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PRINCIPAL INVESTIGATOR: Na-Jin Park

CONTRACTING ORGANIZATION: Alabama University at Birmingham
Birmingham, Alabama 35294-0111

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Na-Jin Park

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Alabama University at Birmingham
Birmingham, Alabama 35294-0111

E-Mail: najinp@uab.edu

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13. ABSTRACT (Maximum 200 Words)

The specific aims of this study were to: (1) examine the association of objective and subjective breast cancer (BC) risk with immune responses; (2) examine the mediating role of psychological distress on the relationship between subjective BC risk and immune response; (3) determine the moderating role of dispositional optimism on the relationship between subjective BC risk and distress; and (4) assess the association between objective and subjective BC risk in healthy women with (FH+) or without (FH-) first-degree relatives (FDRs) with BC. Preliminary analyses with 118 healthy women (57 FH+, 61 FH-) indicated no association between objective and subjective BC risk with immune responses (Aim 1), and no mediating role for psychological distress on the subjective BC risk-immune relationships (Aim 2). However, the moderating role of optimism on the relationship between subjective BC risk and general psychological distress was supported (p=.036), while BC-specific distress was not (Aim 3). Additionally, objective and subjective BC risk showed a positive significant correlations (p=.000). The results indicate additional studies with larger samples of women having strong family history of BC in FDRs and including more measures of IR may advance the understanding of psychological-immune interactions in healthy women with varying degrees of BC risk.

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INTRODUCTION

Based on Selye's framework of Physiological Response to Stress and Lazarus and Folkmans' Transactional Model of Stress (1984), the specific aims of this study are to: (1) examine the association of objective and subjective breast cancer risk with immune responses; (2) examine the mediating role of psychological distress on the relationship between subjective breast cancer risk and immune responses; (3) determine the moderating role of dispositional optimism on the relationship between subjective breast cancer risk and psychological distress; and (4) assess the association between objective and subjective breast cancer risk in 126 healthy women with (FH+) or without (FH-) family history of breast cancer in first-degree relatives (FDRs).

BODY

Task 1. Project Organization: March 2004 ~ June 2004 (4 months)

a. Upon notification of receiving this grant on March 5, 2004, I began preparing all required documents for the University of Alabama at Birmingham (UAB) IRB and the HSRRB approval. While working on the Human Subject Protection document for HSRRB approval, I developed my recruitment materials (flyer, invitation letter, and brochure) and questionnaires (pre-existing psychological instruments, demographics, breast cancer risk information, and other supplementary information).
b. I requested money for participant incentive, parking and office space for meeting the participants. However, I was unable to obtain parking spaces for my participants except for a few one-day parking permits for student lots, which were far from the meeting place and very limited. Parking was a big problem for some participants, especially for those outside of the UAB community since it was almost impossible to find parking space in student lots. Two of the participants received fines for parking violations due to the unavailability of parking space in student lots.
c. I identified all available resources for recruiting participants near the UAB community (UAB reporter, Breast cancer support group, etc). I visited the UAB Interdisciplinary Breast Cancer Clinic and UAB Familial Breast Cancer Clinic and meet staff nurses and Dr. Lisle Nabell, a medical oncologist and co-director of Familial Breast Cancer Clinic, to discuss how to recruit participants through their breast cancer patients.
d. I ordered laboratory supplies for running natural killer cell activity (NKCA) and lymphokine activated killer cell activity (LAKCA) to look at a part of immune responses. Human ELISA

cytokine assay kits will be ordered at the end of data collection for a batch process of cytokine productions (e.g. IFN-g, IL-2, IL-10, and IL-12).

e. I attended monthly Journal Club at the Center for Palliative Care directed by Dr. John Shuster, my co-mentor in behavioral oncology.

Task 2. Subject Recruitment: July 2004 ~ March 4 2005 (8 months)

a. Once my study was announced in the UAB Reporter, a UAB weekly paper, I received overwhelming responses, 49 for the month of July. In the middle of August, 2004, I revised recruitment materials to recruit more healthy women who had at least one FDR diagnosed with breast cancer. As of March 4, 2005, I had 119 participants in my study including 58 women who had a FDR with breast cancer. A sample size of 118 was used for preliminary analysis because one participant had a ductal carcinoma-in situ (DCIS) making her ineligible for this study based on my exclusion criteria. See **Appendix A** for characteristics of sample and significant correlations among major variables.

b. When a volunteer called inquiring about the study, I informed them of the eligibility criteria and asked the potential participant if she was eligible. Although a few reported they were healthy, I later discovered they had pre-existing medical conditions and/or medication excluding them from the study. In the future, information about inclusion/exclusion criteria should be more specific based on my experience from this study. For example, the history of surgical removal of carcinoma without any adjuvant therapy could be considered as an acceptable participant.

c. The main concern from potential participants was about giving a blood sample. They also asked who would perform the procedure. It was at this point that I realized just being a registered nurse would not be enough to ease their fear. I asked Ms. Traci McArdle, RN, BSN, who worked as an oncology nurse for 18 years at UAB hospital and still works as a research nurse with breast cancer patients, to assist me in drawing the blood sample. As a result, participants were comfortable in giving blood samples for this study.

