experienced a 30% reduction of Cohen-Mansfield Agitation Inventory (CMAI) score, with an overall improvement in agitation (mean reduction in CMAI score) of 35% in patients receiving Melissa balm essential oil and 11% in those treated with placebo. Quality of life indices also improved significantly more in people receiving essential balm oil.

Snow et al. (2004) also examined the effect of aromatherapy on agitation in seven patients with dementia in the study design of within-subjects ABCBA (A = lavender oil, B = thyme oil, C = unscented grapeseed oil). The study found no support for the use of purely olfactory form of aromatherapy to decrease agitation in severely demented patients.

On the other hand, Holmes et al. (2002) determined whether aromatherapy with lavender oil was effective in the treatment of agitated behavior in 15 patients with severe dementia in a placebo controlled trial with blinded observer rater, and concluded that lavender oil showed modest efficacy in the treatment of agitated behavior in patients with severe dementia.

MacMahon and Kermodé (1998) undertook a clinical trial of the effectiveness of aromatherapy on motivational behavior in a dementia care setting using an AB design. Baseline data were recorded for two months, followed by two months of treatment data. Findings showed a statistically significant improvement in motivational behavior associated with the use of aromatherapy.

Thus, there have been many studies on the effects of aromatherapy on sleep and behavioral disturbances as mentioned above. However, there have been no studies on the effects of aromatherapy massage on circadian rhythm disturbance, which is frequently observed in the elderly.

One method of measuring the sleep state and circadian rhythms is by monitoring activity levels. This can be done through the use of an actigraph, a motion-sensing device, approximately the size of a man's wrist watch, which is worn on the wrist and is comprised of an accelerometer, a microprocessor, and 32 K of retrievable memory. Actigraphy is a simple, non-invasive method of measuring levels of day- and night-time activity and can be used for precise estimation of the amounts of both day- and night-time sleep. In addition, activity patterns over several consecutive days can be analyzed employing autocorrelational techniques to provide estimates of sleep states and circadian rhythms (Kripke et al. 1978; Taphoorn et al. 1993).

We examined the effect of aromatherapy massage on circadian rhythms in eight elderly subjects in an open semi-comparative trial, comparing parameters in the second week in which aromatherapy massage sessions were given, in 1-week periods (the first and third week) before and after sessions (Imanishi et al. 2010). The % sleep and sleep efficiency during the down period tended to increase, wake minutes after sleep onset tended to be shorter, and the "rhythm pattern" was significantly

higher in the second week than those in the first and/or third week. A higher peak in the 24-h cycle circadian rhythm was noted following aromatherapy massage in the elderly, who often exhibit circadian rhythm disturbances. Furthermore, peaks in the spectrum cycle in the second week seemed to be closer to 24 h than those in the first and third week. These results suggest that aromatherapy massage improves circadian rhythm disturbances.

2.3 Effect of Massage Therapy in Cancer Patients

2.3.1 Usage of Massage Therapies in Cancer

Although massage therapy can benefit patients with cancer, special considerations are needed for these patients. Risks should be minimized and benefits maximized while clinicians feel comfortable dismissing massage therapy with his or her patients (Corbin 2009).

As already mentioned, massage therapy is effective for sedation, relaxation, and the reduction of stress, anxiety, and depression. Thus, massage therapy is expected to be useful for adjunctive cancer treatment in combination with modern Western medicine treatments including surgery, chemotherapy, and radiation.

Ernst (2009) systematically reviewed the effects of massage therapy for cancer palliation and supportive care, searching six databases to identify all trials of classical massage for cancer patients. Fourteen trials met all inclusion criteria. Collectively, they suggest that massage can alleviate a wide range of symptoms: pain, nausea, anxiety, depression, anger, stress, and fatigue. However, the methodological quality of the included studies was poor, a fact that prevents definitive conclusions.

Fellowes et al. (2004) in the Cochrane Collaboration reviewed the effect of aromatherapy and massage for symptom relief in patients with cancer. They searched ten databases and sought randomized controlled trials. The search strategy retrieved 1,322 references. Ten reports met the inclusion criteria and these represented eight RCTs (357 patients). The most consistently found effect of massage or aromatherapy massage was on anxiety. Four trials (207 patients) measuring anxiety detected a reduction post intervention, with benefits of 19–32% reported. Contradictory evidence exists as to any additional benefit on anxiety conferred by the addition of aromatherapy. Evidence for the impact of massage/aromatherapy on depression was variable. Of the three trials (120 patients) that assessed depression in cancer patients, only one found any significant differences in this symptom. Three studies (117 patients) found a reduction in pain following intervention, and two (71 patients) found a reduction in nausea. Although several of the trials measured changes in other symptoms such as fatigue, anger, hostility, communication, and digestive problems, none of these assessments was replicated. They concluded that massage and aromatherapy massage confer short term benefits on psychological wellbeing, with the effect on anxiety supported by limited evidence. The effects on physical

symptoms may also occur. Evidence is mixed as to whether aromatherapy enhances the effects of massage. Replication, longer follow ups, and larger trials are needed to accrue the necessary evidence.

As for breast cancer, many studies have examined the effects of massage therapy on anxiety. Listing et al. (2009, 2010) investigated the efficacy of classical massage on stress perception and mood disturbances in 34 women diagnosed with primary breast cancer randomized into an intervention or control group. For a period of five weeks, the intervention group ($n=17$) received biweekly 30-min classical massages. The control group ($n=17$) received no additional treatment to their routine health care. The Perceived Stress Questionnaire (PSQ) and Berlin Mood Questionnaire (BSF) were used and patients' blood was collected at baseline (T1), at the end of the intervention period (T2), and six weeks after T2 (T3). Women in the intervention group reported significantly lower mood disturbances than that of the control group, especially for anger ($p=0.048$), anxious depression ($p=0.03$) at T2, and tiredness at T3 ($p=0.01$). No group differences were found in PSQ scales, and cortisol and serotonin concentrations at T2 and T3. However, perceived stress and cortisol serum levels ($p=0.03$) were significantly lower than baseline after massage therapy (T2) in the intervention group. Further research is needed to validate their findings.

Billhult et al. (2009) examined the effect of massage on immune function and stress in 30 women with breast cancer by a randomized controlled trial. Results showed that light pressure effleurage massage decreased the deterioration of natural killer cell activity occurring during radiation therapy. Furthermore, it lowered heart rate and systolic blood pressure. No effects were demonstrated on cortisol and diastolic pressure.

Massage therapy induces an improvement in the quality of life. Rueda et al. (2011) suggested in a pilot study that participation in a massage therapy program is both feasible and acceptable to newly diagnosed brain tumor patients experiencing stress. Furthermore, participants in these studies reported improvements in stress and quality of life (QoL) while receiving massage therapy.

Keir (2011) assessed the efficacy of massage therapy on primary brain tumor patients reported psychological outcomes and QoL in a prospective, single-arm intervention. Results showed that as a group, levels of stress dropped significantly between weeks two and three. A trend for the reduction in stress continued through week four. At the end of week four, the Perceived Stress Scale (PSS)-10 scores of all participants were below the threshold for being considered stressed. By the end of the intervention, participants reported significant improvements in three domains, emotional well-being, additional brain tumor concerns, and social/family well-being.

Sturgeon et al. (2009) examined the impact of therapeutic massage on the QoL of 51 patients (mean age of 53 years) undergoing treatment for breast cancer in a pre/post intervention assessment design. Treatment consisted of 30-min treatment per week for consecutive weeks. Results showed that participants experienced a reduction in several QoL symptom concerns after only three weeks of massage therapy. Respondents' cumulative pre- and post-massage mean for state anxiety, sleep quality, and QoL/functioning showed significant improvement.

It has been recognized that not only full body massage, but also topical massage such as leg or foot massage promotes psychological relaxation and reinforces first-line host defense in cancer patients (Noto et al. 2010). Fifteen healthy volunteers rested on a bed for 20 min on the first day, and three days later the subjects received a standardized massage of the legs for 20 min with non-aromatic oil. Twenty-nine cancer patients also received the same standardized massage of the legs. Anxiety/stress was assessed before and just after the rest or the massage using the STAI and visual analogue scale (VAS). Results showed that in healthy volunteers, rest significantly reduced VAS by 34%. In contrast, leg massage significantly reduced both STAI and VAS by 24 and 63%, respectively. In cancer patients, leg massage significantly decreased both STAI and VAS by 16 and 38%, respectively.

Massage therapy is useful for palliative home care. Cronfalk et al. (2009) tried to examine the effects of soft tissue massage (hand or foot) currently used in palliative care nine times over a period of two weeks for the relief of anxiety and pain in 22 patients with cancer. Soft tissue massage generated feelings of existential respite with perceptions of being released from illness for a while. Two categories constituted the basis of these experiences: (1) an experience of thoughtful attention, and (2) a sensation of complete tranquility resulting in the overarching theme “a time of existential respite”.

In addition, massage therapy may be useful for reducing the stress of caregivers. There are a few studies on the effect of massage therapy on mood improvement and anxiety reduction. Goodfellow (2003) determined influences of therapeutic back massage on psychological, physiologic, and immune function variables in caregivers (spouses) of patients with cancer. This group experimental design measured the effects of a 20-min therapeutic back massage at three time points (preintervention, immediately postintervention, 20 min postintervention) on spouses of patients with cancer ($n=42$) randomly assigned to either the experimental or control group. Two-way repeated measures analysis of variance tests determined the effects of therapeutic back massage over the two postintervention time points and resulted in significant group x time interaction on mood ($F[2,40]=14.61, p=0.0005$) and perceived stress ($F[2,40]=28.66, p=0.001$). Significant inverse relationships were found between mood and natural killer cell activity ($r=-0.41, p=0.009, n=42$) and perceived stress and natural killer cell activity ($r=-0.37, p=0.017, n=42$). These results suggest that therapeutic back massage may enhance mood and reduce stress in this population.

Rexilius et al. (2002) also examined the effect of massage therapy and healing touch on anxiety, depression, subjective caregiver burden, and fatigue experienced by caregivers of patients undergoing autologous hematopoietic stem cell transplant in quasi-experimental repeated measures. Twenty-six caregivers assigned to 13 in the massage therapy group and 13 in the control group. All caregivers completed the Beck Anxiety Inventory, the Center for Epidemiologic Studies Depression Scale, the Subjective Burden Scale, and the Multidimensional Fatigue Inventory-20 before and after treatment consisting of two 30-min massages per week for three weeks. Results showed significant declines in anxiety

scores, depression, general fatigue, reduced motivation fatigue, and emotional fatigue for individuals in the massage therapy group. Thus, massage therapy can bring benefits to caregivers of patients with cancer.

2.3.2 Use of Aromatherapy in Cancer

The popular application of aromatherapy is to reduce anxiety, promote relaxation, and increase the wellbeing of patients in palliative care (Wilkinson et al. 1999; Cooke and Ernst 2000; Hadfield 2001; Serfaty et al. 2012). Several studies have centered on anxiety in cancer patients. Corner et al. (1995) evaluated the use of massage and essential oils on the wellbeing of cancer patients by a randomized control trial. They recruited 52 patients with cancer at a UK Cancer Center, with 17 randomized to each massage group and 18 controls. The mean age of patients was 48. Forty-two percent of patients had primary disease, 40% with recurrence. Results showed that anxiety scores reduced significantly over time only for the essential oils massage group. Concerning effectiveness for pain, mobility, ability to work, and communication with family, the essential oils group performed better than the control group.

Wilkinson et al. (1999) also evaluated aromatherapy massage in palliative care in a randomized control study involving full body aromatherapy massage or carrier oil massage three times a week. Eighty-seven patients were recruited with 43 being randomly allocated to an aromatherapy massage group and 44 to a massage only group. The kinds of cancers were various, and 90% of the patients were female. The mean age of patients was 54. Patients in the aromatherapy massage group were given full body massages with carrier oil and roman chamomile essential oil three times weekly, while patients in the control group were given full body massage with carrier oil three times weekly. For the aroma group, significant improvements were found for physical, psychological, QoL, and severe physical and severe psychological subscales of the Rotterdam Symptom Checklist (RSCL), pre to post test. For the massage group, there were no differences in any RSCL subscales from the pre to post test. For the whole group and each group, significant improvements in the STAI-state were noted pre to post tests for each massage.

Kohara et al. (2004) also examined the effects of combined modality treatment consisting of aromatherapy, soaking the feet, and reflexology on fatigue in terminally ill cancer patients in an open study. Twenty patients diagnosed with advanced cancer including nine patients with lung cancer were enrolled. After a patch test was performed, patients received aromatherapy that was accompanied with a foot soak in warm water containing lavender essential oil for 3 min, followed by reflexology treatment with jojoba oil containing lavender for 10 min. Fatigue was evaluated using the Cancer Fatigue Scale (CFS) before, 1 h after, and 4 h after treatment. Total CFS scores improved significantly after this treatment. Among three CFS subscales, physical and cognitive subscale scores were significantly reduced.

We examined how aromatherapy massage influenced psychological parameters in 12 breast cancer patients in an open semi-comparative trial (Imanishi et al. 2009).

One month before aromatherapy massage, as a waiting control period, were compared with those during aromatherapy massage treatment and one month after the completion of aromatherapy sessions. Patients received a 30-min aromatherapy massage twice a week for four weeks (eight times in total).

First, the psychological responses to aromatherapy massage were examined using STAI, POMS, and Hospital Anxiety and Depression Scale (HADS). State anxiety scores of STAI are adequate to determine the short term effects of aromatherapy. In STAI especially, state anxiety scores significantly decreased after each aromatherapy massage session. This result was in accordance with those of Wilkinson et al. (1999).

On the other hand, trait anxiety using STAI and HADS, which are appropriate for the determination of long term effects, gradually reduced over the sessions. There was a significant decrease in trait anxiety scores between one month before and after massage. HADS also showed that anxiety gradually reduced over time, while there were no significant differences in depression scores. Coinciding with our results, Corner et al. (1995) also reported that aromatherapy massage significantly reduced anxiety, although other investigations did not find that aromatherapy had an anxiolytic effect in patients with cancer (Louis and Kowalski 2002; Graham et al. 2003; Soden et al. 2004).

Louis and Kowalski (2002) measured the response of 17 cancer hospice patients to humidified essential oil aromatherapy. Each subject was measured on three different days before and after a 60-min session consisting of: (1) no treatment (control), (2) water humidification (control), or (3) 3% lavender aromatherapy. Results reflected a positive, yet small, change in blood pressure and pulse pain, anxiety, depression, and sense of well-being after both the humidified water treatment and the lavender treatment.

Graham et al. (2003) determined whether the inhalation of aromatherapy during radiotherapy reduces anxiety in 313 patients, randomly assigned to receive either carrier oil with fractionated oils, carrier oil only, or pure essential oils of lavender, bergamot, and cedar wood. Patients underwent assessment by the HADS and the Somatic and Psychological Health Report (SPHERE) at baseline and at treatment completion. Results showed no significant differences in HADS depression or SPHERE scores between the randomly assigned groups. However, HADS anxiety scores were significantly lower at treatment completion in the carrier oil only group compared with either of the fragrant arms. The fragrance alone without massage did not influence psychological conditions of patients with cancer.

Soden et al. (2004) compared the effects of 4-week courses of aromatherapy massage and massage only on physical and psychological symptoms in 42 patients with advanced cancer. They were unable to demonstrate any significant long-term benefits of aromatherapy or massage in terms of improving pain control, anxiety or QoL. However, sleep scores improved significantly in both the massage and the combined massage groups. There were also statistically significant reductions in depression scores in the massage group. In this study of patients with advanced cancer, the addition of lavender essential oil did not appear to increase the beneficial effects of massage. Their results do suggest, however, that patients with high levels of psychological distress respond best to these therapies.

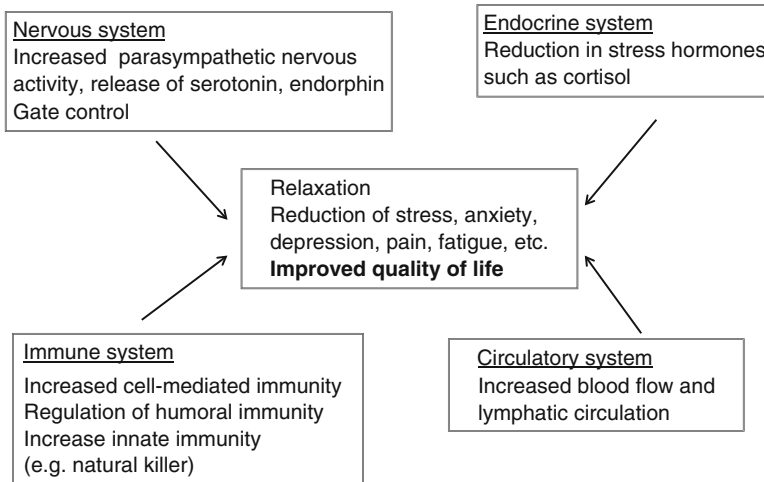


Fig. 2.1 Mode of action of massage and aromatherapy massage in cancer

On the other hand, we found that aromatherapy massage had both short and long term effects on anxiety reduction in breast cancer patients (Imanishi et al. 2009). No significant changes in the waiting control period and significant decreases of anxiety both in the short-term and long-term show that aromatherapy massage holds promise as an effective therapy for breast cancer patients. Further investigations with an increased sample size and improved study design, including a control group, are required to confirm the effect of aromatherapy massage. To do this, it will be important to find a therapy suitable for controls.

Outside psychological therapies, anxiolytic drugs, anti-depressants, and conventional medicine offer no effective interventions to reduce anxiety concerning recurrence and/or metastasis. It has been suggested that aromatherapy massage is a viable complementary therapy that significantly reduces anxiety in patients with malignant brain tumors (Hadfield 2001).

Finally, the author would like to discuss the safety of massage therapy and aromatherapy massage. In general, massage is thought to be safe for patients with cancer, although a few studies have reported adverse effects such as internal hemorrhage due to coagulation disorders, fracture with metastatic cancer in bones, and infection on open wounds or radiation dermatitis. However, we cannot find any evidence to suggest that massage therapy can spread cancer (Corbin 2009).

Massage and aromatherapy massage caused various actions favorable for patients with cancer such as relaxation, reductions in anxiety, depression and fatigue, and improvements in QoL *via* nervous, endocrine, immune, and circulatory systems (Fig. 2.1).

In conclusion, massage therapy including aromatherapy massage in cancer patients would be beneficial for the reduction of anxiety, depression, and stress as well as pain, and is generally safe. Therefore, further studies, especially randomized clinical trials, should be performed.

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Chapter 3

Effects of Massage Therapy on the Relief of Cancer Pain

Sui-Whi Jane, Diana J. Wilkie, Mei-Nan Liao, Randal D. Beaton,
and Yung-Chang Lin

Abstract Despite extensive progress in the scientific understanding and the control of pain, 51–77% of patients with cancer, especially for patients with advanced cancer or approaching end-of-life phase, still experience moderate to severe pain at some time during their illness. This cancer pain can and does erode the quality of life of this patient population. For this and other reasons it is important for health professionals to advocate for appropriate pharmacological and non-pharmacological modalities, such as massage therapy (MT), for pain management in patients with cancer. Evidence from studies reviewed in this chapter documents that patients/subjects in massage groups appeared to have more positive outcomes compared to those in control groups in terms of decreasing pain intensity, nausea or vomiting, fatigue, distressing symptoms, anxiety, depression, and self-reports of relaxation. These and associated effects on measures of physiological arousal (blood pressure) can be documented during massages as well as 5 min, 10–20 min,

S.-W. Jane (✉)

Department of Nursing and Graduate Institute of Nursing, Chang Gung
University of Science and Technology, No 261, Wen-Hwa 1st Road,
Kwei-Shan Hsiang, Tao-Yuan, 333-03, Taiwan
e-mail: swjane@gw.cgust.edu.tw

D.J. Wilkie

Department of Biobehavioral Health Science,
College of Nursing, University of Illinois at Chicago, Chicago, IL, USA

M.-N. Liao

Administration Center of Medical Research Department,
Chang Gung Memorial Hospital, Tao-Yuan, Taiwan

R.D. Beaton

Department of Psychosocial and Community Health,
University of Washington, Seattle, WA, USA

Y.-C. Lin

Division of Hematology/Oncology, Department of Internal Medicine,
Chang Gung Memorial Hospital, Tao-Yuan, Taiwan

and 2–3 h following massage, but not beyond 24 h. In contrast, the most notable inconsistent massage effects are more relevant to sleep, quality of life, and stress adaptation indicators (i.e. heart rate, respiratory rate, cortisol, IgA and α -amylase, natural killer cells or lymphocytes). Future studies with well-designed trials and research directed at the mechanism will clarify potential sensitive indications, subgroup effects in terms of types or dose of massage, types or stage of cancer or type of symptom as well as, the mechanism of massage and in which circumstance it does and does not work. Importantly, MT interventions examined in this systematic review appear to be safe for patients with cancer which is also feasible for patients with advanced cancer or bone metastases and MT appears to enhance the quality of life for this population.

3.1 Introduction

Pain is one of the most common chief complaints among patients with cancer, especially for patients with advanced cancer or approaching end-of-life phase. Patients with metastatic cancers, however, are more likely to have pain compared to those patients without metastatic cancer, 50% (Ahles et al. 1984) to 74% (Cleary 2000) and 15% (Daut and Cleeland 1982), respectively. According to a state-wide survey in Seattle, cancer patients and hospice patients intended to rank pain control as a higher priority than patient samples with the cardiovascular, pulmonary, or neurological disorders (Downey et al. 2009b). In general, pain occurs in approximately 25% of patients with newly diagnosed cancer, 33% of patients undergoing cancer treatment, and in 75% of patients with advanced disease (National Comprehensive Cancer Network 2007). Despite progress in the scientific understanding of pain, 51% (Bonica 1990) to 77% (Cleary 2000) of patients with cancer still experience moderate to severe pain at some time in their illness trajectory and this results in disruption and erosion in their quality of life. Also, their unrelieved pain is both physically and psychologically dangerous, contrary to the notion that it is no more than an annoyance. Many of the dangerous effects of unrelieved pain mimic the effects of opioid analgesics (Table 3.1). Knowing that unrelieved pain can have dangerous consequences should motivate health professionals advocate for appropriate pharmacological and non-pharmacological pain treatments.

Theoretically, 90% of cancer pain can be adequately relieved with relatively simple medical interventions or invasive techniques (Wilkie 1990; Agency for Health Care Policy and Research 1994; De Leon-Casasola 2008) In practice, however, less than 50% of cancer patients actually achieve effective pain relief. This failure to achieve adequate pain relief that is associated with numerous patient and provider barriers (Cleeland et al. 1986; Hill et al. 1990; von Roenn et al. 1993; Oliver et al. 2001), such as patients' reluctance to report symptoms (Ward and Gatwood 2008), patients' hesitation to take analgesic medications due to misconceptions about pain management (Ward et al. 1993), and clinicians' insufficient knowledge about using appropriate analgesics (Janjan et al. 1998).

Table 3.1 Effects of unrelieved pain by body system (Wilkie et al. 2012)

Body system	Effects of unrelieved pain
Immune system	Unrelieved pain causes decreased natural killer cell number, function and activity. Can lead to death.
Pulmonary system	Unrelieved pain causes reflex muscle spasm leads to splinting which decreases pulmonary vital capacity, functional residual capacity, and alveolar ventilation. Leads to atelectasis, which often is followed by pneumonia and hypoxemia.
Cardiovascular system	Unrelieved pain causes sympathetic over activity which increases heart rate (decreased O ₂ to heart), peripheral resistance, BP, cardiac output, and O ₂ use. Leads to hypoxemia and ischemia, especially of the heart and peripheral tissues.
Gastrointestinal system	Unrelieved pain causes increased sympathetic activity, which increases GI secretions and smooth muscle sphincter tone decreases intestinal motility. Leads to gastric stasis and paralytic ileus.
Musculoskeletal system	Unrelieved pain causes segmental and supra segmental reflexes with increased muscle spasm leads to impaired muscle metabolism and to muscle atrophy.
Neuronal plasticity	Unrelieved pain causes primary and secondary hyperalgesia with enabled NMDA receptors and aberrant communication of neurons in the peripheral and central nervous system.
Psychologic	Accompanying unrelieved pain are a number of psychological consequences including anxiety, fear, depression, distress, and suffering, hopelessness, helplessness and a decreased will to live (wish for assisted suicide or euthanasia).

To alleviate severe pain, opioid analgesics are often administered because of their high efficacy and less specific organ toxicity. However, pain treatment with narcotic medications is associated with tolerance and adverse side effects, such as nausea and vomiting, constipation, drowsiness, confusion, urinary retention, itchiness, hyperalgesia, and dependency (Hanks et al. 2010). Thus, patients and clinicians increasingly have looked to complementary and alternative medicine (CAM) interventions, such as massage therapy (MT). MT is one of the most commonly employed interventions used to prevent or reduce pain among cancer patients and in managing cancer pain (Barbour et al. 1986; Bernstein and Grasso 2001; Ferrell et al. 1991; Wilkie et al. 1992). A survey conducted in the 1990's indicated that the prevalence of those using massage in the US general population increased from 6 to 12% (Eisenberg et al. 1998) and massage has been identified as the most popular CAM among adult and child patients with cancer, both in the US (Morris et al. 2000; Gansler et al. 2008) and in the UK (Rees et al. 2000). For instance, the use of MT among children with cancer ranged from 7 to 66% reflecting an increase over the use during the previous decade (McLean and Kemper 2006). In addition to the general public, physicians are increasingly recognizing massage as a useful adjunct in their own practices and 32% of physicians reported having recommended MT to

patients or referred their patients to massage therapists (Boutin et al. 2000; Ernst 2003; Hughes et al. 2008). According to the National Comprehensive Cancer Network practice guidelines (Grossman et al. 1999), MT is also incorporated as an adjunct to conventional medical modalities for pain management, including bone pain management. It becomes apparent that there is an emerging interest, not only in the general public, but also with healthcare providers in the use of MT for managing cancer pain. The most prominent arguments against CAM within the scientific realm, however, lies in the fact that CAM outcome studies have not been rigorous and are plagued with methodological problems such as insufficient sample size, inadequate control condition, and a failure to control for placebo effects. With an emerging emphasis on evidence-based practice in healthcare, it is important to convincingly show the relative benefits of massage with more rigorous approach and/or systematic reviews, so that clinicians can translate the research evidence into best practices and ultimately to improve pain management in the cancer population.

3.2 The Historical Review of MT

The origin of the word massage is derived from the Arabic verb *massa*, meaning to touch, the Greek word *massein*, meaning to knead, and the Sanskrit word *makch*, meaning to strike, press, or condense (Atchison et al. 1996) and has been extensively documented as one of the oldest therapeutic approaches used for healing. In the modern medical practice, MT (synonymous as bodywork) is commonly defined as involving the systematic manipulation of the soft tissue of the body with varying intensity, direction, rate, and rhythm, and motions using primarily the hands of the massage therapist, and is intended to facilitate health and promote well-being (Tappan 1988; American Massage Therapy Association 2012). Dating back to Chinese folk medicine written in the Nei Ching in 2000 BC, MT, has been extensively used for healing purposes in various ancient cultures, such as Indians, Egyptians, Japanese, Persians, Greeks, Hindus, and Romans, for centuries (Cole and Stovell 1991; Cotter et al. 2000). From the perspective of Western medicine, massage was also recognized having the therapeutic benefits for sprains and dislocations by Hippocrates (460–377 BC) who advocated this procedure as “medicine being the art of rubbing” in his book, *On Articulations* (Field 1998, 2002). By the late fourteenth century, this practice was organized into an academic discipline in medical institutions (Cline 2000) and referenced as a medical therapy until the focus of medical care shifted to the biological sciences in the early twentieth century (Braverman and Schuluman 1999; Corbin 2005). The modern Western massage was primarily developed in Sweden by Per Henrik Ling (1776–1839), and was known as Swedish massage. This was a gentle form of massage incorporating some of existing French massage with the application of systematic strokes and deep kneading and stretching to loosen tight muscle and to reduce stress, and is still the most popularly used type of massage in the Europe and United States (Cotter et al. 2000). In the 1970s, massage in the United States found renewed interest, especially for athletes.

Generally speaking, it is increasingly gaining popularity among the healthcare providers globally. Furthermore, there has been an increase in investigations of the therapeutic effects of massage in terms of its physical, physiological, and psychological benefits over the past 30 years.

3.3 Previous Clinical Evidence of Effectiveness of MT

3.3.1 Effects of MT

MT, a form of CAM, is gaining popularity with healthcare providers. However, the most cogent arguments against CAM within the scientific community lies in the fact that CAM studies have been less rigorous methodologically due, in part, to a lack of inclusion of sham procedures massage to control for potential placebo effects of MT (Kaptchuk 2002; Sager et al. 2007). Other methodological challenges from reviewed literature include less rigorous inclusion criteria and research design, failure to consider potential confounding variables, lack of standardized massage doses and protocols, measurement errors, and inadequate sample sizes needed to achieve sufficient statistical power (Moyer et al. 2004; Lafferty et al. 2006; Jane et al. 2008; Wilkinson et al. 2008; Ernst 2009; Kutner et al. 2010; Falkenstiner et al. 2011).

Evidence from existing research studies, investigating a wide range of populations, supports the supposition that massage is a validated means for decreasing pain (Ferrell-Torry and Glick 1992; Grealish et al. 2000; Smith et al. 2002; Chang et al. 2002; Cassileth and Vickers 2004; Hernandez-Reif et al. 2005) and anxiety (Longworth 1982; Sims 1986; Wikinson 1995; Snyder et al. 1995; Field et al. 1997, 1998; Ahles et al. 1999) and lessening physiologic arousal (Fakouri and Jones 1987; Weiss 1990; Meeks 1993; Snyder et al. 1995; Wilkie et al. 2000; Post-White et al. 2003), decreasing sleep disruption (Field et al. 1992, 1999, 2002; Richards 1998) and reducing excess muscle tension (Nordschow and Bierman 1962; Fraser and Kerr 1993; Field et al. 2002). Other benefits documented in the research literature include improvements in local circulation (Wilkins et al. 1950; Wyper and McNiven 1976), lymph flow (Simpson 1991; Williams et al. 2002), reduced fatigue (Field et al. 2002; Rexilius et al. 2002), and enhanced immunity (Groer et al. 1994; Ironson et al. 1996; Diego et al. 2001; Field et al. 2001). To date, however, the results of clinical trials have been inconsistent. This chapter systematically reviews studies and critically analyzing the efficacy of massage in adult patients with cancer in an effort to help clinicians translate validated evidence into best practices.

3.3.2 Types of Massage

Most types of massage have the common intent of calming the patient and promoting generalized well-being, with different forms employing slightly different styles. Certain massage techniques may be more appropriate than others for cancer patients

depending on their specific symptoms and goals. Massage effects may differ depending on which technique is used, how rapidly the stroke is applied, duration of massage, intensity of pressure, and parts of body massaged. Theoretically, the predominate use of rapid firm strokes such as *pétrissage* or *tapotement*, for instance, mainly produce stimulating effects, whereas using long slow *effleurage* stroke will provoke sedative effects (Temple 1967). The various types of massage evolved in Western or eastern cultural traditions are outlined in Table 3.2 (Cotter et al. 2000; Sager et al. 2007; Hughes et al. 2008).

3.3.3 *Safety and Adverse Effects of MT*

In general, MT delivered by registered (or licensed) massage therapists with cautious pre-massage assessment and appropriate modification is considered to be a very safe modality, with minimal complications, for a wide range of applications and for symptom management (Ernst 2003; Corbin 2005; Sager et al. 2007; Hughes et al. 2008). Occasionally, even healthy patients may experience bruising, swelling of massage muscles, a temporary increase in muscle pain, and/or an allergic reaction to skin lubricants, but the absolute risk of these adverse reaction/events were unknown. In a systematic review of 16 case reports and 4 case series (Ernst 2003), a number of adverse events were documented, including cerebrovascular accidents, hematoma, and leg ulcers. Other case reports theorized as serious adverse events included fractures and dislocations, internal hemorrhage, and hepatic hematoma (Trotter 1999), dislodging of deep venous thrombosis and resultant embolisms of the renal artery (Mikhail et al. 1997), as well as the displacement of a ureteral stent (Kerr 1997). In the literature reviewed, the above noted adverse events were based on case reports, were not observed consistently, and the types of massage techniques used or the background of the patients' case conditions were not provided. For these reasons, it was challenging to draw firm conclusions about the cause, nature and event of adverse outcomes/complications of MT. Nevertheless, most adverse events were perhaps more likely associated with massage delivered by non-professional therapists or laypeople or as a result of the use of rigorous massage techniques other than Swedish massage.

There is no evidence reviewed that suggested that massage can spread cancer, although direct pressure over a tumor is usually discouraged. Considering the potential acceleration or initiation of cancer metastases *via* massaging blood or lymph channels, the patient diagnose of cancer has traditionally been a contraindication for MT, especially when the massage is applied locally and with sufficient intensity of pressure to a superficial tumor (Curties 2000). There may be a theoretical risk of increased pain at the affected area (i.e. metastatic bone lesion) or even a fracture due to massage. However, since patient with cancer are prone to suffering certain degree of physical (i.e. pain, sleep disturbance, and lymphedema) and psychological (i.e. uncertainty, anxiety, depression) stress due to the progression of disease, they may need and benefit from some forms of comfort care such as massage to alleviate

Table 3.2 Forms and taxonomy of massage therapy (Field 2002; Sager et al. 2007; Hughes et al. 2008)

Types of massage	Description of techniques
Swedish massage	It involves in effleurage (stroking, gliding movements intended to evoke the relaxing response), petrissage (lifting, squeezing, wringing, or kneading of soft tissues to stimulate deep muscle and to increase circulation), friction (penetrating pressure with fingertips to reduce muscle spasm), tapotement (percussion, rapid striking to stimulate tissues), and vibration (a rapid trembling sensation), and lasts 30–90 min.
Myofascial trigger point therapy (myotherapy)	It is a deep tissue massage to stretches and release fascia or tight connective tissue, including trigger points, using manual pressure, friction, and tools called T-bars and L-bars to relief pain.
Deep tissue massage	Techniques are similar to Swedish massage, except pressure is slower, with medium to deep contact to affect muscle under the superficial layers.
Soft-tissue release	This technique uses specific compression and precise extension, administrated in a systematic manner, to release muscle spasm and scar tissue.
Neuromuscular therapy	It uses static pressure on specific myofascial points to manipulate the muscles, tendons, and connective tissue for pain relief and is thought to balance the central nervous system.
Manual lymphatic draining	It is usually used for postsurgical lymphedema with very gentle, slow, and light-touch hand motions (stationary circles and pumping movement), so lymph is directed from damaged areas toward undamaged vessels. Proximal areas are massage first for dilation of vessels to accept fluid from distal areas of limbs, which are massaged later, enhancing the normal distal-to-proximal lymph flow.
Aromatherapy	Aromatherapy massage is an application of carrier oil and essential oil derived from plants, flowers, stem, barks, or roots that contain chemical components and nutrients that can assimilate into the human body to restore physical, emotional, and spiritual functions. Certain essential oil has its specific properties for particular symptoms.
Medical or orthopedic massage	It addresses the therapists generally use several bodywork modalities, such as muscle testing, heat or cryotherapy, deep tissue work, myofascial trigger point release, range of motion, and stretching and strengthening techniques of muscle groups, to relieve spasm-pain cycles to restore normal function and structural posture.

(continued)

Table 3.2 (continued)

Types of massage	Description of techniques
Rolfing	Rolfing is a structural integration by deep friction massage to release restrictions in the deep fascial planes in the body allowing shortened and tense muscles to relax and lengthen. The goal of Rolfing is to adhere to the concept of mind-body integration and attempts to favorably influence the psychological states as it corrects physical problems.
Trager massage	Trager massage is a hands-on work consisting of gentle rocking, stretching, and rolling movements to relax and enliven tense areas of the body. The movement work emphasizes ease and pleasures in movement and attempts to teach patients.
Acupressure ^a	It is based on the Chinese Meridian System to fortify the yin, yang, and Qi of the body. By using the pressure of thumbs and fingers on acupuncture points on the skin, that are sensitive to bioelectrical impulses and modulate energy flow through meridians and chakras, results in the release of endorphins, thus inhibiting pain.
Shiatsu (meaning finger pressure) ^a	It is a form of Japanese massage and manipulation of acupuncture points and meridians, which are thought to channel vital energy. By applying pressure to Chinese acupuncture points on the surface of the body to stimulate the flow of energy called Ki (Qi or Chi in Chinese), leading to remove Ki blockage or overactivity, to restore areas of Ki depletion, and to stretch and mobilize limbs to facilitate the flow of Ki.
Tui na ^a	It is based on the traditional Chinese medicine theory of the flow of Qi through meridians or energetic pathway by using hand techniques to massage the myofascial and tendon tissue of the body. The manipulation realigns the musculoskeletal and ligamentous relationship.
Reflexology ^a	Reflexology is a form of foot massage designed to harmonize bodily functions and has a healing and relaxing effects. The therapists detect blockages or congestion in the zones or reflex points, then use the finger and thumb pressure to manipulate zones and reflex points in the feet and hands that correspond to all of the organ, gland, muscle, and bone in the body.
Thai massage ^a	It designs to unblock trapped energy and to improve vitality by applying pressure along the meridian channels.

^aIndicated massage is derived from Eastern culture

their distressing symptoms. Unrelieved psychological symptoms may worsen patients' perception of their physical symptoms leading to an increased severity of physical symptoms. Yet, MT has been shown to be more beneficial for patients with

an advanced progression of disease, such as patients with end-of-life stage, in terms of improving the person's physiological, psychological, and social well-beings (Ferrell-Torry and Glick 1992; López-Sendín et al. 2012; Meeks 1993; Wikinson 1995; Wilkinson et al. 1999; Wilkie et al. 2000). In addition, MT may enhance immunity with some evidence showing that it significantly increases the patient's natural killer cells (Diego et al. 2001; Field et al. 2001; Groer et al. 1994; Ironson et al. 1996) and this may counter the proliferation of tumor cells. The current body of work, thus, is more concerned about what technique can be used safely and effectively for patients with cancer by considering the cancer stage, tumor location, and location of any metastatic sites (Gescsedi 2002).

Compared with healthy patients, patients with cancer are more likely to experience adverse side effects and complications of MT. Therefore, MT with cancer patients requires special precautions, such as avoiding areas of receiving radiation therapy as well as areas of radiation dermatitis complicated by pain and infection or bone metastases complicated by fracture, avoiding massage for coagulation disorders complicated by bruising and internal hemorrhage or adjusting the intensity of pressure for those at risk of thrombocytopenia-induced bruising and peripheral neuropathy, and minimizing massage movements that create a rocking motion in patients with nausea and vomiting (Gescsedi 2002; Sager et al. 2007; Hughes et al. 2008). Practitioners should be aware of the above side effects and complications of MT with cancer patients and develop and follow safety protocols prior to and during MT. Jane and colleagues (2009, 2011) proposed the following strategies to ensure the safety of MT for patients with bone metastases: (a) confirming sites of bone metastases with the patient's radiological test and consultations with his/her primary physician for the appropriateness and safety; (b) initiating a pre-intervention evaluation and modifying the MT intervention protocol so as to employ very light and gentle pressure of strokes in the region of bony metastatic sites and avoidance of sites of superficial tumors; and (c) monitoring the patient status consistently for the presence of escalating pain during and following the massage sessions. To date, results from numerous research-based studies indicated that, with special precautions, no adverse events have been reported as a result of MT in patients with cancer including those with bone metastases (Smith et al. 2002; Totch et al. 2003; Stephenson et al. 2007; Kutner et al. 2008; Jane et al. 2009, 2011).

Cotter et al. (2000) posited both systemic (i.e. febrile illness, systematic infection, deep venous thrombosis, congestive heart failure, intoxication or drug use, psychosis and the 24-h period following scuba diving (nitrogen bubble release) and local (i.e. skin breakdown, tissue overlying surrounding malignant tissue, ecchymotic tissue, herniated tissue, varicose veins, abdominal massage during pregnancy, joint manipulation in osteoporosis) contraindications to massage that should be considered and addressed when delivering MT. Other suggested precautions of MT include those for pregnant women who should avoid prolonged positioning on their back. Also, massage therapists should be aware that younger children or young adolescents may have modesty or body image issues and could benefit from work on limbs before proceeding to the back or other areas of the body (Hughes et al. 2008).

3.3.4 *Qualification of the Massage Therapists*

As mentioned earlier, adverse events as a result of massage were more likely when massage was delivered by non-professional therapists or laypeople, so the selection of qualified or certified massage providers is crucial in the area of bodywork. In the United States, the Commission on Massage Therapy Accreditation considers 500 h of training, consisting of 200 h of formal education, 100 h of anatomy-physiology education, and 200 h of adjunct-related education or professional experience, to be a minimum requirement for certification. Additionally to be certified as licensed massage therapist or licensed massage practitioner in the US requires passing an examination offered by the National Certification Board of Therapeutic Massage and Bodywork (Huebscher 1998; Sager et al. 2007; American Massage Therapy Association 2012). In non-licensing US states, a therapist should, at a minimum, have a certified massage therapist.

In Canada, the Canadian Massage Therapists Alliance set a minimum for massage education of 2,200 h. However, diversity exists in terms of the number of hours of education, in terms of the curricula and in the types of educational institution. Some educational institutions have agreements with university for degree completions in science at the baccalaureate level (Sager et al. 2007). For patients with cancer, specialized education and experience for massage therapist working with cancer patients is needed by integrating advanced training program into undergraduate curricula in the regulated provinces in Canada, or providing continuing educational program in the Canada and the USA. Nowadays, some investigations intend to explore the feasibility and efficacy of training non-massage therapist healthcare providers (Jane et al. 2009, 2011) or family caregivers to provide basic massage in patients with cancer, it is due to the concern of limited availability of licensed massage therapist or the continuity of providing comfort care at patient's home (Field et al. 2001; Stephenson et al. 2007; Gorman et al. 2008).

3.4 Systematic Review of MT in Patients with Cancer

3.4.1 *Methodology*

3.4.1.1 *Sampling*

Due to the nature of patients with cancer and related safety concerns, the application of MT might differ from the healthy populations; thus, it is important for clinicians to systematically examine the effects of MT in patients with cancer. In addition, from the perspective of evidence-based practice, systematic reviews, which are regarded as the strongest level of evidence on which to base clinical decisions (Melnik and Fineout-Overholt 2005), involve summarizing large bodies of evidence by the application of scientific strategies that limit bias and random error and the assembly, critical appraisal, and synthesis of all relevant studies (Mulrow and Cook 1998). Reviews used in this chapter consisted of searches of the following

computerized databases: MEDLINE, PubMed, CINAHL, PsycINFO, and Cochrane Library. Also, the bibliographies of relevant studies, especially currently available systematic reviews (Lafferty et al. 2006; Hughes et al. 2008; Jane et al. 2008; Wilkinson et al. 2008; Ernst 2009; Falkenstiner et al. 2011) or meta-analyses (Labyak and Metzger 1997; Moyer et al. 2004), were explored to ensure thoroughness. This literature search examined publications from 1990 to 2012 in English, entering the keywords “CAM”, “massage”, “healing touch”, “non-pharmacological intervention”, “Swedish massage”, “foot massage”, “aromatherapy massage”, “reflexology”, “slow stroke back massage”, “cancer-related pain”, “symptom distress”, “nausea”, “anxiety”, “mood distress”, “depressed”, “physiological relaxation”, “fatigue”, “sleep disorder”, and “quality of life”. Both physical and psychological symptoms experienced by patients with cancer pain are included in this review. Initially, 578 abstracts were found and reviewed; a review of these abstracts resulted in 107 potential relevant studies based on the inclusion criteria.

3.4.1.2 Inclusion and Exclusion Criteria

A total of 29 studies were identified using the following inclusion criteria: (1) subjects were all adults diagnosed with cancer; (2) massage must have employed a single therapy modality with manipulation of soft tissues of the body; (3) one outcome variable was a measured quantitatively; and (4) studies included were either quasi-experimental or experimental design or randomized clinical trial, with statistical analyses. Studies were excluded from this review if they were: (1) published only as an abstract; (2) involved therapeutic touch without direct physical touch; or (3) solely a qualitative study.

3.4.1.3 Extracted Information

Information from each study was extracted systematically, to obtain the following details regarding: (1) author and the year of publication; (2) number of subjects; (3) study design; (4) massage protocol (types of massage technique, number of massage sessions, length of massage, and qualification of therapists); (5) outcome variables; and (6) statistical significance of results.

3.4.1.4 Calculation of Effect Sizes

We calculated effect sizes (ES) based on means and standard deviations of outcome measures. The ES that is known as Cohen’s (1977), represents a standardized mean difference (unit change) between the experimental and control groups in the outcome measures ($ES = \frac{x_e - x_c}{s}$; x_e the means for the experimental group; x_c the means for the control group; S within group standard deviation) (Glass 1976). In general, ES are categorized as small ES (<0.3), medium ES (0.3–0.5), and large ES (>0.5) (Burns and Grove 2009).

3.4.2 Results

The reviewed studies included in this chapter listed in Table 3.3. In the following section, summarized across studies are the characteristics of the sampled studies, subjects, research designs, massage intervention protocols, outcome measures, and quantitative findings.

3.4.2.1 Characteristics of Subjects and Research Design

The majority of studies employed small sample sizes (n 's ranging from 9 to 1,290); studies employed subjects of a wide range of cancer diagnoses and stages of disease (i.e. advanced cancer or end-of-life stage *vs* early cancer), and most subjects/participants received massage concurrently with their cancer treatment protocol. Approximately 65.5% of studies were experimental with pretest-posttest designs or randomized clinical trial or crossover design; and the remaining studies were categorized as quasi-experimental designs due to a lack of randomized group assignment or the lack of a control group. Near half of studies (44.8%) employed standard care as a control group, whereas 11 studies had an active comparison treatment groups, such as aromatherapy, guided imagery, education, acupuncture, healing touch, presence or social attention, as a control condition.

3.4.2.2 Characteristics of Study Massage Interventions

The comparison of intervention effects across studies becomes problematic because of considerable variation in the intervention protocols, including types of massage techniques used, body area massaged, the total dose of massage, the time of day of massage delivered, and the number of massage therapists. The most commonly cited massage was light Swedish massage, followed by full-body massage with diverse stroking techniques (i.e. petrissage, friction, and compression) (massage protocol used in Jane et al.'s work in 2010 and 2011 was shown below), aromatherapy, back massage, hand or foot massage, foot reflexology, myofascial release, and lymphatic draining – all delivered with licensed massage therapists or trained nurses. The intensity and duration of massages ranged from one session of 3–60 min to 15 sessions over three weeks and the total intervention time varied from 6 to 495 min. For studies with a series of massage sessions, the interval between massages ranged from one to three days up to a week. Most studies initiated interventions without respect to time of day, whereas nine studies delivered interventions during the evening hours or the morning time period. To ensure fidelity of delivering the MT, nine investigators either used single therapist or developed a standardized massage protocol to enhance the integrity of intervention administration. In consideration of the safety issues of massage in patients with cancer, authors of five studies suggested avoiding sites of tumor, edema, medical devices, deep vein thrombosis, and open lesions.

