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The Influence of Age Limitation of the German Breast Cancer-Screening Program on Female Patients Older Than 69 Years: A Single-Institutional Retrospective Study

Ahmed Abdelmaqsoud*^a ^aRadiotherapy Department, Südharz Klinikum Nordhausen gGmbH, Nordhausen, Germany

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ABSTRACT

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Background: The breast cancer-screening program is defined as including women between 50 and 69 years old and aims to detect breast cancer in its early stages, which improves the survival outcome. The aim of this study is to explore the differences between female cancer patients at ages between 50 and 69 years old and those older than 69 years regarding the initial tumor stage, method of tumor detection, and conducted oncological treatment.

Methods: Between January 2017 and August 2020, we recruited all breast cancer female patients older than 69 years old who were diagnosed with breast cancer and planned to receive radiotherapy. A similar sample size of female patients between 50 and 69 years old, who were presented to receive radiotherapy at the defined time of the study, was used as a reference group to be compared with the study group.

Results: We identified 132 female patients older than 69 years with breast cancer, who were presented in our department to receive radiotherapy. The control group was represented by 131 female patients at the ages between 50 and 69 years old. The most common stage detected at the time of diagnosis in both groups was stage IA which represented 29% of the study group and 41% of the controlled group. The incidence of Stage IV is significantly higher in the study group (9%) in comparison to the control group (0.8%).

Conclusion: Stage IA is the most common tumor stage detected among female patients older than 69 years as well as those involved in the breast cancer-screening program. The incidence of metastatic disease is significantly higher among patients not involved in the screening program.

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INTRODUCTION

Over the last century life expectancy at birth has increased continuously worldwide. This demographic change is expected to be continued in the next few decades.¹ Cancer is a disease that could affect all age groups but is commonly associated with aging. Many risk factors such as prolonged exposure to different carcinogens and the increase in genomic instability

with aging play an important role making the elderly more susceptible to malignant diseases.²

Breast cancer is the most common malignancy detected among women in Germany and worldwide. The German breast cancer-screening program is defined as including females between 50 and 69 years old aiming to detect and treat breast cancer in its early stages to improve the survival outcome.³ It is well-known that age is an important prognostic factor among females with breast cancer as older age is associated with increased cancer-related mortality.⁴ In the last few years, there was a reevaluation of the age range to be included in the breast cancer screening program worldwide, taking into consideration the

***Address for correspondence:**

Ahmed Abdelmaqsoud, M.Sc,
Niederestrasse 36, 78050 Villingen-Schwenningen,
Nordhausen, Germany
Tel: +493631410
Email: Frag.elsayed@hotmail.com



advantages and hazards of expanding the program to include younger women beginning from age of 40 to the age of 75.^{5,6}

We assumed that the exclusion of females older than 69 years from the German breast cancer-screening program could increase the tumor burden at the time of diagnosis which could limit the treatment options and subsequently impair their life quality as well as the overall survival.

This study aims to explore the differences between patients included in the screening program and those older than 69 years regarding the initial tumor stage, method of tumor detection, the conducted oncological treatment, the treatment intention, and the need for hospitalization during radiotherapy.

METHODS

Between January 2017 and August 2020, we collected all female patients older than 69 years old with histologically confirmed breast cancer, who were referred to our department to obtain radiotherapy. This represents the study group and as a control group we collected a similar sample size of consecutive breast cancer female patients at ages between 50 and 69 years old who were also referred to our department to receive radiotherapy at the defined time of the study. We excluded all female patients younger than 50 years, male patients with breast cancer as well as patients diagnosed with recurrent breast cancer within 5 years after the first diagnosis. The variables to be investigated included age and tumor stage at the time of diagnosis, the method of tumor detection, the type of delivered oncological treatment, the treatment intention whether curative or palliative, and the need for hospitalization during radiotherapy.

Using the American Joint Committee on Cancer (AJCC) TNM Staging System for Breast Cancer and the AJCC Anatomic Stage Groups, all of the patients were categorized into Stages from Stage 0 to Stage IV. The method of detection ranged between self-detected tumors in the breast, the screening mammogram, the clinical examination by the family doctor or gynecologist, and presentation by symptoms of metastatic disease or incendiary findings. The conducted oncological treatment ranged from systemic treatment including chemotherapy or immunotherapy, to surgical intervention or Radiotherapy.

