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Evaluation of effect of self-examination and physical examination on breast cancer☆

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ABSTRACT

Background: Breast cancer is the number one cancer of women in the world. More than 90% of breast cancers can be cured with early diagnosis followed by effective multimodality treatment. The efficacy of screening by breast self-examination (BSE) and breast physical examination (BPx) is best evaluated using randomized screening trials.

Method: A total of 12,660 women aged 35–64 years, 6330 in the intervention group and 6330 in the control group, were randomly selected from four areas of Yazd city, I.R. of Iran. The number of detected cancers along with kind of cancer, staging of cancer, the route of detected cancer and the number of deaths during the first 5 years of the study were collected and analyzed.

Results: No significance difference between the two groups was seen in respect to socio-demographic and socio-economic variables ($P > 0.05$). Subjects in the intervention group had a response rate of 83.5% for attending the health center and 80.2% for visiting the assigned surgeon. A total of 31 and 13 new cases of breast cancer were identified in the intervention and control groups, respectively, of which 48.5% of cases in the intervention group were <50 yr of age. A significant difference between the cumulative incidence of breast cancer in the two groups with a ratio of 2.4 was observed.

Conclusion: BSE & BPx have a significant effect in detecting breast cancers at early stages (<3) suggesting they are effective screening tests with high availability and low costs that can be applied at the community level.

Introduction

Breast cancer is the most prevalent cancer among females and is the number one cancer of women in the world. In middle-income countries, and in many low-income countries, breast cancer has become the most frequent cancer in women, supplanting cancer of the cervix [1,2]. All ages are susceptible and more than 90% of the patients can be cured with early diagnosis followed by effective multimodality treatment, though this is not currently achieved in Iran [3]. Mammography, breast physical examination (BPx) and breast self-examination (BSE) are common tools applied in screening programs. In countries where breast cancer is diagnosed at an advanced stage, screening by BPx with the teaching of BSE as an integral component could be effective in reducing breast cancer mortality [4]. In contrast, mammography is the dominant mode of breast cancer diagnosis in technically advanced countries. Although mammogram-detected non-palpable breast cancers are smaller on average than clinically palpable breast cancers and small breast cancers confer a better prognosis than large ones, evidence shows that survival in the context of mammography screening programs is not predictive of reduced mortality because of lead time bias, length bias, or over-diagnosis [5]. Moreover, recent results

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observed from Canada indicate that annual mammography screening had no effect on breast cancer mortality beyond that of BPx [6], suggesting a greater role for BPx in countries where breast cancer is normally diagnosed at an advanced stage. Since breast cancer ranks first among cancers diagnosed amongst Iranian women, as the second cause of the death in females of all cancer mortalities, onset age of 10 years earlier than developed countries and the vast majority are diagnosed in advanced stages [7–12], a community based trial was planned to evaluate whether BPx combined with BSE can reduce the cumulative incidence of advanced (stage 3 or worse) and mortality from breast cancer in a population of Yazd city, I.R. of Iran.

Methods

The present work is the report of phase II of the Yazd community based trial for the evaluation of the effect of BSE and BPx on the reduction of morbidity and mortality of breast cancer performed in the urban population of Yazd city, I.R. of Iran after approval from the Ethics Committee of Shahid Sadoughi University of Medical Sciences. The trial commenced in 2008 and follow-up is planned to be continued up to 2018.

There are three distinctive phases for this trial of 10 years duration: phase I included a pilot of the questionnaire (3 months) along with gathering the baseline data over a 9 month period; phase II is the active intervention phase with 4 rounds of annual screening by BPX + BSE; phase III the post-screen follow up of 5 years duration.

Data from previous studies were used for the calculation of the required sample size, considering a 30% reduction in breast cancer mortality at a significance level of 0.05 (one-side) and a power of 0.9, a total of 12,660 women age group 35–64 years, 6330 in case group and 6330 in control group, were selected from four areas of the Yazd city. Out of 20 health centers in Yazd city, two health centers from middle socio-economic (SE) areas and two from high SE areas of the city were selected by stratified random sampling, then from each SE area, one of them was randomly allocated to the intervention group and the other to the control group. Appropriate to the number of women of age 35–64 years living in each center, the allocated size was divided into clusters (urban blocks). Having a personal history of breast cancer or detecting the disease at the beginning the study, residing in Yazd city <5 years, suffering from severe illness expecting survival of less than 10 years and not giving permission by subjects to attend the designated center for annual evaluation were exclusion criteria.

