Original Article
Middle East Journal of Cancer; January 2021; 12(1): 97-105

Clinicopathological Behavior of Mucinous Breast Carcinoma in South of Iran: The Shiraz Breast Cancer Registry

Sedigheh Tahmasebi*, MD, Mohammad Yasin Karami*♦, MD, Majid Akrami*, MD, Vahid Zangouri*, MD, Azam Asgari*, MD, Sara Hosseini*, MSc, Azin Sohrabi*, MD, Abdolrasoul Talei*, MD, Nazanin Karimaghaei, MD**

*Breast Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
**Core Medical Trainee, Northumbria Healthcare NHS Foundation Trust, Newcastle upon Tyne, UK

Please cite this article as: Tahmasebi S, Yasin Karami M, Akrami M, Zangouri V, Asgari A, Hosseini S, et al. Clinico-pathological behavior of mucinous breast carcinoma in south of Iran: The Shiraz breast cancer registry. Middle East J Cancer. 2021;12(1):97-105. doi: 10.30476/mejc.2020.82833.1109.

Abstract

Background: Mucinous breast carcinoma (MBC) is a subtype of breast cancer categorized by the presence of extracellular mucin and has more favorable prognosis than invasive carcinoma of no special type of breast cancer. The present study incorporates 27 years of practical experience from a breast disease research center-based series of cases regarding MBC and invasive ductal carcinoma (IDC).

Method: In this retrospective study, we studied the medical documents of 7,739 patients in the Breast Disease Research Center, Shiraz University of Medical Sciences, from December 1993 to January 2019. TNM data, demographic status, pathologic stage, histological grade, hormonal receptor data, recurrence, overall survival (OS), and disease-free survival (DFS) were reviewed. We also statistically evaluated the clinical and histopathological differences of pure, mixed MBC, and IDC using SPSS, version 21.0 (IBM, USA). $P<0.05$ was considered as statistically significant.

Results: A total of 78 and 31 patients were observed to have pure and mixed MBC, respectively, and 5,774 breast cancer patients had IDC. The pure MBC group showed a lower histological grade and pathologic stage and a larger tumor size compared with mixed MBC ($P<0.001$). The pure MBC patients had significantly less perinural and lymphovascular invasion and had less HER-2 positive status in comparison with IDC patients ($P=0.023$). The DFS and OS did not differ the between groups.

Conclusion: MBC is a rare diagnosis with a favorable prognosis due to low lymph node metastases.

Keywords: Mucinous, Breast, Cancer, Invasive ductal carcinoma

♦**Corresponding Author:**
Mohammad Yasin Karami, MD
Department of Surgical Oncology, Shiraz University of Medical Sciences, Zand Ave, Shiraz, Iran
Tel/Fax: 00987132303029
Email: yasinkarami@gmail.com

Introduction

Breast cancer is the most commonly diagnosed malignancy in Iranian women, and it accounts for 21.4% of all cancers.[1] Mucinous breast carcinoma (MBC), especially its pure subtype, is an uncommon and favorable variant comprising 2%

Received: July 13, 2019; Accepted: July 26, 2020

of breast cancers. These lesions usually have a soft gelatinous appearance on gross examination, and they tend to be well-circumscribed. MBC is more prevalent in elderly and postmenopausal women. MBCs are characterized by a cluster of uniform and low-grade atypia, and in some cases there can be more atypia cells floating in a pool of extracellular mucus.[2-7] MBC is categorized into two major subtypes, pure and mixed, primarily based on the cellularity index. Pure mucinous carcinomas are composed of more than 90% mucinous carcinoma.[7] Most pathologists have confirmed that pure MBC diagnosis should be kept for cancers with no less than 90% mucinous part. The mixed subtype also contains an invasive ductal epithelial part without mucin. Pure MBC is an uncommon diagnosis, accounting for less than 2% of all breast cancers.[8,9] The mixed MBC subtype is associated with ductal or lobular carcinoma in situ or invasive cancer.[10] Shiraz Breast Diseases Research Center is the main referral center for diagnosis and treatment of breast cancer in southern Iran. To the best of our knowledge, there is no report on this disease in the foregoing region. The authors aimed to specify different features of MBC and its similarity with invasive ductal carcinoma (IDC). In the second step, we tried to determine the one with a better disease-free (DFS) and overall survival (OS). The present retrospective study incorporated 27 years of experience regarding MBC and IDC with its histological and clinical features.

