



Ph.D. Thesis Summary

**Analysis of contributing factors of the breast cancer mortality
rate in Hungary between 2002 and 2014**

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LIST OF FULL PAPERS THAT SERVED AS THE BASIS OF THE PHD THESIS

- I. **Újhelyi, M., D. Pukancsik, P. Kelemen, E. Kovács, I. Kenessey, N. Udvarhelyi, M. Bak, T. Kovács and Z. Mátrai**
Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol.* 2016; (42):1814 – 1820 **IF: 3.522**
- II. **Újhelyi M, Pukancsik D, Kelemen P, Kovács E, Kenessey I, Bak M, Kásler M, Kovács T, Mátrai Z**
Barriers to Organized Mammography Screening Programs in Hungary: A Questionnaire-based Study of 3 313 Women. *Anticancer Research* doi:10.21873/anticancerres.11xxx (in press) **IF: 1.937**
- III. **Mátrai Z, Kenessey I, Sávolt Á, Újhelyi M, Bartal A, Kásler M**
Evaluation of patient knowledge, desire, and psychosocial background regarding postmastectomy breast reconstruction in Hungary: a questionnaire study of 500 cases. *Med SciMonit.* 2014 Dec 12;(20):2633-42. **IF: 1,433**
- IV. **Újhelyi M, Pukancsik D, Kelemen P, Sávolt Á, Gődény M, Kovács E, Udvarhelyi N, Bak M, Polgár C, Rubovszky G, Kásler M, Mátrai Z**
Breast cancer care quality analysis of the National Institute of Oncology in Hungary according to the requirements of European Society of Breast Cancer Specialists (EUSOMA). *Orv Hetil.* 2016 Oct;157(42):1674-1682. **IF: 0.349**

OTHER PUBLICATIONS RELATED [TO](#) THE THEME OF THE THESIS

- V. **Pukancsik D, Kelemen P, Gulyás G, Újhelyi M, Kovács E, Éles K, Mészáros N, Kenessey I, Pálházi P, Kovács T, Kásler M, Mátrai Z.**
Clinical experiences with the use of ULTRAPRO® mesh in single-stage direct-to-implant immediate postmastectomy breast reconstruction in 102 patients: A retrospective cohort study. *Eur J Surg Oncol.* 2017 Jul;43(7):1244-1251 **IF: 3.522**
- VI. **Pukancsik D, Kelemen P, Újhelyi M, Kovács E, Udvarhelyi N, Mészáros N, Kenessey I, Kovács T, Kásler M, Mátrai Z.**
Objective decision making between conventional and oncoplastic breast-conserving surgery or mastectomy: An aesthetic and functional prospective cohort study. *Eur J Surg Oncol.* 2017 Feb;43(2):303-310. **IF: 3.522**
- VII. **Pukancsik D, Kelemen P, Sávolt Á, Újhelyi M, Kovács E, Zaka Z, Kásler M, Mátrai Z.**
Evaluation of clinicopathological findings and cosmetic outcome of 100 immediate postmastectomy breast reconstruction cases. *Orv Hetil.* 2016 Nov;157(46):1830-1838. **IF: 0.349**
- VIII. **Mátrai Z, Tóth L, Polgár C, Láng I, Gődény M, Sinkovics I, Horváth Z, Bidlek M, Udvarhelyi N, Bartal A, Sávolt A, Ujhelyi M, Kásler M.**
Sentinel lymph node biopsy after neoadjuvant chemotherapy in breast cancer *Magy Onkol.* 2011 Jun;55(2):73-84

1. INTRODUCTION

1.1 Breast cancer incidence and mortality

Breast cancer is one of the most prevalent malignancies and remains a main cause of cancer death for women in the developed world. Across Europe, there is an 8% chance for a woman to suffer from breast cancer before the age of 75 while sustaining a corresponding 2% chance of dying from the disease. The Hungarian National Cancer Registry recorded nearly 7,900 new cases of breast cancer in women, with more than 2,100 deaths in 2014.

1.2 Breast cancer screening

Most breast cancer deaths are caused by the advanced disease that has already spread to the lymph nodes or distant organs. An iimportant public health goal is to disclose breast tumours before they become symptomatic, optimally during stage 0. Therefore, many countries have implemented the organized mammography screening program (OMSP) in order to detect breast cancer at an early stage and reduce breast cancer mortality. The efficacy of mammography screening in preventing breast cancer deaths has been shown in randomized controlled trials, with a mortality rate reduction from 17% to 32%. The Hungarian nationwide OMSP for women 45-65 years of age, with a biannual screening interval was implemented in 2002.