Table 3.3 Summary of reviewed studies on massage therapy in patients with cancer

References	Sample (n)	Research design	Massage protocol	Measurement	Effect size (d)	Massage effects significance
Ahles et al. (1999)	34 BMT	Experimental repeated measures with pre- and post-test Massage vs control	Swedish massage: neck, face, scalp, shoulders 20 min × 9 for three weeks (9 sessions) Licensed therapist: 1	Pain, fatigue, nausea, anxiety, depression, mood, emotional distress Immediate effect	Pain: 0.13 Anxiety: 3.1 Fatigue: 1.84 Nausea: 1.84	↓depression, ↓emotional distress, ↓anxiety, ↓nausea
Cassileth and Vickers (2004)	1,290 (3-year period)	Quasi-experimental with pre- and post-test (one group)	Swedish massage, light touch massage, foot massage 20–60 min Licensed therapist: 12	Pain, fatigue, nausea, anxiety, depression Immediate effect: 5–15 min Long-term effect: 2–5 h; 24–48 h	Pain: 0.66 Anxiety: 1.04 Fatigue: 0.71 Nausea: 0.34 Depression: 0.49	Immediate effect: ↓pain, ↓anxiety, ↓fatigue Length of massage effects: last for 24–48 h Swedish and light touch massage were superior to foot massage
Cornier et al. (1995)	52 40% had metastatic disease	Quasi-experimental repeated measure with pre- and post-test Massage vs aromatherapy or control group	Back massage: NA Weekly 30 min × 8 weeks (8 sessions) Licensed therapist: 1	Anxiety and depression, symptom distress, QoL 24-h duration	NA No mean and SD	Aromatherapy and massage had effects on ↓anxiety, ↓symptom distress Cumulative effect on ↓anxiety at massage 3 Aromatherapy was superior to massage
Curran and Meister (2008)	251 (3-year period)	Quasi-experimental with pre- and post-test	Swedish massage on feet and leg or back neck and shoulder 10–15 min*1 Licensed therapist: 2	Pain, physical discomfort, emotional discomfort, fatigue	Pain: 0.74 Physical: 0.76 Emotional: 0.69 Fatigue: 0.88	↓pain, ↓physical and emotional discomfort, ↓fatigue Massage effects were no relation with gender, age, ethnicity, cancer type

(continued)

Table 3.3 (continued)

References	Sample (n)	Research design	Massage protocol	Measurement	Effect size (d)	Massage effects significance
Downey et al. (2009a)	167 Median survival time: 149 days	RCT Massage vs guided imagery or control (friendly visit)	Light back massage 3.5-min × 2/weeks × 11 treatment Over 10-week period Licensed therapist: NA	Pain, QoL	Pain: NA QoL: NA	Massage vs control: NS Guided imagery vs control: NS
Fernández-Lao et al. (2012)	20 Breast cancer survivors	Randomized single-blind, placebo-controlled crossover Myofascial release vs education (placebo)	Myofascial release followed by barriers approach 40-min × 1 (washout period: three weeks) Licensed therapist: NA	Salivary flow rate, cortisol, IgA, α-amylase	Salivary: -0.60 Cortisol: 0.00 IgA: 0.233 α-amylase: 0.455	Myofascial release: ↑salivary flow rate (parasympathetic effect) Cortisol, IgA, α-amylase: NS Immune function (IgA) was modulated by patient's positive attitude toward massage
Ferrell-Torry and Glick (1992)	9 56% had metastatic disease	Quasi-experimental with pre- and post-test (one group)	Swedish along with myofascial trigger points therapy 30 min × 2 consecutive nights Licensed therapist: 1	Pain, anxiety, SR (immediate effect) Physiologic indicators: HR, RR, MAP (10-min interval)	Pain: 1.13 Anxiety: 1.08 SR: 1.26 HR: 0.19 RR: 0.25 SBP: 0.59 DBP: 0.47	↓pain, ↓anxiety, ↓HR, ↓RR, ↓BP, ↑SR
Grealish et al. (2000)	103	Experimental design with crossover	Foot massage 10 min × 2 consecutive nights Licensed therapist: 2	Pain intensity, SR, HR, nausea 10–20 min interval	Pain: 0.25 SR: 0.61 Nausea: 0.32	↓pain, ↓nausea, ↓HR, ↑SR No gender effect

Hernandez-Reif et al. (2005)	58 Women with breast cancer	Experimental design with pre- and post-test Massage vs control Relaxation vs control	Massage on neck/face, shoulders, arms, legs/ft, back 30-min x 3/per week x 5 weeks (15 sessions) Licensed therapist: NA	Pain intensity, depressed mood, anxiety (immediate effect) Dopamine, NK cells, lymphocytes (long-term effect): week 1 from week 5	Pain: 0.35 Mood: 0.39 Anxiety: 0.79 Dopamine: NA NK cells: NA Lymphocytes: NA	Massage and relaxation group: ↓pain, ↓anxiety ↓depressed mood (week 1) Massage group: ↓depressed mood, ↓anger, ↑vigor (week 5) Massage group: ↑dopamine, ↑NK cells, ↑lymphocytes ↓pain, ↓anxiety HR and MAP: NS No patients reported any adverse effects as a result of MT
Jane et al. (2009)	30 Patients with metastatic bone pain	Quasi-experimental repeated measures with pre- and post-test (one group)	Swedish full-body massage on head, face, neck, arms, back, legs, and feet 45-min x 1 (evening time) Therapist: 1 (trained RN)	Pain intensity, anxiety, relaxation: HR, MAP Immediate, intermediate, long-term effects (16–18 h after MT)	Pain: 1.83 Anxiety: 1.64 HR: 0.01 MAP: 0.11	
Jane et al. (2011)	72 Patients with metastatic bone pain	RCT with repeated measure Massage vs social attention	Swedish full-body massage on head and neck, face, arms, back, legs and feet 45-min x 3 consecutive nights Therapist: 4 (trained RN)	Pain intensity, mood, SR, sleep quality 20-min interval D1-D2-D3 ES: D1	Pain: 0.706 Mood: 0.55 Relaxation: 0.54 Sleep: 0.08	Massage group: ↓pain intensity, ↑mood and SR (D1-D3); ↑sleep quality (D1) Group effects: ↓pain intensity, ↑mood and SR, sleep quality (NS)

(continued)

Table 3.3 (continued)

References	Sample (n)	Research design	Massage protocol	Measurement	Effect size (d)	Massage effects significance
Kite et al. (1998)	58	Quasi-experimental pre- and post-test (one group)	Aromatherapy: scalp, hands, feet, face, legs with 20 kinds of oils 15–60 min (median 45-min)/week x 6 weeks	Psychological distress, physical distress, global benefits Interval: before and after (6th session)	NA	↓anxiety and ↑depression: 50–94% of patients reported improvement in tension, stress, depression, pain, insomnia, tiredness, global benefits No subgroup effect on gender and types of treatment
Kutner et al. (2008)	380 Advanced cancer	RCT Massage vs simple touch	Swedish massage on neck and back, arms, legs and feet 30-min x 3/per week x 2 weeks (6 sessions) Licensed therapist: NA	Pain intensity and mood (immediate effect) Pain interference, symptom distress, QoL, and analgesic use (sustained effect)	NA	Message and simple touch: ↓pain intensity, ↑mood (massage was superior to simple touch for pain and mood) No group effect on pain interference, symptom, QoL, analgesic medication
Meek (1993)	30 Exclude bone metastases	Quasi-experimental repeated measures with pre- and post-test (one group)	Slow stroke back massage 3 min x 2 consecutive nights Licensed therapist: NA	SBP, DBP, HR, ST Immediate: 5-min interval	SBP: 0.27 DBP: -0.2 HR: -0.23 ST: 0.14	↓4.2/min (HR) ↓9.17 mmHg (SBP) ↓6.4 mmHg (DBP) ↓1.45 F (ST)

Mehling et al. (2007)	180 Post-operative cancer	RCT with repeated measures Message+acupunct ure (n=93) vs control (n=45)	Swedish massage (applying kneading and stroke) + acupressure-type foot massage+acupuncture (for pain, anxiety, nausea) 10–30 min (mean = 20 min) × 2 Licensed therapist: NA	Pain, depressive mood, nausea, vomiting, cost for post-operative stay 3-h interval for measurement (D1-D2-D3)	Pain: 0.68 (D1) Mood: NA Vomiting: 0.36 Nausea: NA Cost: NA	Message + acupuncture: ↓pain, ↑mood (D1-D3), ↓nausea and ↓vomiting (D1) Cost: NS Moderate-to-severe pain and mild depression at baseline reported significant trend improvement Patients receiving massage only reported greater pain improvement in pain than in control group Subgroup effect: abdominal (ES: 0.98), prostate (ES: 0.97), and breast (ES: 0.66)
Osaka et al. (2009)	34 Terminal ill cancer patients (median survival time: 38 days)	Quasi-experimental with pre- and post-test design (one group)	Hand massage on upper extremity of one hand (immediate effect) 5-min × 1 Licensed therapist: 1	Anxiety-state CgA (stress biomarker) Satisfaction ES: with-in subjects	Anxiety: 0.71 CgA: 0.68 Satisfaction: NA	↓anxiety (STAI-state) and CgA, ↑Satisfaction with hand massage Group effect: normal group (STAI and CgA significant) Anxious group (STAI significant and CgA NS), satisfied group reported more significant effects

(continued)

Table 3.3 (continued)

References	Sample (n)	Research design	Massage protocol	Measurement	Effect size (d)	Message effects significance
Post-White et al. (2003)	164 Patients under chemo-therapy	Experimental design with crossover (pre- and post-test)	Swedish massage with relaxing music played 45-min x 4 weekly Licensed therapist: 8	Pain, anxiety, fatigue, mood, nausea, HR, RR, SBP, and DBP Medication use, satisfaction Immediate effect	Pain index: 0.33 Pain interference: -0.45 Mood: 0.53 Anxiety: 0.58 Fatigue: 0.33	MT and HT: ↓pain, ↓HR, ↓RR, ↓SBP, ↓DBP, ↑mood, ↓medication use Nausea and satisfaction (NS) MT: ↓anxiety HT: ↓fatigue
Smith et al. (2002)	41 Bone metastases included	Quasi-experimental repeated measures with pre- and post-test massage vs attention (20-min)	Swedish massage 15-30 min x 3 times during 1-week (each session with 24 h apart) Therapist: 1	Pain intensity, pain distress, anxiety, symptom distress, sleep pattern Interval (four-day apart)	Pain: 0.43 Anxiety: 0.71 Symptom distress scale: -0.61 Sleep: 0.62	↓pain, ↓symptom distress and stable sleep pattern
Soden et al. (2004)	42 Palliative care unit	Experimental design with repeated measure (pre- and post-test) Massage (n = 13) vs aromatherapy (n = 16) or control (n = 13)	Swedish massage 30-min per week x 4 weeks (4 sessions) Interval: 1 week after last massage Licensed therapist: 1	Pain intensity, pain descriptor, sleep quality, mood (anxiety/depression), symptom distress	NA	Massage or combined massage (MT + aromatherapy): ↓pain intensity, ↑sleep, ↑anxiety/depression (within-subjects) Pain descriptor, symptom distress (NS) No cumulative effect on pain and mood
Stephenson et al. (2000)	23 Breast (n = 13) and lung (n = 10) cancers	Experimental design with crossover (pre- and post-test) Foot reflexology vs control	Foot reflexology: areas corresponding pain and cancer site 30-min x 1 Licensed therapist: 1	Pain, anxiety Immediate effect	Pain: 0.65 Anxiety: 0.54	↓pain and ↓anxiety

Stephenson et al. (2003)	36 Metastatic cancer	Experimental design with repeated measure (pre- and post-test) Foot reflexology (n = 19) vs control (n = 17)	Foot reflexology: areas corresponding pain and cancer site 30-min x 2 (24 h apart) Licensed therapist: 1	Pain Immediate effect, 3 h, 24-h	NA	↓pain (immediate effect) Pain at 3 h and 24 h (NS)
Stephenson et al. (2007)	86 (dyads) Metastatic cancer	Experimental design with pre- and post-test Foot reflexology vs control (30-min readings by family)	Foot reflexology: nurse-led 15–30 min training + 15–30 min for partner 30-min x 2 delivered by family	Pain (brief pain inventory)/ short-form McGill pain questionnaire Anxiety	NA	↓pain and ↓anxiety Subgroup effect: patients with moderate-to-severe pain (eta squared: 0.23) or anxiety (eta squared: 0.15) had more significant effects
Sturgeon et al. (2009)	51 Breast cancer under treatment	Quasi-experimental with pre- and post-test (one group)	Swedish full-body massage 30-min per week x 3 weeks	Pain, anxiety, nausea and vomiting, symptom distress, sleep, QoL Interval: one week after the last massage	Pain: 0.20 Anxiety: 0.31 Distress: 0.20 Sleep: 0.07 QoL: 0.30	↓anxiety, ↑QoL, ↑ sleep (time to fall asleep, soundness of sleep, sleep satisfaction, quality, and disturbance) Pain, overall sleep quality, symptom distress (NS)
Weinrich and Weinrich (1990)	28	Experimental repeated measures (pre- and post-test) Massage vs control (10-min visit)	Swedish massage: back 10 min x 1 (9:00 am – 12:00 noon)	Pain intensity Immediate and 1-h interval x 2	Pain: 0.04 (immediate effect) 0.08 (1 h) 0.22 (2 h)	No time effect on pain Subgroup effect: a significant immediate effect in male

(continued)

Table 3.3 (continued)

References	Sample (n)	Research design	Massage protocol	Measurement	Effect size (d)	Massage effects significance
Wilkie et al. (2000)	29	Experimental design with pre- and post-test Massage vs control	Full-body massage 30–45 min × bi-weekly × 2 week (4 sessions) Licensed therapist: 5	Pain intensity, emotional distress, relaxation: pulse rate and RR (immediate effect) Longevity, analgesic dose (convert intramuscular morphine-equivalent doses) (1–2 week)	Pain: 0.14 Morphine: -0.57 QoL: 0.66 (global)	↓HR, ↓RR Pain intensity, QoL, and analgesic intake (NS) No gender effect
Wilkinson (1995)	51 76% had metastatic disease	Experimental repeated measure Massage vs aromatherapy	Full-body massage Duration: weekly × 3 week (evening time) Trained nurses: 3	Anxiety (immediate effect) QoL (physical, psychological symptom, global QoL) (long-term effect: 3-week)	Physical: 0.78 QoL: 0.94 Psychological: 0.39	Massage: ↓psychological symptom and ↓state anxiety Aromatherapy: ↓psychological symptom, ↓state anxiety, ↑QoL and physical scales
Wilkinson et al. (1999)	87	Experimental repeated measure with pre- and post-test Massage vs aromatherapy	Full-body massage Duration: 3 times (over 3 consecutive week, evening time) Trained nurses: 4	Anxiety (immediate effect) QoL (physical, psychological symptom, global QoL) (long-term effect: 3-week)	STAI: 0.35 Trait anxiety inventory: 0.12 Physical: 0.50 Psycho: 0.02 QoL: 0.06	Massage: ↓STAI Aromatherapy: ↓STAI, physical and psychological symptom

Wilkinson et al. (2007)	288	Early and advanced cancer	RCT Aromatherapy vs control	Aromatherapy 60-min/session per week x 4 (evening time) Therapist: 12	Anxiety/depression, QoL (pain, fatigue, nausea, global QoL) 6 and 10 weeks after randomization ES: at 6-week	Anxiety: 4.07 Depress: 1.72 Pain: 0.43 Fatigue: 2.51 Nausea: 0.63 QoL: 1.04	↓anxiety and depression at week 6 Anxiety and depression at week 10 (NS) ↓self-report anxiety at week 6 and 10 Self-reported depression at week 6 or 10 (NS) Pain, fatigue, nausea, global QoL (NS) No carryover or long-term effects, only last for two weeks after intervention
Williams et al. (2002)	29	Breast cancer-related lympho-edema	Experimental design with crossover MLD vs simple SLD	MLD: Vodder method to treat neck, trunk, and arms 45 min x 5 days x 3 weeks (15 times) SLD: 20 min x 5 days x 3 weeks Therapist: 3 (MLD)	Excess limb volume, caliper creep, dermal thickness, QoL	Excess limb volume: 0.76 (2 groups) Caliper creep: 0.89 (MLD) Dermal thickness: 0.44	MLD effects: ↓limb volume, ↓caliper readings, ↓dermal thickness, ↓QoL (emotion), ↓pain

Modified from Jane et al. (2008)

BMT bone marrow transplant, *CgA* salivary chromogranin, *D* day, *DBP* diastolic blood pressure, *ELV* excess limb volume, *ES* effect sizes, *HR* heart rate, *HT* healing touch, *MAP* mean arterial pressure, *MLD* manual lymphatic drainage, *MT* massage therapy, *NA* non-applied due to the omission of related information or mean and standard deviation from reviewed studies, *NK* natural killer, *NS* no significance, *QoL* quality of life, *RA* registered nurse, *RCT* randomized clinical trial, *RN* registered nurse, *RR* respiratory rate, *SBP* subacute back pain, *SLD* simple lymphatic drainage, *SR* subjective relaxation, *ST* skin temperature, *STAI* state-trait anxiety inventory

Massage Protocol

The primary goal of this full-body massage was to decrease pain intensity and anxiety, and improved physiological relaxation for patients with metastatic bone pain during an in-patient hospitalization. To maximize therapeutic effects, this intervention should include the following protocol (Field et al. 1996; Wilkie et al. 2000; Smith et al. 2002; Price et al. 2007; Jane et al. 2009).

Pre-massage Preparation

1. The subject was instructed to have the evening meal at least 1 h prior to the intervention or to have the meal after the intervention, remain in bed for at least for 10 min immediately before the intervention, wear loose clothes, and empty his/her bladder.
2. Each massage was performed between 4:00 and 5:00 pm in his/her unit with the door closed and curtain drawn.
3. Prior to the intervention, the subject was instructed to lie first side-lying or prone position, then face-up, close their eyes, take three deep breaths, and refrain any conversation during the entire intervention.
4. Each massage session included unscented massage lotion as a skin lubricant.
5. The subject was asked about their comfort with the room temperature. The application of fan or heater based on the individual's comfort.
6. The massage therapist assesses sites of metastases and any local skin conditions which would be a contraindication to massage intervention.

During Massage Intervention

1. Each massage must be a direct hand-on and skin-to-skin manipulation of the soft tissue of the backside of the body and must last for 45 min, if possible.
2. Each massage should include selected strokes with certain amount of time to eight different body areas, including head and neck, back, gluteus muscles, and four extremities.
3. Selected strokes included:
 - **Effleurage:** rhythmic, long, firm and gliding stroke conforming to the contours of the body using the therapist's whole palm of the hand or the tips of the middle fingers with 5–10 times.
 - **Light petrissage:** rolling, squeezing, and kneading movement of the fingers and thumb done slowly and lightly using the therapist's tips of thumbs or three middle fingers with five to ten times.
 - **Nerve stroke:** very light brushing of the skin with the therapist's fingers or full hand with three to five times.
 - **Light compression:** fingertips are used to lightly compress selected areas of tension using only mild to moderate pressure to the plantar surfaces, shoulders, palms, and possibly to the sacral area with 0–15 s duration.
4. Modification of massage: administration of very light and gentle pressure with Effleurage stroke in the bone metastatic sites and avoidance of sites of superficial tumors, infection, hyperesthesias, wounds, edema, and intravenous catheters.

3.4.2.3 Characteristics of Outcome Measures

Comparability of results across studies in this systematic review was challenging due to the variability of outcome measures employed and instrumentation used, and which are associated with the ES of the outcome measures. Overall, the most striking and prevalent perceived benefits of receiving MT was for the psychological variables (with large to moderate ES) followed by physical or biophysical variables (with small ESs: 0.00–0.21). $ES < 0.2$ is considered as extremely small ES and which may be not clinical important because the relationships between the variables are small and the differences between the treatment and comparison groups are limited (Burns and Grove 2009). The most frequently studied physical and psychological variables included pain intensity (ES: 0.13–1.13), fatigue (ES: 2.51–0.71), nausea (ES: 0.34–1.84) or vomiting (ES: 0.36), symptom distress (ES: 0.20–0.61), sleep quality (ES: 0.07–0.62), subjective relaxation (ES: 0.54–0.61), anxiety (ES: 0.79–3.10), depression (ES: 0.49–1.72), mood status (ES: 0.39–0.53), analgesic dose (ES: 0.57), global quality of life (ES: 0.06–0.94), satisfaction, cost, and bio-physiological parameters, such as heart rate (ES: 0.01–0.23), respiratory rate (ES: 0.20), skin temperature (ES: 0.14), mean arterial pressure (ES: 0.11), excess limb volume (ES: 0.76) or dermal thickness (ES: 0.44), caliper creep (ES: 0.89), stress indicators including urinary cortisol, dopamine, and salivary chromogranin (ES: 0.68), flow rate (ES: 0.60), cortisol (ES: 0.00), IgA (ES: 0.23), α -amylase (ES: 0.45), and immunity (i.e. natural killer cells or lymphocytes).

With respect to the measurement intervals, most studies utilized pretest-posttest research designs with single-time point measurements in conjunction with a variety of measurement intervals from immediately following the massage to 5–10 min; 10–20 min; 1–2 h; 3–5 h; 24–48 h or 2–6 weeks following massage. For studies with repeated measures designs, the interval of measurement ranged from 5 to 10 min or 1 and 2 h or 2–3 weeks. In those studies the massage effects seemed not to be sustained more than for 24 h. For studies with crossover designs, the wash-out period ranged from 24 h to five weeks. With a mean wash-out time of 16.7 days, White et al. compared 4 weekly 45-min sessions of either massage or healing touch to the presence of therapists or standard care conditions in 164 patients. They found significant carryover effects in terms of analgesic use and pain indices, indicating that the value of the variable in the first period influenced responses in the second period. For the rigor of study on MT, thus, the appropriateness of wash-out time period needs to be taken into consideration in studies with crossover design.

3.4.3 Conclusions

In summary, despite variations in the sample sizes, nature of the populations and research designs employed, the complexity of protocols, and the wide range of measurement intervals, outcome variables used, instrumentation, and effect sizes as reported in the literature, the most studies support the supposition that the massages

group outcomes were more positive compared to control group (condition) outcomes in terms of pain intensity, nausea or vomiting, fatigue, distressing symptoms, anxiety, depression, and self-report of relaxation, and physiological arousal (blood pressure) immediately or 5 or 10–20 min or 2–3 h following massage, but not beyond 24 h after termination of massage. In contrast, the most notable inconsistent massage effects were in terms of the responses to complexity and multidimension of stress adaptation, such as sleep, quality of life, and stress indicators, such as heart rate, respiratory rate, cortisol, IgA and α -amylase, immunity (i.e. natural killer cells or lymphocytes). We postulated that the discrepant findings summarized in this review were partly due to the numerous methodological issues identified included less rigorous inclusion criteria, failure to consider potential confounding variables, inconsistent massage doses and protocols, less rigorous research designs, measurement errors, and inadequate statistical power. In the design of future studies, thus, the above methodological issues need to be addressed. Clinical trials with better designs are required to determine indications and contraindications and to ascertain any subgroup effects in terms of types or dose of massage, types or stage of cancer or symptom distressing. In addition, a combination of research focused on potential mechanisms and well-designed clinical trials may clarify how massage works and in which circumstance it works, opening up new research avenues. More importantly, MT in this systematic review appears to be safe for patients with cancer, even feasible for patients with advanced cancer or bone metastases, ensured by initiating a pre-massage assessment and modifying massage protocol with administration of light and gentle pressure in boney lesion.

3.5 The Mechanisms of MT for Pain Control

Despite the promise of mostly positive findings of MT in cancer patients documented in the existing literatures, the mechanical links between manipulation of body tissue and corresponding relief in terms of a broad range of symptoms have not yet been fully elucidated (Moyer et al. 2004; Sager et al. 2007; Cassileth and Keefe 2010). Like other types of relaxation modalities, MT is primarily based on a reciprocal relationship in the human being between the body and the mind (i.e. calming the body automatically calms the mind and calming the mind causes the body to relax). Theoretically, the manipulations of skin and musculoskeletal, such as Swedish massage, induce local biochemical changes that modulate local blood flow and oxygenation in the skin and muscle. These local effects may influence neural activity at the spinal cord segmental level and could modulate the activities of sub-cortical nuclei that influence mood and pain perception. This intrinsic relationship between mind and body and its manipulation is an important target for MT and may help explain how MT reduces suffering for patients with cancer.

In Moyer et al. (2004)'s meta-analysis, a number of potential theories or mechanisms pertaining to MT effects have been posited including: (1) gate control theory of pain reduction: MT could create a stimulus that interferes with the

transmission of the pain stimuli to the brain, effectively “closing the gate” to the reception of pain prior to it being processed; (2) promotion of parasympathetic activity. The pressure applied during MT may stimulate vagal activity, which in turn leads to a reduction of stress hormones and physiological arousal, and a subsequent parasympathetic response of the autonomic nervous system, causing a state of calmness. Nordschow and Bierman (1962) also proposed that a diminished state of excitability of the sympathetic division of hypothalamus and cerebral cortex, which has been observed following MT, could account for physical and mental relaxation; (3) influence on body chemistry. MT could be linked with an increased level of serotonin and endorphins, which may inhibit the transmission of noxious nerve signals to the brain, leading to feelings of well-being; (4) mechanical effects. The manipulations and pressure of MT may break down subcutaneous adhesions and prevent fibrosis and promote circulation of blood and lymph; processes that may lead to reductions in pain associated with injury; (5) promotion of restorative sleep. Deprivation of deep sleep may result in increased levels of substance P and somatostatin and both of these changes have been linked to the experience of pain. MT may reduce pain indirectly by promoting restorative sleep; and (6) interpersonal attention. Some portion of MT effects may result from the interpersonal attention that the recipient experience.

Since the primary focus of this chapter is on the putative effects of MT on cancer pain, the following sections explore the potential underlying mechanisms of MT on pain relief in terms of the potential neural pain mechanisms. The following sections are modified from Wilkie (2012) and are used with permission.

3.5.1 Pain Neural Mechanisms

The neural mechanisms of pain involve a complex process related to transduction, transmission, perception, and modulation of neural signals. These mechanisms represent complex, not fully understood systems, but begin to explain the tremendous variability in pain reported by persons experiencing similar degrees of tissue damage. The transduction and transmission steps of the pain process involve the neurochemical signals of actual or impending tissue damage (nociceptive stimuli) or signals associated with nervous system damage or altered processing of sensory stimuli (neuropathic pain) (Wilkie et al. 2001; von Hehn et al. 2012).

Not all nociceptive stimuli or signals associated with pain are perceived as pain. If there is sufficient modulation of signals and perception of nociceptive or neuropathic events is prevented, there is no pain (Basbaum et al. 2009; von Hehn et al. 2012). Perception is critical to sensing pain. Modulation, either enhancing or inhibiting nociception and neuropathic events, therefore is crucial to pain perception. Most pain management techniques probably mimic endogenous pain inhibition processes. Conversely, pain that is difficult to relieve probably results from enhanced nociceptive signals. Additional details about these four steps provide a foundation for understanding the effects of massage on pain.

Fig. 3.1 Conversion of chemical, heat or pressure stimuli into a neuronal action potential is the first step in the pain process, transduction (Reproduced from Wilkie et al. (2012). With permission)

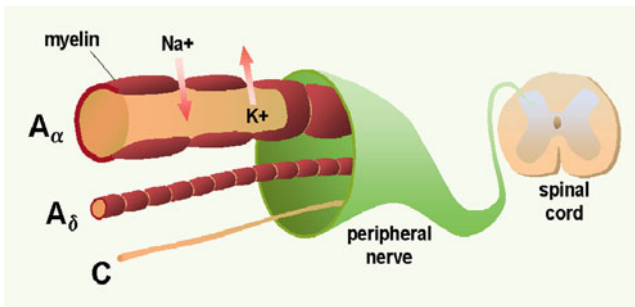
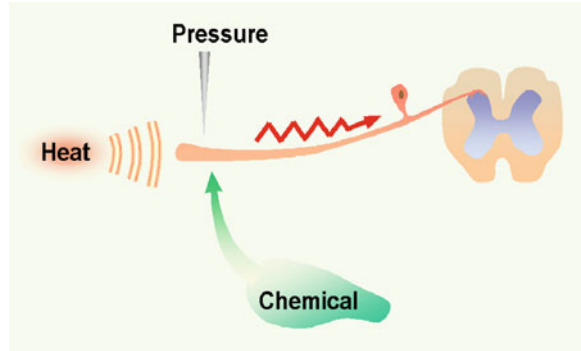


Fig. 3.2 Sensory nerve with large myelinated A- α fiber carrying touch sensation, A- δ and C fibers carrying pain sensation to dorsal horn of the spinal cord (Reproduced from Wilkie et al. (2012). With permission)

3.5.2 Transduction

The first step of the pain process is transduction, which is the conversion of a mechanical, thermal, or chemical stimulus into a neuronal action potential (Fig. 3.1). Peripheral nerve cells are stimulated by tissue damaging (noxious), pressure, heat, or chemical forces. A sufficient nociceptive stimulus generates an action potential at nociceptors (receptors) on A- δ fibers and C fibers. These fibers traverse through the dorsal root ganglia along with the A- α (sensory muscle), A- β (sensory skin) into the dorsal horn of the spinal cord where various connections are made (Fig. 3.2) and along with sympathetic efferent fibers. Norepinephrine, which is released by sympathetic efferent fiber activation, is known to facilitate nociceptive pain signals and activate damaged neurons and thereby contribute to intensified neuropathic pain (Sato and Perl 1991). The relaxing effects of massage may counteract this effect of sympathetic efferent fiber activation and thereby contribute to pain relief in people who have nociceptive, neuropathic, or both of these pain types. Cancer

patients clearly report the pain controlling effects of self-administered massage for pain that has characteristics of both nociceptive and neuropathic pain types (Wilkie et al. 1992).

The A- α and A- β fibers carry the sensations of light pressure to deep muscles, soft touch to skin, and vibration. The A- α and A- β fibers primarily ascend to rostral centers in the dorsal column pathway, but they also make synapses in the spinal dorsal horn close to synapses of the A- δ and C fibers (Fig. 3.2). This dorsal horn connection means that input from touch fibers can enter the spinal cord and synapse or communicate with cells carrying nociceptive input; this mechanism is relevant to some effects of MT, which activates A- α and A- β fibers.

3.5.3 *Transmission*

Once the primary afferent nociceptor has been transduced, the action potential must be transmitted to the central nervous system (CNS) and through the CNS before pain is perceived. The following three steps are involved in nociceptive signal transmission: (1) projection to the CNS; (2) processing within the dorsal horn of the spinal cord; and (3) transmission to the brain. Each step in the transmission process is important in pain perception.

The transmission of the action potential to the central terminal of the neuron is necessary for the cell to deliver the nociceptive signal to cells in the spinal cord. This transmission process requires more time for A- γ fibers than A- α or A- β fibers, both of which are larger and conduct faster than A- γ fibers.

Once the nociceptive signal arrives in the CNS, it is processed within the dorsal horn of the spinal cord. This processing includes: (1) release of neurotransmitters from the primary afferent nociceptor into the synaptic cleft; and (2) binding of neurotransmitters to receptors on nearby cell bodies and dendrites of cells, which may be located elsewhere in the dorsal horn. Some of the primary afferent nociceptor neurotransmitters produce activation, perhaps through cooperation of other neurotransmitters, when bound to receptors whereas others inhibit activation of nearby cells. Cells excited by the primary afferent nociceptor input release other neurotransmitters, which increase the complexity of the neurochemical communication occurring within the dorsal horn (Xu and Yaksh 2011). The net effects of the complex neurotransmitter release can facilitate or inhibit transmission of nociceptive stimuli (Fig. 3.3).

With adequate summation (net excitatory effects) on projection cells, nociceptive stimuli are propagated to the third-order neuron, primarily in thalamus and several other areas of the brain. The axons of the dorsal horn projection cells (second-order neurons) enter the brain through several pathways, including the: (1) spinothalamic tract (STT); (2) spinoreticular tract (SRT); (3) spinomesencephalic tract; (4) spinocervical tract; (5) second-order dorsal column tract; and (6) spinohypothalamic tract. The anterolateral quadrant of the spinal white matter contains all but the second-order dorsal column tract, which traverses in the dorsal column pathway.

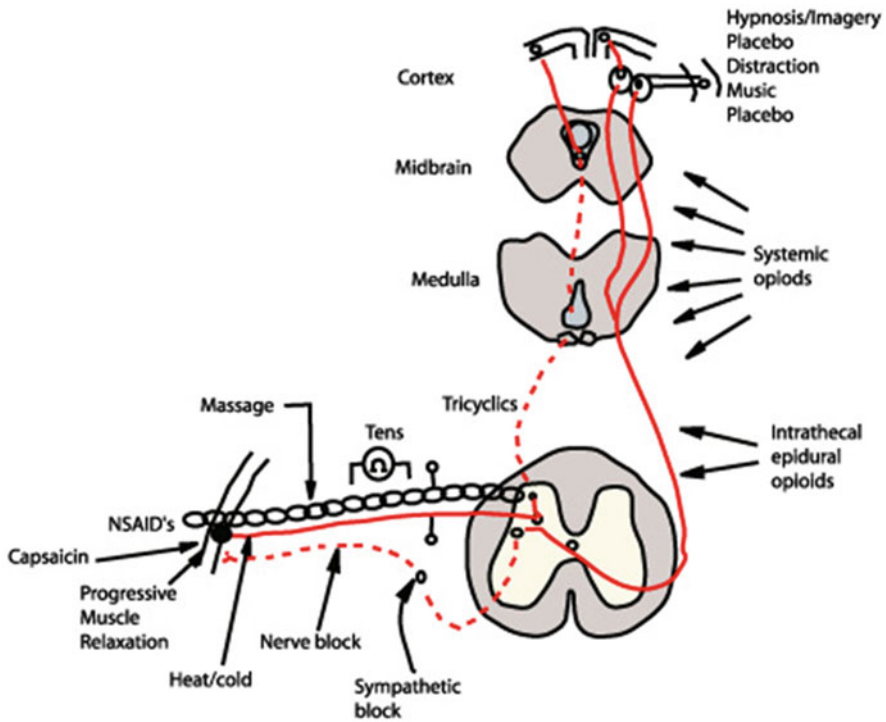


Fig. 3.3 Putting the pain process together: a schematic showing sites of action of commonly used therapies, including massage therapy (Modified from Fields and Levine 1984), pain-mechanisms and management (Reproduced from Wilkie et al. (2012). With permission)

Generally, the STT and SRT are the best-understood nociceptive pathways. The STT segregates into medial and lateral branches near the thalamus with the medial branch terminating in medial thalamus and the lateral branch terminating in lateral thalamus. The lateral branch is known also as the neospinothalamic pathway. The medial branch is known also as the paleospinothalamic pathway or the paramedian pathway. The paleospinothalamic pathway also sends a collateral pathway to the reticular formation and appears functionally similar to the SRT.

3.5.4 Pain Perception

In the brain, nociceptive input is perceived as pain. New data suggest that there is no single, precise location in the brain where pain perception occurs. Instead pain perception involves several brain structures. It is known that the brain is necessary for pain perception; hence no brain, no pain. Until it is understood clearly where pain is perceived, prudent clinical practice involves treatment of any noxious

stimulus as potentially painful, even in the comatose person who does not respond to noxious stimuli. Lack of a behavioral response to a noxious stimulus does not indicate that the person lacks pain perception. This notion is extremely important when providing care to the comatose person with massive injuries or for persons with cancer in the active dying state. Unless there is some reason for assuming that there has been removal of the nociceptive stimuli, which caused pain when the person was awake, it is crucial that pain therapies be continued, even though the person cannot report pain perception or show behaviors usually considered indicative of pain.

Because of the complex neural mechanisms of nociceptive processing, pain is perceived as a multidimensional sensory and emotional experience to which there are cognitive and behavioral responses. In this sense, the use of some forms of relaxation interventions (i.e. music therapy, guided imagery, distraction) or interventions producing relaxing effects (i.e. massage), and cognitive behavioral therapy, might potentially provide clinicians with additional tools for alleviating pain in patients with cancer-related pain.

3.5.5 Modulation

Critical to transmission of nociceptive stimuli and pain perception are the modulatory mechanisms, the final step in the pain process. Evidence has been available for more than 50 years that nociceptive cells in the spinal dorsal horn are selectively inhibited by brain stem stimulation (Melzack and Wall 1965). The dorsolateral funiculus spinal pathway also has been shown to be critical to the inhibition of nociceptive responses in animals. Today, however, we know that spinal modulation may include both inhibition as well as enhancement of nociceptive stimuli.

Massage is one non-drug therapy that may modulate pain. Investigators have postulated a number of explanations for the effectiveness of massage, including the Gate Control Theory of pain (Melzack and Wall 1965) and a general relaxation response (Longworth 1982; Ferrell-Torry and Glick 1993; Meek 1993; Goats 1994; Smith 1998) with improved circulation (Goats 1994), and reduced muscle tension (Danneskiold-Samsoe et al. 1983, 1986; Richards 1993). The relaxing effect of touch (Weiss 1988, 1992; Watson 1997) has been shown to be associated with reduced sympathetic nervous system activation (Weiss 1990) as indicated by decreased pulse and respiratory rates immediately following massage (Moyer et al. 2004). It is well known that increases or reduction in sympathetic nervous system activation plays an integral part in producing physiological (e.g. pulse and respiratory rates), behavioral (e.g. flight, fight-not addressed in this study) and psychological (e.g. mood) responses to stress or relaxation (Henry and Ely 1979; Henry 1992, 1993). It is also well known that sympathetic activation increases pain responses (Sato and Perl 1991). Furthermore, as predicted by the gate control theory of pain and new evidence of pain mechanisms, activation of low threshold A alpha and A beta cutaneous sensory fibers (i.e. by massage) is known to inhibit nociceptive

signals in animals (Willis 1995) and to decrease the perception of pain control in humans (Fields 1987). Gate Control Theory (Melzack and Wall 1965), as modified by our current general understanding of pain mechanisms, postulates ascending and descending mechanisms for pain control, both of which could be modified by massage and an associated relaxation response.

In summary, as previously described more than 50 years ago by the Gate Control Theory of pain (Melzack and Wall 1965), the outcome of activation of nociceptive receptors is multifactorial. The amount of pain perceived by an individual may vary tremendously depending on the context of the situation and other variables including the person's genetic capability to metabolize analgesic drugs. This context and other variables may include other physiological, sensory, affective, cognitive, or behavioral variables, the effects of which cannot be precisely measured physiologically given the limitations of currently available methods. The person's perception of the pain, however, can be measured using a variety of pain scales. Information derived from the scales about the pattern, area, intensity, and nature of the pain, as well as the emotional, behavioral, and cognitive responses to the pain provide the diagnostic foundation for health professionals to intervene. This information helps the health professional to recognize nociceptive and neuropathic types of pain and which can inform clinical decisions regarding appropriate pain relief therapies. Understanding the pain process and genetic alterations in drug metabolism helps health professionals to better interpret pain assessment data and to implement multimodality interventions including MT that can maximize pain relief while, at the same time, minimizing side effects of therapies. Knowledge about neural mechanisms of nociception, pain perception, and pain modulation is vital for clinical decision making and rational management of pain experienced; especially the pain experienced by seriously ill cancer patients.

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Chapter 4

The Effect of Acupressure on Chemotherapy-induced Nausea

Eun Jin Lee and Sherry Warden

Abstract This chapter was to review the effect of acupressure on chemotherapy-induced nausea, the incidence of side effects, and discuss the mechanisms of acupressure. A systematic review approach was used, studies included experimental studies, quasi-review approach was used, studies, preclinical studies, clinical trials, systematic reviews, and meta-analyses. Literatures search was conducted in CINAHL, MEDLINE, and PubMed using the key words acupressure, nausea, and cancer. Studies published in peer-reviewed journals between 1 January 2002 and 31 December 2012, which used acupressure as the sole intervention for one group, were included when they were written in English. After applying inclusion and exclusion criteria, twelve studies were eligible for review. Seven randomized controlled trials, two quasi-experimental studies, and three systematic reviews were found. Six of seven clinical trials showed positive results of acupressure on chemotherapy-induced nausea in 1,341 patients with cancer. However, we cannot conclude that acupressure is effective for nausea due to the small number in the samples and the poor quality of the studies. Furthermore, well-designed studies are needed to examine the effect of acupressure on chemotherapy-induced nausea. Three systematic reviews reported that acupressure may decrease chemotherapy-induced nausea in 11 clinical trials. No side effect of acupressure has been reported, whereas the side effects such as redness, swelling, and tenderness of sea bands have been reported. On the other hand, the mechanism of acupressure can be explained by regulation of substance P, serotonin, cholecystokinin, opioids, the autonomic nervous system.

E.J. Lee (✉)

Nursing Department, Inha University, 100 Inharo Hightech Center 1504,
Namgu Incheon 402-751, South Korea
e-mail: peace-peace@hanmail.net

S. Warden

Emeritus Faculty, University of Kentucky, 413 Cochran Road., Lexington, KY 40502, USA

4.1 Introduction

Cancer is the third leading cause of death in high-income countries (World Health Organization 2012a). The incidence of cancer in 2007 was 472.68 per 100,000 in the US (National Cancer Institute 2012a). The National Cancer Institute reported that 127.47 million dollars was spent to treat cancer in 2010 (National Cancer Institute 2012b). The financial cost of cancer treatment is a burden to patients, their families, and our society. Patients with cancer often suffer from pain, nausea and vomiting, loss of hair, fatigue, skin dryness, insomnia, forgetfulness, sadness, and loss of appetite due to side effects of cancer treatment or cancer symptoms (Liu et al. 2011; Middleton and Lennan 2011). Nausea and vomiting are major side effects of chemotherapy (Middleton and Lennan 2011) as well as major symptoms of cancer. Nausea was experienced by 75.4% of 256 patients with advanced cancer and 63.7% had vomiting (Liu et al. 2011). To treat chemotherapy-induced nausea, competitive antagonists at dopaminergic (D2 subtype) receptors, corticosteroids, cannabinoids, benzodiazepines, olanzapine, NK₁ antagonist such as aprepitant or foraprepitant, 5-HT₃ such as granisetron or ondansetron have been used (American Society of Clinical Oncology 2011; National Cancer Institute 2012c). The average cost of treating nausea and vomiting in patients receiving chemotherapy was US \$170–\$482.46 per chemotherapy course (Avritscher et al. 2010; Hamada et al. 2012). The side effects of anti-emetics are sedation, extrapyramidal reactions, akathisia, hypotension, cog-wheeling rigidity, acute dystonia, and tremors (National Cancer Institute 2012c).

Acupressure can be an option to decrease medical costs and side effects of anti-emetics. Acupressure is a kind of massage involving fingers or hands to stimulate acupuncture points. Acupressure is a non-pharmacological therapy which has been used to manage various symptoms, such as nausea and vomiting, insomnia, fatigue, pain, and dyspnea (Lee and Frazier 2011). Acupressure at Neiguan (PC6) can be easily applied to practice. Nurses can learn acupressure and can teach patients and their families to use acupressure to decrease nausea. Acupressure by nurses would be more effective in inpatient settings because patients might not have the energy to perform acupressure. Most researchers in previous studies used sea bands for 24 h for five days (Fig. 4.1). Even though sea bands are convenient tools for acupressure, due to the possible side effects of sea bands, finger acupressure seems to be safer and more effective. Acupressure for 20 min, once a day, reduced nausea in 150 post-operative patients (Ming et al. 2002).

In traditional Chinese medicine acupressure is based on yin-yang theory and the meridian theory. The body is seen as a subtle balance of two opposing and inseparable forces: yin and yang. Yin symbolizes the cold, slow, or passive principle, while yang symbolizes the hot, excited, or active principle. Health is due to a balanced state of yin and yang, while disease is due to an internal imbalance of yin and yang. This imbalance leads to obstruction in the flow of vital energy (Qi) along pathways known as meridians. Acupressure stimulates meridians, a network of energy pathways throughout the body, to increase the flow of Qi, consequently improving the symptom (National Center for Complementary Alternative Medicine 2012). This chapter was to review the effect of acupressure on chemotherapy-induced nausea, side effects, and the mechanisms of acupressure.

Fig. 4.1 Sea band

4.2 Methods

Literatures search was conducted in CINAHL, MEDLINE, and PubMed using the key words acupressure, nausea, and cancer. Studies published in peer-reviewed journals between 1 January 2002 and 31 December 2012 were reviewed. Inclusion criteria were: (1) studies using acupressure as the sole intervention; and (2) studies written in English. Exclusion criteria were: (1) studies using auricular or hand acupressure, reflexology, shiatsu, and electronic or magnetic devices for nausea; and (2) unpublished papers and abstracts. These intervention methods use a different naming system for the meridians and a different technique from body acupressure. Each experimental study was assessed for quality using the risk of bias tool by the Cochrane group (Moher et al. 2001). This tool consists of six domains: sequence generation; allocation concealment; blinding of participants, personnel, and outcomes; incomplete outcome data; selective outcome reporting; and other sources of bias. Scores range from 0 to 6 and a higher score means higher quality and less risk for bias (Table 4.1). Effect size (Hedges' g) for each study was calculated using the mean values of the acupressure and control groups when provided (Durham University 2012). Effect size is a measure for comparing effectiveness of the intervention between two groups and uses mean and standard deviation to calculate the difference between the two groups (Coe 2000). Pre-post mean for the acupressure group was used alone when the post-mean of the control group was not provided. The names of acupuncture points in this study are based on the World Health Organization (WHO) acupuncture standard (World Health Organization 2012b).

4.3 Results

The review of three databases revealed 25 articles from PubMed, 15 articles from MEDLINE, and 11 articles from CINAHL. Reference lists of these articles also were searched to find other relevant studies. Among 51 articles, 38 articles were

Table 4.1 Effect size and quality of study

Author (Year)	Measure	Quality of study	Acupressure		Control/placebo		Effect size	Confidence interval	<i>p</i>
			Mean	SD	Mean	SD			
Randomized controlled trial									
Roscoe et al. (2003)	Severity of nausea (1–7)	2	2.6	No data	3	No data	232		<0.05
Molassiotis et al. (2007)	Incidence of nausea at day 1	5	0.66	1.6	2.16	2.4	19	0.73	0.04–1.39
Dibble et al. (2007)	Incidence of emesis	1	No data		No data				<0.001
Jones et al. (2008)	Total nausea prevention (0–10)	2	2.7	2.9	3.4	3.0	18	0.23	–0.42 to 0.89
Roscoe et al. (2010)	Mean number of anti-emetic pills at home	4	12.6	6.6	18.5	9.1	32	1.21	0.70–1.73
Suh (2012)	IVNR score at day 4	5	5.48	3.84	10.76	7.54	23	0.89	0.29–1.47
Genç et al. (2013)	Incidence of nausea, vomiting, retching	1	No data	No data	No data	No data	53	–	NS
Quasi-experimental study									
Shin et al. (2004)	Severity of nausea and vomiting at day 4	NA	3.05	2.91	9.5	8.95	20	0.95	0.3–1.6
Taspinar and Sirin (2010)	Severity of nausea (0–10) at day 3	NA	2.47	2.57	4.32	2.78	34	0.68	0.09–1.17

SD standard deviation, *NA* not applicable, *n* number, *NS* not significant

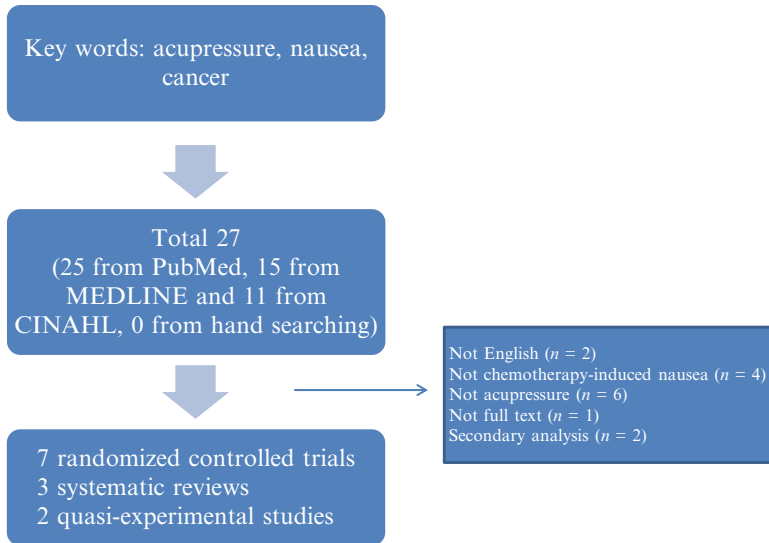


Fig. 4.2 Flow chart of study selection

excluded due to: duplicates ($n=24$), non-English text ($n=2$), nausea not caused by chemotherapy ($n=4$), non-acupressure intervention ($n=6$), secondary analysis ($n=2$) (Roscoe et al. 2006; Lee et al. 2010), and non-availability of full text ($n=1$) (Fig. 4.2). This search resulted in twelve articles that were eligible for review: seven randomized controlled trials, two quasi-experimental studies, and three systematic reviews. Randomized controlled trials use randomization for group assignment to reduce bias and control groups to compare effectiveness between groups, while quasi-experimental studies use pre-post measures but do not use randomization or a control group. Quasi-experimental designs are used when: (1) the efficacy of the intervention has been established and randomization might create ethical concerns; (2) it is difficult to randomize subjects; (3) it is difficult to randomize by location (e.g. by wards); and (4) only a small sample size is available. The limitation of quasi-experimental designs is the risk of bias (Harris et al. 2006). The quality of the studies and effect sizes are summarized in Table 4.1. Roscoe and his colleagues (2003) and Dibble and her colleagues (2007) did not provide data such as mean and standard deviation for each group to calculate effect size. The characteristics of randomized trials and quasi-experimental studies are summarized in Table 4.2. Jones and colleagues (2008), Taspinar and colleagues (2010), Roscoe and colleagues (2010), and Genç and colleagues (2013) did not provide the intervention time for acupressure. Total number of patients from seven studies is 1,341 and 89% of the patients were female. Children under 19 years old made up 1.3% of the subjects.

Table 4.2 The description of acupressure studies

Author (year)	Sample	<i>n</i>	Acupressure point	Tool	Time per day	Days	Measures
Roscoe et al. (2003)	Breast cancer (85%)	739	PC6	Sea band	24 h	5	Severity, frequency of nausea and vomiting, expected efficacy of the wristband
Shin et al. (2004)	Stomach cancer	40	PC6	Finger	15–20 min	5	Rhodes index of nausea, vomiting, and retching
Molassiotis et al. (2007)	Breast cancer	36	PC6	Sea band	24 h	5	Rhodes index of nausea, vomiting, and retching
Dibble et al. (2007)	Breast cancer	160	PC6	Finger	6–9 min	21	Rhodes index of nausea, vomiting, and retching, state-trait anxiety inventory
Jones et al. (2008)	Children with cancer	18	PC6	Sea band	No data	1–5	Morrow assessment of nausea and emesis
Roscoe et al. (2010)	Breast cancer	74	PC6	Sea band	No data	5	Severity of nausea (1–7), mean number of anti-emetic pills at home
Taspinar and Sirin (2010)	Gynecologic cancer	34	PC6	Sea band	No data	5	Severity of nausea (0–10)
Suh (2012)	Breast cancer	120	PC6	Sea band	No data	5	Rhodes index of nausea, vomiting, and retching
Genç et al. (2013)	Lung, breast, or gynecological cancer	120	PC6	Sea band	No data	5	Rhodes index of nausea, vomiting, and retching, functional assessment of cancer therapy general

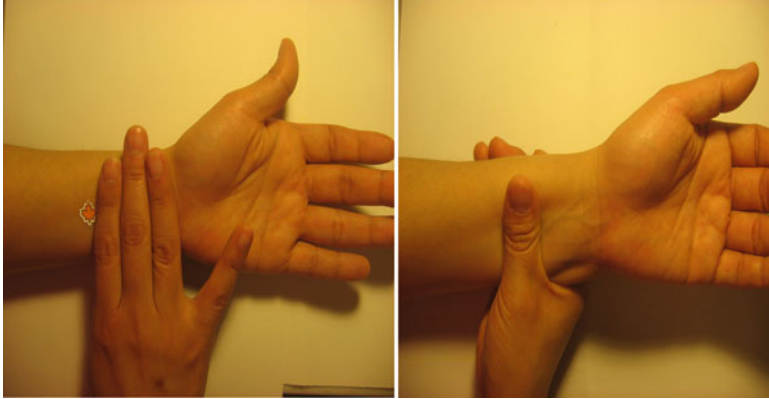


Fig. 4.3 Acupressure at PC6

4.3.1 Randomized Controlled Trials (RCTs)

4.3.1.1 Acupressure Point

All studies used acupoint PC6. PC6 is located at the middle of the inner side of the forearm three fingers width above the wrist crease (World Health Organization 2012b) (Fig. 4.3).

4.3.1.2 Outcome Measures

To measure nausea, studies used the Rhodes index of nausea, vomiting, and retching (Rhodes et al. 1987; Rhodes and McDaniel 1999), the Morrow assessment of nausea and emesis (Morrow 1992), severity of nausea, and a patient report diary (Carey and Burish 1988).

To measure other factors related to nausea, studies used the Functional assessment of cancer therapy scale-general (Cella et al. 1993), expected efficacy of the wrist bands (Roscoe et al. 2003), and the State-trait anxiety inventory (Spielberger 1983).

4.3.1.3 Quality of Studies

The average risk of bias score was 2.85 for the RCTs which indicated that the risk of these studies was moderate to high. Of seven RCTs: the sequence generation was not clear in four studies (Roscoe et al. 2003; Dibble et al. 2007; Jones et al. 2008; Genç et al. 2013); allocation concealment was not clear in four studies (Roscoe et al. 2003; Dibble et al. 2007; Jones et al. 2008; Genç et al. 2013); blinding of participants, personnel, and outcomes was not clear or not used in four studies

(Roscoe et al. 2003; Dibble et al. 2007; Molassiotis et al. 2007; Genç et al. 2013); incomplete outcome data in three studies (Roscoe et al. 2010; Dibble et al. 2007; Genç et al. 2013), selective outcome reporting in four studies (Roscoe et al. 2003, 2010; Jones et al. 2008; Genç et al. 2013); and other sources of bias such as no report of attrition rate and reason, fidelity, and side effects in four studies (Roscoe et al. 2003; Dibble et al. 2007; Jones et al. 2008; Genç et al. 2013).

4.3.1.4 Description of Studies

Acupressure using sea bands continuously for five days significantly decreased nausea and vomiting on the first day of chemotherapy compared to the control group, which received standard care ($n=739$, $p<0.05$). However, there was no significant difference on the second to fifth day of chemotherapy compared to the control group. Females made up 92% of the subjects. In addition, 85% of subjects had breast cancer and 10% of subjects had hematologic neoplasms. This study did not report the mean age of patients and standard deviation for each group (Roscoe et al. 2003). In another study, the use of acupressure with sea bands continuously for five days significantly decreased nausea, vomiting, and retching in patients with breast cancer receiving chemotherapy when compared to a control group receiving standard care ($n=36$, $p<0.05$). The mean age of patients was 49.5 ± 10.5 (Molassiotis et al. 2007). Dibble and her colleagues (2007) randomized patients with breast cancer to the acupressure group, the placebo acupressure group or the usual-care group. The acupressure group used PC6 and the placebo group used Houxi (SI3). There was no significant difference in acute nausea (chemotherapy day 1) among three groups after acupressure. However, there was a significant difference in delayed nausea (chemotherapy days 2–11) and the incidence of vomiting among the acupressure group, the placebo group ($t=3.3$, $p=0.002$, odds ratio=1.3), or the usual-care group ($t=4.91$, $p<0.0001$, odds ratio=1.4, $n=150$). The acupressure group was most effective when compared to the placebo and usual-care groups. The participants performed acupressure for 6–9 min/day for three weeks. They kept a daily log for three weeks and did not report any side effects. The mean age of patients was 49.3 ± 9.4 . This study did not report fidelity and outcome such as the number for each group and the score on the nausea scale for each group. Jones and his colleagues (2008) used a crossover randomized clinical trial design to examine the effect of acupressure on chemotherapy-induced nausea in 18 children with cancer. The effect of acupressure using sea bands was not significantly different compared to the placebo and control groups. The mean age of patients was 11.7 ± 4.2 . The types of cancer varied such as acute lymphoblastic leukemia ($n=4$), rhabdomyosarcoma ($n=5$), Ewing sarcoma ($n=4$), medulloblastoma ($n=2$), and osteosarcoma ($n=3$). Roscoe et al. (2010) reported that patients with high expectancy of acupressure ($n=36$) took fewer anti-emetic pills at home compared to patients with lower expectancy ($n=32$, $p<0.05$). In this study, patients performed acupressure using sea bands for five days. The mean age was 51.5 (28–74) in 74 patients with breast cancer.

