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Research Article

Clinical features and survival outcomes of invasive lobular breast carcinoma

İnvaziv lobüler meme karsinomunun klinik özellikleri ve sağkalim sonuçları

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Abstract

Aim: In this study, we investigated the clinical features and survival outcomes of patients diagnosed with invasive lobular breast cancer who presented to our clinic.

Material and Methods: Patients diagnosed with invasive lobular carcinoma who applied to Cumhuriyet University Oncology Center between 2007 and 2019 were examined retrospectively.

Results: In the study, the files of 1166 female patients with invasive breast cancer were reviewed, and it was determined that 64 of them (5.5%) had the invasive lobular carcinoma subtype. At diagnosis, 30 patients (47%) were in stage I-II, 31 patients (48%) were in stage III, and 3 patients (5%) were in stage IV. According to histopathological evaluations, 60 patients (94%) were found to be estrogen receptor (ER) positive, 53 patients (83%) were progesterone receptor (PR) positive, and 6 patients (9%) were HER2-positive. Regarding the treatments administered, 48 patients (75%) underwent modified radical mastectomy, 15 patients (23%) underwent breast-conserving surgery, 54 patients (84%) received adjuvant chemotherapy, 55 patients (86%) received hormone therapy, and 44 patients (69%) received radiotherapy. During follow-up, metastasis was detected in 14 patients (22%), with a median time to metastasis of 38 months (range 6-76 months). The 5-year overall survival and disease-free survival were 80% and 73%, respectively.

Conclusion: In our study, invasive lobular breast carcinoma was determined to be a common subtype of breast cancer, the majority of which are postmenopausal women, are diagnosed at advanced stages, and histopathologically hormone receptor positivity is common.

Keywords: breast cancer, invasive lobular carcinoma, clinical features, survival

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Öz

Amaç: Bu çalışmada kliniğimize başvuran invaziv lobuler meme kanseri tanılı hastaların klinik özellikleri ve sağkalım sonuçlarını araştırdık.

Gereç ve Yöntemler: Cumhuriyet Üniversitesi Onkoloji Merkezi'ne 2007-2019 yılları arasında başvuran hastalardan, invazif lobüler karsinom tanısı alan hastalar retrospektif olarak incelendi..

Bulgular: Çalışmada 1166 invaziv meme kanserli kadın hastanın dosyası incelenmiş ve bunlardan 64'ünün (5,5%) invaziv lobular meme kanseri alt tipinde olduğu tesbit edilmiştir. Tanıda 30 (47%) hastanın evre I-II, 31 (48%) hastanın evre III ve 3 (5%) hastanın ise evre IV olduğu tesbit edilmiştir. Histopatolojik değerlendirmelere göre hastaların 60'ında (94%) estrogen reseptörü (ER) pozitif, 53'ünde (83%) progesterone reseptörü (PR) pozitif, 6'sında (9%) HER2-pozitif olarak tesbit edildi. Yapılan tedaviler değerlendirildiğinde 48 (75%) hastaya modifiye radikal mastektomi, 15 (23%) hastaya meme koruyucu cerrahi uygulanmıştır ve 54 (84%) hastaya adjuvant kemoterapi, 55 (86%) hastaya hormonoterapi ve 44 (69%) hastaya radyoterapi verilmiştir. Takipte 14 (22%) hastada metastaz tesbit edilmiş olup metastaza kadar geçen süre medyan 38 (6-76) aydı. Hastaların 5 yıllık genel sağkalım ve hastalıksız sağkalım sırasıyla 80% ve 73%'tü.

Sonuç: Çalışmamızda invaziv lobüler meme karsinomu, çoğunluğunu postmenopozal kadınların oluşturduğu, daha çok ileri evrelerde tanı alan, histopatolojik olarak hormon reseptörü pozitifliği yaygın görülen meme kanseri alt tipi olarak tesbit edilmiştir.