1.3 Problems related to ~~Hungarian~~ constant breast cancer mortality rate in Hungary in the last decade

Despite theef well-organized decade-~~old~~ screening programme, while not statistically significant, the Hungarian incidence of breast cancer has been increasing since the implementation of the program. Again a crucial ~~issue~~problem is that ~~the incidence of breast cancer mortality rate~~ in Hungary ~~did not change~~has not changed significantly compared to UK and US between 2002 and 2014 despite theef OMSP.

Another ~~main public health issue is that the Hungarian stage based cross-sectional view of incidence based breast cancer cases has not been analysed~~ yet. To understand the cause of Hungarian constant mortality rate of the decade following ~~decade after~~ the implementation of OMSP there is a basic need ~~for~~investigating the quality cross-sectional view of breast cancer population. There is a **pronounced need to asses proportion of the early staged and advanced breast cancer cases**, which has not been examined properly yet.

Some recent studies have questioned the efficacy of early stage tumour detection on mortality reduction. Some authors believe that advanced breast cancer diagnosis and effective adjuvant therapy may play greater roles in reducing breast cancer mortality than screening. Other studies concluded that OMSP reduces breast cancer-related mortality~~due by~~ decreasing

the percentage of advanced breast cancer cases. ~~__reduces breast cancer related mortality.~~ Consequently the incidence of advanced tumour stages might represent one of the most relevant surrogate parameters for screening effectiveness. The clinical outcomes of early stage breast cancer cases ~~amongbetween~~ patients ~~whothat~~ underwent mammography screening and non-screened symptomatic patients had not been analysed before.

The participation rate ~~ion~~ OMSP is an important factor in breast cancer related mortality reduction. According to the WHO, the breast screening adherence rate should be at least 70% in order to decrease breast cancer mortality. Despite the fact that screening is invitational and free of charge, **the participation rate of the Hungarian OMSP has never reached the required minimum of 70% participation rate and it has not even reached 35** %, which could ~~have effect on~~ affect breast cancer related mortality.

There is an urgent **public health need to explore the participation barriers related to the OMSP in Hungary**. Associations between marital status, education level, socioeconomic characteristics, knowledge, and beliefs about breast cancer and mammography attendance have not been analysed yet in Hungary. It is important to have a valid instrument to answer this question. Neighbouring Central-Eastern European countries such as Austria, **Bulgaria, Latvia, Poland and the Czech Republic have similar living standards, and also present low breast screening coverage rates** comparable to those in Hungary so the problem of low participation rate is European / international.

2. OBJECTIVES ~~AIMS~~ OF THE THESIS

- 2.1 To evaluate quality cross-sectional view of stage based breast cancer incidence for the first time in Hungary.
- 2.2 To analyse the differences between screen-detected and symptomatic early stage ~~eases~~ breast cancer cases for the first time in Hungary.
- 2.3 To compare the overall and disease free survival between screen-detected and symptomatic early stage cases breast cancer cases for the first time in Hungary.
- 2.4 To examine the factors associated with women's screening behaviours, beliefs, and barriers leading to low adherence rates in the Hungarian organized mammography screening program me and to acquire information on the appropriate level of necessary intervention ~~necessary~~ to increase screening participation for the first time in Hungary.
- 2.5 To determine suitable information channels to reach the breast screening target population.

3. PATIENTS AND METHODS

3.1 ~~ANALYSIS THE STUDY OF BREAST CANCER CARE QUALITY~~ ~~ANALYSIS AT THE NATIONAL INSTITUTE OF ONCOLOGY~~ ~~ACCORDING TO~~BASED ON REQUIREMENTS OF EUSOMA

To answer the first question, database ~~has been~~was created and approved by the institutional ethical committee with the aim of evaluating the Hungarian quality cross-sectional view of stage based breast cancer incidence. According to a dedicated breast unit quality analysis ~~EUSOMA of~~ uniformed criteria of EUSOMA ~~a dedicated breast unit quality analysis~~ 119 clinico-pathological data of multimodality treated breast cancer cases were retrospectively analysed from the prospectively ~~kept~~led database of the National Institute of Oncology, Budapest (NIO) between 1 June 2011 and 31 May 2012.

According to the updated international European Society of Medical Oncology (ESMO) Clinical Practice Guidelines for diagnosis, treatment and follow-up, all patients received multimodality oncology treatments and a follow-up at the National Institute of Oncology during the investigation period. Early breast cancer was defined as tumours of not more than five centimetres diameter, with either non-palpable or palpable but not fixed lymph nodes and with no evidence of distant metastases. This corresponds to tumours that are pTis-2, pN0-1, M0 (Stage 0-IIB, except pT3pN0 tumours) as currently defined by the Union for International Cancer Control (UICC) TNM classification of malignant tumours.

