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The Effects of Nursing Back Rub on Pain and Wound Cytokines and The Relationship Between Pre-CABG Mood and Post-CABG Wound Cytokines

Kathlene D. Smith
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To the Graduate Council:

I am submitting herewith a dissertation written by Kathlene D. Smith entitled "The Effects of Nursing Back Rub on Pain and Wound Cytokines and The Relationship Between Pre-CABG Mood and Post-CABG Wound Cytokines." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Nursing.

Maureen Groer, Major Professor

We have read this dissertation and recommend its acceptance:

Mitzi Davis, Stephen Kania, Jan Lee

Accepted for the Council:
Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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Vice Chancellor and Dean of
Graduate Studies

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THE EFFECTS OF NURSING BACK RUB ON PAIN AND WOUND CYTOKINES AND THE RELATIONSHIP BETWEEN PRE-CABG MOOD AND POST-CABG WOUND CYTOKINES

A Dissertation
Presented for the
Doctor of Philosophy
Degree
The University of Tennessee, Knoxville

Kathlene D. Smith
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DEDICATION

This dissertation is dedicated to my husband, and loyal supporter, Lloyd N. Smith.

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I wish to thank all those who helped me in completing the Doctorate of Philosophy Degree in Nursing. I thank Dr. Maureen Groer for her constant support, ideas, assistance, correction and instruction as my Major Professor. She continues to be an inspiration to me. I thank Dr. Mitzi Davis for her energetic encouragement and dedication to my completion of this research. Dr. Stephen Kania deserves recognition as a member of my committee and his willingness to serve in this capacity at the College of Nursing. I especially appreciated his questions during the defense. Dr. Jan Lee is to be commended, as she jumped right into the committee after Dr. Isabelita Guiao had to be replaced. Thank you, Dr. Lee, for your insight and wisdom. Finally, Dr. Guiao contributed greatly to this dissertation by editing and re-editing.

ABSTRACT

This study, guided by psychoneuroimmunology theory, examined the effects of a 10-minute nursing back rub in 20 coronary artery bypass graft (CABG) patients on pain and four proinflammatory wound cytokines (IL-1 β, IL-6, IL-8, and TNF-α). It also examined the relationships between the Profile of Mood States (POMS) and the proinflammatory cytokines. A control group (n = 8) received time with the researcher, and an experimental group (n = 12) received a slow stroke effleurage back rub. All participants initially completed the POMS and after surgery, wound fluid was collected from the mediastinal chest tube before and after the intervention. Analysis showed the experimental group had a significant decrease in pain (df 11, p=0.001). Pretest mean levels of cytokines one hour before the back rub were: IL-1β, 15.1 pg/ml; IL-6, 104,680 pg/ml; IL-8, 6,953 pg/m, and TNF-α, 3.5 pg/ml. Posttest cytokine mean levels were: IL-1β, 13.71 pg/ml; IL-6, 94,658.5 pg/ml; IL-8, 22,431 pg/ml; and TNF-α, 3.6 pg/ml. There were no significant changes in any cytokine levels in either group from pretest to posttest. Great variability in cytokine concentrations was noted in both the experimental and the control group. No significant relationships were found between the POMS Total Mood Disturbance Score (TMDS) and cytokine levels. There was a significant inverse relationship (r = -.560, p=.016) between the POMS score of tension-anxiety and IL-6. There was a significant positive correlation (r = .475, p=.034) between IL1-β and weight. This study has contributed support to a nursing intervention that appears to reduce pain perception, to the understanding of wound cytokine levels in CABG patients, and to psychoneuroimmunology research in that wound fluid IL-6 levels in were lower in patients who were tense/anxious before surgery. Further research needs to be done on wound healing and stress reducing interventions.

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1. INTRODUCTION

The era of "assessment and accountability" began in the late 1980s (Relman, 1988) when biophysiological evidence was called to support psychosocial data for showing the efficacy of nursing interventions. Since then nurses have struggled with responding to such a call. Schwertz and Barry (1994, p.1) noted that, "Cellular physiology may not be a primary focus during daily clinical practice, but it is at the cellular and molecular level that most, if not all, of the therapies that nurses administer exert their effect." Within the last decade, the National Institute of Nursing Research (formerly known as the National Center for Nursing Research NCNR) placed as a nursing research priority the identification of bio-behavioral factors and the testing of nursing interventions that promote immunocompetence (NCNR Outreach, 1993). The nursing back rub is a therapy that can promote immunocompetence.

Touch and Nursing Back Rub

Since nursing began as a profession, nurses have performed interventions involving touch. Generally, such interventions have been in the form of back massages or back rubs. Although other disciplines, such as physical therapy and psychology, have used massage for therapy, a back massage or back rub is primarily a therapeutic act performed by nurses. Touch intervention is considered to be within the field of complementary and alternative medicine. Touch has been used as a therapeutic intervention in various clinical specialties, such as labor and delivery, pediatrics, geriatrics, and orthopedics, to provide comfort and relaxation. Members of various disciplines study the effectiveness of touch in diverse ways. Nurses study "therapeutic touch" (Denison, 2004; Engle & Graney, 2000**).** Physical therapists examine the effect of

deep tissue manipulation and to some degree full-body massage **(**DuPriest, 1993; Nilsson, Christensen & Hartvigsen, 1997**).** Psychologists study the effect of massaging multiple body parts and over many days of therapy **(**Field et al., 1996; Ironson et al, 1996).

Gaps in Touch and Nursing Back Rub Literature

A group of psychologist scientists from the Touch Institute at the University of Miami (TIUM) continue to conduct physiological studies involving stimulation of pressure receptors with deep tissue manipulation. Duration and frequency of intervention vary depending on the age and clinical condition of the participants. In general, the range of sessions per week is two to seven for two to four weeks with duration of 15 to 30 minutes (Field, 1998). Findings from these studies include: a) increased peak airflow in asthma patients; b) decreased glucose levels in children with diabetes; c) decreased anxiety, depression, stress and cortisol and catecholamine levels among various populations; and d) decreased post-operative pain among patients who had gall bladder surgery (Field, 1998**).** They concluded that the pressure stimulation associated with touch may increase vagal activity, which in turn lowers physiological arousal and stress hormone levels, leading to enhancement of immune function**.** However, questions about the underlying mechanisms for the physiologic effects of massage have still been unanswered. The proposed study will examine the effect of nursing back rub on cytokines within wound fluids, in particular, to assist in shedding light on such questions.

Deep tissue massage was found to be beneficial on the cellular level among individuals who are diagnosed to have the human immunodeficiency virus (HIV) by Ironson et al. (1996) at TIUM. For example, after a month of daily 45 minute massages, in an experimental study involving HIV positive individuals, the TIUM scientists found a

significant increase in natural killer cell numbers, natural killer cell cytotoxity, soluble CD8, and the cytotoxic subset of CD8 cells, and a significant decrease in urine cortisol in the experimental group relative to the control group (Ironson et al., 1996). Since massage has been found to influence the immune system in this way, the proposed study will examine cellular processes of the immune system, specifically proinflammatory wound cytokines found in the wound fluids of post-coronary artery bypass (CABG) patients.

Because it is unlikely that professional nurses practicing in medical centers will have the training and time to perform deep tissue massages similar to any of the TIUM studies, it is important to determine if a simple back rub can positively affect pain and the cellular processes in wound healing.

Vast amounts of research literature found in complementary or alternative medicine, use massage as a treatment to provide relaxation, pain relief, improvement in circulation, stimulation of lymph circulation and the assistance in the elimination of metabolic wastes. Nurses, masseurs, physical therapists and other professionals and paraprofessionals have participated in this research. Results from this type of research indicate that massage, as controlled touch, is effective in improving comfort and reducing stress and anxiety. Massage of various parts of the body, using various strokes, for various lengths of time, and for various numbers of massages, has been shown to be effective in boosting the immune system, such as increasing salivary immunoglobulin A (sIgA) concentration (Groer, et al., 1994). Massage has been found to decrease urinary and serum cortisol, pain, heart rate, and blood pressure. There are conflicting results regarding massage and its relationship to respiratory rate. However very little literature provides evidence as to the mechanisms involved to provide these results. By studying

the effects of a nursing back rub at the cellular level, evidence of how massage produces its effects at the molecular level will accumulate. Additionally, several explanations such as increases in endorphins or enkephalins, decreases in epinephrine and stimulation of the pain gate have been studied to determine how pain is decreased with massage but the effect of a massage on cytokine levels has not been found in the literature.

Research has not identified the anatomical locale, the number of massages needed, the type of massage or the duration necessary for the massage to provide results. There is a need from a nursing perspective to provide evidence that ten minutes of back rub is an effective "doable dose".

Nurse researchers have studied massage in multiple patient populations but relatively few have specifically studied the postoperative surgical patient. Only two studies were found that studied massage in CABG patients and this type of massage was not back massage, but 20 minutes of foot massage (Hattan, King, & Griffiths, 2002; Stevensen, 1994). Calmness was significantly increased with the use of foot massage. The nursing intervention of the back massage or back rub needs to be studied on postoperative CABG patients. Furthermore, the length of time needed, or the effective "dose" of the "doable" massage hopefully is not as much as 20 minutes, as nurses cannot feasibly offer this amount of time for one intervention on a busy unit.

Gaps in Mood and CABG Proinflammatory Wound Cytokines

There is a link between preoperative mood and surgical outcomes. Greater fear or distress prior to surgery is associated with longer medical center stays, more postoperative complications, and higher rates of re-admittance to the hospital. The impact of psychosocial interventions administered before surgery has demonstrated positive

effects on postoperative psychological and physical outcomes (Contrada, Leventhal, & Anderson, 1994). Thus, it is conceivable that there is also a link between preoperative mood and immune functioning after surgery.

Kiecolt-Glaser, Marucha, Malarkey, Mercado & Glaser (1995a) suggest that psychological variables influence wound healing, based on the type of surgery and through alteration of the immune system. Surgery is a threatening experience, containing multiple stressful components (Kiecolt-Glaser, Page, Marucha, MacCallum, & Glaser, 1998). Operations considered "minor" produce powerful emotional reactions in patients provoking significant consequences (Johnston & Wallace, 1990). Perhaps psychological variables influence surgical wound healing through alterations of the immune system. However, to date, in general, no research has been reported that links preoperative mood and surgical outcomes and in particular, pre-CABG mood and post-CABG inflammatory wound cytokines.

Wound healing is a dynamic, complex process made so by the presence and interaction of many substances within the wound during the inflammatory stage of wound healing. It has been found that time (Baker, El-Gaddai, Aitken, & Leaper, 2003), type of surgical procedure (Baker & Leaper, 2000), nature of surgical complication (Tarnuzzer & Schultz, 1996), other substances found in the wound (Mast & Schultz, 1996), and stress (Mercado, Quan, Padgett, Sheridan, & Marucha, 2002) influence inflammatory cytokine levels.

Mood might be found to affect wound healing but thus far, reports are contradictory. In general, it would be presumed that decreased inflammatory wound cytokine levels would be associated with higher depression scores because cytokines

assist in the inflammatory phase of wound healing and depression has been found to slow wound healing (Kiecolt-Glaser et al, 1995b). However, Marucha, Cacioppo, Daugherty, & Lee, (2003) reported that proinflammatory cytokine levels in blister wounds were significantly higher among the "lonely" subjects who had higher depression scores compared to their "non-lonely" cohorts who had lower depression scores. To date, to my knowledge, no study has been reported that determined the relationship between pre-operative mood and inflammatory wound cytokine levels after CABG surgery.

Gaps Regarding Stress and Its Relationship to Wound Healing and Interventions

Research that links stress to wound healing has been conducted by the disciplines of psychology, molecular virology, immunology, dentistry, behavioral medicine, biology, medicine, sports physiologists and medical genetics. A thorough review of the nursing literature on wound healing in humans has revealed many descriptive articles regarding how to use new wound healing techniques, with research on the techniques and the physiology of wound healing, but nursing research that links stress and wound healing is scant. Only one nursing study (Holden-Lund, 1988) examined the effects of relaxation with guided imagery on wound healing as determined by visual assessment of the wound. This method of wound healing assessment on surgical patients is not considered effective because sutured wounds do not provide enough visual evidence of healing. Additionally, the study was conducted over 25 years ago, thus more recent data is necessary. The current study addressed the lack of nursing research that links stress to wound healing and used wound fluid cytokine values to analyze the actual wound microenvironment.

Purpose of the Study

The purpose of the study was to determine the effects of nursing back rub on pain and four inflammatory wound cytokine levels in post CABG patients and to determine the relationship between pre-CABG mood and four inflammatory wound cytokine levels of post CABG patients.

Research Questions

1. What are the effects of nursing back rub on pain in post CABG patients?
2. What are the effects of nursing back rub on cytokine levels of interleukin 1-beta (IL-1β), interlekin-6 (IL-6), interleukin-8 (IL-8), and tumor-necroses factor-alpha (TNF-α) in the wound fluids of post CABG patients?
3. What is the relationship between pre CABG mood and pretest IL-1β, IL-6, IL-8, and TNF-α levels in the wound fluids of post CABG patients?

Theoretical Framework

The proposed study will use psychoneuroimmunology (PNI) as the theoretical framework. PNI studies the interactions between the nervous system and the immune system, and the relationship between behavior and health. Landis (1999) defined PNI as the interaction between mind and body and the powerful ways in which emotional, mental, social, and spiritual factors can directly affect health.

Several levels of biological links exist between the immune system and the central nervous system (NCI-NIH, 2002). Chemicals, such as neuropeptides, that convey messages among nerve cells, have been found to "speak" to cells of the immune system and some immune cells manufacture typical neuropeptides. Additionally, the neuroendocrine system, in response to stress, causes the adrenal cortex to secrete

corticosteroids. Corticosteroids have been shown to suppress immune function (Wells-Federman et al., 1995). Thus, the immune system, the central nervous system and the neuroendocrine systems interact continuously with each other. Stress can downregulate immune responses by altering the signals within the network of the nervous, endocrine, and immune systems (Rozlog, Kiecolt-Glaser, Marucha, Sheridan, & Glaser, 1999). The two main pathways that link the brain and the immune system are the hypothalamic-pituitary-adrenal (HPA) axis, and the direct neuronal fiber connections from the autonomic nervous system. Both pathways produce biologically important mediators capable of interacting with cells of the immune system.

The principles of PNI have been applied to several studies. Of particular importance and relevance to the proposed study are the PNI studies conducted by Glaser and associates at Ohio State University (OSU). The Glaser PNI research findings led them to conclude that there are sufficient data to support that psychosocial stressors and/or interventions can modulate the immune system resulting in beneficial health changes. According to Kiecolt-Glaser, McGuire, Robles, & Glaser (2002) wound healing has provided the strongest evidence for such a conclusion. For example, in studies that assessed wound healing, Glaser et al. (1999) noted that psychological stress had measurable negative consequences for proinflammatory cytokines IL-1α and IL-8 production in the local wound.

Intervention

The musculoskeletal system increases in tension and rigidity during stress via motor pathways through the sympathetic nervous system. The antithesis of the stress response is the relaxation response, which has been described as a break in the stress-

symptom cycle (Wells-Federman et al., 1995). Massage can be perceived as a stress-reducing intervention because it has been shown to produce relaxation (Fraser & Kerr, 1993). In general, stress down regulates the immune system. The regulation of the immune system is important to this study because the surgical wound of CABG patients and the specific proinflammatory wound cytokines being measured are directly related to how effective the patient's immune system is functioning.

The behavioral strategy of using the nursing back rub is that a back rub could alter the immune environment of postoperative wounds by decreasing stress. "Given that stress activates neuroendocrine and autonomic pathways known to modulate immune responses and given that immune responses can be conditioned and learned, then it may be possible to use behavioral strategies to modulate immunity" (Landis, 2002, p. 29). To illustrate, Groer et al. (1994) conducted a study that utilized touch in the form of a back massage in a well elderly population. Groer found a significant increase in the concentrations of salivary immunoglobulin A (sIgA) in the experimental group compared to the control group.

In sum, providing evidence for the efficacy and therapeutic value of traditional nursing interventions can be done if the interventions are studied within the PNI framework (Wells-Federman, Stuart, Deckro, Mandle, Baim, & Medich, 1995). Wells-Federman et al. state that viewing nursing interventions through the PNI lens can transform tradition-based practice to knowledge-based practice.

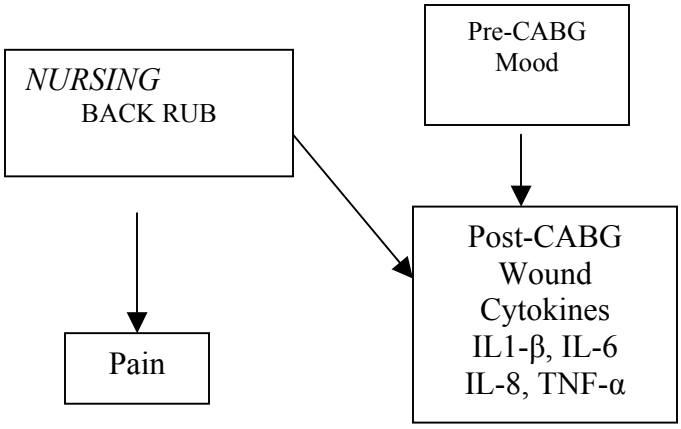

Figure 1 Conceptual Model

The conceptual model (figure 1) for this proposed study was adapted from the conceptual model developed by Kiecolt-Glaser and associates (1998). The Kiecolt-Glaser et al. model is called the "biobehavioral model of the psychological, behavioral and biological pathways that influence wound healing: the central short-term outcome in recovery from surgery" **(**p. 1210**).** Their model illustrates the complex relationships among the relevant domains of wound healing and variables that are believed to influence wound healing through several pathways (Kiecolt-Glaser et al.).

