Histopathological Analysis of Mucinous Breast Cancer Subtypes and Comparison with Invasive Carcinoma of no Special Type.

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Abstract

Background

Mucinous breast cancer (MBC) is a rare histological type of breast cancer characterized primarily by the production and extracellular presence of mucin and it is usually associated with a better prognosis than other invasive breast neoplasms. Because of the low prevalence, MBC biology is not well understood.

Methods

The aim of the present study was to introduce the last 2-year experience regarding MBC pathological diagnostics in our clinical center and comparison of the obtained data with invasive breast carcinoma of no special type (NST) comprising the most common invasive breast cancer.

Results

We identified 24 MBC cases representing 3.09% of all 766 invasive breast cancers, including 15 cases of pure type and 9 mixed MBCs. The median MBC patients' age at presentation was 65.5 years. In comparison to NST, MBC presented a higher T stage with a statistically larger tumor median size, although lower regional lymph node involvement, tumor histological grade and TNM stage.

Conclusion

MBC is a rare type of breast cancer accounting for about 4% of all diagnosed breast cancers. Our findings are consistent with those published in recent years and show significant differences between MBC and NST cancer patients and also highlight differences between pure and mixed MBC emphasizing the essence of their differentiation. MBC is associated with a better long-term prognosis than NST and is characterized by the less aggressive biological behavior expressed through favorable clinicopathologic features in terms of tumor grade, regional lymph node involvement and hormone receptor status.

Background

Breast cancer is the most common invasive female cancer affecting around 14% of women and causing every year approximately 500,000 deaths worldwide. In fact, breast cancer is a heterogeneous group of neoplasms containing a variety of cancers characterized by significantly different biology, clinical course and prognosis. The most common histological type of breast cancer is an invasive carcinoma of no special type (NST) also previously known as invasive ductal carcinoma, not otherwise specified (IDC, NOS). NST is a group of cancers that does not present any specific differentiating features that belong to other histological types of breast cancer. Among the group of other breast cancers, we can distinguish numerous different types, often very rare, including mucinous breast cancer.

Mucinous breast cancer (MBC), also named colloid carcinoma, is a relatively rare histological type of breast cancer, comprising about 4% of all breast cancer cases, although pure type (PMBC) is even rarer

and account for about 2%. MBC is characterized primarily by the production and extracellular presence of mucin. According to the newest WHO classification of tumors of the breast (2019) [1], MBC is classified as a special type of breast cancer and based on its cellularity can be divided into two subtypes:

- The pure type (PMBC), which is composed entirely of tumor cells with extracellular and intracellular mucin part in over 90% of the tumor mass and is more frequent;
- The mixed type (MMBC), which also includes infiltrating components such as ductal or lobular breast cancer-like contains less than 90% of mucin.

PMBC tumors may be classified as hypocellular (PMBC-A) tumors characterized by micropapillary, papillary, tubular, cribriform or cordlike growth pattern and hypercellular (PMBC-B) tumors forming solid nests of cells floating in the mucin. On the other hand, MMBC tumors may be subdivided into two groups based on the amount of mucinous component. According to Lei et al. (2016), it is possible to distinguish mMMBC tumors containing 50–90% of mucinous components and pMMBCs containing 30–50% of mucinous components [2] (Table 1).

Table 1
Characteristics of mucinous breast cancer (MBC) subtypes

MBC subtypes characteristics	
PMBC	> 90% of mucinous components
	PMBC-A – hypocellular tumors; growth patterns: micropapillary, papillary, tubular, cribriform or cordlike
	PMBC-B – hypercellular tumors; growth pattern: sold nests
MMBC	30–90% of mucinous components
	mMMBC – 50–90% of mucinous components
	pMMBC – 30–50% of mucinous components

MBC is usually presented with a better prognosis than NST. Regional lymph node involvement and distant metastases are unusual findings [3, 4]. Some MBCs, mainly mixed type, are associated with ductal and/or lobular neoplasia while some present neuroendocrine differentiation. The etiology of MBC if multifactorial and involves common breast cancer risk factors, nevertheless, data suggest that some factors related to reproductive events (e.g. late menarche, early menopause, childlessness) contribute less to MBC risk than to risk of other histological breast cancer types [5].

