Performance of opportunistic breast cancer screening in Slovenia

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The purpose of the study was to assess performance indicators of opportunistic breast screening carried out in one of the Primary Breast Diseases Centers (PBDC) and to find out if these indicators meet the standards set in "European guidelines for quality assurance in mammographic screening".

The records of 1,896 asymptomatic women, aged between 50 and 69 years who attended PBDC for the first time in the period from October 15 1998 to October 15 2002, were reviewed. In all of them, clinical examination and mammography was done. If necessary, non-invasive additional imaging was also performed in the PBDC. If malignancy could not be excluded, the women were referred to the Institute of Oncology (IO) for additional invasive diagnostic procedures. The data on these findings were collected from the records of the IO. We compared our results with the recommended values of performance indicators valid for organized screening programs as determined by "European guidelines".

Of 1,896 women, 415 (22%) were recalled for additional imaging. In 335/415 women the suspicion for malignancy was excluded with noninvasive diagnostic methods. Invasive diagnostic procedures were applied in 80/415 women. Carcinomas were detected in 23 women, the majority of them (96%) were non palpable. All carcinomas were ductal; 9 (39%), 7 (30.5%), 7 (30.5%) were grade 1, 2 and 3, respectively. One carcinoma was preinvasive; 20 had the tumor size T1, 1 had T2, while in one the size was not specified. The axillary lymph nodes were negative in 14/23 (61%) women with invasive carcinoma and positive in 5/23 (22%). Surgery of the axilla was considered unnecessary in 4/23 (17%). Diagnostic sensitivity in presented cohort was 96%, specificity 79%. After a negative mammogram 1 interval cancer was detected. Compared to the "European guidelines" we achieved satisfactory results in the number and size of detected and interval cancers, but the analysis showed a higher recall rate with too many false-positive results. Efforts should target lowering the recall rate without reducing the cancer detection rate. Compared to Slovenian average, a large percentage of localized breast cancers in our study claim for organized breast cancer screening program in Slovenia at earliest convenience.

Key words: mammography, breast neoplasms, screening program

Due to its high incidence, breast cancer (BC) is a major public health problem worldwide. In 2001, the incidence rate of BC in Slovenia (total population 2 million) was 94.7/100 000, which ranked our country in the middle of the world scale [1]. According to the EUROCARE-3 study, the age standardised relative five-year survival of patients was significantly lower (65.5%) than European average (74.8%) [2]. Despite the recent improvement of five-year survival in Slovenia, a decrease in the mortality rate, such as in the countries with organized screening, has not been observed overall, but only in the youngest age group (30–49) [3]. It is also very upsetting that the percentage of BC detected in localized stage does not exceed 50%, due to an unsuccessful early detection [4, 5].

In Slovenia, breast cancer screening is not organized according to the "European guidelines", but is opportunistic. In each PBDC, women can get clinical breast examination and mammography for diagnostic or screening purpose. Until now, no analysis of performance indicators of PBDCs that perform opportunistic breast screening has been carried out.

The aim of the study was to evaluate the performance indicators in one PBDC and to compare them with the recommended values in "European guidelines" in order to gain some experience that would facilitate the organization of the national screening program, expected to be carried out in a few years in Slovenia.

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Patients and methods

Only asymptomatic women aged 50–69 who visited the selected PBDC (in the city of Domzale) for the first time during the period of 15 October 1998 to 15 October 2002 were included in the study. Of 1,869 women, 13% were found to be at higher risk for BC (relatives of first or second degree with BC) and 17% were on hormone replacement therapy. Our study group represented 16% of women aged 50–69 living in the area covered by this PBDC. They were invited to visit PBDC through local media or referred by gynecologists and general practitioners in the region.

The mammographic unit Planmed Sophie (1998, Planmed, Finland) was used with single-screen recording system (MR Agfa), single-emulsion film combination (MR-DETAIL S, Agfa) and film processor Agfa Mamoray MR 9460. Sensitometry was performed once a week. Once a year, control measurements were performed by a qualified physicist from an institution authorized to control radiology equipment. All mammograms were read by the same radiologist, specially trained in mammography.

Women with negative clinical and mammographic findings were notified by mail. When necessary, women were recalled for further examination because of mammographic or clinically palpable abnormalities. Those with palpable lesion were referred to IO for percutaneous fine-needle biopsy (FNAB). Women with abnormal mammogram first underwent noninvasive diagnostic procedures (additional mammographic views and/or US). If pathology could not be excluded, they were sent to IO for invasive procedures: stereotactic or US-guided biopsy (FNAB or core biopsy, CB) or diagnostic open-biopsy. The latest was done only in case of imaging-cyto-pathologic discordance, if needle biopsy was not feasible, or if the results of FNAB were suspicious for malignancy (at the beginning of the study, we were performing only FNABs; we started with core-biopsies in the year 2000). The details on surgical treatment were obtained from the medical records of IO. The data on interval cancers were obtained from the Cancer Registry of Slovenia.

Basic descriptive statistical methods were used in data analysis.

