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REVIEW

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Recent strategies in diagnosis, screening, prevention, and treatment of breast cancer in young women

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Abstract

As cancer is the leading cause of death worldwide and breast cancer is a significant health concern among young women, it is crucial to consider its substantial morbidity and mortality. Breast cancer (BC) cases must be prioritized and addressed primarily in low- and middle-income countries, as these regions face unique challenges that require solutions despite limited resources. Thus, the primary focus of this review article is to discuss the current state of breast cancer risk, symptoms, diagnosis, prevention, treatment, and research, as well as the challenges and optimal methods that minimize harm to healthy tissues. This review highlights emerging technologies such as 3D imaging, deep inspiration breath-hold techniques, intensity-modulated radiation therapy, volumetric-modulated arc therapy, and aromatase inhibitors. These advancements are vital for overcoming the challenges in breast cancer care. On-going research and collaboration are essential to improve our understanding of breast cancer and its effects on the health and well-being of every woman.

Keywords Breast cancer, Women health, Imaging techniques, Computed tomography, Radiation therapy, Nanomaterials

1 Introduction

From ancient times, women have been regarded as the primary health care providers and decision-makers for health-related issues within their families. Any health concerns in the family are typically addressed or managed by the woman, who serves as the backbone of the family. Therefore, understanding more about women's health is crucial for every individual, as it contributes to the betterment of both their families and society. Women's health has become a significant issue in developing countries due to various barriers and challenges that compel women to neglect their health [1]. Women's health is often primarily defined in terms of reproductive health, which is viewed as a safety concern for younger women and the diseases affecting the female reproductive system. However, the most prevalent conditions affecting women are primarily related to cardiovascular diseases [2]. A woman's health is significantly influenced by her biological and sociocultural environment. Overall, the average life expectancy for women varies based on race and socioeconomic responsibilities. For instance, the average life expectancy for white women is five years higher than that of African American women, standing at 80 years and 75 years respectively in 1997 [3]. In developing countries, women's health remains a crucial issue, but numerous obstacles prevent women from attending to their health needs. The health statistics for women in developing nations reflect a worrying state of well-being. Several factors are vital for maintaining good health. The World Health Organization (WHO) defines health as ''the state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity''. Women's health is a pressing matter in many developing countries due to various issues that force women to overlook their health concerns. Multiple factors contribute to the confounding statistics of poor health among women in developing nations such as India, yet the inability of health systems in many countries to provide accessible care of adequate quality remains a significant concern [4]. Over the decades, their circumstances have changed, yet the situation remains alarming, particularly within disadvantaged and low-income families. As they transition from childhood to adulthood, becoming wives and mothers, numerous factors give rise to health issues among women. Some of these factors include malnutrition, violence against women, abuse, neglect and discrimination, female trafficking and exploitation, illiteracy, early marriage, unintended pregnancy, multiple childbirths, abortions, mental health issues, reproductive health complications, non-communicable diseases, HIV/AIDS, and cancer, among others [5].

Several factors can contribute to the development of cancer. These include specific health patterns, poor nutrition, exposure to harmful radiation, air pollution, obesity, and stress. It is estimated that about 5 to 10% of cancers may be hereditary, which can lead to various types of cancer in women. Cancer is the leading cause of death globally. Various types of cancer are observed in women, with the most common being breast, vaginal, and cervical cancer [6, 7]. Despite advancements in early detection and treatment significantly enhancing survival rates, breast cancer (BC) remains a pressing public health issue, especially in low and middle-income countries (LMICs), due to limited resources for diagnosis and treatment [8]. Therefore, this review article discusses the current state of breast cancer research in young women, advancements in diagnosis, screening, prevention, and treatment, as well as the challenges and optimal methods that minimise damage to healthy tissues.

2 Breast cancer (BC) epidemiology and risk factors

The most common type of cancer among young women is breast cancer (BC); in 2015, there were approximately 2.4 million cases, resulting in around 523,000 deaths [9]. In 2020, about 685,000 women died from BC from an estimated 2.3 million cases [10]. Based on the scenario and demographic projections starting from 2020, the rates remain stable. Eileen Morgan et al. predicted future rates using 2020 figures alongside population data provided by the United Nations Development Programme (UNDP) [11]. The Global Burden of Disease Cancer Collaboration reported that although countries of all income levels have seen an increase in BC incidents, there is significant variation in the disease burden across different income levels in various countries. A standard metric, incorporating quality of life and duration across organs and diseases, was estimated using the disability-adjusted life year. However, in low- and middle-income countries

(LMICs), approximately 69% of the disability-adjusted life years lost due to breast cancer were recorded [12].

There are numerous risk factors for breast cancer (BC), with the most significant being age, gender, family history, reproductive history, estrogen levels, hormonal imbalance, breast density, genetics, alcohol consumption, smoking habits, radiation exposure, and lifestyle (Fig. 1). Aside from sex, one crucial risk factor for BC is age, as the incidence of BC correlates strongly with increasing age. Most BC-associated deaths occur within the age range of 40 to 60 years among women. Therefore, it is essential to undergo mammographic screening for women aged 40 and older [13]. Martine Bellanger has extensively described how economic development in the country is measured by income category, which helps to explain the incidence and mortality of BC in women younger than 50 years, which is comparatively lower. Mortality rates rise as a country's income decreases. The patterns differ from stable to increased mortality rates in women older than 50 years as income rises [14]. Approximately a quarter of BC cases are generally linked to family history [15]. Hannah Brewer detailed the calculation procedure for a Standardised Incidence Ratio (SIR), which she refers to as the 'Family History Score' (FHS). A cohort study conducted in 2003, involved a prospective generation of women aged 16 and older from the general population in the United Kingdom, encompassing over 113,000 women who provided consent and completed a comprehensive questionnaire. Women with first-degree relatives diagnosed with BC have a 1.75-fold higher risk of developing BC compared to those without a family history of related diseases [16]. Factors that increase the risk of BC include early age of menarche and pregnancy-related

