The Efficiency of Breast Cancer Screening in Tbilisi

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Summary
We have analyzed 67,710 cases of screening-diagnostics conducted in 2010-2014 by National Screening Centre, in which 1,197 patients were diagnosed with breast cancer. The prevalence of breast cancer per 1,000 women was 17.7‰. The prevalence of breast cancer cases increases with age and reaches its peak in age group 65-69 (46.7‰). 53% of breast cancer cases were detected at I clinical stage, 35% - at the II, and 12% - at the III-IV clinical stages. With age, the detection of the disease at I stage decreases, while at the II clinical stage it increases. Breast cancer prevalence per 1,000 women (‰) at all clinical stages reaches its peak in age group 60-69. In order to evaluate the diagnostic efficiency of tests during breast cancer screening and estimate the diagnostic value and role of ultrasonography research, we studied the following indicators of diagnostic efficiency of breast physical examination, mammography, ultrasonography and punctate cytological research based on Screening National Centre. While evaluating diagnostic efficiency, we paid attention to the value of tests in differentiating diagnostics between breast cancer and other benign tumors. In order to evaluate the diagnostic efficiency and role of ultrasonography during breast cancer screening, we have additionally compared mammographic and ultrasonography results in cases of breast cancer and other benign tumors. During breast benign tumors, hyper diagnostics occurred in 39.2% of all cases according to mammographic research and only in 15.3% according to ultrasonography research. In other words, ultrasonography research in cases of benign tumors reduces the number of cases of screening hyper diagnostics by 23.9%. During breast cancer, hypo diagnostics occurred in 7.1% according to mammographic research and only in 2.7% according to ultrasonography research. In other words, ultrasonography research in cases of breast cancer reduces the number of cases of screening hypo diagnostics by 4.4% which is very important. It is very important that ultrasonography research at the age of 40-49 increases cases of early diagnostics of breast cancer in I clinical stage.

Key words: *breast cancer, screening, the role and efficiency of ultrasonography, Tbilisi.*

Problems Statement:

In the 1980s, six European countries started breast screening programs. In England, Wales, Scotland and Holland, there is a tendency for reduction in breast cancer mortality, which is connected with diagnosing cancer at its early stage and adequate treatment by screening (Botha J.L. et al., 2003).

American College of Radiology (ACR) analyses (2008) the results of clinical research of Brown University, according to which adding ultrasonography to mammographic research during breast cancer screening increases the number of detected cases of cancer. At the same time, there is an increase in false positive indicators and, therefore, in the number of unnecessary biopsy.

According to Wax A. (2009), breast cancer ultrasonography can be conducted to identify the location of cancer in the breast, which will be used by doctors in biopsy and aspiration procedures.

Nothacker M. Et al (2009) analyzed the results of six cohort researches carried out in 2000-2008, in which both mammographic and ultrasonography research of breast was used in breast cancer screening. In case of negative results of mammographic screening, ultrasonography research of breast revealed the first invasive carcinoma in 0.32% of all cases. This was among the women who, according to American College of Radiology (ACR), were diagnosed with breast tumor of 2-4 type. The majority of cancer cases have been detected by ultrasonography. The potential negative side of ultrasonography for women is connected with the increase in frequency of biopsy.

American Cancer Society (2010) recommends the guidelines of breast cancer screening – annual mammography for early detection of breast cancer must be combined with ultrasonography. Ultrasonography research is particularly seen among women with high risk of breast cancer or during high density of breast tissue.

According to Teh W. and Wilson A.R. (1998), the members of European group of breast cancer screening believe that ultrasonography must be used during diagnostics and screening of breast cancer. The authors think that the role of ultrasonography is the following: breast ultrasonography, as the additional research of mammography and clinical research, makes important corrections in diagnosis, during both palpable and non-palpable breast pathology.

According to Steenhuysen J. (2008), women with high risk of breast cancer benefit from screening during which they get both mammographic and ultrasonography research more than those who only get mammographic screening. Among women with high risk of breast cancer, 50% of all existing breast cancer cases are detected by mammographic screening, while mammography and ultrasonography together detect 80% of existing cases of breast cancer.

According to Schwenk T.L (2008), mammographic screening decreases the frequency of breast cancer mortality by 15-20%. Ultrasonography research enables additional detection of the cases of breast cancer (12 cases of cancer researched by mammographic screening in 2600 women) whose diagnostics was not detected by mammographic screening, especially during dense breast tissue.