Results

Of 1,896 women, 415 (22%) were recalled for additional diagnostic procedures (recall rate). In 335 (18% of all screened, 81% of all recalled), non-invasive diagnostic procedures excluded malignancy. In 80 (4% of all screened, 19% of recalled women), invasive diagnostic procedures were performed, in 8 due to clinical palpable lesion and in 72 due to mammographic abnormalities. Diagnostic algorithm with No. of women and definite findings after all procedures is presented in Figure 1.

A total of 23/1896 (1.2%) cancers were detected in our population; 48% (11/23) with FNAB, 22% (5/23) with CB, 4% (1/23) with percutaneous needle biopsy of palpable lesion, and 26% (6/23) with diagnostic open-biopsy. The malignancy was diagnosed preoperatively in 74% (17/23) of cases. The vast majority of cancers – 96% (22/23) – were nonpalpable, histologically ductal. Histopathologic stage is presented in Table 1 [6]. All patients were treated surgically: in 6 tumourectomy was performed, in 11 quadrantectomy and in 6 mastectomy; 15 of them received radiotherapy after breast conserving surgery.

Screening performance indicators of our study and the recommended values of "European guidelines" are presented in

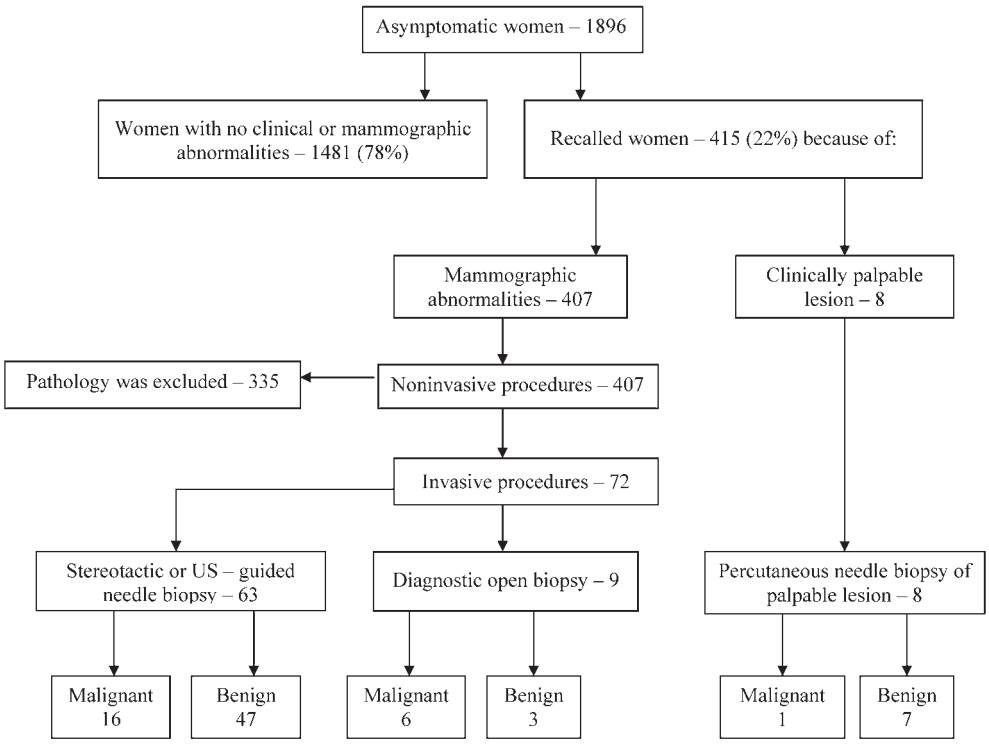

Figure 1. Diagnostic algorithm with No. of women included and No. of definite findings.

Table 2. One interval cancer (BC diagnosed within 12 months after normal mammogram) was diagnosed 8 months after negative mammography.

The sensitivity (the ratio of the No. of BC correctly identified to No. of cancers correctly identified plus No. of cancers not identified, i.e. 23/24) in our study was 96%, while specificity (the ratio of No. of true negative examinations to No. of true negative plus No. of false positive, i.e. 1481/1481 (415-23)) was 79%.

Positive predictive values (the ratio of truly positive lesions to those that tested positive) for recall, FNAB plus CB, diagnostic open-biopsy and surgical (diagnostic and therapeutic) biopsy were 5.5%, 25%, 67% and 88.5%, respectively.

Discussion

Several reports on results of organized screening programmes in West European countries have been published, but there are only few reports on opportunistic screening as it is performed in Slovenia [7–10].

Our results show that some performance indicators (No. of detected cancers <T1b, >T2, interval, node negative cancers and preoperatively confirmed cancers) met the European standards.

The most striking difference was in recall and cancer detection rates. According to the "European guidelines", in the first screening round additional examinations should be performed in less than 10% of women (3% for technical inadequacy and in 7% for clarification of the abnormality seen on mammogram). In further 5% of women, additional images may be taken concurrently with basic examination if they would help to further clarify mammographic appearances [11].

Our recall rate considerably exceeds the standards in many European countries [8, 11–13]. We tried to analyze the possible reasons for this differences.