Methods

The aim of the present study was to introduce the last 2-year experience of the Department of Pathology, Military Institute of Medicine in Warsaw regarding MBC pathological diagnostics and its comparison with NST cancers comprising the most common invasive breast neoplasm.

The material for the present study consisted of histological preparations derived from 776 women diagnosed with invasive breast cancer within the recent two years (2018–2019) in Military Institute of Medicine, Warsaw. We evaluated demographic and clinical data and reviewed pathological findings of MBC and compared them to NST cancers. The material for the present study came from the patients who underwent surgery (modified radical mastectomies or breast conserving surgery methods) and biopsies/excisional biopsies. Tumor slides were evaluated by two independent pathologists. Invasive carcinoma of no special type was found in 592 out of 776 patients (76.29%) and mucinous breast cancer was diagnosed in 24 cases (3.09%).

Histological and immunohistochemical studies were done at the Department of Pathology, Military Institute of Medicine, Warsaw. Tumor samples were initially fixed in 10% phosphate buffered formalin. After 24 hours, fixation tissues were dehydrated in alcohol of gradually increasing concentration (50%, 60%, 70%, 80%, 90%, 96%) and subsequently by pure alcohol and xylene, and afterwards embedded in paraffin. Paraffin blocks were cut into sections (4 μm). The sections were next stained with different methods for diagnostic purposes. Preparations stained with hematoxylin and eosin (H&E) were used to define the tumor histological type (WHO classification, 2019), intensity of division (evaluating the degree of mitotic index as the mean number of mitoses in cancer cells counted in 10 fields of vision at an objective magnification of 400 × (0.17mm^2 surface field)) and histological grade of malignancy (G1-G3).

Constantly, all patients had a basic immunohistochemical profile assessed, i.e. expression of estrogen receptor (ER) and progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). Immunohistochemical methods used paraffin sections attached onto glass slides covered with 2% silane/acetone solution (Merck, Darmstadt, Germany) and dried for 24 hours at 42^{o}C. Before commencing the immunohistochemical procedure, sections were dewaxed by inserting them in a series of alcohols of gradually decreasing concentrations, followed by washing in distilled water. Immunohistochemical assays were performed using the En-Vision™ + complex HRP DakoCytomatic (DAKO, Santa Clara, United States) (En-Vision™ Dual Link System-HRP, DAB+, Code: K4065). In order to determine the expression of steroid receptors, monoclonal antibodies against estrogen (Monoclonal Mouse Anti-Human Estrogen Receptor alpha, 1:50 dilution, Clone: 1D5, Code: IR654, DAKO, Santa Clara, United States) and progesterone (Monoclonal Mouse Anti-Human Progesterone Receptor, 1:400 dilution, Clone: PgR636, Code: IR068, DAKO, Santa Clara, United States) were applied. The study was conducted as follows: histological sections were incubated in an incubator at 60^{o}C overnight and then dewaxed. The following step was to reveal the epitopes by heating slides in a buffer for 45 minutes. Afterwards, preparations were left at 25^{o}C for 30 minutes. Preparations were rinsed in buffer, and then endogenous peroxidase was blocked in 3% hydrogen peroxide. In the following stage, preparations were incubated with an appropriate antibodies. Afterwards, sections were rinsed in a buffer for 15 minutes and then incubated with the visualization reagent for half an hour. Then the preparations were washed in Tris-Buffered Saline, pH 7.6, for 10 minutes, and then were incubated with 3,3′-diaminobenzidine (DAB) (Substrate-Chromogen Solution) for 10 minutes to visualize the color reaction. Subsequently, color reactions were evaluated according to a scale regarding the extent and intensity of staining of nuclei in

tumor cells. Nuclear staining in ≥ 10% of cancer cells was considered positive (+) for estrogen (ER) and/or progesterone (PR) receptor.