Anahtar Kelimeler: meme kanseri, invaziv lobuler karsinom, klinik özellikler, sağkalım

Introduction

Breast carcinoma is a heterogeneous cancer that is divided into subgroups based on histopathology and gene expression patterns [1]. Invasive lobular carcinoma (ILC) is the second most common histological type of invasive breast cancers after invasive ductal carcinoma (IDC), accounting for 5-15% of all breast cancer cases [2]. ILC possesses distinct clinical, pathological, and radiographic features that suggest it is a separate clinical entity [3]. Compared to IDC, classic ILC generally presents with a higher proportion of lower grade tumors, greater positivity for hormone receptors (HR), and fewer cases with Human Epidermal Growth Factor 2 (HER2) amplification [3,4]. Additionally, ILC is more likely to involve lymph nodes, tend to be larger in tumor size, and patients are often diagnosed at more advanced stages. It is usually inclined to be multifocal [3-5]. Studies have also indicated a unique metastatic pattern for ILC, including metastases to the gastrointestinal system, peritoneum, ovaries, orbital cavity, or cerebral meninges [6,7].

Research has shown that the survival of patients with ILC may be better or similar to those with IDC [4,5,8]. However, due to the high risk of late recurrence, long-term follow-up indicate that disease-free survival and overall survival in HR-positive ILC may be worse compared to HR-positive IDC [3,9,10]. In ILC, which is predominantly comprised of hormone-sensitive tumors, early-stage hormone therapy can maintain long-term remission for the patient. Nevertheless, after recurrence or progression, the options and efficacy of treatment following hormone therapy appear to be quite limited for this disease, which has a low responsiveness to chemotherapy. Furthermore, factors contributing to conflicting survival outcomes include the differences in histological subgroup sizes of IDC and ILC patients, histological characteristics of ILC patients, their treatments, differences in follow-up durations, ethnicity, and the impact of sample size in studies. Although ILC is the second most common histological subtype, it is generally represented by a small number of patients in studies. There is a need for studies with larger and more homogenous samples to investigate the prognostic and clinicopathological features that determine survival and treatment response in these patients.

In our study, we aimed to retrospectively investigate the clinical, histopathological, and survival characteristics of patients diagnosed with lobular carcinoma among those who presented to our clinic with invasive breast cancer.

Material and Methods

This study was conducted with 64 patients diagnosed with ILC among 1166 patients treated and followed up for invasive breast cancer at Sivas Cumhuriyet University Faculty of Medicine Oncology Center between 2007 and 2019. Ethical

approval of the study was granted by the Ethics Committee of Sivas Cumhuriyet University Faculty of Medicine (Date: 21.12.2023, No: 2023-12/19). Informed consent was obtained from all individual participants included in the study.

Patient selection

In this study, female patients aged 18 and above with a diagnosis of ILC across all stages were included. Clinicopathological information was obtained from the patient's medical records and pathological reports. At the time of diagnosis, age, comorbidities, family history, menopausal status, and during follow-up, treatments, if any, regions of breast cancer recurrence, and vital status (whether alive or deceased) were obtained from the medical records. Patients with a history of secondary malignancies, including breast cancer, were also excluded from the study as this could have an impact on the results. Patients who had not had a menstrual period for more than six months, who were receiving hormone replacement therapy, who were at least 50 years old, and whose menopause status was not specified in their medical records were considered postmenopausal. At the time of diagnosis, all patients were staged according to the Eighth Edition American Joint Committee on Cancer (AJCC) staging manual. The performance status of the patients was based on the ECOG (Eastern Cooperative Oncology Group) scoring system.

HER2 testing was performed using immunohistochemistry (IHC) or single- or dual-probe in situ hybridization (ISH) tests. Those with IHC 3+ were considered HER2-positive. However, in cases with IHC 2+, the determination was made with concurrent IHC and in situ hybridization (ISH) results. [11]. HR testing for ER and PR via IHC was carried out using the method specified in the ASCO/CAP HR testing guideline [12]. Patients with 1-100% of cells expressing ER or PR were considered HR-positive. Subgroup definitions of the patients as luminal type A and B, HER-2 overexpression type, and triple-negative are based on the St. Gallen International Expert Consensus on the Primary Treatment of Early Breast Cancer 2011 [13].