4.3.2 *Quasi-experimental Study*

Taspinar and Sirin (2010) reported that acupressure using sea bands for five days decreased nausea compared to nausea before acupressure in 34 patients with gynecologic cancer ($p=0.01$). The mean age of the participants was 50.55 ± 10.55 . This study did not use a control group. Seventy six percent of the patients had ovarian cancer. In addition, 23.55% of patients had cancer of the endometrium, cervix, or fallopian tubes. The dosage of anti-emetic medication was reduced significantly after acupressure. Shin and her colleagues (2004) reported that acupressure for 15–20 min per day for five days reduced nausea compared to the control group who received standard care in patients with stomach cancer ($n=40$, $p<0.001$). Seventy percent of the patients were male and the mean age of patients was 52.75 ± 10.91 .

4.3.3 *Systematic Reviews*

Chao and his colleagues (2009) reviewed randomized controlled trials which examined the effect of acupuncture, acupressure, or any other acupuncture point stimulation method for the management of therapy-related adverse events in patients with breast cancer. Chao and his colleagues (2009) included a paper which was written in Chinese. They concluded (based on the positive results of 10 out of 11 studies) that acupuncture, acupressure, electroacupuncture (EA), and drug injection at acupuncture points significantly improved chemotherapy-induced nausea in 761 patients with breast cancer. Chao and his colleagues included four studies which examined the effect of acupressure on chemotherapy-induced nausea (Dibble et al. 2000, 2007; Molassiotis et al. 2007). Dibble and her colleagues (2000) found that a daily 9-min acupressure at PC6 and zusanli (ST36) for 21 days did not reduce acute nausea and vomiting on the day of chemotherapy, but did decrease nausea and vomiting from day 2 to 11 when compared to the control (standard care) and placebo groups (acupressure in inappropriate locations) in 17 patients with breast cancer. Lee and her colleagues (2008) reviewed ten clinical trials to compare the effect of acupressure modalities such as sea bands and finger acupressure on chemotherapy-induced nausea. Four of seven studies using sea bands supported the positive effects and all three studies using finger acupressure supported the positive effects. Sea bands decreased acute nausea, whereas finger acupressure decreased delayed nausea and vomiting. Lee and her colleagues (2008) included two unpublished papers and one abstract. Klein and Griffiths (2004) reviewed two randomized controlled trials (Dibble et al. 2000; Ho 2006). Klein and Griffiths (2004) found that acupressure decreased chemotherapy-induced nausea in 482 patients with cancer.

4.4 Safety and Adverse Effects

Most studies that examined the effect of acupressure did not report whether they had side effects or not. Several studies reported that acupressure did not have side effects (Ezzo et al. 2006; White et al. 2007; Jones et al. 2008). Jones and his colleagues (2008) reported there were no side effects such as bruising, bleeding, swelling, skin irritation, infections, or neurovascular compromise from using sea bands. Ezzo and his colleagues (2006) reviewed 11 studies that examined the effect of acupressure or acupuncture on chemotherapy-induced nausea and vomiting. Ezzo and his colleagues (2006) reported that acupuncture-point stimulation by any method was safe with minimal, transient, and rare side effects. However, there were side effects related to wrist bands/sea bands such as redness, swelling, tenderness, itching, blistering, drowsiness, and headache/dizziness (Norheim et al. 2001; Alkaissi et al. 2002; Lee and Done 2004; Majholm and Moller 2011). Alkaissi and his colleagues (2002) reported a total of 61 adverse events such as discomfort, red indentation, itchiness ($n=15$), headache, dizziness ($n=1$), tightness of the band, swelling or deep marks or blistering at the site of the button ($n=45$) in 410 women. Majholm and his colleagues (2011) found that one third of 134 patients had side effects such as redness ($n=40$), swelling ($n=17$), and tenderness ($n=16$) in the wrist and hand caused by the wristbands. Four patients even reported paresthesias. The local side effects caused by the acupressure wristbands were equally distributed between the PC6 stimulation group and the sham control group. Norheim and his colleagues (2001) reported that 63% in the acupressure group and 90% in the placebo group experienced side effects such as pain, numbness, soreness, and hand swelling from using wristbands.

4.5 The Mechanism of Acupressure on Chemotherapy-induced Nausea

Chemotherapy stimulates the stomach, the chemo-receptor trigger zone in the peripheral nerves, and the vomiting center in the brain (Middleton and Lennan 2011). Nausea and vomiting are caused by harmful stimulation of the vomiting center directly or indirectly *via* one or more of four additional sites: the gastrointestinal tract, the vestibular system, the chemo-receptor trigger zone, and higher centers in the cortex and thalamus. Neural traffic originating in the GI tract moves along afferent fibers of cranial nerves IX (glossopharyngeal) and X (vagal) (Becker 2010). Neurotransmitters that are related to chemotherapy-induced nausea are substance P, serotonin, histamine (H1 and H2), dopamine, acetylcholine, opioids, and numerous other endogenous neurotransmitters. Many anti-emetics block receptors for these substances, thereby inhibiting stimulation of peripheral nerves at the chemo-receptor trigger zone and possibly at the vomiting center (National Cancer Institute 2012c).

A literature search was conducted in CINAHL, MEDLINE, and PubMed using the key words acupressure, mechanism, nausea, and P6/PC6/Neiguan/Neikuan. Some researchers did not use PC6 as a keyword instead they used Neiguan or Neiguan which is the Chinese name for PC6. No study has been published reporting the mechanism of acupressure on nausea. Another literature search was conducted in CINAHL, MEDLINE, and PubMed using the key words acupuncture, mechanism, nausea, and P6/PC6/Neiguan; acupuncture, P6/PC6/Neiguan, and substance P/serotonin/histamine (H1 and H2)/dopamine/acetylcholine/opioids. Clinical trials published in peer-reviewed journals between 1 January 1992 and 31 December 2011 were searched. Inclusion criteria were: (1) studies using acupuncture as the sole intervention for nausea for one group; and (2) studies written in English. Exclusion criteria were: (1) studies using moxibustion, nerve stimulators, or laser acupuncture; (2) studies not using any biophysical measure on outcomes; (3) studies not using PC6; and (4) unpublished papers and abstracts. Acupuncture is a therapy using needles to stimulate acupuncture points, while acupressure is a therapy using fingers. EA uses a small electric current that is passed between pairs of acupuncture needles. From three databases, 27 studies were retrieved from PubMed, 29 from CINAHL and MEDLINE, and four from hand searching. After applying inclusion and exclusion criteria, 18 studies were eligible for review.

According to the previous systematic reviews, acupuncture at PC6 influences the autonomic nervous system by inhibiting sympathetic nerves and increasing parasympathetic nerve activity (Abad-Alegria et al. 2001; Huang et al. 2005; Landgren et al. 2010). Huang and his colleagues (2005) suggested that the relief of nausea and vomiting by acupuncture at the PC6 point can be explained by the parasympathetic nerves (largely mediated by the vagus nerve) which modulate heart and gut. The stimulation of the vagus nerve decreases heart rate and increases peristalsis of the gut. Vagus or vagal nerve is a cranial nerve that regulates talking, swallowing, gag reflex, and parasympathetic activity (McCance and Huether 2002). Increased vagal activity is related to chemotherapy-induced nausea (Morrow et al. 2000), while decreased vagal activity or injury to the vagus nerve is related to the delayed emptying and gastric reflux (Lindeboom et al. 2004). These findings suggest that normal parasympathetic activity may decrease nausea by increasing gastric emptying, while excessive parasympathetic activity may increase nausea by increasing gag reflex.

4.5.1 Autonomic Nervous System

The autonomic nervous system consists of parasympathetic and sympathetic nerves (McCance and Huether 2002). The parasympathetic nerves are located in both the central nervous system (CNS) and the peripheral nervous system (PNS). The parasympathetic nerves function to save and restore energy. The parasympathetic nerves stimulate digestion and increase intestine motility and decrease heart rate, while sympathetic nerves slow digestion and motility (McCance and Huether 2002). Huang and his colleagues (2005) reported that acupuncture at PC6 for 20 min decreased heart rate

measured by electrocardiogram compared to the control group (no acupuncture) in 111 healthy subjects. This finding suggests that acupuncture at PC6 modulates the imbalance of parasympathetic nerve, which is related to nausea.

4.5.2 Serotonin

Serotonin is a neurotransmitter involved with mood, anxiety, sleep induction, and intestinal motility. About 80–90% of serotonin exists in the enterochromaffin cells in the gut, and the remainder is made in serotonergic neurons in the CNS. Serotonin stimulates the emetic center and increases nausea (McCance and Huether 2002). Electroacupuncture (EA) at Jianshi (PC5) and PC6 increased c-Fos immunoreactivity, neurons double-labeled with c-Fos, and either enkephalin or serotonin in all three midline medullary nuclei, especially in the nucleus raphe pallidus in six cats compared to cats with manual acupuncture ($p < 0.05$). These results propose that the medullary raphe nuclei, particularly the nucleus raphe pallidus, process somatic signals during EA and participate in EA-related modulation of cardiovascular function through an opioid or serotonergic mechanism (Guo et al. 2008). EA produces a synergism of the CNS with a direct impact on the uterus through increasing the release of β -endorphin and serotonin into the peripheral blood (Qu and Zhou 2007). Acupuncture at PC6, Shenman (HT7), and Sanyinjiao (SP6) using Jin-3 needling therapy for 45 min, six days per week for six weeks, reduced plasma level of adrenocorticotrophic hormone and platelet content of serotonin compared with the drug and needling group and drug only group in 86 patients with generalized anxiety disorder (Yuan et al. 2007).

4.5.3 Cholecystokinin (CCK) and the Dorsal Vagal Complex

CCK is a polypeptide hormone secreted by the gastrointestinal mucosa. CCK stimulates the gallbladder to eject bile and the pancreas to secrete alkaline fluid and CCK decreases gastric motility (McCance and Huether 2002). Cholecystokinin-A receptors are involved in the induction of meal-like fullness and nausea associated with intraduodenal lipid and gastric distention (Feinle et al. 1996). The dorsal vagal complex located in the brainstem (Charrier et al. 2006) controls the upper digestive tract (Rhoades and Bell 2009). EA at PC6 and ST36 significantly accelerated gastric emptying and concurrently increased vagal activity assessed by the spectral analysis of the heart rate variability, suggesting a possible vagal mechanism in dogs with delayed gastric emptying induced by duodenal distention (Ouyang et al. 2002). EA at PC6 and ST36 speeded up solid gastric emptying measured by scintigraphy in patients with gastroparesis (Xu et al. 2006). EA at PC6 inhibited gastric distention-induced transient lower esophageal sphincter relaxation (gastric reflux), which is related to impairment of the vagus nerve in 12 cats (Lindeboom et al. 2004; Wang et al. 2007).

4.5.4 Opioids

Endogenous opiates such as endorphins, dynorphin, and enkephalins are released into the blood as part of the response to stressful stimuli. Endorphins and enkephalins are widely distributed in the CNS and PNS. The CNS consists of the brain and the spinal cord, while the PNS consists of the somatic nervous system and the autonomic nervous system. High β -endorphin levels increase the pain threshold (McCance and Huether 2002). Chemotherapy-induced nausea is related to decreased levels of opioids (National Cancer Institute 2012c). Li and his colleagues (2001) found that EA (1–2 mA, 5 Hz) at PC5 and PC6 for 45 min activated δ - and μ -opioid receptors in the rostral ventrolateral medulla in 12 cats. EA (2–5 Hz, 2–5 mA) at PC6 for 30 min reduced myocardial ischemia, measured by regional myocardial wall thickening. Intravenous and microinjected naloxone into the rostral ventral lateral medulla prevented the EA-related response. Opioid μ and δ , but not κ , receptors in the rostral ventrolateral medulla are responsible for the EA-related modulation of sympathetic outflow, suggesting that endorphins and enkephalins, but not dynorphins, are the neuromodulators involved in this response (Li et al. 2002). EA (10 Hz) at PC6 for 60 min significantly reduced the number of episodes of retching and vomiting and suppressed retrograde peristaltic contractions compared to EA at weishu (BL21) or ST36 in seven dogs with vasopressin-induced emesis. The anti-emetic effect of EA was canceled by pre-treatment with naloxone but not naloxone methiodide. It is suggested that the anti-emetic effect of acupuncture is mediated *via* the central opioid pathway (Tatewaki et al. 2005). Naloxone methiodide is thought not to cross the blood-brain barrier and is used as a research tool to differentiate between central and peripheral sites of action for drugs acting on opioid receptors (Lewanowitsch and Irvine 2003). EA (1–10 Hz) at Zhongfeng (LR4), PC6, and ST36 for 45 min increased β -endorphin levels compared to sham acupuncture (short stud instead of needles) in 40 participants with colorectal discomfort due to a colonoscopy (Leung et al. 2011).

4.5.5 γ -Aminobutyric Acid (GABA)

GABA is the most widespread neurotransmitter in the CNS (McCance and Huether 2002). A lack of GABA or excessive GABA may cause nausea (Alstermark et al. 2008; Li and Akk 2008). Gabapentin which increases GABA in the brain improved nausea in patients with chemotherapy-induced nausea (Guttuso et al. 2003). EA (2 Hz, 2–4 mA) at PC5 and PC6 for 28 min reduced the release of GABA by 39% during EA and by 44% 15 min after EA in midbrain ventrolateral periaqueductal gray in rats (Fu and Longhurst 2009). These findings suggest that acupuncture at PC5 and PC6 modulates the imbalance of GABA which is related to nausea.

4.5.6 Catecholamine

Catecholamines such as epinephrine, dopamine, and norepinephrine are released at the medulla of the adrenal gland during the stress response (McCance and Huether 2002). Especially, norepinephrine increases nausea by inhibiting gastrointestinal activity (McCance and Huether 2002; Dube et al. 2010). EA (3 Hz, 0.2 ms pulses, 20 mA) at PC6 and Shaohai (HT3) for 30 min decreased blood pressure, heart rate, and plasma norepinephrine and epinephrine levels compared to the control group (Waiguan (TE5), Yinlian (LR11), and tail) in rats with immobilization stress (Yang et al. 2002). EA (3 Hz, 0.2 ms pulses, 20 mA) at HT3 and PC6 for 30 min significantly reduced the expected increases in blood pressure, heart rate, and attenuated plasma levels of norepinephrine and epinephrine in rats with forced immobilization (Yang et al. 2002).

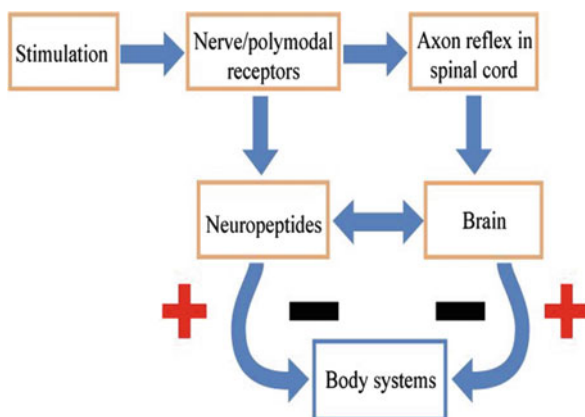
4.5.7 Functional Magnetic Resonance Imaging

EA at PC6 activated the structures of the thalamus and the cortex, but deactivated the structures of the hypothalamus and hippocampus. The brain responses to EA existed in different areas of activation and deactivation despite stimulating the same acupuncture point (Ho et al. 2008). Acupuncture at PC6 selectively activated the left superior frontal gyrus, anterior cingulate gyrus, and dorsomedial nucleus of the thalamus compared to sham acupuncture and tactile stimulation. This result suggests that the effect of acupuncture at PC6 might be mediated by the cerebellar vestibular neuromatrix (Yoo et al. 2004). Acupuncture at PC6 activated typical pain-related areas which are the ventromedial and dorsolateral prefrontal cortex and perigenual anterior cingulate cortex on the cortical level. In the brainstem, needling sensation activated nuclei of the descending pain control system, in which a network of hypothalamus, periaqueductal gray, rostral ventromedial medulla, and ventrolateral medulla was recognized as the source of the heart rate changes (Beissner et al. 2011). The thalamus, cortex, prefrontal cortex, and cingulate cortex are the pathways of vagal afferents, which regulate nausea (Stern et al. 2007). Acupuncture at PC6 activated the right nodule and right uvula of the cerebellum (Ren et al. 2010). The common symptom of cerebellar disorder is nausea (Windle et al. 2001).

4.5.8 Summary of Mechanism

There are several hypotheses regarding the pathways of acupuncture. When acupuncture stimulates the skin, somatic afferent nerves (Higashimura et al. 2009), myelinated nerve fibers (Han et al. 2003), and polymodal receptors

Fig. 4.4 Pathway of acupuncture



(Kawakita et al. 2006) are activated. Myelinated fibers contribute to the afferent input of the autonomic reflex adjustments during EA. Myelinated and unmyelinated fibers are stimulated by EA, although more finely myelinated than unmyelinated fibers are activated by low frequency and low current stimulation (Tjen et al. 2005). The polymodal receptors release neuropeptides as well as activate an axon reflex in the spinal cord (Zhao 2008). The neuropeptides move to tissue and organs to repair functioning. Polymodal receptors have effects on the central neurons (McCance and Huether 2002) as well as peripheral nerve fibers (Xu et al. 2006). The signal moves *via* the spinal cord (Jiang et al. 2010) to the brain. Signals from the brain move *via* efferent nerves to body systems (Fig. 4.4). The effect of acupressure on chemotherapy-induced nausea at PC6 can be explained by regulation of the autonomic system, regulation of CCK and the dorsal vagal complex, and the mediation of neurotransmitters such as serotonin, GABA, and catecholamine. Acupuncture at PC6 may activate different mechanisms according to different factors. Combination with other acupuncture points (Shiotani et al. 2004), types of acupuncture (laser, electro, manual), the frequency and intensity of EA (Wang et al. 2005; Shen and Lai 2007), depth of needling (Ceccherelli et al. 2002), length and diameter of needles, manipulation methods of manual acupuncture (lifting, thrusting, twisting, and twirling) (Zaslowski et al. 2003), duration and intervals between stimulation, individual differences such as genetic (Chae et al. 2006; Kim et al. 2007) or Sasang constitution (Lee et al. 2009), disease status (Toma et al. 2011) or status of yin-yang and five elements (Ahn et al. 2010), or positive/negative perception toward stimulation (Linde et al. 2007) can be factors that affect the response to acupuncture (Fig. 4.5). Sasang constitutional medicine explains that personal variable responses to food and medicinal treatment can be explained by the body constitution typology. Sasang constitutional medicine categorizes people into four body types (TaeYang, TaeEum, SoYang, SoEum) according to their temperaments, body shapes, and other general character features (Lee et al. 2010).

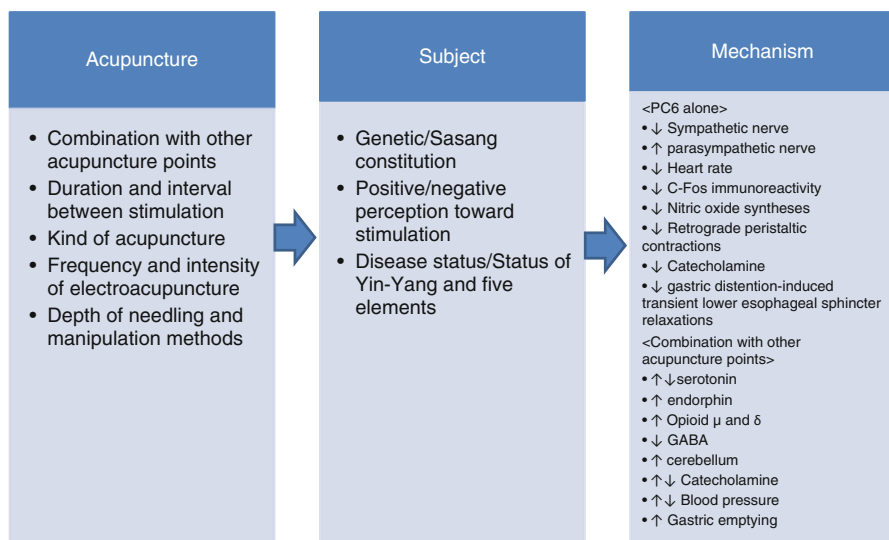


Fig. 4.5 Mechanism of acupuncture at PC6

4.6 Discussion

4.6.1 Sham Acupuncture

There are possible sources of bias in randomized controlled trials to examine the effect of acupressure such as sequence generation; allocation concealment; blinding of participants, personnel, and outcomes; incomplete outcome data; selective outcome reporting, no report of attrition rate and reason, fidelity, and side effects. In addition to these factors, sham acupressure could be a source of bias. Jones and her colleagues (2008) used placebo bands with no internal acupressure button at the same acupressure point. There was no different effect on nausea between acupressure bands, placebo bands, and no bands (Jones et al. 2008). Dibble and her colleagues (2007) used acupressure at SI3 as a placebo acupressure. There was a significant difference between acupressure, placebo acupressure, and usual-care group. Several studies have shown that placebo/sham acupuncture had some effects compared to real acupuncture or other intervention (Enblom et al. 2011; Wechsler et al. 2011; Schliessbach et al. 2012). Schliessbach and his colleagues (2012) used sham acupuncture at LR4 (the same acupuncture point as the real acupoint) with Streitberger needles, which have the blunt needle tips and do not penetrate the skin. Schliessbach and his colleagues (2012) found that both acupuncture and sham acupuncture had an analgesic effect. Wechsler and his colleagues (2011) reported that sham acupuncture was also effective in improving asthma compared to albuterol and placebo inhaler. Enblom and his colleagues (2011) reported that acupuncture

and sham acupuncture were effective in improving nausea and vomiting compared to the standard care in 277 patients with cancer. Acupuncture at a sham acupuncture point (two body-inches proximal to PC6, outside traditional acupuncture points) was used as sham acupuncture. Therefore, any kind of sham acupressure might have some effect on symptoms because stimulation itself such as massage releases neurotransmitters (Listing et al. 2010). Researchers who design randomized controlled trials need to consider the placebo effects of sham acupressure and need to include the control group (usual care) to compare the effect of acupressure.

4.6.2 Mechanism of Acupressure on Chemotherapy-induced Nausea

Acupuncture at PC6 alone activates the parasympathetic nerves, inhibits sympathetic nerves, decreases heart rate, and decreases catecholamines, and recovers blood pressure in patients with hypotension. It is unclear how acupuncture at PC6 changes neurotransmitters because most studies used several points to examine the mechanism of acupuncture. Further studies using neurotransmitters, biophysiological measures, or fMRI are needed to examine the effect of acupressure at PC6. Ming and her colleagues (2002) reported that finger acupressure was more effective than acupressure using sea bands on postoperative nausea. Further studies are needed to examine the effect of different acupressure methods such as finger acupressure or acupressure using sea bands at PC6 on chemotherapy-induced nausea. Acupuncture did not affect blood pressure and heart rate during rest, while acupuncture attenuated blood pressure and heart rate during exercise (Toma et al. 2011). Further studies are needed to examine whether acupressure at PC6 works differently in healthy subjects and unhealthy subjects. There are a few studies which compare the effect of different acupressure protocols (dose, duration, acupuncture points, and the unilateral and bilateral acupressure). Windle and his colleagues (2001) found that there was no difference between the effect of sea bands (either unilateral or bilateral) compared to placebo wrist band (no acupressure button) or no wrist band in 150 patients with postoperative nausea. Further studies are needed to examine which dose (how many minutes per day), duration (how often, three times a day, daily, weekly), treatment period (1 day, 1 week, 2 weeks, 1 month), acupuncture points (PC6, ST36, PC5), and locations (unilateral or bilateral) are more effective in improving chemotherapy-induced nausea.

4.6.3 International Clinical Guidelines for Acupressure

There is no international clinical guideline for acupressure. Therefore the development of an international clinical guideline for acupressure is necessary. The World Health Organization (1999) provided a guideline on basic training and safety in

acupuncture. Even though techniques of acupuncture and acupressure are different, indications and contraindications are the same. Indications for acupuncture are adverse reactions to radiotherapy and/or chemotherapy, allergic rhinitis, biliary colic, depression, dysmenorrhea, pain, headache, nausea, and vomiting (World Health Organization 2003). Some acupuncture points are contraindicated during pregnancy. Acupuncture should not be used in emergencies that require surgical interventions. There is a relative contraindication for acupuncture if patients have bleeding problems. Acupuncture should not be used for the treatment of malignant tumors. Acupuncture may be used for the relief of pain or other symptoms, to alleviate side effects of chemotherapy and radiotherapy (World Health Organization 1999). Filshie and Hester (2006) suggested obtaining verbal consent before beginning acupuncture. They also advise giving treatments weekly or twice weekly to total six treatments. If acupuncture is not effective after six treatments, stopping acupuncture is recommended. If acupuncture is effective, the treatment can be extended until patients have no or fewer symptoms.

4.7 Conclusion

Six of seven clinical trials showed positive results of acupressure on chemotherapy-induced nausea in 1,101 patients with cancer. However, we cannot conclude its effectiveness due to the small number of subjects and poor quality of studies. There is no study which examines the mechanism of acupressure on nausea. Most studies were limited to women with breast cancer. There are a few studies to compare intervention time, period, acupressure points, and delivery method (finger *vs* sea bands; by patient *vs* by researcher). Further well-designed studies are needed to examine the effect and mechanism of acupressure on chemotherapy-induced nausea. Further studies are needed using diverse populations and various types of cancer. Three systematic reviews reported that acupressure may decrease chemotherapy-induced nausea in 11 clinical trials. However, two systematic reviews included unpublished papers and abstracts. The mechanism of acupressure can be explained by regulation of substance P, serotonin, cholecystokinin, opioids, the autonomic nervous system, and the brain areas that regulate nausea. The side effects of acupressure have not been reported, whereas the side effects such as redness, swelling, and tenderness of sea bands have been reported.

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Chapter 5

Effects of Qigong Therapy on Alleviating Symptoms in Cancer Patients: An Overview of Systematic Reviews

Myeong Soo Lee, Byeongsang Oh, David Rosenthal, and Edzard Ernst

Abstract Owing to the limitations and side effects of conventional cancer treatment, especially in relation to quality of life, patients are increasingly utilizing complementary and alternative medicine to supplement health-related outcomes. However, evidence for the safety and efficacy of such treatments is lacking. Qigong is often used to improve the symptoms of cancer patients, although scientific evidence is unclear. The aim of this chapter was to critically evaluate all systematic reviews (SRs) of Qigong for the symptomatic treatment of cancer. We searched 11 electronic databases including MEDLINE, Embase, AMED, the Cochrane Library, six Korean Medical Databases, and a Chinese Database and our departmental files without restrictions on time or language. The search terms involved the following MeSH terms: “Qigong” AND “systematic review OR meta-analysis” AND “cancer”. The methodological quality of all SRs was evaluated using the Overview Quality Assessment Questionnaire. Of 26 potentially relevant publications, five met our inclusion criteria. Three SRs evaluated the effects of both internal and external Qigong. One SR evaluated the effect of internal Qigong, and another evaluated external Qigong. The quality of the SRs was mixed but two SRs had minor flaws only. All SRs noted that the quality of most primary studies was poor. The conclusions of the five

M.S. Lee (✉)

Medical Research Division, Korea Institute of Oriental Medicine,
461-24, Jeonmin-dong, Yuseong-gu, Daejeon 305-811, South Korea

Complementary Medicines, Peninsula Medical School, University of Exeter, Exeter, UK
e-mail: drmslee@gmail.com

B. Oh

Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Sydney Medical School, University of Sydney

D. Rosenthal

Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

E. Ernst

Complementary Medicines, Peninsula Medical School, University of Exeter, Exeter, UK

SRs were inconsistent. The poor quality SRs tended to draw positive conclusions, while the higher quality SRs failed to do so. More than 50% of the primary studies included in the SRs were not randomized and thus open to selection bias, which may be the primary reason for the inconsistency in the conclusions of the SRs. Overall, no clearly positive conclusions were identified. It follows that Qigong as a symptomatic treatment for cancer is currently not supported by sound evidence.

5.1 Introduction

The World Health Organization estimates that 84 million people will die in the next ten years by cancer if action is not taken (World Health Organization 2006). Most cancer patients experience multiple symptoms related to either the cancer itself or late treatment effects. Cancer patients therefore often turn towards complementary or alternative therapies (Wong et al. 2001). Several surveys reported a prevalence range of complementary and alternative medicine (CAM) in cancer from 53 to 88% (Richardson et al. 2000; Dy et al. 2004; Frenkel et al. 2005) and showed that CAM is usually combined with conventional treatments (Richardson et al. 2000). One form of CAM frequently used by cancer patients is mind-body medicine and energy medicine including Qigong (National Center for Complementary and Alternative Medicine 2012).

According to ancient Chinese thought, Qi denotes both essential substances of the human body that maintain its vital activities, and the functional activities of organs and tissues (Xinnong 1987; Shin 2002) (Fig. 5.1). Qi is commonly viewed as vital energy or the life force, and is the source of vitality and strength (Fig. 5.2). Qi acts extensively in the human body by permeating all parts. The meridians in the body are the main pathways through which Qi, or life force energy, moves, and flows. In fact, all of nature, including humanity, is dependent upon this vital force. When Qi flows smoothly, all of life's processes operate rhythmically and harmoniously. If Qi is weak, unbalanced and blocked, the human body succumbs to illness and enters a diseased state. Ultimately, the cause of all disease derives from energetic imbalances. A practical extension of these basic ideas is to diagnose the disease before it manifests in the physical body by measuring the energetic imbalances, and to treat the disease (with energy) by normalizing the energetic imbalances. Therefore, sustaining Qi is more important than anything else in order to keep the body strong and healthy.

Qigong (pronounced chee-gong) is a therapy which maybe belongs to both mind-body medicine and energy medicine. Qigong is an Eastern healing art that uses gentle, focused exercises for the mind and body to increase and restore the flow of Qi with the aim of promoting the healing process, preventing disease and prolonging life (Fig. 5.3). The word Qigong is a combination of two Chinese ideograms: Qi (vital energy) and gong (skill, work, and achievement) (Chen 2007). Thus, Qigong has been described as a way of working with life energy. Qigong aims to restore health by removing Qi blockages. Qigong is intended to be harmonious with the natural rhythms of the environment.

Internal and external Qigong can be distinguished. Internal Qigong is self-directed and involves the use of movements and meditation. It can be performed with or

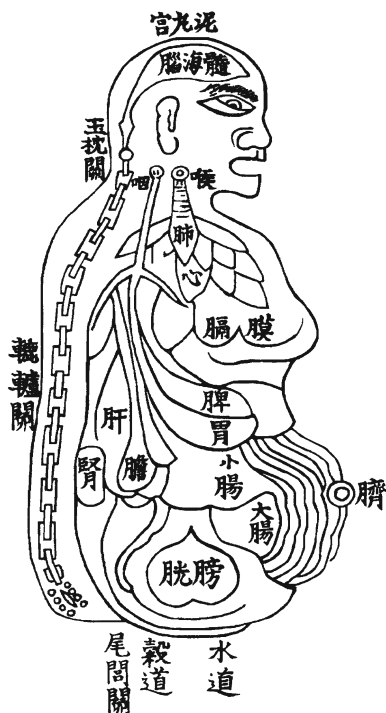


Fig. 5.1 The diagram of the bodily contour and inner organs of *Donguibogam* (registered as Memory of the World). The diagram is in the part of internal medicine of *Donguibogam*. The internal medicine part contains the section of physical shape, essence, Qi, and spirit deals with subjects pertaining to the relationship between the body and nature, as well as the body itself. The diagram visualized the view of nature and the model of the human body of Korean Medicine including the elements of essence, Qi and spirit, together with the five viscera and six bowls. *Donguibogam* is an encyclopaedia of medical knowledge and treatment techniques compiled in early seventeenth century Korea. *Donguibogam* is composed of 2 volumes of the tables of contents, 4 volumes of internal medicine and external appearances, 11 volumes of miscellaneous diseases, 3 volumes of herbal decoction, and 1 volume of acupuncture and moxibustion, totalling 25 volumes (Ahn 2008)

米 + 气 = 氣

rice + steam = Qi

Fig. 5.2 The Chinese character for Qi contains the radicals for both “steam” and “rice”. In its refined forms, Qi moves and flows almost invisibly, like steam. In its denser aspect, it slows or coalesces into form, such as rice (Beresford-Cooke 1996)



Fig. 5.3 The ancient script of process of Qigong scripted in Jade (around BC 600). It consists of 36 Chinese characters (Chen 2007). English translation is like following: “When you breathe deeply to a degree, internally refined Qi will gather. When the refined Qi is fully accumulated, it expands and descends downward (Dantian in the lower abdomen area). When the refined Qi is reinforced to a certain level, it begins to rise up (along the spinal cord) to the head, and then falls down (to the Dantian) again. The internal Qi then circulates around the Ren Du meridians during your daily practice. The universal Qi becomes integrated. It comes in through the top of the head, with the earth Qi, which enters the body through the feet. Thus you will be healthier and more alive while you follow it, and more prone to the effects of aging and death when you don’t”

without a teacher (master) and actively engages people in their own health and well-being. It is best practiced daily to promote health maintenance and disease prevention. This self-practice is thought to facilitate balance and a free flow of energy, contributing to both physical and psychological well-being. There are three major categories of these Qigong forms: movement Qigong, standing pole Qigong, and static form or meditation (Chen 2007). Movement Qigong uses guided physical movements to help practitioners concentrate and induce Qi flow in the body. Static Qigong is primarily meditation based and is used to increase internal power or consciousness stability. Standing pole Qigong falls between movement and static Qigong. Western models of relaxation response and psychoneuroimmunology mechanisms have parallels with the practice of internal Qigong (Ader et al. 1991; Benson and Klipper 1977). External Qigong, in contrast, is a form of energy healing in which a Qigong practitioner sends his Qi into a patient for the purpose of healing (Chen 2007). In this process, a Qigong practitioner directs or emits his Qi to help disrupt Qi blockages in others and force the sick Qi out of the body to relieve pain, balance the Qi flow in the body, and remove disease (Chen 2007). External Qigong can be practiced through the use of either Qi (emitting vital energy) or Yi (consciousness or intentional therapy) or a combination of the two techniques (Chen 2007).

Qigong consists of two main aspects: controlled breathing (or deep breathing), with slow body movements as an aerobic exercise, and relaxation (Ernst et al. 2007). The Qigong exercises are physical stimuli with effects on the cardiovascular and muscular systems. In addition to adaptation processes at the nervous system level, these effects produce better cardiovascular function and may enhance balance and

coordination. This stimulation and relaxation activates and modulates the neurohormonal system to improve the psychological state and enhance immune function.

Some *in vitro* studies (Lee et al. 2001, 2003; Yu et al. 2003) show that emitted Qi or the master's intention affects the activity of natural killer cells, neutrophil function, and human prostate cancer in a positive manner. In addition, it may be possible to store information about emitted Qi in media used for cell culture (Fukushima et al. 2001). However, the true mechanism requires further study. Although neither the Qigong itself nor the mechanism of its effects is understandable or explicable within any paradigm of modern medical science, its effects on the human body are apparent, as is its effectiveness in many clinical and psychological illnesses (Chen 2007).

Qigong has its underpinnings in Eastern medicine and philosophy. So far, it has not been explained scientifically and, from a scientific point of view, it must seem biologically implausible. Despite the absence of a scientific basis, Qigong has been submitted to numerous clinical trials and several systematic reviews (SRs) of these data have recently been published (Lee et al. 2011). They are related to a wide range of conditions: cancer, pain, diabetes, Parkinson's disease, hypertension, and any chronic condition (Lee et al. 2007a, b, c, 2009a, b, 2010; Choi et al. 2008; Lee and Ernst 2009). The conclusions of the SRs tended to be equivocal or contradictory or based on a poor quality SR. The only exceptions are the two SRs on hypertension which both draw positive conclusions, but even these SRs are based on poor quality primary data. Unfortunately their conclusions are far from uniform. This overview is aimed at critically evaluating SRs of Qigong as a symptomatic treatment for cancer patients.

5.2 Methods

5.2.1 Data Sources

Electronic literature searches were carried out in April 2012 using MEDLINE, Embase, AMED, the Cochrane Library, six Korean Medical Databases, and a Chinese Database without restrictions on time or language. The search terms involved the following MeSH terms: "Qigong" AND "systematic review OR meta-analysis" AND "cancer". In addition, our departmental files were hand-searched. The abstracts of reviews were inspected by two authors (MSL, BO), and those meeting the inclusion criteria were retrieved and read in full by both authors (MSL, BO). Reviews were defined as systematic if they included an explicit and repeatable methods section describing the search strategy and inclusion/exclusion criteria.

5.2.2 Study Selection and Data Extraction

All SRs or meta-analyses were included if they evaluated the effect of Qigong on cancer patients with at least two controlled clinical trials (CCTs). SRs evaluating Qigong together with other types of complementary medicine were excluded.

We also excluded the SRs that included mixed populations, such as healthy subjects and cancer patients. Data were extracted independently by two authors (EE and MSL) using pre-defined criteria (Table 5.1). Disagreements were resolved by discussion between the authors.

5.2.3 Assessment of the Quality of the SRs

Judgments of the quality of the primary studies were taken from the respective SRs. The Overview Quality Assessment Questionnaire (OQAQ) was used to evaluate the methodological quality of all included SRs (Oxman and Guyatt 1991; Jadad and McQuay 1996). The assessment score ranges from 1 to 7; a score of 3 or less was considered an indicator of extensive or major flaws, and a score of 5 or more suggested minor or minimal flaws. The two authors assessed the OQAQ independently, and discrepancies were settled by discussion.

5.3 Results

5.3.1 General Characteristics of Included SRs

Our searches generated 26 hits, and five articles met our inclusion criteria. The key data are summarized in Table 5.1 (Chen and Yeung 2002; Lee et al. 2007a, 2010; Chan et al. 2012; Oh et al. 2012a). The first author originated from China ($n=1$) (Chan et al. 2012), Australia ($n=1$) (Oh et al. 2012a), Korea ($n=1$) (Lee et al. 2010), the UK ($n=1$) (Lee et al. 2007a), and the US ($n=1$) (Chen and Yeung 2002). The SRs had been published between 2002 and 2012. They included between four and eight primary studies, including observational studies, clinical trials with no control group and randomized controlled trials (RCTs). Four SRs reviewed both RCTs and non-RCTs (Lee et al. 2007a, 2010; Chan et al. 2012; Oh et al. 2012a). One SR included observational studies in addition to RCTs and non-RCTs (Chen and Yeung 2002). Three SRs evaluated the effects of both internal and external Qigong (Lee et al. 2007a, 2010; Chan et al. 2012). One SR evaluated the effect of internal Qigong (Oh et al. 2012a), and another evaluated external Qigong (Chen and Yeung 2002).

5.3.2 Quality of Included SRs

Based on the OQAQ scores, the quality of the included SRs varied; two SRs had major flaws (Chen and Yeung 2002; Oh et al. 2012a), two had minimal bias (Lee et al. 2007a, 2010), and one SR had moderate flaws (Chan et al. 2012). All reviews identified the quality of most primary studies as poor. Two SRs with lower quality

Table 5.1 Systematic reviews of Qigong for cancer

Author (year)	Type of Qigong	Type of cancer	Number of trials	Quality of trials	Conclusion	Quality of SR OQAQ ^a	Result
Chen and Yeung (2002)	External	Any	10 CCTs	Poor	Qigong therapy may help patients recover from many different diseases at the same time	1	Overall positive
Lee et al. (2007a)	Any	Any	4 RCTs+5 CCTs	Poor	Effectiveness of Qigong is not yet supported	5	Unclear
Lee et al. (2010)	Any	Any	6 RCTs+5 CCTs	Poor	Evidence does not show convincingly that Qigong is effective	5	Unclear
Chan et al. (2012)	Any	Any	8 RCTs+15 CCTs	Poor	It is still too early to draw conclusive statements	4	Unclear
Oh et al. (2012a)	Internal	Any	5 RCTs+5 CCTs	Poor	Support the utilization of medical Qigong by cancer patients	1	Overall positive

CCTs controlled clinical trials, OQAQ Overview Quality Assessment Questionnaire, RCTs randomized controlled trials, SR systematic review

^aThe OQAQ overall score ranges from 1 to 7, OQAQ ≤3 represents extensive or major flaws, OQAQ ≥5 represents minor or minimal flaws

drew positive conclusions (Chen and Yeung 2002; Oh et al. 2012a), while three SRs with minor flaws failed to show conclusive evidence (Lee et al. 2007a, 2010; Chan et al. 2012).

5.3.3 Descriptions of Included SRs

Chan et al. (2012) conducted a SR evaluating the effects of Qigong as supportive cancer care regardless type of Qigong. Eight RCTs were included. The overall effects of Qigong for cancer were not supportive because of high risk of bias and several limitations of primary studies.

Oh et al. (2012a) evaluated the effects of internal Qigong for quality of life (QoL), and survival in cancer patients. They included five RCTs and five CCTs. The results of primary studies were positive. However, the evidence is inconclusive because of the low methodological quality and lack of sample size.

Lee et al. (2007a) published a SR of Qigong for cancer care. Four RCTs and five CCTs were included. All trials related to palliative/supportive cancer care by internal Qigong and none to Qigong as a curative treatment. The notion that internal Qigong is an effective therapy for cancer treatment is not based on data from rigorous clinical trials.

The same group (Lee et al. 2010) updated their previous SR and included six RCTs and five CCTs. The six RCTs failed to show the effectiveness of Qigong as supportive cancer care compared with usual care group. The evidence was not changed with the addition of two RCTs.

Chen and Yeung (2002) reviewed the trials of Qigong for cancer care in China. Ten CCTs included. The authors concluded positively the effects of Qigong for cancer.

The conclusions of the five SRs were not uniform. The poor quality SRs tended to draw positive conclusions, while the higher quality SRs failed to do so. Overall, no clearly positive conclusions were identified.

5.4 Discussion

5.4.1 Appraisals of Included SRs

Our search indicated that the interest in Qigong for cancer care is growing. The results of this overview suggest that the evidence regarding the efficacy of Qigong in cancer treatment is not conclusive. More than 50% of the primary studies included in the SRs were not randomized and thus open to selection bias, which may be the primary reason for the inconsistency in the conclusions of the SRs.

Moreover, the inconsistencies in the primary studies may also be due to different Qigong regimens. In some trials, the dose of Qigong may have been too small to

generate a significant effect. In addition, most primary studies employed different forms of Qigong interventions. There are significant differences between the various forms of Qigong, which poses difficulties in establishing quality standards of treatment. Some types of Qigong applied in the study protocols may not have been suitable for cancer care. This issue should be addressed in future studies comparing the efficacy of the various forms of Qigong. This will require more precise descriptions of the Qigong interventions used in the study and a description of the level of expertise of the instructors.

5.4.2 Adverse Events of Qigong

Qigong appears to be generally safe, and serious adverse effects have not been reported. Some studies have noted adverse events, including headache, dizziness, nausea, mental disorders and psychosis, in individuals who practiced Qigong incorrectly, although these risks have not been formally studied (Ng 1999; Lee 2000; Kemp 2004). Adverse effects were not the focus of this review; regardless, the safety of Qigong needs further research.

5.4.3 Possible Mechanisms of Qigong

Most studies have reported a positive effect of Qigong on the physiological level, although the effects of Qigong on the symptoms of cancer treatment were not consistent. One possible mechanism by which Qigong may improve immune function is the modulation of cytokine and hormone levels, which may counteract the immune deficiency experienced by most cancer patients (Jones 2001; Chen 2004). Others have postulated that Qigong improves micro-circulatory functions, including changes in blood viscosity, the elasticity of blood vessels, and platelet functions (Chen 2004). A third proposed mechanism is an increase in the pain threshold as a result of the relaxation effects (Chen 2004). It is also possible that Qigong induces apoptosis in pancreatic cancer cells and increases or represses PI3K activity in highly enriched PI3K preparations, suggesting that external Qigong could positively or negatively regulate enzymes (such as Akt and Erk1/2) in different settings (e.g. in cancer cells vs normal cells) (Yan et al. 2006, 2008). If these theories are confirmed, they may explain how Qigong leads to clinical improvements in patients.

5.4.4 Possible Interpretation

The fact that there is no good trial evidence in support of Qigong therapy for cancer care is in line with several different interpretations. Qigong may be ineffective, the studies may have been incorrectly designed or the treatment may not have been administered

optimally in the existing studies. For instance, the number of Qigong sessions could have been too small to generate a significant effect, or the type of Qigong or the applied protocol might not have been suitable for cancer care. A clinical study is only truly useful if the intervention used can be replicated, and hence, the type of Qigong employed and a full description are important. There are significant differences between the numerous forms of Qigong, which pose difficulties in establishing quality standards of treatment. A clear description of the Qigong intervention used should be provided together with a description of the level of expertise of the instructors.

5.4.5 Recent RCTs

Further, two RCTs, that tested effects of ten weeks of 90 min Qigong on QoL in cancer patients, were recently published (Oh et al. 2010, 2012b). A two-armed RCT conducted by the University of Sydney assessed the effectiveness of Qigong on QoL, fatigue, mood, and inflammation in various cancer patients compared with usual care control and showed favorable effects of Qigong for improving QoL and mood, and reducing specific side effects of conventional cancer treatment (Oh et al. 2010). Another recent RCT conducted by the same group investigates the effectiveness of Qigong on cognitive function, QoL, and biomarker of inflammation in various cancer patients compared with usual care (Oh et al. 2012b). The results showed beneficial effects of Qigong on cognitive function and QoL. These two RCTs showed favorable effects of Qigong on symptoms of cancer. However, results of the largest trial (Oh et al. 2010) already included in recent SR (Chan et al. 2012). Even though the latest study (Oh et al. 2012b) is included and overall evidence is still inconclusive.

5.4.6 Limitations of This Overview

Our overview has several limitations. Although our search strategy seemed thorough, we cannot totally exclude the possibility that relevant articles were missed. It is also possible that evaluating SRs rather than clinical trials may not capture the relevant details of the primary studies. Furthermore, the fact that the SRs were conducted on primary data of poor quality is a major limitation of this study. Collectively, these drawbacks render our verdict about Qigong less robust than we had hoped.

5.4.7 Perspectives

This overview of SRs focused on the effects of Qigong as supportive cancer care. Collectively, the existing trial evidence is not convincing and does not show Qigong to be an effective modality for supportive cancer care.

Our overview may serve as a stimulus for future Qigong research to become more rigorous. We recommend that researchers study the CONSORT guidelines (Schulz et al. 2010) and that authors of SRs examine the PRISMA guidelines to achieve this goal (PRISMA 2009).

Future RCTs of Qigong for supportive cancer care should adhere to accepted standards of trial methodology. The studies published up to date showed a number of problems that have been noted by other reviews of trials examining the efficacy of Qigong, e.g. expertise of Qigong practitioners, the pluralism of Qigong, frequency and duration of treatment, employing validated primary outcome measures and adequate statistical tests, and heterogeneous comparison groups (Chen and Yeung 2002; Wayne and Kaptchuk 2008). Future studies should be of high quality with a particular emphasis on designing adequate and appropriate control groups.

5.5 Conclusion

Owing to significant methodological flaws in the primary data, the effectiveness of Qigong in cancer treatment remains uncertain. Further studies with robust RCT designs are needed to evaluate the benefits of Qigong for cancer treatment.

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Chapter 6

Effects of Yoga on the Quality of Life in Cancer Patients

Kuan-Yin Lin and Jau-Yih Tsao

Abstract Quality of life (QoL) is a multidimensional concept that includes physical, psychological, and social aspects which can be regarded as a broad term related to the patient's subjective evaluation of life as a whole. Patients with cancer often have to deal with symptoms and treatment-related side effects, which have substantial impact on their QoL. Yoga, as a main component of the mindfulness-based stress reduction and one of the most commonly utilized complementary and alternative medicine therapies, has been studied for its feasibility and effects for cancer patients. Increasing evidence indicates that yoga may be beneficial for people with cancer in improvements of psychological health and QoL. Nevertheless, given different methodologies of the studies, the variety of QoL measures employed, duration of the interventions, and types of yoga, the effects of yoga on QoL in cancer patients are inconclusive. The exact mechanism of yoga or mindfulness-based stress reduction on QoL is not clear. The researchers have proposed and investigated some plausible mechanisms, such as relaxation response, enhancing body awareness, psycho-neuro immunological aspect, and melatonin production. This chapter discusses the evidence for the effectiveness (including safety and adverse effects) of yoga for QoL of cancer patients, includes the underlying mechanisms of yoga on QoL.

K.-Y. Lin • J.-Y. Tsao (✉)

School and Graduate Institute of Physical Therapy, College of Medicine,
National Taiwan University, 3F, No. 17 Xuzhou Road, Taipei, Taiwan
e-mail: jytsaou@ntu.edu.tw

6.1 Introduction

6.1.1 Cancer Epidemiology

Cancer is a major health problem worldwide accounting for about 12.7 million cases and 7.6 million deaths (around 13% of all deaths) in 2008 (Jemal et al. 2011). Due to early detection and advanced treatment of cancer, the overall cancer death rates continue to decrease, in conjunction with increased life expectancy (Jemal et al. 2010). The trend of decreasing mortality rate was seen in the United States where the number of cancer survivors increased from 3 million to close to 12 million between 1971 and 2008 (Parry et al. 2011). However, this trend was not apparent in Asia, where large variation in survival was observed and may be attributed to different levels of development of cancer health services and the availability of trained personnel in urban and rural areas (Sankaranarayanan et al. 2010).

6.1.2 Impacts of Cancer and Treatment

During cancer treatment, fatigue, pain, difficulty remembering, depression, loss of appetite, lack of enjoyment of life, sleep disturbance, distress, difficulty walking, and dry mouth were commonly experienced symptoms (Honea et al. 2007; Karabulu et al. 2010). These psychological and physical symptoms may even persist over the 16-month period following treatment (Brant et al. 2011). Frequent long term physical and functional impairments experienced by cancer survivors include fatigue, musculoskeletal problems, decreased participation in activities, and sexual dysfunction; anxiety or depression may be the psychological long-term effect of cancer (Stein et al. 2008). The disease symptoms and the impact of cancer treatment may negatively influence the patient's quality of life (QoL), increase morbidity, and cause substantial economic burden. Moreover, the financial burden is expected to increase in the future because of the improvements in survival and the costs of care following cancer diagnosis (Karabulu et al. 2010; Yabroff et al. 2011).

6.2 QoL

6.2.1 Definition of the QoL

The World Health Organization (WHO) defines QoL as “individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, social relationships, and environment

(http://www.who.int/mental_health/who_qol_field_trial_1995.pdf). To further define QoL in cancer, Cella, Cherin and Tulsky (Cella and Cherin 1988; Cella and Tulsky 1993) referred QoL as the patients' appraisal of and satisfaction with their current level of functioning compared to what they perceive to be possible or ideal.