Materials and Methods

Study settings

We conducted this survey in Shiraz Breast Clinic, Shiraz, Iran, which is the main referral center for breast cancers in the south of Iran. The registry is affiliated to Shiraz University of Medical Sciences and contains data on more than 7500 breast cancer patients.[11] Breast Cancer Registry includes information on financial status, clinic histopathological characteristics, clinical history and examination, imaging, follow-up, and prognosis data of all patients with breast cancer.

Study protocol

In this retrospective study, we assessed the medical records of 7,739 patients in Breast Disease Research Center (Iran, Shiraz) from December 1993 to January 2019. Complete history and physical examination, bilateral breast

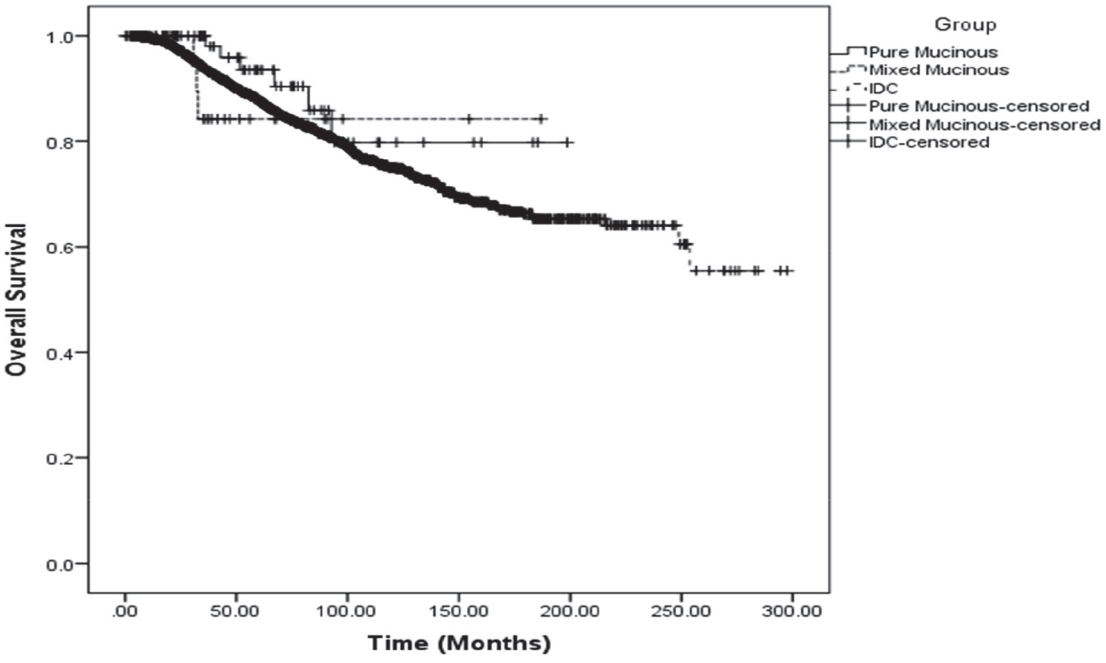

Figure 1. This figure shows patients' overall survival according to pathologic subtype.
IDC: invasive ductal carcinoma

mammography, chest X-Ray radiology, and routine blood and biochemical tests were required for all patients prior to surgery. Exclusion criteria were previous breast cancer, distant metastasis, ductal carcinoma in situ (DCIS), neo-adjuvant chemotherapy, and occult breast cancer presenting with axillary lymph nodal involvement.