Medical records and pathology reports were reviewed, and information on the HER-2, ER and PR status of the patients were collected from the institutional database retrospectively, as well as data on age at the diagnosis, disease grade, stage, and other clinical covariates. The TNM classification was defined by the American Joint Cancer Committee (AJCC) /UICC Breast Cancer Staging 7th Edition.

3.2 THE STUDY OF COMPARISON OF CLINICAL OUTCOME OF SCREEN DETECTED AND SYMPTOMATIC BREAST CANCER CASES

To analyse the differences and compare the overall and disease free survival between screen-detected and symptomatic early stage cases breast cancer cases this study method has been~~was~~ designed. The study was performed in accordance with the Research Ethics Committee of the NIO. A w~~W~~ritten informed consent was always obtained for data collection. The inclusion period was from 1 January 2002 through 31 December 2009. Data were collected from the prospectively led database of the NIO.

~~According to~~Based on the Hungarian guideline on mammography screening the target population was invited for breast screening regionally by invitation letters. Screened (SCR)

breast cancer patients discovered by the mammography screening program of the National Institute of Oncology were collected prospectively. The surely symptomatic (SYM) breast cancer patients with palpable tumours were collected randomly and prospectively from the institutional database by three researchers. The patients included [in](#) the SYM group were newly diagnosed breast cancer patients corresponding to a clinical stage from 0 to II/A with disease discovered by self-examination or via another physical breast examination by [their](#) general practitioner or gynaecologists within the inclusion period. The main reason for breast examination of SYM patients were the changes in the breast shape, skin retraction, nipple inversion, breast pain, a palpable lump, nipple discharge, unexplained redness, swelling or a lump around the collarbone or under the arm. Patients whose disease was discovered by screening were excluded from the SYM group. The database was ~~kept~~ prospectively [based on](#)~~according to~~ the standard methods of all disciplines involved in breast cancer diagnosis, treatment and follow-up, which included all relevant clinicopathological data of the SCR and SYM patients. Some of the patients were included in clinical trials in both groups but nobody has left undertreated.

According to the updated international European Society of Medical Oncology (ESMO) Clinical Practice Guidelines for diagnosis, treatment and follow-up, all patients received multimodality oncology treatments and a follow-up at the National Institute of Oncology. Medical records and pathology reports were reviewed, and information on the HER-2, ER and PR status of the patients were collected from the institutional database retrospectively, as well as data on age at [the](#) diagnosis, disease grade, stage, death, and other clinical covariates. The TNM classification was defined by the AJCC/UICC Breast Cancer Staging 7th Edition. Patients with missing information were excluded. All patients were followed up, and their status was checked from their medical records. All causes of death were included in the analysis of the overall survival (OS). Disease-free survival (DFS) was calculated from the number of months elapsed from surgery until a date of the diagnosis of the first locoregional or systemic recurrence. Patients' OS and DFS were calculated for the entire investigated period until the last visit. The OS and DFS between the SCR and SYM group were compared using the log-rank test and depicted using the Kaplan-Meier method. Qualitative variables are expressed as a number and percentage, and quantitative variables are expressed as the median with minimum and maximum values. For comparison of qualitative data, a chi-square test or Fisher's exact test was applied. Asymmetrical numeric data were analysed using a Mann-Whitney test. Statistical significance was confirmed when P values were <0.05. Data analysis was performed using Statistica 12.0 (Statsoft, Tulsa, OK).

3.3 THE STUDY OF INVESTIGATION OF THE SOCIOECONOMIC FACTORS AND BARRIERS ASSOCIATED WITH LOW ADHERENCE RATE ON MAMMOGRAPHY SCREENING PROGRAM [ME](#) VIA QUESTIONNAIRE

This study was performed in accordance with the Research Ethics Committee of the NIO which conforms to the provisions of the Declaration of Helsinki. The study received non-financial administrative support from the Hungarian AVON Cosmetics Company and the Mellrákinfo advocacy group. A cross-sectional survey was designed to examine women's screening behaviour, beliefs, and barriers to OMSP. The Hungarian breast screening target population of women 45-65 years of age were interviewed anonymously using web-based and printed questionnaires containing 15 structured questions. The questionnaire was designed to assess and report on the psychometric and demographic properties of barriers leading to low participation rates. The sample population was reached *via* e-mail and Facebook campaign through web-based questionnaires by the Hungarian AVON Cosmetics Company. Printed forms were sent by mail and distributed at local social functions by the Mellrákinfo advocacy group and Hungarian AVON Cosmetics Company. To ensure that the study sample was representative of the screening population, only surveys from women 45-65 years of age were accepted. Answering the survey questions was voluntary and anonymous. The data protection law was followed and respected. Questionnaires with unreadable or unclear answers were excluded from the analysis.