6.2.2 Scope and Assessment of QoL

QoL composed of two fundamental constructs, multidimensionality and subjectivity. The multidimensional construct of QoL covers a broad range of content, including physical, functional, emotional, and social well-being, and the subjectivity refers to the patient's perspective on the personal satisfaction with life (Landesman 1986; Cella 1994; Felce and Perry 1995). Because of the multidimensional construct of QoL, the instruments measuring QoL should include: physical functioning (perceived and observed bodily function or disruption and one's ability to perform self care activities), disease- and treatment-related symptoms (pain, fatigue, shortness of breath, hair loss), psychological functioning (distress, anxiety, depression), and social functioning (maintenance of gratifying relationships with friends and intimate relationships with family members, recreation activities) (Cella and Tulsky 1993; Velikova et al. 1999).

QoL instruments have been described as generic or disease-specific. Generic instruments are designed to measure QoL across all the domains of life and allow comparisons to be made with the general population and other illness groups. Disease specific instruments are designed to focus more narrowly for a specific type of cancer or treatment and are more responsive to change (Velikova et al. 1999; Ferrans 2010). Some of the commonly used questionnaires constructed specifically for cancer patients include the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C-30) (Aaronson et al. 1993), Functional Assessment of Cancer Therapy (FACT) (Cella et al. 1993), Cancer Rehabilitation Evaluation System (CARES) (Schag et al. 1991), Functional Living Index Cancer (FLIC) (Schipper et al. 1984), Rotterdam Symptom Checklist (de Haes et al. 1990), and Quality of Life Index (QLI)-Cancer (Padilla et al. 1983; Gunnars et al. 2001). Table 6.1 presents a description of these six instruments.

6.3 Yoga and Mindfulness-based Stress Reduction (MBSR)

6.3.1 Introduction of Yoga and MBSR

MBSR is a structured, group program which combines mindfulness meditation practice, yoga exercises, and mental attention on breathing awareness (Carlson and Bultz 2008; Musial et al. 2011). The efficacy of MBSR for a broad range of chronic disorders has been reviewed and described (Grossman et al. 2004). As a main

Table 6.1 Description of commonly used instruments for measuring QoL in cancer patients

Measure	Domains	Number of items	Scores	Interpretations	Psychometric properties
EORTC QLQ C-30	Functional scales: physical, role, cognitive, emotional, and social; Symptom scales: fatigue, pain, and nausea and vomiting; and a global health and quality-of-life scale	30	Subscale scores transformed into 0–100 scores using an algorithm	Higher scores indicate better health; higher scores on symptom scales mean more intensive symptoms	All interscale correlations were statistically significant, and the correlation was moderate. Most of the functional and symptom measures discriminated clearly between patients differing in clinical status as defined by the Eastern Cooperative Oncology Group performance status scale, weight loss, and treatment toxicity. The responsiveness was also indicated (Aronson et al. 1993)
FACT-G	Physical well-being, social/family well-being, emotional well-being, and functional well-being	27	0–108	Higher scores indicate better QoL	Convergent validity was demonstrated with 0.79 Pearson product moment correlations when compared with the FLIC. Divergent validity was measured using the shortened Marlowe-Crown social desirability scale and a low correlation ($r=0.22$) was found (Cella et al. 1993)

CARES-SF	Physical, psychosocial, medical interaction, marital, sexual, and miscellaneous subscales and items	59	Raw scale scores range, like the items, from 0 (no problem) to 4 (many problems)	Higher scores reflect more problems or worse QoL	CARES-SF is highly related to the CARES ($r=0.98$), has excellent test-retest reliability (86% agreement), concurrent validity with related measures, and acceptable internal consistency of summary scales ($\alpha=0.85-0.61$) (Schag et al. 1991)
FLIC	Physical ability and well-being, psychological well-being, hardship due to cancer, and nausea	22	22–154	Higher score represents a better QoL	Adequate validity and reliability (Schipper et al. 1984)
Rotterdam Symptom Checklist	Physical symptom distress, psychological distress, activity level, and overall global life quality	39	0–100	Higher score indicate higher level of burden or impairment	A scale based on psychological distress was highly reliable (Cronbach's alpha 0.88–0.94). The physical distress is reflected by several dimensions in a homogeneous population (pain, fatigue, gastrointestinal complaints) and unidimensionally in a heterogeneous population. Reliability of the physical distress scales is good (0.71–0.88) (de Haes et al. 1990)

(continued)

Table 6.1 (continued)

Measure	Domains	Number of items	Scores	Interpretations	Psychometric properties
QLI-Cancer	Health/functioning; socioeconomic; psychological/spiritual; and family	69	0-30	High scores are produced by combinations of high satisfaction/high importance responses	The reliability of the QLI is good. QLI had construct and discriminant validity. Concurrent validity between QoL scores and physician estimates of Karnofsky ratings, prognosis, and QoL were poor (Padilla et al. 1983)

CARES-SF Cancer Rehabilitation Evaluation System-Short Form, *EORTC QLQ C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, *FACT-B* Functional Assessment of Cancer Therapy-Breast, *FACT-G* Functional Assessment of Cancer Therapy-General Scale, *FLIC* Functional Living Index Cancer, *QLI* quality of life index, *QoL* quality of life

component of the MBSR program, yoga is a combination of breathing exercise, meditation, and physical postures to promote health and is classified as a mind-body therapy by the National Center for Complementary and Alternative Medicine (Musial et al. 2011).

Although yoga may have been practiced as early as 5,000 years ago, the first known text was documented some 2,500 years ago by the father of yoga, Sage Patanjali (Austin and Laeng 2003). He divided the philosophy of yoga into eight limbs, yama (moral behavior), niyama (healthy habits), asana (physical postures), pranayama (breathing exercises), pratyahara (sense withdrawal), dharana (concentration), dhyana (contemplation), and Samadhi (higher consciousness) (Austin and Laeng 2003).

There are dozens of types of yoga practiced around the world, but Hatha yoga is the most commonly practiced in the West because it emphasizes two of the eight limbs, asanas and pranayama, which are more tangible and practical than other forms of yoga, which may focus more on other limbs (Deutsch and Anderson 2008). Some of the major styles of Hatha yoga include Ananda, Anusara, Ashtanga, Bikram, Iyengar, Integrative, Integral, Ishta, Jivamukti, Kali Ray Triyoga, Kripalu, Kundalini, Phoenix Rising, Power yoga, Svaroopa, Sivananda, Viniyoga, and White Lotus (Collins 1998; Garfinkel and Schumacher 2000; Austin and Laeng 2003).

There has been some research into the benefits of different Hatha yoga styles in cancer populations. Four most commonly studied yoga interventions with cancer individuals are integrated yoga, restorative yoga, Viniyoga, and Iyengar as shown in Table 6.2.

Integrated yoga has been used as an intervention for breast cancer patients (Banerjee et al. 2007; Raghavendra et al. 2007; Rao et al. 2009; Vadiraja et al. 2009a, b), and it consists of a set of asanas, pranayama, meditation, and yogic relaxation. The principles of integrated yoga are attention diversion, mindful awareness, and relaxation to cope with stressful experience (Deutsch and Anderson 2008). One clinical trial has investigated the beneficial effects of Restorative yoga for women with breast cancer (Danhauer et al. 2009).

Different from Integrated yoga, Restorative yoga emphasizes non-violence (ahimsa) and consists of asanas, breathing, and deep relaxation. Viniyoga is a combination of physical stretches and poses, breath control, and meditation, and the poses are coordinated with the breath of the practitioner (Deutsch and Anderson 2008). Littman et al. (2012) has investigated its effects in overweight and obese breast cancer survivors. Iyengar also combines asanas, pranayama, and meditation, but it focuses on precise muscular and skeletal alignment and uses props (belts, blankets, blocks, and chairs) to accommodate special needs (Deutsch and Anderson 2008; Duncan et al. 2008). The impact of Iyengar yoga for breast cancer patients has been studied by several researches (Speed-Andrews et al. 2010; Bower et al. 2011; Galantino et al. 2011).

In addition to the Hatha yoga, Tibetan yoga, another type of yoga, has been studied for its effects in patients with lymphoma (Cohen et al. 2004). Tibetan yoga consists of controlled breathing and visualization, mindfulness, postures from the Tsa lung (channels and vital breath), and the preliminary set of postures from the Trul khor (magical wheel).

Table 6.2 Different styles of Hatha yoga commonly studied in clinical trials

Styles	Studies	Descriptions
Integrated yoga	Vadiraaja et al. (2009a, b) Rao et al. (2009) Raghavendra et al. (2007) Banerjee et al. (2007) Danhauer et al. (2009)	A combination of asanas, breathing exercises, pranayama, meditation, yogic relaxation Asanas, meditation, and breathing are synthesized to develop greater relaxation and internal awareness. The principles of Integrated yoga are attention diversion, mindful awareness, and relaxation to cope with everyday stressful experience A combination of asanas, breathing, and deep relaxation
Restorative yoga		Ahimsa (non-violence) is an emphasis. Poses include centering and meditation, neck and shoulder series, leg stretch (Janu Sirsasana variation) using a strap and circling ankles slowly in both directions, side bend (seated Parighasana), seated twist (Ardha Matsyandrasana variation), simple supported backbend, transition, legs up the wall (Viparita Karani or variation), supported bound-angle pose (Supta Badha Konasana variation), mountain pose, arm and shoulder stretch, supported forward fold, seated sun salutation (Surya Namaskar variation), and reclining twist with a bolster
Viniyoga	Litman et al. (2012)	A combination of physical stretches and poses, breath control, and meditation Poses are coordinated with the breath of the practitioner. Key poses include cobra (bhujangasana), sunbird (chakravakasana), lunges, warrior variations, bridge forward bends, triangle, twists, and corpse (savasana)
Iyengar yoga	Bower et al. (2011) Galantino et al. (2011) Speed-Andrews et al. (2010)	A combination of precise postures (asanas), breathing exercises (pranayama), and meditation focusing on precise muscular and skeletal alignment and using props (belts, blankets, blocks, and chairs)

6.3.2 *Yoga and MBSR Usage Among Cancer Patients*

The recent meta-analysis conducted by Horneber et al. (2012) to summarize data on the prevalence of complementary and alternative medicine (CAM) use in cancer patients included 152 studies with a total of more than 65,000 adult cancer patients from 18 countries. The results showed that the average prevalence of CAM usage among cancer patients was 40%. Moreover, CAM practices were also widely used in the US cancer population with the prevalence of 21%. Of the eight specific complementary and alternative medicine practices (deep breathing, meditation, used special diet, relaxation, guided imagery, yoga, Taichi, and Qigong), yoga was the third most common practice among women and the fifth among men (Fouladbakhsh and Stommel 2010).

6.4 Effects of Yoga/MBSR on QoL in Cancer Patients

Yoga/MBSR has been used as an intervention for psychosocial functioning (Banasik et al. 2011), fatigue (Carson et al. 2007; Banasik et al. 2011; Bower et al. 2012), regulation of cortisol secretion (Banasik et al. 2011), psychological distress (Vadiraja et al. 2009a; Kovacic and Kovacic 2011), anxiety and depression (Ando et al. 2009; Rao et al. 2009; Matousek et al. 2011), modulating circadian patterns of stress hormones (Vadiraja et al. 2009a), stress (Banerjee et al. 2007; Matousek et al. 2011), DNA damage levels, (Banerjee et al. 2007) and sleep quality (Shapiro et al. 2003) in patients with cancer. Results have been generally positive.

6.4.1 *Clinical Studies*

Several research studies support the beneficial effects of yoga/MBSR on QoL in cancer patients. In 2011, Lin et al. (2011) published a meta-analysis and systematic quality assessment of clinical research of yoga for psychological health, QoL, and physical health of patients with cancer. For a clinical trial to meet the criteria of review, the study must have a randomized controlled trial (RCT) design to examine the effects of yoga or MBSR on psychological health, QoL, and physical health of cancer patients. Ten RCTs met the criteria for inclusion from which the authors concluded that yoga group had significantly greater improvements in psychological health: anxiety ($p=0.009$), depression ($p=0.002$), distress ($p=0.003$), and stress ($p=0.006$). The QoL of the yoga groups showed a trend ($p=0.06$) toward more improvement than the control groups. However, the results for the QoL were analyzed from three RCTs (Culos-Reed et al. 2006; Moadel et al. 2007; Danhauer et al. 2009). The authors also warned that results should be regarded as preliminary because of the low to fair quality and small number of studies conducted.

Musial et al. (2011) also published a meta-analysis to assess the effect of MBSR on QoL, mood, and distress in cancer patients. The selection criteria stipulated that the studies must involve a structured MBSR program of at least six weeks duration, to involve cancer patients, and to report at least one quantitative standardized outcome measure related to QoL, mood, or distress. Six studies with a total of 248 patients were included to estimate the effect on QoL, and the overall effect size was 0.29 [$p < 0.001$, 95% confidence interval (CI) 0.17–0.40]. The authors concluded that MBSR programs can improve QoL and mood, and reduce distress in cancer patients. However, further high-quality RCTs are warranted to increase the understanding of the MBSR effects.

Of 15 clinical trials in Table 6.3, seven published RCTs, and eight non-RCTs. The number of participants ranged from 10 to 128. Twelve of the studies focused on subjects with breast cancer (Culos-Reed et al. 2006; Moadel et al. 2007; Raghavendra et al. 2007; Witek-Janusek et al. 2008; Danhauer et al. 2009; Lengacher et al. 2009; Vadiraja et al. 2009b; Speed-Andrews et al. 2010; Ulger and Yagli 2010; Bower et al. 2011; Galantino et al. 2011; Littman et al. 2012), and only three studies included patients who were concurrently receiving adjuvant treatment (chemotherapy or radiotherapy) during the study period (Raghavendra et al. 2007; Danhauer et al. 2009; Vadiraja et al. 2009b).

Among the studies reviewed, three demonstrated insignificant QoL effect with the intervention of yoga/MBSR (Danhauer et al. 2009; Speed-Andrews et al. 2010; Littman et al. 2012), whereas 12 studies reported significant effects (Carlson et al. 2004, 2007; Culos-Reed et al. 2006; Moadel et al. 2007; Raghavendra et al. 2007; Kieviet-Stijnen et al. 2008; Witek-Janusek et al. 2008; Lengacher et al. 2009; Vadiraja et al. 2009b; Ulger and Yagli 2010; Bower et al. 2011; Galantino et al. 2011). Conflicting evidence existed for the efficacy of yoga/MBSR.

Of the three research studies that reported no significant improvement in QoL from the intervention of yoga/MBSR, two were randomized controlled pilot trials, and one of these two was conducted most recently by Littman et al. to investigate the efficacy of a six-month yoga intervention in breast cancer survivors in regards to fatigue, QoL, and weight change. Subjects were post-treatment stages 0–III borderline overweight and obese (body mass index ≥ 24 kg/m²) breast cancer survivors with a mean age of 60 years. The intervention group received facility- and home-based Viniyoga, a Hatha therapeutic style of yoga that involved physical stretches and poses, breathe control, and meditation. QoL measured by the Functional Assessment of Cancer Therapy-General (FACT-G) was assessed at baseline and six months follow-up. Although no statistically significant difference was noted, overall QoL improved to a greater extent from 89.0 ± 9.4 to 90.3 ± 11.0 among women in the yoga group relative to women in the control group (Littman et al. 2012).

Danhauer et al. (2009) included 44 women with breast cancer with a mean age of 55.8 years, and the participants were randomized to the Restorative yoga intervention (ten weekly 75-min classes) or a waitlist control group. The Restorative yoga classes combined asanas, pranayama, and savasana. The results showed a borderline difference in health-related QoL (FACT-B) between the two groups ($p = 0.052$).

Table 6.3 Effects of yoga on quality of life

Authors (year)	n	Type of cancer	Treatment status	Yoga/MBSR group,		Outcome measures		Findings
				frequency and duration	Control group	of QoL	of QoL	
RCT: Littman et al. (2012)	63	Breast cancer	Completion of treatment at least three months prior (except hormonal therapies such as tamoxifen or aromatase inhibitors)	Viniyoga, five times per week for six months	Waitlist	FACT-G	Six-month changes in QoL did not differ between the groups	
Vadira et al. (2009a, b)	88	Breast cancer	Receiving adjuvant radiotherapy	Integrated yoga program, at least three in-person sessions/week for six weeks	Brief supportive therapy (n=44)	EORTC QLQ C30 functional scales	There was significant improvement in positive affect, emotional function, and cognitive function, and decrease in negative affect in the yoga group as compared to controls	
Danhauer et al. (2009)	44	Breast cancer	Eleven received chemotherapy during study, and nine received radiation therapy during study	Restorative yoga, ten weekly 75-min classes	Waitlist	FACT-B	Significant baseline*group interactions were observed for the FACT emotional well-being subscale. Health-related QoL (FACT-B) showed a borderline difference between the two groups (p=0.052)	

(continued)

Table 6.3 (continued)

Authors (year)	<i>n</i>	Type of cancer	Treatment status	Yoga/MBSR group, frequency and duration	Control group	Outcome measures of QoL	Findings
Lengacher et al. (2009)	84	Breast cancer	Completion of treatment within the prior 18 months	MBSR program, weekly 2-h sessions for six weeks	Usual care	Medical Outcomes Short form General Health Survey	Subjects assigned to the MBSR intervention showed higher adjusted mean QoL scores at six weeks including physical functioning, role limitations related to physical health, and energy
Raghavendra et al. (2007)	62	Breast cancer	Receiving adjuvant chemotherapy	Integrated yoga program, 60 min daily during the course of chemotherapy	Supportive therapy	FLIC	There was a significant improvement in QoL during chemotherapy in the yoga group as compared with controls
Moadel et al. (2007)	128	Breast cancer	Not specified	12-week Hatha yoga, 1.5-h weekly	Waitlist	FACT	Significant between group differences on social well-being. For patients not receiving chemotherapy during intervention, significant between group differences on overall QoL, emotional well-being, social well-being, spiritual well-being, and distress mood

Culos-Reed et al. (2006)	38	Breast cancer	A minimum of three months post-treatment	7-week yoga program, 75 min per session	Wait-list	EORTC QLQ C30	Significant differences between the intervention and the control group at post-intervention were seen in global QoL
Non-RCT: Bower et al. (2011)	11	Breast cancer	Completed local and/or adjuvant cancer therapy (except hormonal therapy)	Iyengar yoga, 90 min twice a week for 12 weeks	NA	SF-36	There was significant improvement on the general health subscale of the SF-36
Galantino et al. (2011)	10	Breast cancer	Currently receiving aromatase inhibitors (anastrozole, letrozole, or exemestane)	Iyengar yoga, twice a week for eight weeks	NA	FACT-B	The subjective report of QoL measured with the FACT-B significantly improved
Speed-Andrews et al. (2010)	24	Breast cancer	Completion of primary adjuvant therapy (chemotherapy or radiation therapy)	Iyengar yoga, 90 min per session, 22 times over 12 weeks	NA	SF-36 FACT-B	There were significant and meaningful improvements in generic QoL for bodily pain, the MCS score, vitality, and role-emotional. Borderline significant meaningful improvements were found for the PCS score, role-physical, general health, and mental health. No statistically significant improvements for any of the scales in FACT-B

(continued)

Table 6.3 (continued)

Authors (year)	<i>n</i>	Type of cancer	Treatment status	Yoga/MBSR group, frequency and duration	Control group	Outcome measures of QoL	Findings
Ulger and Yagli (2010)	20	Breast cancer	At least six months post-treatment (chemotherapy or radiotherapy)	Classical yoga program, eight sessions, twice a week	NA	NHP	Quality of life scores after the yoga program were better than scores obtained before the yoga program ($p < 0.05$)
Kieviet-Stijnen et al. (2008)	47	Mixed cancer	Surveillance: 23% hormonal; 17% chemotherapy; 17% radiotherapy; 6% CAM; 21% other; 6%	MBSR training, eight weekly sessions of 2.5 h	NA	10 cm Visual Analogue Scale	Directly after the training patients reported a better QoL, more joy in life, less tension, and fewer physical symptoms
Witek-Janusek et al. (2008)	66	Breast cancer	Eighty-three percent had surgery followed by radiation therapy, no chemotherapy	MBSR program, 8-weekly (2.5 h/week) group sessions	Non-MBSR group that received assessments only	QLI-Cancer	Women enrolled in the MBSR program had improved QoL compared to the non-MBSR group
Carlson et al. (2007)	59	Breast cancer and prostate cancer	No current treatment	MBSR: gentle yoga, eight weekly 90-min group sessions	NA	EORTC QLQ-C30	Improvements were also seen in global QoL scores
Carlson et al. (2004)	69	Breast cancer and prostate cancer	No current treatment	8-week MBSR	NA	EORTC QLQ-C30	Significant improvements were seen in overall QoL

CAM complementary and alternative medicine, EORTC QLQ C30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, FACT-B Functional Assessment of Cancer Therapy–Breast, FACT-G Functional Assessment of Cancer Therapy–General Scale, FLIC Functional Living Index Cancer, MBSR mindfulness-based stress reduction, MCS mental component summary scores, NA not available, NHP Nottingham Health Profile, PCS physical component summary scores, QLI quality of life index, SF-36 Medical Outcomes Study Short-Form Health Survey

Speed-Andrews et al. (2010) conducted a pilot study to evaluate the impact of Iyengar yoga on QoL and psychosocial functioning in breast cancer survivors. All subjects (mean age: 54.8 years) who had completed primary adjuvant therapy participated in the 12-week Iyengar yoga class. Generic QoL was assessed with the SF-36 and Breast cancer specific QoL by the FACT-B scale. Several subscales of SF-36, bodily pain ($p=0.024$), the mental component summary score ($p=0.045$), vitality ($p=0.033$), and role-emotional ($p=0.010$), showed significant and meaningful improvements, but no statistically significant improvements were found in any of the FACT-B scales, even though the overall improvement was clinically meaningful ($d>0.30$).

Of the 12 studies that provided support for the beneficial effects of yoga/MBSR, three included subjects with different types of cancer and were all pre- to post-test studies (Carlson et al. 2004, 2007; Kieviet-Stijnen et al. 2008). The study by Kieviet-Stijnen et al. (2008) measured changes in cancer patients' well-being following MBSR training from pre- to post-treatment and at one year follow-up. After the 8-week training, patients reported a better QoL, which was measured with a 10 cm Visual Analogue Scale, but the effect size for QoL for the pre-follow-up contrasts was small ($d=0.46$). Two studies by Carlson et al. (2004, 2007) included patients who had a diagnosis of stage 0, I, or II breast or early stage (localized to the prostate) prostate cancer. The findings showed that significant improvements were seen in overall QoL (EORTC QLQ-C30) post 8-week MBSR program ($p<0.005$, $d=0.26$) (Carlson et al. 2004) and across one year ($p<0.05$, $d=0.29$) (Carlson et al. 2007). Generally, these clinical trials showed that the beneficial effects of MBSR on QoL could maintain over one year.

Other nine studies reported significant effects of yoga/MBSR on QoL in breast cancer patients with different treatment status, and five of them were RCTs (Culos-Reed et al. 2006; Moadel et al. 2007; Raghavendra et al. 2007; Lengacher et al. 2009; Vadiraja et al. 2009b). A RCT study by Vadiraja et al. (2009b) compared the effects of an integrated yoga program with brief supportive therapy in outpatients with stage II and III breast cancer undergoing adjuvant radiotherapy at a cancer centre. Subjects underwent 6-week integrated yoga or brief supportive therapy prior to their radiotherapy treatment. QoL was assessed using EORTC QLQ-C30. All patients had mastectomy as primary treatment, and the mean age of the participants in yoga group was 46.7 ± 9.3 years, and control group was 48.5 ± 10.2 years. Emotional function ($p=0.001$, 95% CI 6.45–25.33) and cognitive function ($p=0.03$, 95% CI 1.2–18.5) were significantly improved in yoga group as compared to controls. Yoga was more effective than brief supportive therapy to improve QoL and affect in breast cancer outpatient.

Raghavendra et al. (2007) conducted a randomized controlled study that included chemotherapy-naïve stage II and III breast cancer patients receiving adjuvant chemotherapy, and the intervention group practiced an integrated yoga intervention consisted of a set of asanas, breathing exercises, pranayama, meditation and yogic relaxation techniques with imagery during the intervals between chemotherapy cycles. The control group received supportive counseling and coping preparation before the start of the first chemotherapy cycle. FLIC was used to assess QoL. There

was a significant improvement in QoL ($p < 0.001$) during chemotherapy in the yoga group as compared with controls.

Three RCTs that investigated the effects of yoga (Culos-Reed et al. 2006; Moadel et al. 2007) or MBSR (Lengacher et al. 2009) for breast cancer survivors were conducted by Culos-Reed et al. (2006), Moadel et al. (2007), and Lengacher et al. (2009). In a pilot study, breast cancer survivors received either a 7-week yoga program, consisted of gentle breathing, asanas, and relaxation, or a wait-list control. The subjects were approximately 50 years old and 56 months from time of diagnosis. EORTC QLQ-C30 was used for QoL assessment. The repeated measures analysis of variance determined main effects for group in global QoL ($F = 7.36$, $p < 0.01$), emotional function ($F = 6.90$, $p < 0.05$) and decreased diarrhea ($F = 12.20$, $p < 0.01$). In general, the results indicated that the yoga practice had a positive impact on QoL within the intervention group compared to the control group (Culos-Reed et al. 2006).

Moadel et al. (2007) used the FACT to measure patients' subjective reports of QoL and sought to determine the impact of yoga on overall QoL, fatigue, psychological distress, and spiritual well-being among an ethnically diverse sample of breast cancer patients. Subjects in the yoga group received twelve 1.5-h weekly classes and were compared with waitlist control group. The mean age of total sample was 54.81 ± 9.95 years. The comparison of the 71 patients not receiving chemotherapy during the intervention period revealed favorable outcomes for the intervention group in overall QoL ($p < 0.008$), emotional well-being ($p < 0.015$), social well-being ($p < 0.004$), spiritual well-being ($p < 0.009$), and distressed mood ($p < 0.031$).

Another RCT conducted by Lengacher et al. (2009) to determine whether an MBSR intervention compared with usual care is efficacious in improving psychological and physical status in women with stage 0, I, II, or III breast cancer that had completed treatment, used the Medical Outcomes Studies Short Form General Health Survey to measure QoL. The mean age of participants was 57.5 ± 9.4 years. Compared with usual care, subjects assigned to MBSR had significantly higher physical functioning ($p = 0.01$) and physical role functioning ($p = 0.03$) at six weeks.

In addition, Witek-Janusek et al. (2008) conducted a non-RCT that included women recently diagnosed with breast cancer. Subjects self-selected into an 8-week MBSR program or into an assessment only non-MBSR group. QoL measured by the QLI-Cancer was assessed at baseline, at mid-MBSR, at completion of MBSR, and at 4-week post-MBSR completion. The mean age of the participants in MBSR group was 55 ± 10 years, and non-MBSR group was 54 ± 8 years. The results showed that women who completed MBSR reported better total QoL with respect to women in the non-MBSR group ($p = 0.023$). Three single-arm studies that aimed to evaluate the efficacy of yoga intervention for breast cancer survivors also demonstrated positive results in QoL (Ulger and Yagli 2010; Bower et al. 2011; Galantino et al. 2011). Given different methodologies of the studies, the variety of QoL measures employed, duration of the interventions, and types of yoga, the effects of yoga on QoL in cancer patients were inconclusive.

6.4.2 Clinical Guidelines of Using Yoga

There are currently no evidence-based clinical guidelines for using yoga in cancer patients because only limited scientific evidence suggests that yoga may be useful in managing some symptoms of cancer and side effects of treatment, and the results of these studies have been inconsistent or preliminary.

The Society for Integrative Oncology (SIO), an international organization dedicated to encouraging scientific evaluation, dissemination of evidence-based information, and appropriate clinical integration of complementary therapies has developed the evidence-based clinical practice guidelines for integrative oncology. In these SIO practice guidelines, mind-body modalities (meditation, yoga, Taichi, hypnosis, relaxation techniques, music therapy, and other forms of expressive arts therapies) are recommended for incorporation as part of a multidisciplinary approach for reducing anxiety, mood disturbance, and chronic pain and for improving QoL in cancer patients. The grade of recommendation is 1B, meaning that the recommendation is strong, the evidence have moderate-quality and the supporting evidence are RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise). The authors have concluded that mind-body medicine is safe and has good evidence, but time consuming is its limitation (Deng et al. 2009).

Furthermore, the American College of Chest Physicians (ACCP) has published an evidence-based clinical practice guideline to differentiate between alternative therapies and complementary therapies and to describe the evidence base for use of complementary therapies in lung cancer. Although the objectives of this guideline are to evaluate the evidence for complementary therapies in the care of lung cancer patients, the authors have found out that only a few complementary modalities have been studied in patients with a single cancer diagnosis. Hence, symptom-control research conducted with other groups of patients with cancer is also included for evaluation as the results may also be applicable in lung cancer practice. Similar to the SIO clinical guidelines, mind-body modalities are recommended by ACCP as part of a multidisciplinary approach to reduce anxiety, mood disturbance, or chronic pain in lung cancer patients. The grade of recommendation is 1B (Cassileth et al. 2007).

6.5 Safety and Adverse Effects of Yoga/MBSR

As a possible adjunct therapy in cancer patients and survivors, most of the yoga classes are modified and adapted to the response, abilities, and needs of the cancer practitioners. Studies have found yoga to be feasible, well tolerated, and without adverse effects (Danahauer et al. 2009; Vadiraja et al. 2009b; Bower et al. 2011; Galantino et al. 2011; Littman et al. 2012).

Although yoga is generally considered to be safe in cancer patients when practiced appropriately, and currently no evidence has specified contraindications for yoga, some asanas may be dangerous to people with certain medical conditions. For example, Bertschinger et al. (2007) has reported a more than twofold increase

of the intraocular pressure in the headstand position and concluded that patients suffering from glaucoma should be advised not to practice postural (head-down) yoga exercises. Other than people with glaucoma, National Center for Complementary and Alternative Medicine has suggested that people with disc disease of the spine, extremely high or low blood pressure, retinal detachment, fragile or atherosclerotic arteries, a risk of blood clots, ear problems, severe osteoporosis, or cervical spondylitis should also avoid some inverted poses (<http://nccam.nih.gov/health/yoga/introduction.htm>). Moreover, certain conditions or co-morbidities of cancer patient, such as pregnancy, postsurgical care, acute fractures, arthritic flare-ups, cardiovascular disorders, respiratory disease, thyroid conditions, should be cautioned, required special adaptations, and practiced under guidance of a certified and experienced yoga instructor (Austin and Laeng 2003; DiStasio 2008).

6.6 Mechanisms of Yoga/MBSR

As the determinants of the QoL of patients with cancer, the biologic, psychosocial, and spiritual factors have been studied to determine the underlying mechanism of the effects of yoga (Dapueto et al. 2005). Currently, the exact mechanism of yoga/MBSR on QoL is not known; however, researchers have proposed and investigated some plausible mechanisms, such as relaxation response, enhancing body awareness, psycho-neuro immunological approach, and melatonin.

Studies have demonstrated that both yoga breathing and meditation produce a relaxation response, which is a well-established mind/body approach for managing stress and the parasympathetic phase of rest and repair, characterized by decreased metabolism, heat rate, blood pressure, muscle tension, and breath rate, and increased alpha brain wave activity. (Beary and Benson 1974; Lazar et al. 2000; Rakel and Faass 2006; Sarang and Telles 2006; Brown and Gerbarg 2009; Vallath 2010) Moreover, reducing sympathetic (Hoffman et al. 1982) and increasing parasympathetic nervous system tone are related to enhanced spiritual well-being, which is associated with improvements in psychological distress (Philippot et al. 2002; Carmody et al. 2008; Brown and Gerbarg 2009; Chang et al. 2010).

Enhancing body awareness has been indicated as an important element or a mechanism of action for mind-body therapy, such as yoga (Daubenmier 2005; Mehling et al. 2011). A study by Rani and Rao (1994) was conducted to investigate whether the practice of Hatha yoga enhances the one's body awareness. Thirty-six participants were recruited and allocated to either a three-month Hatha yoga training group or a control group. The results showed that yoga-trained group had a significantly better body awareness than the control group (Rani and Rao 1994). Furthermore, Impett et al. (2006) examined the associations between yoga practice and well-being, embodiment, and self objectification over a two-month yoga program and found that more frequent yoga practice was associated with increased body awareness, positive effect, and satisfaction with life, as well as decreased negative effect.

Cancer is often associated with psychological distress, which in turn affects QoL. Chronic stress, such as cancer, leads to the activation of autonomic nervous system

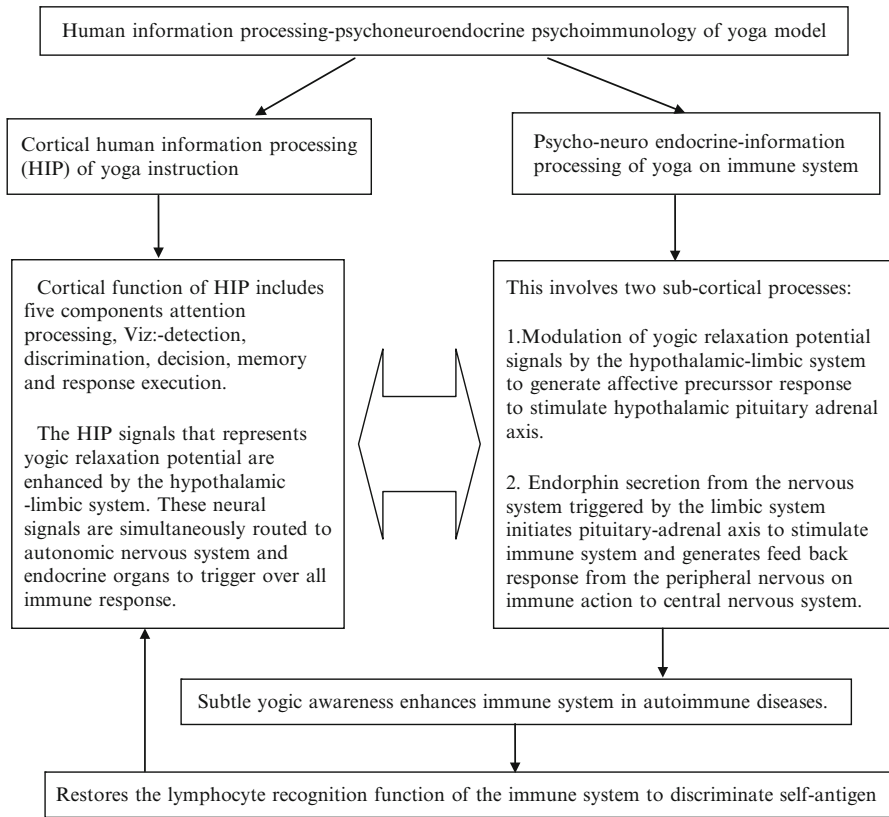


Fig. 6.1 An integrated model of human information processing-psycho-neuroendocrine network for yogic exercise effects on immunity (Reproduced from Kulkarni and Bera (2009). With permission)

and the hypothalamic-pituitary-adrenal (HPA) axis through which catecholamines, glucocorticoids, and other stress hormones and neuropeptides are released. These neuroendocrine stress hormones may suppress the immune response, including natural killer cell activity, phagocytosis, production of inflammatory cytokines, and cytotoxic T cell activity, and promote the initiation and progression of some types of cancer (Reiche et al. 2004; Lutgendorf and Sood 2011). Miller et al. (2008) suggested that psychological interventions such as MBSR may limit the impact of stress on the immune response and may have direct effects on neuroendocrine-immune interactions. Kulkarni and Bera (2009) also reported that the relaxation potential of yoga may produce psycho-neuro-immunological effects by integrating the pituitary-neuro-endocrine network with the cortical information processing aspect of yogic instructions through human information processing and subsequently modulating immune system through hypothalamo-limbic-pituitary-adrenal functions (Fig. 6.1).

Several clinical trials have been conducted to investigate mechanisms of HPA axis functioning underlying yoga/MBSR's potential stress-reduction benefits. Carlson et al. (2003, 2004) investigated the relationships between a MBSR meditation program for early stage breast and prostate cancer patients and QoL, mood states, stress symptoms, and levels of cortisol, dehydroepiandrosterone-sulfate, and melatonin. The results showed that a MBSR program was associated with enhanced QoL and decreased stress symptoms in breast and prostate cancer patients. Also, improvements in QoL were associated with decreased afternoon cortisol levels. The authors concluded that the participation in MBSR program may result in possibly beneficial changes in HPA axis functioning. Most recently, Kiecolt-Glaser et al. (2010) studied healthy subjects to investigate the possible mechanism by which Hatha yoga may have an effect. Participants were screened and classified as novices or experts. In addition to measuring endocrine data (cortisol and catecholamine), they measured skin barrier, heart rate, and immunological parameters [interleukin (IL)-6, soluble IL-6 receptor, tumor necrosis factor- α , C-reactive protein, and lipopolysaccharide-stimulated production of IL-6 and tumor necrosis factor- α]. The results showed that the average serum IL-6 levels of novice yoga practitioner were 41% higher than those of experts, and the odds of a novice having a detectable high sensitivity C-reactive protein were 4.75 times of that of an expert. Also, experts produced less lipopolysaccharide-stimulated IL-6 in response to the stressor than novices. These findings suggested that regular yoga practice may influence physiological functioning and health.

Being proposed as one of the possible mechanisms, melatonin secreted by the pineal gland in the brain primarily at night exhibits immunomodulatory and sedative-like properties (Lieberman et al. 1984; Karasek 2004). It has also been shown to play a significant role in suppressing neoplastic growth in a variety of tumors (Mills et al. 2005; Srinivasan et al. 2011) and in physiological control of stress (Pierpaoli and Maestroni 1987). Clinical trials studying the relationships between melatonin and yoga/MBSR have shown contradictory results. Preliminary study of Massion et al. (1995) has indicated that melatonin may be a relevant outcome variable in assessing psycho-social interventions, particularly for subjects with breast or prostate cancer. Tooley et al. (2000) also concluded from their study that meditation can affect plasma melatonin levels. However, Carlson et al. (2004) reported that the levels of melatonin did not change over the course of an 8-week MBSR program. Moreover, the correlations between melatonin and psychological measures (stress, QoL, and mood) were insignificant.

6.7 Conclusions and Recommendations

Yoga has become increasingly popular as a complementary and alternative therapy for symptom management in oncology. By reducing several cancer-or treatment-related symptoms, yoga may concomitantly improve QoL. Despite the relatively poor quality and heterogeneity of studies for yoga on QoL, the evidence suggests that the use of yoga may have benefits for improving QoL of cancer patients. It has

been proposed that yoga produces a relaxation response, enhances body awareness, has psycho-neuro-immunological effects, and affects melatonin levels that underlie the biopsychosocial mechanisms of yoga. To date, the evidence is insufficient to conclude that yoga is an effective supportive treatment for cancer. Further research is recommended to specify the types or styles of yoga used, to develop and use standardized QoL measures agreed by the research community related, to evaluate the mechanism for the effectiveness of yoga for oncology, and to identify the feasible and effective treatment dose of yoga programs on health outcomes.

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Chapter 7

Efficacy of Mind-body Therapy on Stress Reduction in Cancer Care

Gary Elkins, Aimee Johnson, William Fisher, and Jim Sliwinski

Abstract Psychological stress in cancer patients has been identified as a significant and ongoing problem in oncology. Non-pharmacological interventions have been increasingly employed to facilitate coping with stressful circumstances. Mind-body therapies, which approach healthcare holistically as an interaction between mind, body, and spirit, have been studied as adjunctive therapies to reduce stress, enhance relaxation, reduce anxiety, and improve health outcomes. Mind-body therapies, including mindfulness/meditation, biofeedback, hypnosis, relaxation therapy, art therapy, Qigong, Taichi, and yoga have demonstrated efficacies in their potential to mitigate stress and improve the quality of life of cancer patients and survivors. Though the mind-body literature shows overwhelmingly positive results, methodological deficits hinder adoption as evidence-based palliative care for cancer survivors. Although additional research is warranted, the body of evidence presented in this chapter suggests that clinicians should give serious consideration to mind-body therapies when advising cancer patients and survivors on adjunctive treatment options.

7.1 Introduction

The National Comprehensive Cancer Network has identified emotional and psychosocial distress as significant and ongoing problems for cancer patients and survivors (NCCN 2005). Psychological stress in cancer patients may include anxiety, depression, insomnia, and the fear of dying (Keir 2006). To cope with the stress associated with cancer, patients are increasingly using adjunct non-pharmacological interventions,

G. Elkins (✉) • A. Johnson • W. Fisher • J. Sliwinski
Mind-Body Medicine Research Laboratory, Department of Psychology and Neuroscience,
Baylor University, Waco, TX 76798, USA
e-mail: Gary_Elkins@baylor.edu

such as mind-body therapies (Specia et al. 2000). Mind-body therapies approach health care holistically as an interaction between mind, body, and spirit. This chapter will review a wide body of mind-body therapies including mindfulness/meditation, biofeedback, hypnosis, relaxation, art therapy, Qigong, Taichi, and yoga and report on their respective abilities to mitigate stress and improve the quality of life of cancer patients and survivors. Many of these techniques once considered alternative to mainstream medicine, such as hypnosis and biofeedback, are now widely recognized for their utility to reduce stress, improve mood, enhance relaxation, reduce anxiety and improve health outcomes. The review of mind-body therapies' evidence for efficacy in the treatment of stress was restricted to literature indicating utility for treating cancer-survivors, or studies which show clear logical analogues to cancer treatment. Studies were excluded if they contained inadequate sample sizes ($n < 25$), were not specifically related to cancer or cancer-care, or were not recent, (within the last decade). Although the present chapter is dedicated to the care of cancer patients, it is worth noting that in the treatment of chronic and acute stress, many of these techniques have a broad literature of efficacy across multiple medical diagnoses (Table 7.1).

7.2 Mindfulness/Meditation

Mindfulness and meditation offer cancer patients with limited mobility a viable treatment option for managing stress. Mindfulness-based stress reduction (MBSR) programs have become the most popular meditation based treatment option. MBSR programs combine meditation, yoga, and relaxation practices in an effort to help patients develop less judgmental and more patient attitudes (Carlson et al. 2007).

Carlson and Garland (2005) conducted one of the first studies to examine the effects of an MBSR program on patient health. During this study, 63 male ($n=14$) and female ($n=49$) cancer patients completed an 8-week MBSR program (mean age=54 years). Diagnoses varied, with the most common being breast cancer (59%), prostate cancer (6%), ovarian cancer (6%), and Non-Hodgkin's lymphoma (6%). During the intervention, participants met weekly to practice 90-min of MBSR in small groups. Participants also received a booklet and guided meditation audio recording, and were asked to practice MBSR at home for 45 min, six times per week. A 3-h silent retreat was also offered during the sixth week of the intervention.

Outcome measures were collected at baseline and post-intervention. Results revealed that participant scores for stress measured by Symptoms of Stress Inventory (SOSI) (Spielberger, 1983), sleep quality measured by Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1988), fatigue measured by Profile of Mood States (POMS) (McNair et al. 1971), and mood disturbance measured by POMS, with all measures showed significant improvement following the intervention ($p < 0.001$) (Carlson and Garland 2005). Furthermore, fatigue was found to be significantly correlated with both stress ($r=0.53$, $p < 0.001$) and mood disturbance ($r=-0.39$, $p < 0.01$). Therefore, a large amount of covariance likely exists between these three variables, and reducing fatigue is likely to result in improvement in other areas as well.

Table 7.1 Mind-body therapies for stress reduction in cancer care

Author	Title	n	Modality	Outcome
<i>Mindfulness/meditation</i>				
2005 Carlson & Garland	Impact of mindfulness-based stress reduction on sleep, mood, stress, and fatigue symptoms in cancer outpatients.	63	Eight weeks of mindfulness-based stress reduction along with daily sessions of audiocassette guided meditation.	Patients reported significantly less stress, fatigue, mood disturbance, and sleep problems following the intervention.
2007 Carlson et al.	One year pre-post intervention follow-up of psychological, immune, endocrine, and blood pressure outcomes of mindfulness-based stress reduction in breast and prostate cancer outpatients.	59	Eight weeks of mindfulness-based stress reduction along with daily sessions of audio guided meditation.	Stress and cortisol levels as well as heart rate showed significant improvement at post intervention and 12-month follow-up. Systolic blood pressure also showed significant improvement during post intervention, but was not maintained at follow-up.
2009 Nidich et al.	A randomized controlled trial of the effects of transcendental meditation on quality of life in older breast cancer patients.	130	Patients were randomized into a 7-week transcendental meditation group or a no treatment control group.	Participants in the treatments group experienced significant improvements in quality of life, mental health, and emotional and social wellbeing.
2010 Birmie et al.	Psychological benefits for breast cancer patients and their partners participating in mindfulness-based stress reduction.	42	Eight weeks of mindfulness-based stress reduction.	Patients and their spouses experienced significant improvements in mood disturbance, fatigue, anxiety, depression, tension, and dejection, number of upper respiratory, GI and neurological problems.
2010 Bränström et al.	Self-report mindfulness as a mediator of psychological well-being in a stress reduction intervention for cancer patients – a randomized study.	71	Patients randomized into an 8-week mindfulness-based stress reduction program or a waitlist control group.	Participants in the treatment group reported significantly less stress than controls. They also reported more positive states of mind and less post-traumatic avoidance symptoms. Results were mediated by mindfulness scores.

(continued)

Table 7.1 (continued)

Author	Title	<i>n</i>	Modality	Outcome
2010 Foley et al.	Mindfulness-based cognitive therapy for individuals whose lives have been affected by cancer: a randomized controlled trial.	105	Patients randomized into an 8-week mindfulness-based cognitive therapy program or a waitlist control group.	Patients in the treatment group reported significantly less stress, depression, and anxiety than controls.
<i>Biofeedback</i>				
2005 Kim et al.	Effects of abdominal breathing training using biofeedback on stress, immune, response and quality of life in patients with a mastectomy for breast cancer.	25	Assigned to a biofeedback condition and instructed in abdominal breathing training using biofeedback, 1/week for four weeks or a no treatment group.	Quality of life measures and T3 immune markers showed significant improvements for the biofeedback group.
<i>Hypnosis</i>				
2002 Bakke et al.	The effect of hypnotic-guided imagery on psychological well-being and immune function in patients with prior breast cancer.	25	An 8-week hypnotic imagery intervention.	Patients experienced a significant increase in their number of natural killer cells. Patients also utilized more effective coping methods and reported significantly less depression.
2008 Elkins et al.	Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors.	60	Assigned to a hypnosis condition with five weekly sessions or a no treatment control.	Hot flash scores decreased 68% from baseline in the hypnosis group, and significant improvements in self-report anxiety, depression, interference of hot flashes, and sleep were observed as well.
<i>Relaxation therapy</i>				
2008 Phillips et al.	Stress management intervention reduces serum cortisol and increases relaxation during treatment for nonmetastatic breast cancer.	128	Patients were randomized to either a 10-week cognitive-behavioral stress management intervention or to a single day psycho-education seminar.	Results showed greater serum cortisol reductions in the group receiving the 10-week cognitive-behavioral stress management intervention.

Art therapy

2006

Monti et al.

A randomized controlled trial of mindfulness-based art therapy for women with cancer.

111

Female cancer patients were randomly assigned to an 8-week intervention group or wait-list control.

Compared to control, the treatment group demonstrated a significant decrease in symptoms of distress and quality of life.

2009

Svensk et al.

Art therapy improved experience quality of life among women undergoing treatment for breast cancer: a randomized controlled study.

41

Breast cancer patients were randomized into an art therapy intervention group that attended weekly sessions for five weeks or to a no-treatment control group.

Results indicated that the women who participated in art therapy showed significant positive improvements in physical and psychological quality of life.

Qigong

2006

Lee et al.

Effects of Chan-Chuang Qigong on improving symptom and psychological distress in chemotherapy patients.

67

Quasi-experimental study of 32 participants practicing Qigong for 15 min daily during the first 21-day schedule of chemotherapy vs 35 participants assigned to an undefined control group.

Results showed a significant reduction in symptom distress in the experimental group on day 22. Additionally, significant improvements in pain, numbness, heartburn and dizziness were reported by patients receiving Qigong.

Taichi

2004

Mustian et al.

Taichi Chaun, health-related quality of life and self-esteem: a randomized trial with breast cancer survivors.

31

Patients were assigned to a 12 weeks Taichi group or to a psychosocial support group.

Patients in the Taichi group showed significant improvements in self-esteem when compared to psychosocial support participants. No significant difference was detected for the outcome of health related quality of life.

Yoga

2004

Culos-Reed et al.

Discovering the physical and psychological benefits of yoga for cancer survivors.

38

Patients randomized into a 7-week Hatha yoga intervention group or a waitlist control group.

Intervention participants reported significantly less stress, tension, anger, depression, confusion, and total mood disturbance than did controls.

(continued)

Table 7.1 (continued)

Author	Title	<i>n</i>	Modality	Outcome
2007 Banerjee et al.	Effects of an integrated yoga program in modulating psychological stress and radiation-induced genotoxic stress in breast cancer patients undergoing radiotherapy.	58	Patients randomized into a yoga intervention treatment group or a supportive counseling control group.	Treatment group participants experienced significantly greater improvement in measures of psychological stress, genotoxic stress, depression, and anxiety than did controls.
2007 Raghavendra et al.	Effects of an integrated yoga program on chemotherapy-induced nausea and emesis in breast cancer patients.	62	Patients were randomized into a yoga intervention or supportive care control group.	Yoga was significantly more effective than supportive care in reducing nausea and vomiting. Treatment participants also reported significantly less depression, anxiety, and distress than controls.
2008 Danhauer et al.	Restorative yoga for women with ovarian or breast cancer: findings from a pilot study.	51	Ten weeks of restorative yoga.	Participants reported significantly less state anxiety at two-month follow-up.
2009 Vadiraaja et al.	Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial.	75	Patients randomized into a 6-week yoga intervention group or a supportive therapy control group.	Treatment group participants reported significantly less stress, depression, and anxiety than control participants. Cortisol levels were also significantly lower for treatment group participants.
2010 Thygeson et al.	Peaceful play yoga: serenity and balance for children with cancer and their parents.	49	One 45-min yoga session.	Adolescent cancer patients and their parents reported significantly less anxiety following the yoga session. Younger cancer patients did not report any significant improvements.

In a follow-up to the Carson and Garland (2005) study, Carlson et al. (2007) assigned ten patients with early stage prostate cancer and 49 patients with Stage 0, I, or II breast cancer to an 8-week MBSR program (mean age=54.5 years). Participants attended weekly, 90-min MBSR sessions with no more than 14 other participants. They were also provided with a CD or audio recording with instructions for sensate focus body scan meditation and guided sitting meditation, and were instructed to practice at home daily.

Outcome measures revealed that the intervention significantly reduced participant stress levels as measured by the SOSI ($p < 0.001$) and that these improvements were maintained at six and twelve months follow-up. Heart rate also decreased from baseline to post-intervention ($p < 0.05$) and continued to show significant improvement at the 12-month follow-up period. Cortisol levels also decreased significantly ($p < 0.001$) with a linear downward trend seen from post intervention to one year follow-up. Systolic blood pressure decreased from pre- to post-intervention, ($p < 0.05$) but this difference did not remain significant at six and twelve months follow-up. Finally, the level of pro-inflammatory cytokines also decreased over the course of the study.

The results of this study led the researchers to suggest that relatively brief meditation interventions may lead to significant improvements in the symptomology of cancer patients later in time (Carlson et al. 2007). The authors suggest that, because MBSR teaches patients to be more patient and understanding, patients do not necessarily have to keep practicing meditation to remember these lessons and incorporate them into their daily lives. However, they do suggest that such improvements may be mediated by how long participants have been diagnosed with cancer. Therefore, it is important that patients enroll in a program as early as possible.