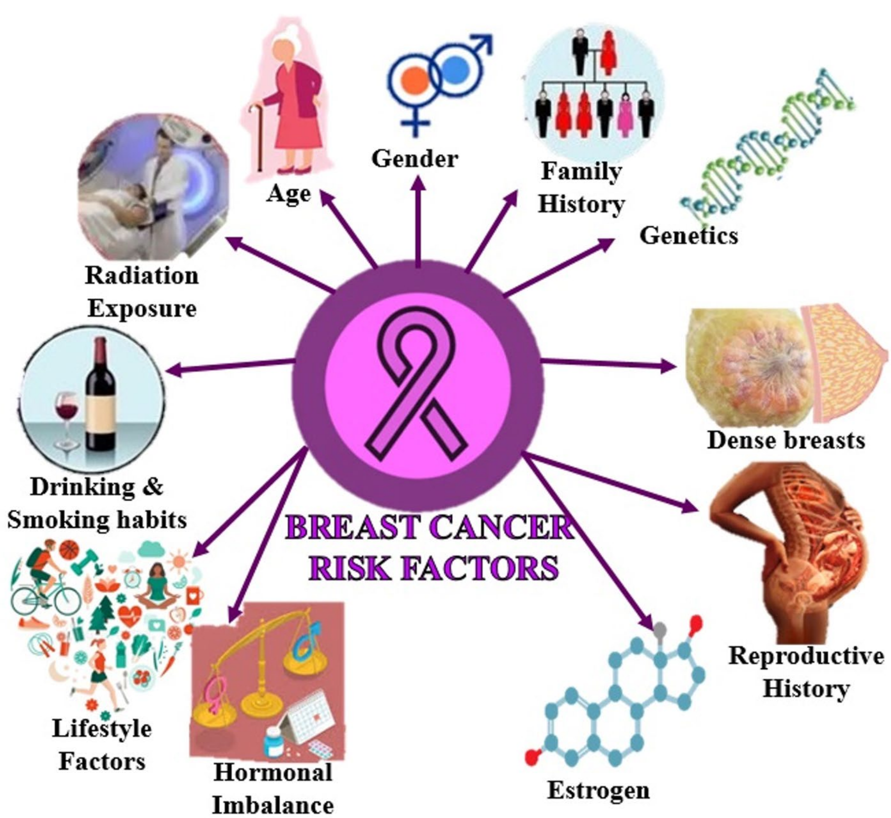

Fig. 1 Risk factors for the breast cancer

factors such as having a first full-term pregnancy at a later age, breastfeeding, parity, years since the last birth, late menopause, and the use of oral contraceptives and hormone replacement therapy (HRT) [17, 18]. Fluctuations in the circulation of estrogen hormone levels are significant factors influencing the risk of BC [19]. Many reproductive risk factors, including pregnancy and HRT, may directly alter hormonal levels. In contrast, other risk factors, such as late menopause and early menarche, serve as lifetime markers of hormonal exposure [20]. For every one-year delay in menopause, there is a 3% increase in BC risk. Additionally, an extra birth or a one-year delay in menarche results in a 5 to 10% reduction in BC risk, respectively [21–23]. Reproductive factors are primarily linked with estrogen status; the relationship between BC and differences in odds ratios (OR) varies between ER + and ER– for parity, e.g., OR: 0.7 versus 0.9 for three or more births compared to nulliparae, and as age increases, the OR for the first birth also increases, e.g., OR: 1.6 versus 1.2 for age ≥ 30 versus < 25 years [23]. The risk of BC associated with estrogen pertains to both endogenous and exogenous estrogens. The ovaries in premenopausal women typically produce endogenous estrogen, and undergoing ovariectomy can reduce BC risk [24]. Exogenous estrogen is derived from HRT and oral contraceptives. Since the 1960 s, oral contraceptives have been widely used; in response to side effects, formulations have evolved. However, if women cease using oral contraceptives for over ten years, their BC risk may decrease [25–27]. Numerous studies indicate that HRT may elevate the risk of BC, with rates increasing from 1.48 to 1.95 over four years [28, 29]. The modern lifestyle significantly contributes to the heightened risk of BC, with factors such as dietary fat intake, excessive alcohol consumption, and cigarette smoking being pivotal. High-fat intake in contemporary diets leads to saturated fats, contributing to poorer prognosis in BC and correlating with a 1.3% relative risk (RR) [30]. Alcohol consumption can elevate estrogen-related hormone levels in the blood and activate estrogen receptor pathways. Epidemiological studies aggregating data from 53 analyses indicated a 32% increase in BC risk among women consuming 35–44 grams of alcohol daily and a 7.1% increase in RR with each additional 10 grams of alcohol per day [31, 32]. Historically, early-age smoking is particularly associated with a heightened risk of BC [33–36]. There remains controversy regarding the relationship between smoking and BC, as mutagens have been identified in breast fluid collected from non-lactating women exposed to cigarette smoke. Furthermore, the risk of BC is elevated in women who both smoke and drink, with a reported RR of 1.54 [37].

3 BC signs and symptoms

Typically, there are no symptoms of BC when the tumour is small, which is why screening is vital for early diagnosis. The physical sign most commonly associated with BC is a painless lump, and sometimes, cancer spreads to underarm lymph nodes, resulting in the formation of a lump or inflammation before the original breast tumour is felt. Hence, a breast lump is considered the most common symptom among women with BC and has a relatively high predictive value for malignancy [38]. The least common symptoms and signs include heaviness or breast pain; persistent changes encompass swelling, skin redness or thickening, and spontaneous nipple discharge, particularly if it involves blood or scaliness. Any specific persistent changes observed in the breast should be examined by a physician immediately [39]. MM Koo has developed a taxonomy of presenting symptoms based on individual symptoms collected from 56 distinct forms of 2,316 women with BC, which include breast lumps at 83.0%, nipple abnormalities at 6.8%, breast pain at 6.4%, breast skin abnormalities at 2.0%, axillary lumps at 1.2%, breast ulceration at 1.1%, back pain at 1.0%, with remaining symptoms being less than 1%. The symptoms are classified into three main categories: (i) Breast lump, (ii) Non-lump breast symptoms (such as breast shape or skin and nipple abnormalities, breast pain), and (iii) Non-breast symptoms (such as neck lumps, axillary symptoms, fatigue, breathlessness, and back pain) (Fig. 2) [40].

3.1 Breast lump

The lump is the first symptom of breast cancer, meaning that a hard lump is more likely to be cancerous if it has irregular edges; however, some cancers can also present with soft, rounded edges. Individuals with a family history of breast cancer are advised to have regular mammograms after the age of 40, as lumps can be too small to be detected by you or your doctor. Lumps may be caused by cysts, fibroadenomas, fibrocystic changes, breast infections, clogged milk glands, injuries, and other factors [41].

3.2 Non-lump breast symptoms

Tenderness, pain, and burning sensations in the breast or nipple may be the primary signs of inflammatory breast cancer. Women with non-lump breast cancer may experience itching of the breast, bloody discharge from the nipple, localised pain, skin sores, dimpled skin resembling an orange, rashes, swelling of the breast, and flat or inverted nipples, among other symptoms [42].

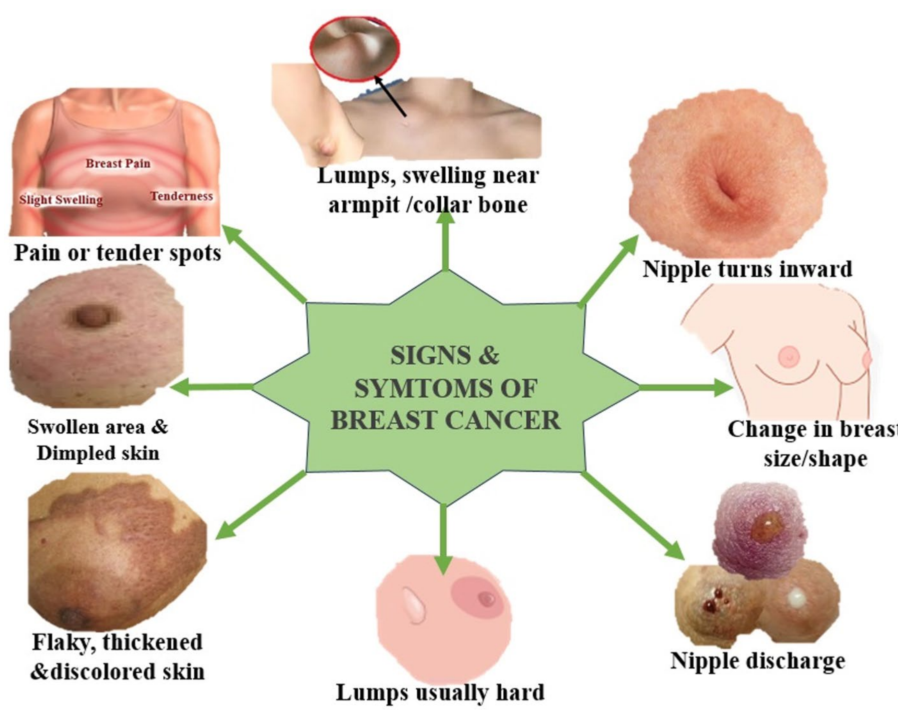

Fig. 2 Graphical representation of sign and symptoms of the breast cancer

4 Advancements in BC diagnosis and screening

Few screening techniques are available for BC, which are classified into imaging and non-imaging techniques. The well-established and most common imaging techniques include mammography, and magnetic resonance imaging (MRI) (Fig. 3). Clinical breast examination (CBE) and liquid biopsy are non-imaging techniques that are still being examined in their formative stages [43].