Within the conceptual model of this study, the nursing back rub was hypothesized to modulate post-CABG pain and inflammatory post-CABG wound cytokines. Specifically, the nursing back rub was hypothesized to decrease post-CABG pain and increase post-CABG wound cytokines. The model also shows that pre-CABG mood wound influence post-CABG wound cytokines.

Theoretical Definitions of Terms

Coronary artery bypass graft (CABG) is surgery that utilizes vessels from other parts of the body for bypasses of obstructed vessels in the heart. Patients can have one

vessel or many vessels bypassed. All of the patients in this study were put on a coronary perfusion bypass machine that circulates the blood through the body while the new vessels are grafted into the heart.

CABG patient is an individual who has had the CABG surgery to bypass blocked coronary arteries using sections of veins from other parts of the body.

Stress response is the increase of corticosteroids, norepinephrine and epinephrine, which may lead to a decrease in immune function (Kiecolt-Glaser et al, 1998). The stress response is triggered when a person perceives a situation to be a threat to his or her physical or emotional well-being and perceives his or her coping abilities to be inadequate to deal effectively with the demand (Wells-Federman et al., 1995).

Immune function is the level of immune variables at inflamed sites during an immune reaction (Kiecolt-Glaser, 1998).

Inflammatory stage of wound healing is the stage of healing occurring more or less during the first 96 hours after injury. At this stage of healing the major cells in the wound are neutrophils followed by macrophages (Carrieri-Kohlman, Lindsey, & West, 1993).

Macrophages are immune cells. They secrete many immune variables including the proinflammatory cytokines Il-1β, Il-6, Il-8, and TNF-α proposed as variables in this study. Macrophages are phagocytes that destroy bacteria and clean up damaged tissues. Macrophages produce chemotaxins for continuing white cell recruitment, and release proteases that lyse necrotic material (Traversa & Sussman, 2001).

Cardiac Surgery Pathway is a printed representation of how the normal course of recovery from CABG surgery is expected to progress. At 18-48 hours after CABG

surgery, the pathway indicates that patients will be: eating soft, low fat, low salt diets, will be up in a chair for meals for at least 30 minutes and walk in the hall three times for 150 feet, be able to use the incentive spirometer to close to pre-surgical levels, be on oral pain medications, receive a sponge bath, have dressings removed except around the chest tube, receive a laxative if has not had a bowel movement, and is to receive cardiac rehabilitation information pamphlets including "Moving Right Along After Heart Surgery".

Nursing back rub is a modified version of the Jensen-Nelson back rub that uses effleurage with a slow stroke for ten minutes (Groer et al., 1994).

Mood will be measured with the Profile of Moods States (POMS) instrument, which measures the variables of tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment. The TMDS adds all of the items except vigor, which is subtracted. The POMS measures dimensions of affect or mood.

Pain will be measured with a visual analogue scale (VAS). The VAS is a horizontal line, 100 mm in length, with labeled anchors at each end to indicate extremes of the variable being studied, with the low end to the left. The participants pain will be measured by a mark made by the patient and will be the number of mm from the left anchor.

Cytokines are protein substances secreted by immune cells and all nucleated cells. They are chemical messengers that act by autocrine, paracrine, and juxtacrine methods. Their actions may be growth stimulating or inhibiting, pro or anti-inflammatory, cause changes in body temperature, fatigue levels, social exploration, mood and appetite and

their levels are affected by stress. Cytokine actions on other cells can increase or decrease synthesis, increase or decrease secretions of other proteins, change migratory activity or act as mitogens to stimulate cell growth. Cytokines released from lymphocytes or macrophages control virtually every aspect of the immune and inflammatory responses, including the coordination of host defense against infection and the host response to injury. The proinflammatory cytokines to be measured in this study are IL-1β, IL-6, IL-8, and TNF-α.

Variables

Nursing back rub and mood are the independent variables and pain and wound cytokine levels are the dependent variables.

Delimitations

This experimental, randomized controlled study was conducted in the southeastern part of the United States. It confined itself to the performance of a nursing back rub or spending time with the participant without the back rub, and collecting data through self-report measures as well as from a biological specimen from CABG patients during the pre and postoperative period.

Limitations

1. The participants were likely to be mostly Caucasian because of the specific location of the study setting. Thus, the findings are not generalizable to the CABG patient population in general.
2. The two collaborating CABG surgeons whose patients comprised the sample were conveniently selected from a community of CABG surgeons who do CABG in the study setting.

3. It is likely that all participants would have received oral pain medication during the study. It is unclear whether it will be the back rub, "time with the researcher", the pain medication or a combination of all that is responsible for any reduction of pain.
4. Many factors affect the inflammatory stage of wound healing. Although a randomized clinical trial design was completed, not all factors can be controlled or measured.
5. Measurement of cytokines through ELISA involves precision. Small deviations in performing ELISA can produce different results. (A trained and experienced lab technician was responsible for measuring cytokine levels to minimize deviations as much as possible).
6. Cytokine measurement is recorded in picograms, so it is possible that the amounts were below the level of detection.
7. Mere awareness of participation in the study could have influenced the responses to the self-report measures. (Hawthorne effect).
8. The participants' desire to project themselves in the best light could have influenced the self-report results (social desirability factor).

Significance

This study extends the extant literature on evidence-based nursing interventions specific to the post-CABG patient. The study also expands our understanding of the effects of nursing back rub on pain and cytokine levels. It informs nursing practice regarding the anatomic location and "dose" of the nursing back rub for post-CABG patients similar to the sample of the study. The study reports two levels of four

proinflammatory cytokines in wound fluids after CABG surgery. Finally, this study expands our understanding of the relationship of mood to four proinflammatory wound cytokines in post CABG patients.

II. LITERATURE REVIEW

The review of the literature will present an overview of the framework of psychoneuroimmunology and research on the intervention of massage. An overview of massage research will be presented because many of these works contribute to the understanding of the effectiveness of touch. The research literature concerning massage will be limited to those studies specifically related to the purpose of this study. Thus, only studies that used the intervention of massage on patients during the perioperative experience will be reviewed. A table of studies that used massage will be displayed for the purpose of indicating a need to determine an effective dose of massage. A review of the literature that discusses the relationship between wound healing and stress will be presented. Additionally, research on the dependent variable of wound cytokines and wound healing will be reviewed.

Psychoneuroimmunology

The definition of PNI by the organizers of the Center for Mind-Body Medicine (Washington, DC) is the interaction between mind and body and the powerful ways in which emotional, mental, social, and spiritual factors can directly affect health (Landis, 1999). Another definition of PNI, from the researchers at OSU (Rozlog et al., 1999) is that PNI is the study of the influence of behavior on brain-immune interactions, and how this affects health. Additionally, psychosocial factors have clinically significant relationships with immune-related health outcomes, including infectious disease, cancer, wound healing, autoimmune disease, and HIV (Kiecolt-Glaser et al., 2002).

Ishigami conducted one of the first known psychoimmunologic investigations in 1919 (Locke, 1982). Ishigami measured tubercle bacilli among chronic tuberculosis

patients during inactive and active phases of the disease and noted a decrease in phagocytic activity in the patient's white blood cells during episodes of emotional excitement. He postulated that the stress of contemporary life led to a decrease in immune function and a resultant increase susceptibility to tuberculosis.

Solomon and Moos (1964), in another early study of the interaction between the mind and the body, found "evidence that emotions play an important role in the pathogenesis of physical disease associated with immunological dysfunction" (p. 657). They noted that particular personality factors in rheumatoid arthritis play a factor in the disease progression. Additionally, other autoimmune diseases, such as ulcerative colitis and hyperthyroidism also point to a relationship between personality factors and the presence of altered immunological responsiveness. They proposed that the adrenal corticosteroids, since they depress lymphocytes and are increased during periods of personal threat, sustained tension, and intense distress, seem implicated in the complex interactions between stress and immunological dysfunction. The major theoretical point of their famous study was that "autoimmunity may be related to relative immunological incompetence and that such immunological incompetence in turn might be related to emotional stress and both anxious and depressive affect, which are associated with elevation of adrenal cortical steroid hormones" (p. 658). Solomon and Moos have been credited with coining the term "psychoimmunology".

It was the discovery by Ader and Cohen (1975), however, that began earnest study into the mind/body connection. It was found that the immune system could be behaviorally conditioned, in other words, the immune system could be taught to respond in a certain manner. In their study, the pairing of a neutral stimulus, saccharin, with

cyclophosphamide, an immunosuppressive agent, resulted in the conditioning of immunosuppression in rats. The results were interpreted as providing evidence for behaviorally conditioned immunosuppression. It was further suggested that the immunosuppression was not mediated directly by a nonspecific elevation in adrenocortical steroids that may be presumed to accompany an illness-induced taste aversion.

Stimuli that are perceived as threatening for either physiological or psychological reasons produce a coordinated response known as the stress response (DeKeyser, 2003). The hypothalamic-pituitary-adrenal axis, through which glucocorticoids are produced, is one response to stress, as cortisol interacts with many immune cells. A second response to stress involves the sympathetic nervous system whose neurotransmitters have receptors on certain immune cells. Additionally, sympathetic noradrenergic nerve fibers directly innervate lymphoid organs of the immune system (Felten, Felten, & Carlson, 1985).

As a result of stress, the body is constantly responding to messages carried throughout its systems. “Data are now available to help explain the way that the mind and body are connected and the way that they communicate. This knowledge may provide the missing link in treating patients.” (Dossey & Guzzetta, 1994, p. 72). Cytokines are diverse chemical signaling messengers secreted by cells of the immune system. Stress has been associated with the altered production and release of cytokines (Agarwal & Marshall, 2001). In fact, stress has been found to impede proinflammatory cytokines (IL1-β and IL-6), thus impeding wound healing (Kiecolt-Glaser et al., 1995; Kiecolt-Glaser et al., 2002).

The Interventions of Touch/Massage/Nursing Back Rub

Review of literature involving CABG patients that relates to the intervention of the nursing back rub will be reviewed. These interventions are Therapeutic Touch (TT) and massage. The term "nursing back rub" was not specifically used in the literature on massage and the CABG patient.

The intervention of the nursing back rub or massage is effective in alleviating distress and providing comfort to patients. Therapeutic massage was found to promote recovery from surgery through reducing autonomic arousal (Menard, 1995) and was also found to significantly reduce pain in surgical patients on the first post-operative day (Chin, 1999). Slow stroke back massage was found to significantly decrease anxiety in CABG patients in the critical care unit (Richards, 1993).

Six review studies on the therapeutic effects of massage, written in the last five years, (Field, 1998; Gauthier, 1999; Hobbs & Davies, 1998; Platt, 2000; Richards, Gibson, Overton-McCoy, & Leigh, 2000; Weinrich, Haddock, & Robinson, 1999) indicate that massage, as a complementary or alternative therapy, has become a popular intervention. Indeed, as mentioned previously in Chapter One, the TIUM conducts research on a variety of different conditions that might benefit from massage (Field, 1998). Field, a prominent investigator from the Institute, noted that massage therapy is older than recorded time and was used as the primary form of medicine before pharmaceuticals. Results from these review studies indicate that the significant effects of massage range from decreasing anxiety, pain, cortisol levels, norepinephrine, epinephrine, heart rate, depression, fatigue and blood pressure to increasing natural killer cells, mood, and range of motion. Because massage has been found to be effective in both

alleviating distress and promoting comfort, and in producing beneficial physiological effects, it can be an important intervention for nurses determined to meet the challenges of providing evidence-based care.

Massage and the nursing back rub has been studied in the areas of healthy women (Longworth, 1982), well elderly (Groer et al, 1994), critically ill patients in intensive care units (Lewis et al, 1997; Tyler, Winslow, Clark, & White, 1990), psychiatry (Field, Morrow, Valdeon, Larson, Kuhn, & Schanberg, 1992), hospice (Meek, 1993), cancer (Weinrich & Weinrich, 1990), and HIV (Ironson, Field, Scafidi, Kumar, Patarca, Price, et al., 1996). What is of importance for this research is the study on the intervention of massage with cardiac and surgery patients. Five studies specifically address the CABG patient (Bauer & Dracup, 1987; Dunbar & Redick, 1986; Okvat, Mehmet, Ting, & Namerow, 2002; Richards, 1993; Stevensen, 1994). Additionally, there were five studies that examined massage with surgical patients (Chin, 1999; Hattan, King, & Griffiths, 2002; Menard, 1995; Nixon, Teschendorff, Finney, & Karnilowicz, 1997; Stevensen, 1994).

All forms of massage involve soft-tissue manipulation that is said to blend mechanical proficiency and artistic sensibility (Bower, Rubik, Wiess, & Starr, 1997). Improper technique can be harmful, thus the procedure must be technically correct. Swedish techniques, the most commonly used, directs blood flow toward the heart to improve circulation. This improvement is said to assist in the removal of waste products and the movement of lymph. It would make sense then, that some of the effects of massage come from an increase in circulating blood and lymph.

Goldstone (2000) noted that a recent review of the literature on massage revealed that the massage intervention is often not explicitly described. Goldstone noted that not all articles mentioned the type of massage stroke, the speed of the massage, amount of pressure applied, and the length of the massage. Goldstone set forth a specification for the description of massage to be used in future research which includes definitions of strokes, purpose of the massage, body areas, frequencies, duration, position of patient, use of conversation, environmental factors, qualifications of the person performing the massage and specification of the type of patient receiving the massage. The specifications would hopefully increase the ability of future researchers to replicate studies and to make more precise conclusions regarding the effects of massage. As a result of this review, the proposed study will specify factors necessary to replicate the massage for future research.

Preoperative Massage Literature

Kim, Cho, Woo and Kim (2001), in an interesting study involving 29 cataract pre-surgical patients, studied the effects of five minute hand massages before surgery on postoperative outcomes of blood pressure, heart rate, and anxiety levels. These parameters were measured before and after the hand massage and five minutes before the end of surgery. Thirty patients, in a control group received no massage. Anxiety was measured using a VAS of ten centimeters and numbered zero to 100. Blood levels of epinephrine, norepinephrine, cortisol, blood sugar, neutrophil and lymphocyte percentages were measured in blood taken before surgery after the intervention and five minutes before the end of surgery. The same surgeon at the same time of day (1pm and 4 pm) performed the same technique under pinpoint local anesthesia. One researcher conducted all the massages using effleurage and petrissage.

Results indicated that there were significant differences in the levels of anxiety that were measured before the massage, after the massage and after surgery. Both the experimental and control groups noted significant decreases in anxiety after the surgery, but the experimental group noted a significant decrease in anxiety before surgery as well. The mean epinephrine, norepinephrine, and cortisol levels decreased after the massage in the experimental group and increased in the control group. Between-group differences in mean levels of epinephrine, norepinephrine and cortisol, before and after the massage, were all significantly decreased.

This study indicated a decrease in the major stress neurotransmitters with a hand massage. Of importance to this study was that a massage for five minutes to a hand of a preoperative patient decreased neurotransmitters since it was proposed that a back massage would be able to decrease sympathetic nervous system activation after surgery. Five minutes of a massage to the hand affected preoperative levels. It was proposed that ten minutes of a back massage would alter levels of stress-inducing neurochemicals postoperatively such that the levels of the cytokines would be affected. Also important to the study that inactivation of the sympathetic nervous system was deemed to be an important factor preoperatively strengthening the model that psychological states may effect postoperative outcomes.

Postoperative Massage Literature

The length or dose of the massage needed for significant postoperative effects has not been determined. Additionally, effective anatomical location and position has not been determined. Further, the best time after surgery, for a massage has not been

determined. A review of the literature on massage after surgery shows differing results and little if any attempt to replicate studies to determine these important factors.

The "dose" or length of time needed for a massage in the following study was not predetermined. Researchers Nixon, Teschendorff, Finney, and Karnilowicz (1997) conducted a study to determine whether therapeutic massage on several body sites, when used as an adjunct to analgesia, would alter patients' perception of postoperative pain. Researchers studied 39 abdominal surgery patients over a five-month time period in a surgical ward of a large metropolitan teaching medical center. The study used an equivalent groups design in a pilot study to assist in determining equivalency in age, gender, ethnicity, country of birth, self-defined pain tolerance, past medical, surgical and anesthetic history, weight, surgical procedure, and previous experience of massage. An important point of the study was that the research protocol was designed to ensure that the massage intervention did not alter the pharmaco-medical management of the patients. Twenty nurses administered the massage after being trained by a masseur in Swedish massage techniques prior to the study. Quality of the massage was said to be monitored by the research assistant and the masseur.

