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Determining Evidence Based Managment of Benign Diseases

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DETERMINING EVIDENCE-BASED MANAGEMENT OF BENIGN BREAST DISEASES

by

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This independent study, submitted by Erin E. Lee in partial fulfillment of the requirements for the Degree of Master of Science with specialization in Family Nurse Practitioner from the University of North Dakota, has been read by the Faculty Advisor under whom the work has been done and is hereby approved.

Faculty Advisor

This independent study meets the standards for appearance, conforms to the style and format requirements of the Graduate School of the University of North Dakota, and is hereby approved.

Director of Graduate Studies
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ABSTRACT

Fibrocystic breast changes, also known as benign breast disease (BBD) can occur in as many as 50-60% of all women. Certain types of BBD have been shown to increase the risk of developing future breast cancer. As primary health care providers, nurse practitioners should be knowledgeable of which conditions place a woman at higher risk in order to provide the best possible care and treatment. These women may have increased anxiety that they will develop breast cancer, since they could be at higher risk than a woman without BBD. Health care providers may not be aware of the current evidenced-based recommendations for proper surveillance of patients with benign breast conditions; thus a review of the current literature and clinical decision models will update clinicians on current practices. Further, the diagnostic tests associated with screening for breast cancer (such as mammography, ultrasound, and biopsy) may be costly, so determining appropriate intervals of screening for each type of BBD is critical to control health care costs and avoid unnecessary testing.

This project included a literature review of current risk models, clinical evaluation tools, and surveillance practices that are used to determine health care management in women with benign breast diseases. The information was summarized into a manuscript accompanied by a post-test and was submitted to *The American Journal for Nurse Practitioners* (NPs). The purpose of this project was to update the NP's knowledge base of this clinical phenomenon by sharing evidence-based practice and ultimately helping to improve the health care management in women with benign breast diseases.

CHAPTER I

INTRODUCTION

This chapter introduces the research problem, purpose of the project, framework, definitions of key terms, and the significance of the problem. Assumptions and limitations of the research project are also discussed.

Statement of the Problem

Benign breast disease (BBD) occurs among many females, and certain types of benign disease have been proven to be an important risk factor for developing breast cancer (Dupont & Page, 1985, Hartmann et al, 2005, and Guray & Sahin, 2006). There are important reasons why this higher risk can affect health care for women. First, women may have increased anxiety that they will develop breast cancer, since they may be at higher risk than a woman without BBD (Andrykowski, 2002). Secondly, health care providers may not be aware of the current evidenced-based recommendations for surveillance of patients with benign breast conditions, so a review of the current literature and clinical decision models needs to be done to provide education of these practices. Also, the diagnostic tests associated with screening for breast cancer (such as mammography, ultrasound, and biopsy) may be costly, so determining appropriate intervals of screening for each type of BBD is necessary to decrease health care costs (Poplack et al, 2005).

Benign breast diseases have often been neglected in comparison to breast cancer, even though there are many more patients with benign breast diseases than patients with breast cancer (Courtillot et al, 2005). As women and healthcare professionals are becoming more aware that benign breast diseases can increase the risk for developing breast cancer, there has been an increasing interest in developing methods of assessing individual risk for breast cancer in order to make decisions on primary and secondary prevention practices (McTiernan, Gilligan, & Redmond, 1997). Different clinical decision models have been developed that can aid a practitioner in recommending screening and healthcare for women with these benign conditions.

Purpose of the Project

The purpose of this project was to research the risk of breast cancer associated with benign breast diseases and also to determine which recommendations of clinical surveillance are necessary in persons with benign breast disease. The project looked at current literature of risk models, clinical evaluation tools, and surveillance practices that are used to determine breast cancer risk in persons with benign breast diseases. This information was compiled into a manuscript for submission to *The American Journal for Nurse Practitioners*, which is aimed at the nurse practitioner reader population. The manuscript was written with a post-test and evaluation form, in the hope that the nurse practitioners would be able to receive continuing education credits for reading the article. The purpose of the manuscript was to update the clinicians' knowledge base of this clinical phenomenon by sharing evidence-based practice.

Conceptual/Theoretical Framework

The theory that was used in this independent project is a learning theory by Malcolm Knowles. The theory of andragogy is an adult learning theory and emphasizes that adults are self-directed and expect to take responsibility for decisions. Knowles bases his theory on four assumptions of the characteristics of adult learners: a) adults need to know why they need to learn something, b) adults need to learn experientially, c) adults approach learning as problem-solving, and d) adults learn best when the topic is of immediate value (Smith, 2007).

Using the assumptions that Knowles outlined in his theory helped facilitate the learning of the nurse practitioners that will read the educational article. First, they will know why they need to learn about benign breast diseases—many of the persons reading the article may have a practice population that includes many women and they could feel the need to learn this information. Secondly, the practitioners will use their experiences to help apply the knowledge they are learning; some of them may have dealt with certain types of benign breast disease in their practice and will be able to apply those situations to the information they are reading. Also, they will approach this learning as problem solving; many practitioners may have had questions about benign breast disease and how to treat it and therefore will take the information and use it to help problem solve each case. Lastly, the practitioners will have some value of learning about benign breast disease—as stated earlier many of the practitioners that will read this article will have an interest or may provide health care to women with these conditions.

Definitions

The major terms that need explanation in this research project are cancer, breast cancer, and benign breast disease. Other terms include surveillance and risk.

Cancer is defined as a pathophysiologic process that causes cells in the body to grow uncontrollably and spread out of control. Clumps of these cells often grow in one area and constitute a "tumor" (American Cancer Society, 2005).

Breast cancer, then, is cancerous cells that have grown in breast tissue. It can involve lobules (glands used in milk production), ducts, and the connective, lymphatic and fatty tissues of the breast (American Cancer Society, 2005).

Benign breast disease (BBD) is a categorical term used to group different types of breast conditions that are currently not cancerous. Benign means "not cancer" or "not malignant"; a benign tumor may grow but does not spread to other parts of the body (Medicine Net, 2007). The conditions of BBD are typically categorized into three subdivisions: nonproliferative lesions, proliferative lesions without atypia, and atypical hyperplasia. In order to classify it into these categories, usually a tissue specimen has to be obtained from a surgery or biopsy sample (Hartmann et al, 2005). One area of confusion in describing the different types of BBD is that different researchers have used their own nomenclature for lesions of the breast. This has produced some inconsistency in the past several years as far as a common vocabulary for these conditions (Courtillot et al, 2005).

Nonproliferative lesions typically encompass benign tumors such as fibroadenoma, lipoma, phyllodes tumor, hematoma, fat necrosis, cysts, and diabetic

mastopathy (Santen & Mansel, 2005). Nonproliferative means that the cells do not grow or increase in number rapidly (MedicineNet, 2007).

Proliferative lesions without atypia include ductal hyperplasia, complex fibroadenoma >3mm in diameter, papilloma, radial scars, and blunt duct adenosis (Santen & Mansel, 2005) . A definition of proliferative is that something is growing and increasing in number rapidly (MedicineNet, 2007).

Atypical hyperplasia involves both atypical ductal hyperplasia and atypical lobular hyperplasia (Santen & Mansel, 2005). Atypical, in general terms, means not normal or typical. In medical language it is often used to refer to the appearance of precancerous or cancerous cells (MedicineNet, 2007). Hyperplasia is an increase in the number of normal cells within a tissue or organ (MedicineNet, 2007). The atypical ductal hyperplasia is therefore an abnormal increase in the ductal cells of the breast whereas atypical lobular hyperplasia is an abnormal increase in the lobular cells.

Fibrocystic changes, fibrocystic disease, or benign mastopathy are all terms that have been used in the past and may be referred to in some of the research to describe benign breast changes (Bilous et al, 2005).

The operational definition for surveillance is close observation of a person.

Risk, for purposes of this project, is defined as relative risk, a term frequently used in research and epidemiological approaches (discussed below).

Relative risk is determined as the probability of an event occurring in the exposed people compared to the probability of the event occurring in the nonexposed people (Gordis, 2004). As an example, it would be the probability of someone with benign

breast disease getting breast cancer compared to the probability of someone without benign breast disease getting breast cancer.

Fine needle aspiration biopsy (FNAB) is a simple, inexpensive technique for obtaining cells from a targeted area of breast tissue (Bilous et al, 2005).