4.1 Mammography

Mammography is considered the cornerstone for breast cancer screening. The most effective method for screening breast cancer is a mammogram due to its lower risk compared to other screening techniques [44]. In 1977, during a meeting convened by the National Cancer Institute (NCI) on breast cancer, the following modifications were enacted: All women over the age of 50 should continue to have annual mammograms. Women with a family history of breast cancer, particularly those with a mother or sister affected, should begin mammography between the ages of 40 and 49, while those with a family history should start from ages 35 to 39 [45]. Some researchers have indicated that the sensitivity of the first mammography during the initial screening interval ranged from 71 to 96%, with the predictive positive value of abnormal mammographic reports needing biopsy ranging from 12 to 78%, which increased with age. The fundamental principle behind mammography relies on the physical properties of X-rays to differentiate various thicknesses of breast tissue, thereby creating an image [46]. A very low-dose X-ray is used in breast mammograms, where the breast tissue is compressed to decrease tissue thickness. This compression aids radiologists in identifying abnormalities more accurately. During the procedure, the breast is placed between two panels, and X-rays are passed from two directions—top-down and side-to-side—to thoroughly examine all tissues. The three main types of mammography available for screening are film mammography (FM), digital mammography (DM), and digital breast tomosynthesis (DBT) [47]. Before 1977, there were no specific guidelines for the early diagnosis of breast cancer. Since then, the NCI of the United States has officially recommended FM as the X-ray imaging technique for breast cancer screening. X-ray imaging produces pictures on film that can be analysed through chemical processing. Since 2000, DM has been

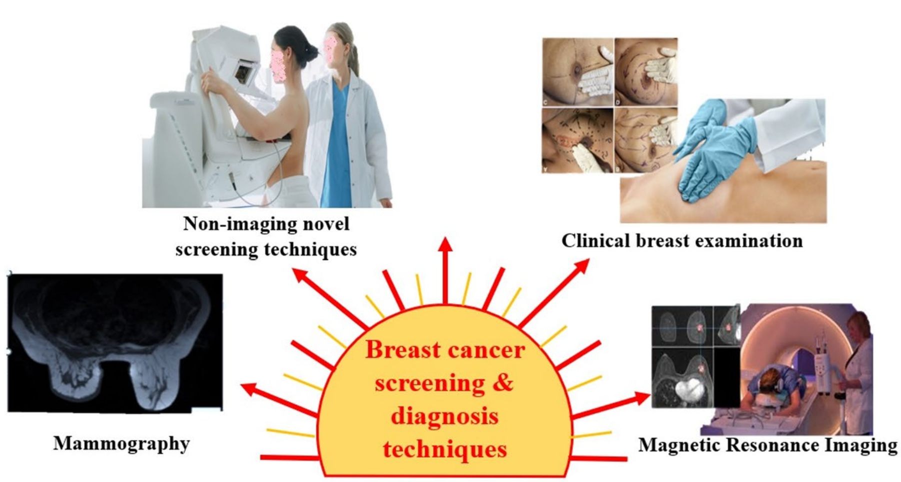

Fig. 3 Diagnosis and screening techniques for the breast cancer

introduced, which employs an electronic detector instead of a conventional screen-film system, displaying images digitally on a high-resolution monitor, thus enhancing screening accuracy by decoupling image acquisition [48]. DBT, an advanced technique, provides a three-dimensional (3D) image by producing a series of images at varying angles around the patient's breast, focusing on the X-ray attenuation coefficients. DBT helps reduce parenchymal overlap, which can create false lesions or obscure cancer, potentially improving the accuracy of breast cancer screening. Although mammography is an effective tool for early detection of breast cancer, various host factors such as age, breast density, and lesion size can influence its effectiveness. Breast density, in particular, has a significant impact as the similar X-ray attenuation of dense fibroglandular tissue and tumours tends to enhance the masking effect due to overlapping tissue or image artefacts, thus reducing contrast between lesions and surrounding tissue. In comparison, mammography sensitivity for extremely dense breasts ranges from 30 to 64%, while for fatty breasts, it is between 76% and 98%. Due to these limitations, an additional supplementary screening tool alongside mammography is essential [49–51].

4.2 Magnetic resonance imaging (MRI)

MRI offers superior soft-tissue resolution, is unaffected by breast density, and can be used for screening only in high-risk patients. It demonstrates high sensitivity for lesions, a notable advantage over mammography, which has lower sensitivity [52]. Women at increased risk of breast cancer may choose MRI despite the longer examination time and higher costs involved. MRI is more effective at detecting smaller tumours than the mammographic screening method. The advanced technique known as abbreviated MRI has been introduced, featuring shorter interpretation time, quicker image acquisition, reduced costs, and improved availability. Kuhl et al. conducted a study involving 443 women, demonstrating that abbreviated MRI significantly reduced image acquisition time to just 3 min for a full breast MRI. Furthermore, abbreviated MRI achieved diagnostic accuracy comparable to that of conventional MRI [53].

4.3 Clinical breast examination (CBE)

CBE is employed as an additional technique for breast screening in LMICs by physicians using breast and axillary palpation. Although several factors affect the sensitivity of CBE, including physician experience, patient age, and body mass index, approximately 5–10% of breast cancer cases can be detected solely through CBE. When the mortality of breast cancer was analysed based on attendance rates to CBE screening rounds, Mittra et al. found that women under 50 years of age who attended all four rounds experienced a significant reduction in the mortality ratio of 0.66 (95% CI 0.53 to 0.83, $P < 0.001$). However, those who attended only three rounds did not benefit, with a mortality ratio of 0.88 (0.60 to 1.27, $P = 0.48$) [54]. Consequently, there remains controversy regarding the effectiveness of CBE as a breast cancer screening tool.

