

Clinical Aspects of Breast Cancer

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Received: July 2022 Accepted: August 2022; Published: September 1, 2022.

Citation: Hani Raka Karrar et al. Clinical Aspects of Breast Cancer. World Family Medicine. 2022; 20(9): 136-142.

DOI: [10.5742/MEWFM.2022.9525148](https://doi.org/10.5742/MEWFM.2022.9525148)

Abstract

Breast cancer is considered one of the major health-care problems and one of the top biomedical research priorities among all biomedical research. Breast cancer is a common but extremely complex disease. The incidence of breast cancer becoming more aggressive is increasing, with around one million and seven hundred thousand new cases that get worse yearly, and this incidence is expected to increase significantly in the next 5–10 years. These rates are suggestive of the slow progress of this disease. Worldwide, Breast cancer is the most common cancer affecting women. The mortality rates for women who are already diagnosed with breast cancer have improved, but even then, the median survival in the metastatic stage is low, around 24 months. For the treatment, chemotherapy is the gold-standard approach for most cancer types and the modest improvement in both survival rates and toxicity reduction. Every newly diagnosed breast cancer should be presented at a multidisciplinary

conference to ensure optimal management by all specialties involved. A careful history of a woman's risk and symptoms and a thorough physical examination are important in the evaluation of breast problems and appropriately timed imaging and diagnostic studies are also important. Early detection of breast cancer at a stage when it is potentially curable and there is the possibility of saving a breast should be the goal of all health care professionals. Also, careful consideration should be given to the unique nature of each tumor and patient. This article aims to provide a brief introduction and the clinical picture of the disease, Etiology, Pathophysiology, Epidemiology, Nutrition, Prevention, and good practice management advice.

Keywords: Breast Cancer, BRCA1 gene, BRCA2 gene, Type one Diabetes mellitus, Type Two Diabetes Mellitus.

Introduction

Breast cancer is considered one of the major healthcare problems and one of the top biomedical research priorities among all biomedical research. The incidence of breast cancer becoming more aggressive is increasing, with around one million and seven hundred thousand new cases that get worse yearly, and this incidence is expected to increase significantly in the next 5–10 years. These rates are suggestive of the slow progress of this disease (1-3). Breast cancer evolves silently, and most disease is discovered on routine screening while other patients may present with an accidentally discovered breast lump, change of breast shape or size, or nipple discharge. Worldwide, breast cancer is the most common cancer affecting women. The mortality rates for women who are already diagnosed with breast cancer have improved, but even then, the median survival in the metastatic stage is low, around 24 months (3). For the treatment, chemotherapy is the gold-standard approach for most cancer types and the modest improvement in both survival rates and toxicity reduction (4, 5). This article aims to provide a brief introduction and the clinical picture of the disease, Etiology, Pathophysiology, Epidemiology, Nutrition, Prevention, and good practice management advice.

Epidemiology

Breast cancer is considered the most common malignancy in women. The incidence of breast cancer varies between countries. Breast Cancer is considered one of the three most common cancers worldwide, along with lung and colon cancer. In 2012, around one million and seven hundred thousand females were diagnosed with breast cancer worldwide, and around five hundred thousand people died from this disease (6, 7). 1 in 8-10 women will get breast cancer during their lifetime. The mortality rate in North America and Europe has decreased, and this has decreased because of the early detection and proper therapies (6, 8). In 2016, There was a drop of eight percent in the mortality rate from breast cancer in Europe (8). Despite the remarkable drop-in mortality rate in Europe and North America, breast cancer cases are growing, and still, it is considered the most common cause of death from cancer in less developed countries such as South America, Africa, and Asia. The cause for this increase is related to the lack of good diagnosis, screening, and therapy (7).