In an additional study, Birnie et al. (2010) investigated whether or not having couples attend a MBSR intervention would prove beneficial for patients and their partners. Twenty-one cancer patients and their cancer free spouses participated in the study. The three most common diagnoses were prostate, breast, and colorectal cancer with rates of 28.6, 19.0, and 14.3%, respectively. Eleven of the cancer patients were male and ten were female. They had a mean age of 62.9 years. The program lasted for eight weeks and consisted of weekly, 90-min, MBSR sessions, and either a 3 or 6-h weekend silent retreat.

Results indicated that both patients and their partners experienced significant improvement in the areas of total mood disturbance ($p = 0.04$), fatigue ($p = 0.05$), and anxiety/tension ($p < 0.001$) as measured by the POMS. Additionally, although improvements in global stress measured by the Calgary (C-SOSI; Carlson and Thomas 2007) failed to reach significance, subscale scores for muscle tension ($p < 0.01$), neurological/gastrointestinal problems ($p < 0.01$), and upper respiratory symptoms ($p < 0.04$) all showed significant improvement following treatment. It is also worth noting that as mindfulness scores rose for cancer patients, their partners exhibited less mood disturbance, ($r = -0.499$, $p < 0.05$). Partners' mood disturbance scores also lowered as patients' stress scores decreased ($r = 0.457$, $p < 0.05$). Patients did not react the same way to changes in their partner's symptom profiles, thus suggesting that the well-being of the cancer patient is more important to both members of the couple.

In an additional MBSR study, Bränström et al. (2010) assigned cancer patients to either a typical 8-week MBSR intervention, ($n=32$) or to a wait-list control group ($n=39$). Cancer diagnoses included breast ($n=54$), gynecological ($n=10$), lymphatic ($n=5$), pancreatic ($n=1$), and neck ($n=1$). All of the patients were women except one, and the mean age of the sample was 51.8 years. Perceived Stress Scale (PSS) (Cohen et al. 1983) scores revealed that treatment participants had significantly lower stress levels than did control participants at post-intervention ($p=0.004$). Intervention participants also experienced significantly more positive states of mind ($p=0.023$) and were less likely to display post-traumatic avoidance symptoms ($p=0.012$) (Bränström et al. 2010). The effects of the intervention were mediated by participants' scores on Five-Facet Mindfulness Questionnaire (FFMQ) (Baer et al. 2008), suggesting that changes in mindfulness were responsible for participant improvement.

Furthermore, Foley et al. (2010) conducted a study in which stage I-IV cancer patients were randomly assigned to either an 8-week mindfulness-based cognitive therapy (MBCT) program ($n=55$, mean age=54.82) or a waitlist control group ($n=60$, mean age=55.52). Seventy-seven percent of the patients were women. Cancer diagnoses varied, with the most common being breast ($n=48$), bowel and colon ($n=9$), lymphoma ($n=8$), prostate ($n=8$), and gynecological ($n=7$). MBCT is an adaptation of MBSR that was originally designed to help patients with depression. MBCT aims to reduce the number of ruminating thoughts that patients contend with, but otherwise follows an outline nearly identical to MBSR. Results indicated that individuals who underwent 2 h of MBCT per week showed significant decreases in their levels of anxiety ($p=0.002$) as rated by the Hamilton Anxiety Rating Scale (HAM-A) (Shear et al. 2001) and depression ($p<0.001$) as rated by the Hamilton Rating Scale for Depression (HAM-D) (Williams 1988). Distress scores on the Depression, Anxiety Stress Scale-short form (DASS) (Lovibond and Lovibond 1995) were also significantly lower for participants receiving MBCT ($p<0.001$).

While these studies demonstrate the popularity of MBSR programs for the treatment of stress among cancer patients, other forms of mindfulness meditation are available. For example, Nidich et al. (2009) conducted a single-blind, randomized control study, in which women with stages II through IV breast cancer were assigned to either a seven session, transcendental meditation program ($n=64$, mean age=64.4) or a standard care control group ($n=66$, mean age=63.3). During transcendental meditation, individuals sit quietly with their eyes closed and focus on quieting their mind while remaining restfully alert. Individuals assigned to the treatment group were taught transcendental meditation by a certified instructor over the course of seven 60–90 min lessons. They were then instructed to practice at home for 20 min twice per day. Outcome data were collected at baseline and every six months thereafter for a period of two years. When compared with control participants, women in the treatment group experienced significant improvements in overall quality of life ($p=0.003$), as well as emotional ($p=0.046$) and social wellbeing ($p=0.003$) as measured by the Functional Assessment of Cancer Therapy-Breast (FACT-B) (Brady et al. 1997, 2002; Nidich et al. 2009). Mental health scores measured by the Short-Form Health Survey (SF-36) (Ware 2000) were also significantly improved ($p=0.017$).

When these studies are examined collectively, they suggest that various forms of mindfulness or mediation can effectively help cancer patients with limited mobility manage their stress. However, the lack of a control group in several of these studies and the omission of physiological measure of stress are limitations. Additional research is warranted in order to fill these gaps.

7.3 Biofeedback

Biofeedback is a process that enables an individual to learn to change physiologic activity to improve health related measures (Association for Applied Psychophysiology and Biofeedback 2011). Many physiologic biofeedback instruments exist to record activities such as brainwaves, heartbeat, breathing, muscle activity, and skin temperature, which in return providing feedback to the participant.

Biofeedback training focused on instructing cancer patients on the use of abdominal breathing exercises has shown promising results in the reduction of anxiety. A study by Kim et al. (2005) evaluated the effects of abdominal breathing training using biofeedback with breast cancer patients upon their completion of chemotherapy. The sample consisted of 25 breast cancer patients whose stages of cancer were not reported. Seventy-five percent of these patients were under the age of 50, and 25% were over the age of 50. Twelve patients were assigned to an experimental biofeedback condition and instructed in the practice of abdominal breathing training utilizing biofeedback once a week for a duration of four weeks.

As part of the quasi-experimental study design, both experimental and control groups completed a initial pre-test and a 4-week post-test. Outcome measures were collected at baseline and post intervention. Patients' assessments included the State Trait Anxiety Inventory (STAI) (Spielberger et al. 1970), the Health-Related Quality of Life Korean Version (Chae and Seo 2010), serum cortisol, T cell subsets (T3, T4, T8), and natural killer (NK) cells. Post-intervention scores indicated a reduction in state anxiety and serum cortisol. However, results were not statistically significant. The abdominal breathing intervention did show significant results on measures of health-related quality of life ($p=0.02$) and T3 markers, ($p=0.04$). Investigation into the mechanism of this potentially beneficially effect is warranted.

7.4 Hypnosis

Hypnosis has proven to be an effective treatment option for managing stress across a wide variety of areas. For example, Elton (1993) showed that 12 weeks of hypnosis therapy significantly reduced stress levels for patients with stress-inducing pain disorders, and that these benefits were maintained at a six months follow-up appointment. Evidence suggests that hypnosis is also effective at reducing stress for individuals undergoing surgery, and has the added benefits of lowering heart rate,

decreasing anxiolytic use, shortening hospital stay, and decreasing blood loss (Enqvist et al. 1995). Finally, several studies have indicated that hypnosis helps boost immune function in individuals under high stress (Gruzelier et al. 2001a, b; Kiecolt-Glaser et al. 2001).

Considering the role that stress plays in disease progression for cancer patients, it is surprising that hypnosis is not a more commonly utilized treatment option. However, limited research is available. For example, Bakke et al. (2002) examined the effects of an 8-week hypnotic imagery intervention on immune function in 25 women with stage I or II breast cancer. During the hypnosis sessions, a trained therapist discussed the negative effects that stress and depression can have on the immune system. Patients were also instructed to picture their immune system working to destroy cancer cells. Following the intervention, depression scores on the Profile of Mood States had improved significantly from baseline ($p=0.039$). Scores on the Ways of Coping Checklist (WCC) (Folkman et al. 1999) also indicated that participants more frequently utilized appropriate coping methods following treatment, such as using positive reappraisal ($p=0.03$) and accepting responsibility ($p=0.04$). These outcomes were maintained at a three months follow-up. Finally, when peripheral venous blood samples were analyzed using a Coulter Stak-S, results indicated that patients' absolute number of NK cells increased significantly from baseline to post-intervention ($p=0.03$), suggesting that the intervention was effective at boosting immune function. However, this result was not maintained at a three months follow-up.

In an additional study, Elkins et al. (2008) randomly assigned female breast cancer survivors to either a hypnosis intervention group ($n=24$, mean age=58.1 years) or a no treatment control group ($n=27$, mean age=55.8 years). Participants in the treatment group received weekly, 50-min sessions of hypnosis. Each session began with a hypnotic induction, which was followed by suggestions for relaxation and coolness. Patients were also instructed to dissociate from hot flashes and to imagine themselves symptom-free in the future. Participants in the treatment group were also provided with an audio recording that allowed them to practice hypnosis at home. Following the intervention, women in the treatment group reported significant improvements in the number of hot flashes experienced, as well as the severity of these hot flashes ($p<0.001$) as measured by the Hot Flash Related Daily Interference Scale (HFRDIS) (Carpenter 2001). These scores were also significantly lower than those reported by control group participants ($p<0.001$). Results also showed that, following treatment, women assigned to the hypnosis intervention reported significantly lower levels of anxiety ($p=0.004$) as measured by the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983), depression ($p=0.003$) as measured by the CES-D, and sleep ($p<0.001$) as measured by the Medical Outcomes Study Sleep Scale (MOS-Sleep) (Stewart and Ware 1992), than did participant in the control group.

Although the results of these studies are promising, additional studies that examine stress as a primary outcome measure are needed in order to determine the appropriate duration of treatment, as well as the most beneficial hypnotic suggestions for patients with different cancer diagnoses.

7.5 Relaxation

Relaxation techniques are the second-most frequently used of the complementary and alternative medicine therapies both for the adult general population as well as cancer patients (Eisenberg et al. 1998; Tindel et al. 2005). Relaxation therapies are designed to provide relief from physical and mental tension (McCaffery and Pasero 1999). The first relaxation studies utilized Jacobson's progressive muscle relaxation (Jacobsen 1929). Since then, several expanded techniques such as jaw relaxation, focused breathing, and abdominal breathing have been developed (Phillips et al. 2008).

Stress plays a role in disease progression for cancer patients; however, limited controlled studies exist that establish an effective relaxation intervention. A recent study examined the effects of a 10-week cognitive-behavioral stress management (CBSM) intervention in 128 women undergoing treatment for non-metastatic breast cancer (Phillips et al. 2008). Patient age ranged from 25 to 69 years (mean age=49.69) with diagnosis classifications being stage 0 (43.8%), stage I (35.2%), stage II (35.2%), and stage III (3.1%). Participants were randomized to either a 10-week CBSM intervention consisting of relaxation, cognitive restructuring, and coping skills or to a single-day psycho-education seminar, which was held at the mid-point of the 10-week CBSM intervention period. Patient scores on the relaxation subscale of the Measure of Current Status (MOCS) (Carver, 2005), as well as serum cortisol levels were collected at baseline, six months follow-up, and twelve months follow-up. Linear growth models analyses were performed, controlling for variables known to affect cortisol (i.e. chemotherapy, disease severity, and caffeine) by including these variables as covariates. Women who received the intervention had a reduction in late afternoon cortisol levels over time in comparison with control, which showed no appreciable decline across 12 months. The intervention group had a small, but significant decrease of 0.01 log-units of cortisol per month ($p < 0.05$). Additionally, results yielded support for the hypothesis that women in the CBSM group would report increased ability to relax across time compared with control ($p < 0.05$). Breast cancer patients undergoing a 10-week CBSM intervention had significantly greater cortisol reductions and increased perceived ability to relax (Phillips et al. 2008). Although the results of this study are promising, additional studies are needed in order to determine the appropriate relaxation intervention for patients with different cancer diagnoses.

7.6 Art

The American Art Therapy Association has defined art therapy as the creative process of art-making to improve and enhance the physical, mental and emotional well-being of individuals of all ages (AATA, 2012). It is based on the belief that the creative process involved in artistic self-expression helps people to resolve conflicts and problems, develop interpersonal skills, manage behavior, reduce stress, increase self-esteem and self-awareness, and achieve insight (AATA, 2012). Art therapy has

been applied in cancer care and rehabilitation, providing a means of imaginative communication and supporting meaning-making processes (Collie et al. 2006). The reported effects of art therapy for cancer care have been improvements in communication, ease of processing traumatic experiences, a reduction of negative symptoms, and improved levels of energy (Luzzatto and Gabriel 2000; Borgmann, 2002; Luzzatto et al. 2003; Nainis et al. 2006; Svensk et al. 2009).

In a study of the efficacy of art therapy, Svensk et al. (2009) reported significant improvements in the quality of life for breast cancer patients. In this study, 41 breast cancer patients (mean age = 59.5 years; tumor classification T1: $n=18$, T2–3: $n=21$, missing data: $n=2$), who were undergoing radiotherapy treatment for breast cancer, were randomized to an intervention with individual art therapy sessions for 1 h a week over five weeks ($n=20$) or to a control group ($n=21$; presumed to be standard care, authors did not specify). Quality of life was assessed using the World Health Organization's Quality Of Life Brief Scale (WHOQOL-BREF) (Harper and Power 1998) and the European Organization for Research and Treatment of Cancer's instrument: the Quality of Life Questionnaire (QOL-BR23) version 1.0 (Sprangers et al. 1996). Measures were provided before randomization and the start of radiotherapy, two months after this, and again six months later. Results from the WHOQOL-BREF calculated by the Mann–Whitney U -test (a non-parametric test of differences between the intervention group and the control group) showed significant differences at the six months follow-up in the domains of overall score ($p=0.003$), general health score ($p=0.024$), and environment ($p=0.034$). Further, when intra-group changes were analyzed using the Wilcoxon's signed ranks test, significant differences appeared in overall scores ($p=0.033$), general health ($p=0.042$), physical health ($p=0.008$), and psychological health ($p=0.045$), though psychological health variables showed significance for controls as well ($p=0.015$). Results from the QOL-BR23 instrument calculated by the Mann–Whitney U -test did not show significant differences between groups. Intra-group analyses using the Wilcoxon's signed ranks tests showed significant differences at six months follow-up in the domains of body image ($p=0.0237$), future perspectives ($p=0.016$), and systematic therapy side effects ($p=0.006$). The authors suggest that the results of the study were a strong support that art therapy was effective in improving the quality of life of breast cancer patients.

An additional study was conducted to examine the efficacy of a newly-developed mindfulness-based art therapy (MBAT) for the treatment of women with cancer (Monti et al. 2006). In this study, 111 women (ages 26–82, mean age = 53.6 years) with a variety of cancer diagnoses (51 breast cancer, 19 gynecologic, 13 hematologic, 5 neurologic, 6 rectal, and 17 others) were randomly assigned to either the intervention group (eight weekly 2.5-h sessions) or to a wait-list control group. The intervention consisted of training in the practice of mindfulness meditation and group art therapy tasks. Home assignments were included, which involved the practice of mindfulness meditation six days a week, for 30 min. The group art therapy component of the intervention focused on non-verbal activities (i.e. the making of directed and spontaneous art productions) that were incorporated with the verbal processes within the group. Outcome measures for this study were the Symptoms

Checklist Revised (SCL-90-R) (Derogatis, 1994), which was included to capture psychological distress and stress-related somatic complaints and was assessed at weeks 0, 8, and 16 of the study. Health-related quality of life was assessed (pre- and post-intervention) with the Medical Outcomes Study Short-Form Health Survey (SF-36) (Ware, 2000). Results of this study showed significant differences in overall scores and in every subscale of the SCL-90-R, with effect sizes ranging from 0.13 to 0.33, with the overall score reporting an effect size of 0.16 (CI 0.08–0.24). Outcomes from the SF-36 showed statistically significant effects for all scale factors, save role-physical and role-emotional with effect sizes ranging from -2.23 to -10.9 , with mental health showing the largest effect size -10.9 ($p=0.001$, CI 16.8 to -4.96). Though this study's results are impressive, it is not possible with this data to determine the relative contribution of art therapy to the efficacy of the overall treatment protocol. Nevertheless, this is encouraging initial data for the potential of MBAT for reducing symptoms of distress and improving key aspects of quality of life for women with cancer.

Though these results are interesting and promising, much of the art therapy literature consists of single-group, quasi-experimental designs, with the few randomized controlled trials utilizing wait-list or no-treatment controls and showing mixed results (Reynolds et al. 2000). Further randomized study employing an active control group (e.g. structured attention) would provide better insight into the efficacy of this technique for cancer patients.

7.7 Qigong

Qigong (pronounced “chē gōng”) is a broad term for describing the practice of the system of healing and energy. This self-training process through Qi (vital energy) and Yi (consciousness or intention) utilizes breathing techniques, gentle movement, and meditation to achieve the optimal state of mind and body (Chen and Yeung 2002).

A quasi-experimental study explored the effect of Chan-Chang Qigong on symptom distress and psychological distress for breast cancer patients receiving chemotherapy (Lee et al. 2006). In this non-randomized study, 32 participants (mean age=44 years, SD=7.51 years) were assigned to an experimental Qigong group, and 35 to a control group (mean age=49, SD=8.13 years). Of the sample of breast cancer patients, 53.7% were classified with a stage II tumor, 62.7% with a tumor size ranging from 2 to 5 cm, 74.6% received radiotherapy before chemotherapy, and 70.1% received a modified radical mastectomy. The experimental group practiced Chan-Chang Qigong for at least 15 min every day during the first 21-day schedule of chemotherapy. Patients practiced Chan-Chang Qigong with proper posture involving stationary standing, circling of the arms, breathing naturally and maintaining the whole body in a state of relaxation. No description of the control group was provided. Patients completed the Symptom Distress Scale (SDS) (McCorkle and Young 1978) and the SCL-90-R (Derogatis 1994) as a measure of psychological

distress at baseline and days 8, 15, and 22 of treatment. Repeated measures analyses of variance (ANOVA) were conducted on measures of symptom distress and psychological distress for each group. Results showed a significant reduction in overall symptom distress in the experimental group on day 22 ($p < 0.05$). Additionally, significant improvements on individual items on the SDS and SCL-90 were observed in pain ($t = 2.18, p < 0.05$) numbness ($t = 3.72, p < 0.01$), heartburn ($t = 2.39, p < 0.05$), and dizziness ($t = 3.72, p < 0.01$). No significant difference was found between groups for psychological distress. However, the item on the SCL-90 measuring “hopelessness about the future” was significant on day 8 ($p < 0.05$).

To date, most studies examining Qigong report that treatment patients show more improvement or better survival rates than patients receiving conventional methods alone (Chen and Yeung 2002). However, these analyses are limited by poor study design and lack of randomization. Additionally, generalization is limited by the fact that the majority of these studies have been conducted in China. Although the literature for the utilization of Qigong in oncology is promising, further cross-cultural, controlled studies are required to generalize efficacy.

7.8 Taichi

Taichi is a Chinese martial art practiced for health promotion and maintenance, which emphasizes a series of postures and movements along with controlled breathing (Reid-Arndt et al. 2012). Taichi is a moderate form of exercise that has been shown to have an intensity that does not exceed 50% of participants maximum oxygen intake (Field, 2010), making it suitable for a wide range of fitness levels (Lan et al. 1996). Research has also shown Taichi can positively affect balance, flexibility, strength, and aerobic capacity (Mustian et al. 2004). Psychological benefits of Taichi may include reductions in tension, depression, and anger, and improved quality of life in a wide range of populations including cancer patients (Jin, 1989; Mustian et al. 2004).

A systematic review of controlled trials on Taichi identified two randomized controlled studies conducted in the United States with sample sizes greater than 25 (Lee et al. 2007). One study compared Taichi to psychosocial support therapy in regards to improvement in health related quality of life and self-esteem (Mustian et al. 2004). The sample consisted of breast cancer survivors with ages ranging from 33 to 78 years (mean age = 52 years, SD = 9 years). All participants were diagnosed with stage 0-III breast cancer and received surgical treatment (61% lumpectomy, 33% mastectomy, 6% bilateral mastectomy). All participants completed the Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F) (Cella and Nowinski 2002) questionnaire to assess health related quality of life and the Rosenberg Self-Esteem Scale (RSE) (Rosenberg, 1965) at baseline, six weeks, and 12 weeks. Participants in the Taichi group practiced for 60 min, three times a week for 12 weeks ($n = 17$) and participants receiving psychosocial support therapy followed same intervals and times as the psychosocial support group ($n = 14$).

A repeated measures analysis of covariance (ANCOVA) was conducted with self-esteem as the outcome variable and baseline self-esteem as the covariate. Results showed a significant difference between the Taichi group and psychosocial support participants on changes in self-esteem at 12 weeks ($F_{1,19} = 7.54$; $p = 0.10$), with the Taichi group showing significant improvements in self-esteem and reduction in psychosocial support group. Although the changes in self-esteem at six weeks were not significantly different ($F_{1,19} = 0.73$; $p = 0.40$), the Taichi group reported improvements in self-esteem while the psychosocial support group showed a decline in self-esteem. No significant difference was detected between groups for the outcome of health-related quality of life as measured by the FACT-F (Mustian et al. 2004). To further investigate the benefits of Taichi for cancer patients, more randomized, controlled trials with larger samples sizes are needed.

7.9 Yoga

Eastern culture has long considered yoga to be an effective treatment option for managing stress. Recent studies indicate that yoga is quickly becoming one of the most widely accepted mind-body therapies in the US as well (Tindel et al. 2005). With the increasing popularity of yoga, it is perhaps unsurprising that many cancer patients, as well as their family members, are beginning to view yoga as a viable adjunct treatment option.

The results of several studies indicate that yoga is indeed effective at helping individuals with cancer manage stress. For example, Culos-Reed et al. (2004) randomly assigned cancer survivors (mean age=51.8 years), the majority of whom were women (93%), to either a 7-week Hatha yoga intervention group ($n=20$) or a waitlist control group ($n=18$). Cancer diagnoses varied, with the majority of patients being diagnosed with breast cancer. Although no differences were seen between groups at baseline, post-intervention results revealed that total stress scores as measured by the Symptoms of Stress Inventory (SOSI) (Leckie and Thompson 1979) were significantly lower for the intervention group than for the control group ($p < 0.05$). SOSI subscale scores for habitual patterns, (e.g. smoking, nail biting, drinking), cardiopulmonary arousal, and emotional irritability were also significantly lower for participants in the yoga intervention group ($p < 0.05$ for all subscales). Additionally, post-intervention scores for anger, tension, depression, confusion, and total mood disturbance, as measured by the POMS, improved significantly for yoga intervention participants ($p < 0.05$ for all subscales), suggesting that yoga is effective at improving the total symptom profile of cancer patients.

In an additional study, Banerjee et al. (2007) randomly assigned stage II and III breast cancer survivors who were undergoing radiotherapy to either a yoga intervention group ($n=35$, mean age=47 years) or a supportive counseling control group ($n=23$, mean age=43 years). Participants in the yoga intervention received instructions on meditation, breathing, and stretching that had been modified to match their limitations. Each yoga session lasted for 90 min, however, the total number of yoga

sessions held was not reported. Results indicated that participants in the intervention group experienced significant improvements in psychological stress ($p < 0.001$) as measured by the PSS, depression ($p < 0.001$) and anxiety levels ($p < 0.001$) as measured by the HADS. Meanwhile, depression, anxiety, and stress actually became worse for participants in the control group. Blood sampling revealed that DNA damage levels were 14.5% lower for participants receiving yoga therapy when compared to control group participants, thus indicating lower genotoxic stress.

In a similar study, Raghavendra et al. (2007) randomly assigned chemotherapy patients with stage II or III breast cancer, to either a yoga intervention group ($n = 28$) or a supportive therapy and coping preparation control group ($n = 34$). Participants in the treatment condition received one, 30-min session of bedside yoga instruction prior to their first session of chemotherapy. They also received audio and videocassettes that guided them through 60-min, in-home, yoga sessions that they were asked to practice daily. Additionally, every ten days a yoga trainer would make a house visit to supervise participants while they completed their yoga session. Participants in the control condition received a 60-min session of supportive-expressive counseling and education prior to their first chemotherapy treatment. Following this initial session, control participants would receive 30-min counseling sessions every ten days, during a hospital visit. Main outcome measures included the frequency and intensity of nausea and vomiting as measured by the Morrow Assessment of Nausea and Emesis (MANE) (Morrow and Carnrike 1988). Results suggested that the yoga intervention was significantly more effective than supportive counseling at reducing nausea frequency and intensity following chemotherapy ($p < 0.01$). Yoga also significantly reduced the rates of anticipatory nausea ($p < 0.01$) and anticipatory vomiting ($p < 0.05$). Furthermore, participant scores on the Beck Depression Inventory (BDI) (Beck et al. 1961), the State Trait Anxiety Inventory, and a symptom distress checklist were significantly lower for participants receiving the yoga intervention than they were for controls for all measures ($p < 0.01$) (Raghavendra et al. 2007). This suggests that yoga may be a successful intervention for controlling symptoms thought to arise from high stress levels.

In a more recent study, Danhauer et al. (2008) asked women who were diagnosed with either ovarian cancer ($n = 37$) or breast cancer ($n = 14$) to complete ten weekly sessions of restorative yoga. The mean age of participants was 58.9 years, and 61% of the participants were undergoing treatment during the study. Each of the ten yoga sessions was led by a certified yoga instructor. Participants completed an average of 5.9 sessions. Outcome measures were recorded at baseline, post-intervention, and two months follow-up. Results revealed that decreases in state anxiety, as measured by the STAI, were not significant from baseline to post-intervention ($p = 0.10$). However, when baseline scores were compared to scores at two months follow-up, the decrease in state anxiety reached significance ($p \leq 0.01$), suggesting that the full-benefits of yoga may not manifest until weeks after participation. However, a control group was not included in the experimental design of the study, eliminating the possibility for comparison.

In an additional study conducted by Vadiraja et al. (2009), women diagnosed with stage II or III breast cancer and undergoing radiotherapy were randomized to either a yoga intervention group ($n = 42$) or a brief supportive therapy control group ($n = 33$).

Participants in the yoga intervention were required to attend a minimum of three 60-min yoga sessions per week for a period of six weeks while undergoing radiotherapy. Each session was taught by a trained yoga instructor at the hospital. Intervention group participants were also asked to complete a self-guided yoga session at home on days when they did not go to the hospital. Participants in the control condition met with a trained social worker for at least 15-min every ten days. They were accompanied by a caretaker, and both were provided instruction on coping and social support. Outcomes included anxiety and depression as measured by the Hospital Anxiety and Depression Scale (HADS), perceived stress as measured by the Perceived Stress Scale (PSS), and biological stress as measured by cortisol sampling. Results revealed that participants in the yoga condition showed a significant decrease in early morning cortisol levels ($p < 0.001$) and also in pooled mean cortisol levels ($p < 0.01$). Additionally, post-intervention cortisol levels were significantly lower for the intervention group when compared to the control group ($p = 0.03$). However, when baseline distress levels were utilized as a control variable, only participants categorized as being under low-distress showed significant drops in cortisol ($p = 0.03$). Anxiety and depression scores were significantly improved at post-intervention for both groups when compared to baseline. However, depression scores for participants in the yoga intervention group were significantly lower than those of the control group ($p = 0.002$), indicating that yoga provided additional benefits not received by patients receiving standard care. Finally, perceived stress scores dropped significantly for participants in the yoga intervention group ($p < 0.001$), but not for participants in the control group ($p = 0.17$).

In a study examining the benefits of yoga in a pediatric population of cancer patients, Thygeson et al. (2010) accrued 11 children and 5 adolescents at an inpatient hematology/oncology unit, as well as 33 parents of inpatient children diagnosed with either cancer or a blood disorder, to participate in one 45-min yoga session. The State Trait Anxiety Inventory for Children (STAIC) (Spielberger et al. 1983) and the STAI were used to measure distress both immediately before and soon after the yoga session. Results revealed that pre- and post-intervention scores did not significantly differ for the child cohort ($p = 0.21$). However, baseline scores for children were already within the normal range. Conversely, anxiety scores were significantly improved in the adolescent cohort ($p = 0.04$) and in the parent cohort ($p < 0.001$). Furthermore, 7 of the 33 parents involved in the study mentioned yoga's ability to reduce stress as the main benefit they received from participating in the study.

These studies lend support to the argument that yoga is effective at helping both cancer patients and their family members manage stress. However, there are some holes in the research literature that should be examined. For example, many of the studies listed here lacked a control group or designated patients receiving standard care as controls. Future studies should attempt to compare the benefits of yoga to other well-known treatment options. Additionally, several of these studies incorporated small sample sizes. While this might provide support for the power of these interventions, large scale studies are needed to confirm these preliminary results. Finally, future studies should incorporate follow-up testing to determine whether or not the benefits of yoga persist over time.

7.10 Conclusion

The body of evidence supporting mind-body therapies' efficacy in the adjunctive treatment of stress in cancer patients is very promising. In particular, support for meditation, hypnosis, Taichi, and yoga is persuasive. Mind-body therapies in general have been shown to have benefit in reducing stress and anxiety, improving mood, increasing hope and raising the quality of life in cancer patients and survivors.

Although the amount and the quality of research in mind-body therapies vary, the potential impacts for cancer patients are myriad and overwhelmingly positive. In considering the requisites for clinical practice guidelines, the grade of research-evidence is often weighed alongside the calculus of the potential benefits *vs* the risks/burdens to the patient. The risks and burdens to patients undergoing mind-body therapies are generally very few and light, and the benefits possibly life-extending in some cases. Therefore, it is recommended that mind-body therapies should be seriously considered as adjunctive treatments to cancer care. Though several mind-body therapy professional organizations provide standards of training, certification, and ethical practice guidelines (e.g. American Society of Clinical Hypnosis), to the best of our knowledge there are not yet published best-practice guidelines for employing mind-body therapy with cancer patients.

This means further research is clearly needed. The number of adequately powered, randomized, and appropriately controlled studies are too few. Future research should involve studies with an active control group (e.g. psycho-education or structured-attention). Also, future studies of mind-body interventions for stress reduction in cancer care should include psychophysiological measures of stress in addition to self-report measures. In many of the current studies, self-report measures are relied upon as primary outcomes. While these measures provide good evidence of subjective changes, physiological measures of stress and anxiety can provide an even more compelling argument for treatment efficacy.

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Chapter 8

Effect of Mindfulness-based Interventions in Cancer Care

Richard Bränström

Abstract Mindfulness meditation as an intervention to promote stress reduction has become increasingly studied and implemented over the last decade and consistently shows promising beneficial effects on psychological well-being. The development of mindfulness is integrated in several structured training programs and therapies such as mindfulness-based stress reduction, mindfulness-based cognitive therapy, as well as programs integrating mindfulness training specifically developed for cancer patients. These programs and therapies have shown promising results in improving different psychological outcomes. In particular, mindfulness-based stress reduction programs have shown a strong potential for changing peoples' experiences of stress-related complaints and increasing well-being. A meta-analysis of results from randomized controlled studies of mindfulness training among cancer patients presented in this chapter gives support for the positive effect of such interventions. Results show moderate intervention effect sizes for increased positive affective outcomes, such as quality of life and frequency of positive experiences; increases in physical health outcomes and measures of mindfulness; and reduction of negative affective outcomes such as depression, anxiety, and perceived stress.

8.1 Introduction

Mindfulness is a concept refers to a state of conscious awareness of present mental states and processes as they are here-and-now and the skills related to conscious awareness involving an observing, accepting attitude to one's own experiences (Bishop et al. 2004). Training of mindfulness skills originates from Eastern

R. Bränström (✉)

Department of Clinical Neuroscience and Department of Public Health Sciences,
Karolinska Institute, Stockholm, Sweden
e-mail: Richard.Branstrom@ki.se

meditation traditions, but during the past decades mindfulness has increasingly been used and integrated into Western forms of stress management interventions and different types of psychotherapy.

The two main components of mindfulness – a self-regulation of awareness towards present mental states and a non-evaluative openness and acceptance towards moment-to-moment experiences – can be trained by practicing various forms of meditation or through mental exercises (Kabat-Zinn 1990). The development of mindfulness is integrated in several structured training programs and therapies such as mindfulness-based stress reduction (MBSR) (Kabat-Zinn 1990), mindfulness-based cognitive therapy (MBCT) (Segal et al. 2002), dialectical behavior therapy (Linehan 1993), as well as acceptance and commitment therapy (Hayes 2005). These programs and therapies have shown promising results in improving different psychological outcomes. In particular, mindfulness based stress reduction programs have shown a strong potential for changing peoples' experiences of stress-related complaints and increasing well-being (Baer et al. 2006; Bishop 2002; Bishop et al. 2004; Carlson et al. 2001; Grossman et al. 2004; Ott et al. 2006; Shapiro et al. 2006; Smith et al. 2005; Speca et al. 2000).

Among patients with cancer and cancer survivors several different interventions and therapies have been used to reduce stress and symptoms related to the diagnosis and treatment of their disease. In particular, the MBSR meditation program developed by Jon Kabat-Zinn (1990) and his colleagues at the Stress Reduction and Relaxation Clinic, Massachusetts Medical Center, and different adaptations of this program have been used. It has been shown to have potential to decrease stress and depression in cancer populations. It has shown positive effects on quality of life (QoL) and decreased stress symptoms in patients with varying cancer diagnoses. Studies have also shown promising results of MBSR programs on sleep disturbances among cancer patients.

In this chapter, a summary of current findings regarding mindfulness-based interventions for cancer patients are presented along with a description of the current knowledge regarding potential mechanisms and a suggested theoretical framework.

8.2 Mindfulness-based Programs for Cancer Patients

8.2.1 MBSR Program

The MBSR program is the most widely used mindfulness program. The program was developed by Kabat-Zinn and his colleagues (1990) at the Stress Reduction and Relaxation Clinic, Massachusetts Medical Center, USA. It was originally developed for patients with chronic pain, but has been applied for patients with a wide variety of medical diagnoses. It is a group-based program with up to 30 participants, and it involves 8–10 weekly sessions and consists of experiential and group exercises. During the program, the theoretical foundations of mindfulness regarding relaxation,

meditation, and the body-mind connection are described. A variety of meditation, relaxation and yoga exercises are practiced during group sessions and at home. Participants are encouraged to practice meditation six days a week at home using an instruction tape during the 8-week period. Training involves body scan meditation, sitting and walking meditation and yoga exercises. The group process is focused on solving problems and challenges regarding successful meditation practice and the everyday application of mindfulness, and learning from each other's experiences. An example of a suggested week-to-week schedule of a MBSR program is presented in Table 8.1.

8.2.2 MBCT

MBCT was developed by Segal et al. (2002) at the University of Oxford and is largely based on the MBSR-program. It is also an 8-week group-based intervention, and follows a manual combining mindfulness training with elements of cognitive therapy. MBCT was originally developed as an approach to prevent depression relapse, but has since been applied to a larger variety of mental complaints such as bipolar disorder, suicidal behavior, and social phobia (Keng et al. 2011), as well as for cancer patients (Foley et al. 2010). Similarly to cognitive behavioral therapy, MBCT puts its focus on helping participants to view thoughts as mental events rather than as facts and to recognize maladaptive automatic thoughts that maintain depressive symptoms (Segal et al. 2002). The difference from traditional cognitive behavioral therapy lies primarily in the emphasis put in MBCT on changing participants' awareness of and relationship to thoughts and emotion, rather than trying to change the content of thoughts and encouraging the development of alternative thoughts. The theoretical assumption is that mindfulness meditation facilitates loosening the association between dysfunctional thoughts and negative emotions.

8.2.3 Variations of Mindfulness-based Interventions

There are a number of alternative mindfulness-based intervention programs that have been developed with influence from MBSR and MBCT programs. Some of these have also been applied among cancer patients. A program independently developed but similar to the MBSR specifically developed for use among cancer patients, mindfulness-based cancer recovery has been developed at the University of Calgary, Canada (Carlson et al. 2010). This program closely resembles the MBSR program but is specifically adjusted for patients with a cancer experience (Specia et al. 2000). Another variant of a mindfulness-based intervention used for cancer patients is mindfulness-based art therapy (MBAT). This program integrates mindfulness meditation training with art therapy within an 8-week supportive group therapy (Monti et al. 2006). The program includes opportunities for both verbal and non-verbal communication and is intended to increase emotion regulation capacity.

Table 8.1 Brief description of a suggested week-to-week schedule of a MBSR program

Week	Theoretical content and group discussions	Practical exercises and homework assignments
1	Introduction to the program and the schedule. Explanation of home assignments and its purpose. Introduction to the concept of mindfulness and its theoretical base.	Introductory mindfulness exercise. The body scan exercise. Distribution of course workbook and audiotapes with recorded exercises for home practice.
2	Group discussion about the experience of past weeks mindfulness practice. Introduction of the seven attitudes of mindfulness practice.	Review of homework. The body scan exercise. One hour of yoga.
3	Group discussion about the experience of past weeks mindfulness practice. Presentation and instruction to yoga exercise. Explanation of awareness and attending to one's moment-to-moment experience with a non-judging attitude.	Short sitting meditation. Description and explanation of sitting meditation homework.
4	Group discussion about the experience of past weeks mindfulness practice. Description of the importance of body posture in sitting meditation. Introduction to the anatomy of stress. Description of how to respond mindfully to stressful events as opposed to reacting automatically.	A short yoga sequence.
5	Group discussion about the experience of past weeks mindfulness practice. More information about the anatomy of stress, its effect on the body, and how to responding mindfully to stressors. A discussion of how to approach and examine emotions mindfully, non-judgmentally, and with curiosity.	Sitting meditation. One hour of yoga.
6	Group discussion about the experience of past weeks mindfulness practice. Further group discussion about styles of communication.	Sitting meditation.
7	Group discussion about the experience of past weeks mindfulness practice. Description and discussion regarding being present and calm in different situations and how to bring mindfulness into everyday life and experiences.	Sitting meditation. Yoga sequence.
8	General group discussion about the participants' experience of the program. Description and discussion about how to uphold regular practice and integrating mindfulness into everyday life.	Body scan exercise. Sitting meditation.

8.3 Effects of Mindfulness Interventions in Cancer Patients – A Meta-analysis

During the last decade, a fair amount of studies have been published that give support for positive effects of mindfulness-based interventions among cancer patients (Smith et al. 2005; Ledesma and Kumano 2009). The large majority of these studies are observational studies without a control group or lacking randomizations to control condition. Despite the methodological limitations of the studies of the effects of mindfulness interventions, there is substantial support for positive effect on indicators of well-being and physical health. To give additional strength to our knowledge about these effects, a meta-analysis of published randomized studies of mindfulness-based interventions for cancer patients was created. Searches in PubMed and PsychInfo databases with keywords “mindfulness” and “cancer” were screened for randomized controlled studies. Five studies were identified that reported adequate results from randomized controlled studies and had quantitative measures of either psychological or health outcomes. The studies reported a number of different outcomes, and for this meta-analysis, outcomes were categorized into four categories: positive affect, i.e. QoL (Monti et al. 2006; Lengacher et al. 2009; Foley et al. 2010); frequency of positive states of mind (Bränström et al. 2010); negative affect, i.e. depression (Lengacher et al. 2009; Bränström et al. 2010; Foley et al. 2010), anxiety (Lengacher et al. 2009; Bränström et al. 2010; Foley et al. 2010), perceived stress (Specia et al. 2000; Lengacher et al. 2009; Bränström et al. 2010; Foley et al. 2010), distress (Monti et al. 2006), negative mood (Specia et al. 2000), and post-traumatic stress symptoms (Bränström et al. 2010); and physical health, i.e. self-reported physical health (Specia et al. 2000; Monti et al. 2006; Lengacher et al. 2009).

The meta-analysis comprised a total of 453 individuals with a mix of different cancer diagnoses, a mean age of 54 years, and in all studies the large majority of participants were women (between 77 and 99%). All but one study (Lengacher et al. 2009) used a waiting-list control group, the control group in this study received care as usual. Details of the studies included in the analysis are presented in Table 8.2. The effect sizes were calculated based on means and standard deviation in intervention and control groups at baseline and post intervention follow-up. Fixed effects models were used to calculate effect sizes and we interpret these as small, medium, or large according to Cohen’s criteria (Cohen 1988), e.g. effect size of $d=0.20$ as small, $d=0.50$ as medium, and $d=0.80$ as large. For studies with several measures within one outcome category, an average effect was calculated within this category. Results are presented in Table 8.3.

The study by Bränström et al. (2010) reports on findings among 71 patients with varying cancer diagnoses and examined an 8-week MBSR group training program. The study showed positive post-intervention effect on perceived stress [effect size (ES)=0.63], post-traumatic avoidance symptoms (ES=0.41), and positive states of mind (ES=0.50). Further, the study showed that those who participated in the intervention reported a significant increase in mindfulness when compared to controls.

Table 8.2 Randomized controlled studies of mindfulness-based interventions for cancer patients

Study number	Author	Year published	<i>n</i>	Type of cancer	Treatment status	Percent male	Mean age	Type and duration of mindfulness training
1	Bränström et al.	2010	71	Mixed	Mixed	1	52	8-week MBSR program (2½h/session)
2	Foley et al.	2010	115	Mixed	Just over two years after initial diagnosis	23	55	8-week MBCT program (2 h/session)
3	Lengacher et al.	2009	84	Breast	Mean 19 weeks after treatment completion	0	58	6-week MBSR program
4	Monti et al.	2006	93	Mixed	Mixed	0	54	8-week MBAT program (2½h/session)
5	Specca et al.	2000	90	Mixed	Not specified	19	51	7-week MBSR program (90 min/session)

MBAT mindfulness-based art therapy, *MBCT* mindfulness-based cognitive therapy, *MBSR* mindfulness-based stress reduction

Table 8.3 Computed mean effect sizes for positive affect, negative affect, physical health outcomes, and measures of mindfulness

Outcome	No. of studies	Total (<i>n</i>)	Mean effect size (<i>d</i>)	95% confidence intervals	<i>p</i>
Positive affect	4	363	0.36	0.16–0.56	<0.001
Negative affect	5	453	0.54	0.36–0.72	<0.001
Physical health	3	267	0.40	0.16–0.63	<0.001
Mindfulness	2	186	0.62	0.32–0.91	<0.001

The increase in mindfulness mediated the effects of the intervention on perceived stress, and post-traumatic avoidance symptoms. This mediation supports the assumption that mindfulness can be increased through exercises and that this increase in mindfulness can lead to positive psychological effects. The intervention study also indicated that the stress reduction intervention influenced the HPA axis functioning. Awakening cortisol was measured and among those with initial low levels of cortisol there was a post-intervention increase in cortisol, and among those with initial high levels there was a post-intervention decreased level of cortisol indicating a “normalization” of HPA axis functioning (Bränström et al. 2012). However, longer-term follow-up of the participants did not show significant effects of the intervention as compared to controls (Bränström et al. 2011b). Suggestions for future studies include the encouragement of continued post-intervention mindfulness training and the integration of mindfulness awareness in everyday life to promote longer-term effects.

The study by Foley et al. (2010) reports on findings among 115 patients with varying cancer diagnoses and examined the effect of an 8-week MBCT program. The study showed large post intervention increases in mindfulness (ES=0.55) and clinically meaningful reductions in depression (ES=0.83), anxiety (ES=0.59), and distress (ES=0.53) among those who participated in the program as compared to the waiting-list control participants. The study gives supports for providing MBCT training among cancer patients.

The study by Lengacher et al. (2009) reports on findings among 84 patients with breast cancer and examined the effect of a 6-week MBSR program. The study showed beneficial post-intervention effects in the group that participated in the program as compared to controls. The program resulted in lower depression, fear of recurrence, and higher energy, physical functioning, and physical role functioning. The study showed clinically meaningful changes on psychological outcomes and provides support for providing MBSR training to breast cancer patients.

The study by Specia et al. (2000) reports on findings among 90 patients with varying cancer diagnoses and examined the effect of a 7-week mindfulness-based training program specifically developed for cancer patients. The study showed beneficial post-intervention effects in the group that participated in the program as compared to controls. The program resulted in lower overall mood disturbance, depression, anxiety, anger, confusion, symptoms of stress, cardiopulmonary and gastrointestinal symptoms, emotional irritability, and cognitive disorganization. Participants in the program further reported higher levels of vigor than control participants. The study showed clinically meaningful changes on psychological and health outcomes and provides support for providing MBSR training to cancer patients.

The study by Monti et al. (2006) reports on findings among 93 women with varied cancer diagnoses and examined the effect of an 8-week MBAT program. The study showed decreased post-intervention symptoms of distress and improved health-related QoL among those who participated in the program as compared to controls. The study showed clinically meaningful changes on psychological outcomes and provides support for providing MBAT training to women with a cancer diagnosis.

8.3.1 Effects on Positive Affect Outcomes

Controlled studies of the effect of mindfulness-based interventions in varying populations have found support for an increase in positive affect, satisfaction with life, and QoL among participants participating in several different programs such as MBSR (Anderson et al. 2007; Nyklicek and Kuijpers 2008; Bränström et al. 2010), MBCT (Kuyken et al. 2008; Foley et al. 2010; Godfrin and van Heeringen 2010), and MBAT (Monti et al. 2006). The meta-analysis of randomized controlled trials (RCTs) studying the effects of mindfulness-based interventions on measures of positive affect among cancer patients presented in this chapter gave an average medium effect size 0.36 on positive affect i.e. QoL and frequency of positive states of mind. This is of particular importance as positive affect has been suggested as an important facilitator promoting persistent and successful coping with stressful circumstances (Folkman and Moskowitz 2000; Folkman 2008), and an increasing number of studies give support for this assumption (Fredrickson et al. 2003; Moskowitz 2003; Moskowitz et al. 2008). However, all studies included in the meta-analysis showing an effect on positive affect had a relatively short follow-up period and reported results shortly after program completion. Only one RCT reports longer-term effects, and this study did not find significant intervention effects on positive affect at six months follow-up after baseline (Bränström et al. 2011b).

The increase in positive affect following mindfulness stress reduction training supports the use of mindfulness stress reduction training to increase well-being among cancer patients. Future research should focus on understanding which specific elements of the mindfulness training influence particular sub-dimensions of mindfulness and psychological outcomes. Studies among patients with specific cancer diagnoses at particular times after diagnosis might clarify when and for whom mindfulness interventions are the most efficient.

8.3.2 Effects on Negative Affect Outcomes

Previous controlled studies of the effect of mindfulness-based interventions conducted among populations with varying complaints have found support for decreases in negative affect such as depression, anxiety, psychological distress,

perceived stress, and post-traumatic symptoms among participants participating in several different programs such as MBSR (Shapiro et al. 1998; Speca et al. 2000; Williams et al. 2001; Anderson et al. 2007; Astin 1997; Koszycki et al. 2007; Sephton et al. 2007; Nyklicek and Kuijpers 2008; Bränström et al. 2010; Grossman et al. 2010), and MBCT (Kuyken et al. 2008; Hepburn et al. 2009; Godfrin and van Heeringen 2010; Thompson et al. 2010), and MBAT (Monti et al. 2006). The meta-analysis of RCTs studying the effects of mindfulness-based interventions on measures of negative affect among cancer patients presented in this chapter gave an average medium effect size 0.54 of negative affect, i.e. depression, anxiety, post-traumatic stress symptoms, perceived stress, distress, and negative mood. All studies included in the meta-analysis showing an effect on negative affect had a relatively short follow-up period and reported results shortly after program completion. Only one RCT reports longer-term effects, and this study did not find significant intervention effects on negative affect at six months follow-up after baseline (Bränström et al. 2011b).

Although more extended follow-up studies are needed, the results give support for a reduction of negative affective states and emotional distress in cancer patients as a result of mindfulness interventions.

8.3.3 Effects on Physical Health Outcomes

Although several smaller studies have demonstrated a potentially beneficial effect of mindfulness interventions on physical health outcomes such as sleep quality, physical well-being, and immunological functioning (Carlson et al. 2003, 2004; Carlson and Garland 2005), only a few controlled studies have shown effects of mindfulness-based interventions on physical health measures such as medical symptoms (Williams et al. 2001), activation in brain regions associated with present-focused self-reference (Farb et al. 2007), and self-reported health (Speca et al. 2000; Monti et al. 2006; Lengacher et al. 2009). The meta-analysis of RCTs studying the effects of mindfulness-based interventions on measures of physical health among cancer patients presented in this chapter gave an average medium effect size 0.40 for self-reported physical health. All studies included in the meta-analysis showing an effect on physical health outcomes had a relatively short follow-up period and reported results shortly after program completion.

Although increased body awareness might potentially increase perceived and reported bodily symptoms, no negative effects of mindfulness have been reported in the studies reviewed. Quite the opposite, the results from the current meta-analysis show increases on indicators of physical health. This is a promising result that lends support for the use of such interventions among cancer patients.

8.3.4 *Effects on Measures of Mindfulness*

A few controlled studies have reported effects of mindfulness-based interventions on different measures of mindfulness (Anderson et al. 2007; Nyklíček and Kuijpers 2008; Bränström et al. 2010). The meta-analysis of RCTs studying the effects of mindfulness-based interventions among cancer patients presented in this chapter gave an average medium effect size 0.62 on measures of mindfulness. Most studies reported an intervention effect of mindfulness training shortly after program completion. However, one RCT reports longer-term effects of mindfulness training and showed continued elevated levels of mindfulness at six months follow-up after baseline in the intervention group (Bränström et al. 2011b).

8.4 **Components of Mindfulness Meditation Interventions**

In the current research literature, there are a number of suggested theoretical models describing the mechanisms through which mindfulness interventions lead to positive outcomes.

Shapiro et al. (2006) describe a model with several components that together explains, mediates, and leads to positive effects of mindfulness training. They describe mindfulness as an inherent state of consciousness that entails “consciously attending to one’s moment-to-moment experience” (Shapiro et al. 2006). Reaching this state is enabled by practicing mindfulness and they describe three axioms that they see as essential building blocks of mindfulness: intention, attention, and attitude. Intention refers to the individual reason behind the initiation and continuation of a mindfulness practice. Attention refers to the self-regulation of attention to internal and external experiences as they unfold in the present moment. Attitude refers to the feelings and thoughts we attach to the experience we encounter as we attend mindfully, with an aim to cultivate a non-evaluative, accepting and curious attitude towards these experiences. They do not see the three axioms as separate processes but rather as simultaneous, interwoven processes that together account directly or indirectly for positive change related to mindfulness practice (Shapiro et al. 2006).

A number of related but more specific processes are described by Brown et al. (2007). They put a focus on the nature of consciousness and its relevance for mindfulness interventions and propose that insight, exposure, non-attachment, enhanced mind-body functioning, and integrated functioning are fundamental processes in the effects to mindfulness practice. According to Brown et al. (2007), practice of being mindful leads to an ability to pay attention in a new way, permitting a more direct contact with phenomena such as thought, emotions, sensations, and events as they occur, with less influence by habitual thought patterns and judgments. An ability to perceive events more objectively and to respond psychologically and behaviorally in a less automatic way is cultivated.

A third model describing the mechanisms of mindfulness has been presented by Baer et al. (2006). She developed a scale to capture different components of

mindfulness, the Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al. 2006, 2008). The instrument was developed by use of an exploratory factor analytic study of five independently developed mindfulness questionnaires. The analysis yielded five factors that appear to represent elements of mindfulness. The five facets were observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience (Baer et al. 2006). Several studies of the validity of the FFMQ supports the possibility to assess mindfulness by means of self-report and has shown a positive relationship between mindfulness and meditation experience (Baer et al. 2008), as well as a buffering effect of mindfulness on the negative effects of stress on psychological and health outcomes (Bränström et al. 2011a).