To examine the appropriate information channels to reach the breast screening target population "Evaluation of patient knowledge, desire, and psychosocial background regarding postmastectomy breast reconstruction in Hungary" [a](#) questionnaire study was used. The questions focused on the decision-making process, emotional impact of the malignant disease, breast loss, attitudes toward reconstruction, changes in family life and social connections, sexual well-being, importance of environmental conditions, patient knowledge regarding breast reconstruction, **sources of information**, and desire for an immediate or delayed procedure. Answering the survey questions was voluntary. The questionnaire and the study structure were approved by the institutional ethics committee. The results of ~~sources of~~ [information gathering](#) on breast reconstruction and fear of losing breast or breast cancer in context of age and education were used in our investigation. All answers were statistically analysed in the context of marital status, educational level, and type of residence using chi-square test; p values <0.05 were considered to be significant. Statistical analysis was performed using PAST 1.86 and Statistica 12.0 (StatSoft, Tulsa, OK, USA).

4. RESULTS

4.1 ANALYSIS OF BREAST CANCER CARE QUALITY AT THE NATIONAL INSTITUTE OF ONCOLOGY BASED ON REQUIREMENTS OF EUSOMA

~~4.0 THE STUDY OF BREAST CANCER CARE QUALITY ANALYSIS OF THE NATIONAL INSTITUTE OF ONCOLOGY ACCORDING TO REQUIREMENTS OF EUSOMA~~

During the study period 906 surgical procedures were performed with the indication of breast malignant, benign or recurrent tumours. The average age was 59 years (range 14-91 years). In case of benign lesions, recurrent tumours the clinical stage was not determined.

The proportion of clinical early stage primary breast cancer cases (Stage 0-IIIB, except T3N0) was 91.29 % (n=755) that decreased to 79.25 % (n=661) after surgical treatment based on ~~due~~ the postoperative pathology assessment (the data of pathological stage were used after primary chemotherapy). 819 (90.4 %) patients received primary surgical procedure and 87 (9.6 %) patients received primary chemotherapy.

The BCS rate was 64% (n=557) and the mastectomy rate was 36 % (n=311) in case of primary surgical treatment in malignant diseases. For 560 (67.4 %, recurrent and benign cases excluded) patients were sentinel lymph node biopsy (SLNB) performed and the incidence of negative lymph nodes was 76.4 % (n=428) and positive was 23.6 % (n=132). The average of removed SLNs was 1.43 (range 1-7). In total for 388 (46.7 %, recurrent and benign cases excluded) patients axillary lymph node dissections (ALNDs) were performed. The average of removed lymph nodes via ALND was 12.67 (range 2-33). The percentage of negative lymph nodes was 51.5 % and 46.7 % for positive lymph nodes. Proportion of patients with invasive cancer and ALND was performed with at least 10 lymph nodes examined was 92.3 %. The average ~~of~~ pathological tumour size was 27.4 mm (range 0-210 mm). The incidence of benign lesions was 4.2 % (n=38), in situ carcinoma was 7,6 % (n=69), invasive carcinoma was 87.4 % (n=791), non-epithelial tumour was 0.2 % (n=2), other was 0.3 % (n=3) and undetermined was 0.3 % (n=3). The incidence of vascular invasion was 29.4 % (n=266). According to the breast cancer subtypes the number of Luminal-A type tumours were 354 (40.8 %), Luminal-B type tumours were 315 (36.2 %), triple negative (TN) cases were 116 (13.4 %) and HER-2 over-expressed tumours were 16 (1.8 %). Proportion of patients with invasive cancer who received postoperative radiotherapy after surgical resection of the primary tumour and appropriate axillary staging/ surgery in the framework of BCT was 94.7 % (n=460). Proportion of patients with endocrine sensitive invasive carcinoma who were offered

endocrine therapy was 99.8 % and the proportion of patients with ER/PR negative invasive tumours ≥ 2 cm and/or regional node positive disease, who received adjuvant chemotherapy, was 98.9 %. ~~According to~~Based on EUSOMA quality indicators the breast cancer care of the NIO is eligible.

4.14.2 THE STUDY OF COMPARISON OF CLINICAL OUTCOME OF SCREEN DETECTED AND SYMPTOMATIC BREAST CANCER CASES

During the inclusion period the NIO as an accredited regional mammography screening centre covered around 2% of the Hungarian target population. During that period 47,718 women were examined by organized nationwide mammography screening programme, and a total of 298 patients were diagnosed with breast cancer, which formed the SCR group.