Kolb T.M. et al. (2002) compared sensitivity index of mammographic and ultrasonography research during heterogenic of high density of breast tissue. According to the authors, out of 105 cases of breast cancer, 60 (57%) were detected by mammography, while 101 (96%) – by ultrasonography.

By comparing mammographic and ultrasonography researches, some researchers priorities mammography for CIS, while during dense breast tissue and small, less than 1 cm, tumors – ultrasonography (Buchberger W. et al., 2000; Kolb T.M. et al., 2002).

Ultrasonography research is particularly effective in women under 50 with high density of breast tissue. In 42 cases of such cancer, mammography detected only 21 (50%) cases, while ultrasonography detected 33 (79%) cases. According to the authors, ultrasonography screening is more effective in young women irrespective of the density of breast tissue (Kolb T.M. et al., 2002).

In case of simultaneous use of mammography and ultrasonography in breast cancer screening, there is less risk of hypo diagnostics and the index is less than 2-4% (Moy L. Et al,. 2002).

Since 2008, there has been breast and cervix uteri cancer screening program in Tbilisi. So far, more than 80000 women have been researched by screening diagnostics.
At the same time, the efficiency of breast cancer screening, the role of ultrasonography and diagnostic value of the program have not been estimated by epidemiological research and there is no academic proof of optimization of advocacy of women's health.

The aim of the research:

To prevent cases of breast cancer by estimating the role of ultrasonography in breast cancer screening among Tbilisi female population, to present academic proof of optimization of advocacy of women's health.

Objectives set up considering the design of the study:

In the scientific research we used the materials of the screening program and the information we received as a result of their realization. In order to estimate the current screening program epidemiologically, the research intends to solve the following task:

- ◊ evaluation of diagnostic efficiency and the role of ultrasonography in breast cancer screening program in Tbilisi (2010-2014).

Target groups and methodology of research:

In 2010-2014, in Tbilisi, 80 585 women were examined within the screening program of breast cancer. In 2010-2014, 84% of mammographic screening cases were conducted in Screening National Centre. As a result of screening diagnostics, in a five-year period, 1 197 patients out of 67 710 were diagnosed with breast cancer.

In order to evaluate the diagnostic efficiency of tests during breast cancer screening and estimate the diagnostic value and role of ultrasonography research, we studied the following indicators of diagnostic efficiency of breast physical examination, mammography, ultrasonography and punctate cytological research based on Screening National Centre: sensitivity, specificity, positive and negative predictive values and efficiency of tests. While evaluating diagnostic efficiency of tests, the result of each research was compared to the final clinical diagnosis of every individual patient based on complex research.

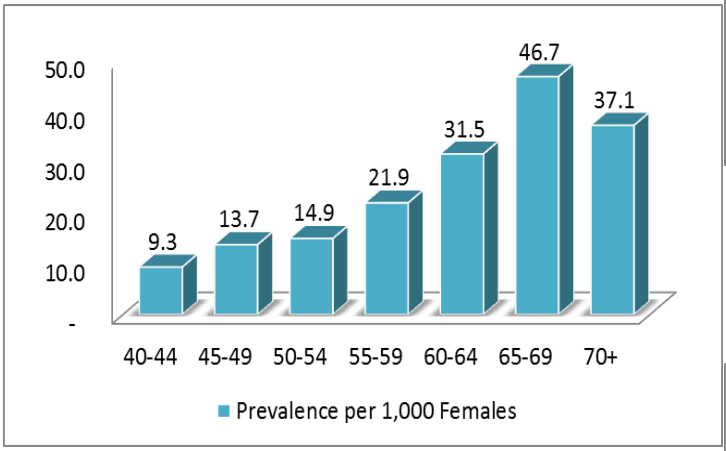
Results of the research:

In the period of 2010-2014, it was performed breast cancer screening in the Screening National Centre. Was investigated and analyzed 67,710 females, which was 84% of total research sample population (see Table 1).