We defined MBC according to the WHO criteria classification.[7] The consistency of MBC diagnosis was examined using the retrospective review of all cases. We retrospectively reviewed the following clinicopathological features: the side of breast involvement, size of tumor, adjuvant systemic therapy (hormone therapy; radiotherapy and chemotherapy), sentinel lymph node biopsy (SLNB) and axillary node dissection (AND) for axillary management, cancer stage using TNM staging system, operation types (lumpectomy vs. mastectomy), histopathology characteristics such as histological grade, subtype, and invasion status, immune-histochemical findings, including Estrogen Receptor (ER), Progesterone Receptor (PR), and HER-2 status, recurrence rate, and DFS and OS. Patients showing +3 were considered positive for HER-2 expression status. Furthermore, those with a concomitant positive fluorescence in situ hybridization (FISH) and HER-2 gene amplification 12 and equivocal (+2) status were considered positive for HER-2. We used American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines criteria version 2013 13 to designate a carcinoma as HER-2 positive. A breast cancer expert pathologist retrieved and reviewed the pathological slides of all available cases. Patients who died from causes other than breast cancer were excluded from the final analysis.

Statistical Analysis

Chi-square test was used to compare the qualitative data. We employed one-way ANOVA and Kruskall-Wallis test tests for quantitative data with and without a normal distribution, respectively. Kaplan-Meier analysis was utilized for OS and DFS data. All analyses were performed using SPSS software® for windows,® version 21.0, and we considered a *P*-value less or equal to 0.05 as statistically significant.

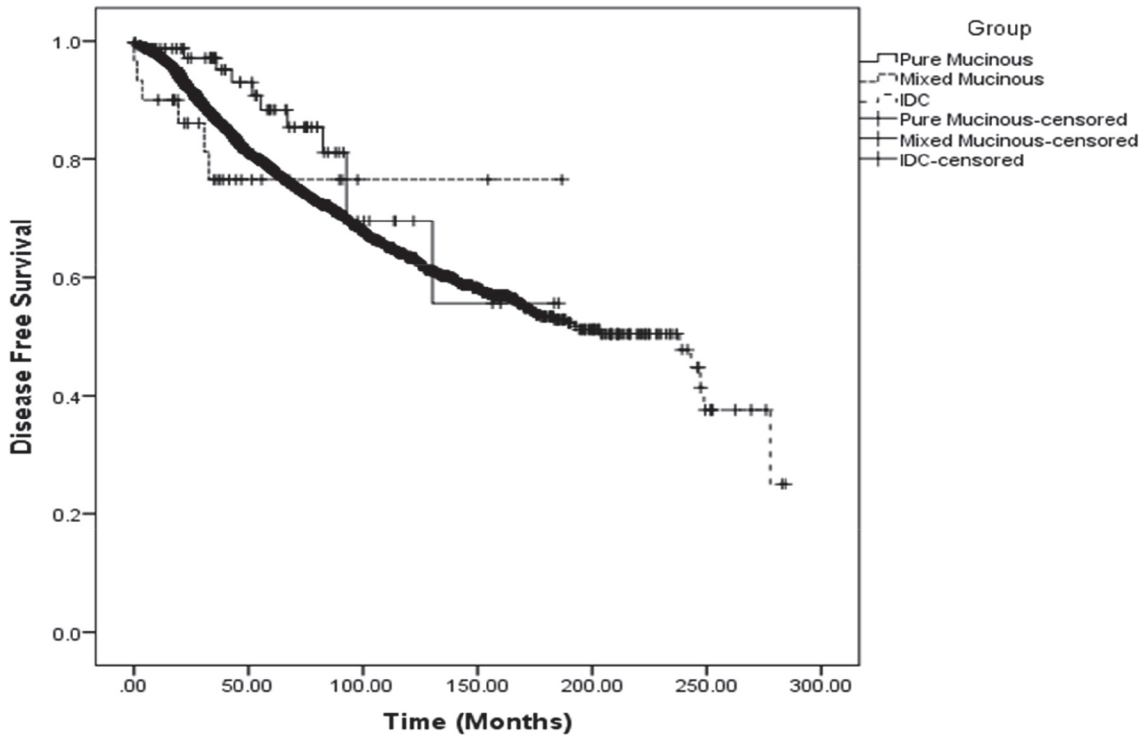

Figure 2. This figure shows patients' disease-free survival according to pathologic subtype.
IDC: invasive ductal carcinoma

Results

A total of 109 women were diagnosed as MBC (78 Pure and 31 Mixed type), and 5,774 patients were diagnosed as IDC. Their mean age was 52.76± 15.87 (54.25±16.08 in the pure MBC and 50.09±15.67 in the mixed MBC) and 48.94±11.58 years in the IDC group, respectively (P<0.001).