For the SYM group, a total of 331 patients were collected randomly from 5351 symptomatic breast cancer patients during the same period. Patients with missing information or who were lost to follow-up were excluded. In total, we analysed data from 279 patients in the SCR group and from 316 patients in the SYM group. The median follow-up was 65 months (range: 13-130 months) for the SCR group and 80 months (range: 18-150 months) for the SYM group. The SCR group presented a significantly less median pathological tumour size than the SYM group ($P < 0.00001$, Mann-Whitney test), and significant differences were observed using the pT classification ($P = 1.6 \times 10^{-7}$, Chi-square test).

The incidence of pTis was significantly higher in the SCR than in the SYM group ($P = 7.2 \times 10^{-5}$). Significant differences in the clinical characteristics were observed ~~according to~~based on breast cancer subtype ($P = 0.003$). The number of triple negative (TN) cases was higher in the SYM group. The number of Luminal-A type tumours was statistically higher in the SCR group than Luminal-B type tumours compared to the SYM group. The incidence of regional lymph node metastasis was significantly lower in the SCR group ($P = 0.0006$). **The incidence of distant metastases was significantly higher in the SYM group than in the SCR group** for the entire investigated period ($P = 0.013$). The incidence of chemotherapy was 17% greater in the SYM group than in the SCR group ($P = 2.9 \times 10^{-5}$, Chi-square test). The BCS rate was 75.9% (n=211) in the SCR group and 74.7% (n=236) in the SYM group ($P = 0.79$; chi-square test). Significant differences were not observed for the type of surgery, in RT and in HT.

The SCR group did not exhibit significantly better OS rates than the SYM group ($P = 0.717$; log-rank). The SCR group did not exhibit significantly better DFS rates than the SYM group. ($P = 0.081$; log-rank).

4.24.3 THE STUDY OF INVESTIGATION OF THE SOCIOECONOMIC FACTORS AND BARRIERS ASSOCIATED WITH LOW ADHERENCE RATE ON MAMMOGRAPHY SCREENING PROGRAM [ME](#) VIA QUESTIONNAIRE

A total of 58,839 questionnaire links were sent *via* e-mail, 21,501 links were sent by Facebook campaign, 500 printed questionnaires were mailed, and 293 questionnaires were completed at social events. The online response rate was 18.32% and 15.2% for mailed forms. A total of 3,313 women between 45 and 65 years of age completed the questionnaire. The majority of responders were married, had completed secondary school or lived in provincial towns. A total of 1,042 women responded to the questions regarding their reasons for not undergoing breast screening. Briefly, the main barriers to participation in the OMSP were work absenteeism (18.9%), fear of painful examination (18.39%) and false beliefs regarding mammography screening (14.94%). Of survey respondents, 13.92% of those who did not attend the OMSP underwent opportunistic screenings; 11.11% answered that their designated screening centre (DSC) was too far from their home. Only 5.49% of those who did not participate in screening reported not having enough information on mammography screening and 4.85% answered that it was too expensive to get to the screening centre. Fear of breast cancer diagnosis prevented 3.58% of non-participants from attending the OMSP, and 2.04% did not participate for fear of mastectomy.

Based on patient marital status and place of residence, the responses were analysed to compare a number of criteria. There was a significant association ($P=0.029$) between the responders' marital status and OMSP attendance, with married women attending breast screenings more frequently than single women. There was also a significant difference ($P=0.038$) between the place of residence and the frequency of mammography examination: women from the capital or from provincial towns more frequently underwent and were more compliant with screening than women who lived in villages. There was a significant association between the responders' residence and the distance from the DSC ($P<0.0001$): women living in the capital or provincial towns had better access to their DSC than those living in villages.

There was a significant association between the place of residence and the travel expenses incurred to reach the DSC ($P=0.009$). Compared to those living in the capital, women in rural populations reported financial difficulties in travelling to their DSC. Female residents of the capital were more likely to choose opportunistic screening compared to those living in rural areas ($P=0.005$). Barriers such as lack of information on mammography

screening ($P=0.001$) and fear of breast loss ($P=0.003$) were also significantly associated with lower education level. Educated women were less likely to fear breast cancer and more likely to have ~~sufficient~~adequate information regarding mammography screening compared to interviewed women with lower levels of education. In the current study, married marital status appeared to be a protective factor against barriers such as feeling embarrassed about the examination ($P=0.0002$) and expenses incurred to reach the DSC ($P<0.0001$).

According to “Evaluation of patient knowledge, desire, and psychosocial background regarding postmastectomy breast reconstruction in Hungary” questionnaire study a higher proportion of patients under age 35 gained information over the Internet, while in older age groups the surgeon was the source of information. Surgeons were the primary source of information for most patients ($P=2.9\times 10^{-5}$). However, if the surgeon and Internet resources were compared with the exclusion of the other sources (e.g., fellow patients, TV, radio, and newspapers), the Internet was the most effective forum for orientation ($P=0.019$). As expected, those with higher educational backgrounds were the most informed ($P=1\times 10^{-5}$).

