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Prevalence of PgR, ER and HER2+ receptors among women with breast cancer by age in Poland

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Introduction. Prevalence of estrogen (ER), progesterone (PgR) and human epidermal growth factor receptors (HER2) vary by age among women with breast cancer (BC). Such variation has a large significance for the prognosis and treatment process. This study characterizes the prevalence of breast cancer subtypes by age in a hospital sample in Poland.
Material and methods. The study population included 735 women with BC aged 27–91 years old (ICD-10: C50) and treated in the years 2009–2011 in the Military Institute of Medicine in Warsaw. Subjects were divided into 2 age categories — 27–44 and 45+ — which included 66 (9%) and 669 (91%) women respectively. In each group prevalence of PgR, ER and HER2+ receptors was investigated.
Results. In both age groups the most frequent BC subtype was luminal A (hormone dependent BC — with PgR and ER receptor expression) — 27–44 years old — 44% and 45+ years old — 56%. The lowest number of cases in the age group 27–44 was luminal B (triple positive breast cancer) — about 15% of cases and for 45+ age group — HER2+ BC — about 11%.
Discussion. Performed research shows relationship between growing age of diagnosis and presence of more desirable features of BC among women aged 55 and more, such as expression of steroid receptors or lack of expression of HER2 receptors, which is a good prognostic indicator for treatment outcomes. In the same time, many studies suggest that more aggressive types of breast cancer (basal-like — triple negative) are more characteristic for younger age groups (under 45 y.o. and younger women in perimenopausal age). Same results have been obtained in own study.
Conclusions. A high incidence of BC in older age groups (45+) and more frequent occurrence of aggressive types of BC among younger women (27–44 years old) indicate the need to educate women from both age groups about risk factors and early symptoms of the disease. As we still have not recognized all BC risk factors, education about well-known agents, such as alcohol intake, overweight and obesity, play significant role in decrease of BC incidence and mortality.

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Key words: breast cancer, PgR, ER, HER2, menopause, primary cancer prevention

Introduction

Mammary gland cancer, commonly called breast cancer (BC) is the most frequent malignant cancer among women in developed and developing countries [1]. In Poland BC incidence has doubled during last three decades. According to the latest Polish National Cancer Registry data in Poland in 2015, there were 18 106 cases of BC (age standardized rate/100 000 — 90.9) and 6319 deaths caused by BC (age standardized rate/100 000 — 31.79). BC is the most common malignant cancer among women in Poland and is the second cause of cancer mortality (after lung cancer, which is the leading cause) [2].

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The clinical characteristics of BC have significant importance for the treatment process and also for further prognosis [3–5]. There are four main subtypes of BC, which were featured in view of expression or lack of expression of specific receptors in BC cells:

— Luminal A with expression of steroid receptors — estrogenic — ER and progesteronic – PgR and lack of expression of HER2 receptor (human epidermal growth factor),
— Luminal B with simultaneously expression of steroid receptors and HER2 receptor (triple positive breast cancer),
— HER2+ with HER2 receptor expression (with simultaneously lack of steroid receptors expression),
— Basal-like with lack of expression of steroid receptors and HER2 receptor (triple negative breast cancer) [6, 7].

Expression of steroid receptors ER, PgR and receptor HER2 is a relevant predictive and prognostic factor in BC. In case of disease with expression of ER and PgR receptors, patients have better prognosis because of more effective response to treatment. Increased expression of these receptors is favorable — it gives better response to hormonal therapy. Lack of ER and PgR receptors leads to increased risk of metastasis. The activity of HER2 receptor contributes to intensified BC development. HER2 receptor is responsible, among others, for multiplication of cells, restriction of apoptosis and causes intensified angiogenesis. Patients with HER2 receptor expression have worse prognosis of the course of the disease — there is a higher risk of metastasis occurrence, higher malignancy and relapse of the disease. This is also a premise for using monoclonal antibodies treatment [8, 9]. BC in which presence of steroid and HER2 receptors is not stated is characterized by the worst prognosis and severe course with frequent relapses. For this group of women targeted treatment is not available [10]. Among BC patients prevalence of PgR, ER and HER2 receptors is diverse (this also applies to their absence). The table below (Tab. I) shows the prevalence.