4.4 Non-imaging novel screening techniques

In the early diagnosis of BC, growing tumors actively release debris into the bloodstream, including cell-free RNA and tumor DNA, which can serve as biomarkers for screening at a molecular level. In this context, liquid biopsies effectively detect tumor particulates in the bloodstream or plasma [55]. Some preliminary analyses have suggested

Table 1 Screening techniques merits and demerits

Technique	Merits	Demerits
Mammography	Detects the changes in structure and calcifications	Detection compatibility is reduced with high density breast tissues
Magnetic resonance imaging	Complete visibility of soft tissue	To identify benign lesion specialized skill is necessary
Clinical breast examination	In LMICs an alternative to mammography screening	Experienced and skilled physician is required
Non-imaging novel screening techniques	Liquid biopsies are useful to detect tumour particulates	Experienced and skilled physician is required

Table 2 Stages of breast cancer

Stage	Description
Stage 0	Carcinoma in-situ (e.g., ductal carcinoma in situ). Tumor cells are confined to the ducts/lobules without invasion into surrounding tissues
Stage I	Tumor ≤ 2 cm in diameter, confined to the breast, no lymph node involvement
Stage IIA	(i) Tumor ≤ 2 cm + spread to 1–3 axillary lymph nodes or near breastbone (microscopic), OR (ii) Tumor > 2 cm but ≤ 5 cm with no lymph node spread
Stage IIB	(i) Tumor > 2 cm but ≤ 5 cm + spread to 1–3 axillary lymph nodes or near breastbone (microscopic), OR (ii) Tumor > 5 cm with no lymph node spread
Stage IIIA	(i) Tumor ≤ 5 cm + spread to 4–9 axillary lymph nodes or near breastbone (enlarged), OR (ii) Tumor > 5 cm + spread to 4–9 lymph nodes
Stage IIIB	Tumor of any size + direct extension to chest wall or skin, including ulceration or swelling (inflammatory breast cancer)
Stage IIIC	Tumor of any size + one or more of the following: (i) 10 + axillary lymph nodes involved, (ii) spread to lymph nodes above/below the clavicle, (iii) extensive lymph node involvement near the breastbone
Stage IV	Tumor of any size + distant metastasis (e.g., to bones, lungs, liver, or distant lymph nodes)

that circulating proteins [56], autoantibodies [57], microRNAs [58], and nucleic acid methylation [59] may be valuable in the early detection of BC as promising biomarkers. Although numerous studies are still in the exploratory phase or clinical trials, it remains very challenging to obtain the data [60]. Consequently, screening with liquid biopsy continues to present a significant challenge in developing higher sensitivity technique for detecting BC. The merits and demerits of various BC screening techniques are outlined in Table 1 [61].

5 Stages of BC

The breast cancer staging outlined in Table 2 adheres to the guidelines established by the American Joint Committee on Cancer (AJCC), 8th Edition. Accurate staging is essential for assessing the prognosis and choosing an appropriate treatment plan. Breast cancer is classified into five stages (0–IV) based on tumor size, lymph node involvement, and the presence of distant metastasis. For clarity, the details are presented in Table 2 [62, 63].

6 Recent strategies for the prevention of BC

Due to the rising incidence of BC in young women and various non-modifiable risk factors, several strategies for the primary prevention of BC have become a key area of interest. The approaches used to reduce the incidence of BC include primary prevention, chemoprevention, and surgical methods, such as mastectomy and/or oophorectomy, for BC prevention.

6.1 Primary prevention

Primary prevention includes dietary modification, exercise, avoidance of tobacco and alcohol, exogenous use of estrogens and progestins, exposure to ionizing radiation, pregnancy, and nursing.

6.1.1 Dietary modification

Diet is considered one of the significant risk factors, and many research studies in humans and animals have reported that diet plays a vital role in the prevention of BC. Obesity, the most common cause of many cancers including prostate, gallbladder, endometrial, breast, ovarian, kidney, liver, and colon cancer, is a major factor. The main mechanisms through which obesity can lead to cancer are (a) increased growth factors like insulin and insulin-like growth factor 1, (b) elevated levels of primary estrogen and other factors affecting metabolism and sex steroid hormones, (c) modifications in adipokines, which are usually involved in regulating the immune system and can affect tumor-regulatory mechanisms, and (d) fostering oxidative stress influenced by factors such as cytokines and low-grade inflammation. Recently, many studies have reported that obesity causes changes in the intestinal microbiome, leading to an increased incidence of cancer. Regardless of weight gain or loss, certain dietary habits affect BC risk; for instance, consumption of red meat, sugary drinks, energy-dense foods, and salt is generally recommended to be reduced for a healthy lifestyle, while adding more fresh vegetables and fruits to the regular diet is advised. There is an inverse relationship between the intake of citrus fruits and dietary fibers and the risk of BC. Modifying dietary patterns not only reduces the risk of BC but can also improve patient diagnosis, treatment, and overall health and survival. The link between BC and obesity has been reviewed in numerous articles due to the increasing prevalence and incidence of both conditions. Being obese or overweight at the time of diagnosis is associated with a worse prognosis in BC patients. Some studies have also reported that folate supplementation alone does not reduce BC risk; however, when combined with alcohol consumption, folate supplementation may decrease the risk of BC [64–68].

6.1.2 Exercise

With the effects of concomitant weight gain or loss, the benefits of exercise in preventing BC can be assessed. A reduced risk of BC was particularly observed in postmenopausal women based on prospective studies examining the dose-response relationship with higher levels of physical activity. Numerous studies have reported that daily physical activity offers many advantages at the cellular level and enhances quality of life, even alongside various drug treatments. Additionally, it reduces the side effects of anti-cancer therapies and improves survival rates after cancer. Therefore, it is crucial to raise awareness of the potential benefits of maintaining a healthy lifestyle and to encourage the supervised performance of physical exercise in a professional and controlled manner. Exercise can also serve as a complementary non-pharmacological therapy for cancer patients [69].

6.1.3 Consumption of tobacco and alcohol

The consumption of tobacco primarily causes cancer in the lungs, mouth, larynx, throat, esophagus, bladder, liver, kidneys, pancreas, stomach, cervix, colon, rectum and acute myeloid leukemia. Staphanie et al. surveyed the smoking status and history of individuals and their impact on BC, reporting that at baseline, smoking status does not significantly predict BC risk ($P = 0.074$). However, smoking duration history is associated with an increased BC risk ($P = 0.007$) in women who smoked for 15 to 35 years. Numerous studies have reported that tobacco-specific nitrosamines and polycyclic aromatic hydrocarbons are tobacco-related carcinogens that are metabolically activated to produce DNA adducts, which can evade cellular repair mechanisms and lead to permanent allelic variants. This disruption may influence the development of BC alongside genetic changes in N-acetyltransferase-2. Furthermore, the carcinogenicity of tobacco is more established, with smoking metabolites generally recognized in the nipple aspirates of women smokers. In addition, the presence of smoking-related DNA adducts has been identified in the epithelial cells of breast milk, indicating that tobacco components can reach breast tissues [70].

The American Cancer Society surveyed over 70,000 women who have consumed alcohol for an average of 13.8 years, with a median follow-up. The study found that among women from British Columbia (BC) who started smoking before their first childbirth, there is a stronger association between smoking and BC incidence. The data indicates that BC incidence among smokers is 24% higher than that of non-smokers, and among former smokers, it is 13% higher than non-smokers. The exact mechanism behind the carcinogenic effect of alcohol is not fully understood, but it may relate to sex hormones, including androgen and estrogen levels. Additionally, alcohol may influence the mutagenic properties of its first metabolite, acetaldehyde, which inhibits DNA damage repair induced by carcinogens. Consequently, alcohol disrupts estrogen pathways by regulating sex steroid levels and estrogen receptors (ERs). The levels of estrogens, androgens, and progesterone significantly increase in women who consume 15–30 g of alcohol daily. Excessive alcohol consumption may negatively influence dietary factors like folate, lutein, zeaxanthin, and β-carotene, which possess anticarcinogenic properties. In these circumstances, low folate levels can impact DNA synthesis and methylation, which, when combined with alcohol, may lead to immunosuppression and immunodeficiency, promoting carcinogenesis [71].