8.5 Mechanisms of Mindfulness Interventions – A Theoretical Framework

There are several possible pathways through which mindfulness might influence psychological functioning. Being mindful may lead to a view of thoughts and feelings as being transient, allowing the individual to view cognitions as “just thoughts” and affects as “just feelings”. This perspective may lead to less automatic thought patterns and rumination and can lead to more effective affect regulation and reduced reactivity to unpleasant states. Mindfulness also involves an acceptance of being with what is as opposed to having the need to alter present unpleasant states and striving towards future, more pleasant goals. This focus on being content with the present situation without constantly striving towards future possible states might in itself generate a greater sense of well-being and happiness that is not conditional on experience. Mindfulness might also promote physical and mental health through the promotion of relaxation and reduction of experiences of heightened physiological stress reactivity. Studies trying to measure different aspects of mindfulness have found increases in mindfulness to mediate the effect of MBSR programs (Nyklicek and Kuijpers 2008; Bränström et al. 2010).

Studies have further indicated an increase in rational decision-making among practitioners of regular mindfulness meditation (Kirk et al. 2011) and greater emotional information processing (Roberts-Wolfe et al. 2012). Of particular importance for the effects of mindfulness on psychological functioning has been the concept of self-compassion. Self-compassion has been described as entailing three major components: self-kindness (being kind rather than self-critical to oneself in instances of perceived inadequacy); common humanity (to see oneself as part of a greater whole rather than as separate and isolated); and mindfulness (in this case to view cognitions as “just thoughts” and affects as “just feelings” without over-identifying with them) (Neff and Vonk 2009). Without being an explicit goal, self-compassion is implicitly integrated into mindfulness-based programs. Although the mechanism of mindfulness is not yet well understood, some studies have found self-compassion to mediate the effect of MBCT on depressive symptoms (Kuyken et al. 2008).

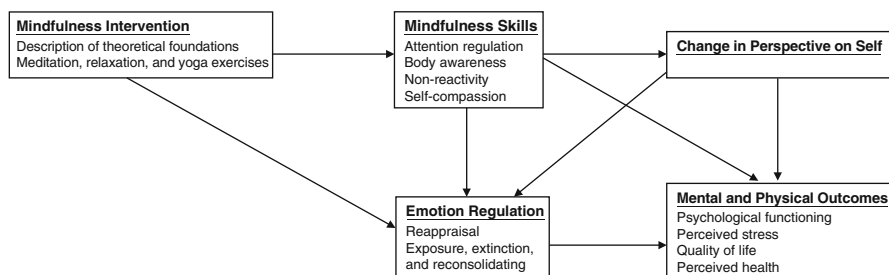


Fig. 8.1 Illustration of a proposed theoretical framework for the mechanisms behind the effects of mindfulness interventions

In a recent review of the mindfulness literature Hölzel et al. (2011) propose a comprehensive theoretical framework integrating earlier suggested models. They suggest that four main components, in combination, can describe the mechanisms behind how mindfulness works: attention regulation; body awareness; emotion regulation, including reappraisal and exposure, extinction, and reconsolidation; and change in perspective on the self. Hölzel et al. (2011) suggest that together these components interact to improve self-regulation. A fuller description of their framework is presented in their article “How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective” (Hölzel et al. 2011) but a summary of each component is provided below. An illustration of the proposed theoretical model, its components, and the relationships between these components are presented in Fig. 8.1.

8.5.1 Attention Regulation

Focused attention is a fundamental aspect of meditation and in mindfulness practice. To increase ability to develop focused attention, practitioners are instructed to continuously pay attention to a specific object or sensation. Even if the mind wanders off, the practitioner is encouraged to return their focus to the chosen object or sensation. In mindfulness meditation, a focus on breathing is an essential starting point for this type of attention training. Participants in mindfulness meditation are typically instructed to focus their attention to their breath without being distracted, the air moving in and out, and the sensation of breathing. If the mind wanders off, they are instructed to make a mental note and return to focusing on their breathing. Self-report studies as well as some studies using cognitive tests and neuroimaging techniques, support the idea that mindfulness meditation practice increases the ability to disregard distractions and direct attention to relevant stimuli, and may lead to enhanced executive attention and attention regulation (Hölzel et al. 2011).

8.5.2 Body Awareness

Body awareness relates to the ability to pay attention to sensations and changes in the body. Exercises to increase the ability to notice bodily sensations are an important ingredient in mindfulness practice. These exercises often focus on the sensation of breathing, walking, scanning the body for tensions and sensations, as well as on integrating body awareness into everyday life. Some self-report studies give support for increased body awareness as a result of participation in mindfulness training programs (Carmody et al. 2008; Bränström et al. 2010). It is hypothesized, and some studies support the idea, that a higher degree of body awareness is related to and facilitates emotion regulation, and increases empathic responses (Hölzel et al. 2011).

8.5.3 Emotion Regulation

Emotion regulation is a complex and multi-componential process in which choice of situations, perception of situation, selective interpretation and appraisal of situation, and response modification can happen automatically or controlled, conscious or non-conscious (Gross 2007). Depending on a person's individual goals, emotion regulation can lead to strengthening, weakening, or maintenance of emotions. Increased awareness of emotional sensation and increased ability to direct attention with less distraction is thought to enhance peoples' ability to successfully regulate emotions. Hölzel et al. (2011) suggests that mindfulness increases the ability to regulate emotions, in particular through two regulatory processes: reappraisal and extinction.

Reappraisal is a process by which a stressful stimuli or situation is interpreted cognitively in a new and less stressful or threatening way so as to change its emotional impact (Gross 2007). A stressful event is seen as neutral, unthreatening, or even beneficial instead of as harmful. Mindfulness is thought to facilitate reappraisal and the process by which an initial appraisal of a threat is reinterpreted and seen in a different light by increased meta-cognitive ability (Garland et al. 2009). Meta-cognition involves taking a mental step back from thoughts and emotions, and thus facilitates reevaluation or shifting of perspectives.

When practicing mindfulness, individuals are instructed to focus their attention to thoughts, feelings, and emotions with an accepting and curious attitude, without direct reactivity. Training involves meeting both pleasant and unpleasant emotions by turning towards them, rather than turning away (Hölzel et al. 2011). This way of exposing yourself to unpleasant emotions when in a relaxed state and in safe circumstances is hypothesized to promote extinction of threatening emotions. Both the increased relaxation associated with mindfulness meditation and the increased attention regulation skills are thought to facilitate extinction as an emotion regulatory strategy. The ability to expose oneself to internal thoughts and feelings without direct reactivity has been measured with the "non-reactivity

to inner experience” – subscale in the FFMQ, and has been shown to increase substantially as a result of participation in a mindfulness training intervention (Bränström et al. 2010).

8.5.4 *Change in Perspective on the Self*

The fourth and last component that describes the mechanisms behind how mindfulness works according to Hölzel et al. (2011) is change in perspective on the self. This refers to a view of the self as transient rather than static. This change is enabled by increased meta-awareness generated by mindfulness training. According to this view internal awareness becomes enhanced through meditation, and this enhanced awareness leads to the ability to observe mental processes with increased clarity and the sense of self can be experienced as an event rather than a static entity (Hölzel et al. 2011). The consequences of this change in perspective on the self is a more positive view of oneself, greater self-esteem, and a more accepting attitude towards ones’ emotional reactions and thoughts. An interview study of cancer patients participating in an 8-week MBSR training program gave support for the significance of the accepting attitude promoted by the program and training, as patients mentioned these aspects of mindfulness as important in interviews after the program (Kvillemo and Bränström 2011).

8.6 Clinical Significance

Getting a cancer diagnosis is coupled with many different stressful experiences both physically and emotionally. In addition to the excessive physiological stress caused by the disease and its treatment, many patients experience psychological stress regarding worries about diagnosis and prognosis, demanding treatments and treatment decisions, and disruption of ordinary life functions and roles (McGregor and Antoni 2009). Following treatment, patients commonly report psychological complaints such as depressive symptoms, anxiety, symptoms of stress, sleep disturbance, fear of recurrence, fatigue, and decreased QoL. Although many of these complaints may resolve over time, many patients experience extended suffering. A recent US study of long-term cancer survivors reported an increased prevalence of serious psychological distress in cancer survivors even among those who had been disease free for five years or more as compared to the general population (Hoffman et al. 2009). That study also showed that long-term psychological distress was more prevalent among those with less education and much more prevalent among younger cancer patients [odds ratio (OR)_{≥65 years}, 95% confidence interval (CI) (reference value); OR_{45–64 years}, 95% CI=2.7 (1.8–4.0); OR_{<45 years}, 95% CI=5.6 (3.3–9.5)].

The findings from the studies included in the current meta-analysis are relevant for clinical practice as they indicate reduced psychological distress and increases on indicators of physical health among patients with a mix of cancer diagnoses. Even though the overall effect sizes were moderate, a reduction of psychological stress in conjunction to a cancer diagnosis and treatment are valuable and should be recommended. Foley et al. (2010) report clinically significant reductions in depression, anxiety, distress, and increased QoL compared to a waiting list control group. Similar results with reduction in perceived stress, post-traumatic stress symptoms, and increased positive affect was reported by Bränström et al. (2010). Clinical meaningful changes with improved psychological status and QoL in MBSR participants as compared to those treated with usual care were also reported by Lengacher et al. (2009). Monti et al. (2006) reported clinically significant reductions in symptoms of distress as well as increases in QoL measures among participants in a mindfulness training program as compared to wait-list controls. Finally, Specia et al. (2000) reported reduction in depression, anxiety, anger, confusion, and overall symptoms of stress, as well as an increase in vigor, among MBSR participants as compared to controls.

8.7 Integration of Mindfulness Meditation in Cancer Care, and Future Directions

Although mindfulness-based interventions for cancer patients holds great promise for reduction of negative mental and physical consequences of a cancer diagnosis, more high quality studies of mindfulness-interventions for cancer patients with active control groups, longer follow-ups, and studies among both men and women are needed to clarify issues such as for whom, when and exactly how mindfulness interventions can be most effective. Further studies should examine questions related to the implementation of mindfulness-based interventions in health care settings such as: Which patients benefit the most from participation in mindfulness training, e.g. type of cancer, disease stage? At what stage in the cancer treatment process should programs be offered? What is the optimal length of a mindfulness-based program? Are there alternative means of program delivery than group based programs e.g. internet-based interventions?

These questions are yet to be answered before we can fully and successfully integrate mindfulness interventions into cancer care. However, the relative low risk with providing patients with this type of treatment coupled with the increasing scientific support for such interventions gives no reason to discourage dissemination and implementation of mindfulness practice in cancer care. To facilitate dissemination and increase the availability of this type of treatments, the development of manual-based easily administered individual, group, and internet-based interventions should be encouraged.

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Chapter 9

Aromatherapy, Physical and Movement-based Therapies on Symptom Management for Cancer Patients

Deborah H. Ndao, Michelle Bombacie, and Diane Rooney

Abstract Aromatherapy, physical and movement-based therapies have been used for centuries to promote health and well-being and manage both physical and psychological conditions. A large number of cancer patients have diminished levels of physical activity and suffer from various types of discomfort, including constipation, shortness of breath, anxiety, negative mood states, sleep disturbances, and fatigue. Randomized controlled trials provide evidence for the use of aromatherapy massage to reduce anxiety, relieve constipation, and improve quality of life, though trials investigating the use of the respiratory administration of aromatherapy among cancer patients have found limited use during radiation therapy and stem cell transplantation. Emerging evidence supports a variety of physical and movement-based therapies for relieving fatigue and improving quality of life, physical conditioning, and aerobic capacity among cancer patients. This chapter summarizes the evidence on the effectiveness of aromatherapy and select physical and movement-based therapies for use as supportive care for cancer patients. Actual case scenarios provide examples for integrating these therapies into clinical oncology care.

9.1 Introduction

The practice of using plants and their essential oils for medicinal, healing, cosmetic, and religious purposes can be traced back more than 5,000 years to ancient Egypt and India (Ball et al. 2009). Later, Hippocrates (460–377 BC) used aromatic fumigation to rid the Greeks of the plague, and after the fall of the Roman Empire, the Arabian Empire was credited in perfecting the distillation process of essential oils.

D.H. Ndao (✉) • M. Bombacie • D. Rooney
Integrative Therapies Program, Division of Pediatric Oncology/Blood
and Marrow Transplantation, Columbia University Medical Center,
161 Fort Washington Avenue, 7th Floor, Room 728, New York, NY 10032 USA
e-mail: dh493@columbia.edu

During the renaissance period, Paracelsus (1493–1591) believed in using plants and their oils as medicine.

Modern day aromatherapy and the use of essential oils are credited to a French chemist and perfumer, Rene Maurice Gattefosse. Although not a believer of the natural health movement, Gattefosse was interested in the properties that essential oils exhibited. In 1910 he burnt his hand in a lab explosion and immediately immersed it in a vat of undiluted lavender essential oil. The pain subsided and by the next day, there was no physical sign of the burn. During the Second World War, Dr. Jean Valet, who was running out of antibiotics, learned of Gattefosse's experiments and started treating his soldiers with essential oils; he discovered most, if not all essential oils, had anti-microbial and anti-bacterial properties.

Essential oils are aromatic volatile liquids that have been distilled from flowers, trees, roots, bushes, barks, seeds, resin, and the rinds of some fruits. The chemical compounds of essential oils, including terpenes, esters, aldehydes, ketones, alcohols, phenols, and oxides, consist of secondary metabolites found in various plant materials and are responsible for the particular fragrances and characteristic odors. The most common form of distillation is steam distillation; other methods include soaking in boiling water, cold-pressing, soaking in alcohol and effleurage, a process in making perfume in which odorless fats or oils absorb the fragrance of fresh flowers.

9.2 Aromatherapy

Aromatherapy refers to the therapeutic use of essential oils. These highly concentrated aromatic substances are either inhaled or applied to the skin during a massage, in a bath, or as a perfume. For application to the skin, essential oils are combined with another substance, such as carrier oil, including almond, jojoba, hemp, and grapeseed oils. When essential oils are inhaled, scent receptors in the nose send chemical messages to the olfactory bulb and then amygdala and limbic system, which produce characteristic effects on target tissues, influencing emotional response, heart rate, blood pressure, and respiration (Lis-Balchin 1997) (Fig. 9.1). Functioning magnetic resonance imaging have supported this claim that the odorant molecules influence the limbic system and its emotional pathways. However, there is also a belief that the effects may partly depend on a person's previous associations or experiences with a particular scent.

Preclinical and clinical studies on aromatherapy have been conducted. Studies on the effects of essential oils have found some to have significant anti-microbial, antiviral, fungistatic, and fungicidal activity (Aridogan et al. 2002; Minami et al. 2003; D'Auria et al. 2005). Additionally, preclinical studies in rats have shown that exposure to various odors can result in stimulation or sedation, as well as changes in behavioral responses to stress and pain. A study on the sedative effects of essential oils and other fragrance compounds (mostly individual chemical components of the oils) on rat motility showed that Lavender essential oil in particular had a significant sedative effect (Buchbauer et al. 1993). Furthermore, studies of abdominal aromatherapy massage have shown to help relieve constipation in palliative care patients (Preece 2002).

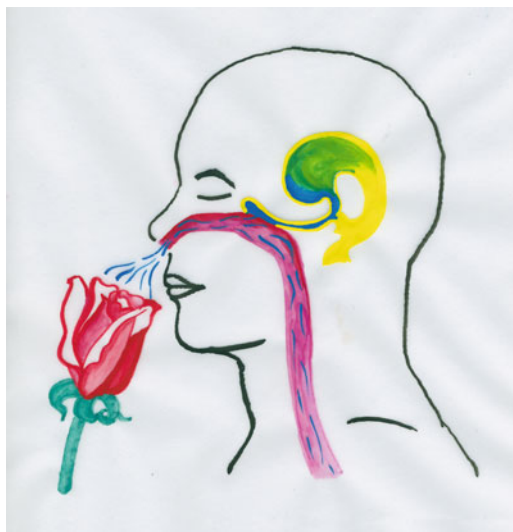


Fig. 9.1 Inhalation aromatherapy. When essential oils are inhaled, aromatic substances (aerosolized volatile odor molecules) pass through the nasal cavity and are absorbed by the nasal mucosa. Scent receptors then send chemical messages along the nervous system to the olfactory bulb and then onto the amygdala and hippocampus of the limbic system of the brain (seats of emotion and memory). Unique to different essential oils, characteristic effects on targeted tissues are produced, influencing emotional response, heart rate, blood pressure, stress levels, hormone balance, and respiration (Reproduced from Mairikke Dau. With permission)

Table 9.1 provides a clinical and evidence-based guide (research support among cancer patients and other adult groups) to using the respiratory administration of essential oils for managing select side effects of cancer treatment. Case examples 1 and 2 illustrate how cancer patients integrate aromatherapy into their clinical oncology care.

Several studies of aromatherapy interventions have been conducted among cancer patients. While some studies focus on the respiratory administration of essential oils others report on the effectiveness of the topical application of essential oils through aromatherapy massage. Although aromatherapy massage interventions among cancer patients have demonstrated some benefit in mitigating various side effects of cancer treatment, it is often unknown if the physical and psychological effects of massage alone provided the benefit, irrespective of the use of essential oils, as has been demonstrated among both healthy subjects and patients in an intensive care unit (Dunn et al. 1995; Takeda et al. 2008).

A Cochrane review of eight randomized controlled trials of aromatherapy and massage among cancer patients reported through 2002 concluded that massage and aromatherapy massage confer short term benefits on psychological well-being, with the possibility of effects on physical symptoms (Fellows et al. 2008). Since the Cochrane review, nine additional randomized controlled trials on the effectiveness of aromatherapy massage and inhalation aromatherapy among cancer patients have

Table 9.1 Essential oils and select inhalation uses for cancer patients

Need/symptom	Essential oil (botanical name)
Anxiety, fear, distress, negative mood	Orange (<i>Citrus cinensis</i>) ^a
	Frankincense (<i>Boswellia carterii</i>) ^a
	Lavender (<i>Lavendula angustifolia</i>) ^{a,b}
	Ylang ylang (<i>Cananga odorata</i>)
	Rosemary (<i>Rosmarinus officinalis</i>) ^a
	Rose (<i>Rosa damascena</i>) ^a
	Sandalwood (<i>Santalum album</i>)
	Lemon (<i>Citrus limon</i>)
	Cedarwood (<i>Cedrus atlantica</i>)
	Chamomile, German (<i>Matricaria recutita</i>) ^a
Depression	Bergamot (<i>Citrus bergamia</i>)
	Sandalwood (<i>Santalum album</i>)
	Lavender (<i>Lavendula angustifolia</i>) ^a
Fatigue	Peppermint (<i>Mentha piperita</i>)
	Spearmint (<i>Mentha spicata</i>)
	Lemon (<i>Citrus limon</i>)
	Bergamot (<i>Citrus bergamia</i>)
	Lavender (<i>Lavendula angustifolia</i>) ^b
	Blend: lavender (<i>Lavendula angustifolia</i>)/geranium (<i>Pelargonium graveolens</i>)/marjoram (<i>Origanum majorana</i>) ^a
Nausea/vomiting	Ginger (<i>Zingiber officinale</i>) ^{a,b}
	Chamomile, Roman (<i>Anthemis nobilis</i>)
	Peppermint (<i>Mentha piperita</i>) ^b
	Spearmint (<i>Mentha spicata</i>) ^b
	Blend: ginger (<i>Zingiber officinale</i>)/spearmint (<i>Mentha spicata</i>)/peppermint (<i>Mentha piperita</i>)/cardamon (<i>Elettaria cardamomum</i>) ^a
Procedural/acute pain	Peppermint (<i>Mentha piperita</i>)
	Wintergreen (<i>Gaultheria procumbens</i>)
	Lemongrass (<i>Cymbopogon flexuosus</i>)
	Clove (<i>Syzygium aromaticum</i>)
	Lavender (<i>Lavendula angustifolia</i>) ^a
	Frankincense (<i>Boswellia carterii</i>) ^a
Sleep disturbances, insomnia	Lavender (<i>Lavendula angustifolia</i>) ^{a,b}
	Roman chamomile (<i>Anthemis nobilis</i>)
	Frankincense (<i>Boswellia carterii</i>)
	Ylang ylang (<i>Cananga odorata</i>)
Shortness of breath	Eucalyptus (<i>Eucalyptus globules</i>)
	Bay laurel (<i>Laurus nobilis</i>)
	Peppermint (<i>Mentha piperita</i>)
	Myrtle (<i>Myrtus communis</i>)

^aResearch evidence in other adult groups^bResearch evidence in cancer

been published. Table 9.2 reviews the outcomes of these additional studies. Adverse events among the studies reviewed included rash following aromatherapy massage (Wilcock et al. 2004) and sweet orange essential oil eliciting a stimulatory effect on the cardiovascular system when used during stem cell infusion (Potter et al. 2011). Several of the studies included in Table 9.2 are discussed in more detail.

In one of the earliest randomized controlled trials investigating the effects of plain massage as compared to aromatherapy massage, patients with heterogeneous cancers (mean age 53.5; M=9, F=78) attending a palliative care center as inpatients or outpatients were randomly assigned to receive three massages using carrier oil (plain massage group) or three massages using carrier oil plus Roman chamomile essential oil (aromatherapy massage group) over three consecutive weeks (Wilkinson et al. 1999). Two weeks after the massage, there were significant reductions in anxiety in the aromatherapy massage group ($p < 0.001$) (as measured by the State-Trait Anxiety Inventory) and an improvement in symptom scores (as measured by the Rotterdam Symptom Checklist): psychological ($p < 0.01$), quality of life (QoL) ($p < 0.001$), severe physical ($p < 0.001$), and severe psychological ($p < 0.01$). The plain massage group showed improvement on psychological, severe psychological, and QoL subscales but the improvements were not statistically significant.

A randomized, single-blinded pilot study investigated the effect of five consecutive days of aromatherapy massage (15–20 min) as compared to plain massage and a control group on constipation and QoL among advanced cancer patients, primarily lung cancer patients (age range 37–82; M=24, F=8) (Lai et al. 2011). Choice of essential oils and base oil were suggested by an aromatherapist; essential oils included bitter orange, black pepper, rosemary, marjoram, and patchouli. As measured by the Constipation Assessment Scale (CAS), constipation scores improved in the aromatherapy massage group (mean difference = -4.16) and plain massage group (mean difference = -2.64), but worsened in the control group (mean difference = +1). Participants in the aromatherapy massage group showed significant improvements in the frequency of bowel movements; there were significant differences in the total number of bowel movements per five days between the aromatherapy massage group and plain massage group ($p < 0.01$), aromatherapy massage group and control group ($p < 0.01$), and plain massage group and control group ($p < 0.05$). Intergroup comparisons, as measured by the McGill QoL for Hong Kong Chinese (MQOL-HK), also demonstrated significant decreases in constipation severity ($p = 0.002$) and improvements in general QoL ($p = 0.028$), physical domain ($p = 0.001$), and support domains ($p = 0.011$); on the other hand, the plain massage group only had improvements in the psychological ($p = 0.016$) and support ($p = 0.027$) domains. Use of massage, with or without aromatherapy stimulated bowel motion and improved QoL, though aromatherapy massage showed greater improvements.

Two clinical trials on the practice of the respiratory administration of essential oils have been conducted among adult cancer patients. One study evaluated aromatherapy during stem cell infusion and the other during radiation therapy. A placebo-controlled, double-blind, randomized trial investigated the effects of inhalation aromatherapy on anxiety during radiation therapy (Graham et al. 2003). A total of

Table 9.2 Use of aromatherapy massage and inhalation aromatherapy as supportive care in cancer and palliative care: table of clinical studies (2003–current)

Study	Design	Subjects	Intervention	Key outcome results
Graham et al. (2003)	Cancer patients undergoing radiation therapy Double-blind randomized controlled clinical trial	<i>N</i> = 313; mean age, 65	Type and duration: Inhalation aromatherapy; necklace; three drops of oil applied before radiation treatment; exposure 15–20 min Aromatherapy group = lavender, bergamot, cedarwood Control group = fragrant carrier oil Control group = non-fragrant carrier oil	Aromatherapy group = no improvements in somatic and psychological health or depression Fragrant carrier control group = no improvements in somatic and psychological health or depression Non-fragrant carrier oil control group = improvements in anxiety scores compared with either of the fragrant arms
Kohara et al. (2004)	Advanced cancer patients Non-randomized clinical trial	<i>N</i> = 20; median age, 64	Type and duration: Aromatherapy massage, footsoak and reflexology; two drops of oil 3-min footsoak + essential oil/carrier oil 10-min reflexology Aromatherapy group = lavender + jojoba carrier oil	Aromatherapy group = improvements in total fatigue scores, and physical and cognitive fatigue subscales at both 1 and 4 h after treatment; no improvement in affective fatigue subscale 1 or 4 h after treatment
Soden et al. (2004)	Advanced cancer patients Randomized, non-blinded controlled clinical trial	<i>N</i> = 42; median age 73 Aromatherapy massage: <i>n</i> = 16 Massage: <i>n</i> = 13 Control group: <i>n</i> = 13	Type and duration: Aromatherapy massage, 4 weeks × 30 min/week Aromatherapy massage group = lavender + sweet almond carrier oil Massage group = sweet almond carrier oil Control group = standard care	Aromatherapy massage group = improvements in pain scores after second massage treatment only; improvements in sleep scores Massage group = improvements in pain scores after second massage treatment only; improvements in sleep scores; improvements in depression scores after second and fourth massage treatment Control group = decline in sleep scores

Wilcock et al. (2004)	Advanced cancer patients Randomized, non-blinded controlled clinical trial	N=46 Aromatherapy massage: n=11 Control group: n=18	Type and duration: Aromatherapy massage, 4 weeks x 30 min/week Aromatherapy massage group= lavender + chamomile + sweet almond carrier oil Control group= standard care	Aromatherapy massage group = no improvements on overall total mood disturbance, quality of life, or physical symptoms; non-significant improvement in mood in all but vigor subscale Control group = no improvements on overall total mood disturbance, quality of life, or physical symptoms; non-significant improvement in mood in all but confusion (deteriorated) and vigor (unchanged) subscales
Wilkinson et al. (2007)	Cancer patients > 3 months prognosis Randomized, single-blinded controlled clinical trial	N=288; mean age, 52.1 Aromatherapy massage: n=144; mean age, 51.5 Control group: n=144; mean age, 52.8	Type and duration: Aromatherapy massage, 4 weeks x 1 h/week Aromatherapy massage group= treatment protocol included 20 essential oils Control group= standard care	Aromatherapy massage group= improvement in clinical anxiety and/or depression at six weeks but not ten weeks when compared to control group; greater improvement in self-reported anxiety at six and ten weeks post-randomization; no improvement in self-reported depression, pain, fatigue, nausea and vomiting, and global quality of life at six and ten weeks post-randomization Control group = no improvement in self-reported depression, pain, fatigue, nausea and vomiting, and global quality of life at six and ten weeks post-randomization

(continued)

Table 9.2 (continued)

Study	Design	Subjects	Intervention	Key outcome results
Potter et al. (2011)	Cancer patients receiving autologous stem cells in ambulatory setting Randomized single-blinded controlled clinical trial	<i>N</i> = 60 Aromatherapy group: <i>n</i> = 23 Orange group: <i>n</i> = 19 Control group: <i>n</i> = 18	Type and duration: Inhalation aromatherapy; three drops of oil inhaled prior and during infusion Aromatherapy group = sweet orange Orange group = sniff or taste orange cut into quarters Control group = deep breathing	Aromatherapy group = increase in heart rate of greater than 20 beats/min; no improvement in tickle/cough or nausea Orange group = improvement in perception of relief with intervention; lower symptom intensity in participants <90 kg; no improvement in tickle/cough or nausea Control group = no improvement in tickle/cough or nausea
Lai et al. (2011)	Advanced cancer patients with constipation Randomized single-blinded controlled clinical trial	<i>N</i> = 45 Aromatherapy massage: <i>n</i> = 13; age range, 37–82 Massage: <i>n</i> = 11; age range, 37–82 Control group: <i>n</i> = 8; age range, 37–82	Type and duration: Aromatherapy abdominal massage, daily × five days, 15–20 min/day Aromatherapy massage group = bitter orange, black pepper, rosemary, marjoram, and patchouli + olive carrier oil Massage group = plain abdominal massage Control group = standard care	Aromatherapy massage group = improvement in total constipation scores; improvements in total number of bowel movements and physical domain of quality of life between plain massage and control groups; improvement in support domain of quality of life between control group Massage group = improvement in total constipation scores; improvements in total number of bowel movements between control group Control group = decline in total constipation scores

Serfaty et al. (2012)	Cancer patients >6 months prognosis with anxiety or depression Randomized single-blinded controlled clinical trial	N=39; mean age, 52.5 Aromatherapy massage: n=20; mean age, 51.1 Control group: n=19; mean age, 54.0	Type and duration: Aromatherapy massage, offered up to 8 x 1-h sessions over ten weeks Aromatherapy massage group=choice of 20 essential oils Control group=cognitive behavior therapy	Aromatherapy massage group=improvements in total mood, depression, and anxiety scores; improvements in the way generally felt in the last week Control group=improvements in total mood, depression, and anxiety scores
Ndao et al. (2012)	Children and adolescents receiving stem cell infusion for malignant and non-malignant disorders Double-blind randomized controlled clinical trial	N=40 Aromatherapy group: n=17; mean age, 11.7 Control group: n=20; mean age, 12.8	Type and duration: Inhalation aromatherapy, diffuser; four drops of oil/h Aromatherapy group=bergamot Control group=fragrant shampoo	Aromatherapy group=greater anxiety and nausea upon completion of infusion and 1 h post-infusion; Pain no longer significant 1 h post-infusion Control group=improvement in anxiety and nausea upon completion of infusion and 1 h post-infusion

313 patients receiving radiation therapy (age range 33–90; M=163, F=150) were randomly assigned to one of three groups: carrier oil with fractionated oils, carrier oil only, or pure essential oils of lavender, bergamot, and cedarwood. All three groups received the oils by inhalation during their radiation therapy. There were no reported significant differences in depression or psychological effects between groups, as measured by the Hospital Anxiety and Depression Scale (HADS) or Somatic and Psychological Health Report (SPHERE). Only the carrier oil only group showed a statistically significant decrease in HADS anxiety scores compared with the other two groups ($p=0.04$).

A randomized single-blinded study evaluated the efficacy of an aromatherapy intervention for reducing symptom intensity of nausea, retching, and/or coughing among adult cancer patients receiving stem cells preserved in dimethyl sulfoxide (age range 40–60+; M=44, F=16) (Potter et al. 2011). The study found that an intervention of tasting or sniffing sliced oranges was more effective at reducing symptom intensity than sweet orange essential oil inhalation aromatherapy or deep breathing ($p=0.032$), as measured on a full-digit numerical scale from 0 to 10.

Safety testing on most essential oils has shown minimal adverse effects, though repeated exposure to lavender and tea tree essential oils by topical administration was shown in one study to be associated with reversible prepubertal gynecomastia (Henley et al. 2007). The effects appear to have been caused by estrogenic and anti-androgenic activities of lavender and tea tree oils. Avoiding these two essential oils is recommended in patients with estrogen-dependent tumors. However, this is the first published report of this type of adverse effect when using products containing tea tree or lavender essential oils.

Case Example 1 Aromatherapy for Anxiety and Stress

Patient: Catherine, a 58-year old woman with metastatic melanoma experiencing anxiety. **Chief complaint:** With a history of anxiety prior to being diagnosed with cancer, Catherine's anxiety and stress levels became extreme as she felt completely out of control and full of fear. She resisted joining a support group because the group environment only made her feel more anxious. **Treatment:** Still anxious after one month of taking a benzodiazepine prescribed by her doctor, Catherine wanted to incorporate a complementary therapeutic modality within her daily routine. She decided to set aside time for an evening bath with either Roman chamomile (*Chamaemelum nobile*) or rose (*Rosa damascene*) essential oil every day. After her bath, Catherine practiced a visual imagery exercise which further helped slow her breathing and heartbeat, resulting in uninterrupted sleep. Catherine woke up refreshed and grounded allowing her to face the day's stresses with a renewed and less anxious perspective.

Case Example 2 Aromatherapy for Headaches

Patient: Isaac, a 52-year old man with glioblastoma multiforme complaining of severe debilitating headaches. Chief complaint: Isaac's headaches could not be fully relieved with prescription medications. The headaches were less intense but still present. He often found it difficult to be around any stimulation such as lights, television or computer games. Treatment: After consulting with his doctor and researching the benefits of aromatherapy, he decided to give essential oils a try. Isaac made an essential oil blend of four drops of wintergreen (*Gaultheria procumbens*) or peppermint (*Mentha piperita*), two drops of lavender (*Lavandula angustifolia*), three drops of German chamomile (*Matricaria recutita*), and two drops of rosemary (*Rosmarinus officinalis CT Cineole*) to help increase mental clarity and concentration. He diluted the drops with grapeseed carrier oil in a three ounce dark glass bottle. Isaac's wife would massage the blend into his feet and calf muscles daily to alleviate the pressure down away from his head. Outcome: Isaac reported that his headaches subsided immediately following the massage. After a week of this daily routine, Isaac's headaches became less frequent and he was able to come out from the dark and join in with life's daily activities.

9.2.1 Precautions and Considerations for Use of Essential Oils

- Synthetic odors produced with the same compounds are synthesized with the aid of chemical solvents and are not considered true essential oils. True essential oils are unadulterated oils derived from a plant source and are considered therapeutic grade oils. If the word "pure" is on the label, only 25% of what is on the label has to be in the bottle. If the word "natural" appears on the label, the oil may be entirely synthetic.
- Always do a patch test with an essential oil to avoid contact dermatitis, especially among patients with a history of adverse reactions to perfume and related scented products. Ylang ylang, lemongrass, jasmine, sandalwood, and clove essential oils are important contact sensitizers (Uter et al. 2010).
- Keep essential oils out of reach of children.
- Citrus oils tend to be phototoxic, therefore cover the local area in sunlight to avoid any adverse reactions.
- Essential oils should be stored in a dark glass container and kept away from exposure to direct sunlight. Keep essential oils away from open flames, sparks or electricity. Applying heat to oil may alter its therapeutic value by changing its chemical composition.
- If applying essential oils with fingers, make sure hands are washed with soap and water before handling contact lenses or touching the eyes. Oils applied to the face should also be kept away from the eyes. Never put oil directly into the ear.

- In rare cases, essential oils may be associated with other specific side effects. For more specific information about side effects associated with aromatherapy, refer to the *People's Desk Reference for Essential Oils* (People's Desk Reference for Essential Oils 1999).
- During pregnancy, avoid the following essential oils: angelica, basil, calamus, celery seed, cinnamon bark, citronella, clary sage, eucalyptus, fennel, hyssop, marjoram, nutmeg, palo santo, rosemary, sage, tansy idaho, tarragon, and wintergreen.

9.3 Physical and Movement-based Therapies

Numerous studies support aerobic exercise as an intervention to improve QoL and manage of fatigue (Mock et al. 2000; Ahlberg et al. 2003). There is also evidence that relaxation techniques can reduce anxiety, particularly related to stressful situations such as receiving chemotherapy (Vickers and Zollman 1999). Physical and movement-based therapies focus the mind on the body using an array of physical activities and breathing or meditative practices, instilling relaxation and promoting overall well-being and wellness (Larkey et al. 2009; National Center for Complementary and Alternative Medicine 2010). Often, these therapies are classified as mind-body exercise or the coupling of muscular activity with mindfulness to achieve self-contemplation (La Forge 1997). To date, there is emerging evidence of the benefits of physical and movement-based therapies as supportive care in the management of a variety of side effects and late effects of cancer treatment. Studies suggest the feasibility of these interventions and the potential of these therapies to help manage a variety of symptoms, including fatigue, QoL, pain, and stress. It has also been suggested that physical and movement-based therapies may counteract the inflammatory process of the stress response, which might have substantial health benefits if practiced regularly. Case examples 3 and 4 illustrate how cancer patients integrate physical and movement-based therapies into their clinical oncology care. Some of the most frequently used physical and movement-based therapies are: dance movement therapy (DMT), Qigong, Taichi (TC), and Pilates.

Case Example 3 Qigong for Quality of Life and Overall Strengthening

Nubia, a 68-year old female, was diagnosed with stage 1 breast cancer, encapsulated in the right breast nine years ago. This past year she relapsed with an osteosarcoma of the right clavicle and femur. In addition to receiving chemotherapy and radiation therapy, she was prescribed one month of physical therapy for her hip following a partial replacement and on-going physical therapy to increase range of motion to her right arm. Nubia endured many side effects, including lymphedema, pain, fatigue, nausea and occasional feelings of hopelessness. Fortunately, Nubia's daughter, Elizabeth, was an Amma massage

(continued)

Case Example 3 (continued)

therapist, and so she provided her mother with daily medical massage. Elizabeth also introduced her mother to Qigong to enhance her quality of life and maintain muscle tone. Performed in her wheelchair with the assistance of her daughter, Nubia practiced the Qigong lung exercise in the morning upon waking up and kidney exercise in the late afternoon before dinner. Though Nubia's right arm was restricted, she was able to execute the exercises with her left arm. She recalls her mother enjoying the movement and believed that the Qigong helped Nubia to relax, increased her circulation, and enhanced her will and strength to live before she passed away.

Case Example 4 Dance Movement Therapy and Qigong for Depression and Fatigue

Alex, an 18-year old male diagnosed with acute myeloid leukemia was isolated to a hospital room for almost one year following bone marrow transplant. No longer capable of going to high school, he missed out on participating in sports and socializing with his peers and became depressed early on in his admission. Inspired by music, Alex enjoyed participating in dance movement therapy three times a week in addition to physical therapy. With a focus on increasing his energy and decreasing his depression, dance movement therapy gave Alex an opportunity to artistically express his emotions while also maintaining his flexibility, circulation, and strength. A few months after his transplant, Alex was diagnosed with capillary leak syndrome with severe hypotension. Also suffering from peripheral neuropathy, Alex lost motivation to partake in physical therapy and became increasingly weak and bed-ridden. In an effort to maintain some physical activity, the massage therapist began incorporating 5 min of Qigong therapy into his massage sessions three times a week to improve his strength. Because he was not able to stand, the Qigong exercises were done in a seated position in bed. The kidney exercise was modified to slight rotation of the waist. Through guided breathing and meditation techniques, Alex was able to relax and feel more at ease and his motivation to interact and engage with his family and practitioners returned.

9.3.1 DMT

Dance as therapy has been valued across cultures for centuries. Involving direct expression through the body, DMT is the psychotherapeutic use of dance and movement to address the physical, emotional, social, and cognitive needs of individuals

(www.adta.org). With the premise that the body holds mental and emotional stress in the form of muscle tension and constrained body movement, DMT helps individuals express themselves through authentic movement to achieve greater self-awareness and well-being (Aktas and Ogce 2005). It is theorized that DMT, through a goal-oriented, systematic treatment process under the supervision of a trained dance movement therapist, may facilitate coping and promote physical activity among cancer patients.

Few controlled trials have rigorously evaluated DMT among cancer patients to date. A Cochrane review identified 17 experimental studies of DMT for improving psychological and physical outcomes in cancer patients, though 14 did not use a randomized controlled or quasi-randomized method of treatment allocation trial design (Bradt et al. 2011). Two randomized controlled clinical trials, using a wait-list control group design, of DMT solely among female breast cancer patients were identified ($n=68$; mean age 57). One study utilized the intervention of authentic movement (6 weekly 3-h sessions) and the other used the Lebed method™ (18 sessions over 12 weeks), consisting of gentle movement to increase lymphatic circulation. No evidence was found to support DMT for the improvement of body image in breast cancer patients; one study reported a large beneficial effect on QoL while the other reported a large beneficial effect on fatigue, though was of high risk for bias. Individually, the studies did not find DMT effected mood, distress, mental health, or shoulder range of motion or arm circumference following lumpectomy or breast surgery among cancer patients.

One recently published small, randomized controlled clinical trial found benefits of a culturally-based, mixed Greek dance, and upper body training exercise program on physical function, depressive symptoms, and life satisfaction in female breast cancer survivors (mean age 57) (Kaltsatou et al. 2011). The intervention consisted of three supervised sessions per week over a period of 24 weeks, and the control group received standard care. Significant differences between groups, favoring the intervention group, were found for both right and left handgrip strength ($p<0.001$), left but not right arm volume ($p=0.028$), 6-min walking test ($p<0.001$), and depression ($p=0.001$) and lifestyle satisfaction ($p=0.001$), as measured by the Beck Depression Inventory and the Life Satisfaction Survey; borderline differences in resting diastolic blood pressure ($p=0.052$) but not resting systolic blood pressure were found.

9.3.2 *Qigong and TC*

The concept of yin-yang, together with that of Qi (an ancient term given to what is believed to be vital energy), has permeated Chinese philosophy over the centuries. Yin and yang represent opposite but complementary qualities. Yin represents the aspect of quiescence, and yang the aspect of activity. Each thing or phenomenon can be itself and its' contrary (Maciocia 1989). Yin and yang are two stages of a cyclical movement, one constantly changing into the other, such as the day giving

way to night. In health, yin and yang are harmoniously blended in dynamic balance (Maciocia 1989). Qi can be translated as energy, vital force, or life force, which manifests simultaneously on the physical and spiritual level (Maciocia 1989). The function of Qi is to transform, transport, hold, raise, protect, and warm.

From a Chinese medical perspective, cancer can cause the blockage of Qi and blood circulation, which can lead to yin-yang imbalance, Qi and blood stagnation, and Qi deficiency. Illness is believed to result from obstruction of Qi flow, or excess or deficiency of Qi. In Chinese medicine lack of movement can also lead to the slowing down or stagnation of Qi and blood, leading to a compromised immune function and a weakening of muscle, tendons, and bones. By correcting the balance or flow of Qi, healing of the body is believed to occur. Chinese medicine based exercise therapies, like Qigong and TC, may benefit the patient by promoting the movement of Qi and blood. This is done by means of exercise, breathing, and the influence of the mind. By stimulating the meridians and Zangfu organs, exercise increases Qi and blood circulation, thereby decreasing pain, relieving stiff joints, and improving muscular strength.

9.3.2.1 Qigong

Dating back more than 3,500 years, Qigong is a vital healing modality in China, with an estimated 60 million people engaging in daily practice (Sancier 1996). The National Center for Complementary and Alternative Medicine (NCCAM) describes Qigong as a component of traditional Chinese medicine that combines movement, meditation, and regulation of breathing to enhance the flow of Qi in the body, improve blood circulation and enhance immune function (National Center for Complementary and Alternative Medicine and Health 2010). Qi refers to energy or vital life force and gong refers to work, or the process of perfecting something through time with constant work and attention. Qi and gong together mean to practice life-force exercises.

By using breathing, intention, movement, meditation, and visualization, Qigong cultivates mindful awareness of the body and is believed to enable one to manipulate Qi in one's own body, or the body of another (Kaptchuck 2000). Having similar effects as the relaxation response in where there is a return to homeostasis of the sympathetic and parasympathetic nervous systems, this balance creates reduced emotional and physical tension, decreased blood pressure, heart rate, and improved immune function. Through a 20-min meditation, the physiologic counterbalance to the fight-or-flight response, in which a deep state of mental and physiological rest, may be elicited. It is suggested that one focuses on a word, sound or phrase, allowing passive disregard of everyday thoughts (www.relaxationresponse.org). There are many forms of Qigong practice. Although these different styles exist, they share the same principle and relationship in Chinese medicine concepts (Micozzi 2011). Two styles that are appropriate to apply in the palliative care setting include medical Qigong and five elements style. In five elements style Qigong the meridians that correlate to each element are opened and closed by the physical movements of the exercise and the Qi is moved

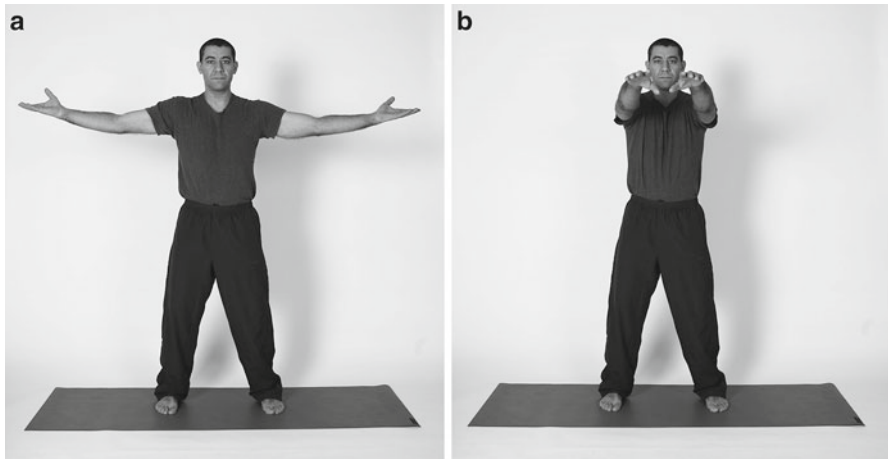


Fig. 9.2 (a) Metal (lung) exercise 1, (b) Metal (lung) exercise 2. Symptoms: grief and sadness, fatigue, immunity. According to traditional Chinese medicine, the lung Qi is related to the immune system through wei Qi. This is the protective layer of Qi which is our defensive energy. Incorporating the lung exercise helps strengthen the body's Qi in order to fight resistance. Strengthening the bodies Qi also increases energy and decreases fatigue (Reproduced from Bisio and Butler (2007). With permission)

through them by the breath. The internal organs related to each element are stimulated also through the movements and breath (Bisio and Butler 2007). Examples of two 5 elements Qigong exercises are illustrated; Fig. 9.2 demonstrates the metal (lung) exercise and Fig. 9.3 demonstrates the water (kidney) exercise.

Qigong practice does not require the ability to move into and hold various poses, and can be modified for those with limited physical ability, even those confined to bed. Patients can be taught specific Qigong practices that are useful for their illness and can be performed in a relaxed standing, sitting, or lying posture. Qigong has the advantage of being easy to learn and causes no extra physical load to patients. From a therapeutic standpoint if a patient is fatigued and weak, movements can be performed in a seated position.

Qigong is frequently used by cancer patients, but has yet to be thoroughly evaluated (Oh et al. 2010). Preliminary studies have shown that some of the benefits of Qigong are decreased heart rate, decreased blood pressure, lowered lipid levels, and enhanced immune function (Oh et al. 2010; Chen et al. 2012). There are numerous reports in the Qigong literature detailing the benefits of this modality. External Qigong, in which a passive subject has his/her Qi balanced by a trained practitioner, has been associated with health improvements. A study by Agishi (1998) found that application of external Qigong resulted in improvement of blood flow, and an increase in regional body temperature. Internal Qigong, in which the subject performs the slow and gentle movements and breathing him/herself, has been associated with enhanced relaxation and its resulting beneficial effects on cardiac and other functions. These included significant improvements in blood pressure, reduced incidence



Fig. 9.3 (a) Water (kidney) exercise 1, (b) Water (kidney) exercise 2, (c) Water (kidney) exercise 3. Symptoms: fear and shock, fatigue, immunity, cold body, will to thrive. According to traditional Chinese medicine the kidneys are directly related to the vital energy in the body. The kidneys house the essence, which is our inherited constitutional potential and are the yin and yang for the entire mind-body connection. Without this connection the life energy becomes depleted and the will to survive declines (Reproduced from Bisio and Butler (2007). With permission)

of stroke, and decreased mortality in hypertensive patients who practiced Qigong and were followed for 20 years (Kuang et al. 1991). Additionally, electrocardiogram findings and retinopathy of 152 hypertensive patients were significantly different in patients in the Qigong group surviving past 20 years from those of controls (Kuang et al. 1991).

A systematic review of nine published controlled clinical trials of the effectiveness of internal Qigong, either as a stand-alone or additional therapy in the treatment of cancer-related symptoms, was conducted through 2006 (Lee et al. 2007a). Of the

nine studies evaluated, four were conducted among advanced cancer patients and four used a randomized controlled trial design. Intervention duration and frequency was not always reported; among studies with available information ($n=4$), Qigong interventions ranged between 3 and 24 weeks in length with varying class-time intensity. The primary study outcomes measured in the randomized controlled trials were health state, survival rate, and QoL. The outcomes primarily measured in the non-randomized controlled trials included strength, appetite, diarrhea, anxiety, depression, fatigue, physical functioning, nausea and vomiting. Author conclusions on the effectiveness of Qigong varied across studies; in one report Qigong was reported as helpful to some extent in improving appetite and in another study, the authors concluded that Qigong was an effective nursing intervention to reduce fatigue and symptom burden from nausea, vomiting, and stomatitis. The review concluded that the effectiveness of Qigong had not yet been adequately measured among cancer patients.

Since the review by Lee et al. (2007a), two additional randomized controlled clinical trials on internal medical Qigong have elucidated the potential benefits of this supportive care intervention among cancer patients (Oh et al. 2008, 2010). Participants in both studies included those in active cancer treatment and those who completed cancer treatment; none reported adverse effects with the intervention. In the first study, 30 patients (age range 35–75; $M=6$, $F=24$) with heterogeneous cancers were randomly assigned to two groups: a standard care control group and an 8-week medical Qigong group with daily home practice and standard medical care. Supervised by an instructor experienced in medical Qigong and Chinese medicine, the 90-min modified intervention consisted of discussion, gentle stretching and body movement, seated postures, and breathing exercise, meditation and visualization. The medical Qigong group reported only clinically significant improved global QoL scores ($p=0.005$) and no other QoL domains scores following the intervention (as measured by the European Organization for Research and Treatment of Cancer QLQ-C30). Also, though there were symptom improvements in nausea, pain, insomnia, constipation, appetite, and diarrhea, as well as a greater reduction in C-reactive protein (inflammation marker) among the Qigong group, the differences did not reach significance.

A subsequent randomized controlled trial investigated the effect of a longer, 10-week, hospital-based medical Qigong intervention, as compared to a standard medical care, on QoL, fatigue, mood, and inflammation among 162 patients (age range 31–86; $M=69$, $F=93$) with heterogeneous cancers. As measured by the Functional Assessment of Cancer Therapy-General (FACT-G), Functional Assessment of Cancer Therapy-Fatigue (FACT-F), Profile of Mood State, between group comparisons demonstrated significant improvements in most outcomes at ten weeks follow-up. Participants in the medical Qigong group reported larger improvements in total QoL ($p<0.001$), all QoL sub-domains (physical well-being, social well-being, emotional well-being, and functional well-being) ($p<0.001$), and cancer-related fatigue ($p<0.001$). Participants in the medical Qigong group also had a greater reduction in total mood disturbance ($p=0.021$) and on four subscales: tension

and anxiety ($p=0.027$), depression ($p=0.029$), lack of vigor ($p<0.001$), fatigue (0.010), and confusion (0.056), but not with anger and hostility. Medical Qigong also showed significantly positive effects on inflammation, as measured by CRP, between groups ($p=0.044$). Dropout, possibly related to the health status of patients, was high in both groups (32% in the medical Qigong group and 35% in the control group).

9.3.2.2 TC

It is said in TC that the mind moves the energy and the energy moves the body. Based on the theory of yin and yang, TC exercises promote balance, coordination, and relaxation. Sometimes referred to as “moving meditation”, TC originated in China thousands of years ago from martial arts and breathing practices. Consisting of a series of self-initiated continuous and rhythmical slow and gentle movements, TC encourages the flow of Qi, or vital energy, and is aerobically equivalent to moderate-intensity aerobic exercise (Mansky et al. 2006). Known for improving functional balance, TC also encourages postural stability through movements that enhance control over the displacement of body mass and emphasize abdominal and lower-extremity muscle function and range of motion in the ankles, knees, and hips (Li et al. 2004). TC may also influence immune function, such as by having positive effects on regulatory T cells.