Four of the five basic techniques of the Swedish massage were included: effleurage, petrissage, friction and vibration. Time of day and anatomical site for the massage was determined by the patient's position and personal preference. Massages lasted for a minimum of two minutes with no maximum time limit, two times a day for seven days or until discharge. Two minutes minimum timing for the massage was set to "allay nurses' concerns about their ability to add massage to their already demanding work schedule".

Prior to surgery, a pain VAS marked no pain and worst possible pain on each end of a ten centimeter long and two centimeter wide scale was given to each patient to determine their perception to pain. The VAS was found to be easy to use and suitable for frequent and repeated use. The amount of pain and the amount of massage in a 24-hour period were summed and divided by the total post-operation days for patients. Data was analyzed by repeated measures analysis of covariance. The independent variable was the group with the subjects in the treatment group representing one level and subjects in the control group as the second level. The dependent measure was the patients' perception of pain over a 24-hour period. Age was considered a covariate.

When controlling for the effect of age and comparing the results for the treatment and control groups, perceptions of pain over a 24-hour period were significantly lower for the age group 41-60 years old, who received a mean of 12.62 minutes of massage in a 24-hour time period. Patients that received less than 12.62 minutes of massage and patients outside of this age group did not have significant decreases in the perception of pain. The researchers noted, "Whether younger patients would have had a similar outcome if they had received massage for the same length of time is unknown." It is also unknown whether older adults in this study would have had a significant decrease in the perception of pain with a longer massage. Additionally, although it was noted that a research assistant and a masseur monitored the quality of the back rub, having 20 different nurses administer the massage could significantly alter the type of massage given. Because five types of massage were given, and they were not differentiated in the results, one type of massage could have been more or less influential to the results.

The use of massage as an adjunct to pharmacological methods of pain relief is appropriate since patients must have pain relief after surgery. It was also important for this study because the variable of pain on a VAS scale before and after the back rub was used to see if pain, even at the level controlled by analgesia, could be further decreased by a back rub. It was proposed that massage could thus serve as an adjunct to routine pain medication administration. The above study did not attempt to measure pain relief pre and post massage, but rather overall perception of pain after the surgery. In contrast, this study used the pain VAS for the immediate effect of massage within what is considered adequate pain control for the post-operative surgical patient. Additionally, the above study did not control for the variable of anatomical location. This may have had a significant effect on the results of the study.

The adequate "dose" of massage to produce significant results in patients is not known as illustrated in Menard's (1995) dissertation research. In this study, the "dose" was greater than three times that of the above study but results were insignificant. Thirty gynecologic oncology post-hysterectomy patients were randomly divided into two groups. One group received routine postoperative care and the other group received a daily 45 minute massage for five days postoperatively. Outcome measures included the POMS, the State-Trait Anxiety Inventory (STAI), self reported levels of pain, amount of pain medication, systolic blood pressure, urinary free cortisol levels, length of medical center stay and amount and kind of follow-up medical services used over a four-week post operative period. There were no statistically significant differences found between the two groups in any of the outcome measures. Results indicated that mean scores for anxiety, and depression, and pain ratings, use of patient-controlled analgesia, mean

systolic blood pressure and cortisol levels were all lower in the experimental group than in the control group. The hypothesis that therapeutic massage promoted recovery from surgery through reducing autonomic arousal was said to be "generally supported".

The study by Menard attempted to determine if a very large "dose" of massage, 45 minutes for five days, was able to significantly alter surgical outcomes. The research did not support the increased effectiveness of a massage in relationship to its "dose". The next study introduced the question of which position is best to conduct massage in postoperative patients in addition to using a "dose" of ten minutes for two days.

Chin (1999), in another study conducted for a dissertation, examined the effects of back massage on stress responses and postoperative pain among gynecological patients. Chin used a pretest-posttest experimental design of 112 Taiwanese subjects. Randomization was achieved by assigning subjects to the massage or control group by permuted block randomization controlling for direction of either a horizontal or vertical incision. A ten-minute massage, in the side-lying position, was given without conversation to the treatment group on the day of surgery and the first postoperative day. The control group received no intervention and were said to rest for ten minutes.

Outcome measures for stress responses included serum cortisol and beta-endorphin concentrations, electromyography of frontalis and trapezius muscles at baseline, post-turning, and pretreatment for both days and post treatment for both days. Self reported physical and psychological tension and the sensation and distress of incisional and muscle pain was measured with a 1-100 VAS.

Chin controlled for pretreatment scores and used a repeated measures ANCOVA to compute the results that showed significantly reduced VAS muscle pain on the first

postoperative day in the massage group. There were no significant differences between the massage and control groups in surgical stress responses, incisional pain and distress of muscle pain. What is interesting about this study is that the researchers found that having patients turn to the side did not increase sensation and distress of incisional pain. Positive and significant relationships were found between distress of incisional pain and psychological and physical tension. Thus, a ten minute, side-lying massage was effective in reducing muscle pain in the hysterectomy patient on the first postoperative day. That there was no decrease in surgical stress responses could be because, as the researcher noted, the EMG measurement might have been more indicative of reduced nerve stimulus if placed at the site of pain. Additionally, tension may not be a valid measure of stress. It is interesting to note that serum cortisol and beta-endorphins were not significantly changed.

Postoperative CABG Massage Literature

The above studies, although utilizing massage for postoperative patients, are not specific to the cardiac surgical patient. The following research used the intervention of massage on post CABG patients. Several studies have been conducted on patients in cardiac units, but very few were found during the literature review that specifically addressed the CABG patient. Stevensen (1994) followed by Hattan (2002), performed foot massage on postoperative CABG patients. Stevenson's hypothesis that aromatherapy combined with foot massage would enhance the psychological well-being of patients without changing physiological parameters was closely related to Hattan's whose aim was to investigate the impact of foot massage and guided relaxation on the well-being of patients who had undergone CABG surgery.

Stevensen (1994) conducted a randomized controlled experiment of 100 CABG patients divided into four groups. One group received no intervention, another group 20 minutes of light conversation, the third group received a 20 minute apricot kernal oil foot massage and the last group received a 20 minute foot massage with neroli essential oil, considered as aromatherapy. Subjects could not be ventilated, paced, receiving mechanical blood pressure support, have a pedal arterial line or have suppurating or infective skin conditions of the foot. Additionally, vital signs had to be within normal limits at the time of the study. Three nurses performed the massage. Physiologic measures of blood pressure, respiration and heart rate were recorded as well as a modified Speilberger STAI State Self Evaluation Questionnaire five times throughout the experiment: one hour before, immediately before, immediately after, one hour after and two hours after the interventions. The modified STAI used three positive indicators: calm, rest and relaxation and three negative indicators: pain, anxiety and tension and were given to the patients verbally. Pain was added to the Speilberger STAI because, "it was thought to be a relevant indicator for this group". No mention was made as to how this might have altered the instrument's reliability or need to consider this. A questionnaire on day five was given to the patients that had received the massage asking to recall their feelings from the massage, their perception of the massage, its benefits, and the length of time that the subjects perceive the duration of the effects of the massage lasted. They were also asked about the timing and frequency of the massage.

Results found no significant differences between age and sex in the groups. The only statistically significant physiological change between the massage and non-massage patients was that respiratory rate decreased and this was found only immediately before

and immediately after the interventions. The psychological results from the two massage groups showed significantly greater on calm, restful and relaxing indicators than from the two control groups. Eighty-two percent of the patients who had foot massage remembered it and 100% of those subjects found the massage beneficial. The neroli foot massage benefits were noted to last from several hours to two days compared to the benefits of plain oil that lasted only minutes. Responses to the questionnaire noted that patients found the massages restful, relaxing, peaceful and calming. Others called the massage "smashing" or "great". Only one patient stated he did not find the massage beneficial.

Hattan (2002) used a randomized controlled experiment with 25 post CABG surgery patients divided into three groups. Subjects had to be English speaking, extubated, and 48 hours postoperative. Subjects were excluded if they were on mechanical blood pressure support, paced or had foot arterial lines and if they were hard of hearing or had a contraindication to massage. Two subjects had surgeries canceled and three withdrew. The control group (n=7) received no intervention and normal unit activity. The second group (n=9) listened to a guided relaxation audio-tape recoding for 20 minutes. The third group (n-9) received a 20 minute foot massage from a trained massage therapist.

Hattan tested subjects in a pretest-posttest design, measuring blood pressure, pulse and respiration. Six VAS scales assessed perceived levels of pain, anxiety, tension, calmness, rest, and relaxation. An open-ended questionnaire asked for positive and negative responses to the massage. Overall differences between pretest and posttest scores were used to statistically test the results with the t-test. The ANOVA was used to

test the differences between the intervention and control groups. Dunnett's multiple comparison test was applied to determine the group responsible for the significant difference.

Results showed there were no significant differences in blood pressure, heart rate and respirations between the three groups. This was important for the proposed study as it had been reported that massage decreased respirations in the previous study. There was a statistically significant effect of foot massage on the variable of "calm". Both the massage and guided relaxation groups showed a trend towards improved psychological well-being. Only three of the massage group returned the questionnaires indicating that they would recommend a massage finding it "therapeutic", "very relaxing", and "soothing and calming".

To summarize these closely related articles to this study, it is apparent that although respirations did decrease in Stevensen's study, it was only transiently and did not adversely affect the patient. No adverse physiological effects occurred in this population as a result of a massage 24-48 hours postoperatively. Additionally, patients recommended a massage, albeit a foot massage. The foot massages produced statistically significant effects on the calm variable in both studies. Guided relaxation did not show these results. Thus, a calm-inducing intervention of massage was seen by this researcher as an effective method to reduce stress in postoperative CABG patients.

Discussion of Table of Studies on Massage

The massage table (Appendix, Table 1) provides a review of the literature that points out one important factor regarding the intervention of massage. Although many studies have produced effects as listed in the right hand column, no one has determined

how long a massage, or dose of massage, must be conducted to consistently obtain those effects. In the busy world of the coronary observation unit, and in fact, for any type of patient on any unit, it is important that a dose of massage be determined. This will happen only when researchers make an effort to specifically address this issue. This study used a ten minute massage because, as evidenced from the chart, ten minutes is about average to elicit effects. Additionally, it is felt that busy nurses will more likely perform a ten minute massage compared to a 20 minute massage if it has been found to be effective in reducing pain, and improving immune functioning in postoperative patients. Studies conducted for more than 20 minutes and over the course of several days have been shown to produce longer lasting results. Although it would be interesting to conduct such a study, money and time make this impossible at the present. The researchers at TIUM have conducted experiments where massages are given for more than 30 minutes and are being performed for many weeks. Thus, one of the rationales for performing a ten minute massage was to attempt to determine an effective dose using ten minutes as a starting point. Future studies may find that decreasing or increasing the duration and number of times necessary to give a massage will produce additional significant and longer lasting results.

Stress and Wound Healing

Research that links stress to wound healing has been conducted by the disciplines of psychology, molecular virology, immunology, dentistry, behavioral medicine, biology, medicine, sports physiologists and medical genetics. A thorough review of the nursing literature on wound healing in humans has revealed many descriptive articles regarding how to use new wound healing techniques with research on the techniques and the

physiology of wound healing but nursing research that links stress and wound healing is scant. Corwin (2000b) noted that further research to improve wound healing outcomes by encouraging supportive sickness behaviors and reducing stress would be intriguing to nurses. Whitney (1999) encouraged investigation into specific cellular responses in response to stress reduction. She argued that the use of stress reduction techniques to improve wound healing rests largely on theory that needs to be confirmed.

Holden-Lund (1988) in a prospective, randomized study of relaxation with guided imagery in patients undergoing a cholecystectomy, found decreased erythema around the wound in the relaxation group. The small sample size (24) may have contributed to the lack of evidence that the intervention improved overall wound healing as measured by a visual assessment inventory. Urinary cortisol levels were lower in the experimental group on the first post-operative day. Wound healing effects by a visual assessment inventory is not appropriate, however, "because most surgical wounds are sutured, direct assessments of healing are not possible" (Kiecolt-Glaser et al., 1998, p. 1214).

Another nurse researcher (McCarthy, 1992) studied rats and the stress of noise. Mc Carthy found that noise stress influenced wound healing by significantly reducing macrophage secretion of IL-1 and neutrophil release of superoxide anion in rats. Both of these molecules are necessary for the proper functioning of neutrophils in wound healing. A replication in human subjects would advance the knowledge of human leukocyte functioning.

A study conducted on mice that were given dexamethasone provided evidence that glucocorticoids produce severe defects in wound healing as indicated by reduced infiltration of inflammatory cells, delayed wound re-epithelialization and impaired

granulation tissue formation. Hubner et al. (1996) studied glucocorticoid-treated mice and isolated RNA from wounded skin. The wounded skin was analyzed for cytokine mRNA expression. IL-1α, IL-1β, and TNF-α mRNAs levels were significantly reduced in the dexamethasone-treated mice. IL-1β mRNA levels were 38% lower compared to the control at day three after wounding as assessed by laser scanning densitometry of the autoradiograms. IL-1α levels (60-70%) and TNF-α levels (55-65%) were even lower in the wounds of dexamethasone-treated mice compared to control mice. The in vivo data demonstrates that glucocorticoids reduce the normal induction of proinflammatory cytokine expression after injury. Thus, impaired expression of these cytokines is associated with wound healing defects.

The work of the research team at Ohio State University in the area of stress and wound healing is extensive. Their study supports the hypothesis that psychosocial factors have clinically significant relationships with immune-related health outcomes including wound healing (Kiecolt-Glaser et al., 1998). Of particular interest to this research is the study that noted an alteration in cytokines by psychosocial factors during wound healing, specifically, the hypothesis addressed whether loneliness altered the expression of cytokines during wound healing (Marucha, Cacioppo, Daugherty & Lee, 2003). Thirty-eight undergraduate students were tested on a loneliness scale. One mm by 5 mm wounds were placed on the palates of 17 of the lonely students and 17 of the non-lonely students. One day after wounding, two mm by 5 mm biopsies were taken from tissue encompassing the wound. The mRNA was isolated from non-wounded tissue and biopsied. Cytokines IL-1 β and IL-8 values were measured. Utilizing an analysis of covariance (ANCOVA) between unwounded and biopsied tissue cytokine values, the

results showed mean scores on the Perceived Stress Scale (PSS) and the Beck Depression Index were significantly higher in lonely compared to non-lonely students ($p<0.0001$). IL-1 β and IL-8 measurements were significantly increased by wounding ($p<0.05$). Furthermore IL-1 β and IL-8 values were increased by more than two fold in wound tissue of lonely versus non-lonely subjects. It was concluded that the higher levels of proinflammatory cytokines in wounds may be responsible for delayed healing. This is just the opposite of what would be expected as an increase in these cytokines would be expected to produce more cytotoxic effects and thus produce a pro-healing environment.

Another Ohio State research study (Glaser et al., 1999) found almost the opposite effects for proinflammatory wound cytokines. In a study of the dynamics of inflammation, blisters were induced on the forearms of 36 women by suction. Samples of wound fluid were aspirated from the blister chambers at five and 24 hours after wounding. Women with higher PSS demonstrated significantly lower production of IL-1α and IL-8. Additionally, women that produced lower levels of both cytokines at 24 hours reported more stress and negative affect, and they had higher levels of salivary cortisol than those with higher cytokine levels. The same conclusion was drawn, that stress has measurable consequences for proinflammatory cytokine production, but for which cytokines and the question is asked, does a particular mood affect different cytokines?

Kiecolt-Glaser et al. (1995) studied the effects of psychological stress on wound healing in 13 women caregivers of relatives with Alzheimer's disease, comparing them to 13 controls matched for age and income. Punch biopsy was used to make three by five mm full-thickness wounds. Peripheral-blood leukocytes from caregivers produced

significantly less IL-1 β mRNA than the leukocytes from the control women. Wound healing, assessed by photography and no foaming after hydrogen peroxide, was complete in 48 days for the caregivers verses 39 days for the control women. Wound healing took an average of nine days, or 24% longer in caregivers than controls.

Kiecolt-Glaser and Glaser have consistently found that human and animal models provide evidence that stress slows wound healing. Marucha (1999) noted that wounds placed on the hard palate of students three days before an exam healed an average of 40% more slowly than those made in the same individuals during summer vacation**.**

Wound Healing and Cytokines

The inflammatory phase of wound healing begins immediately after an injury and continues for approximately three to four days (Carrieri-Kohlman et al., 1993). The inflammatory phase of wound healing is an important phase because it is during this time that tissue is prepared for the formation of new vessels, collagen and epithelial tissue. Healing can be delayed if the inflammatory response is absent or suppressed. Additionally, early post-traumatic inflammation is an important step for cell replication and the foundation of healing (Holzheimer & Steinmetz, 2000). It is during the inflammatory phase that proinflammatory cytokines are called to or secreted into the wound site.