The data was analyzed using SPSS program version 25 (SPSS Inc., Chicago, Illinois, USA). The descriptive analysis was conducted in order to obtain the incidences, standard deviations, and ranges and also to compare different stages and methods of tumor detection in each group. To compare the groups, we used Pearson's chi-squared test and subsequent

Bonferroni corrected post hoc analysis for the significant results.

This retrospective study was conducted according to the Thuringia state hospital law, the ethical principles of the Helsinki Declaration of 1975 and the subsequent revisions. The patient's data were anonymized and stored in a locked software system, and only authorized personnel were allowed to reach the data.

RESULTS

In the defined time of the study, we identified a total of 263 breast cancer female patients, who were planned to acquire radiotherapy. Among these, 132 patients were older than 69 years representing the study group and 131 patients were at ages between 50 and 69 years representing the control group. The median age of the study group was 78 years old (70-92) and the median age of the control group was 60 years (50 to 69).

In both groups, stage IA was the most common stage detected at the time of diagnosis (29% in the study group and 41% in the control group). Meanwhile, stage IIIc had the lowest incidence in the study group (2%) and stages IIIc and IV in the control group (1% for each) (Figure 1).

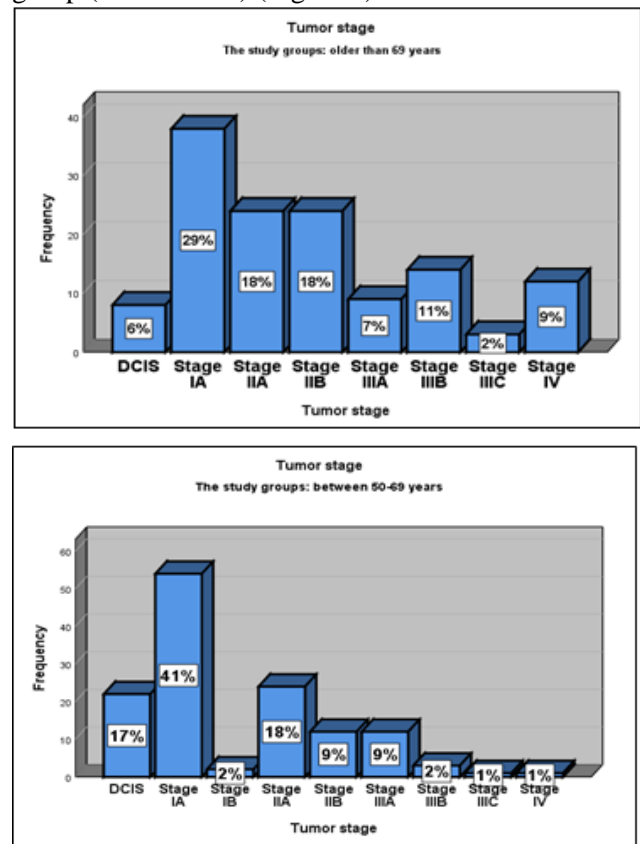


Figure 1. The distribution of the initial tumor stage among both groups

Regarding stage IV disease at the time of diagnosis and with the use of post hoc analysis, we found a significant difference (P-value=0.000) between both



groups with higher incidence among patients older than 69 years (9% vs. 1%). Chi-square test of independence showed that the distribution of the initial tumor stage between both groups was statistically significant (P-value=0.000) as most of the patients (78%) involved in the screening program were concentrated in the early tumor stages (0-IIA), while in the patients older than 69 years the distribution of the tumor stages was more homogenous among all patients (Figure 2).

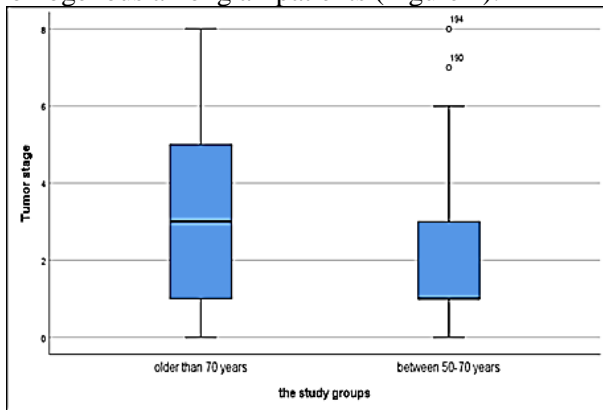


Figure 2. Statistical difference between both groups regarding the initial tumor stage

Regarding the method of tumor detection, self-detection was the most common way (62%) to detect the tumor in the study group, while the tumor was detected by the screening mammogram in 63% of the patients in the control group (Figure 3).