5. DISCUSSION

5.1 ANALYSIS OF BREAST CANCER CARE QUALITY AT THE NATIONAL INSTITUTE OF ONCOLOGY BASED ON REQUIREMENTS OF EUSOMA

~~5.0 THE STUDY OF BREAST CANCER CARE QUALITY ANALYSIS OF THE NATIONAL INSTITUTE OF ONCOLOGY ACCORDING TO REQUIREMENTS OF EUSOMA~~

Applying minimum requirements and quality indicators is essential to improve organisation, performance and outcome in breast care. The evaluation of institutional breast cancer care ~~according to~~based on EUSOMA quality indicators provides quality representative cross-sectional view of Hungarian stage based breast cancer incidence. The limitation of this study is the underrepresented proportion of Stage IV breast cancer cases.

Despite ~~the fact that~~of almost 10 % of patients received primary chemotherapy, the study presented relatively low amount of early stage breast cancer cases. According to the postoperative pathological assessment the proportion of primary early stage (Stage 0-IIB, except T3N0) breast tumour cases decreased from 91.29 % clinical stage rate to 79.25 % pathological stage rate.

According to our statistics Hungarian breast cancer cases represented higher tumour size, tumour stage and percentage of positive lymph nodes compared to Swedish and US statistics. This quality representative cross-sectional view of stage based breast cancer cases

suggests that ~~relatively higher mortality rate in Hungary~~~~Hungarian relatively higher mortality rate~~ could be associated to higher tumour stages at the diagnosis. Further investigation is needed to improve the knowledge regarding the representative cross-sectional view of stage based breast cancer cases to allow appropriate corrective actions leading to improvements in patient care.

5.15.2 THE STUDY OF COMPARISON OF CLINICAL OUTCOME OF SCREEN DETECTED AND SYMPTOMATIC BREAST CANCER CASES

Randomized controlled trials (RCTs) that have evaluated mammography screening have demonstrated a reduction in breast cancer mortality, but unfortunately, the randomized trials are uninterpretable in the modern era, as they were conducted before the era of breast cancer units, before IHC evaluation of receptor statuses to define breast cancer IHC surrogate subtypes, and before the use of modern chemotherapy regimens, given that biological and hormonal therapy are now widely used in breast cancer treatment.

Therefore, the impact of mammographic screening on reducing breast cancer mortality has become an intensively researched topic. A few recent studies have questioned the impact of early detection on mortality reduction and cast doubt on costs for a procedure that yields minimal benefit.

The question arises as to the reason that no differences in OS or DFS were found between the SCR and SYM subgroups. There is a trend of the DFS in favour of the SCR group but it has not reached the statistical significance. The amount of distant metastases was higher in SYM group (17%) compared to SCR group (10%) and as the metastatic breast cancer is an incurable disease, probably, a longer follow-up period might show the statistical significance of DFS and/or OS in favour of the SCR group. But since metastatic breast cancer is still generally an incurable disease with 1 or 2-year average OS, the long term follow-up data are limited. We assume that early breast cancer detection is potentially not the main factor being responsible for reducing mortality in breast cancer. Modern multimodality cancer treatments may play a major role in breast cancer survival. In our investigation, the incidence of chemotherapy was 17% greater in the SYM group than in the SCR group. Adjuvant therapy could be translated into improved outcomes for patients in the SYM group, but it is important to investigate the short and long-term impact on quality of life (QOL) of systemic therapy.

A limitation of this study is the follow-up period. After 10 years of a national screening program, a mortality analysis would be valuable in evaluating the program's effectiveness. In our investigation, the median follow-up time of 65 and 85 months may be

too short to show the real advantages of the screening program^{me}. However, in RCTs, there was a reduction in mortality after 4 years, with an increasing effect up to 10 years. Another limitation of our study is that some of the women in the SYM group might have undergone opportunistic screening, potentially resulting in an underestimation of the benefit of screening.

5.25.3 THE STUDY OF INVESTIGATION OF THE SOCIOECONOMIC FACTORS AND BARRIERS ASSOCIATED WITH LOW ADHERENCE RATE ON MAMMOGRAPHY SCREENING PROGRAM^{ME} VIA QUESTIONNAIRE

To improve breast cancer screening attendance among Hungarian women, it is imperative to have a valid instrument for exploring and understanding the factors associated with their screening behaviour. Our questionnaire has the appropriate psychometric properties to provide insights into tailor-made strategies designed to address the needs of the screening target population.

Our findings highlight that the main reasons for not attending the OMSP were work absenteeism, fear of pain associated with the examination, and false beliefs regarding mammography screenings. ~~To reduce~~Reducing barriers such as work absenteeism, a paid day off might increase women's willingness to participate in the OMSP. It would be important for employers also to participate in helping their employees utilize preventative measures.