Task 3. Data Collection and Management: July 2004 ~ March 4 2005 (8 months)

a. I have ran all 119 NKCA and LAKCA assays in the lab. All instruments including pipettes, incubator, centrifuge, and gamma counter have been calibrated periodically and well-maintained. I followed the exact guidelines for monitoring radioactive material use while

performing those immune assays. I attached my certificate of radiation safety training in **Appendix B**.

b. After collecting data, individual objective breast cancer risk was assessed using the Breast Cancer Risk Assessment Tool for Health Care Providers based on the modified Gail model (NCI, 2001). I mailed a copy of their breast cancer risk assessment outcome along with a summary of breast cancer screening information. I attached an example of my mail packet in **Appendix C**.

c. I created a data codebook and entered questionnaire and lab data regularly, which gave me a sense of monitoring the quality of data. Close monitoring of data must be begun with the start of data collection.

d. I completed the annual UAB IRB training course and Research Compliance training course pertaining to human subject protection and research ethics. I attach my IRB training certificate for 2004 in the **Appendix D**.

e. I attended a variety of seminars from the School of Public Health, Comprehensive Youth Violence Center, Center for Health Promotion, Center for Aging and Comprehensive Cancer Center to enhance my understanding of various research skills and study populations in the current bio-behavioral study.

KEY RESEARCH ACCOMPLISHMENTS

- Successful recruitment and data collection: 119 out of final sample size 126
- Poster presentation at the Graduate Student Poster Presentation in the School of Nursing at the University of Alabama at Birmingham (UAB), July 30, 2004.
- Poster presentation at the 19th Annual Conference of the Southern Nursing Research Society (SNRS), Atlanta, GA. February 3-5, 2005.
- Submitted an abstract for the 4th Era of Hope meeting, Philadelphia, PA, June 8-11, 2005

REPORTABLE OUTCOMES

- Abstract for poster presentation at the 19th SNRS conference. See **Appendix E**.
- Abstract for the 4th Era of Hope meeting, June 8-11, 2005. See **Appendix F**.

CONCLUSIONS

Most of all, I appreciate your support for a beginning researcher like me to have such a precious learning opportunity working with people in the real world. They were enthusiastic in doing something meaningful to overcome breast cancer as well as researchers. They were willing to share their own story about breast cancer with me. They inspired me with direction of my future study. I appreciate their participation and enthusiasm in my study.

In summary of the preliminary analyses with 118 participants (61 FH-, 57 FH+), there was no association between objective and subjective breast cancer risk with NKCA and LAKCA (Aim 1) and no mediating role for psychological distress on the subjective breast cancer risk-immune relationships (Aim 2). However, the moderating role of optimism on the relationship between subjective breast cancer risk and general psychological distress measured by the Profile of Mood States (POMS; Shacham, 1983) was supported ($p=.036$), while cancer-specific distress measured by the Impact of Event Scale (IES; Horowitz, Wilner, & Alvarez, 1979) was not (Aim 3). In addition, objective and subjective breast cancer risk showed a positive significant correlations ($p=.000$) (Aim 4).

The results of preliminary analyses indicate additional studies with larger samples of women having strong family history of breast cancer in FDRs and including other measures for immune response may help to advance the understanding of psychological-immune interactions in healthy women with varying degrees of breast cancer risk. The findings of this study can be applicable in developing better preventive approaches against breast cancer for general population in the future.