Material and methods

The material for the study was clinical data on prevalence of steroid and HER2 receptors among women with BC (ICD-10: C50) in the age groups 27–44 and 45+ years old. Tissue sections were taken from women with BC, treated in the years 2009–2011 in the Military Institute of Medicine in Warsaw, Poland. Obtained biological material has been stained using immunohistochemistry methods and all personal data of the patients has been anonymized. Primary research group consisted of 1116 patients in the age of 27–91 years old. However, because of the fact that in the diagnostic process in some cases there were doubts about the expression of specific receptors, these cases have not been included in the final research group that consisted of 735 patients. The group has been divided into 2 age categories: 27–44 and 45+ years old which consisting of 66 (9%) and 669 (91%) women respectively. The criterion for group division was perimenopausal age — 45 years old. Additionaly data have been divided into 4 following groups by hormone profile:

— presence of progesterone and estrogen receptors with lack of HER2 receptor (luminal A),
— presence of progesterone, estrogen and HER2 receptors (luminal B),
— lack of progesterone and estrogen receptors with presence of HER2 receptor (HER2+),
— lack of progesterone, estrogen and HER2 receptors (basal-like).

Data were also grouped by age into 14 five-years age ranges: 20–24, 25–29, …, 80–84, 85 years and more. Data were analyzed with the use of Microsoft Excel Software ver. 15.22 (160506) and Jointpoint Trend Anylysis Software ver. 4.5.0.1. Level of statistical significance was set to alpha = 0.05.

Table I. Prevalence of PgR, ER and HER2+ receptors in breast cancer [2], [10], [11]

Receptor	Estimated prevalence in BC
ER	80%
PgR	40–70%
HER2	20–30%
– (basal-like breast cancer)	15–20%

Limitations of the study

As the study is based on preliminary data only, some limitations have occurred. We did not analyse all of the biological aspects of BC, such as HER2 amplification or Ki67 expression and others, but only the chosen ones. Moreover, we decided to limit the size of the sample and include only fully confirmed cases.

Results

In the age group 27–44 years old, 15.2% of women had BC with expression of ER, PgR and HER2 receptors (luminal B) which constituted the lowest percent of all BC types in analysed age group. 16.7% patients had breast cancer with HER2 receptor expression (HER2+ without steroid receptors expression). Further, 24.2% of women had basal-like BC without ER, PgR and HER2 receptors expression. The biggest group constituted women with BC with expression of ER and PgR receptors, without HER2 receptor expression (luminal A) — 43.9%.

In the age group 45 years old and older, the lowest percent was breast cancer with HER2 receptor expression — 11,1% of women. Triple negative breast cancer constituted 15,1% of all cases in this age group, triple positive — 18%. The most frequent was breast cancer with steroid receptors expression (PgR, ER) — 55,8% (Fig. 1).

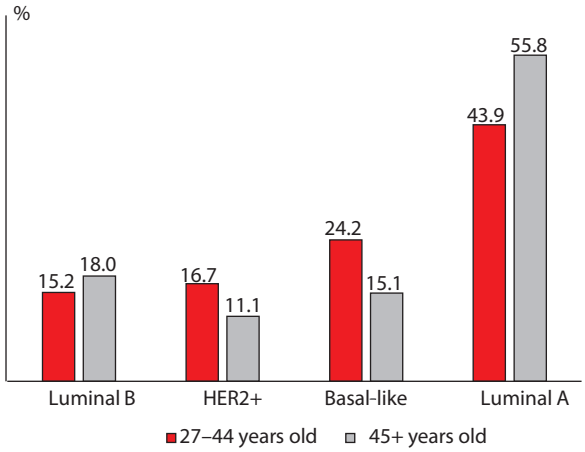

Figure 1. Breast cancer prevalence by hormone profiles in the age groups 27–44 and 45+ years old

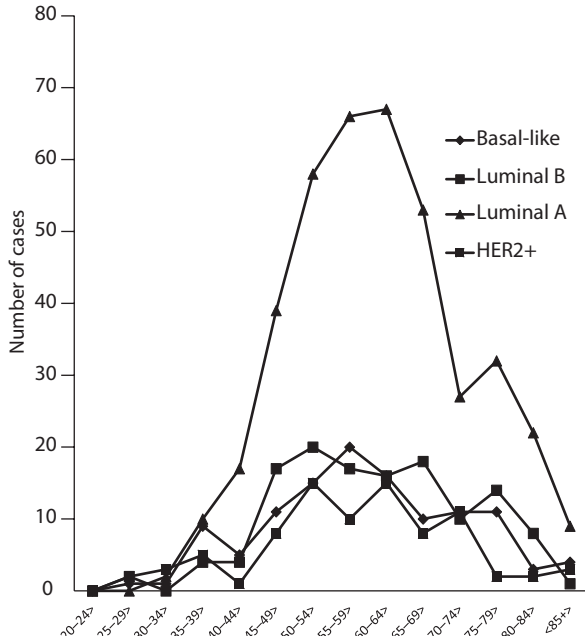

Figure 2. Hormone profile of women with breast cancer in the age of 27 years old and older

In the analyzed two age groups there is an analogy concerning the most frequent type of breast cancer. Luminal A BC (with ER and PgR expression) was identified among the highest percent of women in the age group 27–44 years old — 43.9% and in the age group 45+ — almost 56%. Luminal B BC occurred among the lowest percent of women in the age group 27–44 years old — 15.2%, meanwhile in the age group 45+ the lowest number was BC with HER2 receptor expression (without steroid receptors expression) — 11.1%.