Core biopsy involves obtaining either single or multiple tissue samples from the breast by either vacuum assisted or conventional means (Bilous et al, 2005).

Significance of the Project

Benign breast diseases affect many females; incidence is generally not well-estimated, probably due to the fact that some females may not even know they have a benign breast condition (Courtillot et al, 2005). In one post-mortem review by Goehring and Morabia (as cited in Courtillot et al, 2005), it was estimated that one out of two women develops some degree of fibrocystic breast disease during her lifetime and one out of five women will develop a fibroadenoma. Therefore this information could affect the health care of many females. There is a chance that men can develop BBD as well, but this project focused on the diagnosis and treatment of BBD in women, because the disease occurs much more frequently in women.

Since some types of benign breast disease have been shown to have an increased risk of developing later breast cancer (Dupont & Page, 1985, Hartmann et al, 2005, and Guray & Sahin, 2006), the disease can have significant implications on health, psychosocial, and economical levels.

If benign disease is ignored and the proper surveillance methods are not practiced in the management of this condition or preventive techniques (such as the Breast Self Exam (BSE)) are not explained to the patient, there could be consequences. This disease

could develop into breast cancer that is diagnosed at a later stage, which may be much more difficult to treat and could possibly be terminal.

On a psychosocial level, having "lumpy" breasts or a specific lump, (which is common in benign breast disease) may create anxiety for a woman, since many women assume that any lump could signify breast cancer. Some studies have shown that women with a diagnosis of BBD have higher anxiety levels than women without BBD (Woodward & Webb, 2001, and Meechan, Moss-Morris, & Petrie, 2005). The worry and anxiety that this "lump" could develop into breast cancer can have an impact a woman's quality of life. Women with BBD need appropriate education to assure them that they have a benign condition, but also to alert them that their risk for developing cancer is slightly higher than someone without benign disease. Women also need to know how often they should be monitored in order to detect breast cancer, should it occur.

Lastly, the economic ramifications of surveillance testing should be considered. Determining the importance of whether or not a patient with benign disease needs an ultrasound/mammogram or a fine-needle biopsy due to their clinical presentation can save many health care dollars. If every woman with benign disease had a biopsy, this could have a significant impact on the health care dollars and insurance claims, due to a higher collective cost of healthcare for such women. Being able to determine correctly which patients have the highest risk and need those diagnostic procedures could save patients and medical facilities a substantial amount of money.

Therefore, due to these factors, determining the risk of developing breast cancer and the proper preventive recommendations and screenings for women with BBD is an important task, and this information needs to be communicated to practicing clinicians.

conditions. After the literature was reviewed, a manuscript with continuing education credits available was developed and was submitted to a national women's health or nurse practitioner journal for publication. The framework used in developing this project included ideas from Malcolm Knowles' adult learning theory of andragogy. This research project was significant because this disease can affect medical, psychosocial, and economical aspects of a patient's care.

CHAPTER II

LITERATURE REVIEW

Introduction

Benign breast disease has been heavily researched as to its role in the development of breast cancer, and there are numerous studies and informational articles related to this topic. Some of the more common factors that have been researched relate to each specific BBD classification and its associated risk for developing breast cancer. For example, atypical hyperplasia, which is a classification of BBD has been associated with higher risk rates. Other areas that have been researched are the risk in persons with BBD and with a family history of breast cancer. Other factors, such as dietary and genetic markers, have also been related to BBD and risk for breast cancer.

Another area associated with estimating breast cancer risk is the use of risk-models and/or clinical decision models that can aid clinicians in determining appropriate surveillance for patients, depending on their risk factors and their classification of BBD. Some of the more popular risk models include the Gail, Claus, Berry, and Rosner Models (Claus, 2001; Chen et al., 2006; MacTiernan, Gilligan, & Redmond, 1997; & Tartter, Galdos, Smith, Estabrook, & Rademaker, 2002). Some of these models are statistical formulas that calculate each woman's risk probability.

On the other hand, rather than using detailed statistical formulas to aid in risk estimates, simpler clinical decision tools (flow diagrams) have been used to determine the appropriate medical surveillance and testing for benign breast conditions. These decision

tools can be used as an aid to health care providers in discovering the path of surveillance for each specific woman based on her history.

Understanding the risk associated with BBD is important for health care providers, because the increasing use of ultrasound and mammography has also increased the frequency of breast biopsies, most of which yield benign findings (Hartmann et al., 2005). With education on the risk models and clinical decision tools, clinicians will be able to provide appropriate economic and patient-specific surveillance against breast cancer.

Benign Breast Disease Classification and Risk for Breast Cancer

Morphologic features of the breast undergo vast changes from early adolescence to menopause; these features range from ducts, lobules, and intra- and interlobular stroma to features that exhibit fibrous change and cyst formation. Most often these changes are due to hormonal factors: increased cell proliferation occurs during the luteal phase of the menstrual cycle. Different developments occur more frequently in each age group: fibroadenomas are more common in women mid-adolescence into their 20s, while women in their 30s to 40s seem to exhibit diffuse nodularity. But what seems to be the the most important classification of these changes is the degree of cellular proliferation, which is categorized histologically from a biopsy sample (Santen & Mansel, 2005).

Numerous research studies have found that women who have had a benign breast biopsy have varying subsequent risk for developing breast cancer, according to the histological classification of BBD. Numerous research studies have found that in women with nonproliferative lesions the risk is minimal, with proliferative lesions without atypia

the risk is moderate, and the risk increases substantially with a diagnosis of atypical hyperplasia (AH) (Collins et al., 2006).

A large, retrospective cohort study completed by Hartmann et al. (2005) reported on the risk of breast cancer according to BBD histologic findings (classification), age at diagnosis of BBD, and the strength of family history. This study included 9,087 women that were studied for a median of 15 years; these women received a diagnosis of BBD at the Mayo Clinic between 1967 and 1991. The relative risks were estimated by comparing the number of observed breast cancers in the population to the number expected, based on the rates of breast cancer in the Iowa SEER (Surveillance, Epidemiology, and End Results) registry. The populations of both studies were demographically similar. The relative risk associated with AH was 4.24 (95% CI, 3.26 to 5.41), 1.88 for proliferative changes without atypia (95% CI, 1.66 to 2.12), and 1.27 for nonproliferative lesions (95% CI, 1.15 to 1.41). Associations between risk of breast cancer and histologic findings, age at diagnosis of BBD, and strength of the family history were examined using Cox proportional-hazards regression models. Since this study involved tissue review, compared the site of the biopsy with subsequent breast cancer diagnosis, and had a large sample size, the results should be considered reliable. One factor that should be considered, however, is that the study did not make adjustments for other risk factors for breast cancer (using risk models discussed later in this chapter).

While many research projects have determined that the atypical hyperplasia conditions of BBD are associated with higher risk, few have determined the specific risk for the lower categories of BBD (LC-BBD). Wang et al. (2004) reviewed biopsy reports from the Breast Cancer Prevention Trial cohort sample to determine whether or not the

LC-BBD indicated higher risk. The unique aspect of this research was that it made adjustments for the other risk factors for breast cancer (age at menarche, number of first-degree relatives with breast cancer, age at menopause, age at first live birth, and number of previous breast biopsies) using the modified Gail model (a risk model to be discussed later). The findings showed a higher relative risk (RR) of breast cancer in patients with LC-BBD 1.60 (95% CI, 1.17 to 2.19). Problems with these findings include that participants recruited to be in this cohort were either 60 years of age and older (more likely to get breast cancer) or aged 35-59 and estimated to have a RR of 1.66 of developing breast cancer within 5 years (1. 6 times more likely than an average person to get breast cancer), and also the fact that other studies have not adjusted for other risk factors of breast cancer. Due to these considerations, it is difficult to compare the findings to those of other studies or to be able to generalize them to a larger population.

Communicating these risks to the patient needs to be done in a simplified manner—patients will usually not understand what a relative risk means unless it is explained in simplified terms (Elmore & Gigerenzer, 2005). For example, the patient with BBD may not know what a 1.66 relative risk means for them, but if you explain to them that a relative risk of 1.00 would mean that they have equal risk of developing breast cancer than a person without BBD, and a RR of 2.00 would mean they are twice as likely, that can give the patient a reference point with which to compare.