Human epidermal growth factor receptor 2 (HER2) expression was determined using the HerceptTest™ Dako test (Code: K5204). It enables the HER2 detection using a polyclonal antibody against this protein (Rb A - Hu HER2 - Rabbit Anti-human HER2 Protein). HER2 status was determined by assessing protein expression on the membrane of tumor cells using immunohistochemistry or by assessing the number of *HER2* gene copies using fluorescence *in situ* hybridization (FISH). HER2 expression level was determined based on the maximum area of staining intensity as follows: strong circumferential membranous, staining > 30% of invasive carcinoma cells was graded 3+, moderate, circumferential membranous staining in ≥ 10% of invasive tumor cells or strong circumferential membranous staining in > 30% of cells was designated as 2 + staining, weak and incomplete membranous staining in invasive tumor cells was marked as 1 + and no staining was scored 0. Score 0 and 1 + were considered negative for *HER2* amplification. Score 3 + was considered positive. Score 2 + was considered equivocal and FISH was ordered for confirmation. *HER2* was considered to be amplified if the average HER2 copy number was ≥ 6 signals/cells or ER2/CEP17 ratio ≥ 2 [6]. Positive and negative control preparations were formerly performed.

All statistical analyses were performed with SPSS software v. 12.0 for Windows. The χ^2 and Fisher's Exact Tests were used appropriately. Differences were considered statistically significant when $p \leq 0.05$.

Results

We identified 24 MBC cases representing 3.09% of all 766 invasive breast cancers diagnosed in our clinical center within recent two years (2018–2019) and compared obtained data with the characteristics of invasive carcinoma of no special type comprising the most numerous type of breast cancer (76.29% in the present study), hence, most often diagnosed (Table 2). In the group of mucinous breast cancer, we identified 15 pure mucinous breast cancer (PMBC) and 9 mixed mucinous breast cancer (MMBC) (Table 2).

Table 2
Distribution of histological types in the group of 776 patients with invasive breast cancer

Type	No.	%
Invasive carcinoma of no special type (NST)	592	76.29
Invasive lobular carcinoma	98	12.63
Mixed ductal and lobular invasive carcinoma	32	4.12
Mucinous (colloid) carcinoma (MBC)	**24**	3.09
Tubular carcinoma	10	1.29
Metaplastic carcinoma	8	1.03
Carcinoma with medullary features	7	0.90
Invasive micropapillary carcinoma	5	0.81
	776	100.00

At the time of primary diagnosis, the vast majority (95.8%) of MBC patients were postmenopausal women. The median MBC patients' age at presentation was 65.5 (range: 35–88) years versus 60.0 (range: 27–91) for NST. It shows that MBC usually affects older women, especially in the postmenopausal period. The difference was statistically significant with p-value = 0.009. Comparing MBC subgroups, the mean age of PMBC patients was 64.1 years and 69.7 years of MMBC, respectively (Fig. 1, Table 4).

At the time of diagnosis 83.3% of MBC patients presented a palpable mass in the breast, whereas the remaining 16.3% were diagnosed after the preventive mammography. The laterality of the neoplasm was right-sided in 14 (58.3%) patients and left-sided in the remaining 10 (41.7%) women. All cases were unifocal.

Gross examination of MBCs showed a glistening, gelatinous lesion with pushing margins and fairly soft consistency. Typical of examined MBCs was mucoid material separated by usually fragile septa seen on the cut section. The majority of lesions were well circumscribed and bosselated. The tumors ranged in size from 0.7 cm to 4.0 cm (mean size 2.19 cm, PMBC mean size 2.46 cm; MMBC mean size 2.01 cm); tumor size was assessed as pT1 in 13 patents, pT2 in 9 patients and pT4 with 2 patients, with no pT3 cases. Only 3 (12.5%) patients presented regional lymph node involvement and only those who were diagnosed with MMBC (pN0–21 patients, pN1–2 patients, pN3–1 patient), while no distant metastases (M0) were identified.