Considering all BC types in all investigated age groups, BC occurs most often among women between 45 and 60 years old. The biggest difference in the number of cases was observed between luminal A and other types of this disease. In case of other three types of BC (basal-like, luminal B and HER2+) in the age group 27–91 years old, the difference in the number of cases between these groups was not significant (Fig. 2).

Prevalence of basal-like BC increases with women's age up to the age of 55. Average percentage change in subsequent 5-years age groups was 7.3% [95% CI = (1.9; 13.1)]. After the age of 55 prevalence of this type of BC decrease. Average percentage change (APC) in the 5-years age groups was 4.9% [95% CI = (–8.9; –0.7)].

Luminal B BC prevalence increases with age up to the age of 50. Average percentage change in subsequent 5-years age groups was 12.1% [95% CI = (4.3; 20.4)]. After the age of 50 prevalence of this type of BC did not change at the assumed significance level: APC = 3% [95% CI = (–6.1; 0.2)].

Prevalence of luminal A BC increases with women's age up to the age of 45. APC in 5-years groups was 19.6% [95% CI = (5.9; 35.1)]. Prevalence of this type of BC stabilizes among women in the age group 45–60 years old with APC = 6.5% [95% CI = (–9.8; 3.1)] in subsequent 5-years age groups.

In the investigated group, prevalence of BC with HER2 expression receptor increases with age up to the age of 60. APC in subsequent 5-years age group was 5.7% [95% CI = (1.2; 10.3)]. After this age (60 years old) prevalence of HER2+ BC decreases. APC in 5-years age groups was 7.7% [95% CI = (–14.8; –0.1)].

Discussion

In our study the most frequent type of BC regardless of age was luminal A BC (hormone-dependent breast cancer with expression of ER and PgR receptors (and without HER2 expression). The results indicate that this type of BC is more common among women aged 45 and older (in perimenopausal and postmenopausal age), affecting almost 60% of women with BC, while in the age group 27–45 it was about 44% of women. Dębska and Potemski reported similar conclusions, finding that 75% of women with diagnosed BC have steroid receptors expression. Additionally, this regularity is

Table II. Breast cancer by age group and hormone profile

Age group	Number of cases (n)	Luminal B	HER2+	Basal-like	Luminal A
20–44	66	10	11	16	29
45+	669	121	74	101	373

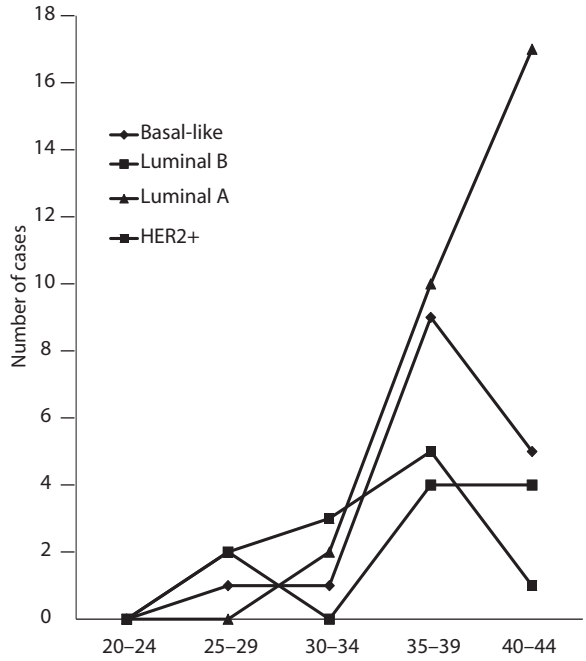

Figure 3. Hormone profile of women with breast cancer in the age group 20–44 years old

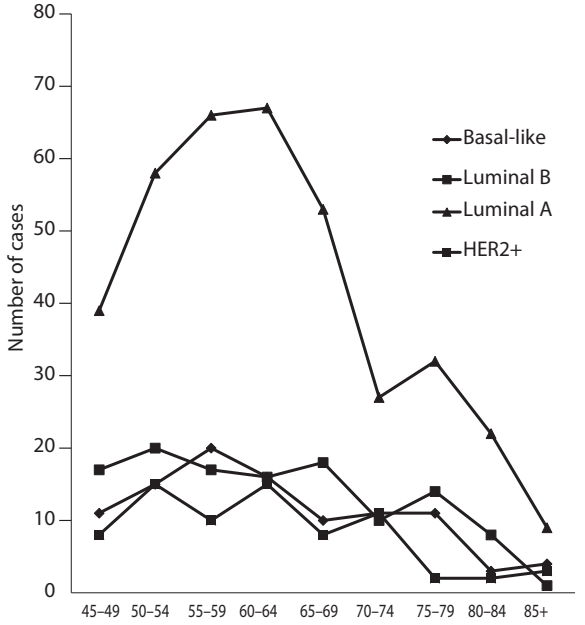

Figure 4. Hormone profile of women with breast cancer in the age group 45 years old and older