Benign Breast Disease and Family History of Breast Cancer

Since many women are diagnosed with having BBD, determining other risk factors besides the classification type of BBD (such as atypical hyperplasia or the category of proliferative lesions) is imperative. Another commonly researched risk

factor is family history of breast cancer. In most literature, family history of breast cancer is defined as a first-degree relative having the disease, which would be a mother or sister. Some studies classify the risk into strength of association, depending on the number of first-degree family members with breast cancer.

Hartmann et al. (2005) conducted a large cohort study (listed earlier) using follow-up survey data to determine family history risk. The classifications of family history were none, weak, and strong. Strong family history was at least one first-degree relative with breast cancer before the age of 50 years or two or more relatives with breast cancer with at least one being a first-degree relative. Any lesser degree of family history was classified as weak. For women with BBD and no known family history of breast cancer, the relative risk was determined to be 1.18 (95% CI, 1.01 to 1.37), compared to 1.43 for women with a weak family history (95% CI, 1.15 to 1.75) and 1.93 for women with a strong family history (95% CI, 1.58 to 2.32). Thus, the results found that family history was a risk factor independent of histologic findings; therefore there was a positive risk associated with family history of breast cancer but the risk was not any higher or lower depending on what type of BBD the woman had. This study did not examine women without BBD and risk for breast cancer, so the study findings are applicable only to women with a diagnosis of benign breast disease.

Webb et al. (2002) reported that women with a family history of breast cancer have an increased risk of being diagnosed with BBD, in particular the high-risk classifications (atypical hyperplasia and proliferative changes with atypia). Family history (FH) was defined as a first degree relative (mother or sister) having the disease. Data were obtained from the Nurses' Health Study II cohort, with a final population

sample of 1465 women after appropriate exclusions were taken into consideration. The results found that the risk for having a diagnosis of BBD in women with a family history decreases as age of the person increases. The relative risk (RR) for biopsy-confirmed diagnosis of BBD was 2.08 at age 25-29 years to 1.31 at age 45-50 years. However, one factor that could play a role in these results is the fact that women with a family history of breast cancer are more likely to seek medical advice for a breast lump, due to their increased awareness and concern of having breast cancer.

Dupont and Page (1985) reported that positive FH and diagnosis of AH had a substantially increased breast cancer risk (RR 11.0, 95% CI, 5.5-24.0) (as cited by Hartmann et al., 2005). Contrasting these results was a similar study by Collins et al. (2006), who did a nested case-control study of 2005 women enrolled in the Nurses' Health Study. Family history was defined the same (a first degree relative: mother or sister with breast cancer) as the Webb et al. study. All women involved in the Collins et al. study had a previous benign breast biopsy. Cases were defined as women with breast cancer that had a previous benign biopsy and controls were women that had a previous benign biopsy and who continued to be free of breast cancer. The levels of BBD (on biopsy results) were categorized in the 3 typical classifications, and results showed that compared to women with nonproliferative lesions and positive FH, women with proliferative lesions without atypia and a positive FH had a higher breast cancer risk (odds ratio 2.45, with a CI of 95%) than women with no FH (odds ratio 1.51, CI 95%). There was not a significant increase in risk of women with AH and positive family history. Contrasting the results from this research was that of Dupont and Page (1985), who reported in an earlier study that positive FH and diagnosis of AH had a substantially

increased breast cancer risk (RR 11.0, 95% CI, 5.5-24.0). The sample in this study was slightly smaller, which could explain the difference in the results. Conclusions of the Collins' et al. study (2006), since this was the most recent performed and reviewed all similar studies, was that the influence of family history on the risk of breast cancer in women with AH remains an unresolved issue. The authors state that risk assessment and management and recommendations for these women should be based on the presence of AH and do not need to be altered in those with a positive FH of breast cancer.

Since there are such varying results in each of these studies, it is difficult to determine which findings are the most reliable. However, all of the studies showed that positive family history in people with BBD increased the risk for breast cancer, so these patients can be encouraged to be screened more frequently than those with no family history of the disease.

Models and Assessment Tools Used to Predict Risk Breast Cancer Risk in BBD

Determining risk of developing breast cancer is a concern that many women have, and many research projects and screening methods have been evaluated, including risk models, decision tools, and cytology indexes. The use of one or more of these can help clinicians tailor a plan of surveillance for each individual patient.

Risk models are used to predict either relative or absolute risk for developing breast cancer. Commonly known risk models are the Gail, Claus, and Rosner models. These models are statistical formulas that have assigned certain risk factors for developing breast cancer numeric values in order to determine risk. For example, age at menarche, age at first live birth, and family history of breast cancer are some of these factors. Some risk factors that have not been taken into consideration are degree of breast

density, plasma levels of free estradiol, bone density, weight gain after menopause, and waist-to-hip ratio (Santen & Mansel, 2005). There are also tools that can help assess a woman's genetic risk, (due to the BRCA1 or BRCA2 gene mutation) including BRCAPRO and the Myriad tables (C. Grimm, personal communication, February 11, 2008).

The Gail model is the risk model that is the most widely used—it is also known as the Breast Cancer Risk Assessment Tool that is located on the National Cancer Institute's website. This model took data from the Breast Cancer Detection Demonstration Project (BCDDP) and used it to predict both five-year and lifetime (up to age 90) probabilities of developing invasive breast cancer. The factors that are used in this model include family history of breast cancer, personal history of benign breast biopsies (AH or not), age at first live birth, current age, and age at menopause. The researchers included these factors based on the results of a logistic regression analysis of data from a case-control study (2852 cases to 3146 controls matched by age, race, center, date, and length in study) of the BCDDP subjects (Claus, 2001). While this model is the most popular one used, it does have disadvantages. For example, the sample includes only Caucasian women and the model does not take into account the woman's age at diagnosis or whether or not the relatives with breast cancer are first- or second-degree. The Gail model has been tested and shown to slightly overpredict the absolute risk in premenopausal women (MacTiernan et al., 1997). Since these studies were completed, the model now uses an adjusted formula. A new formula similar to the Gail model that includes mammographic density (Chen et al., 2006) has been tested recently; however, studies need to be replicated in order to validate this new formula.

The Rosner model is another model that incorporates family history and environmental risk factors, using data from the Nurses' Health Study. It uses a multiplicative logistic model that assumes that the number of pre-cancerous cells increases multiplicatively with time, and exposures or risk factors may affect the rate of increase differentially over time. Recent additions to this model take into account Body Mass Index (BMI), alcohol use, and age at use of hormones such as oral contraceptives or estrogen replacement therapy. Disadvantages of this model are that it is not currently in a formula accessible to clinical oncologists and it does not provide estimates of absolute risk. As it is developed, this model may become popular because it includes common factors that are applicable to women (Claus, 2001).

The Claus model is a genetic model that used data from the Cancer and Steroid Hormone Study (CASH), a population-based case-control study of breast cancer. One advantage over the BCDDP model (Gail model) is that age of onset of the breast cancer of relatives is included. However, it does not take into account any other risk factors, leaving it at a disadvantage to other models. This sample was also taken from Caucasian women, so risk estimates may not be applied to other ethnic groups; also, a confidence interval was not reported.

In general, the Gail model is the most frequently used and most useful for women without an extensive history of breast cancer. For women in whom the primary risk factor is a strong family history of breast cancer, the Claus model is the most appropriate. Researchers have addressed the need to develop better models that incorporate detailed genetic information and environmental risk factors to validate new and existing models.

Clinical Decision Tools and Other Assessment Techniques

Women usually seek treatment for a palpable breast mass, or a clinical practitioner may discover a mass during a clinical exam. BREASTAID (**B**reast **R**isk **E**valuation **A**nd **S**coring System **T**o **A**id **I**n the **D**iagnosis of Mammary Masses) is a relatively new clinical decision rule (CDR) tool being developed. This CDR development has three goals: 1) to accurately predict the probability of malignancy in women with palpable solid breast masses, 2) to be practical enough to be used by a general surgeon or primary care clinician, and 3) to compare to the current method of practice, which is the triple-test method. The study was conducted on 380 women (small sample size) and found that the BREASTAID model can reduce the open biopsy rates by almost 40%--however, the study does recommend all patients with a mass to have FNAB for cytology review. The authors stated that the tool requires much more study before it should be applied clinically (Osuch, Reeves, Pathak, & Kinchelow, 2003), but it has the potential to conserve health care dollars while offering patients and clinicians assurance that clinical follow-up is a safe alternative to open biopsy.