Cytokines are soluble proteins secreted by lymphocytes, macrophages and neutrophils that instruct immune cells to alter proliferation, differentiation, secretion or activity (Zeller, McCain, & Swanson, 1996). Cytokines regulate the intensity and duration of the immune response by stimulating or inhibiting other cells. More than 80 different cytokines have been identified and include the interleukins, interferons, tumor

necrosis factor and colony-stimulating factors. Cell membranes, or the plasma membrane is important for regulatory and protective functions. Outside of this is the extracellular fluid containing innumerable chemical signals, including neurotransmitters, hormones, growth factors, and cytokines. The cytokines as chemical signals constantly bombard the plasma membrane with information and directives. "The information contained in these chemical signals is indispensable for coordination of intercellular function and maintenance of cellular homeostasis and essential for the survival of the whole organism." (Schwertz & Barry, 1994, p. 2).

Holzheimer and Steinmetz (2000) measured local and systemic concentrations of cytokines in surgical wounds and found that cytokine levels are markedly higher systemically indicating a compartmentalization of the immune response. Compartmentalization is important because the control of tissue repair requires temporal and spatial confinement of cytokines. The balance of cytokines within wound fluid controls normal or abnormal wound healing.

Since it is postulated that the inflammatory response that occurs after cutaneous wounding is a prerequisite for healing (Gallucci et al., 2001), it is important to recognize inflammatory cytokines that are called to the site. The cytokines of interest to this study are IL-1β, IL-6, IL-8, and TNF-α because these cytokines are found in wound fluid during the inflammatory phase of wound healing. IL-1 is one of the most important immune response modifying interleukins (Indiana State University web site, 2002). A deficiency of IL-6 has been found to delay wound healing in mice (Gallucci et al., 2001). Accumulation of IL-6 can lead to production by alkaline phosphatase of adenosine and subsequent protection from ischemic injury (Gallo et al., 1997). IL-8 is hypothesized to

enhance gap junctional intercellular communication between fibroblasts in granulation tissue, which increases the rate of granulation tissue maturation (Moyer, Saggers, Allison, Mackay, & Ehlich, 2002). Production of the inflammatory cytokines IL-1, IL-6, and TNF α can be considered as one of the local vital reactions after wounding (Ohshima, 2000). IL-6 was shown to exhibit an ability to stimulate keratinocyte proliferation. Ono (1999) noted that cytokine modulation of the repair process in transitory wounds remains a very important subject for investigation.

Mast and Schultz (1996) noted that the process of skin wound healing begins at the moment of tissue injury and that it was the same whether the injury was intentional, as in surgery, or unintentional, as in trauma. They characterized some of the cytokine interactions. TNF-α was noted to initiate the pro-inflammatory cascade and to induce IL-1β synthesis during skin wound healing. It was noted that research provided evidence that low levels of TNF-α produced in normal, non-infected skin wounds may improve healing, but longer exposure to higher levels of TNF-α reduced tensile strength. TNF-α was known to upregulate its own synthesis by macrophages and in synergy with IL-1β, to regulate synthesis of collagen and matrix metalloprotainases. Both TNF-α and IL-1β are mitogenic for fibroblasts. IL-1β was known to increase proliferation of smooth muscle cells and vascular endothelial cells and to attract neutrophils and macrophages. Mast and Schultz noted that the ratios of TNF-α and IL-1β and their natural inhibitors p55 and IL-1 receptor antagonist, in mastectomy wound fluids are significantly higher in acute wounds than in chronic wounds, indicating a close regulatory environment within a normal healing wound.

Wound Fluid Kinetics

As noted previously, the wound environment is constantly changing. It is important to note that no literature regarding the kinetics of wound fluids after CABG surgery was found. All of the following studies include proinflammatory cytokines but some of the studies include other substances found in the wound as well. Only those related to this study will be included in the discussion.

Holzheimer and Steinmetz (2000) collected wound fluid samples from 28 patients undergoing an elective reduction mammoplasty, via a miniflap drainage system connected to a vacuum. Wound fluid was collected four times a day at three, four, six, nine, 26, 34, 54 and 58 hours postoperatively for as long as the wound produced drainage. Levels of IL-6, IL-8, and soluble TNF receptor-1 (indirect TNF-α release) were measured in wound fluids and plasma and all levels were higher in the wound. IL-6 levels increased from 93.7 ng/ml at three hours to 271.7ng/ml at seven hours postoperatively, an increase of 300%. Levels of IL-6 remained significantly elevated nine hours after the operation when compared to levels at three hours postoperatively and decreased significantly at 54 hours after operation. IL-8 levels in wound fluid were increased from 11 ng/ml at four hours postoperatively, which was almost significantly elevated when compared to the baseline level at three hours. Soluble TNF-1 levels increased steadily from three hours (3.3 ng/ml) until its peak at 11.1ng/ml at 50 hours postoperatively.

These findings are significant for this study in that the levels of these cytokines were measured at close intervals and the measurements show changes and some of them were significant. It is also important that these changes are taking place during the inflammatory time period. Additionally, the wound fluid is most likely fluid that would

be similar to mediastinal wound fluid and three of the four proposed cytokines were measured in this study. Frequent measurements may contribute to a clearer understanding of TNF-α levels.

To assist in determining if different wound sites have different levels of cytokines, Baker and Leaper (2000) compared levels of several biological factors in colorectal and breast wound fluids from 50 cancer patients (24 breast and 26 colorectal) undergoing elective surgery for cancer resection. Fluid was collected from tube drains on the first postoperative day. Proteinases, their inhibitors, and cytokine profiles were compared but only levels pertinent to this study will be reported. IL-6, IL1-β and TNF-α were all significantly greater in colorectal wound fluid than breast wound fluid. IL-6 levels were 37.3 ng/ml in breast fluid and 63.8 ng/ml in colorectal patients. IL1-β levels were 66 ng/ml in breast fluid and 161 ng/ml in colorectal fluid. TNF-α levels were 11.5 ng/ml in breast fluid and 32.9 ng/ml in colorectal fluid. Differences were attributed to the possibility that the rate of wound healing may be faster in breast surgery than colorectal surgery or that there were differences in the extensiveness of the surgeries. Also, colorectal surgery has an increased risk of contamination/infection compared with breast surgery, thus a need for more proinflammatory cytokines.

The above study, reported to be the first to compare acute surgical levels of these cytokines during the first 24 hours postoperatively, indicates that indeed, different wound sites may have different levels of cytokines. It did not measure changes in cytokine levels over time, which might indicate that the temporal changes are consistent, but at a higher concentration. All wound fluid, thus far, has been collected from patients that have had cancer. Thus, since different surgery sites noted different cytokine kinetics in wound fluid

after surgery, perhaps different disease states also reflect different cytokine kinetics after surgery. Again, no studies have been found that have measured cytokines in wound fluids collected after CABG surgery.

Taniguchi (2002), also sampling wound fluids from cancer patients, selectively researched pro and anti-inflammatory cytokines (IL-6, IL-8, IL-10) and vascular endothelial growth factor (VEGF), from both venous blood and pleural fluid, to study their kinetics and mutual relationships after major lung resection. Pleural fluid was collected from two thoracic tubes, which were constantly aspirated with –10 cmH2O pressure. Chest tubes in CABG patients are also connected to continuous suction but with –20 cmH2O pressure. It is important to note, for this study, that Taniguchi specifically mentioned that no severe complications such as respiratory failure, pneumonia, liver dysfunction or renal failure occurred postoperatively after fluid collection, as the wound samples were collected from chest tubes with continuous suction. It was suggested that the thoracic tubes might be used to collect hourly cytokine levels as a useful marker for evaluating the degree of trauma caused by thoracic procedures.

Samples of wound fluid were collected at three and six hours, and at 9 am on days one, two, three and five postoperatively. Additionally, Taniguchi set a specific morning time collection, assisting with the diurnal cortisol fluctuations that might influence cytokine levels, thus avoiding this variability. Control venous samples, taken before surgery, and control pleural samples were collected just after thoracotomy. Serum levels of cytokines after surgery were significantly higher than controls. Additionally, concentrations of cytokines in pleural fluid were about 100-fold greater than those in serum and in controls. It was suggested that that when the concentrations of cytokines in

pleural fluid are markedly higher than serum cytokine levels, serum cytokine levels are strongly influenced by the amount of cytokines produced per hour in pleural fluid. IL-6 and IL-10 reached their peaks six hours and one day after surgery (IL-6 177,000 pg/ml and IL-10 481 pg/ml). IL-8 peaked at three to six hours postoperatively (IL-8 19,700 pg/ml). Hourly cytokine levels were calculated by multiplying the concentration by drainage volume per hour, thus mean production levels were presented on a daily graph. IL-6 decreased on a linear basis from three hours to day five. IL-10 was very similar to IL-6, decreasing daily, except there was more of a decrease at day two. IL-8 decreased in the same manner until day three, then increased slightly. The presentation of these values is a very useful marker for this study. Taniguchi noted that during wound healing, the period until day three after surgery corresponds to an inflammatory phase, while the period later than day three corresponds to a proliferative phase during which angiogenesis occurs. Additionally, because the surgery was conducted on cancer patients, it was noted that overexpression of angiogenic factors, such as IL-8 and VEGF might promote the recurrence of metastasis of cancer cells.

Finally, daily profiles of cytokines (Baker, El-Gaddai, Aitken, & Leaper, 2003) from peritoneal wound fluid following colorectal surgery from drainage tubing in 52 patients showed significant positive correlations between the levels of inflammatory cytokines, IL-6, TNF-α, and IL-1β to each other: IL-6 and TNF-α on days one through three, IL-6 and IL-1β on days one, four, and five, and TNF-α and IL-1β on days one through six. TNF-α levels were constant, as in previous studies, from day one to day five. IL-1β peaked on days one and six in patients that did not have complications, but for those that did have complications, IL-1β (days one, three and six) and IL-6 (day 6) were

all significantly greater. Interestingly, IL-1β consistently correlated with various surgical parameters, including the length of the surgical procedure, the estimated blood loss during surgery, whether a stoma had been fashioned, and whether there were postoperative complications, which the researchers attributed to an increased inflammatory response that may be present in these patients. It is likely that stress plays a role in the level of this cytokine.

The above studies on substances present in the wound during the inflammatory stage of wound healing and sequential sampling of the fluids to determine the kinetics with possible interactions between the substances denotes a very complex, dynamic environment. More study is needed to determine the optimal level of cytokines and other substances present for different types of surgical procedures and for different types of wounds. What is important for this study is that it has been determined that cytokine levels are influenced as a result of time, procedures, complications and other substances found in the wound. Thus, it is fairly easy to suggest that there are other factors, such as stress and stress-reducing techniques that might also influence wound cytokines.

Kinetics of Mediastinal Lymphatic Fluid

The mediastinum is the space between the two pleural sacs. It contains all structures of the thorax except the lungs, the caudal vena cava and the right phrenic nerve. Mediastinal wound fluid is not static within the mediastinal space, but is constantly flowing through the space via blood vessels and the lymphatic system. Fluid in the pleural space transmits transpleural forces involved in normal respiration, with fluid being filtered into the pleural space along a vertical pressure gradient (Lee & Olak, 1994). There is a net movement of the fluid from the costal pleura to the mediastinal and

interlobar regions with pleural fluid being resorbed primarily through lymphatic stomata on the parietal pleural surface. Additionally, lymphatic drainage from the peritoneal cavity to the mediastinal lymph nodes has been reported (Shih, Coupal, & Chia, 1993).

It is important to conceptualize pleural movement because the nursing intervention of a nursing back rub was studied as an influence on wound cytokines such that there will be detectible changes in cytokine levels. Because fluid is constantly moving through the mediastinal space, it is likely that there will be changes in cytokine levels, as concentrations will be constantly changing. Pleural fluid turnover is estimated to be approximately 0.15 ml/kg/hour with increasing filtration with respiration increasing this rate to 30 ml/hour. Thus it is estimated that pleural lymph flow could attain approximately 700 ml/day or approximately 40% of the overall lymph flow (Miserocchi, 1997). Postoperative mediastinal fluid drainage averages 917 ml after adult cardiac operations (Belisle & Hardy, 1996).

It is also important to remember that serum levels of cytokines and the levels of cytokines within the mediastinal compartment are not equal, but that the ratios are constantly changing during the healing process. With this in mind, it is conceivable that levels of cytokines could be measurably altered by a stress reducing intervention.

Summary

As this literature has presented, massage, administered during the perioperative experience has been effective in reducing anxiety, stress neurotransmitters, and pain. It is apparent that the best dose for the intervention of massage, in the form of a nursing back rub, as well as the site on the body to perform the massage has not been determined, especially in the CABG patient. Also presented in the literature review were studies

indicating that wound cytokines during the inflammatory stage of wound healing are dynamic for various reasons. There is evidence that links stress to wound healing noting that stress has increased the time needed for wounds to heal. There is confusion in the literature regarding the effects of mood on cytokine levels, as individuals that were lonely were found to have an increase of cytokines in their wounds. Thus, there was a need to study the relationship of wound cytokines to preoperative mood and to examine a postoperative nursing intervention that may significantly alter the levels of certain proinflammatory cytokines and pain among CABG patients.

Drugs have intervened on components of cell-signaling with cardiac patients in the past (Schwartz & Barry, 1994). Schwartz and Barry go on to note that other interventions, such as stress reduction therapies that interact with cell-signaling pathways may be found in the future. The nursing back rub, a stress reducing intervention, may interact with the cell-signaling pathways of cytokines. It is with this understanding that the nursing back rub and CABG surgery are linked in this study.

III. METHOD

The purposes of this study were two-fold: 1) to determine the effects of a nursing back rub on pain and the levels of four proinflammatory cytokines in the wound fluids of postoperative CABG patients; and 2) to describe the relationship between preoperative mood and the levels of the four proinflammatory cytokines in the wound fluid. The study questions are:

1. What are the effects of nursing back rub on pain in post CABG patients?
2. What are the effects of nursing back rub on the cytokine levels of IL-1 β, IL-6, IL-8, and TNF-α in the wound fluids of post CABG patients?
3. What is the relationship between pre CABG mood and pretest cytokine levels of IL- β, IL-6, IL-8, and TNF-α in the wound fluid of post CABG patients?

The study design, operational definitions, sample and setting, the protection of human subjects, instruments used, data collection procedures, and data analysis will be described below.

Study Design

An experimental design was used for the first two questions and a correlational design for the third question. An experimental design is one in which is the researcher controls (manipulates) the independent variable and randomly assigns subjects to either the experimental or control group (Polit & Hungler, 1999). In this study, the experimental group had the "nursing back rub" and the control group had "time with the researcher". A correlational design will provide an approach to investigate the relationship or association between the independent (pre-CABG mood) and the dependent variable CABG wound

cytokine levels (wound cytokines during the inflammatory stage of wound healing). The correlation design asks the question, ”To what extent is mood before CABG surgery related to four proinflammatory cytokine levels in the wound fluid of CABG patients?”

Operational Definitions

Nursing Back Rub In this study, the nursing back rub is described as follows: 1) three, slow effleurage circles of light pressure are made that begin near the vertebrae and move across the trapezius, infraspinatus, and pectoralis major muscle group beginning in an upward direction; 2) circles will continue down the lateral portion of these muscles and back toward the vertebral column; 3) three more circles are made in the opposite direction over the lower portion of the trapezius, infraspinatus, and upper portion of the latissimus dorsi muscles; 4) in the reverse direction, three circles are made between the areas of thoracic vertebrae 12 and the iliac crest over the midsection of the latissimus dorsi; 5) three slow, moderately pressured, 12-inch strokes are made in up and down directions in the perivertebral region of the back. As described this set of nursing back rub procedures is adapted from the massage procedure described by Jensen-Nelson (1948). The nursing back rub lasted 10 minutes. Extra gentle, certified, organic, anti-allergenic oil was used for lubrication.

Time with the researcher was ten minutes of general conversation centered on the working of an easy crossword puzzle.

Wound Cytokine levels were the measurement of cytokine concentrations of IL-1 β, IL-6, IL-8, and TNF-α.

Pain was operationally defined as the measurement in millimeters from the left to the right on the VAS instrument.

Pre-CABG mood was operationally defined as the sum total score or the TMDS of the variables within the Profile of Moods States (POMS) instrument.

Pretest cytokine level was operationally defined as the levels of cytokines before the nursing back rub or time with the researcher.

Sampling Design

Non-probability sampling and randomized assignment of the participants to the study groups were used in this study. The participants were not randomly chosen to have heart surgery, but were randomly selected to enter into the study. Thus, a convenience sample was utilized. However, through random selection, all potential participants within the patient pool of the two collaborating CABG surgeons had an equal chance of participating in the study. As noted by Polit and Hungler (1999), for cases in which the phenomena under investigation are fairly homogeneous within the population, the risks of bias may be minimal. The participants were randomized to the intervention or control group such that each participant had an equal probability of assignment to either treatment or control group. Each participant was asked to pick one piece of folded paper from a container of 35 pieces of such folded paper in which the word **"**during**"** or "later**"** was printed. As a "during" or "later" piece of paper was picked a blank folded paper was replaced to maintain the same chance of choosing "during" or "later".