Table 1. The number of researched women and detected cases of breast cancer during breast cancer screening in Tbilisi in 2010-2014 and the prevalence of breast cancer per 1000 women according to age

Age group	Total number of researched women	The number of detected breast cancer cases	The prevalence of breast cancer per 1000 researched women
40-44	16391	153	9.3
45-49	15880	218	13.7
50-54	14692	219	14.9
55-59	10401	228	21.9
60-64	6636	209	31.5
65-69	3360	157	46.7
70+	350	13	37.1
Total	67,710	1,197	17.7

Drawing 1. The prevalence of breast cancer according to age group per 1000 researched women at Tbilisi Screening Centre in 2010-2014



As a result of screening diagnostics, within a five-year period, 1,197 patients out of 67,710 were diagnosed with breast cancer. The prevalence of breast cancer is 17.7‰ per 1,000 women.

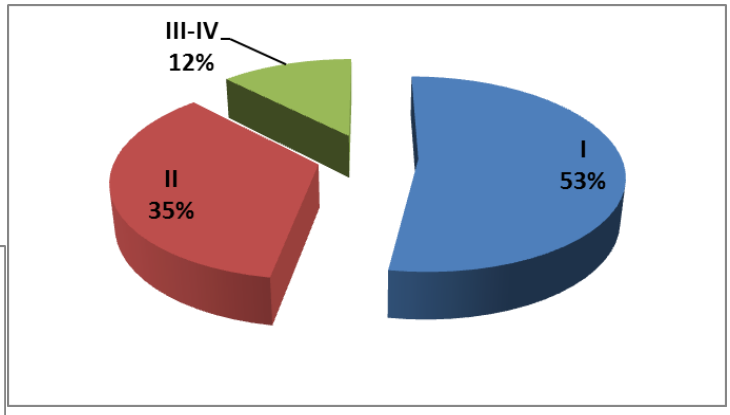
The prevalence of breast cancer per 1000 women according to age group is shown in Drawing 1. The prevalence of breast cancer cases is increasing with age and reaches its peak in age group 65-69 (46.7‰).

Table 2. The number of detected breast cancer cases according to age group and research years conducted in 2010-2014 by Screening National Centre in Tbilisi

Age group	2010	2011	2012	2013	2014	2010-2014
40-44	23	13	41	41	35	153
45-49	34	36	53	59	36	218
50-54	39	22	46	60	52	219
55-59	41	22	58	51	56	228
60-64	24	34	47	59	45	209
65-69	28	13	35	41	40	157
70+	10	1	2	0	0	13
Total	199	141	282	311	264	1,197

The number of detected breast cancer cases in Tbilisi according to age group and research years conducted in 2010-2014 by Screening National Centre is shown in Table 2, while the number of detected breast cancer cases according to age groups and clinical stages are shown in Table 3.

Drawing 2. Rates of clinical stages of breast cancer provided by the Screening National Centre in Tbilisi in 2010-2014.



Drawing 3. The number of detected breast cancer cases according to age groups and clinical stages conducted in 2010-2014 by Screening National Centre in Tbilisi

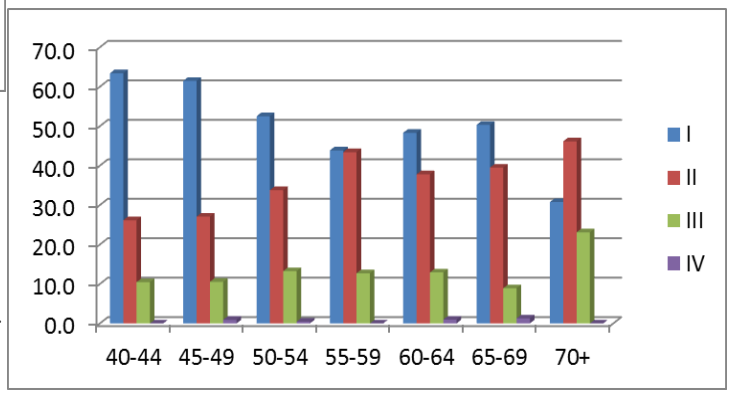


Table 3. The number of detected breast cancer cases according to age groups and clinical stages conducted in 2010-2014 by Screening National Centre in Tbilisi