One common and trusted source of guidelines in oncology is the National Cancer Center Network (NCCN). There is a specific guideline that has detailed algorithms used in the screening and diagnosis of breast cancer (C. Grimm, personal communication, February 11, 2008) and is used by clinicians in the decision-making process of determining what types of testing to do depending on the situation. For example, if a woman presented with a breast lesion, the algorithms would describe what further testing should be done to evaluate the lesion.

One area being recently developed is cytomorphology, which has been used to determine risk in breast tissue aspirates. Masood (2005) developed the Masood Cytology Index, which is a cytological grading system that looks at cellular arrangement, pleomorphism, myoepithelial cells, anisonucleosis, nucleoli, and chromatin clumping, and comes up with a total score of each specimen. Scores range from 6-24, and are separated into the following categories: (a) nonproliferative disease with atypia (6-10), (b) proliferative disease without atypia (11-14), (c) atypical hyperplasia (15-18), and (d) cancer (19-24). These researchers took 100 breast aspirates and scored them according to these criteria, and then compared the score category with the histological diagnosis, and found that the results were highly concordant. This index will allow separation of hyperplasia from neoplasia and may determine whether or not patients need chemoprevention. But since this is a newer index and was only tested on a small sample size, reproduction of the findings will need to occur before using it on a larger patient population.

Another new technology in breast cancer screening is using 3-D ultrasound instead of 2-D, which was shown in a small study by Cho et al. (2006) to have slightly higher sensitivity, specificity, and negative predictive values of determining benign from malignant solid breast masses. The results, whereas the 3-D results were more accurate, were not significantly higher than the 2-D images. More studies will need to be done to determine if 3-D imaging would be the preferred method in diagnosis of breast lesions.

Psychological Implications of Benign Breast Diseases

As discussed earlier, many women fail to be reassured about their benign breast condition following a benign diagnosis (Meechan, Collins, Moss-Morris, & Petrie, 2005).

A woman with a known "breast lump" for example, may have increased anxiety or worry that she has or will develop breast cancer in the future. Knowing what types of benign breast diseases are at higher risk can help a health care provider convey proper education to these patients and reassure them that they are receiving the proper surveillance necessary to discover breast cancer, should it occur.

Andrykowski et al. (2002) did a small study of 100 women that examined the impact of benign breast biopsies on distress and the perceptions of risk for breast cancer. Interviews were conducted with the women after their biopsy results, and also at 4 and 8 months post-biopsy. Compared to a matched group of healthy women that did not have a breast biopsy, the benign breast group experienced greater breast-cancer specific stress at the baseline measurement, which was taken right after the initial biopsy. Their stress did decline, however, and was close to the matched control at the 8-month post-biopsy interview.

In a similar study, Meechan et al. (2005) found that a significant proportion of women who received a benign breast symptom diagnosis experienced uncertainty. They also found that women who were not reassured were more likely to have a lower education level (high school) and that this group could benefit from some additional education about breast symptoms and a benign diagnosis. The authors also reported that women with high levels of anxiety, stress, and general worry about their health needed further reassurance in the immediate phase following a benign diagnosis.

In contrast, a literature review of women's anxieties surrounding breast disorders found that women with benign breast disorders and women with breast cancer had similar levels of anxiety and distress in the period of discovering the problem to receiving a

diagnosis, but that the anxiety levels fell much more quickly in women with a benign diagnosis (postdiagnosis) (Woodward & Webb, 2000).

Economic Impact of Surveillance Methods on Health Care

As far as the economic impact of different types of surveillance during screening for breast cancer, there is little information found in the literature. However, with each type of test done to screen for cancer, it is an additional cost to the patient. There needs to be a balance between providing the appropriate testing frequently enough to discover breast cancer and treat it in its early stages, and not testing so often that health care resources are being wasted unnecessarily.

Poplack et al. (2005) did a comparison study of the costs of screening mammography. The main conclusions of the study found that the largest total cost of screening mammography was the screening views alone (those mammograms not associated with other procedures). However, the highest costs per capita were associated with patients that needed to have interventional procedures done during mammography (such as a needle biopsy).

Recommendations for Management of Benign Breast Conditions

Since patients with BBD appear to be at higher risk of developing breast cancer, it is necessary for practitioners to be aware of evidence-based practice in regards to health-care management of these conditions. One of the most reported methods is "triple testing", which is a combination of 1) clinical examination, 2) imaging (mammography and ultrasound), and 3) nonsurgical biopsy (core needle biopsy or fine-needle aspiration). Triple testing is commonly used in women who have a significant clinical finding—for example, an asymmetrical thickening or a discrete palpable mass (Brennan, Houssami, &

French, 2005). Determining accuracy of the triple test methods is important: clinical exams have been estimated to have 54 percent sensitivity and 94 percent specificity, and also depend on the thoroughness and technique of the examiner (Santen & Mansel, 2005). Mammography has a false-negative rate (incorrectly diagnoses a lump as negative when it is positive) of approximately 10 to 20 percent and also can fail to see 9-22% of palpable breast cancers. One review of 4,943 fine-needle aspirations noted 87 percent sensitivity for the diagnosis of cancer (Hammond, Keyhani-Rofagha, & O'Toole, 1987), while another review of 3,545 fine-needle aspirations reported a 9.6 percent false-negative rate (Kline, Joshi, & Neal, 1979). If all three of these tests (in the triple-test method) appear benign, a breast lesion can be considered to be benign with an approximate 98% accuracy (American Cancer Society, 2003).

Clinical judgment is required to provide a balance between the intense surveillance needed for some and the risk of overdiagnosis in others, since up to 80% of women who have had a breast biopsy do not have cancer (Graf et al., 2004). Graf et al. (2004) conducted a small study to determine whether palpable solid breast lesions with benign morphology on mammography and ultrasound (US) can be managed with short-term follow up (6-month intervals for 2 years), without doing a breast biopsy. In their sample (n=108) this type of follow up was acceptable but more data are needed to determine if this is a correct conclusion.

There are several methods of obtaining a biopsy. Open-surgical biopsy is the most invasive. Other less invasive techniques include (a) fine core-needle biopsy, (b) image-guided (with ultrasound or MRI) core-needle biopsy, and (c) image-guided vacuum-assisted biopsy. A European prospective multi-center study examined 538

lesions, to determine the accuracy, reproducibility, and clinical value of MR-VAB (MRI-guided vacuum biopsy), since it has been shown to acquisition a larger tissue volume (allowing for reduction in sampling error), which can be important in histologic diagnosis of in situ malignancies or borderline lesions (Perlet et al., 2006). No false-negative diagnoses occurred, and the findings indicated that the MR-VAB offers excellent accuracy, so this may be one technique that is used more frequently in the years to come.

Nodularity, which is a common clinical finding that is usually physiologic, can be managed with clinical surveillance and a repeat examination in 2-3 months, if found in women less than 30 years old. However, if a women over age 30 presents with a localized nodularity, she should be further tested with mammography and/or ultrasound since there is a small percentage of breast cancers that present this way. If there is a clinical concern, fine needle biopsy or core biopsy should be performed (Brennan et al., 2005).

Cysts are another very common breast finding—they are a localized collection of fluid in the breast that are benign and are not associated with an increased risk for developing into breast cancer. Peak incidence of breast cysts is in the age group of 30-50 years. Some cysts are impalpable, but others can present clinically as lumps that are smooth, mobile, and sometimes tender. Ultrasound is usually better at diagnosing and characterizing cysts. Most do not require follow-up unless they become symptomatic (accompanied by discomfort) at which time the cyst(s) can be aspirated (Brennan et al., 2005). Cysts that are difficult to differentiate on imaging may also need to be aspirated; sometimes a tissue specimen is sent for cytology review, especially if the aspirate is

bloody or there is a residual solid component in the breast after aspiration (Vargas H., Vargas, M., Gonzalez, Eldrageely, & Khalkhali, 2004; Morrow, 2000).