Sample

A subset of the CABG patient population that met the inclusion criteria was randomly selected to participate in the study. The sample included 20 CABG patients who were divided into the intervention (n=12) and the control (n=8) groups. Due to the detailed lab testing and costs involved, there were fewer participants in the study than in

other such studies where significant positive effects of massage on calmness (n=25) (Hattan, King & Griffiths, 2002), anxiety and sleep (n=69) (Richards, 1993), and anxiety and calmness (n=100) (Stevensen, 1994) were conducted.

Inclusion criteria for participation in the study were: 1) English language proficiency; 2) age older than 21 years; 3) any gender or race; 4) approval of assigned registered nurse for the patient to receive the intervention; 5**)** achievement of the cardiac surgery pathway guidelines of a large metropolitan medical center in the southeastern region of the United States (see p. 13 for description of the cardiac surgery pathway); and 6) vital signs (blood pressure, pulse rate, temperature, and respiratory rate) within normal limits throughout the intervention and post CABG data collection.

A CABG patient was excluded if: 1) a mechanical/chemical blood pressure support, pacing or arterial lines were needed: 2) vital signs were not within normal limits at the time of the intervention; and 3) a history of diabetes mellitus, peripheral vascular disease, poor wound healing, the use of anti-inflammatory medication or other obvious immunologic influences or immunologically related health problems, e.g. cancer, or autoimmune disease was reported.

It was anticipated that narcotics would effectively manage most pain at the time of the intervention. It was also expected that there would still be pain sensation that the chemical intervention had not obliterated.

The control group (n=8) treatment was normal unit procedures with participants receiving ten minutes of normal conversation and/or work on an easy crossword puzzle after the first wound fluid was collected. The experimental group (n=12) received a ten-minute nursing back rub conducted by this researcher after the first collection of the

wound fluid. Only the researcher administered the back rub to assist in controlling for external factors. Differences in how the back rub were administered was almost entirely eliminated by having only the researcher conduct the intervention. Participants were told that they had a 50% chance of receiving a back rub for the purposes of the study but if desired, would be able to receive one after the second cytokine sample. Four of the control group decided to not receive a back rub.

Setting

The study took place in a large metropolitan medical center in the southeastern region of the United States. The cardiac observation unit and the intensive care unit were used in this medical center.

Protection of Human Subjects

Before participants were recruited the researcher received Institutional Review Board (IRB) approval from the Fort Sanders Regional Medical Center and the University of Tennessee College of Nursing and the Office of Research. Written informed consent (Appendix) was obtained from each participant before data collection began and the participant had the CABG. Verbal affirmation of consent was obtained before the intervention was conducted. Care was taken to ensure that potential participants did not feel coerced into participation during recruitment by allowing patients time to think about whether they would like to participate and by verbal reassurance that it was "ok" if they did not want to be in the study.

An information sheet (Appendix) was given to all potential participants. The information sheet described the: 1) nature of the study; 2) purpose of the study; 3) nature of the participants' involvement in the study; 4) expected duration of the intervention; 5)

potential risks of participation; 6) potential benefits of participation; 7) manner in which anonymity will be assured; 8) intervention and data collection procedures to be followed; 9) right to withdraw at any time during the study without loss of care, benefits or privileges and 10) e-mail address and telephone number of the researcher and faculty advisor.

There was no direct benefit or incentive for participants but the opportunity to have a nursing back rub or to receive individual attention from the researcher. Previous studies and the researcher's own pilot work found that approximately 18 hours post CABG, patients tolerate a back rub without experiencing an increase in pain or discomfort and/or change in heart rate or cardiac rhythm. Instead patients welcomed the back rub and stated that it made them feel better.

During the study participants were monitored for heart rate and cardiac rhythm. No participant was withdrawn from the study due to adverse changes in heart and/or cardiac rhythm. No participant withdrew; except three patients did not recover adequately from the surgery to meet the inclusion criteria for continuing in the study. Two of these would have been in the experimental group and one in the control group.

To insure confidentiality, no names were attached to any specimen, questionnaire, or form; they were coded for organization purposes only. The completed forms and questionnaires are kept in a locked cabinet at the researcher's home and will be thus for at least three years. Specimens will be kept indefinitely at the College of Nursing Walker Lab. Participants were assured that all data used in any presentations or publications will not contain their identities. Only the researcher and the faculty advisor have access to

completed instruments. A hired laboratory technician did have access to the specimens but only participant numbers were on the specimen tubes.

Instruments

Profile of Mood States (POMS) The POMS (McNair, Lorr & Droppleman, 1971) was used to measure mood (Appendix). The POMS is a 65- item measure of distressful, affective states that were experienced during the past week including the day of assessment. The POMS consists of six subscales: 1) tension-anxiety (9 items); depression-dejection (15 items); anger-hostility (12 items); vigor-activity (8 items); fatigue-inertia (7 items); and confusion-bewilderment (7 items). The POMS is a five-point Likert scale in which an individual responds to the items as "Not at all"; "A little"; "Moderately"; "Quite a bit"; and "Extremely". The sum of the POMS score is known as the Total Mood Disturbance Score (TMDS) The TMDS ranges from –32 to 232. Researchers are encouraged to utilize the TMD score whenever a single global estimate of affective state is wanted. The internal consistency of the POMS ranges from .87 to .92 and its test-retest reliability ranges from .68 to .74 (McNair, Lorr, & Droppleman, 1971). Six factor analytic replications were conducted in the development of the POMS giving evidence of the factorial validity of the six mood factors. Validity studies that have been conduced are numerous including predictive (Lorr, McNair, Weinstein, Michaux & Raskin, 1961), construct and content validity (Pugatch, Haskell & McNair, 1969), and concurrent validity (Bowler, Mergler, Schwarzer, Bowler & Rauch, 1991) with the Beck Depression Scale. The POMS has been used in several studies involving diverse heart and surgical populations including CABG patients (Cronin, Logsdon & Miracle, 1997; Rankin, 1990), lung cancer surgical patients (Uchitomi, Mikami, Nagai, Nishiwaki,

Akechi & Okamura, 2003), and cardioverter defibrillator patients (Carroll, Hamilton, & Kenney, 2002). It takes approximately three to five minutes to complete the POMS, making it a useful and simple tool to administer before surgery.

Visual Analog Scale (VAS) Pain was measured in terms of intensity (Gift, 1989) with a specific Visual Analogue Scale (VAS) that the researcher developed (Appendix). This VAS is a 100 mm horizontal line with the left end labeled "No Pain" (0 mm) and at the right end, "Worst Pain" (100 mm). Participants were asked to mark a point on the line that represented the intensity of pain experienced immediately before and after the intervention. Pain was measured in millimeters by measuring the distance from the low end of the scale to the subject's mark (Gift, 1989). The VAS concept of measuring pain was chosen because the researcher wanted the pain variable to be a continuous variable. Several studies (Hattan, 2002; Schooler, 1998; Stevensen, 1994) used similar VAS scales. In general, the validity of VAS scales have been established: construct validity, by Price, McGrath, Rafii, & Buckingham (1983); Seymour (1982) reported on the discriminant validity; criterion-related validity was reported by Wewers & Lowe (1990); and concurrent validity was reported by Ahles et al, (1984).

Enzyme-linked Immunosorbent Assay (ELISA) ELISA was used to measure cytokine levels for IL-1 β (Pierce Biotechnology, Inc., Rockford, IL.), IL-6 (Ebioscience, San Diego, CA), IL-8 (American Laboratory Products Company, Windham, NH), and TNF-α (Ebioscience, San Diego, CA). The ELISA is an assay based on the immunological detection of peptides. Immunoassays rely on antibody that specifically detects the cytokine that is being measured. In this experiment, an enzyme-linked immunosorbent assay was used as opposed to a radioimmumnoassay. Both assays are

considered to have an exquisite specificity for a particular cytokine due to the use of monoclonal antibodies (Kronfol & Remick, 2000). Because only a portion of the cytokine is recognized by the antibody it is possible that the assay only measured the degraded fragment of the protein and not the biologically active material. A bioassay, as opposed to an ELISA, indicates not only if the cytokine is present, but whether it is biologically active as well (Kronfol & Remick, 2000).

Assays were visualized using a standard curve that demonstrated a direct relationship between optical density and cytokine concentration. In other words, the higher the optical density, the higher the cytokine concentration in the sample. When cytokine measurements fell outside the standard curve, concentrations were calculated by plotting the standard curve on a linear graph, then drawing a horizontal line to intersect with the standard curve. This procedure was necessary for the IL-6 and IL-8 cytokine concentrations levels, however, these levels were only slightly higher than the highest standard for IL-6 and slightly lower than the lowest standard for IL-8. The data were analyzed using the Fit/SplineLOWESS function in GraphPad Prism.

Recruitment Procedure

Potential participants were accessed through word of mouth in the medical center or doctors' offices where the collaborating CABG surgeons practiced. Potential participants were approached within a week before their scheduled CABG surgery and were given the Information Sheet **(**Appendix**)** to read and consider participation. Potential participants had the opportunity to ask questions before giving their informed consent.

Data Collection Procedures

After the consent form was signed potential participants were screened for eligibility. They were given a questionnaire (appendix) consisting of health-related questions such as history of smoking and diseases, as well as sociodemographic questions including sex, age, weight, and race. If they were eligible, the POMS was administered at that time.

Approximately 36 (range 30 – 45) hours after the CABG, participants were assessed for further eligibility to continue in the study. If participants met the inclusion criteria relative to the cardiac surgery pathway guidelines, data collection ensued in the following manner: 1) the pretest VAS was administered; 2) pretest wound fluid was collected from the self-sealing drainage tubing using a sterile needle attached to a 12 milliliter syringe after cleaning the tubing with alcohol; 3) a 10 - minute intervention (nursing back rub or time with researcher) was performed; 4) post test VAS was administered; and 5) approximately after one hour after the intervention, posttest wound fluid was collected from the self-sealing drainage tubing in the same manner as above. Wound fluid specimens were collected in serum tubes (Vacutainer: Becton Dickinson Labware), and taken to the Walker Lab the College of Nursing at the University of Tennessee, Knoxville. Wound fluid was centrifuged for ten minutes at 1500 rpm at 0 ° C to extract any cells in a pellet and the supernatant was removed and stored at –80 ° C until assayed.

At the time the assays were run, specimens were allowed to thaw. Specimens and standards were set up in duplicate on all cytokine kits in 96 well microtiter plates. ELISAs were performed by using sandwich-type kits according to the manufacturer's

instructions. IL1-β, (rabbit) IL-6 and TNF-α used purified anti-human antibody and, I-L 8 used biotinylated rabbit anti-human polyclonal antibody, to detect the cytokines in the samples. Samples were diluted 1:1000 to fall within the standards range for IL–6 and IL-8. IL-1β and TNF-α did not require dilution. The intra and inter assay coefficients for the in ?? lab for TNF-α and IL-6 was less than 10% not computed for IL-1 β and IL-8.. Absorbance was measured photometrically at an optical density of 450 nm. Cytokine concentration was determined by interpolation with the standard curve.

Intervention Procedure

The "nursing back rub" or "the time with the researcher" was approximately 40 hours (30 – 45) post-CABG. Such timing was crucial for two reasons: 1) the wound healing process is in the inflammatory stage**;** and 2) the participants met the inclusion criteria relative to the cardiac pathway guidelines. The nursing back rub was administered in the position of choice of the patient. Such position could be sitting in a chair, dangling on the side of the bed, or lying on either side in the bed.

Data Analysis

Standard univariate descriptive statistics were used to describe the sample characteristics and demographic variables such as mean age and weight. Descriptive statistics were used to compute the mean, mode and median of scores of all variables. Tests for normality were conducted to determine whether parametric or nonparametric tests were appropriate.

Research Question #1 What are the effects of nursing back rub on pain in post CABG patients?

Since there were no severe deviations from normality, repeated measures analysis of variance (ANOVA) was conducted to compare the changes in pain among post CABG patients. A repeated-measures ANOVA was used to answer this question because two measures of the same dependent variable (pain) were collected at two points in time. The F-statistic was computed to test for differences in the experimental participants versus the controls, which is the between-subjects effect. Another F-statistic was computed to test for differences across time, which is the within-subjects effect. This statistic indicated whether, across both groups, the mean change in pain differed before and after the interventions. An alpha level of .05 was the criteria of statistical significance. Paired t-tests were then run to determine an interaction effect or if there was a differential treatment effect at the different points in time.

Research Question #2 What are the effects of a nursing back rub on the cytokine levels of IL- β, IL-6, IL-8, and TNF-α in the wound fluids of post CABG patients?

To determine if both groups were similar in levels of cytokines before statistical analysis was conducted, t-tests were run on pre-cytokine levels. It was determined that there were no significant differences between the control and treatment group in these measures thus the groups were similar. A repeated measures ANOVA was conducted to compare the changes in cytokine levels. A repeated-measures ANOVA was used to answer this question because two measures of the same dependent variable (cytokines) were collected at two points in time. The F-statistic was computed to test for differences in the experimental participants versus the control participants, or the between-subjects effect. Another F-statistic was computed to test for differences across time, or the within-subjects effect. This statistic indicated whether, across both groups, the mean of the

cytokine levels IL- β, IL-6, IL-8, and TNF-α differed before and after the interventions. Paired t-tests were not run to determine an interaction effect or a to see if there was a differential treatment effect at the different points in time because there was not a significant change over time. An alpha level of .05 was the criteria of statistical significance.

Research Question #3 What is the relationship between pre-CABG mood and pretest cytokine levels of IL- β, IL-6, IL-8, and TNF-α in the wound fluid of post CABG patients?

To determine if both groups were similar before statistical analysis was conducted, t-tests were run on POMS scores. It was determined that there were no significant differences between the control and experimental group in these scores. Pearson's correlation was used to determine the relationship between pre-CABG mood (TMDS) and each of the pretest cytokine levels of IL- β, IL-6, IL-8, and TNF-α in the wound fluid. All data analyses were conducted with the SPSS software program.

Summary

This chapter discussed the methods and procedures that were used for data collection and analysis to address the study questions of whether a nursing back rub can affect cytokine levels in wound fluids and pain in post CABG surgery patients and whether there is a relationship between preoperative mood and wound cytokines.

IV. RESULTS

Twenty participants completed the study with eight participants in the control group and 12 in the experimental group. The mean age of the total sample was 61.5 years (range 48 to 82). The mean age in the treatment group was 60.9 years (range 48 to 82) and 62.5 years (range 48 to 80) in the control group. There was one male African American in the control group. There were three females and five males in the control group and two females and ten males in the experimental group. Although the random distribution of the participants by sex into the groups was not equal, an analysis of posttest cytokines indicated that sex of the participant did not contribute significantly to the results.

Mean weight for the total sample was 180.7 pounds (range 109 to 265.5): (experimental group:184.7 pounds [range 109 to 265.5], control group: 174.9 pounds [range 123 to 261]). (Appendix, Table 2 and Table 3) Participants were asked what other medical conditions they had besides coronary artery disease. Four participants had hypertension in the experimental group and three participants had hypertension in the control group. Three participants had gastric reflux disease (GERD) in the experimental group. Three participants in the experimental group had high cholesterol. Three of the experimental participants had a previous myocardial infarction (MI) and one control group member had an MI history. One participant in each group had a hiatal hernia. Two participants in the experimental group and one in the control group had arthritis. Other reported conditions in the experimental group included gout, kidney stone, hyperlipidemia, atrial fibrillation, and benign prostatic hyperplasia. Other reported

conditions in the control group included sleep apnea, kidney stone, anemia, and hyperlipidemia.

Independent pretest t-tests were run on cytokines and pain levels to determine if the groups were similar before final analyses of the data. (Appendix, Table 4 and Table 5) There were no significant differences noted between the two groups. The following results will address the three questions of this study. The first question asked how a nursing back rub affected pain in post CABG patients and will be addressed first.

Pain

Pain was measured on a visual pain scale that ranged from 0 mm to 100 mm with 0 being no pain and 100 mm indicating the worst pain ever felt. Pain was measured before and after the back rub or time with the researcher. The mean pretest pain in the experimental group was 39.8 mm (range 3 to 89.5 mm, SD 28.2) and dropped to 17.2 mm (range 0 to 52 mm, SD 17.6) post-back rub. The mean pretest pain in the control group was 44.1 mm (range 5 to 100 mm, SD 35.3) and dropped to 40 mm (range 3.5 to 95 mm, SD 35.2) post-time (Appendix, Table 6).

The mean change from pre to post test in pain was 22.6 mm (range 2 to 65mm, SD 18.5) for the experimental group. The mean change in pain in the control group was 4.1 mm (range –20 to 29 mm, SD 14.4) (Appendix, Table 7). Analysis, using repeated measures analyses of variance (ANOVA) with two time points (before and after) by group interaction, showed that pain did change significantly ($F_{1,18} = 5.696$, $p = 0.028$). There was a small change of pain in the control group, but a very large decrease in pain for the experimental group. Analysis using paired t-tests showed that the control group

did not have a significant decrease in pain (p=0.450) and the experimental group had a significant decrease in pain (df 11, p=0.001) (Appendix, Table 8, Figure 2).