In comparison to NST, MBC presented a higher T stage with a statistically larger tumor median size (2.19 cm for MBC and 1.92 cm for NST, p = 0.018). Moreover, patients with MBC were introduced with lower N stage (p = 0.007), lower tumor grade (p = 0.005) and lower TNM stage (p = 0.037). All these clinicopathological features are summarized in the Tables (Table 3, 4).

Table 3
Comparison of the clinicopathological features between mucinous breast cancer (MBC) and invasive carcinoma of no special type (NST).

	MBC		NST		p
	No. of patients	%	No. of patients	%	
Age	65.5	0.0	60.0	0.8	0.009
Median	66.0	4.2	60.0	4.9	
average	35–88	8.3	27–91	15.5	
range	0	16.7	5	31.4	
<=30	1	25.0	29	27.9	
31–40	2	37.5	92	14.7	
41–50	4	8.3	186	4.7	
51–60	6		165		
61–70	9		87		
71–80	2		28		
>=81					
Median size	2.19 cm		1.92 cm		0.018
Tumor size (T)	1	4.2	12	2.0	0.748
T1a	2	8.3	54	9.1	
T1b	10	41.7	232	39.2	
T1c	9	37.5	248	41.9	
T2	0	0.0	9	1.5	
T3	2	8.3	37	6.3	
T4					
Nodal status (pN)	21	81.7	354	59.8	0.007
pN0	2	8.3	142	24.0	
pN1	1	4.2	63	10.6	
pN2	0	0.0	33	5.6	
pN3					

	MBC		NST		p
	No. of patients	%	No. of patients	%	
Tumor grade	0	0.0	46	7.8	0.005
G1	22	91.7	321	54.2	
G2	2	8.3	189	31.9	
G3	0	0.0	36	6.1	
Gx (necrosis/autolysis)					
Estrogen receptor status	7	29.2	215	36.3	0.474
ER-	17	70.8	377	63.7	
ER+					
Progesterone receptor status	9	37.5	241	40.7	0.925
PR-	15	62.5	351	59.3	
PR+					
HER2 status	20	83.3	488	82.4	1.000
HER2 0/1+	0	0.0	32	5.4	
HER2 2+	4	16.7	72	12.2	
HER2 3+					
Stage (TNM)	4	16.7	262	44.3	0.037
I	9	37.5	224	37.8	
II	11	45.8	77	13.0	
III	0	0.0	29	4.9	
IV					

Table 4
Comparison of pure and mixed mucinous breast cancer with NST cancer of the breast

	MBC - total	PMBC	MMBC	NST
Number of patients	24	15	9	592
Mean age at diagnosis	66.0	64.1	69.7	60.0
Patients aged over 80	2	2	0	28
OS 5-year (%)	95.8%	100%	88.9%	75.3%
DFS 5-year (%)	91.6%	93.3%	88.9%	70.2%
Local recurrence (%)	8.3%	6.7%	11.1%	29.8%
Median size	2.19 cm	2.46 cm	2.01 cm	1.92 cm
Tumor size (T) (no, %)	1 (4.2)	0	1 (11.1)	12 (2.0)
T1a	2 (8.3)	1 (6.7)	1 (11.1)	54 (9.1)
T1b	10 (41.7)	5 (33.3)	5 (55.6)	232 (39.2)
T1c	9 (37.5)	8 (53.3)	1 (11.1)	248 (41.9)
T2	0	0	0	9 (1.5)
T3	2 (8.3)	1 (6.7)	1 (11.1)	37 (6.3)
T4				
Nodal status (pN) (no, %)	21 (87.5)	14 (93.3)	7 (77.8)	354 (59.8)
pN0	2 (8.3)	1 (6.7)	1 (11.1)	142 (24.0)
pN1	1 (4.2)	0	1 (11.1)	63 (10.6)
pN2	0	0	0	33 (5.6)
pN3				
Tumor grade (no, %)	0	0	0	46 (7.8)
G1	22 (91.7)	15 (100.0)	7 (77.8)	321 (54.2)
G2	2 (8.3)	0	2 (22.2)	189 (31.9)
G3	0	0	0	36 (6.1)
Gx (necrosis/autolysis)				
Estrogen receptor status (no, %)	7 (29.2)	3 (20.0)	4 (44.4)	215 (36.3)
ER-	17 (70.8)	12(80.0)	5 (55.6)	377 (63.7)
ER+				