Fibroadenomas are focal areas of change in the breast tissue that occur due to overgrowth of both stroma and epithelium. They can be solitary or multiple, and also palpable or not palpable. On clinical exam they are usually round or oval in shape, feel firm and rubbery, smooth, and are mobile; usually pain is not felt, but occasionally premenstrually the patient will have tenderness in the area of the fibroadenoma. If they are found benign after using the triple testing method, fibroadenomas can either be managed with surgical excision or clinical surveillance, depending on the age and patient preference (Brennan et al., 2005). Also, they are not usually associated with an increased risk for breast cancer.

Atypical ductal hyperplasia (ADH), one of the forms of AH, has been found to be high risk for future development of breast cancer. The finding of ADH lesions is associated with a 20-50% rate of cancer in adjacent tissue, so the biopsy should be followed with a surgical excision to exclude invasive disease. Estrogen receptor (ER) is over expressed in ADH lesions (60% of cells) compared to normal epithelium (25-30% of cells); ER promotes growth and proliferation of breast epithelial cells and may be a cause of progression to breast cancer. Therefore, Tamoxifen therapy (if appropriate for the patient) has been shown to decrease the rates of cancer significantly in women with ADH lesions (Arpino, Laucirica, & Elledge, 2005), since Tamoxifen helps prevent transcription of the estrogen-receptive genes (National Cancer Institute, 2002). A recent overview of breast-cancer prevention trials showed a reduction of 50 percent in the RR of breast cancer with Tamoxifen. However, there are also side effects of this medication,

including an increased risk for thromboembolic events, endometrial cancer, and cataract development, so the risk of these events needs to be compared to the benefit of using the medication (Santen & Mansel, 2005).

The other form of AH, atypical lobular hyperplasia (ALH), is another type of BBD that has been shown to have higher risk of developing into breast cancer. More trials need to be done to clarify the recommendations of management of this category of BBD. However, currently women with ALH can be managed with careful follow-up of yearly mammography and clinical breast exams. Tamoxifen has also been used in some patients with this condition, and bilateral mastectomy is considered in certain situations but can have psychological consequences (Arpino et al., 2005).

Conclusion

As breast cancer is a significant disease in women—in 2006 an estimated 211,240 new cases were diagnosed and approximately 40,970 persons died from the disease (American Cancer Society, 2005), practitioners need to be aware of which patients are at higher risk to develop it. Women with certain types of BBD are known to be at higher risk, depending on the histologic classification of their biopsy; for example, women with atypical hyperplasia (either ductal or lobular) have been shown to have the highest risk, especially if they have a family history of breast cancer in a 1st degree relative. Other factors that have been proven to increase this risk in women with BBD are a family history of breast cancer and certain environmental factors. However, cysts and fibroadenomas, which are often common in women, are not significantly associated with an increased risk for breast cancer. Also, new research studies are evaluating more

accurate methods of screening for breast cancer, such as digitalized mammography, and 3-D imaging.

The most widely used, clinically accepted recommendation of surveillance for women with BBD is the "triple test" method, which includes a clinical exam, imaging, and non-surgical biopsy (FNAB or core-needle biopsy). Many women who present with a breast mass for the first time should have the triple testing, but since a large percentage of biopsies are benign (up to 80%), clinicians need to display good judgment on determining if repeat biopsies are necessary after a diagnosis of BBD. Risk models, clinical decision models, and guidelines and/or algorithms can be used in combination with the triple test to help provide an appropriate plan for the patient based on risk estimates, with the goal being early detection or prevention of breast cancer.

CHAPTER III

PROJECT/DISCUSSION

Introduction

This chapter discusses target audience for this project, the plan for the project, and the methods that were used to evaluate it. Also included are the expected results and implications for nursing that deal with practice, research, education, and policy. The purpose of this project was to complete a comprehensive review of the literature to determine evidenced-based management for practitioners to follow when providing health care to women with benign breast diseases.

Population/Sample for the Project

The target audience of this project was the readers of a national nurse practitioner journal. Assumptions of this project were that after reading the article, the readers would become more knowledgeable about the different types of benign breast diseases, the importance of implementing the appropriate surveillance methods in women with these conditions, and appropriate resources and risk models to use in risk assessment. A manuscript developed as part of this project has been submitted to *The American Journal for Nurse Practitioners*.

Methodology/Procedures/Plan

In order to determine appropriate information on the types of benign breast diseases and current evidence-based management recommendations, a review of the literature on benign breast diseases was completed. The information obtained in the

literature review was organized into a journal article manuscript, complete with tables, a list of resources, continuing education questions, and an evaluation form. The article was written in an easy-to-read format that would hopefully grab the reader's attention. To determine the author had correctly summarized and interpreted the literature related to current clinical practice in managing women's breast health, the manuscript was reviewed by a physician that specializes in breast diseases. Her comments were integrated in editing the manuscript. The manuscript was also reviewed for editorial comments by a nursing professor that has extensive experience as an editor of various journals.

In order to implement this project, several women's health journals were contacted to determine their interest in the topic. Of the journals that indicated interest in the topic, *The American Journal for Nurse Practitioners* was selected for several reasons: (1) the journal is available in both online and paper versions, making it accessible to more clinicians, and (2) the journal publishes articles that offer continuing education credits. The manuscript was written using the guidelines established by the journal. Upon completion, it was submitted for approval. Knowles' Theory of Andragogy was used as a theoretical framework in writing the manuscript.

Evaluation Plan for the Project

The American Journal for Nurse Practitioners has an evaluation tool that is placed at the end of each CE article that is published. (Refer to Appendix C.) Assuming that the manuscript is accepted for publication, the article will be evaluated using this evaluation instrument by all readers who choose to complete the application for continuing education credit. One evaluative measure would be to determine how

frequently the article had been read by asking the journal editors how many persons had submitted an application for CE credits; It was difficult to evaluate the success of the project, considering the fact that the manuscript was still pending approval at the writing of this paper. If approved, it would also be difficult to determine how many pracitioners actually read the article. One way of determining if the article had been read would be to ask the journal editors how many persons submitted for the CE credits; it might also be possible to ascertain the content of their comments on the evaluation (i.e., how well the objectives were met, and the effectiveness of the article).

Expected Results of the Project

The general expectation of this project is that the readers of the journal article learned new information that they could use in their clinical practice. From the new information, they will hopefully be able to provide appropriate medical, psychosocial, and economical care for their patients with benign breast disease. In addition, the author of this article mastered this information and will be able to use it in her future clinical practice. Further, the experience of writing an article for a national publication also helped build confidence.

Expected Implications for Nursing: Practice, Research, Education, and Policy

This project has numerous implications for nursing in areas of practice, research, education, and policy. In the practice arena, if the readers of this journal article left with new evidence-based knowledge that would better help them treat patients with benign breast disease, this will help them provide appropriate, relevant, and cost effective care for women with BBD. The hope is that after they learn the information presented in this article, they will use the recommended surveillance methods in order to discover breast

cancer at an early stage. Practitioners should incorporate this knowledge into their history and physical of a woman's exam. Many practitioners are already teaching women how to do a self-breast exam; however, they can incorporate information about BBD and any personal risk associated with breast cancer. Also, some practitioners may not have been aware of the resources that were listed in the article and may want to incorporate the algorithms for breast surveillance and diagnosis into their practice. Another consideration is that a facility may want to develop a patient education pamphlet on different types of surveillance used in the monitoring and screening of breast conditions, in order to provide a patient-friendly way for women to learn about benign breast disease. Facilities can make teaching more relevant to women by using breast models to help differentiate between types of breast lesions.

In the research realm, perhaps after reading about this topic a clinician will develop further questions that he or she may be motivated to conduct further research. Perhaps a health care organization may see several patients with benign breast disease throughout the year and may want to begin a research study on another type of factor pertaining to BBD. The field of breast health has been extensively researched and is ever evolving, and there may be grants or scholarships available to a practitioner or facility who is interested in this topic. Areas that are currently being highly researched include the digital mammography and breast MRI capabilities, as well as medications used in the prevention and treatment of breast cancer. Some examples of research areas the author thought of that could be addressed in the future are: (1) does intake of certain dietary products affect risk of developing benign breast diseases, or (2) does benign breast disease correlate with a higher body mass index?