A non-systematic review of TC trials among a number of populations supports the potential benefits of TC to improve physical conditioning and reduce cardiovascular disease risk and psychological stress in adult cancer survivors (Mansky et al. 2006). In contrast, a systematic review of four clinical trials of TC as a supportive care intervention for cancer patients preliminarily recognized that TC has shown improvements in self-esteem, total distanced walked, and grip strength among adults with cancer with no adverse event, but concluded there is not yet enough evidence to support the application of this intervention (Lee et al. 2007b).

Since the review by Lee et al. (2007b), five additional reports on the effectiveness of TC among cancer patients have been published; Table 9.3 reviews the outcomes of these additional studies. Three of the five reports discuss finding on the same sample of breast cancer patients following the completion on cancer treatment, and only one study was conducted among advanced cancer patients. Attendance compliance and drop out were common, possibly due to a long intervention period, ranging from 12 to 24 weeks. Consistent with earlier findings, these new reports provide additional evidence in the application of TC for cancer patients in improving aerobic capacity and strength with no adverse effect. Additionally, the research begins to support the findings that TC may help decrease BMI, maintain stable insulin levels, and improve flexibility and quality of life among cancer survivors. Preliminarily, the research also suggests TC may improve select immune markers among cancer survivors and handicap scores and physical functioning among terminal cancer patients.

Table 9.3 Use of Taichi as supportive care in cancer and palliative care: table of clinical studies (2008–current)

Study	Design	Subjects	Intervention	Key outcome results
Mustian et al. (2008)	Breast cancer patients, 1 week – 30 months following completion of cancer treatment Randomized controlled clinical trial	<i>N</i> = 21; mean age, 52 TC group: <i>n</i> = 11 Control group: <i>n</i> = 10	Duration and frequency: 12 weeks, 3 × 60 min/week TC group = supervised yang-style TC + breathing, meditation, imagery Control group = supervised psychosocial support	TCC group = improvements at 6 and 12 weeks in aerobic capacity, muscular strength, flexibility, and quality of life Control group = decline in aerobic capacity, muscular strength, and quality of life at 12 weeks; improvements in abduction flexibility at 12 weeks
Hui et al. (2008)	Advanced cancer patients Non-randomized clinical trial	<i>N</i> = 21	Duration and frequency: 18 weeks, 1 × 30 min/week TC group = supervised 18-form TC	TC group = improvements in functioning capacity, flexibility, balance, and overall handicap scores; improvements in handicap domains (independence, mobility, orientation, social integration, and occupation)
Lee et al. (2010)	Gastric cancer patients, within two years following gastrectomy Non-randomized clinical trial	<i>N</i> = 21; mean age, 58	Duration and frequency: 24 weeks, 1 × 60 min/weeks + 12 weeks self help education TC group = supervised sun and yang style TC with Qigong + self help lifestyle education	TC group = improvements in white blood cell and monocyte percentages; no improvement in depression, HRQOL, or other immune markers

<p>Janelains et al. (2011)</p> <p>Breast cancer patients, 1 week – 30 months following completion of cancer treatment</p> <p>Randomized controlled clinical trial</p>	<p>$N=19$; mean age, 53</p> <p>TC group: $n=9$; mean age, 54</p> <p>Control group: $n=10$; mean age, 53</p>	<p>Duration and frequency: 12 weeks, 3 x 60 min/week</p> <p>TC group = supervised yang-style TC +breathing, meditation, imagery</p> <p>Control group = supervised psychosocial support</p>	<p>TC group =improvements in decreased BMI and maintenance of insulin levels</p> <p>Control group = increase in BMI and insulin levels</p>
<p>Sprod et al. (2012)</p> <p>Breast cancer patients, 1 week – 30 months following completion of cancer treatment</p> <p>Randomized controlled clinical trial</p>	<p>$N=21$; mean age, 52</p> <p>TC group: $n=11$</p> <p>Control group: $n=10$</p>	<p>Duration and frequency: 12 weeks, 3 x 60 min/week</p> <p>TCC group = supervised yang-style TC +breathing, meditation, imagery</p> <p>Control group = supervised psychosocial support</p>	<p>TC group =improvement in total HRQOL, physical functioning, physical role limitations at six weeks, social functioning at 12 weeks, and general mental health at 6 and 12 weeks</p> <p>Control group = improvements in social functioning and vitality at six weeks</p>

BMI body mass index, HRQOL health-related quality of life, TC Taichi

9.3.3 *Pilates*

Developed by Joseph Pilates in the early 1900's, the Pilates method of exercise is a movement-based mind body therapy that mixes elements of gymnastics, martial arts, yoga, and dance. Coordinating breath with movement, Pilates strengthens and builds muscle control to improve flexibility, strength, and posture (Latey 2002). Though several systematic reviews suggest mixed results on the effectiveness of Pilates for relieving pain and improving function in adults with back pain (La Touche et al. 2008; Lim et al. 2011; Posadzki et al. 2011), a recent systematic review of the effects of Pilates among healthy people reported strong evidence for this exercise therapy to improve flexibility and dynamic balance and moderate evidence to support its use to enhance muscular endurance (Cruz-Ferreira et al. 2011).

As only three small studies to date have studied the use of Pilates specifically among breast cancer patients (Keays et al. 2008; Eyigor et al. 2010; Stan et al. 2012), limited evidence is available to guide the clinician on directing cancer patients in the appropriate use of the method. Table 9.4 reviews the current research available on Pilates among cancer patients. All interventions were under the guidance of a Pilates instructor and utilized mat-based exercises. Interventions varied in intensity and were either 8 or 12 weeks in length. The research is suggestive of promising improvements in observed physical performance and shoulder mobility among breast cancer patients.

Though two studies reported no adverse effects and no development of lymphedema over the course of the intervention, one study reported a 1.6% mean increase in interlimb volume in the affected arm, with one patient developing a new onset of lymphedema and another experiencing a worsening of established lymphedema, warranting caution for the endorsement of pilates exercises in the affected arm for women at risk for lymphedema (Stan et al. 2012). Additional research is needed to explore the potential risks and benefits of Pilates as an intervention for cancer patients to increase physical activity and functional capacity, improve body composition and image, and improve flexibility and muscular endurance.

Table 9.4 Use of Pilates as supportive care in cancer and palliative care: table of clinical studies

Study	Design	Subjects	Intervention	Key outcome results
Keays et al. (2008)	Breast cancer patients with axillary dissection, ≥ 6 months following radiation therapy Nonconcurrent, randomized multiple baseline single-subject design	$N=4$; mean age, 57	Duration and frequency: 12 weeks, 3 \times 60 min/week + home program 12 weeks, 1x/week Pilates group = supervised Pilates on apparatus + unsupervised Pilates on mat	Pilates group = modest improvements in shoulder abduction and external rotation range of motion
Eyigor et al. (2010)	Breast cancer patients, no evidence of disease, following completion of surgery, radiation, and/or chemotherapy Randomized controlled clinical trial	$N=52$; age range, 18–75 Pilates group: $n=27$; mean age, 49 Control group: $n=15$; mean age, 50	Duration and frequency: 8 weeks, 3 \times 60 min/week + 8 weeks home program of daily exercises + 3 \times 20–30 min walk Pilates group = supervised Pilates on mat + home program Control group = home program	Pilates group = improvements in functional capacity, depression, quality of life (functional) Control group = improvements in functional capacity Between group comparison showed improvements in functional capacity in Pilates group only
Stan et al. (2012)	Breast cancer patients, 6–52 weeks postmastectomy Non-randomized clinical trial	$N=13$; age range, 33–65	Duration and frequency: 12 weeks, increasing intensity (4 weeks, 2 \times 45 min/week; 4 weeks, 3 \times 45 min/week; 4 weeks, 4 \times 45 min/week) Pilates group = supervised Pilates on mat	Pilates group = improvements in affected shoulder abduction and internal rotation, neck rotation toward unaffected side, and neck flexion; improvements in quality of life (except emotional well-being), mood (vigilance-activity, fatigue-inertia, total mood disturbance), and body image (health evaluation, body area satisfaction)

min minute

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Chapter 10

Safety and Side Effects of Non-pharmacological Interventions as a Therapy for Cancer

Anne M. Williams, Caroline E. Bulsara, and Anna S. Petterson

Abstract Persons diagnosed with cancer are increasingly using non-pharmacological interventions as a therapy for cancer, either independently or in addition to usual medical treatment. Within mainstream medical systems, information availability and access to these therapies is generally limited and patients' usage is commonly self-initiated. Self-initiation raises issues regarding personal safety, efficacy of the intervention, and the minimisation of potential side effects. A search was undertaken to identify relevant scientific literature related to the use of 15 non-pharmacological interventions widely used in cancer populations as therapy: acupuncture, biofeedback, exercise, meditation, music, visualization/guided imagery, yoga, kinesiology, massage, reflexology, healing touch, Qigong, Reiki, and transcutaneous electrical nerve stimulation. These interventions were classified as mind-body, touch-based or energy-based therapies. This literature search was not intended to be a systematic review, but a comprehensive assessment of current scientific publications relating to the safety and side effects of each intervention. This chapter reveals that such interventions had been used

A.M. Williams (✉)

Clinical Nursing and Midwifery Research Centre, Edith Cowan University,
Joondalup, WA 6027, Australia

SolarisCare Foundation, Nedlands, WA 6009, Australia

Centre for Nursing Research, Sir Charles Gairdner Hospital,
Nedlands, WA 6009, Australia

C.E. Bulsara

Clinical Nursing and Midwifery Research Centre, Edith Cowan University,
Joondalup, WA 6027, Australia

Brightwater Care Group, Osborne Park, WA 6017, Australia

A.S. Petterson

Clinical Nursing and Midwifery Research Centre, Edith Cowan University,
Joondalup, WA 6027, Australia

SolarisCare Foundation, Nedlands, WA 6009, Australia

in a number of different countries worldwide, in a variety of cancer populations, to address approximately 23 different symptoms associated with the experience of cancer. For all of the interventions reviewed, the recorded occurrence of side effects was minimal. Safety issues and precautions were rarely discussed in the literature relating to these non-pharmacological therapies, apart from the literature relating to the use of exercise. For hospitals considering the use of non-pharmacological interventions, a framework to facilitate the safe administration of non-pharmacological interventions as a therapy for cancer is presented. There are six main elements of this framework: the considered selection of non-pharmacological interventions, recruitment of quality practitioners, provision of oncology education and preparation for the care of persons with cancer, the use of clinical practice guidelines for each intervention, careful monitoring of persons receiving non-pharmacological interventions, and adherence to the principles of occupational health and safety. It is important that these elements are addressed by hospitals offering non-pharmacological interventions. In addition, the provision of detailed and accurate information to enable patients to continue certain therapies independently and after hospitalisation is also essential.

10.1 Introduction

In 2008, it was reported that more than seven million deaths worldwide were caused by cancer and this figure is expected to rise to more than 13 million in the next 20 years (World Health Organisation 2012). The treatment regime for persons diagnosed with cancer varies and is dependent upon the type and stage of the cancer diagnosed. For many, treatment will involve surgery, radiation/and or chemotherapy. The common physical side effects of these medical treatments may include: nausea and vomiting, pain, fatigue, hair loss, and skin reactions. In addition, psychological distress and disruption to normal social patterns are also common.

There is evidence to suggest that persons with a diagnosis of cancer are increasingly using non-pharmacological interventions as a therapy for cancer to help relieve the unpleasant side effects associated with some medical treatment. These therapies are being used both independently and in addition to usual medical treatment (Roberts et al. 2005; Robb et al. 2008). Patients in both the United Kingdom and the United States of America have been found to be using complementary and alternative medicines (CAMs) (which include non-pharmacological interventions) without the knowledge of their healthcare team (Roberts et al. 2005; Corner et al. 2009). The self-initiation of these non-prescribed therapies raises issues regarding personal safety, efficacy of the intervention, and the minimisation of potential side effects.

Non-pharmacological interventions can be defined broadly as interventions which are not derived from pharmacology. Oh et al. (2010) defined non-pharmacological interventions as non-biological, as they were interventions which were not ingested. These interventions can be categorised into four main areas:

1. Psychological and social (psychosocial): this includes interventions such as cognitive behavioural therapy, counselling, art, and narrative therapy.

2. Mind-body: this includes interventions such as acupuncture, aromatherapy, biofeedback, exercise, meditation, music, visualisation/guided imagery, and yoga.
3. Touch-based: this includes interventions such as kinesiology, massage, and reflexology.
4. Energy-based: this includes interventions such as healing touch, Qigong, Reiki, and transcutaneous electrical nerve stimulation (TENS).

There is a tendency in the literature to include all of these interventions under the banner of CAMs, which also includes a number of interventions which are taken internally, such as herbal medicine, Bach/other flower remedies, vitamins, homeopathy, and traditional Chinese medicine. It is important that non-pharmacological interventions are viewed exclusively as nil by mouth interventions. This chapter will focus on three areas of non-pharmacological intervention: mind-body, touch-based, and energy-based. Given that the psychological and social impact of cancer has been widely researched and is a field of study within the area termed psycho-oncology, the authors decided not to include this. In addition, the use of psychological social support is rarely self initiated by a person with cancer diagnosis and it is usually accessed *via* a referral process.

10.2 Method

A number of individual non-pharmacological interventions were identified which related to the areas of interest: mind-body, touch-based, and energy-based. A search was undertaken to identify relevant scientific literature related to the use of these interventions in cancer populations. This literature search was not intended to be a systematic review, but a comprehensive assessment of current scientific publications. The objectives of this assessment were to identify:

1. The number of literature items (within a defined period of time) which related to specific non-pharmacological therapies which described use with a cancer population.
2. The methods by which specific non-pharmacological therapies had been used.
3. The type of cancer population/s which had been targeted by the non-pharmacological therapy.
4. The type of symptoms for which the non-pharmacological therapy had been used.
5. The number of literature items which discussed safety or side effects of the non-pharmacological therapy and a description of these.

The database CINAHL was searched primarily to identify items of scientific literature. Some literature was also located through: MEDLINE, Cochrane Library, ProQuest Dissertations and Theses, and PsycARTICLES. A consistent search strategy was employed and literature published during the period January 2001 to December 2011 was retrieved. In circumstances where more than 200 articles were identified for that time period, only research published in the previous five years was accessed. To ensure that a comprehensive representation of literature was reviewed, both complete articles and abstracts were assessed. Wherever possible full articles were

Table 10.1 A review of the literature for non-pharmacological interventions as a therapy for cancer in relation to safety and side effects

Non-pharmacological intervention	Number of studies	Safety	Side effects
Mind-body			
Acupuncture (five years only)	40	6	2
Aromatherapy	22	2	1
Biofeedback	16	0	0
Exercise (five years only)	46	35	6
Meditation	31	1	2
Music	56	1	1
Visualization/guided imagery	41	0	0
Yoga	36	1	0
Touch-based			
Kinesiology	2	0	0
Massage	7	2	1
Reflexology	14	3	1
Energy-based			
Healing touch	3	0	0
Qigong	1	0	0
Reiki	4	1	1
Transcutaneous electrical nerve stimulation	6	1	3
Total	325	53	18

accessed, however, a decision was made to include abstracts when the article was either unavailable locally or in a foreign language. This ensured that worldwide literature was included.

The scientific evidence for each of these areas was assessed in terms of potential safety and side effects in patients with a diagnosis of cancer. A number of interventions identified in the initial search list yielded no research based articles for the selected time period. These included: Bowen (touch-based), craniosacral (touch-based), pranic healing (energy-based), and self-controlled energy neuro adaptive regulator (SCENAR) (energy-based). The final number of non-pharmacological interventions assessed was 15, and the total number of literature items assessed was 325 (Table 10.1).

10.3 A Literature Review of Non-pharmacological Interventions

10.3.1 *Mind-body*

Mind-body techniques can assist patients create positive emotional changes which can influence both physical and emotional well-being. Eight mind-body interventions

were reviewed in relation to being suitable therapies for patients diagnosed with cancer: acupuncture, aromatherapy, biofeedback, exercise, meditation, music, visualisation/guided imagery, and yoga.

10.3.1.1 Acupuncture

Acupuncture has long been used in Eastern healthcare to aid the treatment of symptoms and to improve health. The intervention usually involves the use of very thin sterile needles being inserted through the skin at various points on the body to stimulate energy flow. The manipulation of needles into specific combinations of points called meridians, allows the body to return to its regulated flow of energy or Qi (pronounced chee). The flow of Qi is considered necessary in order to maintain physical and emotional wellbeing.

The literature search for acupuncture yielded over 200 references over a 10-year period; therefore only a 5-year period was assessed. Forty studies were identified in which acupuncture had been used as a therapy for cancer. Several types of acupuncture apart from the traditional approach were apparent in the literature. These types were ear acupuncture (Walker et al. 2007), acupuncture similar to TENS (Wong et al. 2010), self-administered acupressure (Harris and Zick 2010), and magnetic acupressure (Bao et al. 2011). The main cancer groups in which the use of acupuncture had been researched were: breast cancer, prostate cancer, head and neck cancer, gynaecological cancer, and patients in the palliative care phase. The symptoms treated using acupuncture included pain (Mehling et al. 2007; Hopkins Hollis 2010; Bao et al. 2011; Baxter 2011), hot flashes (Deng et al. 2007; Walker et al. 2007; Frisk et al. 2008; Lee et al. 2009; Beer et al. 2010; Radtke et al. 2010; Locke et al. 2011), quality of life (Molassiotis et al. 2007; Cho et al. 2008; Dean-Clower et al. 2010), xerostomia (Cho et al. 2008; Meidell and Rasmussen 2009; Simcock et al. 2009; O'Sullivan and Higginson 2010; Wong et al. 2010; Baxter 2011), nausea and vomiting (Nystrom et al. 2008; Konno 2010; Taspinar and Sirin 2010; Enblom et al. 2011), fatigue (Balk et al. 2009; Harris and Zick 2010; Locke et al. 2011), lymphoedema (Cassileth et al. 2011), peripheral neuropathy (Donald et al. 2011), and hiccups (Adeline et al. 2010). Acupuncture had been used in several studies for symptoms related to either chemotherapy or radiotherapy.

A systematic review of 98 case reports between the years 1965–1999, identified 202 safety incidents. These incidents were primarily infections and physical injury as well as fainting and vomiting (Lao et al. 2003). These authors noted that incidents decreased after 1988, which probably resulted from improved training of practitioners and protocols. Of the literature reviewed for this chapter, six studies commented on the apparent safety of acupuncture as observed in the participants (Walker et al. 2007; Simcock et al. 2009; Adeline et al. 2010; Crew et al. 2010; Cassileth et al. 2011; Filshie and Rubens 2011). Two studies documented adverse side effects, both studies were conducted with patients in the palliative care phase (Meidell and Rasmussen 2009; Lim et al. 2011). Unusual minor sensations in the limbs of two participants were noted by Lim et al. (2011). Meidell and Rasmussen (2009) noted the occurrence of

tiredness, a dry mouth, and three haematomas. Filshie (2001) warned of serious risks for patients with cancer using acupuncture which included spinal cord transection, muscle spasm, infection, cellulitis, and excessive sleepiness. The risks identified by Filshie were largely based on anecdotal evidence and she suggested that urgent work was needed to clarify the risks. Although this was recommended by Filshie ten years ago, it would appear that this work is still to be undertaken.

10.3.1.2 Aromatherapy

Aromatherapy is the use of fragrant substances distilled from plants. When inhaled or absorbed through the skin during massage, these aromatic oils stimulate the body's tissues.

Twenty items of literature were identified which described the use of aromatherapy as a therapy for cancer. Apart from the inhalation of essential oils, aromatherapy had been used as a massage, either by self (Barclay et al. 2006) or by a therapist (Dunwoody et al. 2002), and as a foot soak (Kohara et al. 2004). Aromatherapy in the literature reviewed had been used to minimise pain (Soden et al. 2004; Wilkinson et al. 2007), anxiety (Robertshawe et al. 2008; Imanishi et al. 2009; Stringer and Donald 2011), nausea and vomiting (Wilkinson et al. 2007), constipation (Lai et al. 2011), lymphoedema (Barclay et al. 2006), malodour in wounds (Gethin 2011), and fatigue (Kohara et al. 2004). Aromatherapy was also used to improve sleep (Soden et al. 2004) and quality of life (Wilcock et al. 2004). Aromatherapy had been used predominately for cancer patients in the palliative care stage. Breast cancer was the only cancer which was specifically referred to. Aromatherapy had also been used in paediatric patients. The essential oils used in the literature reviewed were: lavender, chamomile, eucalyptus, orange, tea tree, and sandalwood. In some circumstances a blend of oils had been used.

Two articles discussed the safety of using aromatherapy (Dunwoody et al. 2002; Louis and Kowalski 2002). Dunwoody et al. (2002) emphasised the importance of using a therapist who was trained in both aromatherapy and oncology. Wilkinson et al. (2008a) identified skin rashes and digestive disorders as occasional adverse side effects. Fellowes et al. (2008) suggested that caution was needed for some skin types. Clinical practice guidelines have been developed and published by Lee (2003) and Williams et al. (2009), these detail the safe use of aromatherapy in clinical settings. These guidelines highlighted the importance of an educated therapist, as well as caution in shared hospital rooms.

10.3.1.3 Biofeedback

Biofeedback is an intervention in which specific information, which is not normally apparent, is provided to participants through the use of specially designed equipment regarding the physical functioning of their body. For example, electrodes placed on the body can provide information about skin temperature and heart rate

through a visual monitor. Some equipment can be linked into computerised programs for more detailed analysis. The provision of this physical information is provided in addition to health education. The aim of biofeedback is to improve physical functioning through monitoring of personal effect.

Sixteen items of literature were identified which described the use of Biofeedback as a therapy for cancer. Eight areas of focus were identified from the work in this area: stress relief (Cohen 2010; Groff et al. 2010), pain relief (Tsai et al. 2007), constipation (Collins and Burch 2009), respiration (Kim et al. 2005; George et al. 2005, 2006; Masselli et al. 2009), faecal incontinence (Allgayer et al. 2005; Bartlett et al. 2011; Kim et al. 2011), urinary incontinence (Floratos et al. 2002; Burgio et al. 2006; Lilli et al. 2006), dysphagia (Crary et al. 2004), and quality of life (Zhang et al. 2006). No safety or side effect issues were noted in any of these studies which used a variety of biofeedback techniques.

10.3.1.4 Exercise

There has been some academic discussion in the literature around the differences between physical activity and exercise. However, for the purposes of this chapter, the most relevant definition of exercise is as follows: exercise is physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective (Caspersen et al. 1985).

The literature search for exercise yielded over 200 references for a 10-year period; therefore only a 5-year period was assessed. Forty-six items were identified in which exercise had been used as a therapy for cancer. Kirshbaum (2005) noted that having received a cancer diagnosis, some view an exercise program as a way of coping with disease and treatment and regaining a measure of control over their illness. Growing evidence also supports the physical and psychological benefits of exercise for those undergoing treatment for cancer (Young-McCaughan and Arzola 2007; Sander 2008; Galvão et al. 2011). In addition to exercise during the active treatment phase, secondary prevention amongst breast cancer survivors is increasingly being highlighted as important through leading a more proactive lifestyle which includes exercise and healthier diet (Rabin et al. 2006). While these results must be viewed with some degree of caution, they would suggest that performing low to moderate exercise could provide the greatest benefit and little risk to cancer patients (Rabin et al. 2009).

Exercise as an intervention has been primarily researched in breast cancer populations (McNeely et al. 2006; Rabin et al. 2006). Research into the use of exercise in prostate cancer patients is starting to emerge in the literature (Galvão et al. 2011). Positive findings have been reported for those patients who added low to moderate exercise to their treatment regime (Dimeo et al. 1997). One reported benefit is that exercise assists in maintaining muscle mass in patients undergoing mainstream treatment (Sander 2008). There is also a growing body of research suggesting that mild to moderate exercise can improve side effects of lymphoedema in breast cancer patients

(Cheema and Gaul 2006; Hayes et al. 2009; McNeely et al. 2010). In addition, regular physical exercise can be promoted safely even for those who have completed high dose chemotherapy and bone marrow transplants (McNeely et al. 2010; Jones et al. 2011). However, the positive outcomes anticipated from persons with cancer engaging in an exercise program are not yet conclusive. A recent systematic review and meta-analysis by McNeely et al. (2010), noted that of the 14 studies reviewed, most did not focus sufficiently on adverse side effects or longer term safety of an exercise regimen for cancer patients. There are still many unanswered questions about which type and levels of intensity of exercise provides the most benefits for a particular subgroup of cancer patients. More information is also required to test which strategies to promote exercise adherence would be most appropriate for a cancer population.

Of the literature reviewed, only six papers mentioned adverse side effects of exercise. Of those, one systematic review and one meta-analysis identified studies with no specific incidence of adverse side effects (Velthuis et al. 2010; Jones 2011), three papers reported no incidence of adverse side effects in individual studies (Cheema and Gaul 2006; Newton et al. 2011; Schmitz 2011). One reported specific adverse side effects in terms of physiological impairments (Schmitz and Speck 2010). A review of the risks and benefits of exercise among breast cancer survivors identified lymphoedema as a potential problem. To minimise side effects it was suggested that timing after surgery be considered and that caution be applied to patients with compromised immune function and anemia (Schmitz and Speck 2010). Thirty-five papers mentioned safety. The issues most often noted were around the occurrence and reduction of lymphoedema (Sander 2008; Hayes et al. 2009; Kwan et al. 2011). One meta-analysis (Jones et al. 2011) noted that of the studies analysed, few addressed the issues around safety adequately. It is likely that the provision of supervision and monitoring through a structured exercise program would assist in minimising any safety risks. Other health conditions, such as heart disease, would also need to be considered and assessed before embarking on an exercise program.

10.3.1.5 Meditation

Meditation was widely introduced to Western culture in the 1960s (Kabat-Zinn 2003), it is an intervention which aims to bring about a relaxed body and calm mind. There are a number of different types of meditation (Matchim et al. 2011) that generally involve focusing attention on the senses of the body, which then allows thoughts to recede. A goal of meditation is to reach a state of relaxed awareness. Lutz et al. (2008) noted that meditation techniques have varied practices and anticipated outcomes for the practitioner.

Thirty-one items of literature were identified which described the use of meditation as a therapy for cancer. The majority of that literature specifically mentioned the use of mindfulness meditation and in particular the mindfulness-based stress reduction (MBSR) approach. First developed by Kabat-Zinn at the University of Massachusetts in 1970s, MBSR incorporates an awareness of moment-by-moment

experiences that arises from purposeful attention, along with nonjudgmental acceptance of the experiences, in conjunction with the use of Hatha yoga postures (Ott et al. 2006). Other types of meditation included Kundalini yoga meditation (Shannahoff-Khalsa 2005), Integrative restoration meditation (Pritchard et al. 2009), and transcendental meditation (Nidich et al. 2009).

Meditation had been used most often with breast cancer patients. Other patient populations included prostate (Shannahoff-Khalsa 2005), gynaecological (Brotto and Heiman 2007), and haematopoietic stem cell transplantation patients (Bauer-Wu et al. 2008). It was often used with outpatients receiving either chemotherapy or radiotherapy (Ando et al. 2009; Pritchard et al. 2009), and had been used in palliative care patients (Matchim and Armer 2007). The symptoms treated with meditation included anxiety and depression (Tacon 2006; Ando et al. 2009; Sharplin et al. 2010), stress (Pritchard et al. 2009; Branstrom et al. 2010), psychological states including promoting wellbeing (Carlson and Garland 2005; Birnie et al. 2009; Lengacher et al. 2009), quality of life (Bauer-Wu et al. 2008; Nidich et al. 2009), physical functioning (Ando et al. 2009; Lengacher et al. 2009), immune function (Carlson et al. 2003; Horowitz 2010), sexual dysfunction (Brotto and Heiman 2007), fatigue, and sleeplessness (Shapiro et al. 2003; Smith et al. 2005).

Two items of literature commented on the absence of side effects related to the use of meditation in cancer populations (Smith et al. 2005; Branstrom et al. 2010). Smith et al. (2005) suggested that there was a risk when using MBSR in persons who had psychotic episodes, personality disorders, or who were at risk of suicide. Interestingly, Brotto and Heiman (2007) describes the use of extensive use of MBSR in psychiatric populations. The extent to which MBSR presents a risk in certain disorders requires further exploration. Preliminary clinical practice guidelines for the use of meditation in hospital have been developed by Williams et al. (2009).

10.3.1.6 Music

Music is the production of harmonious sounds, it has been defined as “an art of organising sound in significant forms to express ideas and emotions through the elements of rhythm, melody, harmony, and colour” (Macquarie Dictionary 1998, p.1419).

Fifty-six items of literature were identified in which music had been used as a therapy for cancer. Music had been used in a variety of different ways such as through listening to different types of recorded music (Smith 2001; Kwekkeboom 2003), listening to live music such as choirs (O’Callaghan et al. 2010), and participating in the playing of musical instruments (Staneslow 2007; Tourin 2007). Two of the items described the combined use of music with guided imagery (Beebe and Wyatt 2009; Lai et al. 2010). The use of a music therapist was described as an important component in this approach (Lally 2007; Hart 2009).

Music had predominantly been used to reduce anxiety (Li 2004; Bulfone et al. 2009; Galaal et al. 2011; Lin et al. 2011), pain (Na Choliburi et al. 2004; Kwekkeboom 2010; Nguyen et al. 2011), nausea and vomiting (Sadat-Hoseini 2009; Mahon and

Mahon 2011; Pieszak 2011), and fatigue (Chuang et al. 2010; Kwekkeboom 2010). Music was described as being used in populations of patients with gastric cancer (Li 2004), breast cancer (Christenson 2003; Bulfone et al. 2009; Chuang et al. 2011), liver cancer (Jin and Zhao 2011), and gynaecological cancer (Chi 2009). Music has been used in both children (Ishola 2009) and adolescents (Abad 2003). It had been used with patients having chemotherapy (Bulfone et al. 2009; Lin et al. 2011), radiotherapy (Smith 2001) and in palliative care (Pawuk and Schumacher 2010; Sales et al. 2011). It has also been used for oncology staff (O'Callaghan 2001) and families (Krout 2003).

Regarding the safety and side effects of using music as an intervention for cancer patients, Beebe and Wyatt (2009) stressed the importance of using a trained music therapist. Hartwig (2010) conducted a qualitative study of 17 healthcare professionals caring for palliative care patients in Tanzania. A few potential side effects from music were identified in that study, such as possible distress from inappropriate words, potential feelings of harassment if a church choir is used, and issues when music was too loud.

10.3.1.7 Visualisation/Guided Imagery

The terms visualization and guided imagery are both used to describe the same intervention. When using this approach, imagination is initiated using sounds and vision to promote pleasant feelings (Rusy and Weisman 2000).

Forty-one items of literature were identified which described the use of visualisation/guided imagery as a therapy for cancer. A number of studies combined guided imagery with other non-pharmacological interventions, such as acupuncture (Sawada et al. 2010), music (Beebe and Wyatt 2009; Lai et al. 2010), reflexology (Wyatt et al. 2007) and cognitive behavioural group therapy (Cohen and Fried 2007). Visualisation/guided imagery had been used to improve quality of life (Freeman et al. 2008; Loizzo et al. 2010; Sawada et al. 2010), immune function (Lengacher et al. 2008; Salgado 2009; Kang et al. 2011), and personal strength (Rossman 2002). In other studies it was used to reduce anxiety and depression (Linde and Stuart 2002; Sloman 2002), dyspnoea (Lai et al. 2010), nausea and vomiting (Coleman 2003), fatigue (Cohen and Fried 2007; Kwekkeboom et al. 2010), and pain (Solito 2009; King 2010; Kwekkeboom et al. 2010).

The research conducted into the use of visualisation/guided imagery has predominately been in populations of patients with breast cancer (Kinney et al. 2003; Cameron et al. 2007; Kang et al. 2011), gynaecological cancer (Kwekkeboom 2001; Lengacher et al. 2006; Loizzo et al. 2010), and prostate cancer (Charalambous 2010; Cohen et al. 2011). It has also been used with patients undergoing chemotherapy (Coleman 2003; Sawada et al. 2010), and patients in the palliative care setting (Miller and Hopkinson 2008; Lai et al. 2011). Thomas (2009) described an educational module for healthcare professionals to ensure that visualisation/guided imagery was used safely; however specific issues of safety were not described. No adverse side effects were apparent in any of the literature which discussed the use of visualisation/

guided imagery. Preliminary clinical practice guidelines for the use of visualisation/guided imagery in hospitals have been developed by Williams et al. (2009).

10.3.1.8 Yoga

Yoga is defined by Birdee et al. (2008) as: a body of practices with an ancient history originally derived from India. In Sanskrit, the word yoga derives from “yug” meaning to yoke, referring to the discipline of aligning the mind and body for spiritual goals. Yoga has also been practised for potential health benefits, with increasing attention in popular culture to prevent illness and treat disease. The definition of yoga encompasses a variety of practices which may include postures (asanas), breathing exercises (pranayama), meditation, mantras, lifestyle changes (e.g. diet, sleep, hygiene), spiritual beliefs, and/or rituals.

Thirty-six items of literature were identified which described the use of yoga as a therapy for cancer. Of the literature reviewed, the majority of studies were related to patients with breast cancer (Desai et al. 2010; Banasik et al. 2011; Kovacic and Kovacic 2011). Other studies included nonspecific cancer types (Selman et al. 2012), three were prostate cancer (Carlson et al. 2003, 2004; Shannahoff-Khalsa 2005), and one was conducted with a paediatric cancer population (Thygeson et al. 2010). Symptoms that were reported as being evaluated were nausea (Culos-Reid et al. 2006; Raghavendra et al. 2007), pain (Carson et al. 2007; Speed-Andrews et al. 2010), sleep disturbances (Smith et al. 2006), fatigue (Cohen et al. 2004; Banasik et al. 2011), hormonal imbalances (Vadiraja et al. 2009), postural problems (Selman et al. 2012), and psychological distress (Vadiraja et al. 2009; Kovacic and Kovacic 2011).

DiStasio (2008) noted that patients and health care teams should be made aware of the safety concerns and potential risks and benefits of yoga when in active cancer treatment phase. No other articles reported on adverse side effects or on the potential safety concerns for patients with cancer. A systematic review by Smith and Pukall (2009) however, expressed caution regarding yoga and highlighted the need for larger studies to demonstrate the safety aspects of yoga for cancer patients, particularly during active treatment phase. Given that some forms of yoga practice can be a more intensive exercise, it was evident that this may be potentially harmful to less physically active individuals, particularly during the active treatment phase. The systematic review also noted that it was difficult to draw conclusive evidence as to the benefits and safety of yoga for cancer patients because most of the studies reviewed were limited in terms of their scientific rigour.

10.3.2 Touch-based

Three touch-based interventions were reviewed in relation to being used as a therapy for patients diagnosed with cancer: kinesiology, massage, and reflexology.

10.3.2.1 Kinesiology

Kinesiology studies the motion of the human body whereby the diagnosis is based on the theory that muscle dysfunction is secondary to subclinical structural, chemical, or mental dysfunction in other parts of the body (Hoffman 2009). Kinesiology therapists assess patients by observing posture, gait, muscle strength, range of motion, and by touching the patient. These observations may be combined with more common methods of diagnosis, such as a health history and physical examination. During a kinesiology treatment, the patient might be asked to hold a body part in a certain position while the therapist tries to push it out of that position. The relative strength differences are thought to help the kinesiologist identify internal imbalances. The therapist might also press on key trigger points to find out if they cause muscle weakness. In order to restore muscle strength, the kinesiologist may apply manual stimulation and relaxation techniques to key muscles. The treatment may also include joint manipulation or movement, reflex procedures, manipulation of the head, or other types of treatment.

Kinesiology is a widely used therapy amongst those providing therapeutic relief for a range of chronic conditions. However, the use of kinesiology amongst cancer patients has not been widely researched. A thesis by Mc Gowan (2010) of University of Western Ontario in the area of kinesiology focused more on the benefits of physical activity and movement for colon cancer patients. Another study by Finnerty and Thomason (2010) reported the use of kinesiology tape in assisting breast cancer patients with oedema. Although these studies reported benefits, there was neither mention of potential side effects nor safety.

10.3.2.2 Massage

Massage is one of the most universally used methods of healing the body, and there are a variety of massage techniques. Essentially, the hands are used in a range of motions over the skin.

Seven items of literature were identified in which massage had been used as a therapy for cancer. Several large, robust scientific studies indicated that there are a number of benefits to massage as a touch-based therapy for cancer patients at varying stages of their illness trajectory. Most notably, the reduction in anxiety and pain were observed (Kutner et al. 2008; Aghabati et al. 2010). A study in 2008 noted that pain and fatigue were reduced through therapeutic massage technique with cancer patients undergoing chemotherapy (Cassileth et al. 2008). There is also a body of research indicating the benefits of massage as a non-invasive therapy during times of immunosuppression for children and adults with cancer (Hughes et al. 2008). The caveat being that the therapy should be administered by health professional in a health care setting.

A few studies have accounted for the potential negative side effects and safety of soft tissue massage as part of the study protocol. Although it is maintained that soft tissue has few if any negative side effects for cancer patients (Wilkinson et al. 2008a), there were a small number of identified studies noting that rare side effects could be

observed amongst some patients with cancer. A systematic review (Wilkinson et al. 2008a) reported a case of skin rash in one patient and another study reported on physical discomfort experienced after a massage session (Cambron et al. 2007).

A study by Kutner et al. (2008) reported on any adverse events during a trial into massage therapy *vs* simple touch and noted that of the few adverse events reported (e.g. heart attack) that these were more likely to be related to overarching health condition of the patient and not directly linked to the therapy. Thus, adverse events were infrequent, similar in both groups, and did not seem to be related to the massage therapy.

Two studies discussed the safety issues in relation to massage. A lack of clear regulatory process for administering of therapies such as soft tissue massage was discussed by Cassileth et al. (2008). A systematic review of massage for lower back pain suggested that the benefits of massage are stronger when a trained therapist is used (Furlan et al. 2008). Preliminary clinical practice guidelines for the use of massage in hospitals have been developed by Williams et al. (2009).

10.3.2.3 Reflexology

Reflexology is system of healing which is based on the principle that reflexes in the hands and feet correspond to various organs and organ systems in the body (Jonas 2005). Thus it is a specialised form of hand or foot massage that is derived from the Chinese practice of acupressure.

Eleven items of literature were identified which described the use of reflexology as a therapy for cancer. In addition, three systematic reviews were also located. Few of these reported on the safety or side effects of reflexology. Of the three which did, one study qualitatively explored the experience of adverse side effects in addition to reporting on the overall benefits and outcomes (Ross et al. 2002). In this study, eight patients reported effects which included foot discomfort, nausea, shaking, and sleep disturbance. A systematic review of reflexology as effective for symptom relief amongst cancer patients (Wilkinson et al. 2008b), noted that only one in five studies had taken the safety and adverse side effects into account. A Japanese study by Kohara et al. (2004) explored a combined modality treatment of aromatherapy, foot soak, and reflexology relieves fatigue in patients with cancer and reported that no safety issues were associated with of this modality of treatment.

Literature not specific to the use of reflexology in patients with a diagnosis of cancer has cautioned the use in patients with fever, phlebitis, severe pain with unknown cause, skin eruptions or rashes, enlarged varicose veins, burns, infections, new surgery, acute conditions with unknown cause, fracture sites, and in some pregnancy cases (Mackey 2001). Griffiths (1996) suggested that care should be taken when using reflexology for patients with depressive or manic conditions, as well as epilepsy. The evidence for these cautions, however, is not stated by either author. Griffiths also notes that some patients have reported experiencing flu-like symptoms for several days following treatment. Preliminary clinical practice guidelines for the use of reflexology in hospitals have been developed by Williams et al. (2009).

10.3.3 Energy-based

Four energy-based interventions were reviewed in relation to being used as a therapy for patients diagnosed with cancer: Reiki, healing touch, Qigong, and TENS.

10.3.3.1 Healing Touch

Healing touch is a relaxing, nurturing energy-based therapy. Gentle touch is thought to assist in balancing physical, mental, emotional, and spiritual well-being. Healing touch works with personal energy field to support the body's own natural ability to heal.

Three studies were identified in which healing touch had been used as a therapy for cancer; all were quantitative, randomized controlled trials. In each study a positive effect was attributed to the healing touch intervention. Loveland Cook et al. (2004) found an increase in quality of life, vitality and physical functioning, and that pain experience was decreased. Post-White et al. (2003) found that healing touch reduced pain and fatigue in patients undergoing chemotherapy and it induced relaxation and improved mood states. Lutgendorf et al. (2010) found that immunity was improved and the occurrence of depression was decreased in patients with cervical cancer. No safety or side effect issues were noted in any of these studies which used healing touch.

10.3.3.2 Qigong

Pronounced "chee-gung", Qigong is a practice of aligning breath, movement, and awareness for exercise, healing, and meditation. Qigong is traditionally viewed as a practice to balance Qi (chi) or what has been translated as intrinsic life energy. Typically, a Qigong practice involves rhythmic breathing, coordinated with slow stylized repetition of fluid movement and a calm mindful state. There are four main divisions of Qigong, depending on the goal of the practitioner and are defined as spiritual, medical, martial, and athletic. However, there is some overlap between the divisions.

Only one study was identified in which Qigong had been used as a therapy for cancer. In this study the focus was on women with breast cancer and Qigong it was used to improve the blood cell counts following chemotherapy. The results of this small quasi-experimental study suggested that Qigong could decrease leukopenia (Yeh 2006). No safety or side effect issues were noted.

10.3.3.3 Reiki

Reiki is a form of gentle hands-on treatment therapy using energy fields within and around the body. The result is a deeply relaxing experience, increasing the body's natural ability to heal itself. The term Reiki is a Japanese word meaning universal life energy. Reiki is believed to influence a person's physical and spiritual health by realigning and strengthening the body's flow of energy (American Cancer Society <http://www.cancer.org>).

Four studies were identified in which Reiki had been used as a therapy for cancer; three were quantitative and one was a discussion paper reporting on case studies. Reiki in these studies had been used as a therapy for pain (Olson et al. 2003), anxiety (Potter 2007), and fatigue (Tsang et al. 2007). No side effect issues were noted in any of these studies which used Reiki. Tsang et al. (2007) suggested that patients may have felt safer using Reiki because they had the support from their oncologists.

10.3.3.4 TENS

TENS is an energy-based therapy which provides electrical energy stimulation through electrodes attached to the skin connected to a device (usually battery operated and portable). There are a variety of devices commercially available and different levels of nerve stimulation can be administered.

Six studies were identified in which TENS had been used as a therapy for cancer. In one study it had been used for patients with breast cancer (Robb et al. 2007), in another for patients undergoing chemotherapy (Roscoe et al. 2003). In four studies it had been used for pain relief (Robb et al. 2009; Searle et al. 2009; Bennett et al. 2010), in one study for skin flap necrosis (Atalay and Yilmaz 2009), and another study for the relief of nausea and vomiting related to chemotherapy (Roscoe et al. 2003). A systematic review of the use of TENS for cancer patients (Robb et al. 2008) suggested that the adverse events from the use of TENS were minimal. Some patients using TENS have been reported as withdrawing from the trials due to an increase in pain. Three patients out of 41 withdrew in the trial by Robb et al. (2007) for adverse side effects of TENS. Pain increased for two patients and one patient had a skin reaction. Five patients out of 19 withdrew in a trial by Bennett et al. (2010) for adverse side effects. The condition of three deteriorated, two patients had increased pain, although it was not clear, however, whether this pain was due to the use of TENS or other reasons. One patient dropped out of the trial by Robb et al. (2007) because of a skin reaction. Minor skin irritations and burns have been noted previously with the use of TENS when it is incorrectly applied (Lynch and Simpson 2002). Searle et al. (2009) noted the importance of ensuring that patients are educated and supervised when first using the device. Hypoallergenic electrode pads are available for persons susceptible to skin irritations (Rusy and Weisman 2000). Preliminary clinical practice guidelines for the use of TENS in hospitals have been developed by Williams et al. (2009).

10.3.4 Summary of Literature Review

The assessment of literature related to the use of non-pharmacological interventions for patients diagnosed with cancer resulted in the review of 325 items of literature for 15 interventions (Table 10.1). The majority of literature was for the acupuncture and exercise, and the literature for these interventions was only reviewed for five years because of the large number of items published over a 10-year period. All other interventions were reviewed for a 10-year period. In terms of safety and side effects,

Table 10.2 Symptoms addressed by the non-pharmacological interventions

Symptoms	Non-pharmacological interventions
Anxiety and depression	Acupuncture, aromatherapy, biofeedback, healing touch, massage, meditation, music, reflexology, Reiki, visualization/guided imagery
Blood cell count	Qigong
Circulation	Reflexology
Constipation	Aromatherapy
Dysphasia	Biofeedback
Dyspnoea	Biofeedback, reflexology, visualization/guided imagery
Fatigue	Acupuncture, aromatherapy, healing touch, massage, meditation, music, reflexology, Reiki, visualization/guided imagery
Faecal incontinence	Biofeedback, reflexology
Hiccups	Acupuncture
Hot Flushes	Acupuncture
Immune function	Healing touch, massage, meditation, reflexology, visualization/guided imagery
Lymphoedema	Acupuncture, aromatherapy, exercise
Malodour in wounds	Aromatherapy
Nausea and vomiting	Acupuncture, aromatherapy, music, TENS, visualization/guided imagery
Oedema	Kinesiology
Pain	Acupuncture, aromatherapy, biofeedback, healing touch, massage, meditation, music, reflexology, Reiki, TENS, visualization/guided imagery
Peripheral neuropathy	Acupuncture
Quality of life	Acupuncture, aromatherapy, biofeedback, healing touch, meditation, exercise, visualization/guided imagery
Rehabilitation	Exercise, healing touch
Sexual dysfunction	Meditation
Wound healing	Reflexology, Reiki
Urinary incontinence	Biofeedback, reflexology
Xerostomia	Acupuncture

TENS transcutaneous electrical nerve stimulation

acupuncture and exercise reported the most side effects, although this could be related to the greater number of literature items reviewed. For all other interventions the safety and side effects were assessed as minimal.

A close examination of the literature retrieved, revealed that the 15 non-pharmacological interventions assessed had been used for the relief of 23 unpleasant symptoms of cancer and its treatment. Table 10.2 documents the type of intervention associated with specific symptoms. The symptoms most addressed by the use of these non-pharmacological interventions were: anxiety and depression, fatigue, and pain. In addition, 15 different groups of cancer populations were documented as using the 15 non-pharmacological interventions assessed (Table 10.3). The populations most using these non-pharmacological interventions were women with breast cancer, patients undergoing chemotherapy, and patients in the palliative phase.

Table 10.3 Cancer population using non-pharmacological interventions

Cancer population	Non-pharmacological interventions
Adolescent	Music
Bone marrow transplant	Exercise
Breast	Acupuncture, biofeedback, exercise, healing touch, kinesiology, meditation, music, Qigong, TENS, visualization/guided imagery
Cervical	Healing touch
Chemotherapy	Acupuncture, exercise, healing touch, meditation, music, TENS, visualization/guided imagery
Colon	Kinesiology
Gastric	Music
Gynaecological	Acupuncture, healing touch, meditation, music, visualization/guided imagery
Hematopoietic stem cell transplantation	Meditation
Head and neck	Acupuncture
Liver	Music
Paediatric	Aromatherapy, music
Palliative	Acupuncture, aromatherapy, biofeedback, meditation, music, visualization/guided imagery
Prostate	Meditation, visualization/guided imagery
Radiotherapy	Meditation

TENS transcutaneous electrical nerve stimulation

From the literature reviewed, the reported side effects, possible risk factors and suggested precautions were identified and outlined in Table 10.4. The accuracy and extent of risk in terms of the safety and side effects associated with each of the 15 therapies assessed was difficult to determine and further research would be required to confirm the occurrence of the specified side effects and risk factors. An assessment of the effectiveness of the precautions suggested is also warranted. The need for further research is clearly evident in seven of the non-pharmacological interventions which had no reference to side effects, risk factors or precautions. As this assessment of literature included abstracts, the assessment of some items of literature may have been limited by the lack of detail accessed.

10.4 A Preliminary Framework for the Safe Administration of Non-pharmacological Interventions as a Therapy for Cancer in the Hospital Setting

A number of hospitals around the world now offer non-pharmacological interventions alongside mainstream medicine. In the USA, a recent survey identified that 42% of 714 hospitals were offering at least one non-pharmacological intervention. The most popular

Table 10.4 Side effects, risk factors and suggested precautions

Intervention	Reported side effects	Possible risk factors	Suggested precautions
Mind-body			
Acupuncture	Infections, physical injury, fainting, vomiting, unusual sensations in limbs, haematomas, tiredness, dry mouth, spinal cord transection, spasm, cellulitis	Nil noted	Quality practitioner Use of infection control principles
Aromatherapy	Skin rashes, digestive disorders	Some skin types	Quality practitioner Caution in shared rooms Nil noted
Biofeedback	Nil noted	Nil noted	Structured exercise programs Physiological monitoring
Exercise	Lymphoedema, skeletal complications	Timing after surgery Compromised immune function Anemia	Nil noted
Meditation	Nil noted	Psychotic episodes Personality disorders Persons at risk of suicide	Nil noted
Music	Distress, harassment	Inappropriate words Noise level Personal taste Nil noted Active treatment phase	Quality practitioner
Visualization/guided imagery	Nil noted		Nil noted
Yoga	Nil noted		Nil noted
Touch-based			
Kinesiology	Nil noted	Nil noted	Nil noted
Massage	Skin rashes, physical discomfort	Nil noted	Quality practitioner
Reflexology	Foot discomfort, nausea, shaking, sleep disturbance	Fever, phlebitis, severe pain (unknown cause) skin rashes, enlarged varicose veins, burns, infections, new surgery, fractures sites, pregnancy, depression, epilepsy	Quality practitioner

Energy-based

Healing Touch

Qigong

Reiki

Transcutaneous electrical
nerve stimulation

Nil noted

Nil noted

Nil noted

Increased pain, skin reactions, burns

Nil noted

Nil noted

Nil noted

Some skin types

Nil noted

Nil noted

Nil noted

Supervision for first use
Education

of these interventions were pet therapy, massage, and music/art (<http://gantdaily.com/2011/11/14/hospitals-offering-complementary-medical-therapies/>). Hospitals known for providing non-pharmacological interventions in the USA include: Sloan Kettering Cancer Centre, New York; Anderson Cancer Centre, Texas; and the Grinnell Regional Medical Centre, Iowa. In the United Kingdom, hospitals offering non-pharmacological interventions include the Dorset Cancer Centre, and the Portsmouth Hospital. In Thailand the Arokhayasala Centre for cancer patients offers both pharmacological and non-pharmacological interventions. Within Australia, a review of hospitals in state of New South Wales in 2005 found that it was mostly mind-body and touch-based therapies which were being used in hospitals. No energy-based therapies were reported (<http://www.cancerinstitute.org.au/incite/issue-1/complementary-therapies>). Organisations currently offering non-pharmacological interventions within Australia include the SolarisCare Foundation in Western Australia and the Peter MacCallum Centre in Victoria. A further organisation in Australia is the Olivia Newton-John Cancer and Wellness Centre at the Austin Hospital, Victoria.

For hospitals considering the use of non-pharmacological therapies in hospital, a framework was developed for this chapter. This framework is primarily based on the ten years' experience of the SolarisCare Foundation (Western Australia) which facilitates for the safe administration of non-pharmacological interventions as a therapy for cancer. There are six main elements of this framework: considered selection of non-pharmacological interventions, recruitment of quality practitioners, provision of oncology education and preparation for the care of persons with cancer, the use of clinical practice guidelines for each intervention, careful monitoring of persons receiving interventions, and adherence to the principles of occupational health and safety (Fig. 10.1).