More than 82% of the pure subtype tumors were well-differentiated. The tumors were more located in the left breast than in the right one. In the mixed subtype group, more than 44% of the tumors were moderately-differentiated, and 20% and 36% were poorly-and well-differentiated, respectively. The clinical stage-difference was statistically significant among groups (P=0.001).

The pure MBC group had higher stage 1 and 2 tumors (88.4 %), and the mixed MBC group had more stage 2 and 3 patients (80.5%). The pure mucinous breast cancer group had a significant correlation with a lower pathological grade (P<0.001), as well as, less tumor size (P<0.001) compared with mixed MBC. The pure MBC patients presented with better histological differentiation and correlated with low-grade tumors, more ER and PR expressions, larger tumor, and less lymph node metastasis in comparison with the IDC patients.

To evaluate the local invasion, perineural and lymphovascular invasions were considered. Although not part of a standard pathology report around the world, perineural invasion is a standard and common report in Iran. The pure MBC patients had significantly less perineural and lymphovascular invasions, respectively, compared with IDC (P<0.001, P=0.002). In all of these subtypes, IDC had a poorer prognostic factor compared with pure MBC. The pure MBC subtype had less lymphovascular invasion than the mixed subtype (33.8% vs. 50%; P=0.002). 60% of the MBC patients (71.8% in the pure and 48.4% in the mixed subtype) had localized cancer; whereas, 33.02% (28.1% in the pure and 51.6% in the mixed subtype) had regional lymph node metastasis; none of the patients had distant metastases.

The pure MBC group showed more ER and less PR expression compared with the mixed subtype group (88% and 78.4% (P= 0.058) vs. 82.8% and 79.3% (P=0.27)), respectively. We detected HER-2 positivity in 9 (14.1%) of the pure MBC cases and 8 (33.3%) of the mixed MBC cases. In half of the mixed MBC, HER-2 positivity was in the mucinous component.

The IDC group showed lower ER and PR expression than the pure MBC group (76.9% vs. 88 %, P=0.058; 78.4% vs. 71.4%, P=0.27). Pure MBC group had more HER-2 negative cases compared with the IDC group (85.5% vs. 70.3%, P=0.023), (Table 1).

Larger tumors were seen in the mixed MBC compared with pure MBC and IDC cases (3.79±3.16 cm vs. 3.02±1.97 cm and 2.68±1.50, P< 0.001). However, the mean of tumor size was higher in the pure MBC than in the IDC groups (P<0.001).

We detected left breast involvement in 55.1% and 60% of the pure and mixed MBC cases, respectively, and 52 % of the IDC cases (P=0.58). Surgical breast cancer management was assessed in all patients. Accordingly, lumpectomy was done in 47.4%, 56.7%, and 51.4 % of the pure and mixed MBC and IDC patients, respectively (P=0.66).

Besides, 86.59% of the cases with MBC and 94.5% of the cases with IDC received chemotherapy (P=0.001). The rate of radiotherapy was 60.9% and 79.5% in the pure MBC and IDC groups, respectively (P=0.001). Moreover, 81.3% of the IDC cases and 88.6% of the pure MBC ones underwent hormonal therapy (HT) (P<0.001).

The mean OS (Figure 1) was 172.77±10.00, 162.38±12.98, and 219.59±3.92 months for pure MBC, mixed MBC, and IDC, respectively; the mean DFS (Figure 2) was 142.02±02, 146.95±14.46, and 177.99±3.47 months for pure MBC, mixed MBC, and IDC, respectively. The Kaplan–Meier analysis results showed no statistically significant difference between MBCs and IDCs in terms of OS rate (P=0.42); no difference existed among the three groups concerning the DFS rate (P=0.28).