more characteristic for women in postmenopausal age [12]. De Kruijf et al. also show a relationship ($p < 0.02$) between ER, PgR receptors expression and age (research group — 822 women with BC) [13]. Some research indicates a relationship between a woman's age at BC diagnosis time and their prognosis for recovery. Diab et al. show in their study performed on two cohorts of women with BC (50 828 and 256 287 patients) a relationship between increasing age of diagnosis and the presence of more desirable features of BC among women aged 55 and older, such as expression of steroid receptors or lack of expression of HER2 receptors, which is a good prognostic indicator for treatment outcomes [14].

According to Kolečkova's et al. study, which investigated BC tissue from 632 women in terms of presence of steroid receptors, HER2 receptor expression and corelation with age, the most agressive BC types (basal-like and HER2+ BC) are more prevalent in younger age groups — 20–39 years old women. This study also shows a correlation between occurance of estrogene receptors — ER and age of women with BC ($p < 0.0001$) [15]. De Kruijf et al. also indicate a relationship ($p < 0.02$) between younger age of women and more frequent basal-like BC occurence [13].

Our analysis leads to similar conclusions — basal-like BC and HER2+ BC occurred in 24.2% and 16.7% of cases respectively in the younger age group, while among women in the age of 45 and older it was 15.1% and 11.1% of cases respecitvely. Less aggressive types of breast cancer with presence of ER and PgR receptors were more characteristic for women in older age groups both in Kolečkova's et al. and in our study.

Anders et al. shows less frequent occurrence of steroid receptors with simultaneous presence of more frequent HER2 receptor expression among younger women. Analysis carried out on the group of women counted 784 patients with early BC proves that BC among young women is a specific type of this disease and it is kind of "unique biological unit" [16]. Moreover, Anders et al. in other study underline that prognosis of survival for women with diagnosed BC under of the age of 40 years is much worse in comparison to older patients. Younger age in BC is an independent factor contributing to worse prognosis for the course of treatment [17].

A study carried out by Jenkins et al. among 3947 women with BC also shows that with increasing age of women, the number of cases of luminal A BC grows with simultaneously decrease of basal-like BC cases. However, authors of the study claim that taking into the consideration each type of BC, the age of diagnosis is not independent prognostic factors for treatment effects [18].

From studies cited by Ribnikar et al. performed in two research groups counted respectively 1427 and 9885 women with BC it follows that in perimenopausal age (women in the age about 50 years old) lack of ER and/or PgR receptors and expression of HER2 receptor were observed, especially among younger women. Similar conclusions have been developed in own studies [19].

Conclusions

Conducted study confirms that prevalence of specific receptor profiles in BC patients varies by age of the women. BC with HER2 receptor expression and basal-like BC are more characteristic for younger age group — 27–44 years

old. Luminal A and luminal B BC are more frequent among patients aged 45 and older.

The border point for significant increase of number of BC cases was perimenopausal age (about 45 years old), which may suggest that the change of women's hormonal status plays a key role for BC development, regardless its receptor profile.

High incidence of BC in older age group (45+) and more frequent occurrence of aggressive types of BC among younger women (27–44 years old) indicate a need of education of women from both age groups about risk factors and early symptoms of the disease. However, taking into consideration the increasing incidence of BC among younger women, this group should be a subject of particular interest.

As we still do not know enough about BC origin and treatment options for some women with BC are limited (basal-like BC), primary prevention and mammography remain efficient tools in BC incidence and mortality reduction.

Primary prevention of well-known factors contributing to BC (for example obesity and overweight, alcohol consumption, diet rich in saturated fats) is even more important when we consider features of BC in the research group and general population. Receptor profile of BC has significant meaning for treatment process. In the investigated group the most frequent was luminal A BC with best prognosis. Early detection of this type of BC may contribute to more effective treatment, shortening the treatment time and in the long term may lead to mortality reduction and savings for health care systems. Similarly, in case of more aggressive BC types (basal-like and HER2+ BC) effective actions for early detection may contribute to mortality reduction, also in the younger age group.

Abbreviations

BC — breast cancer
ER — estrogen receptor
PgR — progesterone receptor
HER2 — human epidermal growth factor receptor
APC — average percentage change

Conflict of interest: none declared

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