	MBC - total	PMBC	MMBC	NST
Progesterone receptor status (no, %)	9 (37.5)	4 (26.7)	5 (55.6)	241 (40.7)
PR-	15 (62.5)	11 (73.3)	4 (44.4)	351 (59.3)
PR+				
HER2 status (no, %)	20 (83.3)	14 (93.3)	6 (66.7)	488 (82.4)
HER2 0/1+	0	0	0	32 (5.4)
HER2 2+	4 (16.7)	1 (6.7)	3 (33.3)	72 (12.2)
HER2 3+				

Histological examination allowed us to identify 15 (62.5%) pure (PMBC, hypocellular/paucicellular variant) and 9 (37.5%) mixed (MMBC) mucinous breast cancers occurred usually with an invasive (ductal and/or lobular) or intraductal component noted mostly at the periphery of the tumor mass. One case with the presence of necrotic tissue in the central part of the tumor was found. Among MMBCs there were found 7 cases with an invasive ductal component, 1 with an invasive lobular component and 1 with the presence of intraductal non-invasive carcinoma. *In situ* component presented a micropapillary, papillary, tubular or cribriform/comedocarcinoma pattern usually associated with prominent extracellular mucin production.

Typically, the microscopic features were individual epithelial cells or small clusters variable in shape with occasional tubular structures formation, floating in lakes of mucin subdivided by gentle fibrous septa containing fine capillaries. MBC cells usually present marked nuclear atypia, prominently visible nuclei, vesicular nucleoli and a moderate amount of cytoplasm. MMBC typically manifests neuroendocrine differentiation expressed as cytoplasmic argyrophilia and/or expression of neuroactivity markers: chromogranin, synapthophysin, neuronal-specific enolase whereas PMBC represents the typical non-endocrine variant [7].

Discussion

MBC is rarely seen in clinical practice, representing about 4% of all diagnosed invasive breast cancer, prevails mainly in postmenopausal women and usually affects older patients compared to other invasive breast cancer types [8] and is extremely rarely diagnosed in younger women under 35 years of age (1%) [4]. The mean age at diagnosis was 66 years compared to 60 years for NST patients. Considering MBC subtypes, PMBC affected younger women than MMBC (64.1 versus 69.7 years, respectively). Molecularly, MBC belongs most frequently to the luminal A subtype of breast cancer, which is characterized by the expression of genes typical for glandular cells that form the inner layer of normal ducts and lobules of the breast (inner luminal cells). Luminal A cancers show a strong expression of estrogen receptor (ER) genes and genes associated with the regulation of its function (*LIV-1*, *HNF3A*, *XBP1*, *GATA3*).

Compared to NST cancer, MBC presented with a higher T stage and hence by larger tumor size (2.19 cm vs 1.92 cm, respectively) which was also reported by Park et al. (2010) [9]. Nevertheless mucinous breast cancers are usually associated with smaller tumor size [2, 10, 11]. Although in our study MBC was presented with a larger tumor size than NST at the time of primary diagnosis, tumor size (T) appears not to be a significant independent factor associated with the severity of the disease because the mucin component comprises the majority of the tumor mass [12]. It stays in concordance with the American Joint Committee on Cancer (AJCC) staging system in which tumor size is not a meaningful factor in MBC [13]. It is presumed that in some cases a large amount of mucin is answerable for hiding the disease until an extensive size is reached [14]. Some studies report tumor size as a prognostic factor, a less valuable one than nodal involvement [2, 4, 15].