Diagnosis

Breast cancer is mainly diagnosed through either screening or a symptom such as pain or a palpable mass (9). But imaging methods are the primary diagnostic approaches that can offer useful information on patients' breast cancer among the various diagnosis platforms. It has been demonstrated that several imaging techniques, including mammography, MRI, PET, CT, and single-photon emission computed tomography (SPECT), can be used to diagnose and track patients with breast cancer at different stages. Employing biochemical biomarkers including proteins, DNA, mRNAs, and microRNAs in addition to imaging techniques could be used to develop new diagnostic and treatment approaches for patients with breast cancer (10). Mammography screening can help identify breast cancer at an earlier stage, which is associated with reduced mortality. According to a recent systematic review of screening program studies, screening decreased breast cancer mortality for women who were invited to the program by around 23% and by about 40% for regular participants. Most screening programs have switched from two-dimensional (2D) analog mammography to full-field digital mammography (FFDM) within the past ten years. The effectiveness of screening programs is projected to rise as a result of digital mammography (DM), which is linked to modest increases in detection rates and decreases in false positives. It serves as the comparison in this evaluation and is the current standard for the majority of mammography programs (11). According to randomized controlled trials, screening mammography reduces breast cancer mortality by 30%. Mammography does have its limitations, though, with a sensitivity of only 70%. Cancers may not show up on mammography, especially in women with dense breasts. Magnetic resonance imaging (MRI) of the breast is undisputedly the most sensitive of imaging methods to detect cancer, with a higher cancer detection rate than mammography, digital breast tomosynthesis, and ultrasound. Its present limitations include its relatively expensive costs, prolonged examination, and reading times, which prevent it from being used widely as a screening tool for women with an average risk of breast cancer (12). For axillary staging, sentinel node biopsy is still the preferred method over PET/CT, which is not advised for initial diagnosis. However, PET/CT can give important insights into several histological characteristics of the primary tumor, although its value and possible implications are not yet fully understood (13). The use of different imaging techniques has several disadvantages, including cost, a lack of sensitivity, and a lack of specificity. Therefore, it would appear that developing novel biomarkers that could overcome the constraints of imaging techniques is needed. One of the key components of diagnosing and monitoring breast cancer patients is the use of various biomarkers. The right biomarkers could help us improve our knowledge of the cellular and molecular mechanisms underlying the pathogenesis of breast cancer. These findings may be used to develop efficient therapy strategies and track treatment responses in breast cancer patients (10).

Risk Factors

Some factors help increase the development and progression of breast cancer. Several well-established risk factors are associated with the development of breast cancer which include: Age, while the percentage of breast cancer increases with age, the female sex has more chance to develop breast cancer than the male, and early menarche women have a high risk to develop breast cancer than others, and women with a family history of breast cancer in a first-degree relative (mother, sister, daughter) are highly suspected to get breast cancer more than other women especially if cancer has been diagnosed pre-menopausally. Women who have pre-menopausal first-degree relatives with breast cancer have a three- to fourfold increased risk of developing breast cancer than women who do not (14).

Signs and Symptoms

1. Breast mass

Detection of a breast mass is considered one of the most common breast signs for which women seek medical advice. Mainly breast masses are caused by benign lesions. Smooth and rubbery masses related to fibroadenoma in ladies in their 20s and 30s or cysts in ladies in their 30s and 40s (15-17).

2. Breast pain

Breast pain is usually related to cystic changes in premenopausal ladies and rarely comes with breast cancer. Breast pain is mainly associated with Postmenopausal women because of the effect of estrogen replacement therapy due to the effect of fibrocystic changes (18, 19).

3. Other

Other symptoms such as erythema, Edema, nipple discharge, and retraction of the skin are highly associated with malignancies (17, 19).

Management

1. Goal of therapy

The main goal of therapy is to decrease morbidity, mortality, and the economic cost of breast cancer. The treatment of breast cancer is multidisciplinary and can include surgery, radiation, and chemotherapy (20).

2. Surgical therapy

During the beginning of the 20th century, women diagnosed with breast cancer were treated with radical therapy, mastectomy, or Breast conservation surgery (21, 22). Nowadays, the primary treatment for local lesions of breast cancer is surgical intervention (23-25).