The five-year OS rates were 93.5%, 84.2%, and 87.8% for pure MBC, mixed MBC, and IDC,

Table 1. The comparison between pure, mixed mucinous breast cancer and IDC

Characteristics	Mucinous		IDC	*P*-value
	Pure Mucinous N (%) 78(1.3)	Mixed Mucinous N (%) 31(0.5)	N (%) 5774(98.1)	
Age (years)	54.25±16.08	50.09±15.67	48.94±11.58	<0.001
Mean (Max-Min)	(28-96)	(25-83)	(18-97)	
Sex				
Female	78(100)	31(100)	5739(99.4)	0.71
Male	0	0	35(0.6)	
Tumor size (centimeters)	3.02±1.97	3.79±3.16	2.68±1.50	<0.001
Mean (Max-Min)	(0.4-14)	(0.5-14)	(0.5-18)	
Breast				
Right	35(44.9)	12(38.7)	2775(48.06)	0.58
Left	43(55.1)	19(61.3)	2999(51.93)	
Operation				
Lumpectomy	37(47.4)	18(58.06)	2966(51.4)	0.66
Mastectomy	41(52.6)	13(43.3)	2808(48.6)	
Chemotherapy				
Yes	58(84.1)	26(92.9)	4854(94.5)	0.001
No	11(15.9)	2(7.1)	280(5.5)	
Radiotherapy				
Yes	39(60.9)	22(78.6)	3905(79.5)	0.001
No	25(39.1)	6(21.4)	1004(20.5)	
Hormonal therapy				
Yes	62(88.6)	26(86.7)	4025(81.3)	0.23
No	8(11.4)	4(13.3)	923(18.7)	
Recurrence				
Yes	7(9)	7(22.6)	1130(20.2)	0.047
No	71(91)	24(77.4)	4476(79.8)	
Grade				
I (Well differentiated)	28(82.4)	9(36)	1048(20.8)	<0.001
II (Moderately differentiated)	5(14.7)	11(44)	2992(59.6)	
III (Poorly differentiated)	1(2.9)	5(20)	1003(19.9)	
Lymphovascular invasion				
Yes	22(33.8)	14(50)	2916(55.5)	0.002
No	43(66.2)	14(50)	2341(44.5)	
Perineural invasion				
Yes	4(6.2)	11(39.3)	1523(29)	<0.001
No	61(93.8)	17(60.7)	3734(71)	
Axillary node involvement				
Positive	20 (28.2)	16(51.6)	2876(52.1)	<0.001
Negative	51 (71.8)	15(48.4)	2642(47.9)	
N				
N0	51(71.8)	15(48.4)	2642(47.9)	0.003
N1(1-3)	13(18.3)	5(16.1)	1458(26.4)	
N2(4-9)	5(7)	6(19.4)	879(15.9)	
N3(>10)	2(2.8)	5(16.1)	539(9.8)	
ER				
Positive	66(88)	24(82.8)	4219(76.9)	0.058
Negative	9(12)	5(17.2)	1267(23.1)	
PR				
Positive	58(78.4)	23(79.3)	3902(71.4)	0.27
Negative	16(21.6)	6(20.7)	1561(28.6)	
HER-2				
Positive	9(14.1)	8(33.3)	1277(29.7)	0.023

Table 1. The comparison between pure, mixed mucinous breast cancer and IDC (continued)

Characteristics	Mucinous		IDC	*P*-value
	Pure Mucinous N (%) 78(1.3)	Mixed Mucinous N (%) 31(0.5)	N (%) 5774(98.1)	
Negative	55(85.9)	16(66.7)	3024(70.3)	
Breast cancer subtypes				0.078
HR+/HER2- (Luminal A)	51(79.7)	14(58.3)	2550(59.7)	
HR+/HER2+ (Luminal B)	6(9.4)	6(25)	796(18.6)	
HR-/HER2+(HER2 positive)	3(4.7)	2(8.3)	465(10.9)	
TNBC	4(6.3)	2(8.3)	459(10.7)	
TNM staging				0.001
I	19(31.7)	5(17.9)	1227(23.9)	
II	34(56.7)	12(42.9)	2456(47.9)	
III	7(11.7)	8(28.6)	1360(26.5)	
IV	0	3(10.7)	89(1.7)	

IDC: invasive ductal carcinoma, ER: estrogen receptor, PR: progesterone receptor, TNBC: triple negative breast cancer

respectively (Figure 1). The five-year DFS rates were 88.3%, 76.5%, and 78.3% for pure MBC, mixed MBC, and IDC, respectively (Figure 2). Table 2 shows the multivariate analysis to estimate the risk factors of nodal involvement.