6.1.4 Exogenous use of estrogens and progestins

Most researchers reported that using formulations containing both progesterone and estrogen after menopause increases BC risk; however, the exact role of female exogenous hormones in causing BC is still unclear. While only estrogen use after menopause is linked to a higher risk of endometrial cancer, it is considered safe for women who have undergone a hysterectomy and does not show signs of increasing the risk of developing BC. One researcher discussed the duration of unopposed estrogen use, the role of progestins, types of hormone replacement therapy (HRT), and cancer features associated with HRT [72]. Due to the connection between BC and HRT, a minimal duration of HRT use is recommended for symptom control, especially under chronic disease management. Many reports suggest that higher doses of estrogens and progestin in birth control pills (BCPs) are more likely to raise BC risk [73]. A study in Denmark involving 1.8 million women using temporary hormonal contraceptives found that BCPs and intrauterine devices releasing progestins showed an average 20% increase in BC risk among women. Based on epidemiological evidence, it can be strongly suggested that the use of both estrogens and progestogens contributes to BC risk, with a very high risk observed during the premenopausal years [74, 75].

6.1.5 Exposing to ionizing radiation

Typically, most cancers can be induced by ionizing radiation, notably exhibiting a linear dose-response for many solid tumors. Considering the heightened sensitivity in children, the most radiosensitive organs include the thyroid gland, breasts, bone marrow, brain, and skin. A study indicated that infants who received radiation at one time to treat specific benign lesions, such as hemangioma and enlarged thymus, faced particular risks. In cases of hemangioma, infants treated with an average of 30 cGy experienced a 40% increased risk of BC, while those receiving an average of 70 cGy for an enlarged thymus had an excess risk of 250% for developing BC. This excess risk persists for up to 50 years following radiation exposure. Research on multiple chest X-ray radiation exposure used in monitoring tuberculosis (TB) treatment in young women and adolescent girls shows increased BC mortality with greater radiation doses during numerous X-ray examinations. These examinations monitor the spinal curvature of girls with scoliosis, revealing that the increased BC risk becomes apparent after 15 years of radiation exposure and can remain elevated for up to 50 years. Numerous studies have reported an increased BC risk among young women who underwent CT scans of the heart, concluding that young adults under 23 years of age who received more than 2 CT scans of the heart faced more than double the risk of developing BC over the standard 10 years [76–78].

6.1.6 Pregnancy and nursing

An increased risk of BC was observed in all age groups immediately following childbirth. Langer et al. reviewed new cases of BC diagnosed between 1993 and 2009, totalling 16,555 cases. There were 117 instances of pregnancy-associated breast cancer (PABC) in women either during pregnancy or within 12 months after delivery. It was noted that the BC risk was higher in women whose first full-term pregnancy (FFTP) occurred after the age of 35 compared to those who completed their FFTP at a younger age, specifically under 26 years. Genin AS et al. studied and recorded 276 BC cases among 282 patients, discovering that 14.5% of these were PABC cases. In a survey of all the PABC patients, the ratio of BC cases was 30:70 between pregnancy and the year following delivery, with 36 patients diagnosed during pregnancy and 25 diagnosed in the subsequent year [79, 80].

6.2 Chemoprevention

6.2.1 Overview

Chemotherapy remains a fundamental component of BC treatment, especially in young women, who are more likely to present with aggressive subtypes such as triple-negative and HER2-positive breast cancers. It is often used in both neoadjuvant (pre-surgical) and adjuvant (post-surgical) settings to reduce tumor size, eliminate micrometastatic disease, and improve overall survival outcomes. Commonly used chemotherapeutic agents include anthracyclines (e.g., doxorubicin), taxanes (e.g., paclitaxel, docetaxel), and alkylating agents (e.g., cyclophosphamide), often administered in combination regimens tailored to tumor biology and patient factors [81].

Many drugs have been developed to treat cancers linked to somatic mutations and genomic changes. However, there are notable signs of reluctance regarding the use of germline genetic data in drug development for malignancy prevention. To lower cancer risks, a larger number of individuals could currently benefit from non-pharmaceutical measures addressing cancer risk factors, such as alcohol, tobacco, and infectious diseases. Efforts are needed to prevent cancer based on genetics, including genes influenced by normal polymorphisms that modulate cancer risk. Although many trials remain underutilized, there are opportunities to develop advanced targeted agents for cancer chemoprevention based on human germline genetics. These efforts require support from funding programs by international and national agencies. To prevent breast cancer in high-risk women, the Food and Drug Administration (FDA) has approved medications such as tamoxifen (TAM) and raloxifene, which are selective estrogen receptor modulators (SERMs). These SERMs exhibit a pro-estrogenic effect in some organ systems and an anti-estrogenic effect in others. Chemoprevention relies on external agents, such as supplements or medications, to inhibit or slow the onset, recurrence, or progression of cancer. The United States FDA has approved numerous compounds for clinical use in cancer prevention of cancer [81, 82].

6.2.2 Selective Estrogen receptor modulators (SERMs)

Financial support was provided by the US National Cancer Institute in the early 1990 s to conduct the BC prevention trials in women and reported in 13,388 pre and post-menopausal women. The first FDA- approved chemo- preventive agent for both pre- and postmenopausal women is tamoxifen (TAM), which can reduce the risk of ER- positive BC by 30 to 60% in high- risk individuals. Overall, 49% of invasive BC patients received TAM, leading to a risk reduction of over 40% across all age subgroups. The FDA also approved the second- generation selective estrogen receptor modulator (SERM) raloxifene for preventing BC in high- risk populations. Compared to randomized trials with TAM, raloxifene gained approval based partly on prospective findings [83]. By the time the trial commenced, the FDA had already approved raloxifene for treating osteoporosis in postmenopausal women. A systematic review conducted by the United States Preventive Services Task Force (USPSTF) reported that TAM decreased the incidence of invasive BC with placebo by 7 events per 1, 000 women over five years [84]. However, the use of TAM is associated with increased risks of cataracts, vasomotor symptoms, venous thromboembolic events (such as pulmonary embolus, stroke, and deep vein thrombosis), and endometrial cancer. Raloxifene demonstrated a similar effect on ER-positive BC with fewer side effects compared to tamoxifen. The FDA has approved both drugs for the prevention of BC in high- risk individuals. Randomized clinical trials have been conducted in high- risk postmenopausal women using aromatase inhibitors (AIs) like exemestane and anastrozole, which significantly reduce the risk of ER- positive BC and are used in conjunction with SERMs for BC prevention. AIs inhibit the aromatase enzyme, blocking the conversion of androgens to estrogen. They also have more favorable side effect profiles and greater efficacy than SERMs. Consequently, USPSTF recommends that physicians prescribe lower- risk drugs, including TAM, raloxifene, and AIs, to women at elevated risk for BC who have a low risk of adverse side effects [85–89].

6.2.3 Specific subgroups: histopathologic alterations and breast density findings which increase risk

Many variations of benign breast disease were identified through excisional breast biopsy, which is directly linked to an increased risk of BC. These variations can generally be categorized into usual hyperplasia, atypical hyperplasia, and lobular carcinoma in situ (LCIS). The risk of developing BC in women with atypical hyperplasia increases by 1.5-2%, while for those with usual hyperplasia, it rises by 50–100%. In patients with LCIS, the risk is 2% per year, compared to less than 0.4% per year in other healthy women. Women with LCIS or atypical hyperplasia may face a lifetime risk of BC exceeding 30%. There are very few indicators in high-risk patients that assist treating physicians in determining whether a patient will develop invasive BC and the potential extent of the disease. Due to the unclear distinction between individuals with LCIS and atypical hyperplasia, many women may develop BC, presenting a counseling challenge regarding risk reduction; thus, surgical strategies and chemoprevention can have beneficial effects. It has not been conclusively reported that reducing mammographic breast density (MBD) leads to a decreased risk of BC. MBD measurements were taken before starting tamoxifen and at intervals of 12 to 18 months, continuing for at least 54 months. A reduction in MBD was noted within 18 months of tamoxifen treatment, which persisted for at least 54 months. On average, a decrease of around 13.4% in MBD was observed after 54 months of tamoxifen treatment in women aged 45 years or younger, and a decrease of 1.1% in women aged 55 years or older [90].