According to the results of our questionnaire study, women with lower levels of education - mainly those who completed only primary school (were less likely to have sufficient information on breast screening, and they were more likely to fear of mastectomy compared to women with higher levels of education) mainly those who had completed secondary school or university. According to the questionnaire study "Evaluation of patient knowledge, desire, and psychosocial background regarding postmastectomy breast reconstruction in Hungary" education level and awareness residence showed significant associations. There is a need for a multi-pronged strategy to inform and educate women about breast awareness and bring about a behavioural change.

According to the "Evaluation of patient knowledge, desire, and psychosocial background regarding postmastectomy breast reconstruction in Hungary" questionnaire study the source of information on breast reconstruction was correlated with ^{the} level of education and most information coming from the medical staff, doctors or from the Internet. Consequently, the patient navigator system, employing prevention nurses, general practitioners or other specialties could decrease the actual willingness₂ and the information

channels [such as due](#) the internet could decrease the future target population's willingness participation on breast screening by offering education of breast awareness.

Fear of pain in the examination was the second most common reason for avoiding mammography examinations. According to a previous study, discomfort was reduced when women were provided with written or verbal information, and when a breast cushion was used. Providing verbal or written information, as well as supporting women during the examination, is a simple and easily achievable intervention and can help to reduce pain during screening mammography. Use of alternative breast compression strategies or premedication with acetaminophen has not been reported to significantly reduce breast pain and discomfort.

The non-participants described other barriers such as long waiting times in clinics, unorganized DSCs, dissatisfaction with facility staff, difficulties in changing scheduled mammogram appointments, and a lack of concern about breast cancer. Only two-thirds of responders had received an Invitation Letter for Screening (ILS) in the previous 2 years, which is below the minimum 70% adherence rate required by the WHO to reduce breast cancer mortality. Further investigations are needed to determine the causes for the lack of receipt of ILS.

Married status appeared to be a protective factor against barriers, including embarrassment regarding the examination, financial challenges associated with travelling to the DSC and avoiding breast screening. There is [a](#) strong positive association between relationship and participation behaviour in mammography screening, which is also supported by other authors. Excessive distance to reach the DSC was the fifth most frequent barrier to breast screening. Statistical comparative analyses indicated that living in villages or in single households were associated with lower participation rates because of financial difficulties and problems in travelling long distances to the DSC. Well-situated units with advanced promotion about public transportation and parking facilities may encourage greater uptake. Rural women require special attention because of their lower participation rates in mammography examination. Patient navigation, free public transport for the day of screening, specialized round-trip bus lines, or mobile breast screening units may help to overcome these barriers. The strength of our survey study was that the Hungarian mammography screening target population 45-65 years of age was interviewed regardless of whether the participants had received an ILS.

6. CONCLUSIONS

Early tumour detection is very important in breast cancer treatment and in clinical outcomes. As breast cancer mortality depends on the stage of the diagnosis and oncological outcomes are generally more favourable during early stages of disease before symptoms appear in symptomatic diseases. Despite mammography screening, with the aim of mortality reduction, the incidence of breast cancer mortality rate in Hungary has not changed significantly since 2002.

Answer of the Answering question 2.1. question of the thesis: According to the evaluation of institutional breast cancer care ~~according to~~ based on EUSOMA quality indicators Hungarian women with breast cancer represented higher tumour stage compared to western countries. The percentage of early stage breast cancer cases was lower compared to US and Sweden. This quality representative cross-sectional view of stage based breast cancer cases suggests that the Hungarian relatively higher mortality rate in Hungary could be associated to higher tumour stages at the diagnosis.

Answering questions 2.2. and 2.3. of the thesis: Answer of the 2.2. and 2.3. questions of the thesis: According to the comparison of SCR and SYM groups patients with non-palpable early stage breast cancers diagnosed via population-based breast screening ~~had not~~ did not have better survival rates than those with symptomatic cancers. The reason why there were no differences in OS and DFS remains unclear. The potential drawback of symptomatic early stage tumours compared to non-palpable early stage tumours could be equalized by modern breast cancer molecular subtype-based personalized multimodality oncology treatments. There is a trend of the DFS in favour of the SCR group but it has not reached the statistical significance. The amount of distant metastases was higher in SYM group compared to SCR group and as the metastatic breast cancer is an incurable disease, probably, a longer follow-up period might show the statistical significance of DFS and/or OS in favour of the SCR group. Further investigations and longer follow-up are needed to answer these questions.