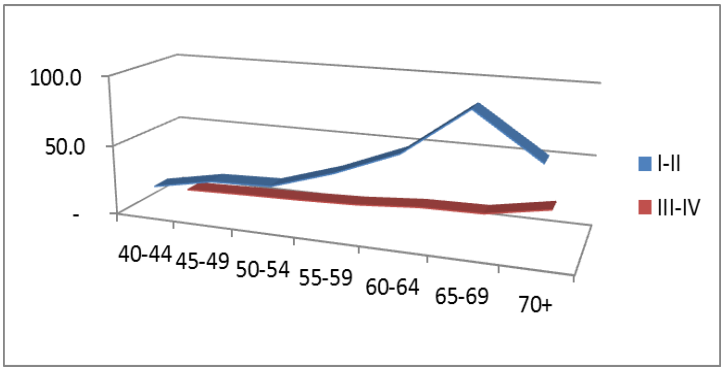
Age group	Total number of detected cases of breast cancer	Stage							
		I		II		III		IV	
		Abs. number	%	Abs. number	%	Abs. number	%	Abs. number	%
40-44	153	97	63.4	40	26.1	16	10.5	0	0.0
45-49	218	134	61.5	59	27.1	23	10.6	2	0.9
50-54	219	115	52.5	74	33.8	29	13.2	1	0.5
55-59	228	100	43.9	99	43.4	29	12.7	0	0.0
60-64	209	101	48.3	79	37.8	27	12.9	2	1.0
65-69	157	79	50.3	62	39.5	14	8.9	2	1.3
70+	13	4	30.8	6	46.2	3	23.1	0	0.0
Total	1,197	630	52.6	419	35.0	141	11.8	7	0.6

53% of 1,197 cases of breast cancer were detected in the I clinical stage, 35% -in the II stage and 12% - in the III clinical stage. With age, there are less cases of detecting the disease in the I stage and more cases of the disease in the II clinical stage. The prevalence of breast cancer in all clinical stages reaches its peak at the age of 60-69 (see Drawing 2, 3 and 4).

Table 4. The prevalence of breast cancer according to clinical stages and age per 1000 women researched in 2010-2014 at Screening National Centre in Tbilisi

Age group	Clinical Stage			
	I	II	III	IV
40-44	13.2	5.5	2.2	-
45-49	18.9	8.3	3.2	0.3
50-54	17.5	11.3	4.4	0.2
55-59	21.5	21.3	6.2	-
60-64	34.0	26.6	9.1	0.7
65-69	52.5	41.2	9.3	1.3
70+	25.3	38.0	19.0	-

Drawing 4. The prevalence of breast cancer according to stages and age per 1,000 women researched in 2010-2014 at Screening National Centre

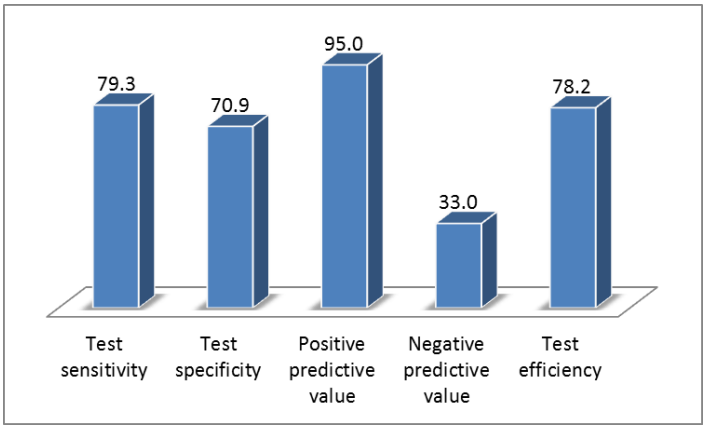


While evaluating the efficiency of diagnostics, the emphasis was put on the values of tests in the process of differentiating between breast cancer and benign tumors.

Table 5. The comparison of the results of clinical diagnosis and breast physical examination conducted in 2010-2014 at the Screening National Centre during differentiating diagnostics between breast cancer and benign tumors

Breast physical examination	Clinical diagnosis				
	Breast cancer		Breast benign tumor		
	Total number	%	Total number	%	Total
Breast cancer	949	95.0	50	5.0	999
Breast benign tumor	248	67.0	122	33.0	370
Total	1,197	87.4	172	12.6	1,369
χ^2= 192,0; p<0,001					

Drawing 5. Evaluation of the efficiency of differentiating diagnostics between the cases of breast cancer and benign tumors conducted in the Screening National Centre in 2010-2014



The comparison of the results of clinical diagnosis and breast physical examination during differentiation diagnostics between breast cancer and benign tumors is shown in Table 6.