3. Chemotherapy

Adjuvant chemotherapy after surgery is recommended for patients at high risk of recurrence. Also, chemotherapy may be needed in a patient with one of the following criteria: Estrogen receptor negative tumor, Progesterone

receptor negative tumor, HER2 gene negative tumor, HER2 gene positive tumor, larger tumor size, and positive lymph nodes. Mainly the decision to use chemotherapy should be based on a balance of survival benefits and risk for complications (26, 27).

4. Radiotherapy

Radiation therapy is an important integral part of the treatment of breast cancers from preinvasive to metastatic stages (28, 29). The role of radiation treatment in breast cancer in women with early diagnosis has been long established. Postmastectomy radiation has been a matter of contention for decades (30-32).

Prevention

One of the important roles in modern medicine is to enhance the efficacy of health prevention through conducting research that focuses mainly on primary prevention, risk factors modification to early detection of the disease, and quick beginning of treatment (secondary prevention) (20).

1. Primary Prevention

Primary prevention includes the main causes leading to the disease occurrence, and increasing or enhancing the immune system in the population (33).

1.1 Diet

World Cancer Research Fund and American Institute for Cancer Research recommended a healthy diet as the primary prevention for breast cancer and that helps to maintain proper body weight. A healthy diet includes vegetables, fruits, cereals, and legumes, with little red meat and a little salt. Also, they recommended avoiding sweet beverages, high calorie food, and alcoholic beverages (33).

1.2 Obesity

There is a strong relationship between obesity and increasing the risk of breast cancer. The main cause is high-calorie meals which lead to weight gain and eventually obesity (34, 35). Body Mass Index (BMI) is commonly used to determine underweight, overweight, and obesity, which is calculated by dividing body weight in kilograms by the square of height in meters (kg/m²). BMI range include: BMI range include: <18.50 (underweight), 18.5–24.99 (normal body weight), ≥25.00 (overweight), ≥30.00 (obesity) (36).

1.3 Alcohol

Increasing alcohol consumption will increase the risk of cancer. Also, ethanol and its metabolism substance and acetaldehyde play a role in increasing the risk of cancer (37-39).

1.4 Physical Activity

The relationship between breast cancer and physical activity is stronger among women who have undergone menopause. Physical activity has a positive impact on mental health among patients suffering from malign tumors (40, 41).

2. Secondary Prevention

Secondary prevention aims at terminating the process of disease development before its full symptoms are diagnosed, which may prevent the development of a malign tumor. Secondary prevention includes Mammography (MMG), Ultrasonography (USG), Magnetic Resonance Imaging (MRI), and Breast Self-Examination (BSE). Mainly, these screening types are targeted at specified groups characterized by a greater risk of malignancy (42, 43).

2.1 Mammography

Mainly mammographic screening is used for asymptomatic women. Also, it is used as a diagnostic for women with signs or symptoms of breast cancer. Any sign of breast cancer should be communicated to the radiologist with the referral for a diagnostic mammogram. National Cancer Institution and American Cancer Society recommend screening mammograms every year for asymptomatic women 40 years and older (10, 44, 45). Mammography screening works by testing mammary gland cancer, and it is conducted on women in the age group 50–69 (46).

2.2 DIGITAL MAMMOGRAPHY [DONE]

Digital mammography is similar to standard mammography but the main advantage of this device is that images can be stored digitally, enhance the brightness or contrast, and be transmitted by mobile phones for remote consultation (46, 47).

2.3 Ultrasonography

Ultrasonographic screening is used to differentiate between solid and cystic breast masses when a palpable mass is not well seen on a mammogram (48). The main advantage of ultrasonography is it is safe, has no ionizing radiation, and is non-invasive. It's mainly used as a complement to other diagnostic examinations, and also, used to conduct biopsies under ultrasonography control. But still, the low specificity is the main disadvantage of this device (43).

2.4 Magnetic Resonance Imaging

Magnetic Resonance Imaging works by testing the mammary gland by magnetic resonance. It is very similar to ultrasonography. It is safe, has no ionizing radiation, and is non-invasive. It works complementary to mammography by increasing the detection of malignant lesions (43, 49).