The first encounter for both groups was in their homes for the signing of an informed consent form and gathering of primary data, then, subjects in the intervention group were invited to their local health center for the teaching of BSE and undertaking BPx by a general physician. Four annual follow-up visits at the health center were arranged for the subjects in this group. Subjects in the control group were checked and questioned by an annual telephone call to enquire of their morbidity and mortality. The information on morbidity and mortality was checked through the active Cancer and Death registry systems available through the Deputy for Health affairs of the University. The main outcome measures of the study were comparison of cumulative incidence of advanced breast cancer (stage 3 or worse), survival rate of breast cancer and mortality rate from breast cancer between the study groups. The required data such as demographic and socio-economic characteristics at the beginning of the study, the number of detected cancers in 5 years along with kind of cancer, staging of cancer, the route of detected cancer (BSE/BPx) and the number of deaths occurred at the first 5 years of the study were collected for the two groups. Data were analyzed using SPSS software applying statistics like frequencies, percentage, mean (SD) and testes of chi-square, student t-test with 95% confidence level.

Results

The final analysis included a total of 12602 subjects (6302 & 6300 individuals in intervention and control group respectively). The reason for the exclusion of 28 women from the intervention and 30 in the control group is due to them having already been diagnosed with breast cancer at the beginning of the study. Demographic and socio-economic characteristics of subjects in both experimental and control groups is shown in Table 1. No difference was seen with respect to age, marriage age, family size, number of live births and total family income. There was no statistically significant differences ($p > 0.05$) between the frequency distribution of marital status, occupation and education levels in the two groups. The majority of women were married (94.3% and 94.1% in intervention and control groups respectively), householder (90.0% and 91.0%, respectively) and low educated (62.9% and 67.4%, respectively).

The overall response rate of subjects in both intervention and control groups showed that both had acceptable communication and cooperation during 5 years (Table 2); subjects in the intervention group showed a mean response rate for attendance at the health center of 83.5% and 80.2% for attending the assigned surgeon. Out of five potential appointments, 63.8% of subjects in the intervention group completed all five and visited the general physician at the health center, 4.9% did not respond at all. In the control group, a mean response rate of 96.5% was seen to a phone call made by social workers.

The most common kind of tumor observed in the intervention group was infiltrating ductal carcinoma (51.5%) followed by infiltrating medullary carcinoma (22.5%). Table 3 shows the characteristics of the breast cancers detected during 5 years in the two groups; a total of 31 and 13 new cases were identified in the intervention and control groups, respectively of which 15 (48.5%) of the cases in the intervention group were <50 yr of age. A pathology report on two subjects in the intervention group and one subject in the control group were not available. The cumulative incidence at 5 years in the intervention and control groups were 49.4 and 20.6 per 100,000 respectively. Fifteen cases (48.5%) in the intervention group were primarily detected by BSE and the others (51.5%) were identified by BPx by the general physician. Two cases in the

Table 1
Demographic & socio-economic characteristics of subjects in both experimental & control groups.

Group Variable mean(SD) Age	Intervention N = 6302 45.84 (6.75)	Control N = 6300 46.02 (7.38)
Age at Marriage	17.82 (3.40)	17.75 (3.30)
Family size	4.21 (1.31)	4.20 (1.52)
Number of live birth	3.69 (1.61)	3.74 (1.74)
Total monthly family income	$2800	$2600
Marital status		
Married	5942 (94.3)	5928 (94.1)
Single	38 (0.6)	79 (1.2)
Other	322(5.1)	302 (4.7)
Occupation		
Housewife	5672 (90.0)	5733 (91.0)
Employed	630 (10.0)	567 (9.0)
Education		
Illiterate	693 (11.0)	844 (13.4)
Primary school	3270 (51.9)	3402 (54.0)
Middle school	1638 (26.0)	1436 (22.8)
Others	700 (11.1)	617 (9.8)

Table 2
Overall measures and response rate of subjects in intervention and control groups.

	First yr. N (%)	Second yr. N (%)	Third yr. N (%)	Fourth yr. N (%)	Fifth yr. N (%)
Intervention group (n = 6302)					
Invited to Health center	6300 (100)	6202 (98.5)	6168 (97.9)	6092 (96.7)	6066 (96.2)
Subject's Response rate	5324 (84.5)	5147 (83)	5236 (84.9)	5129 (84.2)	5106 (82.1)
Referred by general physician	187 (3.7)	139 (2.7)	147 (2.8)	118 (2.3)	139 (2.7)
Visited surgeon	152 (80.8)	118 (81.3)	134 (88.1)	87 (70.7)	111 (80.0)
Control group (n = 6300)					
Successful contact rate	6300 (100)	6182 (98.0)	6098 (96.8)	6092 (96.6)	6007 (95.3)

intervention group and one in the control group are known to have died from breast cancer.

The nodal status and tumor size of the ascertained breast cancers in the two groups is presented in Table 4. Although the mean tumor size of those with known size is the same in the two groups (3.0 cm), there were more node positive and large cancers ascertained in the intervention group than the control.

