J Arch Mil Med. 2021 December; 9(4):e120371. https://doi.org/10.5812/jamm.120371.

Published online 2022 January 24. **Review Article**

Design of Comprehensive System for Screening, Diagnosis, and Treatment of Breast Cancer in Armed Forces

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Received 2021 October 17; **Accepted** 2021 November 23.

Abstract

Context: In the present study, we aimed to design a comprehensive system for screening, diagnosing, and treating breast cancer in the armed forces.

Methods: We conducted a focused group meeting (FGM) and article review to evaluate one-stop clinics. Review studies with a standard design based on the PRISMA guidelines and the "Cochrane Handbook" to conduct data analysis were reviewed in the article review phase. In addition, for data extraction in the initial phase, the text of each session with specialists was read and discussed to get the general atmosphere of the meetings.

Results: In the present study, we observed the importance of better diagnosis and treatment of army cases, as mentioned in previous studies. Thus, we should use one-stop clinics to screen, diagnose, and treat army cases with breast cancer. In the present study, we designed this system and reviewed the best results in screening, diagnosis, and treatment of breast cancer in army cases.

Conclusions: A general and regular one-stop clinic dedicated to rapid diagnosis in a comprehensive cancer center can be a highly effective model of care, although not directly linked to screening structures.

Keywords: Comprehensive System, Screening, Diagnosis, Treatment, Breast Cancer, Armed Forces

1. Context

The history of breast cancer dates back to about 1,500 years B.C. In addition, ancient Egyptians reported the first breast cancer case more than 3,500 years ago (1, 2). Breast cancer is the most common type of cancer and a leading cause of mortality from cancer in women worldwide (3). Almost 1.38 million new cases of breast cancer were diagnosed in 2008. Approximately 50% of all breast cancer cases and almost 60% of mortality cases are detected in low-income countries (4, 5). In addition, diagnosis, treatment, and survival vary in social groups with different jobs and financial statuses (6, 7).

The armies offer an exclusive chance to study the expansion of breast cancer in a population with full knowledge of occupation and time (8). Employed women in army locations and the wives of military personnel are at an enhanced risk of industrial chemicals exposure (9). In addition, in the United States (US), it was mentioned that these cases are more involved in jobs, such as auto mechanics, than the general public and were under an enhanced risk of industrial chemicals exposure (10, 11).

As the importance of this study is clear, this study aimed to design a comprehensive system for screening, diagnosis, and treatment of breast cancer in the Armed Forces, as a systematic review and meta-analysis in Iran. Thus, in this review, we will highlight the diagnostic techniques that will be evaluated along with treatment approaches.

2. Methods

2.1. Search Strategy and Study Selection

We reviewed articles and interviewed experts for data collection, which were done in two phases. In the article review phase, review studies have a standard design based on the PRISMA guideline and the "Cochrane Handbook" (12) to conduct the data analysis and then review them.

The authors searched in international databases including ScienceDirect, Scopus, and PubMed/Medline, and national databases such as Elmnet, Magiran, Scientific Information Database [SID], and Barkat Knowledge Network

System. Google Scholar was used to search for the gray literature. The search was done in July 2021, and all published and online articles before the mentioned date were searched. The following keywords were used to search the databases: “Breast Cancer Diagnosis," "Comprehensive System for Breast Cancer," "Armed Forces," "Breast Cancer Screening," "Breast Cancer Treatment," "epidemiology," and “prevalence."

In addition, an expert team involved in breast cancer management was invited to hold FGM. The team included a general surgeon, a radiologist, an oncologist, an epidemiologist, and a general practitioner. The minimum number of meetings was 5, and if the required goals were not achieved, the number of meetings could be increased. The conversations made in each session were recorded, and then its content was implemented to collect data. Before the start of the project, informed consent was obtained from the participating team to record conversations. Participants were asked to make decisions based on the need to localize breast cancer screening in the sessions.

2.2. Inclusion and Exclusion Criteria

The obtained articles in Persian and English languages that evaluated breast cancer of armed forces in treatment and diagnosis without time restriction were evaluated. Furthermore, the literature with only book chapters, abstracts, review articles, congress abstracts, inadequate data, or no relevant data was excluded.

2.3. Data Extraction

The required data of primary retrieved studies were extracted and abstracted independently by two authors, and in case of discrepancies, the other members of the research team were consulted to reach an agreement. The following specifications of studies were extracted: the first author’s name, region, country, publication year, study period, the sample size of the study, and methods of diagnosis and treatment in army cases.

In addition, for data extraction from specialists in the initial phase, the text of each session with specialists was read and discussed to get the general atmosphere of the meetings.