The thesis does not suggest that mammography screening does not reduce breast cancer mortality, but supports the evidence that mammography screening reduces the rate of advanced breast cancers. As breast cancer deaths are caused mostly by an advanced disease that has already spread to the lymph nodes or distant organs, an important public health goal is to increase adherence rate on mammography screening. Increased knowledge regarding the barriers to mammography screening provides information to extend our knowledge ~~one of~~ breast cancer screening and effective treatment in Central-Eastern European countries.

Answering question 2.4. of the thesis~~Answer of the 2.4. question of the thesis:~~ Our findings highlight that the main reasons for women to not attend OMSP included work absenteeism, fear of painful examination, lack of information, and false beliefs regarding mammography screenings. ~~To reduce~~Reducing barriers such as work absenteeism, a paid day off may increase women's willingness to attend the OMSP. In order to increase screening compliance, environment and facility staff ~~are~~is very important factors associated with the women's satisfaction and therefore their participation in future screenings. A patient navigator system employing prevention nurses could help to organize an effective screening programme by offering education on breast awareness, screening invitations, and managing appointments for biennial mammograms. Married women more regularly receive breast screening compared to single women; marital status seems to be a protective factor against barriers like embarrassment and financial difficulties that may prevent travelling to the DSC. Single women and rural female residents require special attention because of their lower participation rates ~~infer~~for mammography exams. In these populations, patient navigation, free public transportation, specialized round-trip bus lines, or mobile breast screening units may help to decrease these screening barriers.

Answering question 2.5. of the thesis: Answer of the 2.5. question of the thesis: In the following, using applicable information channels as the internet for the future screening target population and the patient navigation system, employing prevention nurses, general practitioners or other specialties could provide feasible breast cancer awareness for the current~~actual~~ screening target population in conclusion of increased breast screening participation.

ÖSSZEFOGLALÁS: A rosszindulatú emlődaganatok korai felfedezése jelentősen befolyásolja az onkológiai kezelést és a túlélést. A korai stádiumban, még tünetmentesen felfedezett emlőrákok esetében kedvezőbb az onkológiai kimenetel, ellentétben a lokálisan előrehaladott vagy már távoli áttétet adó esetekkel. Mortalitást csökkentő célja ellenére a szervezett lakossági mammográfiás szűrés érdemben nem csökkentette a halálozást Magyarországon.

Válasz az első célkitűzésre: A magyar emlőrák populáció EUSOMA egységes nemzetközi kritériumrendszere szerint végzett keresztmetszeti vizsgálata alapján a korai emlőrákok aránya kisebb volt összehasonlítva az Egyesült Államokkal vagy Svédországgal.

Válasz a második és a harmadik célkitűzésre: A vizsgáltunk alapján a mammográfiás emlőrák szűrés nem csökkentette a mortalitást a korai emlőrákos betegek esetében összehasonlítva a szimptomatikus korai emlőrákos esetekkel. A szimptomatikus emlőrákos betegek túlélését növelő faktorok között szerepe lehet a korszerű személyre szabott adjuváns terápiának és diagnosztikus modalitásoknak, melyek képesek kiegyenlíteni a későbbi diagnózis miatt kialakult különbségeket. Hogy választ kapjuk arra, hogy miért nem volt különbség a teljes és a betegségmentes túlélésben a két csoport között további vizsgálatokra van szükség. Vélhetően hosszabb utánkövetéssel a szűrésen kiemelt és a szimptomatikus csoportok között a teljes és/vagy betegségmentes túlélésben különbség adódhat a szűrési csoport javára. A kérdés megválaszolására további vizsgálatok szükségesek.

Válasz a negyedik célkitűzésre: A mammográfiás szűréstől való távolmaradás leggyakoribb okaként a munkahelyi hiányzást jelölték meg, továbbiakban gyakori okként a félelem a fájdalmas vizsgálatról és károsnak tartott mammográfiás vizsgálat került megnevezésre. A részvételi arányok növeléséhez elengedhetetlen a megfelelő információ biztosítása és oktatás az emlőrák szűrés fontosságáról és elérhetőségéről. Továbbá egy szervezett betegirányító rendszer, könnyen elérhető szűréssel kapcsolatos információk felületek, szabadnap biztosítása, elérhető távolságban lévő szűrőközpontok kialakítása a vidéki lakosság számára és a szűrésre ingyenes tömegközlekedés biztosítása javíthatja a mammográfiás szűréseken való részvételt.

Válasz az ötödik–negyedik célkitűzésre: Az aktuális szűrésre behívott célcsoport az egészségügyi személyzettől, illetve kezelőorvosától szerzi a legtöbb információt, a jelenleg fiatalabb a jövőbeli szűrésre behívásra kerülő célcsoport pedig az internetről gyűjti azt. A megfelelő információs csatornák célzott alkalmazásával javítható a szervezett lakossági mammográfiás szűréseken való részvételi arány.

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