For nursing education, if there are readers of the article that teach at nursing schools, they should incorporate this information into their teaching curriculum of nurse practitioner students, especially in women's health and family nurse practitioner programs. National certifying bodies (such as the American Nurses' Credentialing Center or the American Academy of Nurse Practitioners) could include questions regarding different types of benign breast disease into their entrance-level exam for nurse practitioners. On the opposite side of things, nurse practitioners (acting as the teacher to their patients) would be better able to educate women (especially those with BBD) on the risk factors associated with developing breast cancer and be able to answer questions the patient may have.

Lastly, for policy considerations the article should cause some participants who are involved in administration to change the policies in which their clinicians practice, or encourage them to implement new policies involving treating patients at risk for developing breast cancer, perhaps by incorporating a specific clinical decision making model or guideline. It should spur a provider to develop a standing order protocols for imaging or biopsy to be used by that health care facility. Another idea could be to add breast-health risk questions to a facility's health history questionnaire; these are sometimes used in annual physical exams to identify patient's risk factors for specific diseases. Some examples for questions to include would be 1) does the woman have a family history of breast cancer?, 2) has she ever had a breast biopsy?, or 3) has she ever had an abnormal mammogram?

Chapter Conclusion

The information found during the literature review was arranged and written into a manuscript of journal article format, complete with tables, continuing education questions, and an evaluation tool at the conclusion of the article. The manuscript was submitted to *The American Journal for Nurse Pracitioners* and is currently pending approval for publication. This project can have several implications in four areas of nursing, including practice, research, education, and policy.

APPENDICES

Appendix A
Manuscript of Management of Benign Breast Diseases

Evidence-Based Management of Benign Breast Diseases

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Abstract

Fibrocystic breast changes, also known as benign breast disease (BBD) can occur in as many as 50-60% of all women. Certain types of BBD have been shown to increase the risk of developing future breast cancer. As primary health care providers, nurse practitioners should be knowledgeable of which conditions place a woman at higher risk in order to provide the best possible care and treatment. This article provides a review of the pathophysiology and types of benign breast diseases, screening and/or diagnostic tests used to monitor BBD, and statistical models that are used in determining risk of developing future breast cancer in these patients.

Introduction

One out of two women is estimated to develop some degree of benign breast disease during her lifetime.[1] Breast masses are a clinical problem that can present to a health care provider, either by the woman finding a lump herself during self-breast examination, or by the provider during the clinical exam. Even though there are many more women with benign breast conditions than with breast cancer, benign breast diseases have been neglected in regards to treatment recommendations.[1] As primary care providers, nurse practitioners need to be aware of the current management recommendations of benign breast lesions.

Although the disease is considered to be benign, some types of benign breast disease have been shown in large studies to be an important risk factor for later development of breast cancer. The risk is often dependent on the histological classification of the breast lesion.[2] Some types of benign disease can carry a risk greater than five times what a woman without benign disease would have. Since breast cancer is

the most common cancer in women, in all races and ethnicities,[3] understanding the changes that may occur during early development of cancer may help provide more accurate assessment of risk and individualization of therapy.[4]

Understanding risk and recommendations for management can also help with patient counseling, since a diagnosis of benign disease can have psychological impact. Women who had some type of benign breast pathology found on their mammogram were more likely to fear that they would develop breast cancer than women with normal mammogram results.[5-8]

Breast Physiology

Once a breast mass has been identified, the practitioner's role shifts from risk assessment to exclusion of cancer and provision of education and reassurance to the patient.[9] Having an understanding of the histologic changes that are associated with benign diseases and why some carry a higher risk of developing into breast cancer can aid the practitioner with his or her role.[4]

The term fibrocystic breast disease was often used in the past to describe "lumpiness" or thickened areas in the breast.[10] Now, the term "fibrocystic change" is preferred, since this histologic change may affect up to 50 to 60 percent of women.[11] Most women who were previously labeled as having "fibrocystic breast disease" may simply have breast tissue that is experiencing normal physiologic changes.[9] Due to fluctuations of estrogen and progesterone during the menstrual cycle, milk glands and ducts enlarge and breasts retain fluid. During the luteal phase, changes occur that result in an increased rate of cell proliferation—breast size can increase by up to 15 percent.[11] This normal glandular fluctuation may be why assessment of breast masses in younger

women proves to be challenging.[12] The benign lesions that form are thought to result from repeated stimulation by the estrogen and progesterone;[11] the lesions are under the complex system of local factors and systemic hormonal controls.[1]

Fibrocystic changes (FCCs) are the most frequent disorder of the breast and are seen commonly in premenopausal women 20 to 50 years old; incidence begins to rise in the 20s and peaks in the 40s and 50s, as opposed to malignant disease in which incidence increases after menopause and with age.[13] The fibrocystic changes in the breasts may be multifocal and bilateral, often presenting as breast pain and tender nodularities.[13] Types of FCCs include cysts, fibroadenomas, epithelial hyperplasia (with or without atypia), papillomas, and apocrine metaplasia[13] and are further placed into the three-tiered histological classification system that was developed by Dupont and Page in 1985 as either 1) nonproliferative lesions, 2) proliferative lesions without atypia, or 3) proliferative lesions with atypia. Table 1 describes the key terms and definitions of breast disorders.

(Insert Table 1 here)

Risk Associated with Breast Cancer Development

Women can be separated into high-risk and low-risk groups based on a determination of histological classification for the biopsy sample.[14] The tissue sample is taken either from needle aspiration, core biopsy, or open excision of tissue.

Nonproliferative findings on breast biopsy have a relative risk (RR) of breast cancer of 1.27, those with proliferative changes but no atypical cells have a RR of 1.88, whereas those with atypical hyperplasia have a RR of 4.24. These relative risks are the chances that someone with these conditions would develop breast cancer compared to

someone with normal breast tissue. Relative risks of benign breast disease on histologic examination are described in Table 2. The relative risk of developing breast cancer also appears to be independent of a family history (FH) of breast cancer,[14] and one study showed that the risks associated with BBD were the same across races.[15]

(Insert Table 2 here)

Another well accepted risk for developing breast cancer is having a first-degree family member with the disease.[16] However, having a family history of breast cancer does not appear to correlate with the specific types of benign breast disease.[2,17]

Risk Models

Women and health care professionals are becoming more aware that there are several factors that can affect the risk for breast cancer, so recently there has been interest in developing formulas to assess an individual's risk. Most of these risk assessments involve determining a woman's individual demographic information and health and family history into a quantitative (percentile or numerical score) or qualitative (high, medium, or low risk) estimate.[18]

The risk of breast cancer is commonly determined by practitioners with the use of the Gail model, also known as the Breast Cancer Risk Assessment Tool. This is the model that has been used by the National Cancer Institute, and can be found at http://www.cancer.gov/bcrisktool/. Variables that are taken into account in this risk model include age of the woman, age at menarche, age at birth of first live child, number of previous benign breast biopsies, and number of first-degree relatives with breast cancer.[19] However, the Gail model is not as accurate in a person with a strong family

history of breast or ovarian cancer, as the formulas have not been adjusted to account for these variables.

Other models include the Rosner, Claus, and Berry models. These models can be helpful in women with a FH that includes second-degree maternal or paternal relatives with breast cancer.[11,18,20] Other tools include the BRCAPRO model and Myriad tables listed in Figure 1. These are statistical models that use software to assess the probability that an individual carries a deleterious mutation of the BRCA1 or BRCA2 gene, based on family history of breast and ovarian cancer.

(Insert Figure 1 here as a sidebar)

Types of Surveillance

A number of methods are used to evaluate breast lesions, ranging from simple history and physical exam to more sophisticated methods involving ultrasound or biopsy. These methods are listed in Table 3 and will be explored below.