2.4. Risk of Bias

The author assessed the quality of studies using the strengthening the reporting of observational studies in epidemiology (STROBE) checklist to check the risk of bias. Based on the extracted results, the primary studies were categorized into three groups: low, medium, and high quality, and then a subgroup analysis was performed based on study qualities.

2.5. Publication Bias and Sensitivity Analysis

Egger’s linear regression test and Funnel plot were used to explore the publication bias. The sensitivity analysis was performed via evaluating the effect of a study on the pooled prevalence estimate calculated by removing a study from a total of studies each time.

2.6. Statistical Analysis

At first, we did a primary descriptive analysis of included studies. Then, for each study, the methods of screening, diagnosing, and treating breast cancer in army cases were evaluated. In the following, the opinions of experts were also examined. In the end, these comments were summarized and integrated, and a system was developed to evaluate army patients with breast cancer.

The conversations of each FGM session were recorded, implemented, and analyzed in the following steps: (1) first, in the initial phase, the text of each session was read and discussed until getting the general atmosphere of the meeting; (2) then, in the second phase or summarization, the data were coded and categorized based on content; (3) in the end, analysis was done to compare the enrolled articles.

3. Results

Our results were based on FGM and search in search engines, as a review study mentioned in the following.

3.1. Screening

It is estimated that one-third of cancers are completely cured with early detection and timely treatment. With a comprehensive cancer control program, a significant number of patients can be treated or live longer, while late detection leads to increases in treatment costs, resources wasted, and the need for supportive care services (13). An early detection program is the establishment of a systematic or organized screening program that includes the following sections: early screening and early detection, diagnosis, treatment, follow-up, and rehabilitation of patients (14, 15).

Early diagnosis refers to increasing public awareness and health personnel about the signs and symptoms of breast cancer to facilitate early diagnosis (16). In other words, the diagnosis is made in the lower stages of the disease. Screening means performing a diagnostic test in an asymptomatic population, and its purpose is to identify people before the onset of the disease or people suspicious of the disease (17, 18). Two common forms are:

3.1.1. Organized Screening

The establishment of a systemic screening program for a specific population is referred to as a facility, institution, local government, or national health care delivery system (19). This approach leads to the earliest detection among the population and the most significant focus on resources for early detection (20). Organized screening coordinates that all people in a particular community, even those out of reach, for example, by mail, are encouraged to have mammograms regularly (21).

3.1.2. Organized Screening in Iran is Done at Three Levels

3.1.2.1. Level 1 Organized Screening

In the first level, in the health centers, the physician or midwives obtain the required history and record the data, based on the "form of care for women aged 20 to 69 years to prevent and control common cancers in women." At this stage, while evaluating the person classifying her (normal or high risk) and justifying her about her health condition, the necessary measures are taken, and if the person is over 40 years old, she is referred for mammography (22). If the person has problems such as breast pain, sores, touching the mass, etc., and the measures taken by the first level have not been effective in improving the person's condition, for further evaluation, she will be referred to the level 2 breast cancer experts. Health workers' responsibility is to record the results of examinations in the office of "registration of referrals of women aged 20 to 69 years for the prevention and control of common gynecological cancers" in health centers (23, 24).

3.1.2.2. Level 2 Organized Screening

In this level, the health unit with level 2 experts is known as the women's care unit (25). The second level expert, using the form of "Comprehensive care and services for breast diseases," makes a complete evaluation of the patient, and according to his condition, the necessary measures are taken; if necessary, the patient is referred to higher levels (26, 27). After completing the treatment, the person is returned to the doctor of the relevant health center with feedback, the follow-up, and the recommendations of the second-level expert. In other words, the second level expert is the link between the first level and the third level (28, 29).

3.1.2.3. Level 3 Organized Screening

In the third level, a treatment protocol is designed for patients diagnosed in the program after a specialized examination performed at the provincial level (30). This protocol should be evidence-based and based on guidelines developed by a national committee (31). All the documents are included in the first level and family records. The results of follow-ups and actions in the referral office and care form are recorded daily by the relevant health staff (32, 33).

3.2. Unorganized or Opportunistic Screening

Outside of a formal screening program, if she is in good health, she should be screened and undergo a complete diagnostic evaluation of an abnormal finding (29). In this program, the early detection of breast cancer at an intangible stage is provided only for women who have access to screening tests or are in the field of specific health services (24, 34).

3.3. Screening System Design

In a screening program, the proportion of symptomatic people is much lower than the number of asymptomatic people, but in cases where resources are limited, it is better to pay attention to the early detection of symptomatic people. According to the World Health Organization, breast and cervical cancer screening is a priority if resources are limited. Cervical cancer screening is more effective than breast cancer (35). Therefore, a breast cancer diagnosis will be a priority only if the prevalence of breast cancer is three times more than that of cervix cancer.