10.4.1 Considered Selection of Non-pharmacological Interventions

A literature review should be conducted for each new non-pharmacological intervention adopted. This review should determine the potential benefits as well as the possible safety and side effect issues associated with the intervention. Where possible, interventions which have either state or national organisations that provide standards of practice and protocols should be used. It should be noted that for some non-pharmacological interventions, the evidence base for their effectiveness is low. For these interventions the guiding principle, *primum non nocere* (do no harm) should be used, especially as regards safety and potential side effects.

10.4.2 Recruitment of Quality Practitioners

The recruitment of potential practitioners should begin with a state and national police check, followed by a rigorous assessment of therapy membership affiliation. A face-to-face interview is essential and therapists should have worked in their field for at least 8 h a week for a period of one year.

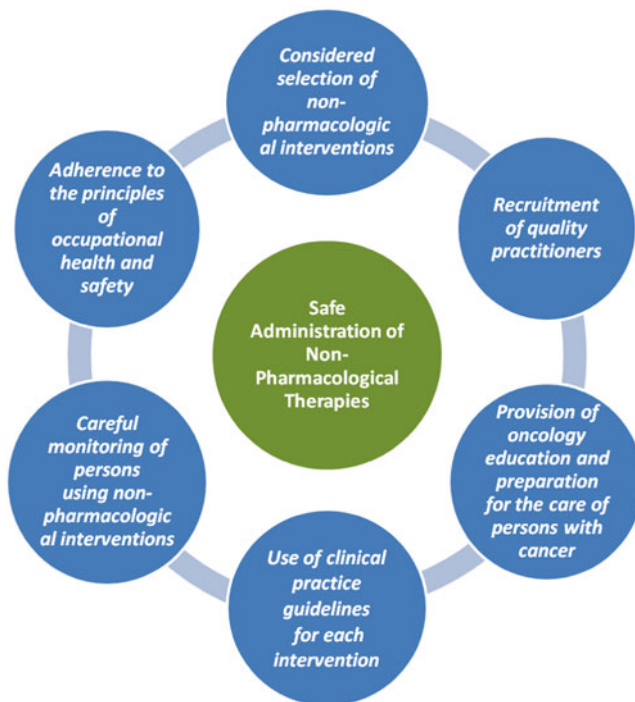


Fig. 10.1 Framework for the safe administration of non-pharmacological interventions as a therapy for cancer

10.4.3 Provision of Oncology Education and Preparation for the Care of Persons with Cancer

Provision of oncology education and preparation for the care of persons with cancer is essential. This preparation should include supernumerary time spent interacting with patients and current therapists, to provide an opportunity for both parties to assess suitability. Initial education and follow-up sessions after the first 12 months are recommended. An emphasis on psycho-social care, particularly active listening is an important part of this education.

10.4.4 The Use of Clinical Practice Guidelines for Each Intervention

Clinical practice guidelines should be developed for the administration of any non-pharmacological therapy. These guidelines should be developed in collaboration with therapists and all therapists employed would be required to be familiar of the details contained within these guidelines. Potential side effects and safety issues

should be contained within the guidelines. Although some organisations have developed their own clinical practice guidelines, access to published guidelines is currently limited.

10.4.5 Careful Monitoring of Persons Using Non-pharmacological Interventions

All patients should sign a consent form prior to receiving non-pharmacological interventions. Patients should be allocated an identification number and basic demographic details should be kept. It is important that the type of therapy provided and date are recorded in the patient's file and any side effects noted and addressed.

10.4.6 Adherence to the Principles of Occupational Health and Safety

It is essential that the principles of occupational health and safety are adhered to. These principles include consideration of infection control such as the use of clean equipment and linen for each patient, strict hand hygiene practices, and the availability of single use needles for acupuncture. Therapists also need to be protected against injury and an awareness of risk factors in the environment and the safe management of these should be part of their preparatory and ongoing education.

10.5 Summary and Conclusions

This chapter has reviewed the safety and side effects of non-pharmacological interventions used as therapies for cancer. A literature search of 15 non-pharmacological interventions was conducted in the areas of mind-body, touch-based, and energy-based therapies. The majority of literature had been published in relation to use of acupuncture and exercise, followed by music and visualization/guided imagery. The review revealed that these interventions have been used worldwide in a variety of cancer populations. For all of the interventions reviewed, the recorded occurrence of side effects was minimal. Exercise recorded the most comments regarding side effects. Safety issues and precautions relating to these non-pharmacological interventions were rarely discussed in the literature, apart from in relation to exercise.

Two conclusions can be drawn from the analysis of this literature on non-pharmacological interventions. Either safety and side effects are not an issue and therefore do not require a thorough explanation, or the research exploring safety and side effects is lacking and more work needs to be conducted in this area. In 2001,

Filshie (2001) suggested that more research was urgently needed to explore the side effects and risks associated with the use of Acupuncture in cancer populations. However, no evidence of further research could be identified. A greater emphasis on these issues would clearly assist healthcare practitioners and patients in their choice and application of non-pharmacological interventions.

From the literature reviewed, it seems likely that for the majority of non-pharmacological interventions, there are minimal side effects. There were indications however, that more research is needed to ensure that acupuncture and exercise in particular, are used safely to minimise any adverse effects. The publication of clinical practice guidelines for the safe use of these interventions is recommended. Of the other interventions assessed, minimal safety and side effect issues were apparent. In a recent survey of 381 patients with a diagnosis of cancer in Australia, only seven patients reported experiencing side effects when using complementary and alternative medicines. However, as this survey included biological, ingestible therapies such as vitamins, it is difficult to assess which therapies resulted in adverse effects (Oh et al. 2010). More work focussing on potential safety issues is recommended. It was apparent that the term complementary and alternative therapies in the literature can be misleading when assessing the effect of non-pharmacological therapies, as this tends to include all therapies. Concerns are regularly raised by the medical profession in relation to biological therapies (Wernecke et al. 2004) and maybe it is time to make a clear distinction in our language between biological/pharmacological therapies and non-pharmacological therapies, as described in this chapter.

Although not the focus of this chapter, it was readily apparent that the evidence base for a number of non-pharmacological interventions is currently low and well designed studies with large samples lacking. Difficulties with recruitment were noted, and the use of placebo's and control groups insufficient. The overriding view within the healthcare field today is that quality care is associated with the use of approaches which reflect the best level of evidence (Pearson 2006). It would however be unfortunate if healthcare practitioners avoided the use of these therapies, or did not make patients aware of their existence, due to a current lack of evidence. In addition, there is evidence to suggest that a psychological benefit can be achieved through the use of these therapies in terms of increasing a person's feelings of control during a time of disempowerment (Davidson et al. 2005). It is essential that an element of common sense is embraced alongside the evidence based medicine movement. Until we have developed the evidence base for non-pharmacological interventions, we need to ensure that these therapies are used in a safe way, applying defined principles to minimise any risk to patients.

A framework for the safe administration of non-pharmacological interventions within the hospital setting has been presented in this chapter. It is essential that the elements presented here are considered when these interventions are offered to patients with a cancer diagnosis. The use of quality practitioners and the close monitoring of patients would particularly be important. In addition, the provision of detailed and accurate information for patients to continue certain therapies, independently and following hospitalisation, is also essential.

Increased use of non-pharmacological interventions by cancer patients throughout the world, have made the regulation of these interventions an important issue for policymakers. Currently, regulation and monitoring of providers and practitioners varies between and within countries. For example, in Canada they are regulated by individual provinces, but in Australia discussions on the options for regulation of unregistered health practitioners have only just commenced. The current policy of the British Medical Association suggests that complementary medicine should be regulated by a statutory authority (<http://web.bma.org.uk/pressrel.nsf/wall/98705BD6917D74A0802569A5005D920A?OpenDocument>).

A regulatory framework and guidelines for non-pharmacological interventions in oncology will be one of the biggest challenges of the future. As patients continue to seek alternatives to mainstream care, a new healthcare approach is needed; one in which patients can safely embrace both conventional and non-conventional therapies. This approach needs to encourage and facilitate communication between patients and their healthcare providers about the use of non-pharmacological interventions, to ensure that these interventions are used in a safe, effective and informed way.

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Chapter 11

Integrating Non-pharmacological Therapies with Western Medicine in Cancer Treatment

Gulbeyaz Can

Abstract Each year, ten million people are diagnosed with cancer around the world and global cancer rates are increasing. There is also a rise in the number of cancer survivors living with symptoms and disabilities as a result of their disease and/or its treatment. Generally pharmacological interventions are recommended for symptom management, because most of the studies shown their sufficient strong empirical evidence of effectiveness. However, some research results indicate that physical and cognitive modalities have benefit in management of pain; psycho-education in reducing fatigue; acupuncture, acupressure, cognitive distraction, psycho-educational support and hypnosis in management of nausea and vomiting; and cryotherapy in prevention of chemotherapy induced nail changes. Resistance exercise was found to be effective in reducing the severity of fatigue. A significant effect was found for music therapy in pain management, for psychosocial intervention specific for fatigue, and oral cryotherapy for mucositis. In conclusion, there is an urgent need for well-designed randomized controlled trials to test the effectiveness of non-pharmacological interventions.

11.1 Introduction

Cancer is a major burden of disease worldwide, and it is perceived as a frightening and untreatable disease that implies death. Each year, ten million people are diagnosed with cancer around the world and global cancer rates are increasing. At the same time, there is also a rise in the number of cancer survivors living with symptoms and disabilities as a result of their disease and/or its treatment. Cancer treatments and the disease itself may cause different symptoms such as anxiety, fatigue, nausea and

G. Can (✉)

Istanbul University Nursing Faculty, Abide-I Hurriyet Cad, Caglayan, Istanbul, Turkey
e-mail: gulbeyaz@istanbul.edu.tr

vomiting, anorexia, pain, and constipation, which decrease the physical functioning and quality of life (QoL) of the patients (Deng et al. 2009). Most of these symptoms are multidimensional, complex, and subjective phenomena that “reflect changes in the bio-psycho-social functioning of the patients”. Some are acute, with an onset that corresponds closely with the timing of treatment, such as nausea and vomiting, whereas others may last beyond treatment, such as fatigue (Lotfi-Jam et al. 2008). Therefore, the symptom management becomes a very important issue in cancer patients and a vital aspect of oncological care (Barsevick 2007). Generally pharmacological interventions are recommended for symptom management, because most of the studies shown their sufficient strong empirical evidence of effectiveness. However, there are many non-pharmacological interventions such as acupuncture, acupressure, exercise, music therapy, relaxation, cognitive distraction, psycho-educational support, hypnosis, oral hygiene programs, including mouthwashes, cryotherapy, and dietary changes that can be recommended for prevention, controlling or treating disease- or therapy-related symptoms (Lotfi-Jam et al. 2008; Deng et al. 2009). With regard to symptoms, the non-pharmacological management of pain, fatigue, nausea and vomiting, mucositis, constipation, diarrhea, hair loss, nails changes and psychological distress is fundamental for cancer patients and discussed in detail below.

11.2 General Symptoms

11.2.1 Pain

Pain is one of the most common symptoms associated with cancer. It occurs in approximately one quarter of patients with newly diagnosed malignancies, one third of patients undergoing treatment, and three quarters of patients with advanced disease. Unrelieved pain denies patients comfort and greatly affects their activities, motivation, interactions with family and friends, and overall QoL. Strong evidence supports many cancer pain interventions and pain guidelines state that pain can be alleviated through the careful use of analgesic drugs combined with non-pharmacological strategies. The use of physical modalities (e.g. massage, physical therapy) and cognitive modalities (e.g. hypnosis, relaxation, and distraction) may provide extremely beneficial adjuncts to pharmacologic interventions. However, attention should also be focused on psychosocial support and providing education to patients and families (Swarm et al. 2012) (Table 11.1).

Pain guidelines recommend education about pain. Two systematic reviews addressed this issue and supported the beneficial effect of the education and counseling for pain (Allard et al. 2001; Devine 2003). The role of physiotherapists in palliative care is primarily defined by expert opinion, which is not backed up by good quality evidence. However, an absence of research evidence does not mean that a service or treatment is ineffective, just that we don't know for certain yet. Because the maintenance or improvement of the functional component of QoL and

Table 11.1 Definition of non-pharmacological therapies used for pain management

Term	Definition
Acupuncture	A method of producing analgesia by inserting fine, wire-thin needles (about the diameter of a strand of hair) into acupoints along a specific meridian (meridians are channels in the body that transport energy) on the body
Healing touch	A form of complementary and alternative medicine based on the belief that vital energy flows through the human body. This energy is said to be balanced or made stronger by practitioners who pass their hands over, or gently touch, a patient's body
Homeopathy	Homeopathy based on the belief that natural substances, prepared in a special way and used most often in very small amounts, relieve pain and restore health. According to these beliefs, in order for a remedy to be effective, it must cause in a healthy person the same symptoms being treated in the patient
Hypnosis	A behavioral intervention process whereby patients learn to focus attention on thoughts or images unrelated to a source of distress (i.e. pain). The patient is relaxed through a meditation-like excursion to pleasant locations and/or activities while a clinician introduces suggestions of calmness and well-being
Massage therapy	An ancient form of healing that involves the therapeutic manipulation of the painful soft tissues of the body by various hand movements (e.g. rubbing, kneading, pressing, rolling, slapping, tapping, effluage)
Mind-body interventions	Mind-body medicine focuses on the communication between mind and body and the powerful ways in which emotional, mental, social, and spiritual factors can directly affect health. Mind-body interventions include relaxation, imagery, meditation, hypnosis, yoga, and others
Music therapy	Treatment that uses music to help relieve pain or stress and promote well-being
Psychoeducational interventions	The use of counseling, support, and structured educational interventions, through the use of interactive media (audiotapes, computer-assisted, telephone, video) to provide specific information on self-care measures for patients with pain

significant improvements in pain are noted in patients who received optimized levels of physiotherapy time and resources (Dalacorte et al. 2011).

Previous studies have supported the value of massage for relieving pain in patients with cancer (Wilkie et al. 2000; Cassileth and Vickers 2004; Kutner et al. 2008; Jane et al. 2009), and found that this intervention yielded a considerably better effect in patients with strong pain perception [Visual Analogue Scale (VAS)>4] (Cassileth and Vickers 2004; Kutner et al. 2008; Jane et al. 2009). However, Downey et al. (2009) could not prove the effectiveness of massage therapy in terminal oncological patients. Positive studies shown that the reduction of pain after massage

therapy lasting up to 18 h (Wilkie et al. 2000; Kutner et al. 2008; Jane et al. 2009) and its immediate effects is higher than longer-term effects (Wilkie et al. 2000; Kutner et al. 2008). Kutner et al. (2008) and Wilkie et al. (2000) studied the patients' consumption of analgesics after they had received massage therapy and compared it with the previous dosage. While the decrease in the consumption of analgesics was not statistically significant, the dosage of analgesics was subject to less fluctuation (Wilkie et al. 2000). Although there is evidence that massage therapies can influence the symptoms of pain in a positive way (Fellowes et al. 2008; Falkensteiner et al. 2011) most of authors state that study limitations (small sample size, lack of adequate control groups) and conflicting results made firm conclusions impossible (Pan et al. 2000; Sagar et al. 2007; Myers et al. 2008) and further well-designed large trials with longer follow-up periods are needed to be able to draw firm conclusions about the efficacy and effectiveness of massage for cancer patients (Wilkinson et al. 2008).

Unrelieved persistent pain commonly causes patients to seek relief with alternative medicine, including homeopathy, acupuncture, healing touch, and music therapy (Dalacorte et al. 2011). Although there is little scientific evidence for the efficacy of most of these strategies for controlling persistent pain the use of mind-body modalities are recommended as part of a multidisciplinary approach to reduce chronic pain and improve QoL of cancer patients (Deng et al. 2009; Dalacorte et al. 2011). A Cochrane's review concluded that touch therapies may have a modest effect in pain relief (So et al. 2008). The research results and meta-analysis suggest that music therapy and music medicine interventions may have a beneficial effect on pain and the QoL of cancer patients (Bradt et al. 2011). They showed that listening to music reduces pain intensity levels and opioid requirements, but the magnitude of these benefits is small and therefore its clinical importance is unclear (Cepeda et al. 2006). Although the magnitude of the efficacy of music therapy varies between previous studies, some researchers suggested that music therapy relieved cancer pain (Beck 1991; Zimmerman et al. 1989) whereas others did not (Curtis 1986). The effect of music therapy on pain management was supported by enough strong empirical evidence by randomized controlled trials and systematic review conducted in last years. A randomized controlled trial performed by Huang et al. (2010) found that 30 min of music listening provided 50% relief in 42% of the music group compared to 8% of the controls, the large effect sizes indicating that music was very helpful for pain. Another randomized controlled trial of 120 breast cancer patients who received Personal Controlled Analgesia (PCA) following radical mastectomy showed that music therapy has both short- and long-term positive effects on alleviating pain. In this study, music therapy was found to reduce the pain score in the intervention group significantly compared with the control group with a mean difference (CI 95%) of -2.38 (-2.80 to -1.95), -2.41 (-2.85 to -1.96), and -1.87 (-2.33 to -1.42) for the first, second, and third post-tests, respectively. Similar results were found for VAS and Present Pain Intensity (PPI) scores (Li et al. 2011). Recently, a systematic review indicated that music interventions might have beneficial effects on pain in people with cancer and stated that music therapy had moderate pain-reducing effect (SMD = -0.59 , CI 95% -0.92 to -0.27 , $p=0.0003$) (Bradt et al. 2011).

11.2.2 *Fatigue*

The National Comprehensive Cancer Network defines cancer-related fatigue (CRF) as a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer-related treatment that is not proportional to recent activity and interferes with usual functioning (Berger et al. 2012). Cancer patients can experience fatigue at different stages of disease. The prevalence of fatigue during cancer treatment ranges from 25 to 99%, after successful cancer treatment, it can still be a problem in up to 38% of cancer survivors and can persist for many years (Goedendorp et al. 2009). The specific non-pharmacological interventions as activity enhancement, physically-based therapies, and psychosocial interventions have the strongest evidence base for managing fatigue (Berger et al. 2012) (Table 11.2). Specifically, multi-modal exercise and walking programs, restorative approaches, supportive-expressive, and cognitive-behavioral psychosocial interventions show promising potential for ameliorating CRF (Kangas et al. 2008).

Current literatures suggest that the role of exercise on managing fatigue is likely to be beneficial, because some reviews concluded that exercise had a positive effect on fatigue (Conn et al. 2006; McNeely et al. 2006), others found no effect of exercise on fatigue (Stevinson et al. 2004; Knols et al. 2005; Jacobsen et al. 2007). Two meta-analyses confirm that exercise during cancer treatment is beneficial in improving fatigue, especially among breast and prostate cancer patients (Velthuis et al. 2010; Brown et al. 2011). Subgroup analysis in patients with breast cancer showed a significant reduction in CRF in favor of the aerobic exercise groups. Supervised aerobic exercise programmes were more effective in reducing CRF than home-based exercise programmes, which did not lead to significant reductions in CRF. Due to a limited number of data a subgroup analysis of home-based and supervised aerobic and resistance exercise programmes in prostate cancer patients showed no significant reduction in CRF in favor of the exercise group (Velthuis et al. 2010). Brown et al. (2011) confirmed that cancer survivors engaging in moderate-intensity resistance exercise modulated CRF levels more than those engaging in low-intensity resistance exercise or low to moderate intensity, aerobic exercise. Finding of the efficacy of resistance exercise reducing CRF was somewhat unexpected (Brown et al. 2011). Current guidelines for cancer patients emphasize the importance of participating in aerobic exercise, complimented with resistance and flexibility exercises, and often make no or minimal mention of resistance exercise. The exercise program itself should be individualized based on patient's age, gender, type of cancer, and physical fitness level. Exercise interventions must be used with caution in patients with bone metastasis, thrombocytopenia, anemia, fever or active infection, limitations secondary to metastasis or other illnesses (Berger et al. 2012).

A Cochrane review found that the effectiveness of psychosocial interventions specific for fatigue was significantly higher (80%) compared to interventions not specific for fatigue (14%). The significant effects was reported for psychosocial interventions, that specifically focused on management of fatigue, such as education

Table 11.2 Definition of non-pharmacological therapies used for fatigue management

Term	Definition
Energy conservation and activity management	Energy conservation is the deliberate and planned management of one's personal energy resources to prevent their depletion. Energy conservation strategies include planning, delegating, setting priorities, pacing, resting, and scheduling activities that require high-energy use at times of peak energy. Balancing rest and activity during times of high fatigue allows for maintaining adequate energy to carry out valued activities and reach important goals
Exercise	Exercise is any planned, structured, and repetitive bodily movement performed during leisure time that incorporates cardiovascular, strength, and/or flexibility conditioning of any intensity with the intent of improving or maintaining one or more components of physical fitness, performance, or health
Massage therapy	This ancient form of healing involves the therapeutic manipulation of soft tissues of the body by various hand movements (e.g. rubbing, kneading, pressing, rolling, slapping, tapping). Massage therapy can elicit the relaxation response as measured by decreases in heart rate, blood pressure, and respiration. Often, massage is complemented by the use of aromatherapy (i.e. essential oils combined with a carrier cream or oil to manipulate the soft tissues)
Progressive muscle relaxation	Progressive muscle relaxation is a technique that involves the sequential tensing and relaxation of major skeletal muscle groups with the aim of inducing relaxation. Focused breathing, with all attention centered on the sensations of breathing, including the rhythm and rise and fall of the chest, often is used along with progressive muscle relaxation
Psychoeducational interventions	Psychoeducational interventions for fatigue include cognitive-behavioral techniques, education or information provision, psychotherapeutic interventions, and supportive strategies to modify factors that may trigger or intensify cancer fatigue and to elicit behaviors that may effectively manage cancer-related fatigue. Psychoeducative interventions may be delivered individually or in groups, and multiple components often are included in single interventions. Interventions may be tailored or standardized and may include materials that are written, audiovisual, or web-based
Yoga	Yoga is an ancient Eastern science that incorporates stress-reduction techniques such as regulated breathing, visual imagery, and meditation, as well as various postures

about fatigue, self-care or coping techniques, activity management, learning to balance between activities and rest. Interventions that did not focus on fatigue, e.g. interventions that aimed to reduce depression or pain, showed that fatigue did not decrease with depression or pain management (Goedendorp et al. 2009).

Complementary therapies such as massage therapy, yoga, muscle relaxation, and stress reduction based on mindfulness have been evaluated in pilot studies. The preliminary data suggest that they may be effective in reducing fatigue in cancer patients (Berger et al. 2012).

Few randomized controlled trials of yoga in patients with cancer have been published. However only several studies conducted with breast cancer patients and survivors have shown beneficial effects of yoga interventions on fatigue. In one study, 31 breast cancer survivors were randomly assigned to yoga ($n=16$) or health education ($n=15$), shown that fatigue severity declined significantly from baseline to post-treatment and over a three months follow-up in the yoga group relative to controls ($p=0.032$) (Bower et al. 2012). Other published studies of yoga in patients with breast cancer have used participants as their own controls. In a pilot study of 13 patients with metastatic breast cancer, women participated in an 8-week program that included gentle yoga postures, breathing exercises, meditation, didactic presentations, and group interchange. During the two pre-intervention weeks and the final two weeks of yoga, fatigue level were measured daily. On the day after yoga practice, participants experienced significantly lower levels of fatigue (Carson et al. 2007). In another single-arm pilot study, the feasibility and preliminary efficacy of a yoga intervention for fatigued breast cancer survivors based on the Iyengar tradition was also evaluated. Twelve women were enrolled in the trial, and 11 completed the full 12-week course of treatment. There was a significant improvement in fatigue scores from pre- to post-intervention that was maintained at the three months post-intervention follow-up (Bower et al. 2011). These results support the acceptability of yoga intervention and suggest that it may have beneficial effects on fatigue for breast cancer patients. However, results require replication in a larger.

The effect of progressive muscle relaxation training on fatigue was assessed in a prospective, quasi-experimental study with control group. Twenty-seven patients with breast cancer undergoing adjuvant chemotherapy (14 individuals formed the progressive muscle relaxation group, 13 individuals formed the control group) were attend to the study. Progressive muscle relaxation training was given to the progressive muscle relaxation group, but not to the control group. The effect of the progressive muscle relaxation training was measured at different stages of the treatment and findings indicated that progressive muscle relaxation training would improve fatigue in patients with breast cancer undergoing adjuvant chemotherapy (Demiralp et al. 2010).

Two studies assess the efficacy of mindfulness-based cognitive group therapy in reducing severe chronic fatigue in cancer survivors with mixed diagnoses. In the first study, fatigue was a secondary endpoint measured with a subscale of the Profile of Mood States. This study examined the effects of an 8-week Mindfulness-Based Stress Reduction (MBSR) program on the sleep quality of a heterogeneous sample of 63 cancer patients. An 8-week MBSR program that involved 90-min weekly

sessions of meditation and hatha yoga was apply as intervention. There was no randomization to a control group in this study. Statistically, fatigue was significantly improved after eight weeks of MBSR training. Improvements in sleep and fatigue were not correlated, which suggests that this intervention might have had an effect on fatigue independent of the improved sleep outcome. Based on this pilot evidence, authors state that a randomized, controlled trial with adequate power would be warranted (Carlson and Garland 2005). In the second study, participants were randomly selected from a cohort and allocated to an intervention and a waiting list condition. Fatigue severity was assessed before and after the 9-week intervention. The intervention group had a follow-up nine months following the intervention. The mean fatigue score at post-measurement was significantly lower in the intervention group than in the waiting list group corrected for pre-treatment level of fatigue and treatment effect was maintained at six months follow-up (van der Lee and Garssen 2012). However, results require replication in a larger randomized controlled trial.

11.3 Gastrointestinal Symptoms

11.3.1 *Nausea and Vomiting*

Nausea and vomiting are common symptoms in cancer patients as a result of either treatment-related toxicity or complications directly or indirectly related to the cancer (Naeim et al. 2008). Although recent surveys indicate that the symptoms of nausea and vomiting may be less common and bothersome than has previously been reported (Glare et al. 2011), sometimes these symptoms can give rise to medical complications, including poor nutrition, dehydration, electrolyte imbalances, physical and mental deterioration, which can adversely affect patients' QoL (Hawkins and Grunberg 2009). In some cases, patients may refuse to continue potentially beneficial treatment regimens due to treatment-associated nausea and vomiting (Hawkins and Grunberg 2009). So successful interventions to prevent, manage, and treat nausea and vomiting is vital to decrease the distress associated with the symptoms and promote well-being and QoL for patients and their families (Tipton et al. 2007).

Pharmacological interventions were the only interventions that were supported by enough strong empirical evidence to prevent, manage, and treat nausea and vomiting. However, guidelines indicate that dietary changes, acupuncture, acupressure, guided imagery (GI), progressive muscle relaxation, music therapy, psycho-educational support and hypnosis can be recommended in conjunction with pharmacological interventions as non-pharmacological interventions for management of nausea and vomiting (Garrett et al. 2003; Ezzo et al. 2006; Tipton et al. 2007; Lotfi-Jam et al. 2008) (Table 11.3).

In the prevention of nausea and vomiting environmental stimuli, such as sights, sounds, smells, fatty, spicy, and highly salted food should be avoided. Small, but frequent meals and flavonoid-rich fruits and vegetables also might be recommended

Table 11.3 Definition of non-pharmacological therapies used for nausea and vomiting management

Term	Definition
Acupuncture and acupressure	Acupuncture usually entails the needling of specific points on the body surface. The acupoint most commonly investigated and accessible for nausea and vomiting is Neiguan (PC6), which is located on the anterior surface of the forearm, approximately three finger-widths from the wrist crease. The PC6 point is stimulated either with an acupuncture needle (acupuncture) or by a wristband with a protruding knob or by finger pressure (acupressure)
Ginger	A plant herb used for the treatment of nausea and vomiting. Ginger has aromatic, spasmolytic, carminative and absorbent properties that suggest direct effects on the gastrointestinal tract
Guided imagery	A behavioral technique that uses imagination to form a relaxing, pleasing mental image, often preceded by relaxation techniques and/or music. This technique can serve as a form of distraction to aid in reducing chemotherapy-induced nausea and vomiting
Hypnosis	A behavioral intervention process whereby patients learn to focus attention on thoughts or images unrelated to a source of distress (i.e. nausea or vomiting). The patient is relaxed through a meditation-like excursion to pleasant locations and/or activities while a clinician introduces suggestions of calmness and well-being
Progressive muscle relaxation	Progressive muscle relaxation is a technique that involves the sequential tensing and relaxation of major skeletal muscle groups with the aim of inducing relaxation. Focused breathing, with all attention centered on the sensations of breathing, including the rhythm and rise and fall of the chest, often is used along with progressive muscle relaxation
Psychoeducational interventions	The use of counseling, support, and structured educational interventions, through the use of interactive media (audiotapes, computer-assisted, telephone, video) to provide specific information on self-care measures for patients with chemotherapy induced nausea and vomiting

(Harris 2010; Glare et al. 2011). In a double-blind, randomized clinical trial the effect of concord grape juice on management of chemotherapy-induced nausea and vomiting (CINV) was assessed by Ingersoll et al. (2010). This study found that flavonoid-rich fruits and vegetables may provide additional protection against CINV, but authors state that the effect of grape juice flavonoids on CINV should be investigated in further research with a larger sample to determine whether the preliminary findings of this study are supported (Ingersoll et al. 2010)

In the literature indicated that psycho-educational and psycho-social care have beneficial effects for nausea and vomiting in cancer patients (Devine and Westlake

1995; Tipton et al. 2007; Roscoe et al. 2010). Contrary to results of these studies, in the study performed by Roscoe et al. (2010), a structured nursing intervention did not differ the incidence of anorexia, nausea, and emesis symptoms as compared to standard care (Jahn et al. 2009). To maximize the utility of this knowledge for clinicians, more research is needed to evaluate the relative effectiveness of different types of psycho-educational care.

Behavioral approaches, such as relaxation and distraction, may decrease psychological arousal and distress by refocusing the patient's attention on something else, and increase the patient's feelings of control over the symptoms of nausea and vomiting (Glare et al. 2011). There have been few studies of effect of these therapies in cancer patients. Massage has been reported as effective intervention for nausea and vomiting (Fellowes et al. 2008; Wilkinson et al. 2008). Relaxation training, which utilizes progressive muscle relaxation and GI, has been successful in reducing nausea and vomiting in some studies (Arakawa 1997; Molassiotis 2000; Molassiotis et al. 2002; Yoo et al. 2005), but not in others (Troesch et al. 1993; Arakawa 1995).

Progressive muscle relaxation training (PMRT) may be beneficial for preventing or managing nausea and vomiting in patients receiving chemotherapy. Several studies examined this effect of PMRT either alone or in combination with other interventions and found that PMRT considerably decreased the duration (Molassiotis 2000; Molassiotis et al. 2002) and intensity of nausea and vomiting (Molassiotis 2000), and have beneficial effect on the incidence of delayed nausea and vomiting (Arakawa 1997). However, the effect of PMRT on nausea and vomiting was not verified in a pilot study with Japanese patients. In this study, both treatment and control groups showed similarly decrease in nausea and vomiting (Arakawa 1995). In another study, the effectiveness of PMRT and GI in reducing the anticipatory nausea and vomiting (ANV) and post-chemotherapy nausea and vomiting (PNV) of patients with breast cancer was assessed. The results of this study indicate that PMRT and GI were associated with both the improvements in ANV and PNV of patients with breast cancer (Yoo et al. 2005). The use of GI for nausea was supported by a meta-analysis of 15 studies. Clinically significant reductions in nausea were found, but the effect on vomiting could not be analyzed because of the low incidence of vomiting in the studies that were reviewed (Luebbert et al. 2001). In a group of patients receiving cisplatin-based chemotherapy, Troesch et al. (1993) assessed the influence of GI on chemotherapy-related nausea and vomiting. In this study, both groups received the same standard anti-emetic regimen while the experimental group additionally used a chemotherapy-specific GI audiotape. Findings revealed that there were no statistically significant differences in the nausea and vomiting experience between the two groups when measured at five different times during chemotherapy administration (Troesch et al. 1993).

Over the past decade, several published reports have shown that acupuncture can be used for CINV. Ernst and Lee (2010) stated that evidence supported the use of acupuncture in treating of CINV experienced by cancer patients. There are a variety of acupuncture-point stimulation techniques that have been examined in treating chemotherapy-induced nausea, vomiting, or both. These techniques include methods

that involve needles, electrical stimulation, magnets, or acupressure (Naeim et al. 2008). There are two positive Cochrane reviews for the effect of acupuncture in the prevention of post-operative nausea and vomiting (Lee and Fan 2009) and chemotherapy-induced nausea (Ezzo et al. 2006). Ezzo et al. (2006) demonstrated some beneficial effects of acupuncture-point stimulation on chemotherapy-induced acute nausea and vomiting in adult cancer patients with the anti-emetic regimen recommended by the American Society of Clinical Oncology. No statistically significant effects were reported for delayed nausea or vomiting in this study. Stimulation with needles and electroacupuncture reduced the incidence of acute emesis, but not the symptom of acute or delayed nausea compared with controls (Ezzo et al. 2006).

Similar to acupuncture, another non-pharmacological intervention commonly used for nausea and vomiting is acupressure. A Cochrane review state that acupressure is effective intervention to reduce acute nausea, but not acute vomiting and the use of self-administered acupressure may be suggested to patients (Ezzo et al. 2006). Another review performed by Lee et al. (2008a) evaluated the effects of two specific acupressure modalities (acupressure band and finger acupressure). In this study, four of seven acupressure band trials supported the positive effects of acupressure, whereas three acupressure band trials yielded negative results regarding the possible effects of acupressure. However, all the studies with negative results had methodological issues. In contrast, one quasi-experimental and two randomized finger acupressure trials all supported the positive effects of acupressure on CINV control. The reported effects of the two acupressure modalities in each phase of CINV produced variable results. Acupressure bands were effective in controlling acute nausea, whereas finger acupressure controlled delayed nausea and vomiting. The overall effect of acupressure was strongly suggestive, but not conclusive. Differences in the acupressure modality, the emetic potential of chemo-therapeutic agents, anti-emetic use, and sample characteristics of each study made study-to-study comparisons difficult. Acupressure should be strongly recommended as an effective, non-pharmacological adjuvant intervention for CINV control if its positive effects are reproduced in future acupressure clinical trials (Lee et al. 2008a).

Lee et al. (2008b) evaluate the relationship between nausea and exercise during and after adjuvant cancer treatment [chemotherapy and radiation therapy (RT) or chemotherapy alone]. This longitudinal, single-blinded, three-arm, randomized controlled trial stated that exercisers experienced significantly less intense nausea than non-exercisers at the completion of adjuvant cancer treatment. A moderate level of aerobic exercise is related to less intense nausea at the completion of adjuvant cancer treatment. A moderate level of aerobic exercise is recommended during adjuvant cancer treatment because of the possibility of reducing nausea intensity, as well as alleviating other symptoms from adjuvant cancer treatment (Lee et al. 2008b).

A meta-analysis performed by Richardson et al. (2007) examined the effectiveness of hypnosis in management of CINV and revealed that hypnosis could be a clinically valuable intervention for anticipatory and CINV in children with cancer. Six randomised controlled trials were included in this meta-analysis and five of the included trials were assessing paediatric patients aged from 5 to 18 years and one adults aged

from 19 to 49 years. Most trials included training in self-hypnosis. The duration of hypnosis sessions varied between studies. Control groups included treatment as usual, therapist contact and cognitive-behaviour therapy. Positive results were reported for nausea and/or vomiting in all five studies assessing children, but there were no significant differences between groups for nausea and/or vomiting in the study assessing adults cancer patients. Further research into the effectiveness, acceptance, and feasibility of hypnosis in CINV, particularly in adults, should be suggested.

Ginger has also been studied for its efficacy in management of CINV. Ginger has been successful in prevention of nausea and vomiting after major gynecologic surgery (Nanthakomon and Pongrojapaw 2006), but not in CINV (Manusirivithaya et al. 2004; Zick et al. 2009). In a randomized, double-blinded crossover study with 48 gynecologic cancer patients receiving cisplatin-based chemotherapy, ginger was not found to be effective in treating acute nausea, nor was it significantly different from metoclopramide in delayed nausea (Manusirivithaya et al. 2004). Zick et al. (2009) stated that ginger provided no additional benefit for reduction of the prevalence or severity of acute or delayed CINV when given with 5-HT₃ receptor antagonists and/or aprepitant.

11.3.2 Mucositis

Mucositis, an inflammation of the mucous membranes, is a commonly occurring side effect of chemotherapy and radiation. Mucositis disrupts the function and integrity of the oral cavity, affects functional status and QoL of the patients. Its incidence is high in cancer patients receiving head and neck RT and moderate in patients receiving myelo-suppressive chemotherapy for solid tumors. Many interventions for managing mucositis exist, however, some are based in tradition or expert opinion and have not been studied in large randomized controlled trials (Eilers and Million 2011) (Table 11.4).

The Multinational Association of Supportive Care in Cancer/International Society for Oral Oncology (MASCC/ISOO) guideline recommended oral care protocols using a soft toothbrush, patient and staff education regarding the oral care protocols (Keefe et al. 2007). In the past, a Cochrane review reported some evidence of benefit of oral care in the prevention of mucositis, but this benefit was not shown in the last version of this review (Worthington et al. 2011, 2007). Therefore, using oral care protocols involving basic oral care that includes a soft toothbrush that is replaced regularly recommend for practice based on the literature, because good oral health is related to overall health and wellness and it is integral to the prevention and treatment of mucositis. Most of the studies have included basic oral care as a comparison with new therapies often fail to show the desired significant difference, which contributing support for the importance of basic oral hygiene (Keefe et al. 2007; Eilers and Million 2011).

Application of ice chips or other frozen edible liquids have been successfully tested in mucositis prevention in patients treated with bolus 5-FU and suggested for

Table 11.4 Definition of non-pharmacological therapies used for mucositis management

Term	Definition
Oral care protocols	The foundation of an oral care protocol is good oral hygiene. This protocol includes an interdisciplinary educational plan that clinicians use to educate patients and families about components of oral care in prevention and management of oral mucositis. Components of basic oral care include consistent, regular, and thorough brushing with a soft toothbrush that is changed on a regular basis; daily flossing; frequent rinsing with bland rinses such as sterile water, normal saline, or sodium bicarbonate; and use of oral moisturizers. The oral care protocol should be feasible, tolerable, and easy to maintain and must be specific to a patient's diagnosis and treatment. Prior to treatment, a baseline oral assessment needs to be completed and a dentist should be consulted
Cryotherapy	The use of ice chips and/or ice-cold water for the prevention of oral mucositis. Patients are to suck on ice and/or hold ice-cold water in their mouths prior to, during, and after rapid infusions of mucotoxic agents with a short half-life. Cryotherapy is based on the theoretical and conceptual model of vasoconstriction decreasing exposure of the oral cavity mucous membranes to the mucotoxic agents

bolus edatrexate and in patients receiving high-dose melphalan. The use of cryotherapy in these studies is based on the assumption that when used together with short-term intravenous chemotherapy agents, cryotherapy causes local vasoconstriction and the blood flow to the oral mucosa slows down, the distribution of the drug among the cells decreases and, as a result, the risk of oral mucositis formation also decreases. Since bolus 5-FU has a short half-life authors suggested that around 20 min, oral cooling for 30–45 min immediately before and after chemotherapy administration may reduce the frequency of oral mucositis. This effect of cryotherapy was assessed in many studies (Worthington et al. 2011, 2007). A recent randomized controlled trial of 60 cancer patients who received to infusion of 5-FU with leucovorin also support these results. In this study, oral mucositis in the patients was evaluated at 7, 14, and 21 days after chemotherapy. In the majority of patients receiving cryotherapy, oral mucositis was not observed (Grade 0) at 7 and 14 days. Similarly, incidence of Grades 1, 2, and 3 oral mucositis in the experimental group was quite a bit lower when compared to the control group ($p < 0.05$). On day 21, no statistically significant difference between the experimental and control groups was determined based on the development of oral mucositis ($p > 0.05$) (Katrancı et al. 2012). In another study, long term effects of cryotherapy evaluated in 40 patients with multiple myeloma scheduled to receive melphalan 200 mg/m² followed by autologous stem cell transplantation. Patients were randomly assigned to receive oral cryotherapy or room temperature normal saline rinses 30 min before and for 6 h after high-dose therapy. In this study, the normal saline group was compared to patients using cryotherapy experienced less grade 3–4 mucositis (14% vs 74%,

$p=0.0005$). Patients receiving cryotherapy also had statistically lower uses of narcotics and total parenteral nutrition, although there were no differences in length of hospitalization or weight loss (Lilleby et al. 2006). However, in two Cochrane reviews, cryotherapy also found to be beneficial in the prevention of all the outcome categories of mucositis – any, moderate, and severe, and cryotherapy for patients receiving bolus chemotherapy with short half-life (bolus 5-FU and melphalan) was identified as “likely to be effective” intervention. No statistically significant difference for all levels of mucositis found for 30 min vs 60 min cryotherapy (Worthington et al. 2011, 2007). It is hypothesized that the cold temperature induces vasoconstriction in the mucosal tissues and prevents delivery of the noxious medication to the area. The main limitation of this method is its applicability only with drugs that have a short plasma half-life and it cannot be used in patients with head and neck or esophageal malignancies (Eilers and Million 2011).

Bardy et al. (2008) conducted a systematic review of honey in oncology care. Unfortunately, the article had only limited relevance for mucositis prevention and treatment. However, weak unreliable evidence with substantial heterogeneity that honey may be beneficial in the prevention of any mucositis shown in a Cochrane review for head and neck cancer undergoing RT or chemo-radiotherapy (Worthington et al. 2011).

11.3.3 Constipation

Despite the frequency of significant constipation, no randomized trial data have been found to support any particular non-pharmacological intervention in prevention and management of constipation. Patient education is, therefore, a central part of prevention: ensuring privacy and comfort to allow a patient to defecate normally; increasing fluid and fiber intake and encouraging activity within the patient’s limits are recommended in the literature (Larkin et al. 2008; Librach et al. 2010). Ensuring privacy (visual, auditory, and olfactory) health care providers should encourage the patient to sit on the toilet 20 min after breakfast. Abdominal massage may be useful in some patients for the prophylaxis and treatment of constipation. Although dietary fiber supplements have been shown to increase stool weight and decrease transit time, the amount of fiber required (50% increase in bowel frequency would require a 450% increase in fiber intake) to have an effect is unrealistic. Adequate fluid intake is equally important to bowel function and the effectiveness of dietary fiber. Research suggests that the prevention of constipation requires at least 2 L of fluid per day and at least 1.5 L is required for the safe use of dietary fiber supplements (Larkin et al. 2008; Librach et al. 2010). Although there is evidence to support the link between exercise and constipation (Cordain et al. 1986; Lotfi-Jam et al. 2008), research in the general adult population has shown only a weak correlation between constipation and physical activity and, in fact, increasing exercise was shown to be more likely to improve well-being than to reduce constipation (Tuteja et al. 2005).

11.3.4 Diarrhea

Diarrhea is a common and significant problem among cancer patients who undergoing 5-FU based chemotherapy, or taking irinotecan, targeted agent such as erlotinib, gefitinib, sorafenib, sunitinib, imatinib, and bortezomib in their chemotherapy regimen. However, cancer treatment regimens that include RT to the abdominal region for cervical, ovarian, prostate, sigmoid, or colorectal cancer can cause RT-induced diarrhea, enteritis, and colitis in more than 80% of patients with cancer (Cherny 2008). So successful interventions to prevent, manage, and treat diarrhea can be vital to decrease the distress and promote well-being and QoL of these patients.

Pharmacological interventions were the only intervention that was supported by enough strong empirical evidence to prevent, manage, and treat diarrhea. However, guidelines indicate that dietary changes and hydration also may be recommended for prevention and management of diarrhea. Because a transient lactase deficiency with lactose malabsorption can occur with any form of mucosal injury to the gastrointestinal tract, milk products should be avoided. Special attention should be given to patients who are incontinent of stool due to the risk of pressure ulcer formation (Cherny 2008).

Another approach tested for the prevention of RT-induced diarrhea is the use of probiotics. Randomized clinical trials have demonstrated efficacy of in decreasing the incidence and grade of RT-induced diarrhea (Narayan et al. 2010; Visich and Yeo 2010). Delia et al. (2007, 2002) conducted two double-blind, randomized clinical trial to investigate the efficacy of probiotics on prevention of RT-induced diarrhea in patients with cancer. The primary outcomes considered in these studies were incidence and severity of RT-induced diarrhea, daily number of bowel movements, and the number of days of lopermide use as a rescue medication. Two study results showed that the use of probiotic dramatically reduced severity of RT-induced diarrhea and the daily number of bowel movements, and increased the number of days of lopermide used as a rescue medication. The authors concluded that probiotics are effective intervention in the management of RT-induced diarrhea. Another double-blind, randomized controlled trial was conducted to determine whether a probiotic drink containing *Lactobacillus casei* reduced the incidence of RT-induced diarrhea in patients with gynecologic cancer. Eighty-five patients undergoing pelvic RT (45–50 Gy, conventional fractionation) for either cervical carcinoma or endometrial carcinoma were randomly assigned to a yogurt drink containing *L. casei* or liquid yogurt placebo. Patients recorded their number of bowel movements and scored stool consistency. Results demonstrated that diarrhea of grade 2 or greater and/or the use of loperamide was observed in 24 of 41 patients (58.5%) in the placebo group and 30 of 44 patients (68%) in the probiotic group ($p=0.57$). No differences were found in the median time to the presentation of grade 2 or greater diarrhea or the need for loperamide (Giralt et al. 2008). Although these studies showed that probiotics improved the patients' status, the safety and efficacy of specific probiotics must be evaluated and described by further randomized controlled trials (Narayan et al. 2010; Visich and Yeo 2010).

11.4 Cutaneous Symptoms

11.4.1 Hair Loss

Chemotherapy-induced alopecia (CIA) is a distressing side effect that causes significant clinical morbidity. Shorten or completely cut of hair can decrease perception of significant hair style change during thinning, along with decreasing and eliminating the daily slow psychological trauma of removing shed hairs off a pillow case or shower drain (Chon et al. 2012). Patients with hair loss experience considerable physical change; they also undergo psychological stress and changes in self-esteem. Research results showed that the negative effects of alopecia on body image, self-esteem, and psychological functioning might be decreased by patient education and support (Chon et al. 2012). A computer-imaging intervention has been described by McGarvey et al. (2001) reduced the psychological stress of alopecia by desensitizing women to hair loss before it is experienced. But makeup techniques and hair/headpiece suggestions to women with CIA was not found to be more successful in improving changes in body image than standard counseling (Nolte et al. 2006). Another intervention is the social support for a patient with cancer by shaving one's head. Family members, friends, and teammates will sometimes "go bald" to raise awareness for the affected individual and share a part of the difficult experience. Anecdotal response to this gesture has been overwhelmingly positive (Chon et al. 2012).

In the prevention of CIA, scalp cooling is another non-pharmacological interventions introduced in the 1970s. It stimulates local vasoconstriction, thus decreasing the amount of chemo-therapeutic agent reaching the follicle. The efficacy of scalp cooling has been investigated in seven randomized clinical studies, six of which found cooling to be effective with varying degrees of success. It has become an increasingly effective method to prevent hair loss, especially when anthracyclines or taxanes are used, but should not be used if chemotherapy is given with a curative intent in patients with generalised haematogenic metastases because this intervention has some concerns. A recent retrospective cohort study of women with breast cancer found a low incidence of scalp metastases (1.1%), all of which occurred in patients who used scalp cooling at some point in their therapy. In none of the cases, the scalp was the first isolated site of relapse (Lemieux et al. 2009). However, because of safety concerns and a lack of evidence of product effectiveness, the US Food and Drug Administration banned the sale of such items in 1990 (Chon et al. 2012).

11.4.2 Nail Changes

Chemotherapy induced nails changes result from toxicity arising in the various nail constituents, such as the matrix, nail bed, periungual tissues, or blood vessels in the fingers (Scotté et al. 2005). A review of published studies by Minisini et al. (2003) showed that the overall incidence of these changes is as high as 44%. Many factors

may affect the development of nail toxicity and that cryotherapy is the first proven measure used effectively in the prevention of the nail toxicity. Scotté et al. (2005, 2008) were able to reduce the incidence of nail toxicity by using a glycerin-containing elasto-gel thermal glove or sock, cooled to -25°C and worn on the hand or foot just before, during, and after docetaxel infusion. The frozen glove delayed the median time to occurrence of nail toxicity compared with the control group. The median time of the occurrence of nail changes in this study was 106 days for the protected hand and 58 days for the control hand (Scotté et al. 2005). However, no statistically significant difference in nail toxicity incidence and time to occurrence of nail changes was found between the frozen gloves/socks protected group and the unprotected group in the study performed by Can et al. (2012). Further randomized controlled studies using this intervention are warranted to determine the effect of using the frozen glove/sock on taxane-related nail changes.

11.5 Psychological Distress

Having cancer may result in intense emotional, physical, and social suffering. Depression is one of the most common mental health problems in cancer patients with prevalence ranged from 5.1 to 30.1%. However the prevalence of adjustment disorder of cancer patients was 15.4% (10.1–21.6) and anxiety disorders 9.8% (6.8–13.2) (Mitchell et al. 2011). Mind-body modalities are strongly recommended to be incorporated into a multi-disciplinary approach in reducing anxiety, mood disturbance, and improving QoL of cancer patients (Deng et al. 2009). The use of cognitive behavioral therapy approaches provided in an individual format can assist cancer survivors in reducing emotional distress (anxiety, depression) and improving QoL of these patients (Osborn et al. 2006).

A meta-analysis to investigate whether aromatherapy or massage, or both, decreases psychological morbidity of the cancer patients was performed by Fellowes et al. (2008). In this study, the most consistently found effect of massage or aromatherapy massage was on anxiety. Four trials (207 participants) measuring anxiety detected a reduction post intervention, with benefits of 19–32% reported. Contradictory evidence exists as to any additional benefit on anxiety conferred by the addition of aromatherapy. The evidence for the impact of massage/aromatherapy on depression was variable. Of the three trials (120 participants) that assessed depression in cancer patients, only one found any significant differences in this symptom (Fellowes et al. 2008). Wilkinson et al. (2008) also suggested that massage might reduce anxiety in patients with cancer in the short term.

Music is another intervention used to decrease anxiety prior to or during surgical procedures, to decrease tension during chemotherapy or RT, to improve mood, and to improve QoL of cancer patients. Research results suggested that music therapy and music medicine interventions might have a beneficial effect on anxiety, mood, QoL, heart rate, respiratory rate, and blood pressure in cancer patients. No support was found for depression of patients (Bradt et al. 2011).

11.6 Conclusion

Nowadays information about the use of non-pharmacological therapies in cancer treatments and their effectiveness are steadily increasing. Clearly, some progress has been made in establishing clear scientific evidence for the use of several non-pharmacological interventions in clinical management of cancer- or treatment-related symptoms, but a great deal of research to test the effectiveness of non-pharmacological intervention is still needed.

Some non-pharmacological interventions (music therapy for pain, cognitive modalities for psychological symptoms, exercise for fatigue, acupuncture and acupressure for nausea and vomiting, and oral cryotherapy for mucositis) have the strongest scientific evidence base to support their use in clinical practice, so these interventions should be implemented in medical guidelines for effective symptom management. There is also promising, but limited, evidence to support the use of cryotherapy for the prevention of chemotherapy-induced nail changes. However, the scientific evidence underlying this intervention is very preliminary and the use of these modalities as part of standard clinical care in oncology for the management of nail changes is premature. Integrative non-pharmacological interventions used by many cancer patients in the management of their cancer- and treatment-related symptoms have already been sought. The scientific community should continue conducting and funding research to provide detailed scientific evidence and resources necessary for health care providers to prescribe these non-pharmacological interventions effectively as part of standard care and to assist cancer survivors in choosing which intervention will best suit their needs.

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