(Insert Table 3 here)

Screening versus Diagnosis: A "diagnostic" test is performed in a woman with a reported symptom of possible breast disease, such as a lump, discharge, or skin change[21] whereas a "screening" test is performed in someone who is asymptomatic. Breast cancers that are detected in a screening test have better prognostic outcomes than those diagnosed after symptoms have occurred.[22]

The Triple Test: Triple testing is the standard of care for any woman who presents with a palpable mass in the breast tissue. This process involves three components: 1) the clinical breast examination, 2) breast imaging, which may include mammography or ultrasound, and 3) nonsurgical biopsy.[9]

History & Physical: A thorough history and physical exam of the breasts and chest wall should be completed in a woman presenting with a breast lesion. History components focus on symptoms, risk factors for breast cancer (which include age at menarche, age at first live birth, family history of breast cancer, number of previous breast biopsies, waist to hip ratio, age at menopause, and any use of estrogen or progestin therapy). Physical exam is palpation of the breast and chest wall while the patient is both sitting and lying, identifying discrete lumps, and examining for regional lymph nodes. The consistency of the lesion should be determined and whether or not it has marginated borders, as well as assessment for symmetry of the breasts and any nipple discharge.[11]

Breast Imaging Reporting and Data System (BI-RADS) Classification: This classification system is used by radiologists to report the findings of an ultrasound, mammogram, or MRI in a standardized way. This classification is often seen on the report that is sent to the health care provider.[23] Categories are listed from 0 to 6: Category 0 means that there was an unsatisfactory assessment and additional imaging is needed. Category 1 is "negative" and routine follow-up is recommended. Category 2 means that there were benign findings such as fibroadenoma or cysts and no malignancy is suspected. Category 3 is a "probably benign lesion" where short-term follow-up is indicated (such as a repeat imaging study in 4-6 months). Categories 4, 5, and 6 range from suspicious abnormality to known malignancy.[24]

If the BI-RADS finding of the ultrasound or mammogram is a Category 3 or "probably benign lesion," periodic mammographic surveillance of the lesion every 4 to 6 months is recommended instead of jumping ahead to tissue diagnosis.[25, 26] This has proven to be effective and to help limit costs associated with interventional procedures.

Ultrasound: Ultrasound is frequently used to distinguish between cysts and solid tumors, but can also be used to help differentiate benign from malignant solid lesions of the breast.[9,27] Ultrasound is commonly used in women younger than 35 years of age due to their dense breast tissue, whereas mammography is used in most other women.[11]

Mammography: This test uses radiographic images to determine abnormal tissue composition of the breast and is the most common imaging test for breast tissue. The radiographic appearance of each woman's breast varies because of differences in the tissue composition (fat, stroma, and epithelium). Fat will appear dark on a mammogram, whereas epithelium and stroma are dense and look light (which is otherwise termed mammographic density).[28]

Women with dense tissue in 75% or more of the breast as measured by mammography have a risk four to six times greater of developing breast cancer than a women with little to no dense tissue.[28,29] Digital mammography has been shown to detect more breast tumors in women with dense breasts than film mammography[29] and sometimes an ultrasound in combination with a mammogram can result in better detection of malignant lesions.[26] Also, comparing prior mammograms of the patient to a current one can improve the overall reading.[30]

Fine-needle aspiration biopsy (FNAB): This diagnostic tool is used to assess breast lesions. It has high specificity, sensitivity, and positive-predictive value.[31] However, an experienced pathologist is needed to read the results due to the minimal number of cells collected. In recent years, some institutions have replaced FNAB with core biopsy and vacuum-assisted core biopsy since more cells are collected and the histologic diagnosis is easier to determine.

Core biopsy: In contrast to FNAB, core biopsy is more invasive, time-consuming, and expensive, but can have some advantages over FNAB. This is becoming the standard of care for histologic classification of breast lesions. The benefits include the use of histologic examination with which pathologists are more familiar and the ability to distinguish *in situ* from invasive carcinoma. Vacuum assisted core biopsy takes a larger sample of tissue and is highly accurate and effective in diagnosis of breast lesions.[31] Guidance with ultrasound or magnetic resonance can also be used to perform core biopsies.[32, 33]

Open biopsy: A surgical incision is made in the breast and a tissue sample is surgically removed in this method. If possible, the use of less-invasive techniques for surveillance such as FNAB or core biopsy should be used since this can decrease the morbidity and costs that are associated with open surgical biopsy.

Other: Newer technologies are emerging and have been shown to improve accuracy of diagnosis. These methods include digital mammography, computer-aided detection, breast MRI, and positron-emission mammography.[34]

A commonly used reference of guidelines for evaluation and diagnosis is available from the National Cancer Center Network (NCCN) at http://www.nccn.org/professionals/physician_gls/f_guidelines.asp?button=I+Agree.

Management for Different Types of Benign Breast Diseases

Fibroadenoma (FA): This is the most common lesion of the breast, occurring in 25% of asymptomatic women with peak incidence between the ages of 15 and 35.[13] In young women the FA is smooth, round, or lobulated, firm with discrete swelling and high mobility. Mammography is not indicated in women < 35 years with dense breasts;

ultrasonography is the best imaging method for these women. As far as the risk of developing subsequent breast cancer, Dupont and Page[1] concluded that there is no increased risk for a woman with a simple FA and no family history of breast cancer. Lesions can simply be treated with observation and followed with ultrasound every 6 months for 2 years and once yearly thereafter, but some physicians prefer an excision for tissue diagnosis.[11,13] If a triple assessment has concluded benign histology in women >25 years, a conservative approach is acceptable. If any feature is atypical or if the patient wishes to have it removed, surgery may be indicated.

Cysts: Asymptomatic cysts are often managed with no treatment, and they do not increase the risk of developing breast cancer. Cysts cannot reliably be distinguished from a solid mass by clinical exam so either ultrasound or FNAB are used.[13] Ultrasound is often a better tool for diagnosing cysts than mammography. Follow-up is not necessary unless the patient develops pain, in which case the cyst can be aspirated directly or under ultrasound guidance.[9,35] If the cyst is atypical or has bloody or tenacious aspirate, the fluid can be sent to cytology for assessment. The cyst can be reevaluated four to six weeks later and if there is no reoccurrence the cyst can be managed with routine mammographic or ultrasound surveillance.[35,36] Cysts that reoccur often despite repeated aspiration or that display atypical cytology can be removed with fine-needle or excisional biopsy.[37]

Papilloma: A solitary intraductal papilloma has slightly increased risk of developing into cancer. If a papilloma is suspected from the FNAB or core biopsy, surgical excision is recommended for full pathological assessment to rule out intraductal papillary carcinoma.[38]

Atypical hyperplasia (both ductal and lobular): This is the benign finding with the highest associated risk of developing into a future invasive breast cancer, especially in a woman who also has a family history of breast cancer. A finding of atypical hyperplasia (AH) on biopsy is often associated with a 20-50% rate of cancer in immediately adjacent breast tissue, so the biopsy should be followed by a surgical excision of tissue in that area to exclude any invasive disease and to prevent cancer from occurring.[4,38,39] A second recommendation has been to treat women that have AH with the anti-estrogen Tamoxifen. The National Surgical Adjuvant Breast and Bowel Project P-1 found that in women with ADH (ductal hyperplasia) that were on Tamoxifen therapy the relative risk for invasive breast cancer was reduced by 86%; although Tamoxifen therapy does carry other risks such as endometrial hyperplasia and increased risk of thromboembolic events.[4] In any woman with AH, the recommendation is routine follow-up of both breasts.[13]

In situ breast carcinoma, both ductal (DCIS) and lobular (LCIS): There can be several types subclassified by the pathologist depending on the cell nuclei's appearance. Treatment is dependent to some extent on the classification of the lesion. Current recommendations include complete excision of the lesion with attention to the margins, due to the high risk of development into an invasive cancer. Women with these types of lesions need to have close surveillance of both breasts,[38] and it is recommended that referrals be made to surgery and oncology.

Even though 80% of biopsies prove to be benign,[26]it has been shown that increased surveillance following a benign breast biopsy is necessary due to the risk of cancer development. The recommended schedule of follow-up is imaging either by

mammogram or ultrasound and a clinical breast examination by a breast surgeon at 6 months, 1 year, and 2 years after the benign biopsy.[40]

Implications for Practice

Since benign breast diseases occur in so many women, nurse practitioners need to be aware of the types of BBD and their associated risk of development into breast cancer as well as recommendations for surveillance and management. This knowledge will help provide adequate health care for women that are affected by these conditions and also assist in educating them about the plan of care and rationale which may alleviate concern they may have about their condition.