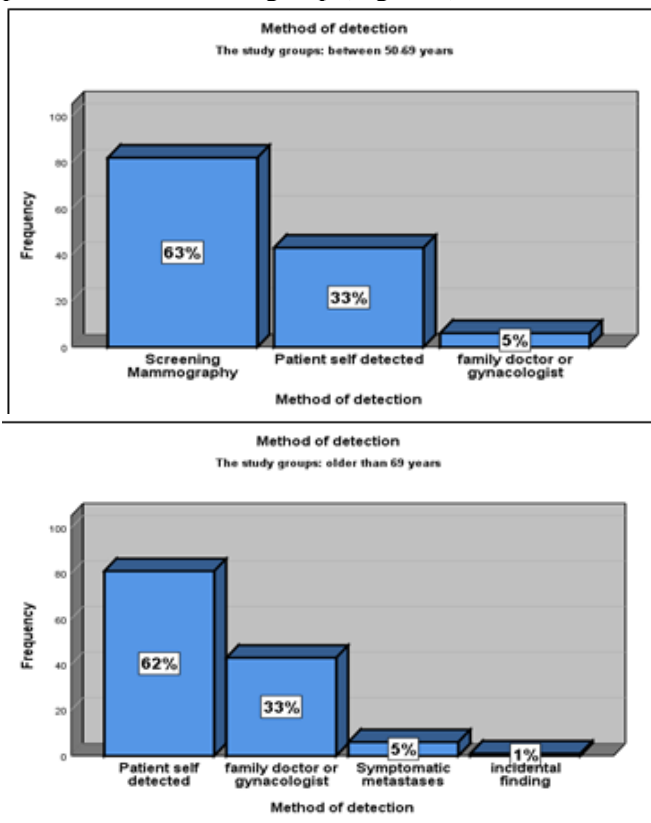


Figure 3. The method of tumor detection among both groups

In terms of conducted oncological treatment, we observed in our study that 92% of the patients older than 69 years old were suitable for surgical intervention with either breast conservative surgery or mastectomy. On the other hand, almost all patients (99%) in the control group were operated. Regarding systemic treatment, 22% of the patients in the study group received chemotherapy, in comparison to 51% in the control group (Figure 4). It is important to note that in early tumor stages with a low risk of recurrence there was no need to conduct chemotherapy and in spite of the higher incidence of stage IV disease in the study group, the capability to obtain chemotherapy was still lower than that in the control group. Nearly all patients in both groups received radiotherapy with 98% in the study group (either with curative intent in early stages or as palliation in the metastatic situations as for brain or bone metastases). On the other hand, all patients (100%) in the control group received radiotherapy.