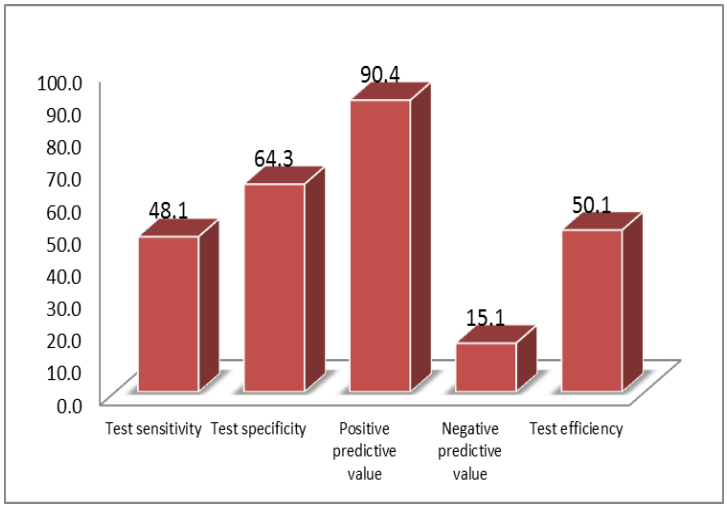
Mammography	Clinical diagnosis				
	Breast cancer		Breast benign tumor		Total
	Abs. number	%	Abs. number	%	
Breast cancer	572	90.4	61	9.6	633
Breast benign tumor	618	84.9	110	15.1	728
Total	1,190	87.4	171	12.6	1,361
χ^2=9,2 ; p=0,002					

According to the research conducted at Screening National Centre in 2010-2014, out of 1 369 women, 1,197 (87.4%) patients were diagnosed with breast cancer, while 172 (12.6%) – with benign tumors. Clinical diagnosis of breast cancer in 949 (95%) and breast benign tumors in 122 (33%) cases were also made by breast physical examination.

The ratio of diagnostic efficiency of breast physical examination in differentiating diagnostics is shown in Drawing 5. The sensitivity of breast physical examination is 79.3%, its specificity – 70.9%, the ration of predicting positive results of tests – 95.0%, the ration of predicting negative results of tests – 33.0% and ratio of test values - 78.2%.
Table 6. The comparison of the results of clinical diagnosis and breast physical examination conducted in 2010-2014 at the Screening National Centre during differentiating diagnostics between breast cancer and benign tumors
The comparison of the results of clinical diagnosis and breast physical examination to differentiate between breast cancer and benign tumors is shown in Table 6. 1,190 (87.4%) out of 1,361 women researched at the Screening National Centre in 2010-2014 were diagnosed with breast cancer, and 171 (12.6%) – with benign breast tumor. Clinical diagnosis of 572 (90.4%) cases of breast cancer and 110 (15.1%) cases of benign breast tumor was also confirmed by mammography.

The efficiency of mammography diagnostics in differentiating diagnostics is shown in Drawing 6. Mammography sensitivity ratio was 48.1%, specificity ratio – 64.3%, ratio of predicting positive results – 90.4%, ratio of predicting negative results – 15.1%, and ratio of values – 50.1%.

Drawing 6. Evaluation of mammographic efficiency in differentiating diagnostics between the cases of breast cancer and benign tumors carried out in the Screening National Centre in 2010-2014



The comparison of clinical diagnosis with the results of ultrasonography in differentiating diagnostics between the cases of breast cancer and benign tumors is presented in Table 7.

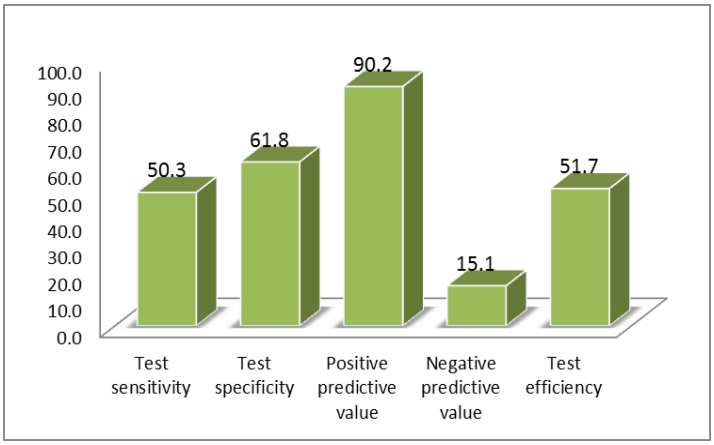
1,191 (87.5%) out of 1,361 women researched at the Screening National Centre in 2010-2014 were diagnosed with breast cancer, and 170 (12.5%) – with benign breast tumor. Clinical diagnosis of 599 (90.2%) cases of breast cancer and 105 (15.1%) cases of benign breast tumor was also confirmed by ultrasonography.