Discussion

Pure MBC accounts for roughly 1.3% of all breast cancer patients in our study population. This retrospective comparative study revealed the less aggressive manner of pure MBC compared with IDC. In our database, pure MBC patients presented with better histological differentiation and association with low-grade tumors, more ER and PR expression, larger tumor, and less lymph node metastasis compared with the IDC patients.

In Europe, United States of America, and China, MBC patients are usually postmenopausal and older than IDC cases.[5,14-17] MBC Korean patients are younger than IDC patients.[6] In our study, this tumor occurred in older Iranian than IDC cases.

Axillary lymph node metastasis in MBC patients was rare but seemed to worsen the breast cancer prognosis. Some studies found that node-positive MBC patients were more likely to have recurrence and poor prognosis.[18-22] Axillary metastasis incidences ranged from 19% to 64% in MBC.[6,17] We also observed this trend in the present study (28.2% in pure and 51.6% in mixed and 52.8% in IDC). Pure MBC had a better prognosis than mixed MBC and IDC due to the status of axillary lymph nodes.[15] It seems that pure MBC was correlated with a better short-term prognosis and similar long-term survival compared with IDC, which is consistent with our study.[5,18,23,24]

The presence of lymphovascular invasion (LVI) is associated with an increased risk of axillary lymph node and distant metastases. Our database reported LVI in 33% of MBC and 55% of IDC, which is significantly higher than expected.

In the previous studies, younger age, higher T stage, high histologic grade, and a negative ER status correlated with a higher axillary lymph node metastasis in MBC cases.[14,15]

In the present study, younger age at diagnosis and larger tumor size had a relationship with axillary nodal involvement in MBC. Tumor size was an independent factor for estimating the risk factors of nodal involvement in pure MBC. MBC showed significantly higher nodal metastasis rate regarding larger tumor sizes. Tumor size was an independent prognostic factor in Di Saverio et al.'s study, while size was less significant than lymph node involvement status and age in pure MBC patients.[5] In some recent studies, no statistically significant associations were detected between tumor size and axillary lymph node metastasis.[15,25] In some others; meanwhile, nodal positivity was found to be correlated with larger tumors in MBC, which is in line with our study.[5,6,19] Diab et al.

Table 2. Multivariate analysis for the estimation of the risk factors of nodal involvement in MBC, pure MBC, and IDC

Subgroups	Risk Factors	OR	*P*-Value	95% C	
				Lower	Upper
Pure MBC	Negative ER	0.536	0.620	0.046	6.301
	Negative PR	0.361	0.350	0.042	3.066
	Negative HER-2	0.302	0.278	0.035	2.626
	Age at diagnosis	1.029	0.242	0.981	1.078
	Tumor size	0.457	0.010	0.253	0.828
MBC	Negative ER	0.561	0.602	0.064	4.925
	Negative PR	0.637	0.646	0.093	4.364
	Negative HER-2	0.614	0.507	0.145	2.594
	Age at diagnosis	1.043	0.044	1.001	1.086
	Tumor size	0.649	0.011	0.465	0.907
IDC	Negative ER	1.469	0.007	1.111	1.943
	Negative PR	0.977	0.863	0.753	1.268
	Negative HER-2	1.488	0.000	1.280	1.730
	Age at diagnosis	1.009	0.002	1.003	1.015
	Tumor size	0.765	0.000	0.726	0.806

MBC: mucinous breast cancer, IDC: invasive ductal carcinoma, ER: estrogen receptor, PR: progesterone receptor, TNBC: triple negative breast cancer, OR: odds ratio, CI: confidence interval

showed better DFS for MBC vs. IDC.[19] Our study showed that MBC patients had similar long-term DFS and OS compared to IDC.