6.3 Immuno-prevention

Immunoprevention typically boosts the immune system's ability to identify and respond to tumor-specific antigens, helping to inhibit the onset of tumors or malignant transformations. With the implementation of cancer vaccines, immunoprevention has been in practice for some time. The development of hepatocellular cancer has shown an 80% reduction thanks to a vaccine for the hepatitis B virus (HBV). Genomic instability, a well-known hallmark of cancer, is directly linked to immune responses. The unstable genomes of tumor cells acquire numerous mutations, resulting in unique tumor-specific antigens (TSAs) within the tumor genome, which can serve as targets for the immune system. Currently, the most effective applications of immunoprevention include HBV and human papillomavirus (HPV) vaccines for virally induced tumors. TSAs are still being researched to create vaccines for non-viral tumors. In contrast, secondary prevention involves other forms of immunotherapy, such as immune checkpoint inhibitors, which have demonstrated clinical potential [91, 92].

6.4 Surgical approaches to BC prevention by mastectomy

The guidelines for these therapies are generally based on known risk implications and are frequently updated according to the latest available data. The identified driver genetic mutations among the BC, including BRCA 1 & 2, PTEN, TP53, STK11, CDH1, ATM, PALB2, NBN, CHECK2, and NF1, each have specific implications for future BC risk. The American Society of Breast Surgeons currently recommends that risk-reducing bilateral mastectomy is a valuable approach for women without BC who carry a known deleterious mutation in BRCA 1 & 2, TP53, CDH1, or PALB2. If the patient has a family history of BC, risk-reducing mastectomy is preferred for consideration in cases with deleterious mutations in ATM or CHEK2. Generally, screening is advised to begin at the age of 30 for NF1 and STK11 and at the age of 40 for NBN. A bilateral risk-reducing mastectomy is recommended for women with a prior history of therapeutic mantle radiation and a diagnosis of lobular carcinoma in situ (LCIS). After discussing with the patient the individual benefits and risks, such as family history and known deleterious genetic mutations that increase BC risk, mastectomy is not recommended as a standard procedure for reducing the risk in the contralateral breast of women diagnosed with cancer in the ipsilateral breast. For risk reduction in women at genetically high risk, bilateral salpingo-oophorectomy (BSO) may be considered. BSO reduces the risk of BC in premenopausal women with BRCA 1 & 2 mutations by approximately 50%, similar to tamoxifen, compared to a 90% reduction in women who undergo bilateral mastectomy. Additionally, BSO reduces the risk of ovarian cancer in these patients by 90% [93].

Surgery remains the cornerstone of BC treatment in young women, typically involving either breast-conserving surgery (BCS) or mastectomy, depending on tumor size, location, and patient preference. Advances in surgical techniques have improved cosmetic outcomes while maintaining oncological safety [93].

7 Novel strategies for the treatment of BC

There are various types of treatments for BC patients based on the stage of the disease. The different treatments include radiation therapy, surgery, chemotherapy, immunotherapy, targeted therapy, and hormone therapy. Many novel types of treatment are also being studied in clinical trials. Above all, BC treatment may cause several side effects, and follow-up care is required [94]. The available data describes radiation therapy and its significant impacts on disease control, survival, and mortality, clearly illustrating the effective influence of radiation therapy on BC and critical organs. This leads to a focus on applying advanced techniques to enhance the benefits of radiation for BC patients. Although the computed tomography (CT) imaging technique was established in 1972, it was not widely available in radiation oncology departments until the late 1990 s. Particularly for internal mammary nodes (IMN), treatment planning with CT became increasingly evident for tangential field setups, accommodating suboptimal target ranges and addressing lateral and medial breast tissue and tumors [95]. Adequate coverage of IMN and breast targets exposed to substantial volumes of radiation was also observed with sophisticated photon- based radiation therapy (RT), including intensity- modulated RT (IMRT). Appropriate regional node coverage similarly raised concerns due to meta-analyses showing substantial lung exposure and excess mortality in pulmonary-related irradiated BC patients. Therefore, standard care in CT treatment planning is now crucial for 3 D dose distribution calculation, achieving a good balance between the competing goals of tumor control and safeguarding critical organs [96]. The patient is securely positioned for an optimal beam array and then stabilized in a specific patient immobilization device for CT treatment planning. The produced CT images are imported into a CT treatment planning unit, which defines targets such as the tumor bed, nodal regions, and block- out areas for organs at risk (OARs). In CT treatment planning, the physician collaborates with physics and dosimetry teams to provide improved radiotherapy sources (protons, electrons, photons), beam angles, energies, field shapes, and sizes, aiming for dose distributions that concentrate on target regions while minimizing the prescribed dose to normal adjacent tissue. Techniques include IMRT, 3 D conformal radiation therapy (3 D- CRT), volumetric arc therapy (VMAT), active scanning proton therapy, or passive double- scattering therapy.

7.1 Three-dimensional conformal radiation therapy

In this therapy, treatment is based on axial CT of 3 D target volumes contoured rather than on underlying bony anatomy, 2 D images, skin incisions, surface anatomy, and organs at risk (OARs) such as the lung and heart. Numerous outline guidelines have been published to target and block the OAR [97, 98]. Nowadays, several studies are being conducted on the coverage of target areas and avoidance of OARs. A particular plan described a review on radiation dose distribution, designating size, shaping, angle, and number as key factors, alongside how much radiation can be delivered through a given field. The evaluation of the treatment plan must also consider the reliability or robustness of the plan. Based on the clinical situation, target coverage can be prioritized while assessing OARs. Various factors influence this, including breast size and shape, thorax shape, expanders, the proximity of the heart to the chest wall, and the impact of radiotherapy implant dosimetry. Treating internal mammary nodes (IMNs) in left-sided BC women presents challenges due to the left ventricle's proximity to the chest wall and the nearby left anterior descending artery. Although the treatment portals in modern 3 D plans and historical 2 D plans are similar, 3 D plans are selected based on target dose and OAR considerations. To treat IMNs, the breast wall, and low axilla, a parallel opposed photon tangent field with a common beam arrangement is necessary, matched with the anterior photon field that treats supraclavicular nodes and the high axilla. A small posterior field is often required to increase the dose to the high axilla from the anterior field. Particularly in tangential fields, smaller fields can be introduced within larger fields to enhance dose homogeneity, and materials that hold radiation wedges may be applied in the beam path. To achieve OAR control goals, electrons can be utilized in conjunction with photons [99]. Given the limited radiation goals for OARs, a general treatment planning objective should ensure that 90–95% of the prescribed dose is received by 95–100% of the entire volume of the target.