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APPENDICES

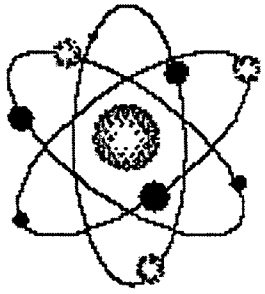
A. Characteristics of Sample & Significant Correlation Outcomes

Table1. Characteristics of Sample (N=118)

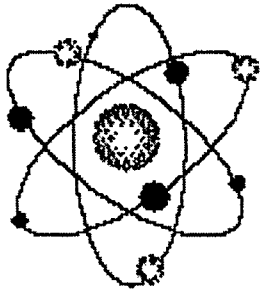
	Frequency	Percent (%)
Family history		
No family history	61	51.7
1st degree family history	57	48.3
Race		
Caucasian	64	54.2
African American	49	41.5
Others	5	4.3
Employment		
Unemployed, homemaker, retired, disabled	16	13.6
Part time	25	21.2
Full time (40 & over 40 hrs)	70	59.3
Other (student, self-employment)	7	5.9
Marital status		
Married	54	45.8
Living with a partner	7	5.9
Widowed	3	2.5
Separated	4	3.4
Divorced	15	12.7
Single/Never married	35	29.7

Table2. Correlations among major variables (* significant at <.05, ** significant at <.001, ns non-significant)

	Objective breast cancer risk	Subjective breast cancer risk	General distress (POMS)	Cancer-specific distress (IES)	Optimism (LOT-R)	NK 25:1	NK 12:1
Objective breast cancer risk		.320** .000	ns	ns	ns	-.182* .049	-.226* .014
Subjective breast cancer risk			.325** .000	.225** .014	-.362** .000	ns	ns
General distress				.405** .000	-.524** .000	ns	ns
Cancer-specific distress					-.391** .000	ns	ns
Optimism						ns	ns



UAB



The Department of Occupational Health and Safety
Radiation Safety Division
certifies that

Na-Jin Park

has successfully completed a course in

Radiation Safety Training

William B. Bass, Radiation Safety Officer

August 18, 2004

B. Certificate of Radiation Safety Training

C. Example of Mail Packet to Participants

October 13, 2004

Dear Participant,

I would like to thank you for your participation in my dissertation project: **Genetic Risk of Breast Cancer, Distress, and Immune Response.** This was an exciting learning experience for me and I hope that you will benefit from the information enclosed.

What was used to assess your breast cancer risk?

I have enclosed your individual breast cancer risk assessment result. This tool is available for your review at **http://bcra.nci.nih.gov/brc**. It was originally used to calculate the risk status of women who participated in a large National Cancer Institute Breast Cancer Prevention Trial.
The risk assessment is based on some selected risk factors but not every factor is included. For example, although the number of first-degree relatives (mother, sister, and daughter) with breast cancer is included, other risk factors such as family history of breast cancer in second-degree relatives (grandmother, aunt, and niece) are not included. Therefore, you should keep in mind that this risk assessment result is only a very rough estimate for you.

Why should you follow the guidelines for breast cancer screening?

The causes of breast cancer are not fully known, although a number of risk factors have been identified. Furthermore, there are individual differences: While some women with many risk factors never develop breast cancer, others with few or no risk factors develop breast cancer. Being a woman itself is the #1 risk factor for breast cancer. The risk increases as women gets older, especially after age 40. There are things you can do to lower your risk of developing breast cancer (eating right, exercising, maintaining a healthy body weight, staying away from alcohol), but no one yet knows how to prevent the disease. This is why you should follow the Guidelines for Breast Cancer Screening & Early Detection.

Your risk category and breast cancer screening

I have enclosed the breast cancer screening recommendations for women at average risk and at increased risk. If you have an estimated **5-year risk less than 1.7%** on your risk assessment, you are **at average risk**. If you have **a 5-year risk $\geq$ 1.7%** on your risk assessment, you are **at increased risk**. Follow the guidelines appropriate for your risk.

I hope this information helps you understand your breast cancer risk. If you have any questions or concerns, please feel free to contact me. Thank you again for your participation.

Sincerely,

Na-Jin Park, RN, PhD Candidate
School of Nursing
University of Alabama at Birmingham
(205) 934-7572
najinp@uab.edu

Screening Recommendations for Women *at Average Risk* for Breast Cancer

	Susan G. Komen Breast Cancer Foundation 1.800 I'M AWARE www.komen.org	American Cancer Society 1.800.ACS.2345 www.cancer.org
Mammography		
Ages 40–49	Every year	Every year
Ages 50–69	Every year	Every year
Ages 70+	Every year	Every year
Clinical Breast Exam		
	At least every 3 years between ages 20–39	At least every 3 years between ages 20–39
Breast Self-Exam		
	Monthly beginning by age 20	Beginning in 20s, review benefits and limitations of self-exam with health care provider. Choice to perform self-exam is up to the individual.