The optimal effectiveness of screening tests in diagnosis has been proven; however, the lack of an appropriate and low-cost screening program, the risks and concerns about the adverse effects of screening under the age of 40, errors in false-positive screening results, and beliefs among women in the community can be other reasons for the rejection of screening. Due to the effect of early detection of breast cancer in terms of ease of inhibiting cancer progression, lower treatment costs, and improving family quality of life, breast cancer screening is essential (11). The guide to breast cancer screening in Iranian women was designed according to global standards.

3.4. Diagnosis

3.4.1. Breast Self-examination

Most breast cancers are detected by the patient (48%) and then by breast imaging (41%), and only 11% of them are identified by physical examination (36). Although the incidence of breast cancer is low in young women, the importance of early breast examination is such that it becomes a habit (37, 38). The main components of breast examination include: (1) position; (2) palpation; (3) pads of fingers are too sensitive for palpation; (4) pressure; (5) perimeter; (6) pattern of search; (7) patient education (36, 39).

3.4.2. Mammography

It currently plays a vital role in the early diagnosis of breast cancer. At present, according to mammography screening studies in the age group of 60 - 50 years of age, it can cause a decrease in mortality in women in this age group (23). Diagnostic mammography may be performed to further evaluate the breast in women who present with one of the suspected symptoms of breast cancer, such as a discharge or skin changes in the breast (40, 41).

3.4.3. Ultrasonography

It is preferred in young women with signs and symptoms of breast diseases as a sensitive method. The quality of the information obtained from the ultrasound depends on the individual's skill. The method of recording in ultrasonography, such as the BIRADS mammography reporting system, is not standardized (42). Some lesions can only be diagnosed by ultrasound, which is the preferred diagnostic method for differentiating solid masses from cystic masses. It should be noted that there are more false positives in ultrasound than in mammography (43, 44).

3.4.4. Magnetic Resonance Imaging

This method examines lesions that have not received sufficient information by examination or mammography. In many cases, magnetic resonance imaging (MRI) is used to examine the breast following breast resection surgery (45). The incidence of cancer at the surgical site can be well investigated with this method. MRI is very sensitive but not specific. For this reason, a biopsy is not necessary if any mass is detected in this procedure (45). Enhancement of images with gadolinium allows for more differentiation between benign and malignant masses. In addition, the number of false positives in this method is much higher than in other methods. At present, this method is more suitable in people with BRCA1 and BRCA2 gene mutations with a history of breast cancer (22, 46).

3.4.5. Positron Emission Tomography Scan

Positron emission tomography (PET) is a method to study metabolic activity. In this method, radioactive fluorodeoxyglucose is used, which is metabolized by tissue with high metabolism, and the tumor area is identified. It is conducive to diagnosing latent breast lesions. This method is primarily used to examine latent breast cancer metastases at the time of diagnosis or follow-up and has no role in diagnosing or screening breast cancer (47, 48).

3.5. Treatment

In cancer care, specialists in different cancer treatment areas work together to a patient's treatment plan as a team of multidisciplinary (49). Cancer care teams include care professionals, such as physician assistants, oncology nurses, pharmacists, counselors, nutritionists, etc. (35, 50).

3.6. Surgery

3.6.1. Lumpectomy

Removal of the tumor, and in invasive types, radiation is recommended, especially in larger tumors and negative hormone receptors (51, 52).

3.6.2. Mastectomy

This is a surgical method of total breast removal. There are several types of mastectomies. Nipple-sparing mastectomy may be a treatment approach in patients with a BRCA1 or BRCA2 gene mutation or women with a moderate-risk gene mutation, like CHEK2 or ATM (53, 54).

3.7. Radiation Therapy

- External-beam radiation therapy
- Brachytherapy
- Intra-operative radiation therapy (55)

3.8. Therapies Using Medication

Drugs can reach cancer cells throughout the body.

The types of systemic therapies used for breast cancer include: (1) immunotherapy, (2) chemotherapy, (3) targeted therapy, (4) hormonal therapy (56, 57).

3.9. Chemotherapy

Common drugs include: (1) epirubicin (ellence); (2) docetaxel (taxotere); (3) capecitabine (xeloda); (4) ixabepilone (ixempra) (58); (5) paclitaxel (taxol); (6) carboplatin (available as a generic drug); (7) pegylated liposomal doxorubicin (doxil) (59); (8) fluorouracil (5-fu); (9) cisplatin (available as a generic drug); (10) cyclophosphamide (available as a generic drug); (11) eribulin (halaven) (60); (12) gemcitabine (gemzar); (13) vinorelbine (navelbine); (14) methotrexate (rheumatrex, trexall); (15) protein-bound paclitaxel (abraxane) (61).