The period from the date of diagnosis to the last follow-up or death was assessed as overall survival (OS), and the period from the date of diagnosis to the date of recurrence/distant metastasis, date of death, and for those without recurrence/metastasis, the last follow-up date was assessed as disease-free survival (DFS).

Statistics Analysis

Version 23 SPSS (IBM Corp., Armonk, New York, USA) program was used for statistical analysis. Descriptive statistics (medians, frequencies and percentage) were calculated for patient demographics, clinic characteristics, pathological characteristics, treatments received by patients and recurrence-metastasis patterns. Kaplan-Meier test was used to determine survival times. p value of <0.050 was considered statistically significant.

Results

In this study, 1166 patients with invasive breast cancer were screened, and 5.5% (n=64) of these were of the ILC histological subtype. The median age of these patients was 52 (range 36-83), and 61% (n=39) were postmenopausal at the time of diagnosis and 45% (n=29) of patients had comorbidities, primarily hypertension. A family history of breast cancer was present in 31% (n=20) of patients, while 9% (n=6) of patients were found to have bilateral breast cancer. According to the staging at diagnosis, T1 tumors were identified in 23% (n=15) of patients, T2 in 45% (n=29), T3 in 22% (n=14), and T4 in 9% (n=6) of patients. Moreover, 67% (n=43) of patients were N-positive, with N2-3 comprising 42% (n=27) of patients, and based on staging, 48% (n=31) of patients were at stage III at diagnosis. Table 1 displays the demographic and clinical characteristics of the patients.

When evaluating the pathological characteristics of the patients, 94% (n=60) were ER-positive, 83% (n=53) were PR-positive, and 10% (n=6) were HER2-positive. The median Ki67 was assessed at 12.5% and 47% (n=30) of patients were identified as luminal A, 40% (n=26) as luminal B, HER2-negative, 8% (n=5) as luminal B, HER2-positive, 2% (n=1) as HER2-positive, and 3% (n=2) as triple-negative. The presence of an intraductal component was observed in 67% (n=35) of patients, and of these, 77% (n=27) had an intraductal component ratio of less than 25%. Multifocality was identified in 29% (n=17) of patients. Table 2 summarizes the histopathological characteristics of the patients.

The median follow-up period was 89 months (range 6-252), and Table 3 shows the treatments given to the patients and their recurrence-metastasis patterns. Accordingly, 75% (n=48) of patients underwent modified radical mastectomy (MRM) and 86% (n=55) underwent axillary dissection (AD). It was found that the majority of patients received adjuvant treatment (chemotherapy, hormone therapy, and radiotherapy at rates of 84%, 86%, and 69%, respectively). In early stage disease, local recurrence was observed in 8% (n=5) of patients. Again, during follow-up, it was determined that metastasis developed in 22% patients (n=14) and the most common site of metastasis was bone (93%, in 13 of 14 patients).The median time to metastasis was assessed at 38 months (range 6-76).

Table 1. Demographic and clinic characteristics of patients

	Number of patients n=64	%
Age (median, year)	52 (36-83)	
ECOG Performance status		
0	40	63
1	22	34
2	2	3
Menopausal status		
Premenopausal	25	39
Postmenopausal	39	61
Comorbidity	29	45
Diabetes mellitus	9	14
Hypertension	20	31
Heart disease	4	6
Family history		
No	44	69
Yes	20	31
Bilateral breast cancer		
No	58	91
Yes	6	9
CEA		
Normal (<2.5 ng/mL)	43	78
High (≥2.5 ng/mL)	12	22
CA 15-3		
Normal (<30 U/mL)	39	70
High (≥30 U/mL)	17	30
T stage		
T1	15	23
T2	29	45
T3	14	22
T4	6	9
N stage		
N0	21	33
N1	16	25
N2	14	22
N3	13	20
Stage		
I	9	14
II	21	33
III	31	48
IV	3	5