Cytokines

Tests of normality were performed on pretest cytokine levels of IL-1β, IL-6, IL-8 and TNF-α (Table 4.8). Distributions of the variables were examined by independent t-tests on the means noting that there were departures from normality. Thus, cytokine levels were log10 transformed. Normality tests run on the log-transformed cytokine values found the data was now normally distributed for all cytokines. (Appendix, Table 9)

Levels of cytokines, IL-1β, IL-6, IL-8 and TNF-α were measured in wound fluids one hour after the back rub and control group intervention. The pretest cytokine measures for the sample are as follows: mean level of IL-1β, 15.1 pg/ml (range 1.11 to 46.24 pg/ml, SD12.4); IL-6, (table shows dilution of 1:1000) 104,680 pg/ml (range 17,450 to 240,000 pg/ml, SD 68.9); IL-8, (table shows dilution of 1:1000) 6,953 pg/ml (range 490 to 26,220 pg/ml, SD 6.7); and TNF-α, 3.5 pg/ml (range .09 to 9.12 pg/ml, SD 2.6). Posttest cytokine measures for the sample are as follows: mean level of IL-1β, 13.71 pg/ml (range .55 to 34.87 pg/ml, SD 9.0); IL-6, 94,658.5 pg/ml (range 24,780 to 242,000 pg/ml, SD 65.8); IL-8, 22,431 pg/ml (range 490 to 374,940 pg/ml, SD 83); and TNF-α, 3.6 pg/ml (range .81 to 8.21, SD 2.0) (Appendix, Table 11). Appendix table 12 describes the statistics of the levels of cytokines by group.

Four repeated measures ANOVA with time by group interactions for transformed pretest cytokine levels: tIL-1β (F [1,18] 2.765, p=.114); tIL-6 (F[1,18]=.123, p= .730);

tIL-8 (F[1,18]=.043, p=.838); and tTNF-α (F[1,18] = .065, p= .801) indicated that there were no significant interactions by group over time. There were no significant changes in any cytokine levels in either group from pretest to posttest. Great variability was noted in both the experimental and the control group. Since there were no significant changes by time in either group paired t-tests were not performed.

Mood

The POMS scores for the 20 participants indicated that TMD scores had a mean of 25.35 (range –11 to 103, SD 30.13) (Appendix, Table 13). To determine the relationship between pre CABG TMD scores and pretest cytokine levels in post CABG wound fluids, the Pearson Product Correlations were performed. Results indicated no significant relationships (IL1 β, r = -.008, p=.973; IL-6, r = -.404, p=.096; IL-8, r = -.097, p=.701; TNF-α, r = .258, p=.272) between pre CABG TMD scores and pre-treatment cytokine levels (Appendix, Table 14).

Additional Findings

Review of the correlation tables indicates that there is a significant inverse relationship (r = -.560, p=.016) between the POMS score of tension-anxiety and the wound cytokine IL-6. As tension-anxiety is increased, IL-6 is decreased in the wound fluid (Appendix, Figure 3).

When non-transformed cytokine levels were correlated with body weight (Appendix, Table 15) using Spearman's rho Nonparametric Correlation there was a significant positive correlation (r = .475, p=.034) between IL1-β and weight. This suggests that as weight increased so did IL1-β levels.

V. DISCUSSION

This study was conducted to answer the call for biophysiological evidence that supported the psychosocial data showing the efficacy of nursing interventions. The results of this study have contributed to answering this call by providing evidence that a nursing back rub significantly decreases pain in CABG patients, by describing four cytokine levels at two time points in wound fluids of CABG patients, and by linking one preoperative mood, tension-anxiety, to wound cytokines.

The first purpose of this study was to determine the effects of nursing back rub on pain in CABG patients. In the sample of 20 CABG patients, the results provided evidence that a nursing back rub can significantly reduce postoperative pain in CABG patients. The second purpose of this study was to determine the effects of nursing back rub on four proinflammatory wound cytokines in CABG patients. The data did not provide evidence that a ten-minute nursing back rub had an effect on wound cytokines one hour after the back rub. The third purpose of this study was to determine the relationship between pre-CABG mood and four proinflammatory cytokine levels. Although the TMD score was not significantly associated with wound cytokines, there was a significant negative relationship between the POMS tension-anxiety score and the IL-6 cytokine. Additionally, a significant correlation was found between IL-8 and the weight of participants.

The results from this experiment did address the gaps found in the literature regarding; 1) a nursing touch intervention (back rub); 2) CABG proinflammatory wound cytokines; and 3) mood and its relationship to wound healing with an intervention designed to reduce stress. This study narrowed the gap regarding the touch of a back rub

but it appears to have both narrowed and widened the gaps in regards to cytokines and wound healing.

The back rub was conducted in such a manner that it can be easily replicated. Because of the setting of the experiment, it was difficult to follow the specifications as set forth by Goldstone (2000). However, definitions of strokes, purpose of the massage, body area, frequency, duration, qualifications of the person performing the massage and specification of the type of patient receiving the back rub were all explicated. The position of patient, use of conversation, and environmental factors were not controlled, thus this might be a limitation for future back rub studies.

The participant determined the conversation between the researcher and the participant during the back rub or the time with the researcher. If the participant was quiet, then the researcher was quiet. If the participant desired to talk more than work on the crossword puzzle, than the researcher engaged in general conversation. The majority of participants talked some, and then were quiet. One participant in the control group did not want to talk at all, so the researcher sat with him. It was noted that those that received the back rub were less likely to talk.

External factors involving the environment might have influenced the results. In particular was the interruption of the ten minutes by various "others" such as nurses, doctors, and respiratory therapists. Although the interruptions were brief and very little talk occurred, these interruptions might have influenced the results. Another possible environmental influence was the sounding of various alarms such as the oxygen monitor in the next room or the noises from the hallway. It was very difficult to make the room as quiet as the researcher would have liked it to be.

Nursing Back Rub and Pain

That the results are consistent with the results of the researchers at the Touch Institute at the University of Miami (TIUM) such that pain was significantly reduced with a back rub is not a surprising. What gap this study narrows is that a ten minute back rub was a duration that effectively lowered post-operative pain. Further, simple effleurage strokes, only on the back, did significantly decrease pain, suggesting that techniques requiring formal education are probably not necessary for pain relief in this population.

Although an increase in proinflammatory wound cytokines by a nursing back rub was not found, a bio-behavioral effect was detected. Patients reported decreased tension and frustration after the back rub. Patients also verbalized that the back rub was relaxing. One patient noted that he was ready to, "Kill his surgeon!" until he received the back rub. He expressed profound gratitude after the back rub. These results support the need for further research, perhaps of a qualitative nature, to determine the meaning of the back rub.

Pain was significantly reduced, perhaps through vagal effects. Field (1998) suggested that touch may increase vagal activity, which lowers physiological arousal, and stress hormone levels. Massage may relieve pain through the release of enkephalins, the emotional contact of a caring touch that induces a sense of well-being, or by soft tissue manipulation thus improving circulation, removing lactic acid and irritants (McRee, Noble, & Pasvogel, 2003). Perhaps the back rub did work in this manner. Further research is needed to explicate the mechanism, especially since opioids are produced and released in response to stress and/or pain (Rabin, 1999). If stress increases opioid

secretion, and the back rub is meant to decrease stress, then it makes sense that opioids would decrease as stress decreases.

McRee, Nobel and Pasvogel (2003) studied the effects of thirty minutes of Swedish massage on the posterior portion of the body preoperatively, on pain, cortisol and prolactin levels postoperatively. It was hypothesized that massage would decrease pain, cortisol and prolactin levels by decreasing anxiety. No significant decreases were found in pain or cortisol levels. Prolactin levels were studied because prolactin has been found to increase during the physiological response to stress and increased mental vigilance. No significant decreases were found in prolactin levels. Thus, the decrease in pain noted from this experiment are most likely not because the back rub decreased serum levels of cortisol or prolactin. However, measuring these levels in wound fluids might lead to further explications of the mechanisms involved in pain reduction through a back rub.

The mechanism for how the back massage decreased pain could have been by lowering substance P levels. Substance P levels and the pain of fibromyalgia were reduced through 30-minute massages twice a week for five weeks (Field, Diego, Cullen, Hernadez-Reif, Sunshine, & Douglas, 2002). DeVane (2004, p. 1) suggests that the substance P "neuropeptide is an integral part of central nervous system pathways involved in psychologic stress." DeVane notes that endogenous substance P is released as part of the response to stress. Additionally, substance P is considered to be a modulator of nociception, or a regulator of pain. Thus, it might be feasible that the back rub, by decreasing the participant's stress, also decreased pain levels. That one light back rub for

ten minutes might reduce stress such that it influences the effects of substance p is an exciting possibility.

Nursing Back Rub and Cytokines

There was a great amount of variability in the wound cytokine levels both between subjects and within subjects which hampered analyses of differences. Some subjects had cytokine levels that increased with the back rub and others had levels that decreased. Participants in both groups had no changes in cytokine levels. This degree of variability has been reported elsewhere in non-intervention studies (Weissflog, Kroegel, Lettmann, Grahmann & Hasse, 1999; Baker et al., 2000). Thus, on reflection, it was a stretch to believe that a ten minute intervention would affect the wound cytokine environment. Other limitations that might have affected the results are that fluids could not be collected at the same time point after surgery on every participant. The researcher was not able to control for this due to timing of surgeries and only one researcher to collect the fluids. Thus, the diurnal influence in cytokine levels may have influenced the results. Only one participant had to have the second wound fluid collection more than the one hour time period and this was less than a one hour delay. Another limitation is that cytokine levels might not have had time to have an effect in one hour because the downregulation of immune system, via the macrophage, might not have had time to be evident.

Additionally, increases in proinflammatory wound cytokines may or may not be what is optimal for wound healing in the CABG patient. It has not yet been determined which mix or what concentration of cytokines is optimal for wound healing in CABG patients. This is the only study reported in the literature that has measured these cytokines

in wound fluids of CABG patients. Further research on anti-inflammatory cytokines, cell types and growth factors and other wound factors, including their interactions with each other must be undertaken to have a clearer picture of the optimal wound site. Further research is needed in determining effects of dose on stress-reducing interventions, which potentially could alter wound cytokines. Kiecolt-Glaser, Marucha, Atkinson and Glaser (2001), in the one psychoneuroimmunological intervention study designed to specifically study wound repair and immune function, used whole blood in the analysis of IL-1β levels rather than wound fluids. Thus, more intervention studies using different stress reducing interventions or one of greater intensity are needed.

Landis (2002) asked if it were possible that behavioral strategies might modulate immunity. It is possible that the immune system must be conditioned through multiple sessions of a stress reducing intervention much like the massages studied by the researchers at TIUM. If this is the case, then a ten minute back rub might be effective with more doses per day or over days for an effect to be recognized by the wound cytokines that were studied in this experiment. Although Groer et al. (1994) found a significant increase in sIgA with a ten minute back rub, this "dose" might not be effective in altering the complex wound environment.

As noted previously, this study described the levels of four proinflammatory cytokines at two points in time. It is impossible to compare these levels with other CABG studies of cytokines because no CABG studies were found in the literature. A comparison of these levels with other types of surgeries or wounds is of interest. Table A-16 compares the levels of the four cytokines with other levels found in wound fluids from colorectal, thoracotomy, and mammary reduction surgeries, pleural effusions from

medical conditions, split graft wound drainage and blister wound drainage. Mediastinal wound fluids may be different in concentrations from other wounds because cytokines could be diluted in the pleural fluid that is naturally present in the mediastinal space. Thus, cytokine levels in CABG patients could be entirely different than those found in other wounds. The levels found in this study, however, revealed they are consistent with other wound fluids.

In a review of the table, this study is the only study that described the levels of all four cytokines. Other studies included one to more than 32 time points. This study combined the two time points because they were only one hour apart. Perhaps a greater length of time between collections of wound fluids would have contributed to the body of knowledge in a more significant manner by analyzing the kinetics of these cytokines in CABG wound fluids.

The number of participants in this study was comparable to the numbers included in other studies. Considerable variance in concentrations of cytokines in wound drainage, as noted by Weissflog et al. (1999), is obvious when comparing studies. However it is interesting to note that the levels found in this study are comparable to the other studies with the exception of IL 1-β.

IL1-β concentrations ranged from .55 to 46.24 pg/ml (mean 14.4 pg/ml considering both time points) in this study that is lower than levels found in all the other studies. The results of this study are closest to those patients that had pleural drains from mastectomy (Baker et al., 2000, mean 66 pg/ml, range 3-341 pg/ml) and non-empyema patients that had pleural fluid (Silva-Mejies, Gambia-Antinolo, Lopez-Cortes, Cruz-Ruiz, & Pachon, 1995, <30-97 pg/ml). It would appear that pleural drainage post CABG might

contain the lowest levels of IL1 β of the wounds thus far studied. Additionally, this study supports Baker et al. (2000) that not only the type of surgery influences wound cytokine concentrations, but where the surgery site is located as well.

Silva-Mejias et al., (1995) measured IL1-β levels in 102 pleural effusions of different etiologies. Silva-Mejias, et al. noted that IL1-β levels ranged from 30-97 pg/ml in those patients whose etiology of pleural fluids were from congestive heart failure, ascites, abdominal malignancy, pneumonia and multiple other causes. In patients whose fluids arose from bacteria producing empyema, IL1-β levels were >200 pg/ml. The levels from this research fall within the same levels of this study, as indicated earlier, which further suggests that pleural levels and wound levels of IL1-β are similar. This is not surprising as the inflammatory process could be at work in effusions due to the disease process. Additionally, since IL1-β is increased in patients with empyema the levels found in this study are consistent with sterile wounds in these CABG patients.

The levels of IL-6 in this research ranged from 17,450 – 242,000 pg/ml which is very consistent with the levels IL-6 in other studies except Ono et al. (1995) who described substantially less IL-6 (13,500 pg/ml) on day 5 post operatively. IL-6 peaked at day two in the study of postoperative mammary reduction patients by Holzheimer and Stinemetz (2000) and fell significantly on day five. Holzheimer and Stinemetz suggest that this probably reflected the influx of inflammatory cells into the wound and the phase of wound healing. This research supports their finding since IL-6 is secreted by activated macrophages that are numerous in the wound during the inflammatory phase.

Levels of IL-8 (range 490 to 374,940 pg/ml) were skewed due to one outlier that had a post intervention level that was more than ten times that of any other participant.

When that cytokine level is factored out of the comparison, the range of IL-8 is 490 to 26, 222 pg/ml that compares with skin blister fluids (Glaser et al., 1999), but is greater than either of the pleural fluid studies (Holtzheimer & Stinemetz, 2000; Taniguchi, 2002). Taniguchi noted that although IL-8 decreased 24 hours after surgery, it increased significantly on day five. It was suggested that IL-8 was a proinflammatory cytokine until day two then functioned as an angiogenic factor later in the healing wound. Indeed, IL-8 levels were 19,000 pg/ml six hours after thoracic surgery for lung resection due to lung cancer and 13,000 pg/ml on day five. A closer review of all the levels of IL-8 in this research reveals that the 87.5% of the patients in this study did have comparable levels to that of all pleural studies, suggesting that the levels of IL-8, when factoring out the outliers, are relatively predictable in pleural fluids one to two days postoperatively regardless of surgery.

The CABG patient that had the outlier value of IL-8 was a white male, 82 years old, who weighed 170 pounds. He did not smoke and reported a previous appendectomy, cholecystectomy and arthritis as his other medical conditions. This participant did receive the back rub. Why his value was so significantly higher than that of the others could have been because of experimental error in cytokine measurement.

The researcher did not thoroughly review the anesthesia medications of patients during surgery or those administered in the first 24 hours. This is a limitation that might have altered cytokine levels. It is unknown whether patients received medications that might have influenced the immune response such as corticosteroids during this period. It is known that participants received pain medication containing aspirin.

Mood and Wound Cytokines

TMD scores can range from –32 to 232 when all six identifiable moods or affective states are added together and vigor is subtracted. The mean of the TMD score of the participants was 25.35 (range –11 to 103, SD 30.13). These scores reflect participants that are relatively not "disturbed". The highest score is less than one-half of the worst total mood score. Additionally, there was little variability among the 20 participants. This might explain why there was not a significant relationship between the mood and the cytokine levels. If participants had been more "disturbed" wound cytokines might have been more affected, therefore more research into a more "disturbed" population is needed.

POMS data collection from 1986 through 1991 showed a mean score of 33.4 (SD 37.1) for females and 27.2 (SD 31.8) for males (McNair, Lorr & Droppleman, 1971). This data was collected from 1986 through 1991 on a sample of 2,360 adults ages 18 – 65 participating in a "self help" smoking cessation research program. It can be assumed then, that participants were about as emotionally disturbed as those trying to stop smoking before smoking since the scores are similar.

Additional findings from this study were discovered when the TMDS was further divided into the six sub-factors. The mean tension-anxiety scores for the participants in this study were 12.25 (SD 7.64). Scores for females in the POMS normative data was 12.8 (SD 7.9) and for men 12.3 (SD 7.0). Participants were very similar in tension/anxiety to controls in a smoking cessation program.