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Table 1: Key Terms and Definitions

Term	Definition	Comments
Localized nodularity	• Normal "lumpy" or nodular tissue; generally found in upper outer quadrants of the breast	• Common finding, especially in young women • Usually a physiological change, but some breast cancers may present this way
Fibroadenoma	• Focal area of change in breast tissue, usually the lobule • Caused by overgrowth of benign breast elements, (both stroma and epithelium) • Feels round or oval, firm, rubbery and smooth, and is mobile; may be tender	• Peak incidence in younger women ages 15-35 • Hormonal factors may be important, as fibroadenomas fluctuate during menstrual cycle and pregnancy • Usually unilateral but may present in both breasts
Breast Cysts	• Localized collection of fluid in the breast • If palpable, soft to firm, smooth, mobile, and sometimes tender	• Common; occurs in women of all ages but most often in premenopausal women between 35 and 50 years of age (Guray 2006)
Fibrocystic Change	• Nonspecific term that was commonly used in the past to describe a range of benign breast diseases • May refer to breast tissue that feels nodular or shows benign changes on imaging or with biopsy	• Often women who were previously labeled as having fibrocystic breast disease displayed nodular breast tissue that was undergoing normal physiological cyclical changes.
Papilloma	• Lesion of the epithelium of mammary ducts;	• Serous nipple discharge can be a presenting symptom

	central ones are usually solitary while multiples can occur in the periphery	• Surgical excision is sometimes recommended to rule out intraductal papillary carcinoma
In situ breast carcinoma	• Some epithelial cells have undergone malignant change but have not invaded through the basement membrane of the duct or lobule (are not "invasive" carcinoma yet)	• Can be classified into high, intermediate, and low nuclear grade depending on appearance of the cell nuclei • Needs to be excised and closely monitored with follow-up
Nonproliferative Changes	• Classification in which cells do not have proliferative changes	• Includes cysts, simple fibroadenoma, diabetic mastopathy, lipoma, mastitis
Proliferative changes without Atypia	• Classification of a lesion in which there is proliferation of cells but they are not atypical on appearance	• Normal ductal hyperplasia, complex fibroadenomas, papillomas, blunt duct adenosis, or radial scars
Atypical Hyperplasia	• Overgrowth of the cells that line either the ducts or lobules of the breast; it is called either ductal hyperplasia or lobular hyperplasia	• Atypical ductal hyperplasia and atypical lobular hyperplasia

(Some terms adapted from[1,9,13,41,42])

Table 2: Relative Risk of Benign Breast Diseases on Histologic Examination

Risk	Proliferation	Histologic Findings
No increase	Minimal (Non-proliferative)	Fibrocystic changes: cysts and ductal ectasia, mild hyperplasia, nonsclerosing adenosis; simple fibroadenoma; miscellaneous
Small increase (Relative Risk, 1.5-2.0)	Proliferative without atypia	Usual ductal hyperplasia, complex fibroadenoma, papilloma or papillomatosis, radial scar, blunt duct adenosis
Moderate increase (Relative Risk, >2.0)	Proliferative with atypia	Atypical Ductal Hyperplasia and Atypical Lobular Hyperplasia

(Adapted from Santen RJ, & Mansel R, 2005)

Table 3: Types of Surveillance

Clinical Breast Exam	• Examination of the breast tissue and surrounding areas from health care provider
Mammography	• Uses radiographic imaging to detect breast lesions
Ultrasound	• Ultrasound waves are used to detect breast lesions
Biopsy: 1) FNAB (Fine Needle Aspiration Biopsy)	• Simple, inexpensive, reliable, & rapid • Uses a thin needle that is guided into the area of the breast abnormality while the doctor is feeling the lump. Ultrasound may be used to guide it (stereotactic needle biopsy)
2) Core biopsy (CNB)	• Conventional or vacuum-assisted • Larger needle than in FNAB; removes small cylinder of tissue (1/16" in diameter and ½" long) from the breast abnormality • Can be done in the clinic with local anesthesia
3) Surgical biopsy	• Surgery may be needed to remove all or part of the lump to examine it under a microscope; An excisional biopsy is used to remove the whole lesion as well as surrounding margin of normal appearing breast tissue, sometimes with the guidance of mammography or ultrasound

(Information adapted from American Cancer Society, 2003 and Bilous et al, 2005)

Figure 1: Helpful Sources Regarding Management of Benign Breast Diseases and helpful patient references:

1. National Cancer Center Network Guidelines for Oncology
http://www.nccn.org/professionals/physician_gls/f_guidelines.asp?button=I+Agree
2. BRCAPRO: Model and software program for genetic counseling of women at high risk of hereditary breast and ovarian cancer
http://astor.som.jhmi.edu/BayesMendel/brcapro.html
3. Reference for the Myriad tables—used to assess genetic risk
http://www.myriad.com/products/cancerrisk.php American Academy of Family Physicians: Breast Problems in Women www.familydoctor.org/519.xml
4. American Academy of Family Physicians: Breast Cyst Aspiration
www.aafp.org/afp/20031115/1983.html
5. Mayo Clinic: Patient handout: Breast Lumps
http://www.mayoclinic.com/print/breast-lumps/BR00013
6. American Cancer Society: Cancer Reference Information on Noncancerous Breast Conditions
http://www.cancer.org/docroot/CRI/content/CRI_2_6X_Non_Cancerous_Breast_Conditions_59.asp?sitearea=
7. Susan G. Komen Foundation website: excellent patient resource
http://www.komen.org
8. Breast Cancer.org: excellent patient information
http://www.breastcancer.org

Appendix B
Post-Test of Management of Benign Breast Diseases

Please answer the following questions:

1. **True or False** Benign breast changes can affect up to 50-60 percent of women.

2. **List the three components of the triple test method, which is the standard of care for all breast masses.**

_____, _____,_____

3. **Which histological classification of benign breast disease is associated with the highest risk of developing into a later breast cancer (Relative-Risk >2.0)?**
   a. Atypical hyperplasia
   b. Proliferative changes without atypia
   c. Nonproliferative changes

4. **Which type of breast biopsy removes a small cylinder of tissue (1/16") with a needle that is guided into the lesion?**
   a. Fine-needle aspiration biopsy
   b. Core biopsy
   c. Surgical biopsy

5. **True or False** Women with extensive mammographic density (on mammogram) do not have an increased risk of developing breast cancer.

6. **True or False** A lesion that is classified as atypical hyperplasia (either ductal or lobular) on biopsy should be surgically excised.

7. **Matching: Match the definition with the corresponding term.**

   A. ____ Localized collection of fluid in the breast; commonly occurs in women aged 35-55.
   B. ____ Focal area of change in the breast, usually the lobule; common in women aged 15-35.
   C. ____ Lesion of the epithelium of the mammary ducts; serous discharge is often a presenting symptom.
   D. ____ Normal "lumpy" or nodular tissue; common in young women and may be a normal physiologic change, but some cancers can present this way.

   1. Fibroadenoma
   2. Breast cyst
   3. Localized nodularity
   4. Papilloma

Answers to questions:

1. True
2. Clinical breast exam, imaging (either mammography or ultrasound), and biopsy (usually core biopsy or fine-needle aspiration biopsy)
3. a
4. b
5. False
6. True
7. A:2, B:1, C:4, D:3

Appendix C
Evaluation Tool of Article

Management of Benign Breast Diseases
Evaluation Form

Procedure:
To receive credit and your exam score:

- Read the article.
- Complete and return the post-test.
- Provide the information requested below.

Evaluation Form:

Please use the following scale to evaluate the extent to which this program met the educational objectives. Circle one response for each.

5=Excellent 4=Very Good 3=Good 2=Fair 1=Poor

Upon completion of this activity, participants should be able to:

1. List some common types of benign breast diseases and their associated risk of developing into breast cancer 5 4 3 2 1
2. Describe the components of the triple test in assessing a breast mass 5 4 3 2 1
3. Discuss the types of surveillance that are recommended for each type of benign breast disease 5 4 3 2 1

Please evaluate the effectiveness of this article. Circle one response for each parameter.

4. Timeliness 5 4 3 2 1
5. Relevance of the content to advanced nursing practice 5 4 3 2 1
6. Effectiveness of teaching/learning materials 5 4 3 2 1
7. Achievement of learner's objectives 5 4 3 2 1

Time required to complete the offering: _____Hours _____Minutes

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