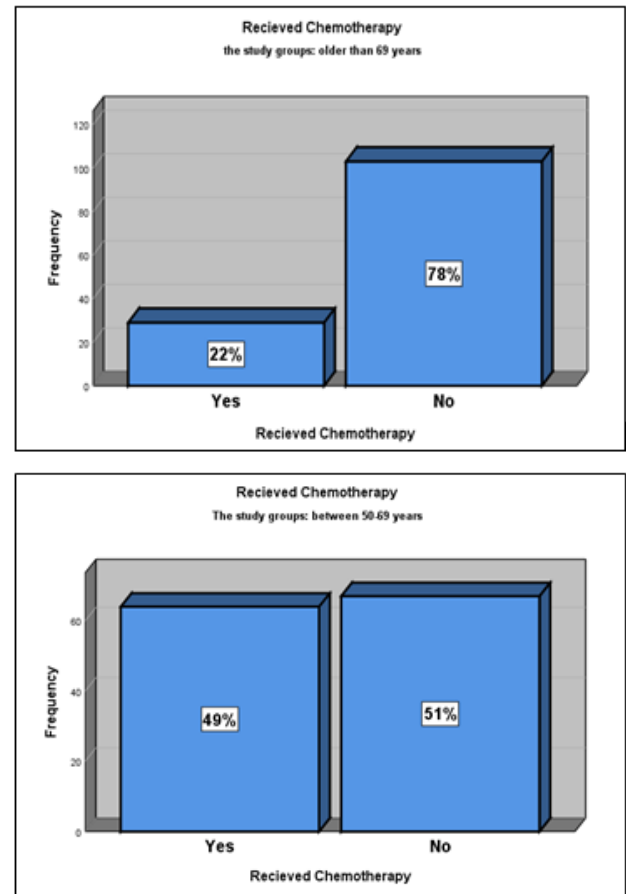


Figure 4. The application of chemotherapy among both groups

The comparison of both groups according to received oncological treatment showed a significant statistical difference in the application of chemotherapy and surgical intervention but no significant difference regarding radiotherapy. We excluded the hormonal therapy from the analysis as



most of the patients treated with curative intent in our department receive it after radiotherapy.

The need for hospitalization was also significantly higher in the study group (55%) because of comorbidities, the complication of previous oncological treatment such as chemotherapy, the need for supportive treatment in metastatic situations, or immobility. This could raise the total costs of the applied treatment which represents an additional burden on the medical insurance. However, 35% of the patients received in the control group the radiotherapy on an out-patient basis (Figure 5).

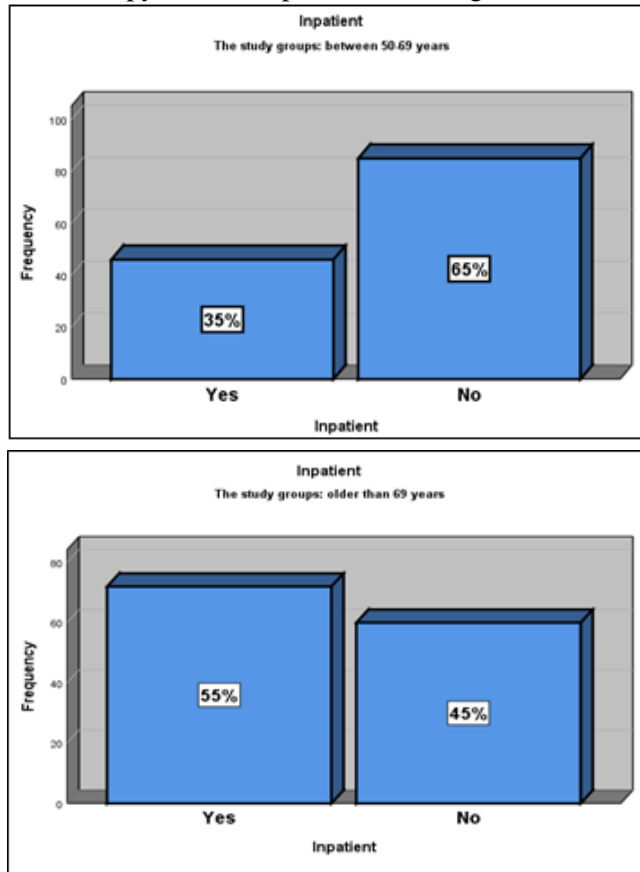


Figure 5. The need of hospitalization during radiotherapy among both groups

DISCUSSION

The worldwide improvement of health care systems including early detection of diseases through screening programs, and the continuous improvement of the medical technologies and treatment options side by side with increased self-awareness, healthy lifestyle, and regular medical control have positively improved the life expectancy in the last decades. This improvement is expected to continue until 2050.¹ Aging is a well-known risk factor associated with increasing the incidence of malignancies. Different biological changes together with extrinsic and intrinsic genomic transformation are responsible for this high incidence.²

Breast cancer is the most common malignancy among women in Germany and worldwide with more than 2 million newly diagnosed cases worldwide every year. It is also responsible for the highest incidence of tumor-related mortality among women with more than half a million death cases yearly worldwide. In Germany, there are approximately 70,000 new breast cancer cases annually. The German program of screening mammograms was first conducted in 2005 and from this time forward expanded the coverage of the program nationwide. The aim is the early detection and treatment of breast cancer in women between 50 and 69 years old in order to decrease the breast cancer-related mortality. The reason for this age limitation was explained by the assumption that the benefit of the screening among elderly females (older than 69 years) without symptoms has not been yet clarified.^{3,7} That could be understood as the costs of mass screening and subsequently, the treatment of early detected breast cancer among this age group of the population would not influence their life expectancy. On the other hand, to decrease the radiation exposure and the potential carcinogenic effects of the mammogram excluded women younger than 50 years old.