2.5 Breast Self-Examination

Breast Self-Examination is a self-method. It has an important role in detecting cancer at an early stage. The main advantage of this test is it has no cost, it is available, can be done at home, and does not need technical training. But still, it is not sufficient to confirm the detection of cancer (50, 51).

2.6 Biopsy

Fine-needle aspiration (FNA) biopsy is generally used to obtain samples from a solid mass for cytology (52, 53).

3. Special Cases

3.1 Pregnancy

Since mammography is not performed in pregnant patients, the signs and symptoms during pregnancy are usually a suspicious palpable non-painful lump in the breast. In pregnancy the breast may undergo changes because of the normal physiological changes of the breast enlargement during pregnancy and the diagnosis tends to be delayed, leading to a worse prognosis in pregnant women. It is strongly advised that suspicious or palpable mass persisting > 2 weeks during pregnancy are investigated, even though 80% of breast lesions during pregnancy will be benign (54-56).

3.2 Male

Carcinoma of the male breast is a rare condition that accounts for less than 1% of all cases of cancer in men. Breast cancer occurs at a very low incidence in males, while the whole world's focus is on female breast cancer (57).

3.3 Black Population

Breast cancer makes up 30% of all types of cancer found in women. Before then lung cancer was the leading cause of cancer deaths in black women but that has changed. Nowadays about 12% of black women get breast cancer during their lifetime. Black women have the highest rates of breast cancer compared to other races (58).

4. Nutrition and Breast Cancer

General diet characteristics and individual dietary factors play an important role both in the development and the prevention of breast cancer. A healthy lifestyle, including weight management and a high-quality diet such as one that includes omega three fatty acids, natural antioxidants, and fibers are strongly related to better breast cancer outcomes, while unhealthy lifestyle, obesity, and poor dietary habits characterized by excessive intake of high-caloric foods which are rich in sugar and saturated fats will lead to an increase in the risk of postmenopausal breast cancer, recurrence, and mortality rate (59, 60).

5. Follow-Up

The American Society of Clinical Oncology recommends to do one mammogram screening annually, and one visit every 3 to 6 months for the first 3 years, one visit every 6 to 12 months in 4 and 5 years, then annually in patients who have undergone breast-conserving surgery with radiation. (61).

Conclusion

Breast cancer is a common but extremely complex disease. Every newly diagnosed breast cancer should be presented at a multidisciplinary conference to ensure optimal management by all specialties involved. A careful history of a woman's risks and symptoms and a thorough physical examination are important in the evaluation of breast problems, and appropriately timed imaging and diagnostic studies are also important. Early detection of breast cancer at a stage when it is potentially curable and there is the possibility of saving a breast should be the goal of all health care professionals. Also, careful consideration should be given to the unique nature of each tumor and patient.

DEFINITIONS, ACRONYMS, ABBREVIATIONS

BC; BREAST CANCER.

BRCA1; BREAST CANCER GENE 1.

BRCA2; BREAST CANCER GENE 2.

BSE: BREAST SELF-EXAMINATION.

MMG: MAMMOGRAPHY.

USG: ULTRASONOGRAPHY.

MRI: MAGNETIC RESONANCE IMAGING.

Authors' Contributions

'H. Karrar' supervised the team and direct the research. 'M. Noh' wrote the introduction, epidemiology, complication, and Conclusion paragraph. 'B. Alanazi' wrote the special cases. 'W. Aldoweirah' wrote the introduction. 'A. Hakami' wrote the relation between breast cancer and nutrition. 'R. Alharbi' wrote the diagnosis. 'B. Alanazi' wrote the special cases. 'W. Alanazi' wrote the introduction. 'W. Alzahrani' wrote the treatment. 'F. Alanazi' wrote the epidemiology. 'N. E. Alshammari' wrote the special population. 'N. H. Alshammari' wrote the Risk Factors. 'H. Alzahrani' wrote the risk factors. 'A. Alghamdi' wrote the Sign and symptom. The authors had full access to the data and take full responsibility for the integrity of the data. All the authors gave their approval for the submission of the final manuscript.