In the present study MBC patients presented a higher hormonal receptors expression (ER, PR) and also HER2 gene overexpression, which is untypical, but probably depends on a non-representative group of only four HER2-positive MBC cases reported. Previous studies also investigated that MBC was more often associated with steroid hormone receptors (ER, PR) expression, which is followed by the present results, in which the positive rates for ER and PR were 70.8% and 62.5% in MBC and 63.7% and 59.3% in NST, respectively [16, 17]. The contemporary guidelines do not recommend chemotherapy or anti-HER2 therapy for hormone receptor-positive MBC, regardless of its HER2 status. In the study by Gwark et al. (2019) 11.8% of all 471 cases of PMBC were HER2-positive. Group of hormone-positive, lymph node-negative and HER2-positive cases with tumor size exceeding 3 cm presented worse disease-free survival (DFS) rates, thus authors suggested a potential role of trastuzumab usage in this particular subgroup [15].

Considering MBC subtypes, PMBC shows a higher T stage, and slightly lower N stage and tumor grade (G1-G3) when compared to MMBC. PMBC seems also to express steroid hormones receptors (ER, PR) more often than MMBC, which is reversed in the case of HER2 expression. The results concerning nodal involvement stays in concordance with data provided by other studies, in which MMBC presented a greater capacity to metastasize [14, 18]. On the other hand, in the study by Marrazzo et al. (2020) it was MMBC, that demonstrated a greater mass and higher T stage. What is worth mentioning, the obtained results were not statistically significant [14]. As far as hormonal status is concerned, the expression is suspected to be similar in both studied cases [18], nonetheless, some studies suggest a higher incidence of luminal-A type among PMBC and higher incidence of luminal-B type among MMBC [14].

Diagnostic procedures pose some difficulties as MBC might resemble a benign lesion. The differential diagnosis could be challenging, because MBC typically presents as a round -shaped, well-circumscribed lesion, with misleading homogeneous isoechoic and normal posterior acoustic appearance at ultrasound examination [19]. At radiological diagnostics, MBC often shows non-mass mammographic findings, and even calcifications or focal asymmetries may be missed. PMBC demonstrate less suspicious imaging features than cases of MMBC and could be mistaken for non-malignant breast lesions [20].

Typically MBC is a slow-growing tumor and shows infrequently regional lymph node involvement, nonetheless a metastatic disease worsens the survival rates and is regarded as the most significant

prognostic factor [18]. Regional lymph node involvement and lymphovascular invasion were observed in the present study in the vast minority of MBC cases (12.5%), compared to NST (40.2%) (p = 0.007) which is comparable with other authors reporting the mean lymph node metastatic disease in 15% of MBCs [21]. It is also important to distinguish MMBC from PMBC in terms of nodal involvement frequency (22.2% in MMBC versus 13.3% in PMBC), which was also observed in the previous studies, e.g. study by Marrazzo *et al.* (2020) which reported nodal involvement in 31.58% of MMBC and in 11.11% PMBC patients respectively [14]. Differentiation of PMBC from MMBC is also important since pure type has a better prognosis [22].

It is also significant to search for additional microscopic features, such as micropapillary patterns, related to significantly worse overall prognosis [23]. A lobular component present in the tumor structure is usually associated with microscopic features of cell polarization loss, decreased cell to cell adhesion and lack of neuroendocrine differentiation. Calcifications seen in conjunction with MBC often correspond to the invasive ductal component, and whenever visible, should prompt to search for this component. Also, neuroendocrine differentiation, defined by cytoplasmic argyrophilia and/or immunoreactivity to markers such as chromogranin, synaptophysin and neuronal-specific enolase, might be present within the tumor. Previous studies reported that the presence of neuroendocrine differentiation is associated with unfovorable 5-year and 10-year survival rates, overal survival and desease-free survival therefore neuroendocrine differentiantion is a poor prognostic indicator for mucnous breast cancer patients [24].