In spite of the fact that not all women allowed to be screened in Germany (50 -69 years old) participate in the program (about 50%),⁸ it still plays an important role in the early detection of breast cancer (in our study 63 %). The national association of statutory health insurance as well as the statutory health insurance companies in Germany bear the costs of screening mammograms starting from the age of 50 years and then every 2 years until the age of 69 years. Another reason for this age limitation is the cost of widening the coverage to include elderly females. This deficiency of early detection among these women could be reflected in the disease burden represented by the initial tumor stage and subsequently in the treatment strategies and treatment costs.

Most European countries have similar age limits for their breast cancer screening programs (between 50 and 70 Years). However, the Dutch National Breast Cancer Screening program allowed women between 50 and 75 years of age to be included.⁹ In England, the National Health Service (NHS) conducted the AgeX trial to assess the risks and benefits of offering an extra screen to women aged 47-49 and 71-73. The trial began in 2009 and was planned to continue until 2026.¹⁰ In March 2020, the routine breast screening was suspended in England due to the COVID-19 pandemic and in May 2020, it was decided to end the randomization in AgeX.¹¹

This study shows that in comparison to females involved in the screening program the tumor stage



distribution at the time of diagnosis among elderly patients is significantly different. Stage IA is still the most common initial stage detected in both age groups but with weak representation among elderly patients (29% vs. 41%). There is also a significantly increased incidence of stage IV disease among patients excluded from the screening program (9% in comparison to screened patients 1%).

As it is expected the screening program helps to downstage the initially detected tumor stage. Patient awareness plays a very important role in tumor detection, especially by excluded females (older than 69 years) which represent the most common method of tumor detection in our study. Remarkably, the screening mammogram shows results similar to self-detection among the control group (63% vs. 62%). In the second place come the routine medical examinations conducted by the family doctor or the gynecologist. Both (self-detection and medical examination) were responsible for about 95% of tumor detection in females excluded from the program.

In our study, 92% of the patients excluded from the screening program were surgically operated but in this group 9% of the patients were already in stage IV disease at the time of the diagnosis. This could mean that all non-metastatic patients were subjected to local surgical intervention (BCS or MRM). Nevertheless, chemotherapy is only feasible for selected patients in this age group. In our study Radiotherapy was observed to be a well-tolerated non-invasive treatment modality acceptable to elderly patients. There was no significant difference between both groups in terms of radiotherapy application.

The need for hospitalization is significantly higher in elderly patients not only because of the advanced tumor stage but also because of the prevalence of comorbidities among this group of population.

Recommendations

We recommend inducting a nationwide cost-benefit study in order to calculate the financial burden

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of widening the screening program to include women until the age of 80 years old. According to our results, self-detection and the regular clinical examination are the most common methods of breast cancer detection among females older than 69 years; therefore it is convenient to encourage raising awareness about breast cancer in this age group including learning self-examination. This could be achieved by targeted information campaigns or by creating a parallel clinical screening program for females older than 69 years using a combination of medical clinical examination and breast ultrasound. This could improve the early disease detection with reasonable costs in comparison to the screening mammogram.

CONCLUSION

In our study, we observe that Stage IA was the most common tumor stage initially detected among breast cancer female patients older than 69 years as well as those allowed to be involved in the breast cancer-screening program (age between 50-69 years). The incidence of metastatic disease was significantly higher among patients excluded from the screening program. Self-detection represented the most common method of tumor detection in this group of patients. Surgery and radiotherapy remained the most feasible treatment options among elderly patients but with a higher incidence of hospitalization. It is necessary to evaluate the risks and benefits of widening the age coverage of the breast cancer-screening program to include elderly females.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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