Ethical Approval

An ethical approval statement is not applicable, because this study is based exclusively on published literature.

References

- DeSantis C, Howlader N, Cronin KA, Jemal A. Breast cancer incidence rates in U.S. women are no longer declining. *Cancer Epidemiol Biomarkers Prev*. 2011;20(5):733-9.
- DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. *CA Cancer J Clin*. 2014;64(1):52-62.
- Greaney ML, Sprunck-Harrild K, Ruddy KJ, Ligibel J, Barry WT, Baker E, et al. Study protocol for Young & Strong: a cluster randomized design to increase attention to unique issues faced by young women with newly diagnosed breast cancer. *BMC Public Health*. 2015;15:37.
- Schmidt C. Immunology: Another shot at cancer. *Nature*. 2015;527(7578):S105-S7.
- Adams JU. Genetics: Big hopes for big data. *Nature*. 2015;527(7578):S108-S9.
- Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-86.
- Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65(2):87-108.
- Malvezzi M, Carioli G, Bertuccio P, Rosso T, Boffetta P, Levi F, et al. European cancer mortality predictions for the year 2016 with focus on leukaemias. *Ann Oncol*. 2016;27(4):725-31.
- Fuller MS, Lee CI, Elmore JG. Breast cancer screening: an evidence-based update. *Med Clin North Am*. 2015;99(3):451-68.
- Jafari SH, Saadatpour Z, Salmaninejad A, Momeni F, Mokhtari M, Nahand JS, et al. Breast cancer diagnosis: Imaging techniques and biochemical markers. *J Cell Physiol*. 2018;233(7):5200-13.
- Hodgson R, Heywang-Köbrunner SH, Harvey SC, Edwards M, Shaikh J, Arber M, et al. Systematic review of 3D mammography for breast cancer screening. *Breast*. 2016;27:52-61.
- Leithner D, Moy L, Morris EA, Marino MA, Helbich TH, Pinker K. Abbreviated MRI of the Breast: Does It Provide Value? *J Magn Reson Imaging*. 2019;49(7):e85-e100.
- Paydary K, Seraj SM, Zadeh MZ, Emamzadehfard S, Shamchi SP, Gholami S, et al. The Evolving Role of FDG-PET/CT in the Diagnosis, Staging, and Treatment of Breast Cancer. *Mol Imaging Biol*. 2019;21(1):1-10.
- Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN. Proportion of breast cancer cases in the United States explained by well-established risk factors. *J Natl Cancer Inst*. 1995;87(22):1681-5.
- AMB, RVS, JME, AAO. Breast cancer biomarkers: risk assessment, diagnosis, prognosis, prediction of treatment efficacy and toxicity, and recurrence. *Curr Pharm Des*. 2014;20(30):4879-98.
- Winters S, Martin C, Murphy D, Shokar NK. Breast Cancer Epidemiology, Prevention, and Screening. *Prog Mol Biol Transl Sci*. 2017;151:1-32.
- Peairs KS, Choi Y, Stewart RW, Sateia HF. Screening for breast cancer. *Semin Oncol*. 2017;44(1):60-72.
- Shamsi M, Pirayesh Islamian J. Breast cancer: early diagnosis and effective treatment by drug delivery tracing. *Nucl Med Rev Cent East Eur*. 2017;20(1):45-8.
- Černíková Anna K, Kráčmarová Klůzová L, Pešoutová M, Tavel P. Patient delay in presenting symptoms of breast cancer in women in the Czech Republic. *Klin Onkol*. 2021;34(1):40-8.
- Coughlin SS, Smith SA. The Impact of the Natural, Social, Built, and Policy Environments on Breast Cancer. *J Environ Health Sci*. 2015;1(3).
- Fischer JP, Wes AM, Tuggle CT, Nelson JA, Tchou JC, Serletti JM, et al. Mastectomy with or without