ECOG Performance status: Eastern Cooperative Oncology Group Performance status, CEA: carcinoembryonic antigen, ng/mL: nanogram/milliliter, CA 15-3: Cancer Antigen 15-3, U/mL: Unit/milliliter

Table 2. Pathological characteristics of patients

	Number of patients n=64	%
ER status		
Negative	4	6
Positive	60	94
PR status		
Negative	11	17
Positive	53	83
ER (median, %)	90 (10-100)	
PR (median, %)	75 (15-100)	
Ki67 (median, %)	12,5 (5-60)	
HER2 status		
Negative	58	91
Positive	6	9
Histological Subtypes		
Luminal A	30	47
Luminal B (HER2-negative)	26	40
Luminal B (HER2-positive)	5	8
HER2-positive	1	2
Triple Negative	2	3
Grade (n=64)		
1	29	45
2	26	41
3	9	14
Lymphovascular invasion (n=50)		
Negative	24	48
Positive	26	52
Perineural invasion (n=51)		
Negative	31	61
Positive	20	39
Intraductal component (n=52)		
Absent	17	33
Present	35	67
Intraductal component ratio (n=35)		
<25%	27	77
≥25%	8	23
Multi-centricity/focality (n=59)		
Absent	42	71
Present	17	29
Tumor necrosis (n=46)		
Absent	39	85
Present	7	15
Extracapsular invasion (n=43)		
Absent	16	37
Present	27	63

ER: Estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor2

Table 3. Treatments received by patients and recurrence-metastasis patterns

	Number of patients n=64	%
Surgery		
Absent	1	2
MRM	48	75
BCS	15	23
Axilla surgery		
Absent	2	3
SLNB	7	11
AD	55	86
Adjuvant Treatments		
Chemotherapy	54	84
Hormonotherapy	55	86
Radiotherapy	44	69
Local relapse	5	8
Metastasis	14	22
Metastasis sites		
Bone	13/14	93
Brain	3/14	21
Lung	3/14	21
Liver	6/14	43
Time to metastasis (median, month)	38 (6-76)	

MRM: Modified Radical Mastectomy, BCS: Breast Conserving Surgery, SLNB: Sentinel Lymph Node Biopsy, AD: Axillary Dissection

The survival outcomes of the patients are shown in Table 4. Accordingly, the 5-year OS and DFS were 80% and 73%, respectively, while the 10-year OS and DFS were found to be 63%. Figure 1 shows the OS curves of the patients, and figure 2 shows the DFS curves.

Table 4. Survival outcome of patients

Number of patients n=64	5 years %	10 years %	p value
Overall survival	80	63	
Overall survival according to stage			
Stage I	100	100	<0.001
Stage II	95	87	
Stage III	67	40	
Stage IV	33	-	
Disease-free survival	73	63	
Disease-free survival according to stage			
Stage I	100	80	<0.001
Stage II	95	89	
Stage III	58	45	
Stage IV	-	-	

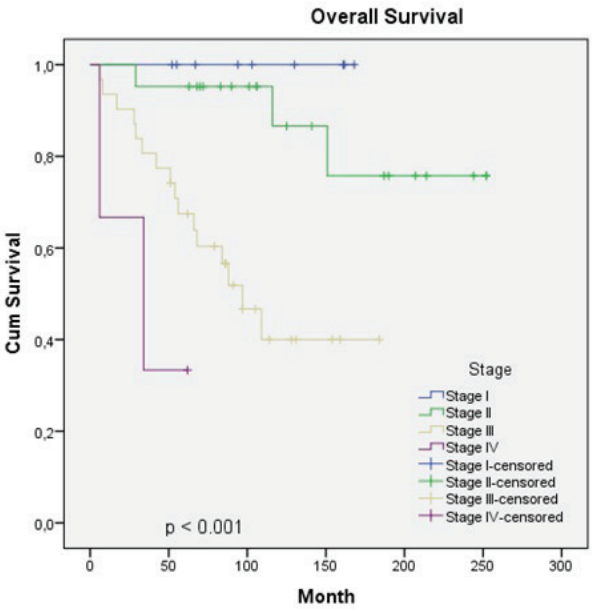

Figure 1. Overall survival curve of patients with invasive lobular carcinoma according to stages