Bearing in mind the mucinous biology of this type of breast cancer, it is worth mentioning that overexpression of mucin 1 (MUC1) – a glycoprotein involved in the metastasis in various malignancies, was proved to worsen the prognosis of patients with breast cancer, including mucinous ones [25]. The possible mechanism might be correlated with the elevation of programmed death-ligand 1 (PD-L1) transcription by MUC1, and consequently, contributing to the immune escape of the aggressive forms of tumors [26]. The majority of PMBC overexpress the secreted mucin, mucin 2 (MUC2) [27]. Moreover, these cases are more resistant to chemotherapy that might be linked to the MUC2 overexpression [28]. Astashchanka et al. (2019) demonstrated that MUC2 plays an essential role in mediating the processes of apoptosis, proliferation, and metastasizing in breast cancer cells [28].

MBC has a specific molecular identity different from NST [29]. Moreover, a lower genetic instability is a characteristic MBC feature, compared to NST and lobular breast cancers as well [30]. It was reported, that almost all MBCs have a normal diploid stem line, unlike NST and lobular cancers. It has been proved, that aneuploidy correlates with higher tumor grade (G) and stage (TNM) [31].

MBC prognosis is more favorable compared to NST cancers. PMBC patients showed better overall survival (OS) and DFS rates than those for NST patients, but not significantly different from MMBC. MBC patients had a 5-year DFS rate of 91.6% (versus 70.2% of NST) and a 5-year OS of 95.8% (versus 75.3% of NST), that is similar to findings reported by Bea et al. (2011) [32] and Cao et al. (2012) [10]. Some studies have reported that MMBC and NST patients are characterized by a significantly poorer prognosis than those with PMBC [4, 33].

Limitations of this study encompass a limited number of patients that might affect the achieved results. It brings us to another drawback that is the fact of a single-center study. The juxtaposition of results obtained in the different clinical centers would present a broader view of the discussed subject. Nonetheless, we strongly believe that outcomes acquired in our center are a meaningful puzzle piece in the knowledge concerning MBC.

Conclusions

MBC is a rare type of breast cancer accounting for about 4% of all diagnosed breast cancers. Our findings are consistent with those published in recent years and show significant differences between MBC and NST cancer patients and also highlight differences between PMBC and MMBC emphasizing the essence of their differentiation. Although it is crucial from the practical point of view and helps to predict the overall prognosis, there are still no tailored treatment strategies for MBC subtypes. Fortunately, all ones are characterized by a significantly better prognosis compared with NST patients. MBC is associated with a better long-term prognosis than NST and is characterized by the less aggressive biological behavior expressed through favorable clinicopathologic features in terms of tumor grade, regional lymph node involvement and hormone receptor status. Without any doubts, further research is needed to obtain a broader understanding of the biology of this breast cancer subtype resulting in even better survival rates.

Abbreviations

MBC – mucinous breast cancer

PMBC – pure mucinous breast cancer

MMBC – mixed mucinous breast cancer

MUC1 – mucin 1

MUC2 – mucin 2

NST – invasive breast carcinoma of no special type

OS – overall survival

DSF – disease-free survival

Declarations

Ethics approval and consent to participate

The work described in this article has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) on medical research involving human subjects; the ethical

principles defined in the Farmington Consensus of 1997.
The study was approved by the Bioethics Committee of the Medical University of Warsaw.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

MB designed the work, analyzed and interpreted data, performed literature analysis; MF performed laboratory work and literature analysis ; ABK drafted the work and substantially revised it.