Table 7. The comparison of clinical diagnosis with the results of ultrasonography in differentiating process between the cases of breast cancer and benign tumors carried out at the Screening National Centre in 2010-2014

Ultrasonography	Clinical diagnosis				
	Breast cancer		Benign breast tumor		Total
	Abs. number	%	Abs. number	%	
Breast cancer	599	90.2	65	9.8	664
Benign breast tumour	592	84.9	105	15.1	697
Total	1,191	87.5	170	12.5	1,361
χ^2=8,7 ; p=0,003					

Efficiency ratio of ultrasonography in differentiating diagnostics is shown in Drawing 7. Ultrasonography sensitivity ratio was 50.3%, specificity ratio – 61.8%, ratio of predicting positive results – 90.2%, ratio of predicting negative results – 15.1%, and ratio of values – 51.7%.

Drawing 7. Evaluation of ultrasonography efficiency in differentiating diagnostics between the cases of breast cancer and benign tumors in the Screening National Centre in 2010-2014



The comparison of the results of punctate cytological and biopsy histology researches in differentiating diagnostics between the cases of breast cancer and benign tumors is presented in Table 8.

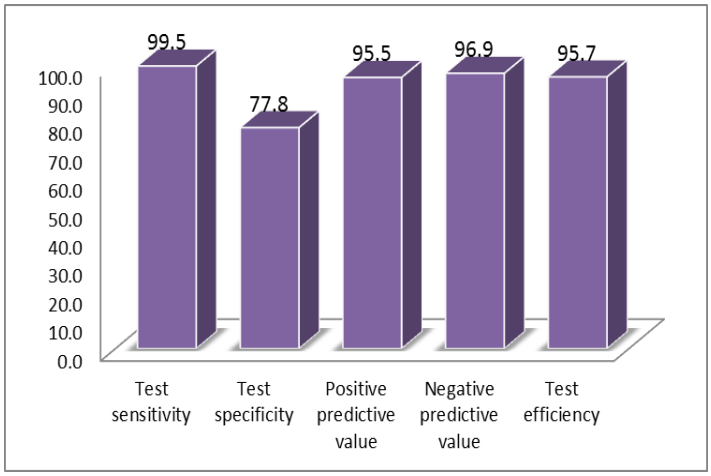
Table 8. The comparison of the histological conclusions and the results of punctate cytological research in differentiating diagnostics between the cases of breast cancer and benign tumors carried out in the Screening National Centre in 2010-2014

Cytological research	Histological diagnosis				
	Breast cancer		Benign breast tumor		Total
	Abs. number	%	Abs. number	%	
Breast cancer	379	95.5	18	4.5	397
Benign breast tumour	2	3.1	63	96.9	65
Total	381	82.5	81	17.5	462
χ^2=330,0; p<0,001					

381 (82.5%) out of 462 women researched at the Screening National Centre in 2010-2014 were diagnosed with breast cancer according to histological examination, and 81 (17.5%) – with benign breast tumor. The diagnosis of 379 (95.5%) cases of breast cancer and 63 (96.9%) cases of benign breast tumor was also confirmed by cytology.

The ratio of diagnostic efficiency of cytological research in differentiating diagnostics is presented in Drawing 8. Cytological sensitivity ratio was 99.5%, specificity ratio – 77.8%, ratio of predicting positive results – 95.5%, ratio of predicting negative results – 96.9%, and ratio of values – 95.7%.

Drawing 8. Evaluation of the efficiency of punctate cytological research in differentiating diagnostics between the cases of breast cancer and benign tumors carried out in the Screening National Centre in 2010-2014



In order to evaluate the value and role of ultrasonography diagnostics during screening diagnostics of breast cancer, we have additionally compared the results of mammography and ultrasonography in the cases of benign tumors and breast cancer (see Tables 9, 10 and Drawings 9, 10).