Screening Recommendations for Women *at Increased Risk* for Breast Cancer

National Comprehensive Cancer Network	Clinical Breast Exam	Mammogram	Breast Self- Exam
5-year risk of invasive breast cancer of 1.7% or higher in women age 35 and over.	Every 6-12 months	Every year	Encouraged
Strong family history of breast or ovarian cancer (for example, 2 or more first-degree relatives with breast cancer or ovarian cancer)	**Under age 25**		
	Every year	Not recommended	Encouraged
	Age 25 and over		
	Every 6-12 months	Every year	Encouraged
American Cancer Society	Women at increased risk (e.g. family history, genetic tendency, past breast cancer) should talk with their doctors about the benefits and limitations of starting mammography screening earlier, having additional tests (e.g. breast ultrasound or MRI), or having more frequent exams.		

NCI Breast Cancer Risk Assessment Tool
Your Individual Risk for Invasive Breast Cancer

4/4/2005
Name: xxxx

Age:	36
Age at first period:	15
Age at first birth:	29
Number of first-degree relatives with breast cancer:	1
Number of breast biopsies:	None

Race: White

Five-year risk of invasive breast cancer

Patient:	0.6%
Woman with average risk factors:	0.3%

Lifetime risk of invasive breast cancer

Patient:	17.6%
Woman with average risk factors:	12.5%

Risk at age 65 of invasive breast cancer

Patient:	8.7%
Woman with average risk factors:	6.0%

What do the numbers mean?

5-year risk

Based on the data provided your estimated risk for invasive breast cancer over the next 5 years is 0.6%, compared over the same time period to that of 0.3% for a woman of your age with average risk factors.

This also means that your estimated risk for NOT getting invasive breast cancer over the next 5 years is 99.4%.

Your estimated risk for invasive breast cancer of 0.6% would not have been high enough to qualify for the Breast Cancer Prevention Trial. In this trial, women ages 35 and older at high risk for invasive breast cancer who had a 5-year risk of 1.7 or higher qualified for entry.

Lifetime risk

Your estimated lifetime risk (to age 90) for invasive breast cancer is 17.6%. A woman of your age with average risk factors would have an estimated risk of

invasive breast cancer of 12.5%.

Do NOT compare your lifetime risk with the 1.7% cutoff used by the Breast Cancer Prevention Trial. It is the 5-year risk which should be compared to 1.7%, rather than the lifetime risk.

Risk at age 65

Your estimated risk at age 65 for invasive breast cancer is 8.7%. A woman of your age with average risk factors would have an estimated risk at age 65 of invasive breast cancer of 6.0%.

Do NOT compare your risk at age 65 with the 1.7% cutoff used by the Breast Cancer Prevention Trial. It is the 5-year risk which should be compared to 1.7%, rather than the risk at age 65 .

University of Alabama at Birmingham

Institutional Review Board for Human Use
CERTIFICATE OF TRAINING

This is to Certify that

Na-jin Park

has successfully completed Managing the Perils of Investigator-Initiated Research (OHRP), and has earned 1.5 credits of Continuing Education training in the protection of human subjects in research.

Awarded on
December 10, 2004
by the Institutional Review Board for Human Use,
at The University of Alabama at Birmingham

Investigators and other personnel involved in human subjects research at UAB must complete the initial training requirement and 1.5 credits of continuing IRB training each calendar year. Attendance at Managing the Perils of Investigator-Initiated Research counts toward the Continuing Education IRB training requirement for the year. This certificate may be printed for use in records and funding applications.

F Urthaler MD
Ferdinand Urthaler, MD
Chairperson, UAB IRB

Sheila Deters Moore
Sheila Deters Moore, CIP
Director, UAB IRB

Office of the Institutional Review Board for Human Use
470 Administration Building
701 20th Street South

Phone: (205) 934-3789
Fax: (205) 934-1301
Email: irb@uab.edu

D. IRB Training Certificate for 2004

E. Abstract for Poster Presentation at the 19th SNRS Conference

THE IMPACT OF BREAST CANCER RISK, PSYCHOLOGICAL DISTRESS, & DISPOSITIONAL OPTIMISM ON IMMUNE RESPONSES IN HEALTHY WOMEN

Na-Jin Park, MSN / Duck-Hee Kang, PhD
University of Alabama at Birmingham
School of Nursing
1530 3rd Avenue South, Birmingham, AL 35294
Key Words: Breast Cancer Risk, Distress, Immune Response

Background: Breast cancer is a multifactorial disorder influenced by gene-environment interactions. Family history of breast cancer, especially in first-degree relatives (FDR) is a known risk factor of developing breast cancer. Women who have FDR diagnosed with breast cancer, therefore, may perceive themselves to be at high risk, often exaggerating their risk, and experiencing undue psychological distress. Psychological distress, in turn, negatively affects immune response such as natural killer cell activity (NKCA) and lymphokine activated killer cell activity (LAKCA) that play an important role in tumor defense mechanism. Optimism, on the other hand, is known to moderate risk perception and psychological distress.