Cronin (1997) studied 86 women before CABG surgery using the POMS depression and tension scales. The mean score for the women on the depression scale was

6.81. Mean scores for the participants of this study for depression were 7.7, indicating that participants were slightly more depressed. The range of depression scores on the POMS, as noted previously, is 0-60. Thus, it appears that both groups were not significantly depressed. The mean tension/anxiety score for the women was 8.81 in Cronin and for this study the mean for tension/anxiety score was 12.25. Tension/anxiety scores for the POMS can range from 0-36. The participants of this study were tenser than those in Cronin's study.

In a study conducted by Goodfellow (2003), a therapeutic back massage of 20 minutes in 42 spouses of cancer patients had a significant positive effect ($p = .0005$) on the TMDS, pointing out again, that another administration of the POMS after the back rub might have provided further evidence-based support for the back rub. Goodfellow's study utilized a back rub, lasting ten more minutes and which also included several minutes of petrissage. It would have been interesting to note whether the ten minute, effleurage back rub would also have had a significant positive effect on TMDS. The mean TMDS was 34 (~ range -11 to 68). Depression scores means were 12 in the experimental group. The evident comparison between the two groups is that spouses of cancer patients were generally more depressed with a negative mood than preoperative CABG patients.

This study did not support McCarthy's (1992) study of a reduction of IL-1 in rats that were stressed with noise. Two reasons might be that noise stress is not equal to any of the variables found in the POMS and rats may have a different wound environment. This study did possibly support the finding of Hubner et al. (1996) that increased levels of corticosteroids reduces the normal induction of proinflammatory cytokines after

injury. Another study that measure corticosteroid levels of participants would assist in explicating the Hubner et al. finding.

A significant negative relationship of tension to IL-6 was found. The POMS was given at least 40 hours before the cytokine level was collected however this relationship does suggest a preoperative influence of tension/anxiety on wound fluid dynamics. It is possible that high pre-operative anxiety was associated with postoperative anxiety, but this was not measured. Although neutrophil granulocytes are the dominant leukocyte subpopulation for up to 12 hours in a wound, an increase in macrophages and monocytes occurs after 12 hours (Weissflog et al., 1999). Different cell types, such as macrophages, monocytes, lymphocytes, fibroblasts and endothelial cells, can produce identical cytokines. Thus, it is possible that tension, through neuro-endocrine pathways, might have affected one of the cell types that secrete IL-6. Stress has been implicated in the increase of serum IL-6 (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002), but increased tension has not been correlated to lower IL-6 levels in wound fluids before.

Kiecolt-Glaser et al., (1995) noted that serum IL1β levels were lower in caregivers of demented relatives that reported significantly more stress. The study indicated that decreased levels of serum IL1β might be one immunological mechanism underlying the observed slowing of wound repair in the stressed caregivers. IL1β levels in the wound fluids of this study did not show any significant differences between those individuals that had higher TMDS. However, stress, as measured by the Perceived Stress Scale (PSS), which measures the degree to which subjects perceived their daily life during the preceding week as unpredictable, uncontrollable, and overloading, might be significantly correlated to IL1β wound fluid levels. Additionally, further research using

serum IL1β levels, in addition to wound fluid levels, might increase the understanding of the relationship between serum and wound fluid cytokine levels. This is necessary if researchers continue to link low proinflammatory serum cytokine levels with defects in wound repair.

Glaser et al., (1999) did find significantly lower production of IL-8 in wound fluids in women with higher stress scores. Again, the PSS was used to measure stress. Perhaps it is the unpredictability, the lack of control and overloading that contributes to the lower levels of wound IL-8 and not a person's overall mood. It is also possible that blister wound fluids have less variability than CABG wound fluids, thus the correlation is more readily detected.

It is interesting to note that the back rub was selected as an intervention to reduce stress and tension but the mood tension-anxiety was the one significant negatively correlated factor with IL-6 ($r= -.560$, $p=.016$). How did pre-surgical tension and anxiety effect cytokines? This question points out a limitation of the study, which is that POMS was only measured before surgery. Had POMS been measured after surgery, it would have given a clearer picture of what the patient's mood was after surgery and the correlations of mood to post surgical cytokines could have been repeated on the second tension-anxiety score. However, this research does support the findings of Kiecolt-Glaser et al. (1995) and Glaser et al. (1999), which suggest that stress influences wound healing. Preoperative tension/anxiety did have a negative effect on postoperative wound cytokine levels, that of IL-6. This study contributes to the body of knowledge by the significant finding that IL-6 levels in wound fluids decrease significantly when a patient is more tense/anxious before surgery.

A further explanation for the decrease in wound IL-6 levels in patients that were tenser or more anxious might be that these conditions are known to increase glucocorticoid production. Rabin (1999) has found that glucocorticoids may contribute to the development of a predominantly Th2 response of the CD4 population of leukocytes. Th2 cells inhibit macrophage function that secrete significant numbers of the IL-6 cytokine. Thus, a significant decrease in wound fluid IL-6 is possible. It would not be difficult to extrapolate that the ill effects of a decrease in the inflammatory cytokines at this time of wound healing might be detrimental to the process and thus support a slower healing wound.

The final finding from the study is the significant positive relationship between weight and IL-1β ($r=.475$, $p=034$) indicating that as weight increased IL-1β increased. In a study of mice and plasma lipid levels (Kirii, Niwa, Yamada, Wada, Saito, Iwakura, Asano, Moriwaki, & Seishima, 2003) found no significant differences in body weights and plasma lipid levels between the two groups of mice at 12 and 24 weeks of age when IL-1β levels were higher. However, Zhang, Kumar, Barnett and Eggo (2001) noted that TNFα stimulated the release of IL-1β from preadipocytes and adipocytes up to 20-fold. Thus, since IL-1β is secreted from adipocytes, it may be that as more a person weighs, the more adipocytes they would have, thus, more IL-1β. No other wound cytokine studies reported this finding, thus further research is needed.

Summary

This study has contributed to the knowledge base of nursing by giving nurses an evidence-based ten-minute nursing intervention to decrease pain in CABG patients. Additionally, this study has contributed to the understanding of wound cytokine levels in

CABG patients. Further research needs to be done on wound healing and stress reduction interventions, however, the state of the science has been positively influenced by the significant finding that IL-6 levels in wound fluids decrease significantly when a patient is more tense/anxious before surgery.

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APPENDIX

Table A-1. Massage Table

Duration	Researcher	Year	Results
6 min	Longworth	1982	Decreased anxiety
30-45 min	McKechnie	1983	Decreased HR and tension
3 min	Fakouri	1987	Decreased HR, BP Increased skin temp
6 min	Bauer	1987	No changes "felt good"
20 min	Kaada	1989	Increased plasma endorphins
10 min	Weinrich	1990	Decreased pain in males
1 min	Tyler	1990	Increased HR, Decreased s VO_2
30 min	Field	1992	Decreased STAI, sCort, Increased sleep
30 min x5d	Field	1992	Decreased anxiety, depression, sCort (day1)
3 min	Meek	1993	Decreased HR, BP, Increased skin temp
5 min	Fraser	1993	Decreased anxiety by EMG, BP, HR
30 minx2	Ferrell-Torrey	1993	Decreased pain, anxiety, HR, RR
20 min	Stevensen	1994	Foot massage Decreased pain, anxiety, tension
10 min	Groer et al	1994	sIgA concentration increased significantly
3 min	Corley	1995	No change HR, BP, EMG, Increased skin temp
45 min	Menard	1995	No significant changes, deceased pain, anx, dep
15-30 min	Dunn	1995	Decreased anxiety
30 min 5x	Sunshine	1996	Decreased anxiety, depression, s Cort
30 min over weeks	Field	1997	Decreased depression, anxiety, s Cort
1 minX	Lewis	1997	Decreased sVO2 stopped
6 min	Richards	1998	Increased sleep and efficiency
20 min	Field	1998	Decreased anxiety, s Cort, Increased affect
30 min	Hernandez-Reif	1998	Decreased diastolic BP
10 min	Chin	1999	Decreased pain
20 min	Hattan	2002	Increased calmness
15-30minx3	Smith	2002	Decreased pain and symptom distress

Table A-2. Demographic Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
age	20	48.00	82.00	61.5500	9.59427
weight	20	109.00	265.50	180.7550	45.12638

Table A-3. Demographic Statistics by Group

group		N	Minimum	Maximum	Mean	Std. Deviation
Treatment	age	12	48.00	82.00	60.9167	10.06757
	weight	12	109.00	265.50	184.6750	41.27683
Control	age	8	48.00	80.00	62.5000	9.42641
	weight	8	123.00	261.00	174.8750	52.76481

Table A-4. Pre-test T-Test (pg/ml)

	group	N	Mean	Std. Deviation	Std. Error Mean
tIL_8pre	Treatment	12	.7309	.37250	.10753
	Control	8	.8194	.33968	.12010
tIL_6pre	Treatment	12	1.9150	.29252	.08444
	Control	8	1.9407	.36836	.13024
tIL_ilibpre	Treatment	12	1.1285	.39185	.11312
	Control	8	1.0418	.21545	.07617
tIL_tnfapre	Treatment	12	.5607	.31283	.09031
	Control	8	.6084	.19089	.06749
pain1	Treatment	12	39.8333	28.19279	8.13856
	Control	8	44.0625	35.25665	12.46511

Table A-5. Pre-test T-Test

	t-test for Equality of Means		
	t	df	Sig. (2-tailed)
tIL_8pre	-.539	18	.597
tIL_6pre	-.174	18	.864
tIL_ilibpre	.568	18	.577
tIL_tnfapre	-.384	18	.705
pain1	-.298	18	.769

Table A-6. Pain Level Descriptive Statistics

group		N	Minimum	Maximum	Mean	Std. Deviation
Treatment	pain time 1	12	3.00	89.50	39.8333	28.19279
	pain time 2	12	.00	52.00	17.2083	17.57640
Control	pain time 1	8	5.00	100.00	44.0625	35.25665
	pain time 2	8	3.50	95.00	40.0000	35.20856

Table A-7. Change Scores in Pain

group		Minimum	Maximum	Mean	Std. Deviation
Treatment	change in pain	2.00	65.00	22.6250	18.54004
Control	change in pain	-20.00	29.00	4.0625	14.36374

Table A-8. Significance of Difference in Change in Pain- Paired T-Tests

group			t	df	Sig. (2-tailed)
Treatment	Pair 1	pain1 - pain2	4.227	11	.001
Control	Pair 1	pain1 - pain2	.800	7	.450

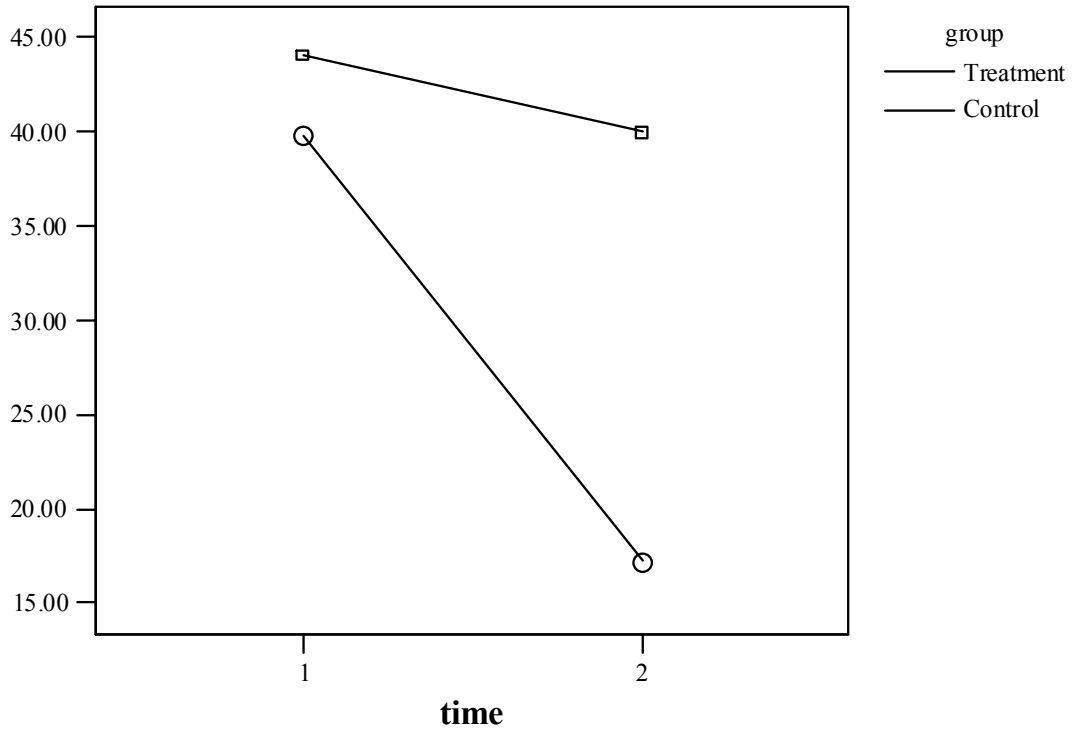

Figure 2. Change in Pain Graph

Table A-9. Test of Normality of Cytokines (pg/ml)

	Kolmogorov-Smirnov		
	Statistic	df	Sig.
il8_pre	.183	20	.079
il8_post	.489	20	.000
il6_pre	.151	20	.200
il6_post	.247	20	.002
ilib_pre	.254	20	.002
il1b_post	.246	20	.002
tnfa_pre	.163	20	.169
tnfa_post	.157	20	.200

Table A-10. Test of Normality of Log Transformed Cytokines (pg/ml)

	Kolmogorov-Smirnov		
	Statistic	df	Sig.
tIL_8pre	.103	20	.200
tIL_8post	.176	20	.106
tIL_6pre	.082	20	.200
tIL_6post	.126	20	.200
tIL_ilibpre	.132	20	.200
tIL_ilibpost	.162	20	.179
tIL_tnfapre	.111	20	.200
tIL_tnfapost	.106	20	.200

Table A-11. Descriptive Statistics of Cytokine Levels

	N	Minimum	Maximum	Mean	Std. Deviation
il8_pre pg/m.	20	.49	26.22	6.9531	6.71396
il8_post pg/ml	20	.49	374.94	22.4315	83.04538
il6_pre pg/ml	20	17.45	240.00	104.6799	68.90693
il6_post pg/ml	20	24.78	242.00	94.6585	65.82266
ilib_pre pg/ml	20	1.11	46.24	15.1080	12.41355
il1b_post pg/ml	20	.55	34.87	13.7130	8.97380
tnfa_pre pg/ml	20	.09	9.12	3.5013	2.65180
tnfa_post pg/ml	20	.81	8.21	3.6895	2.01210
Valid N (listwise)	20				

Table A-12. Descriptive Statistics of Pre and Post Test Cytokines in Experimental and Control Groups

group		N	Minimum	Maximum	Mean	Std. Deviation
Treatment	IL 8 pre pg/ml	12	.49	18.21	6.3424	5.78838
	IL 8 post pg/m	12	.49	374.94	33.8424	107.44664
	IL 6 pre pg/ml	12	35.06	240.00	101.7041	76.37981
	IL 6 post pg/ml	12	33.84	242.00	100.1563	77.63837
	IL 1b pre pg/ml	12	1.11	46.24	17.5940	14.77829
	IL 1b post pg/ml	12	.55	34.87	14.1248	9.79141
	TNFa pre pg/ml	12	.09	9.12	3.5549	3.09936
	TNFa post pg/ml	12	.81	8.21	3.4209	2.02611
Control	IL 8 pre pg/ml	8	1.43	26.22	7.8690	8.25249
	IL 8 post pg/ml	8	.90	14.36	5.3151	4.39666
	IL 6 pre pg/ml	8	17.45	185.26	109.1438	60.68281
	IL 6 post pg/ml	8	24.78	185.37	86.4119	46.45765
	IL 1b pre pg/ml	8	5.83	25.jk07	11.3789	6.96973
	IL 1b post pg/ml	8	6.54	32.44	13.0952	8.19734
	TNFa pre pg/ml	8	1.12	7.10	3.4208	1.99485
	TNFa post pg/ml	8	1.62	7.60	4.0924	2.05641

Table A-13. Descriptive Statistics of POMS Scores

	N	Minimum	Maximum	Mean	Std. Deviation
Anger/hostility	20	.00	22.00	6.7500	7.24660
Depression/ dejection	20	.00	39.00	7.7000	9.50955
Tension/anxiety	20	1.00	28.00	12.2500	7.64251
Fatique/inertia	20	.00	27.00	10.1000	7.59432
Confusion/ bewilderment	20	1.00	20.00	8.2500	5.13886
Vigor/activity	20	10.00	27.00	19.7000	4.87852
Total mood disturbance score	20	-11.00	103.00	25.3500	30.13701