Discussion

The present study was designed to evaluate the efficacy of BSE and BPx in reducing the frequency of breast cancer presenting at stages III and more, and reduction in mortality due to this cancer. Secondary prevention through screening appears to be the most promising intervention available to increase the incidence of cancer detected at an early stage and decrease the incidence of cancer presenting at a late stage [13]. In our study the good participation rate and acceptance of women in both groups, also the high quality of services delivered by the health professionals, especially the general practitioners, resulted in a higher probability of 2.4 fold in detecting breast cancer in the intervention group compared to the control from the use of BSE and BPx, as well as the detection of cancers with stages less than 3 (1.58 fold).

There are two potential reasons why more breast cancers were ascertained in the intervention than the control group in this study. The first is that the follow-up post cessation of annual screening has so far been too short to exceed the lead time gained by the use of BSE and BPx. In general, the lead time gained by these two approaches to breast cancer early detection is not believed to be long - of the order of a year. This would suggest that a lead-time effect does not completely explain the discrepancy seen. The other explanation is that despite the good overall response of the women in the control group to the annual telephone follow-up conducted by social workers, some women who had developed breast cancer either were non-responders, or hid the fact of breast cancer occurrence from the social workers. These possibilities are reenforced by the relative absence of node positive and large cancers ascertained in the control group. It is possible that further follow-up of the two cohorts (including if possible visits to homes and neighbors of non-respondents) may help to resolve this inconsistency. It is possible that if more resources had been utilized to improve the awareness of breast cancer and its curability if detected early in the base population of the study, the discrepancy would not have occurred, as it is known that such education is needed in Iran [14,15].

Although there is a low sensitivity (54%) for BPx, the specificity is high (94%) [16] resulting in the conclusion, in contrast to mammography, that BPx may be more relevant in women aged 40–49 years than older women when more healthy women

Table 4
Nodal status and tumor size of the ascertained breast cancers.

	Intervention group	Control group
Number of nodes involved		
None	6	6
1–3	12	5
4 or more	9	1
Unknown	4	1
Tumor size (cm)		
<1.0	2	0
1.0–1.4	2	4
1.5–1.9	3	1
2.0–3.9	13	5
4.0 or more	7	3
Mean size	3.0	3.0
Unknown	4	0
Total	31	11

Table 3
Characteristics & statistics of Breast cancer detected in both intervention and control groups.

Group and year intervention	No. of detected cancers in 5 years	Stage			Detected by BSE	Detected by BPx	No. of deaths due to cancer in 5 years
	(total = **31**)	I	II	III			
Year 1	5	1	4	0	2	3	2
Year 2	11	2	5	4	7	4	
Year 3	4	1	2	1	1	3	
Year 4	2	1	0	1	1	1	
Year 5	9	2	4	3	4	5	
Control	(total = **13**)						
Year 1	2	0	2	0	–	–	1
Year 2	3	1	1	1	–	–	
Year 3	1	0	1	0	–	–	
Year 4	2	2	0	0	–	–	
Year 5	5	0	4	1	–	–	
5yr.Cumulative incidence		5 yr cumulative incidence stage <3					
Intervention group	49.4/100000	30.2/100000					
Control group	20.6/100000	19.07/100000					
p-value	**<.05**	**<.05**					

are < 50yrs old. In this study about 50% of women with cancer in the intervention arm were under 50 yr of age, similar to the findings of Harrichi et al. in which the highest frequency of malignancies was observed in the 40–49 age group (31.8%) [17]. This is, in fact, the current scenario seen in developing countries where because of the population pyramid the majority of cancers are identified at earlier age compared with developed countries [18–20]. According to a study in India by Okonkwo et al. it was estimated that the cost-effectiveness of BPx screening for breast cancer compares favorably with that of mammography in developed countries [21]. This is due to high rates of cancer amongst women less than 50 yr, and the non-availability, inaccessibility and higher costs of mammography in developing countries. Considering the low awareness, attitude and practice of women in developing countries for the prevention of breast cancer [22–24], it may be expected that with low cost screening programs BSE and proper BPx besides creating a good healthy behavior amongst women can detect cancers at the earlier stages. In our study, the most common type of malignant lumps was infiltrating ductal carcinoma which is similar to findings of other studies [25–28]. The limitations of the study were not completing follow-up in the intervention and control group and not analyzing the survival time due to low number of deaths observed in two groups. The follow-up of the study will need to be continued for a few more years to obtain definitive results.

Conclusion

The results of study showed that the cumulative incidence to 5 years in the intervention and control groups were 49.4 & 20.6 per 100,000 respectively, an overall excess of 240%, also 158% for detecting stages <3 cancers. It may concluded BSE & BPx have a significant effect in detecting breast cancers at early stages suggesting they are effective screening tests with high availability and low costs that can be applied at the community level. However, the deficit in identified breast cancers is as yet unexplained. Further follow-up may clarify.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Ethical approval

The study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences.

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