3.10. Hormonal Therapy

Hormonal therapy is different from menopausal hormone therapy (MHT) (62) and could be given before surgery to shrink a tumor, make surgery more straightforward, and/or lower the risk of recurrence. This is called neoadjuvant hormonal therapy (63).

3.10.1. Types of Hormonal Therapy

- Tamoxifen
- Aromatase inhibitors (AIs)
- Ovarian suppression or ablation (62, 64).

3.11. Targeted Therapy

3.11.1. HER2-Targeted Therapy

- Ado-trastuzumab emtansine or T-DM1
- Pertuzumab, trastuzumab, and hyaluronidase-zzxf (phesgo) (65)
- Pertuzumab (perjeta) (66)
- Trastuzumab (67)
- Neratinib (nerlynx) (68).

4. Discussion

In this study, we conducted an FGM and article review to evaluate one-stop clinics. The concept of one-stop clinics has been known since the 1990s (69), and they provide facilities for all the necessary tests in patients with breast diseases, including examination, ultrasonography, mammography, biopsy, needle aspiration, and report of a single needle. Reference can be made, and results are presented. These clinics provide services to symptomatic individuals and lead to a precise and rapid diagnosis. These multi-purpose clinics usually have radiologists, cytologists, breast surgeons, and radiologists. By examining the results of FGM in another study and accompanied with ideas of breast experts, the availability of this type of one-stop public clinic with screening programs can improve women's understanding of screening and mammography attendance, which was in line with previous studies (70).

Breast disease specialists believed that medical expenses in one-stop clinics would be reduced due to the concentration of facilities in one clinic. In the study by Delaloge et al., each patient's medical cost in a one-step diagnostic test at the clinic was estimated at €420 and the operating cost per day at 3,700 € (70). Given the complexity of this type of assessment and the very little data available for comparison, 420 € is a reasonable cost compared to other studies (71).

Previous studies have shown that the sensitivity and specificity of one-stop clinics for benign or malignant lesions are excellent (72). Delaloge et al. found that 75% of people with suspected breast lesions allow doing an accurate diagnostic method. As expected, immediate diagnosis involves most patients with mass lesions, 87% of whom can be accurately diagnosed on the first day (70).

According to the best results described in breast centers, the overall diagnostic accuracy of this one-step process seems to be very high (70). Studies have also shown that one-stop clinics can significantly reduce the time to visit a specialist (73).

In addition to these benefits, there are studies on the ineffectiveness of one-stop clinics. Despite the savings that may result from less consultation, there are reports that a large number of staff at one-stop clinics can lead to higher costs for patients with this condition (74). In addition, we have shown that one-stop clinics are associated with a reduced time for general practitioners (GPs) to make a diagnosis. In addition, none of the studies in this study discussed the effect of clinics in the diagnosis of cancer (75), which was in contrast with our results.

The vast majority of studies have concluded that patient-centered one-step clinics are an efficient way of diagnosis. There is no consensus on the management of one-stop clinics. In addition to the cost of these clinics, some authors have argued that other methods can be used instead of this method (76). In contrast, others have argued that the difficulties arising from various evaluations that lead patients to the hospital mean that restructuring is necessary to simultaneously evaluate, counsel, and manage patients (77). Another group of researchers believed that diagnostic tests should be performed separately from counseling so that they do not lead to the inevitability of tests (78).

Our results were in line with other studies in this field who evaluated some methods in diagnosis and treatment in a particular group, such as army cases, which clear the importance of paying attention to differences in different groups of society, especially in armed forces, for diagnosis and treatment of those with breast cancer.

4.1. Conclusions

Our results in this review study were in line with other studies in this field that found the importance of better diagnosis and treatment of army cases to use one-stop clinics for screening, diagnosis, and treatment of breast cancer. In the present study, we designed this system and reviewed the best results in breast cancer screening, diagnosis, and treatment in army patients. Therefore, we can reduce the time to diagnosis and enhance the patient's prognosis and condition. However, a general and regular one-stop clinic dedicated to rapid diagnosis in a comprehensive cancer center can be a highly effective model of care, although not directly linked to screening structures.

Footnotes

Authors' Contribution: All authors equally participated in manuscript preparation and submission.

Conflict of Interests: We have no conflict of interests.

Data Reproducibility: Input data for the analyses are available from the corresponding author on request.

Funding/Support: The Aja University of Medical Sciences funded our study.

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