Briefly, mucinous carcinoma had a favorable prognosis and infrequent lymphatic metastasis compared with IDC. Pure mucinous carcinoma had a better prognosis than mixed mucinous breast carcinoma.[18] The five-year disease-free survival rates ranged from 81% to 94%. Late distant metastases might occur in pure mucinous carcinoma.[26] In a multivariate analysis of 11,422 patients with pure mucinous carcinoma, tumor size was found to be an independent prognostic indicator yet less significant than nodal status.[27] In another study, tumor size was not a significant prognostic factor and did not affect the survival since most of the tumor volume consisted of mucin.[28]

MBC treatment is based on breast conservation and axillary staging via sentinel lymph node biopsy and administration of adjuvant radiotherapy associated with post-operative hormone therapy in hormone-responsive (ER/PR) tumors.

Trastuzumab is approved for the treatment of advanced breast cancer and as adjuvant therapy for early-stage HER-2-positive tumors.[29] Adjuvant chemotherapy can be omitted in cases with favorable risk factors.[10]

In this study, while the authors included information from the main breast cancer registry in Shiraz, study samples may not be representative of the whole nation, which can be considered as a limitation.

In conclusion, MBC patients were older and presented favorable characteristics, including less nodal involvement, lower tumor stage, more ER, PR receptors expression, and less HER-2 expression. This can be attributed to the fact that mucinous carcinoma is more prevalent in the older population, in whom ER and PR are expressed more often than in younger women. Similarly, there were lower rates of HER-2 overexpression, which impactsthe selection of an appropriate therapy.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgment

The authors would like to thank Shiraz University of Medical Sciences, Shiraz, Iran, and the Center for Development of Clinical Research of Nemazee Hospital for their support. We are also grateful to Dr. Nasrin Shokrpour for editorial assistance. The present article was part of a surgical oncology fellowship thesis written by

Dr. Mohammad Yasin Karami.

Conflict of Interest

None declared.