7.1.1 Deep-inspiration breath hold (DIBH)

To enlarge the distance between the anterior chest wall and the heart, DIBH techniques are employed to minimize the exposure of the heart to radiation, as proven by several studies. Yamauchi et al. reported that the use of DIBH resulted in a decrease in the radiotherapeutic heart dose for patients with left-sided BC and the implementation and recommendation of DIBH are considered for underweight and patients with a normal BMI. It was found that DIBH provided approximately a 50% reduction in dose compared to a free breathing plan [100]. Dincoglan et al. noted that the use of active breathing control with moderate DIBH (ABC-mDIBH) in patients undergoing radiotherapy for left-sided BC improves normal tissue sparing, reduces dose, and leads to a decrease in treatment-related mortality and morbidity. DIBH requires active patient participation, but some patients may find it difficult to comply, which may limit its practicality with advanced techniques like IMRT, as they may require longer delivery times. Demiral et al. studied the utility of the ABC technique in right-sided early-stage breast cancer (ESBC) and reported that incorporating ABC-mDIBH into adjuvant radiation therapy significantly improved OAR outcomes in right-sided ESBC patients [71].

7.1.2 Prone positioning

BC patients are typically treated in a supine position with both arms immobilized overhead. This positioning offers advantages such as enhanced patient comfort, better visualization of actual field borders, and assurance that there is no underlap or overlap when matching fields. In some cases, breast tissue can fall away from the treatment point or become bulged, resulting in excessive exposure of the underlying tissues to tangential photon fields. In these instances, repositioning patients to a prone position can be beneficial, allowing the breast to shift away from the treatment point. Researchers from various institutions have analyzed and reported on the penalty score, which is calculated from the absolute mean dose to the breast, lungs, heart, and tumor bed for both supine and prone plans for each patient. They confirmed that there is a reduction in the penalty score when transitioning from supine to prone due to the dosimetric advantages of the prone [101]. However, this position may not always be effective if the heart is close to the radiation field, and accurate field matching can be challenging during regional node irradiation. Therefore, prone positioning may only be used in breast treatment patients along with 3D-CRT or IMRT methods [102]. In the future, the applicability of prone positioning may increase.

7.2 Intensity-modulated radiation therapy

The IMRT employs multiple beams and the direct machine parameter optimization technique to achieve a thin film with precise thickness over a large area of high-dose distribution to the target volume. It was designed with two tangential angles tailored to the target shape and maximizing lung volume sparing. The left and right tangential angles were initially set at 235∘ and 55∘, respectively. An increment in the tangential angles was established, resulting in a total of eight irradiation fields, each separated by 20∘–30∙. A dosimetrist selects the beam angle using 3D-CRT and analyzes the dose distribution to encompass the maximum area of the target while adhering to the constraint goals for the OAR. If they proceed with IMRT, the OAR constraint goals and target coverage are integrated into the system to select beam shapes and angles in the treatment planning system [103].

7.3 Volumetric modulated Arc therapy

Volumetric modulated arc therapy (VMAT) is a type of IMRT that achieves conformality with high doses while requiring less delivery time. VMAT continuously delivers radiation in an arc around the patient as the gantry rotates, whereas IMRT uses numerous independent beam angles. During radiation delivery in VMAT, multiple parameters can also be adjusted, such as dose rate, gantry rotation speed, field shape, and orientation. A beam model must allow continuous changes in the dose rate and the rotational speed of the gantry to achieve the necessary level of modulation, with the maximum gantry rotation speed set at 4.8° per second [104].

IMRT and VMAT techniques produce (conformality, creating a thin film with precise thickness over a large area of high dose while exposing normal tissue to low-dose radiation. However, these techniques carry a higher risk of cardiac diseases compared to 3D-CRT when the volume of the heart receives 5 Gy. The mean heart dose with the VMAT plan for left-sided BC is 3.8 ± 1.4 Gy, and for right-sided BC, it is 2.6 ± 0.7 Gy, whereas the doses are 5.8 ± 4.4 Gy for left-sided BC and 0.9 ± 0.2 Gy for right-sided BC with 3D-CRT. A reduction in hazardous radiation dermatitis has been observed with IMRT in several randomized trials comparing IMRT to 2D or 3D-CRT [105, 106]. However, these techniques necessitate longer follow-up to monitor both heart disease and the potential for increased second malignancies.

7.4 Proton therapy

Even though protons and photons are particles, protons have energy and are heavy, and relatively massive but photons are pure energy and have no masses, and travel a particular distance. The penetration depth of the proton may be controlled, as there is no doorway beyond the targeted tumor. In proton therapy, most of the dose is deposited at a specific point known as the Bragg peak, while along its path, it deposits much less energy than photons. In nature maximum dose goes into the target whereas with photons maximum dose is generally deposited beyond the target, even so for 3D-CRT, VMAT, or IMRT techniques. The protons-specific property permits the application of anterior enface beams directly aimed at the target towards the respiratory motion direction on behalf of tangentially. Innumerable studies have shown that < 1 Gy of mean heart dose with proton therapy for overall IMNs [107]. In a few cases, DIBH can even reduce cardiac dose but sometimes not necessary. Proton therapy can also be used to avoid the contralateral lung and even ipsilateral lung V5 and V20 values are typically decreased by approximately 50% when compared to conventional 3D-CRT. Proton therapy significantly also delivers minimal low-dose radiation to V5, and V10 or with similar or reduced moderate-to-high-dose radiation to V20, and V40. From all the techniques proton therapy also reduces or removes contralateral breast wall dose and also provides minimal overall integral dose [108]. The dose reductions may lead to a reduction rate of second malignancy even in medial contralateral BC. Proton therapy may be delivered through passive-scattering or scanning techniques. A scanning technique can obtain intensity-modulated proton therapy with a minimal skin dose than passive-scattering methods, but if both are used, it leads to a larger skin dose than usually most photon methods, which causes enhanced radiation dermatitis risk.

The other potential advantage of proton therapy is that allows anterior field treatment with arms akimbo rather than projecting, which may enhance patient comfort during the delivery of treatment. The enface beams are towards the direction of respiratory motion, reducing the risk of loss of target coverage during respiration.

7.5 Nanomaterials-based drug delivery therapy

Novel drug delivery systems, such as nanotherapeutics, represent one of the most rapidly advancing fields designed to address the problems associated with conventional formulations, including poor oral bioavailability, inadequate aqueous solubility, lack of targeting, and nonspecific biodistribution [109]. Both hydrophobic and hydrophilic drugs can incorporate nanoparticles and can be administered through various routes, including ocular, parenteral, oral, nasal, and topical. Schematic representations are shown in Fig. 4.

Liposomes: Recent advancements in the treatment of breast cancer, such as TAM-citrate loaded sustained release liposomes, transdermal TAM encapsulated lipoplex, gemcitabine and TAM-loaded liposomes, TAM-loaded stealth liposomes, TAM encapsulated in lipid vesicles, daunorubicin with TAM stealth liposomes, and thermosensitive liposomes, have been developed and proven effective in the co-delivery of tamoxifen