Purpose: Based on the Selye's framework of Physiological Response to Stress and Lazarus and Folkman's Transactional Model of Stress, the specific aims of this study are to: (1) examine the impact of objective and subjective breast cancer risk on immune responses; (2) examine the mediating role of psychological distress on the relationship between subjective breast cancer risk and immune responses; (3) determine the moderating role of optimism on the relationship between subjective breast cancer and psychological distress; and (4) assess the association between objective and subjective breast cancer risk in healthy women with or without family history of breast cancer in FDR.

Methods: For this cross-sectional, descriptive study, a convenience sample of 126 healthy women complete self-report questionnaires of objective and subjective breast cancer risk, psychological distress and optimism and provide a blood sample once. Objective breast cancer risk is calculated using the modified Gail model. NKCA and LAKCA are determined by a chromium-51 release cytotoxicity assay using K562 target cells. Multiple regressions will be used to test the magnitude of impact of (objective vs. subjective) breast cancer risk on NKCA and LAKCA (Aim 1) and a mediating and moderating role of psychological distress and optimism on the subjective breast cancer risk-immune relationships (Aim 2 & 3). Pearson's correlation coefficients will be used to test the relationship between objective and subjective breast cancer risk (Aim 4).

Discussion/Relevance: Findings of this study will advance the understanding of psychological-immune interactions in healthy women with varying degrees of breast cancer risk, which may contribute to developing better preventive strategies against breast cancer for general population in the future.

This research is supported by the Department of Defense Breast Cancer Research Program under award number W81XWH-04-1-0352.

G. Abstract for the 4th Era of Hope Meeting, June 8-11, 2005

THE IMPACT OF BREAST CANCER RISK, PSYCHOLOGICAL DISTRESS, & DISPOSITIONAL OPTIMISM ON IMMUNE RESPONSES IN HEALTHY WOMEN

Na-Jin Park, M.S. And Duck-Hee Kang, Ph.D.
University of Alabama at Birmingham
1530 3rd Avenue South, Birmingham, AL 35249
E-mail: najinp@uab.edu

Breast cancer is a multifactorial disorder influenced by gene-environment interactions. Family history of breast cancer, especially in first-degree relatives (FDR) is a known risk factor for developing breast cancer. Women who have FDR diagnosed with breast cancer may therefore perceive themselves to be at high risk, often exaggerating their risk, and experiencing undue psychological distress. Psychological distress, in turn, negatively affects immune responses such as natural killer cell activity (NKCA) and lymphokine activated killer cell activity (LAKCA) which play important roles in tumor defense mechanisms. Optimism, on the other hand, is known to moderate risk perception and psychological distress.

Based on Selye's framework of Physiological Response to Stress and Lazarus and Folkman's Transactional Model of Stress, the specific aims of this study are to: (1) examine the association of objective and subjective breast cancer risk with immune responses; (2) examine the mediating role of psychological distress on the relationship between subjective breast cancer risk and immune responses; (3) determine the moderating role of dispositional optimism on the relationship between subjective breast cancer risk and psychological distress; and (4) assess the association between objective and subjective breast cancer risk in healthy women with (FH+) or without (FH-) family history of breast cancer in FDR.

For this cross-sectional study, a convenience sample of 94 healthy women (33 FH+, 61 FH-) completed self-report questionnaires for objective and subjective breast cancer risk, psychological distress and dispositional optimism and provided a blood sample. Objective breast cancer risk was calculated using the modified Gail model. NKCA and LAKCA were determined by a chromium-51 release cytotoxicity assay using K562 target cells.

Preliminary analyses indicated no association between objective and subjective breast cancer risk with NKCA and LAKCA (Aim 1), and no mediating role for psychological distress on the subjective breast cancer risk-immune relationships (Aim 2). However, the moderating role of optimism on the relationship between subjective breast cancer and psychological distress was supported (p=.013) (Aim 3). In addition, objective and subjective breast cancer risk showed a positive significant correlation (p=.003) (Aim 4).

The results of these preliminary analyses indicate additional studies with larger samples of women having family history in FDR may help to advance the understanding of psychological-immune interactions in healthy women with varying degrees of breast cancer risk, and aid in developing better preventive strategies against breast cancer in the future.

The U.S. Army Medical Research and Materiel Command under W81XWH-04-1-0352 supported this work.