References

1. Rezaianzadeh A, Peacock J, Reidpath D, Talei A, Hosseini SV, Mehrabani D. Survival analysis of 1148 women diagnosed with breast cancer in Southern Iran. *BMC Cancer.* 2009;9:168. doi: 10.1186/1471-2407-9-168.
2. Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histologic types of breast cancer. *Br J Cancer.* 2005;93(9):1046-52.
3. Li CI, Moe RE, Daling JR. Risk of mortality by histologic type of breast cancer among women aged 50 to 79 years. *Arch Intern Med.* 2003;163(18):2149-53.
4. Thurman SA, Schnitt SJ, Connolly JL, Gelman R, Silver B, Harris JR, et al. Outcome after breast-conserving therapy for patients with stage I or II mucinous, medullary, or tubular breast carcinoma. *Int J Radiat Oncol Biol Phys.* 2004;59(1):152-9.
5. Di Saverio S, Gutierrez J, Avisar E. A retrospective review with long term follow up of 11,400 cases of pure mucinous breast carcinoma. *Breast Cancer Res Treat.* 2008;111(3):541-7.
6. Bae SY, Choi MY, Cho DH, Lee JE, Nam SJ, Yang JH. Mucinous carcinoma of the breast in comparison with invasive ductal carcinoma: clinicopathologic characteristics and prognosis. *J Breast Cancer.* 2011;14(4):308-13.
7. Sinn HP, Kreipe H. A brief overview of the WHO classification of breast tumors. *Breast Care.* 2013;8(2):149-54.
8. Hanagiri T, Ono K, Baba T, So T, Yamasaki M, Nagata Y, et al. Clinicopathologic characteristics of mucinous carcinoma of the breast. *Int Surg.* 2010;95(2):126-9.
9. Anderson WF, Chu KC, Chang S, Sherman ME. Comparison of age-specific incidence rate patterns for different histopathologic types of breast carcinoma. *Cancer Epidemiol Biomarkers Prev.* 2004;13(7):1128-35.
10. Park S, Koo J, Kim JH, Yang WI, Park BW, Lee KS. Clinicopathological characteristics of mucinous carcinoma of the breast in Korea: comparison with invasive ductal carcinoma-not otherwise specified. *J Korean Med Sci.* 2010;25(3):361-8.
11. Talei A, Tahmasebi S, Akrami M, Zangouri V, Rezaianzadeh A, Arasteh P, et al. The Shiraz Breast Cancer Registry (SBCR): study design and primary reports. *J Pers Med.* 2018;15(6):471-9.
12. Wolff AC, Hammond MEH, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *Arch Pathol Lab Med.* 2007;131(1):18-43.
13. Wolff AC, Hammond MEH, Hicks DG, Dowsett M, McShane LM, Allison KH, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *Arch Pathol Lab Med.* 2013;138(2):241-56.
14. Louwman MW, Vriezen M, Beek MWv, Nolthenius-Puylaert MC, Sangen MJ, Roumen RM, et al. Uncommon breast tumors in perspective: incidence, treatment and survival in the Netherlands. *Int J Cancer.* 2007;121(1):127-35.
15. Avisar E, Khan MA, Axelrod D, Oza K. Pure mucinous carcinoma of the breast: a clinicopathologic correlation study. *Ann Surg Oncol.* 1998;5(5):447-51.
16. Cao AY, He M, Liu ZB, Di GH, Wu J, Lu JS, et al. Outcome of pure mucinous breast carcinoma compared to infiltrating ductal carcinoma: a population-based study from China. *Ann Surg Oncol.* 2012;19(9):3019-27.
17. Fu J, Wu L, Jiang M, Jiang T, Hong Z, Wang F, et al. Clinical nomogram for predicting survival outcomes in early mucinous breast cancer. *PLoS One.* 2016; 11(10):e0164921.
18. Komaki K, Sakamoto G, Sugano H, Morimoto T, Monden Y. Mucinous carcinoma of the breast in Japan. A prognostic analysis based on morphologic features. *Cancer.* 1988;61(5):989-96.
19. Diab SG, Clark GM, Osborne CK, Libby A, Allred DC, Elledge RM. Tumor characteristics and clinical outcome of tubular and mucinous breast carcinomas. *J Clin Oncol.* 1999;17(5):1442-8. doi:10.1200/JCO.1999.17.5.1442.
20. Fisher ER, Gregorio RM, Fisher B, Redmond C, Vellios F, Sommers SC. The pathology of invasive breast cancer a syllabus derived from findings of the National Surgical Adjuvant Breast Project (Protocol no. 4). *Cancer.* 1975;36(1):1-85.
21. Rasmussen BB, Rose C, Christensen I. Prognostic factors in primary mucinous breast carcinoma. *Am J Clin Pathol.* 1987;87(2):155-60.
22. Vo T, Xing Y, Meric-Bernstam F, Mirza N, Vlastos G, Symmans WF, et al. Long-term outcomes in patients with mucinous, medullary, tubular, and invasive ductal carcinomas after lumpectomy. *Am J Surg.* 2007;194(4):527-31.
23. André S, Cunha F, Soares J, Bernardo M, E Sousa JM, Cortez F. Mucinous carcinoma of the breast: a pathologic study of 82 cases. *J Surg Oncol.* 1995;58(3):162-7.
24. Toikkanen S, Kujari H. Pure and mixed mucinous carcinomas of the breast: a clinicopathologic analysis of 61 cases with long-term follow-up. *Hum Pathol.* 1989;20(8):758-64.

25. Paramo JC, Wilson C, Velarde D, Giraldo J, Poppiti RJ, Mesko TW. Pure mucinous carcinoma of the breast: is axillary staging necessary? *Ann Surg Oncol.* 2002;9(2):161-4.
26. Yang M, Li X, Chun-Hong P, Lin-Ping H. Pure mucinous breast carcinoma: a favorable subtype. *Breast Care (Basel). 2013;8(1):56-9.*
27. Righi L, Sapino A, Marchio C, Papotti M, Bussolati G. Neuroendocrine differentiation in breast cancer: established facts and unresolved problems. *Semin Diagn Pathol.* 2010;27(1):69-76.
28. Memis A, Ozdemir N, Parildar M, Ustun EE, Erhan Y. Mucinous (colloid) breast cancer: mammographic and US features with histologic correlation. *Eur J Radiol.* 2000;35(1):39-43.
29. Komenaka IK, El-Tamer MB, Troxel A, Hamele-Bena D, Joseph KA, Horowitz E, et al. Pure mucinous carcinoma of the breast. *Am J Surg.* 2004;187(4):528-32.