Table 9. The comparison of the results of mammography and ultrasonography in detecting the cases of benign breast tumors at the Screening National Centre in 2010-2014

Mammography (BIRADS)	Ultrasonography				Total
	2, 3		4, 5		
	Abs. number	%	Abs. number	%	
2, 3	171	84,7	**31**	15,3	202
4, 5	**47**	39,2	73	60,8	120
χ^2= 71,2; p<0,001					

During breast benign tumors hyper diagnostics occurred in 39.2% of all cases according to mammographic research and only in 15.3% according to ultrasonography research. In other words, ultrasonography research in cases of benign tumors reduces the number of cases of screening hyper diagnostics by 23.9% (χ^2= 71,2; p<0,001).

Drawing 9. Comparison of results of mammography and ultrasonography during benign tumors detected at the Screening National Centre in 2010-2014

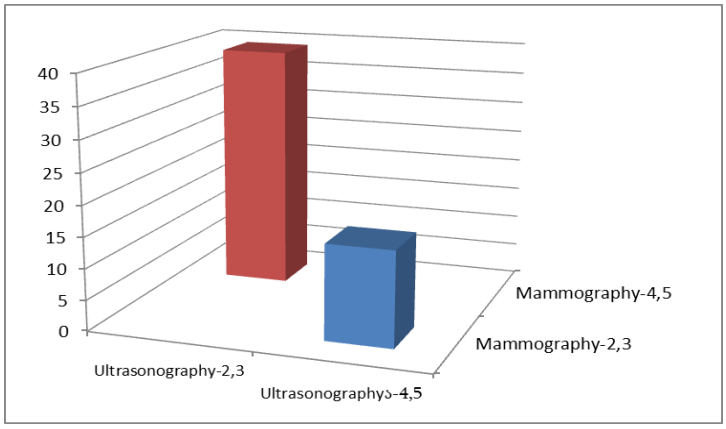
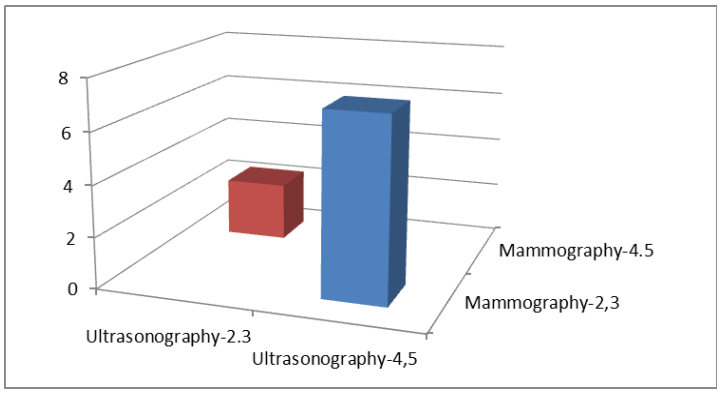


Table 10. Comparison of results of mammography and ultrasonography during breast cancer detected at the Screening National Centre in 2010-2014

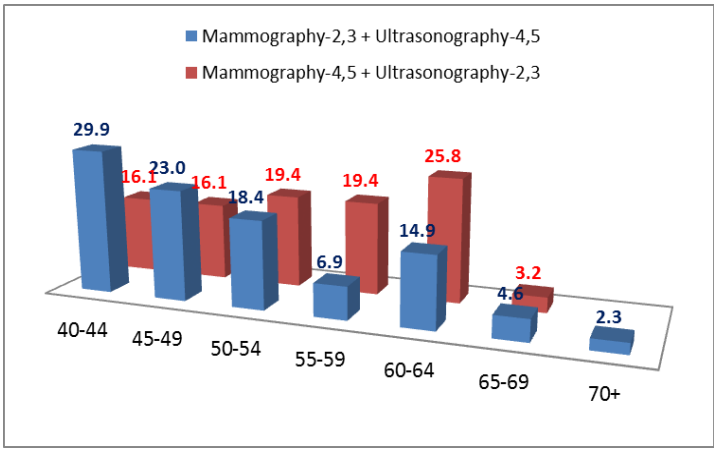
Mammography (BIRADS)	Ultrasonography				Total
	2, 3		4, 5		
	Total number	%	Total number	%	
2, 3	1,136	92,9	**87**	7,1	1,223
4, 5	**31**	2,7	1,116	97,3	1,147
χ^2= 1930,0; p<0,001					

Drawing 10. Comparison of results of mammography and ultrasonography during breast cancer detected at the Screening National Centre in 2010-2014