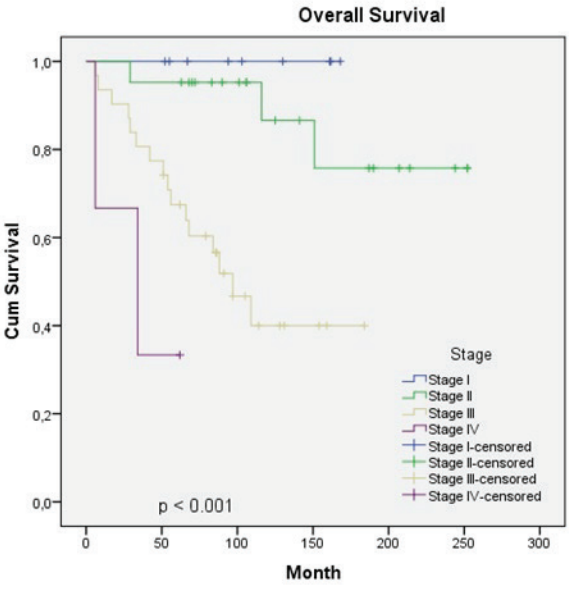

Figure 2. Disease-free survival curves of patients with invasive lobular carcinoma according to stages

Discussion

In our study, we aimed to evaluate the clinical characteristics and survival outcomes of patients diagnosed with invasive lobular breast cancer who applied to our clinic. We identified the frequency of ILC among all invasive breast cancers as 5.5%. The majority of these patients, who were postmenopausal, had a history of bilateral breast cancer in 9% of cases. Most patients

were N-positive, with 48% of patients diagnosed at stage III. Histopathologically, while HR positivity was high, HER2 positivity was as expected at low rates (94% and 9%, respectively). The presence of an intraductal component was common. Surgically, MRM with AD was performed more frequently than BCS and SLNB. The median time to metastasis was 38 months, and in the follow-up, 13 of the 14 patients who developed metastases had bone metastases. When looking at survival outcomes, the 10-year OS and DFS were found to be 63%.

Studies have shown that the frequency of histological subgroups, HR status, and factors associated with survival in breast cancer may vary among different races and ethnic groups [14,15]. A retrospective cohort analysis by Findlay-Shirras et al. found that 14.7% of all patients with invasive breast cancer between 1991 and 2015 were diagnosed with ILC [15]. This study highlighted a general increase in the rate over the years, with the ILC rate at approximately 10% in 1991 and rising to 15.9% in 2015. In this study, about 5% of the total 9352 ILC patients diagnosed between 2010 and 2015 had bilateral breast cancer. Indeed, it was observed that all bilateral breast cancers in these years were of ILC histopathology. In a study conducted by Oesterreich S. et al., the clinicopathological features of a total of 33662 IDC and ILC breast cancer patients from three clinical centers were retrospectively compared [3]. Of these patients, 3617 (10.7%) were in the ILC group, and an increasing trend in the incidence of ILC over time was identified [3]. In a retrospective evaluation of IDC and ILC patients by García-Fernández A. et al., the proportion of ILC patients was found to be 8.4% [4]. In our study, however, we identified the frequency of ILC among all invasive breast cancers as 5.5%.