- immediate implant reconstruction has similar 30-day perioperative outcomes. *J Plast Reconstr Aesthet Surg*. 2014;67(11):1515-22.
22. Veronesi U, Saccozzi R, Del Vecchio M, Banfi A, Clemente C, De Lena M, et al. Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. *N Engl J Med*. 1981;305(1):6-11.
23. Matsen CB, Neumayer LA. Breast cancer: a review for the general surgeon. *JAMA Surg*. 2013;148(10):971-9.
24. Kaufman CS. Increasing Role of Oncoplastic Surgery for Breast Cancer. *Curr Oncol Rep*. 2019;21(12):111.
25. Wyld L, Audisio RA, Poston GJ. The evolution of cancer surgery and future perspectives. *Nat Rev Clin Oncol*. 2015;12(2):115-24.
26. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med*. 2004;351(27):2817-26.
27. Albain KS, Barlow WE, Shak S, Hortobagyi GN, Livingston RB, Yeh IT, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. *Lancet Oncol*. 2010;11(1):55-65.
28. Pfeffer RM. Radiotherapy for Breast Cancer: Curing the Cancer While Protecting the Heart. *Isr Med Assoc J*. 2018;20(9):582-3.
29. Rodin D, Knaul FM, Lui TY, Gospodarowicz M. Radiotherapy for breast cancer: The predictable consequences of an unmet need. *Breast*. 2016;29:120-2.
30. Krug D, Baumann R, Budach W, Dunst J, Feyer P, Fietkau R, et al. Current controversies in radiotherapy for breast cancer. *Radiat Oncol*. 2017;12(1):25.
31. Bradley JA, Mendenhall NP. Novel Radiotherapy Techniques for Breast Cancer. *Annu Rev Med*. 2018;69:277-88.
32. Castaneda SA, Strasser J. Updates in the Treatment of Breast Cancer with Radiotherapy. *Surg Oncol Clin N Am*. 2017;26(3):371-82.
33. Kolak A, Kamińska M, Sygit K, Budny A, Surdyka D, Kukielka-Budny B, et al. Primary and secondary prevention of breast cancer. *Ann Agric Environ Med*. 2017;24(4):549-53.
34. Orecchioni S, Reggiani F, Talarico G, Bertolini F. Mechanisms of obesity in the development of breast cancer. *Discov Med*. 2015;20(109):121-8.
35. Allott EH, Hursting SD. Obesity and cancer: mechanistic insights from transdisciplinary studies. *Endocr Relat Cancer*. 2015;22(6):R365-86.
36. Jeon YW, Kang SH, Park MH, Lim W, Cho SH, Suh YJ. Relationship between body mass index and the expression of hormone receptors or human epidermal growth factor receptor 2 with respect to breast cancer survival. *BMC Cancer*. 2015;15(1):865.
37. Castro GD, Castro JA. Alcohol drinking and mammary cancer: Pathogenesis and potential dietary preventive alternatives. *World J Clin Oncol*. 2014;5(4):713-29.
38. Frydenberg H, Flote VG, Larsson IM, Barrett ES, Furberg A-S, Ursin G, et al. Alcohol consumption, endogenous estrogen and mammographic density among premenopausal women. *Breast Cancer Research*. 2015;17(1):103.
39. Liu Y, Nguyen N, Colditz GA. Links between alcohol consumption and breast cancer: a look at the evidence. *Womens Health (Lond)*. 2015;11(1):65-77.
40. Castelló A, Martín M, Ruiz A, Casas AM, Baena-Cañada JM, Lope V, et al. Lower Breast Cancer Risk among Women following the World Cancer Research Fund and American Institute for Cancer Research Lifestyle Recommendations: EpiGEICAM Case-Control Study. *PLOS ONE*. 2015;10(5):e0126096.
41. Kruk J. Lifestyle components and primary breast cancer prevention. *Asian Pac J Cancer Prev*. 2014;15(24):10543-55.
42. Weigel S, Heindel W, Heidrich J, Heidinger O, Hense HW. Reduction of Advanced Breast Cancer Stages at Subsequent Participation in Mammography Screening. *Rofo*. 2016;188(01):33-7.
43. Mehnati P, Tirtash MJ. Comparative Efficacy of Four Imaging Instruments for Breast Cancer Screening. *Asian Pac J Cancer Prev*. 2015;16(15):6177-86.
44. Apantaku LM. Breast cancer diagnosis and screening. *Am Fam Physician*. 2000;62(3):596-602, 5-6.
45. McDonald ES, Clark AS, Tchou J, Zhang P, Freedman GM. Clinical Diagnosis and Management of Breast Cancer. *J Nucl Med*. 2016;57 Suppl 1:9s-16s.
46. Fiorica JV. Breast Cancer Screening, Mammography, and Other Modalities. *Clin Obstet Gynecol*. 2016;59(4):688-709.
47. Sechopoulos I, Teuwen J, Mann R. Artificial intelligence for breast cancer detection in mammography and digital breast tomosynthesis: State of the art. *Semin Cancer Biol*. 2021;72:214-25.
48. Kolb TM, Lichy J, Newhouse JH. Occult cancer in women with dense breasts: detection with screening US--diagnostic yield and tumor characteristics. *Radiology*. 1998;207(1):191-9.
49. Yang S-N, Li F-J, Liao Y-H, Chen Y-S, Shen W-C, Huang T-C. Identification of Breast Cancer Using Integrated Information from MRI and Mammography. *PLOS ONE*. 2015;10(6):e0128404.
50. Godavarty A, Rodriguez S, Jung YJ, Gonzalez S. Optical imaging for breast cancer prescreening. *Breast Cancer (Dove Med Press)*. 2015;7:193-209.
51. Akhtari-Zavare M, Latiff LA, Juni MH, Said SM, Ismail IZ. Knowledge of Female Undergraduate Students on Breast Cancer and Breast Self-examination in Klang Valley, Malaysia. *Asian Pac J Cancer Prev*. 2015;16(15):6231-5.
52. Schmidt RA. Stereotactic breast biopsy. *CA Cancer J Clin*. 1994;44(3):172-91.
53. Klimberg VS, Rivere A. Ultrasound image-guided core biopsy of the breast. *Chin Clin Oncol*. 2016;5(3):33.
54. Ulery M, Carter L, McFarlin BL, Giurgescu C. Pregnancy-associated breast cancer: significance of early detection. *J Midwifery Womens Health*. 2009;54(5):357-63.