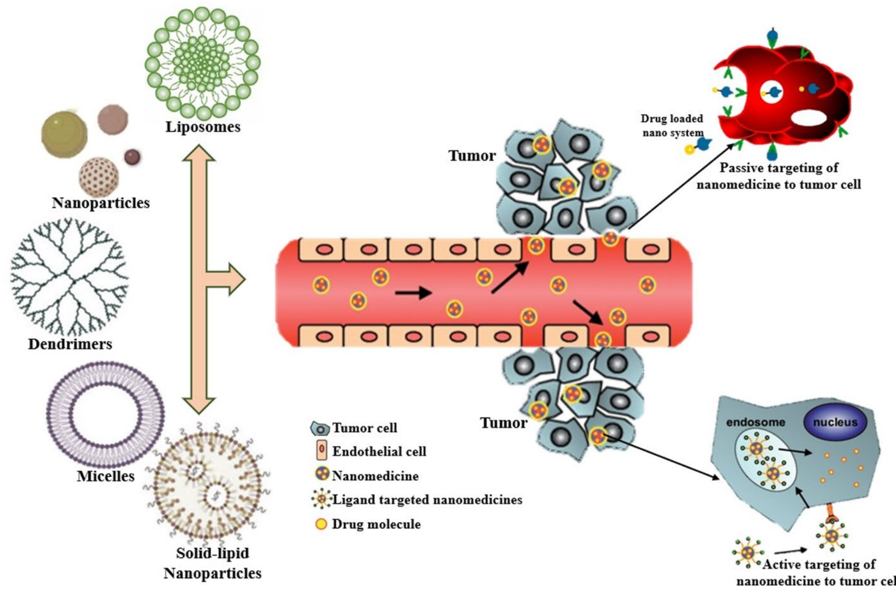

Fig. 4 Schematic representation of nanotechnology and mechanism of drug targeting for the treatment of breast cancer

and imatinib in breast cancer. Targeted liposomes are prepared by inserting ligands of proteins, antibodies, peptides, and carbohydrates on the liposomal surface for various breast cancer receptors like antitransferrin, anti-HER2, antilectins, and anti-ER, enhancing treatment effectiveness [110–112].

Nanooarticles: The increased use of nanoparticles for delivering anticancer agents via the intravenous route offers numerous advantages over other administration methods, such as enhancing the solubility profile of poorly soluble drugs and reducing the metabolism of anticancer drugs by encapsulating them in the hydrophilic and hydrophobic cores of the nanoparticles, which also aids in effective passive targeting of anticancer agents in breast cancer treatment. Furthermore, nanoparticles possess a larger surface-to-volume ratio for drug loading, which contributes to a prolonged plasma half-life and improved biodistribution profiles compared to conventional chemotherapy agents [113, 114].

Dendrimers: Dendrimers are a promising new drug delivery technology that aims to overcome the current limitations of anticancer drugs. They enhance drug solubility, improve drug bioavailability, reduce adverse effects, and their sustained drug release properties minimize toxicity to healthy cells under physiological conditions. In tumor conditions, they facilitate faster drug release and absorption through BC cells, owing to their unique structural characteristics and versatile surface functionality which arise from highly branched macromolecules with defined sizes and shapes. This leads to increased drug loading and specific release kinetics. The exploration of dendrimers as nanocarriers opens up potential for effective and innovative solutions in various dosage forms [115–117].

Micelles: are formed by amphiphilic, single-layer self-assembly architectures consisting of repeating surfactant molecule units at low concentrations, along with separately existing surfactant molecules. An increase in surfactant concentration leads to the aggregation of micelles within a narrow concentration range, culminating in the critical micelle concentration. These micelles can accommodate hydrophobic drugs, such as

TAM cores, which are enclosed in hydrophilic polymers that protect them from degradation by the surrounding environment. Due to their small size, ranging from 20 to 80 nm, these micelles can easily penetrate tumors through the surrounding leaky vasculature and remain there for extended periods [118].

Solid-lipid nanoparticles: Researchers describe additional advantages associated with a novel dosage form of hybrid nucleoside-lipid-based preparation using sorafenib-loaded NPs. Depending on the charge of the nucleoside lipid, the solid lipid NPs (SLNs) exhibited either negative or positive zeta potential values. Sorafenib-loaded SLNs demonstrate more effective anticancer activity than the free drug when tested on four distinct cell lines from breast and liver cancers. This effectiveness is attributed to the biocompatible nature of SLNs, which can accommodate large quantities of drugs used in the treatment of various types of tumors by overcoming the resistance mechanisms of cancer cells. The primary advantages of SLNs include their ability to cross biological barriers and enhance cellular uptake of drugs through passive, co-transport, and active mechanisms, maintaining the drug at the target site for an extended period with the use of non-toxic nanocarriers, as well as improving the bioavailability of poorly soluble drugs even via pulmonary administration [117, 118].

8 Challenges and future prospective

The widely recognized causes of cancer are influenced by a combination of environmental exposure and genetic susceptibility. To prevent BC, we must gain a deeper understanding of both environmental factors and genetics. The primary risk factor for BC is widely regarded as the management of lifetime endogenous estrogen exposure to breast epithelium, which contributes to BC risk. The role of metabolic genes in carcinogenesis is currently a relatively new area of research. Individual differences in estrogen metabolism linked to genetic polymorphisms and mutations should be outlined in women who are at high risk of BC when exposed to certain exogenous estrogens.

Additionally, a greater number of bioactive agents found in plant foods has demonstrated antiangiogenic and antitumor effects in experimental models. Such research should undoubtedly prompt an assessment of the feasibility of their use in chemoprevention. For many of these agents, clinical trials are very limited, often contradictory, nonexistent, or inconclusive, making it extremely difficult to determine their efficacy in chemoprevention and the necessary regimens to achieve the desired health benefits. In this regard, significant effort is needed to enhance the design of clinical trials and to pay special attention to target patients, along with the pharmacokinetics and pharmacodynamics of the agents [119]. The role of immunoprevention in cancer research can be elevated, as the immune system is an adaptable, living entity that can be enhanced by vaccines and tumor-specific antigens to inhibit or prevent the onset of tumors or control tumor growth [103].

9 Conclusion

The present review discusses breast cancer epidemiology and risk factors, signs and symptoms, advancements in screening and diagnosis, stages of breast cancer, novel techniques in BC treatment, progress in the prevention of breast cancer, and the challenges and prospects over the past few decades, which can enhance early detection, treatment, and prevention of BC in young women. The description of epidemiology and risk factors clarifies the reduction and control of BC risk factors from young to elderly populations. The elaboration on the signs and symptoms associated with risk factors may inform individuals when to see a doctor, aiding in the early detection of BC. The challenges include addressing global disparities in outcomes, metastatic disease, and the necessity for a better understanding of BC etiology. Recent advances in screening, such as mammography and computer- aided detection, can now produce detailed images required for diagnostic purposes. Additionally, digital mammography facilitates the transmission of 3 D images over long distances. MRI plays a vital role in breast imaging, particularly for high- risk patients, alongside mammograms or ultrasounds, especially when physical exams yield indeterminate results. Ultrasound is also a crucial technique in breast imaging, particularly for young women with denser breasts or when a lump is palpable. These advances demonstrate that we are closer to overcoming significant logistical barriers to enhance screening and care for BC. Over the past two decades, breast biopsy techniques have drastically improved, and image- guided core biopsy methods have reduced the need for excisional biopsies for diagnosis. Both ultrasound and MRI are now significantly more effective in providing the necessary information for developing treatment plans, which are tailored to each individual and markedly increase the chances of saving each woman's life. Emerging technologies like AI, 3 D, DIBH IMRT, and VMAT hold promise in addressing these challenges and reforming BC care. However, ensuring equitable access to these advanced diagnostic and therapeutic technologies remains a critical challenge. Many low- and middle-income countries (LMICs) face infrastructural, economic, and healthcare workforce limitations, which may hinder the implementation of these newer treatment modalities. Addressing these global disparities in access is essential to achieving comprehensive and inclusive progress in breast cancer care. Therefore, it is imperative that future research and policy also focus on scalable, cost-effective strategies tailored to resource-constrained settings. Continued collaboration, innovation, and global investment are essential to improve breast cancer outcomes for every woman, regardless of geographical or economic background.

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