In the study conducted by Oesterreich S. et al., it was identified that patients with ILC were diagnosed at more advanced stages with larger tumors and more lymph node involvement compared to IDC (17.7% with T3-4 tumors and 15.4% with N2-3 involvement, respectively). The same study showed more HR positivity and HER2 negativity in the ILC group, with a higher proportion of grade 1-2 patients compared to IDC [3]. In the study by García-Fernández A. et al., when looking at the clinicopathological features of these patients, it was shown that tumors were more likely to be multifocal/multicentric, HR-positive, HER2-negative, and had a lower proliferative index compared to IDC patients [4]. This study also significantly found more lymph node involvement (44.6% vs. 37.0%, p=0.04) and T3-4 tumor rate (9.4% vs. 5.6%) in ILC patients. The prevalence of stage IIB and III patients was significantly more common in ILC patients compared to IDC patients (37.4% vs. 25.3%, p=0.006). In our study, T3-4 tumors were seen in 31% and N2-3 involvement in 42% of patients, supporting the literature. Similarly, in our study, the majority of patients were HR-positive (ER-positive 94% and PR-positive 83%), HER2-positive (9%), with grade 1-2 tumors seen in 86% of patients. Consistent with this finding, in a retrospective analysis that included 864 ILC patients by Kee GJ et al., the HER2 positivity rate was determined to be 10.1% (87 patients) [16].

In the study conducted by Oesterreich S. et al., it was found that statistically significantly more mastectomies were performed in the ILC group compared to IDC (60% vs. 50%) [3]. García-Fernández A. et al. also highlighted the necessity for more re-excisions and/or mastectomies, thus the mastectomy rates were higher in patients with ILC compared to those with IDC (39.3% vs. 22.2%) [4]. This finding is supported by other studies [9]. In our study, the MRM rate was 75% while the BCS rate was evaluated at 23%. The high rate of MRM in this patient group, who often present at an advanced stage, is an expected outcome.

Oesterreich S. et al. identified that in patients with ER-positive ILC, disease-free survival and overall survival were statistically significantly worse compared to those with ER-positive IDC [3]. However, García-Fernández A. et al. demonstrated that the frequencies of recurrence/metastasis, EFS, and OS durations were similar between patients with IDC and ILC [4]. Chamalidou C. et al., in their large population-based study that included over 20 years of follow-up, assessed the survival and excess mortality rate ratio of patients with ILC and IDC [17]. In the study that evaluated a total of 17,481 patients, the excess mortality rate ratio for patients with ILC was lower compared to those with IDC during the first five years following surgery, but in the subsequent 10-15 years, the excess mortality rate ratio for patients with ILC increased compared to IDC [17]. Findlay-Shirras et al. found the 5, 10, and 15-year OS rates for patients diagnosed with ILC to be 82.7%, 65.3%, and 50.2%, respectively [15]. In our study, the 5 and 10-year OS rates were found to be 80% and 63% respectively, consistent with the literature. Similarly, in our study, the 5 and 10-year DFS rates were identified as 73% and 63%, respectively.

Limitations

Limitations of the study include retrospective analysis, small number of patients, lack of more detailed molecular and genetic testing, lack of evaluation of treatment and responses after relapse/metastasis, and disease progression characteristics. It is not known whether the patients have any germline mutations.

Conclusion

Whether ILC has a better prognosis compared to IDC remains controversial. Although the outcomes of comparative studies are debated, there is a general consensus that patients, who present at an older age with larger tumor masses, more lymph node involvement, and consequently at a more advanced stage, have good early survival rates. The histopathological characteristics of the tumor suggest an expected course of milder and slower progression. Long-term follow-ups become increasingly important for patients with ILC due to the rising risk of recurrence-metastasis.

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Conflict of interests

The authors have no relevant financial or non-financial interests to disclose.

Availability of data and material

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author's contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mukaddes Yılmaz. The first draft of the manuscript was written by Mukaddes Yılmaz and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

The present study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Sivas Cumhuriyet (Date: 21.12.2023, No: 2023-12/19).