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Figures

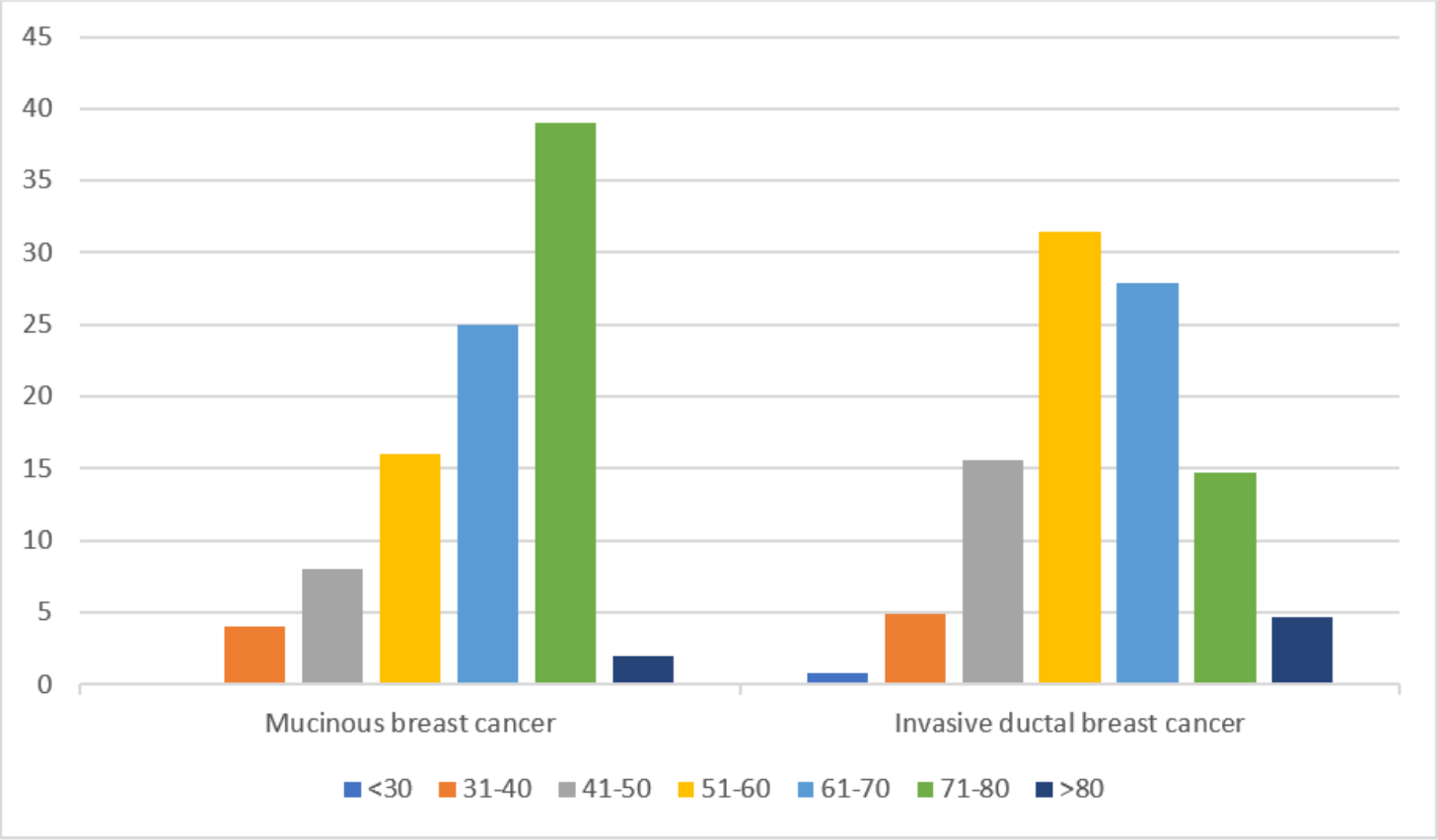

Figure 1

Age distribution of patients with mucinous and invasive carcinoma of no special type