It was not possible to monitor separately additional examinations due to technical reasons and due to mammographic abnormality. Our recall rate included also invasive diagnostic procedures in 8 clinically palpable lesions.

Our radiographers do not have the competence to decide whether additional views should be taken at the time of the initial examination. As well the majority of abnormalities were clarified by additional views or US, which could also be due to inadequate compression, i.e. unexperienced radiographer [14].

Regular biennial mammography might find a tumor that has grown in between and become detectable but is still small. Being aware that our women are not examined in two-year intervals, each mammogram was precisely checked and every abnormality was additionally examined. Early recall after 6–12 months that would certainly reduce recall rate was not used. The single mammography reader was a potential weakness of the study. Double reading and the arbitration of the third expert may considerably reduce the number of additional examinations [11, 14–17]. Nevertheless a possible reason for higher recall may also be the mistaken belief in Slovenia that an interval carcinoma is an indication of incompetence of radiologists and not a fact that cannot be completely avoided. The fear from overlooking a tumor encourages additional examinations that frequently (in 50% to 90% of cases) do not confirm the cancer.

According to the "European guidelines", initial screening should detect a three-fold age-specific incidence of BC in the observed region [11]. In the case of Slovenia, the incidence of BC in women aged 50–69 was 1.78/1,000, so we expected to detect 5.3 BC/1,000 screened women, while in fact 12/1000 were found [1]. One of the reasons might be due to higher (13%) percentage of women with family his-

Table 1. Histopathologic stage of tumor (pT)

	STAGE							
CARCINOMAS	pTis	pT1mic	pT1a	pT1b	pT1c	pT2	pT3	Tx
No	1	0	2	6	12	1	0	1
%	4.4	0	8.7	26	52.1	4.4	0	4.4
Grade 3				1	4	1		1
Grade 2	1		1	2	3			
Grade 1			1	3	5			
Neg. axillary status			1	5	7			1
Pos. axillary status				1	3	1		
Unknown ax. status	1		1		2			
Metastatic disease	0	0	0	0	0	0	0	0

Table 2. Performance indicators in our study compared to recommended values in European Guidelines

Performance indicators	Our study	European guidelines
Cancer detection rate (per 1,000)	12	3 x incidence*
Recall: (%) – technical reason – mammographic abnormality	total 22	 3 7
Preoperative diagnosis (%)	74	>70
Ductal carcinoma in situ (DCIS) (%)	4.4	>10
Invasive breast cancer (IBC) (%)	95.6	<90
IBC </= 10 mm (%)	35	>20
IBC > T2 (%)	4.4	<25
Negative axillary nodes (%)	61	>70
PPV** of open-surgical biopsy (%)	88.5	>50
Benign to malignant biopsy ratio	0.13 : 1	1 : 1

*Incidence in Slovenia in 2001, in the age group of 50–69 years was 1.78 cancer/1,000 women, PPV** – positive predictive value

tory of BC in our study. These women are on the one hand more interested to attend breast examinations, while on the other hand they are at higher risk of having BC [18]. Therefore, women in our group are not completely comparable to general population screened in organized programs.

Higher percentage of BC detected may also be due to higher recall rate, as some studies showed that the number of additional examination is, to certain extent, proportional to the number of detected BC [8, 12, 19, 20]. One study showed that the detection of each of poorly discernible BC, which might turn out to be interval cancer in later screening cycles, would require to recall 100–400 women to additional examinations [21]. In the United Kingdom, the priority was to detect the highest possible number of invasive BC, even on account of more numerous additional examinations. In the Netherlands, the main concern was to keep the number of women unnecessarily recalled as low as possible, even on account of lower number of BC cases detected [8, 22].

In the field of invasive diagnostic procedures in our PCDC we followed the "European guidelines". Thus, few breast surgeries were performed without preoperative biopsies; the majority of BC was confirmed preoperatively with an encouraging ratio between surgically treated benign and malignant changes of 0.13:1.

The data of the Cancer Registry of Slovenia showed that in 2001, less than 50% of BC were detected in localized stage [1]. In our study, localized disease was found in 61% of detected BC with additional undefined stage in 4 patients (17%) because the axillary lymph nodes were not surgically removed. Among these 4 cancers, 2 were smaller than 1 cm and their axillary lymph nodes would be probably negative, so we can assume that in our study about 70% (61%+(17%/2)) cancers were node negative (Tab. 1).

Conclusion

The results of the present study confirmed that the analyzed PBDC with its technical facilities and staff was adequate to attain the recommended values of the majority of performance indicators valid in organized screening programs. Efforts to improve mammographic screening in the planned Slovenian organized screening programs should target lowering the recall rate without reducion cancer detection rate.

A considerably high percentage of BC cases detected in our study in localized stage that was app. 20% higher than that of Slovenia in 2001 is a most conclusive proof of efficient early detection. Slovenia would act most sensibly if recommendations by European guidelines were taken into account in the forthcoming development of organized screening program.

As a further point, our experience could provide motivation for the countries in similar situation to the one in Slovenia, to take the steps towards a nation-wide BC screening program throughout the evaluation of opportunistic screening program in a selected PBDC.

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