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References

1. Perou CM, Sørlie T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature. 2000 17;406(6797):747-52. https://doi.org/10.1038/35021093.
2. Thomas M, Kelly ED, Abraham J, Kruse M. Invasive lobular breast cancer: a review of pathogenesis, diagnosis, management, and future directions of early stage disease. Semin Oncol. 2019;46(2):121-132. https://doi.org/10.1053/j.seminoncol.2019.03.002.
3. Oesterreich S, Nasrazadani A, Zou J, et al. Clinicopathological features and outcomes comparing patients with invasive ductal and lobular breast cancer. J Natl Cancer Inst. 2022;114(11):1511-1522. https://doi.org/10.1093/jnci/djac157.
4. García-Fernández A, Lain JM, Chabrera C, et al. Comparative Long-term Study of a Large Series of Patients with Invasive Ductal Carcinoma and Invasive Lobular Carcinoma. Loco-Regional Recurrence, Metastasis, and Survival. Breast J. 21(5):533-7. doi: 10.1111/tbj.12455. Epub 2015 Jul 17.
5. Silverstein MJ, Lewinsky BS, Waisman JR, et al. Infiltrating lobular carcinoma. Is it different from infiltrating duct carcinoma? Cancer. 1994 15;73(6):1673-7. https://doi.org/10.1002/1097-0142(19940315)73:6<1673::aid-cncr2820730620>3.0.co;2-b.
6. Raap M, Antonopoulos W, Dammrich M, et al. High frequency of lobular breast cancer in distant metastases to the orbit. Cancer Med. 2015 Jan;4(1):104-11. https://doi.org/10.1002/cam4.331.
7. Mathew A, Rajagopal PS, Villgran V, et al. Distinct pattern of metastases in patients with invasive lobular carcinoma of the breast. Geburtshilfe Frauenheilkd. 2017;77(6):660-666. doi:10.1055/s-0043-109374.
8. Fortunato L, Mascaro A, Poccia I, et al. Lobular breast cancer: same survival and local control compared with ductal cancer, but should both be treated the same way? analysis of an institutional database over a 10-year period. Ann Surg Oncol. 2012 Apr;19(4):1107-14. doi: 10.1245/s10434-011-1907-9. Epub 2011 Sep 13.
9. Adachi Y, Ishiguro J, Kotani H, et al. Comparison of clinical outcomes between luminal invasive ductal carcinoma and luminal invasive lobular carcinoma. BMC Cancer. 2016;16:248. doi:10.1186/s12885-016-2275-4.
10. Pestalozzi BC, Zahrieh D, Mallon E, et al. Distinct clinical and prognostic features of infiltrating lobular carcinoma of the breast: combined results of 15 International Breast Cancer Study Group clinical trials. J Clin Oncol. 2008; 26(18):3006-3014. doi:10.1200/J Clin Oncol.2007.14.9336.
11. Wolff AC, Hammond ME, Schwartz JN, et al. American Society of Clinical Oncology; College of American Pathologists. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. J Clin Oncol. 2007 Jan 1;25(1):118-45. doi: 10.1200/JCO.2006.09.2775.
12. Hammond ME, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol. 2010 Jun 1;28(16):2784-95. doi: 10.1200/JCO.2009.25.6529.

13. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B, Senn HJ; Panel members. Strategies for subtypes--dealing with the diversity of breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol. 2011;22(8):1736-47. doi: 10.1093/annonc/mdr304.
14. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by race and ethnicity among women 50 years of age and older. Cancer Epidemiol Biomarkers Prev. 2002;11(7):601-7.
15. Findlay-Shirras LJ, Lima I, Smith G, Clemons M, Arnaout A. Population Trends in Lobular Carcinoma of the Breast: The Ontario Experience. Ann Surg Oncol. 2020;27(12):4711-4719. doi: 10.1245/s10434-020-08895-8.
16. Kee GJ, Tan RY, Rehena S, et al. Human epidermal growth factor receptor 2 positive rates in invasive lobular breast carcinoma: The Singapore experience. World J Clin Oncol. 2020:24;11(5):283-293. doi: 10.5306/wjco.v11.i5.283.
17. Chamalidou C, Fohlin H, Albertsson P, et a. Swedish western and south-eastern breast cancer groups. Survival patterns of invasive lobular and invasive ductal breast cancer in a large population-based cohort with two decades of follow up. Breast. 2021;59:294-300. doi: 10.1016/j.breast.2021.07.011. Epub 2021 Jul 22.