55. Macdonald HR. Pregnancy associated breast cancer. *Breast J.* 2020;26(1):81-5.
56. Shao C, Yu Z, Xiao J, Liu L, Hong F, Zhang Y, et al. Prognosis of pregnancy-associated breast cancer: a meta-analysis. *BMC Cancer.* 2020;20(1):746.
57. Jaiyesimi IA, Buzdar AU, Sahin AA, Ross MA. Carcinoma of the male breast. *Ann Intern Med.* 1992;117(9):771-7.
58. Moormeier J. Breast cancer in black women. *Ann Intern Med.* 1996;124(10):897-905.
59. George SM, Bernstein L, Smith AW, Neuhouser ML, Baumgartner KB, Baumgartner RN, et al. Central adiposity after breast cancer diagnosis is related to mortality in the Health, Eating, Activity, and Lifestyle study. *Breast Cancer Research and Treatment.* 2014;146(3):647-55.
60. De Cicco P, Catani MV, Gasperi V, Sibilano M, Quaglietta M, Savini I. Nutrition and Breast Cancer: A Literature Review on Prevention, Treatment and Recurrence. *Nutrients.* 2019;11(7).
61. Khatcheressian JL, Wolff AC, Smith TJ, Grunfeld E, Muss HB, Vogel VG, et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting. *J Clin Oncol.* 2006;24(31):5091-7.