Table A-14. Pearson Product Correlation of POMS Scores Using Log Transformed Cytokines

		tIL_8pre	tIL_6pre	tIL_ilibpre	tIL_tnfapre
anger/ hostility	Pearson Correlation	.207	-.090	.196	.140
	Sig. (2-tailed)	.382	.707	.407	.555
depression/ dejection	Pearson Correlation	.012	-.374	-.085	.187
	Sig. (2-tailed)	.959	.104	.723	.431
tension/ anxiety	Pearson Correlation	-.054	-.566	-.269	.232
	Sig. (2-tailed)	.822	.009	.251	.324
fatique/ inertia	Pearson Correlation	.076	-.271	-.067	.255
	Sig. (2-tailed)	.751	.248	.779	.278
confusion/ bewilder	Pearson Correlation	-.026	-.083	.014	.236
	Sig. (2-tailed)	.913	.729	.955	.317
vigor/ activity	Pearson Correlation	-.214	.318	.065	-.057
	Sig. (2-tailed)	.366	.171	.785	.813
total mood disturbance	Pearson Correlation	.089	-.417	-.073	.265
	Sig. (2-tailed)	.708	.067	.760	.259
painchange	Pearson Correlation	.046	-.366	.037	.130
	Sig. (2-tailed)	.849	.112	.877	.585

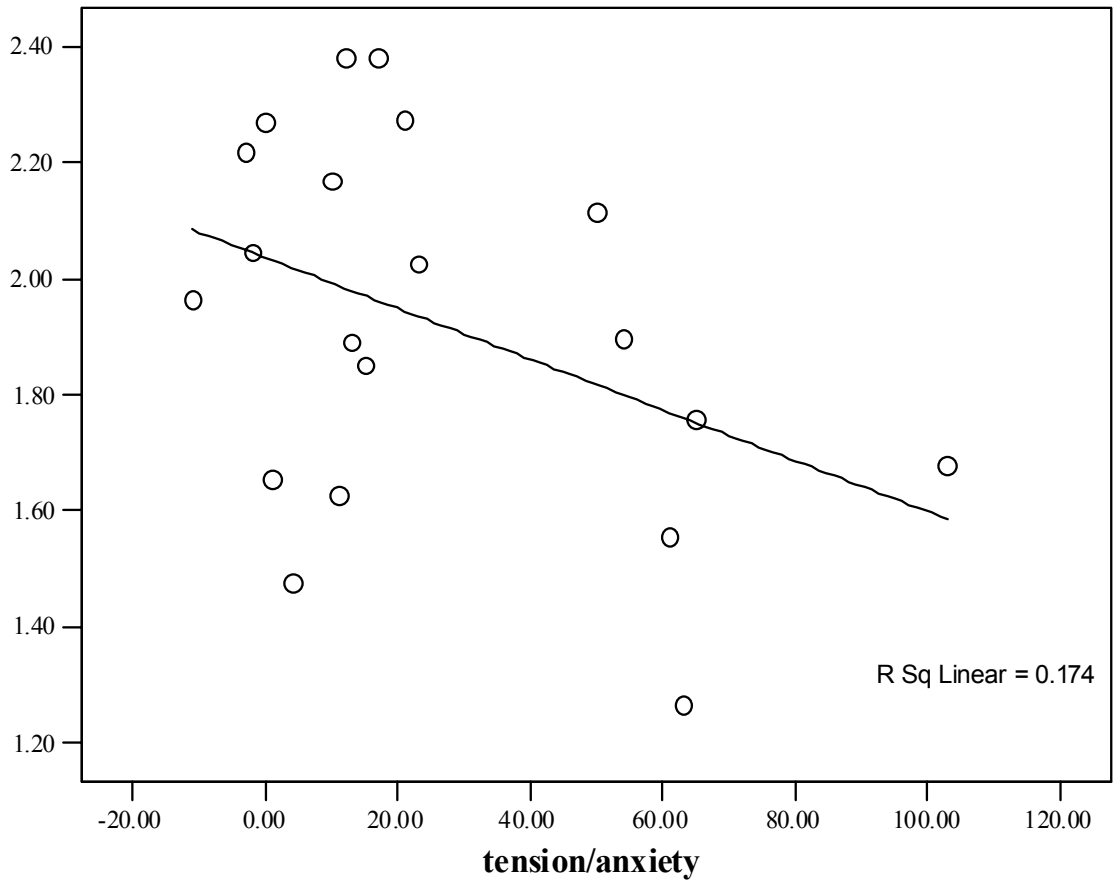

Figure 3. Negative Relationship of Tension-Anxiety and IL 6

Table A-15. Spearman rho Correlation Between IL-1β and Weight

			age	weight
Spearman's rho	il8_pre	Correlation Coefficient	-.132	.327
		Sig. (2-tailed)	.602	.185
		N	18	18
	il6_pre	Correlation Coefficient	.063	-.148
		Sig. (2-tailed)	.804	.559
		N	18	18
	ilib_pre	Correlation Coefficient	-.218	.475(*)
		Sig. (2-tailed)	.355	.034
		N	20	20
	tnfa_pre	Correlation Coefficient	.192	-.102
		Sig. (2-tailed)	.419	.668
		N	20	20

* Correlation is significant at the 0.05 level (2-tailed).

Table A-16. Wound Cytokine Studies

Studies	IL-1β pg/ml	IL-6 pg/ml	IL-8 pg/ml	TNF-α pg/ml
Smith 2004 20 patients mediastinal wound fluid 1-1.5 day post op	.55-46.24	17,450 – 242,000	490-374,940	.09-9.12
Baker et al. 2003 52 patients colorectal wound fluid 1,2 + days post op	1) 3-3,502 2) 5-5,071	1) 9,928-456,408 2) 5,500-242,076		1) 0-193 2) 0-167
Taniguchi et al, 2002 (means) 10 patients pleural fluid cancer 1,2+ days post op		1)177,000 2)approx 140,000	1)approx 5000 2)approx 2,000	
Baker et al. 2000 50 patients 24 pleural wound fluid 26 colorectal wound fluid 1 day post op	pl 3-341 ca 5-2,145	pl 90-146,700 ca 11,500-269,600		pl .4-41.5 ca 7.5-105.4
Holtzheimer et al. 2000 (means) 28 female patients pleural wound fluid (mam red.) 1,1.5 +days post op		1)180,000 1.5) 200,000	1)8,000 1.5)3,500	sTNFR-1 1)8000 1.5)11,000
Glaser, et al. 1999 36 female patients skin blister fluid 5 hours/1 day post op			5° 400-3,100 1)100,000-130,000	
Weissflog et al. 1999 21 patients pleural fluid cancer and no cancer .5-,2+ days post op				.5) 84 2) 80-3500
Ono et al. 1995 (means) 24 patients burn patients skin graft fluid 5th day post op	4,690	13,500		
Silva-Mejies et al. 1995 102 patients thoracentesis fluid pleural effusions/not surgery	No empyema <30-97 empyema >200			
Ono et al. 1994 20 patients burn patients skin graft fluid 5th day post op	0-65,000			
Grayson et al. 1993 (means) 13 patients burn thigh skin graft fluid 1,2+ days post op				1) 58 2) 68

Information Sheet

I am conducting a research study for completion of my dissertation. I am a nurse desiring to know more about what helps patients after surgery and what nurses can do to make patients more comfortable. I also am studying wound healing.

You, if you decide to participate in my research study, will be one of about 70 other participants. having coronary artery bypass surgery. I am interested in the effects of a nursing back rub after surgery on pain and wound healing.

The 3 forms I need you to complete for this research will take a total of about 20 minutes of your time. I will spend a total time of about one hour with you. You will be asked to sign a consent form, answer questions about your mood, complete an information sheet about yourself and rate your pain. The back rub will take ten minutes. The collection of the wound fluid will take less than 5 minutes each of the two times.

The study participants will be divided into two groups. One group will receive a nursing back rub and the other group will receive ten minutes of my time. For those of you that are not in the group receiving the back rub, I will give you one after I collect the second vial of fluid from your wound. I will take the wound fluid from your chest tube using sterile technique.

You will be involved with very little risk during this study. If you do not like the back rub or do not want to answer the questions you may choose to stop at any time. There is a minimal risk of infection during the wound fluid collection. I will use sterile needles to withdraw the fluid and use preventive measures to protect us from infection. There are potential benefits of this study, in that the results will help nurses know what may benefit patients after surgery and to know how moods might affect wound healing.

No one except my professor and I will have any records about your answers or information. I will assign numbers to you from the beginning and label all specimens with those numbers. I will be storing records in a locked file drawer to which only I will have the key.

If you have any questions about this study, please ask at any time.
Thank you

Kathlene D. Smith, RN
(865) 974-4151 email: ksmith6@utk.edu
ksmith6@utk.edu

Dr. Maureen Groer
(865) 974-7615
mgroer@utk.edu

University of Tennessee College of Nursing

The Effects of a Nursing Back Rub on Pain and Wound Cytokines and the Relationship of Preoperative Mood to Wound Cytokines.

Principal Investigator: Kathlene D. Smith, MSN
(865-974-4151 & ksmith6@utk.edu)
Sub-Investigator: Maureen Groer, PhD
(865-974-7615)

This study is being conducted at Fort Sanders Regional Medical Center in conjunction with the University of Tennessee College of Nursing. This study is being performed as a requirement to complete a nursing PhD program.

WHY AM I BEING ASKED TO TAKE PART IN THIS RESEARCH STUDY?

This is a research study. Research studies only include patients who choose to take part. You are being asked to take part because you are scheduled to have coronary bypass graft surgery (CABG). It is up to you to decide whether or not to take part. Please read this consent carefully and take your time to make your decision.

WHY IS THIS STUDY BEING DONE?

The major purpose of this research is to obtain information about what helps patients after surgery and what nurses can do to make patients more comfortable. This study is also being done to find out more information about wound healing as well as to complete the requirements of a PhD. in nursing.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

If you choose, you will be one of 70 people to take part in this study.

WHAT IS INVOLVED IN THE STUDY?

You will be asked to complete three forms which will take about 20 minutes of your time. If you choose to participate you will be asked to answer questions about your mood, complete an information sheet about yourself and rate the pain you experience. The questions will help the Principal Investigator understand how a nursing back rub may help reduce pain and influence wound healing.

Study participants will be divided into two groups. Using a sterile technique, fluid will be collected from a tube located in your chest. One group of participants will receive a nursing back rub and the other group will receive ten minutes of the Principal Investigator's time. For those that are not in the group receiving the back rub, a back rub will be performed, if you so desire, after the collection of the second vial of fluid from your chest tube. Total participation in this study will take approximately one hour of your time.

HOW LONG WILL I BE IN THE STUDY?

You will only be in this study as long as you are in the hospital.

WHAT ARE THE RISKS OF THE STUDY?

You will be exposed to very little risk during this study. If you do not like the back rub or do not want to answer the questions you may stop either at any time. Although a sterile technique will be used for obtaining fluid from your chest, there may be a small

risk that you will be exposed to germs that can cause an infection. You will be treated appropriately by your physician if this occurs.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There may be potential benefits to taking part in the study although you may experience none of them directly. It is hoped that the information gained in this study will help nurses know what may benefit patients after surgery and to know how moods might affect would healing. It is hoped this study will help improve nursing care in the future.

WHAT OTHER OPTIONS ARE THERE?

You have the option of not participating in the study and receiving the care routinely given to patients after CABG surgery is performed.

WHAT ABOUT CONFIDENTIALITY?

Under federal privacy regulations, you have the right to determine who has access to information regarding your medical condition, treatment, and means of payment (called "protected health information" or PHI). Your information will be kept as confidential as possible. By signing this consent form you are giving the Principal Investigator the right to use and disclose your PHI for purposes only related to this research study.

In addition to the Principal Investigator, the University of Tennessee Institutional Review Board and the Covenant Health Institutional Review Board may require access to your information. An Institutional Review Board is an independent committee that reviews research to ensure that patient's rights are protected.

The Principal Investigator will assign a specific number to your information and label all specimens with that number. Your specimens and information will be stored in a locked file drawer to which the Principal Investigator only can open. No reference will be made in verbal or written reports which could link you to the study.

WHAT ARE THE COSTS?

If you choose to participate, the study will be performed at no additional cost to you. The wound fluid evaluation has already been paid for by Sigma Theta Tau International, Inc (an organization that gives grants to support nursing research).

WHAT ABOUT LIABILITY?

Fort Sanders Regional Medical Center as a member of Covenant Health and The University of Tennessee College of Nursing do not provide reimbursement nor have funds budgeted to cover injures experienced as a result of participating in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may stop the study procedures (questionnaires, back rub, wound fluid collection) at any time. Choosing not to take part will not result in any penalty or loss of benefits to which you are otherwise entitled. If you decide to withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research related injury, you should call Kathy Smith, MSN. Her number is listed on the front page of this document.

For questions about your rights as research participant, you can call the Covenant Health Institutional Review Board Office at 865-541-1814.

PATIENT STATEMENT OF UNDERSTANDING

I have read the description of the clinical trial and have been offered the opportunity to have my questions answered. I understand that this clinical trial is a research study designed to obtain information about what helps patients after surgery and what nurses can do to make patients more comfortable. I also understand this research study is being conducted in order for the principal investigator, Kathy Smith, MSN, to complete the requirements to obtain a PhD in nursing. I know enough about the purpose, procedures, risks and benefits of the study to determine that I am willing to participate.

My signature below serves as permission for the Principal Investigator to access my PHI. My signature below also indicates that I have chosen to participate in the study. Once I sign and date this consent, I will be given a copy for my records.

_____ _____

Patient Signature Date

_____ _____

Investigator Signature Date

_____ _____

Person Obtaining Informed Consent Signature Date

INFORMED CONSENT FORM

The effect of a nursing back rub on pain, and wound cytokines in postoperative coronary artery bypass graft patients and the relationship of preoperative mood on wound cytokines.

You are invited to participate in a research study. The purpose of this project is to study preoperative mood and postoperative wound healing during the early stages of healing. Another purpose of this study is to look at how a back rub will might affect pain and early wound healing.

INFORMATION

This research study will ask you to complete short demographic and mood questionnaires. You will also be asked to report your levels of pain. Before surgery, you will be randomly assigned to one of two groups. One group will receive a back rub for ten minutes and one group will receive ten minutes of time with the researcher 18-48 hours after surgery. If you would like, if you have been assigned to the group that does not receive a back rub, you may request a back rub after the researcher has completed collecting the 2 wound fluid samples. The researcher will collect fluid from your wound by taking it from the tube in your chest incision before and after the back rub or time with the researcher. This study will take approximately one hour of your time for completion of questionnaires, self rating of pain, the collection of fluid from your wound and the back rub or time with the researcher. This study will involve about 70 other participants. No deception will occur in this study as you, the participant will have complete knowledge of every portion of every stage of the study.

RISKS

The risk of feeling discomfort, stress, or pain is unlikely, but you will be able to stop the back rub at any time, or stop being in the study at any time if you desire. You will be continuously monitored for heart rate and heart rhythm during the back rub and if there are any adverse changes the back rub will stop immediately. There are minimal risks involved in taking wound fluid samples. Sterile needles will withdraw fluid from the tube in your chest and precautions to prevent infection will be used. The nurse involved in this research will not be able to provide you with normal nursing care but will notify appropriate staff if you need someone.

EMERGENCY MEDICAL TREATMENT

The University of Tennessee does not "automatically" reimburse participants for medical claims or other compensation. If you require emergency medical treatment from this research you will be responsible for the costs.

BENEFITS

The benefits of this study are to assist in the provision of good patient care after surgery.

CONFIDENTIALITY

The information in the study records will be kept confidential. Data will be stored securely and will be made available only to persons conducting the study unless you specifically give permission in writing to do otherwise. No reference will be made in oral or written reports which could link you to the study.

CONTACT

If you have questions at any time about the study or the procedures, you may contact the researcher, Kathlene D. Smith, RN, at UTK College of Nursing, 1200 Volunteer Blvd.,

Knoxville, TN and (865) 974-4151, email or Dr. Maureen Groer 974-7615. If you have questions about your rights as a participant, you may contact the Compliance Office at the of the Office of Research at (865) 974-3466.

PARTICIPATION

Your participation in this study is voluntary; you may decline to participate without penalty. If you decide to participate, you may withdraw from the study at anytime without penalty and without loss of benefits to which you are otherwise entitled. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

CONSENT

I have read the above information and agree to participate in this study. I have received a copy of this form.

Participant's name (print) _____

Participant's signature _____

Date _____

PERSONAL INFORMATION QUESTIONNAIRE

ARE YOU MALE OR FEMALE? _____

HOW OLD ARE YOU? _____

HOW MUCH DID YOU WEIGH BEFORE SURGERY?

_____

WHAT IS YOUR RACE? _____

IF YOU SMOKE, HOW MANY CIGARETTES A

DAY?_____

WHAT OTHER MEDICAL PROBLEMS OR CONDITIONS DO

YOU HAVE?

PAIN SCALE

PLACE MARK ON LINE THAT SHOWS YOUR PAIN

NO PAIN _____ **WORST PAIN**

Vita

Kathlene Duncan Smith was born in St. Charles, Illinois on May 16, 1952. She was raised in Wheaton, Illinois and graduated from Wheaton Academy in 1970. She attended Moody Bible Institute, DuPage Junior College, and graduated from the University of Tennessee, Knoxville and received a B.S. in nursing in 1976. Kathlene also received a M. S. in exercise physiology (1987) and a M. S. in nursing (1991) from the University of Tennessee, Knoxville. Kathlene completed requirements for the doctorate in nursing at the University of Tennessee, Knoxville.