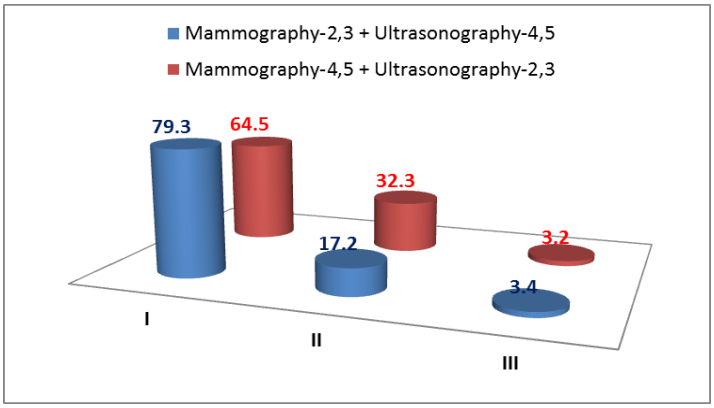


During breast cancer, mammographic research detected hypo diagnostics in 7.1% of all cases and only 2.7% of cases were detected by ultrasonography research. In other words, ultrasonography research in cases of breast cancer reduces the number of cases of screening hypo diagnostics by 4.4% (χ^2= 1930,0; p<0,001).

Drawing 11. Comparison of results of mammography and ultrasonography in detecting breast cancer according to patients' age, carried out at the Screening National Centre in 2010-2014



Drawing 12. Comparison of results of mammography and ultrasonography in detecting breast cancer according to the stages of clinical disease, carried out at the Screening National Centre in 2010-2014



It should be noted that the ultrasonography research in age group 40-49 increases the number of early detection of breast cancer at the I clinical stage (see Drawings 11 and 12).

Conclusions:

1. We have analyzed 67 710 cases of screening-diagnostics conducted in 2010-2014 by National Screening Centre, in which 1 197 patients were diagnosed with breast cancer. The prevalence of breast cancer per 1000 women was 17.7%. The prevalence of breast cancer cases increases with age and reaches its peak in age group 65-69 (46.7%).
2. 53% of 1 197 cases of breast cancer were detected in the I clinical stage, 35% -in the II stage and 12% - in the III-IV clinical stages. With age, there are less cases of detecting the disease in the I stage and more cases of the disease in the II clinical stage. The prevalence of breast cancer in all clinical stages reaches its peak at the age of 60-69.
3. In differentiating diagnostics between breast cancer and benign tumors, the ratio of ultrasonography sensitivity was 50.3%, specificity ratio – 61.8%, ratio of predicting positive results – 90.2%, ratio of predicting negative results – 15.1%, and ratio of values – 51.7%.
4. During breast benign tumors, mammographic research detected hyper diagnostics in 39.2% of all cases and only 15.3% were detected by ultrasonography research. In other words, ultrasonography research in cases of benign tumors reduces the number of cases of screening hyper diagnostics by 23.9% (χ^2= 71,2; p<0,001).
5. During breast cancer, mammographic research detected hypo diagnostics in 7.1% of all cases and only 2.7% were detected by ultrasonography research. In other words, ultrasonography research in cases of breast cancer reduces the number of cases of screening hypo diagnostics by 4.4% (χ^2= 1930,0; p<0,001).
6. Carrying out both mammographic and ultrasonography research at the age of 40-49 increases cases of early diagnostics of breast cancer in I clinical stage.
7. During breast cancer screening, diagnostic efficiency of ultrasonography research is high and its role is important in early diagnostics of cancer during dense breast tissue, in women aged 40-49, during differentiating diagnostics between breast cancer and benign tumors, during small tumors to make morphological research of punctate and biopsy.

Recommendations:

1. To increase the effectiveness of early detection of breast cancer and screening program, to decrease the number of cancer burden and hypo diagnostic cases, it is recommended to use both mammography screening and ultrasonography research in the following situations:
   - ◊ High density of breast tissue
   - ◊ Among women aged 40-49
   - ◊ During differentiating diagnostics between breast cancer and benign tumors
   - ◊ During small tumors to make morphological research of punctate and biopsy.
2. Epidemiological evaluation of the role of ultrasonography research, academic explanation of the advocacy of women's health and education of female population – teaching them self-examination of breasts and working out the habit of regular screening, will help optimize preventive management of breast cancer, and the implementation of the acquired recommendations into practice will create scientifically proved basis for the social and economic progress.

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