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Original Article

Delayed Surgical Treatment and Survival Outcome in Breast Cancer

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Abstract

Background: For decades, there was inconsistency regarding the association between delay in treatment initiation (surgery) and survival outcomes in breast cancer patients. Therefore, this study aimed to evaluate the impact of the interval between diagnosis and curative surgery on survival outcomes in patients diagnosed with breast cancer.

Methods: This retrospective study was conducted on patients with stage I-III breast cancer referred to Imam Hossein Hospital in Tehran between 2011 and 2013. The Kaplan-Meier survival analysis and Cox proportional hazard model were performed to investigate the effect of delay in time from diagnosis to surgery and its effect on patients' overall survival.

Results: analysis of 93 patients who were treated with surgery at Imam Hossein Hospital showed the interval between diagnosis and surgery using various subgroup (cut-off value: 15, 30, and 45) had no effect on overall survival. However, surgery over 60 days after biopsy may be associated with worse overall survival (p=0.017). Cox proportional hazard model for comorbidities (HR and 95% CI: 0.2; 0.05-0.8, p<0.05) and distant metastasis (HR and 95%CI: 0.06; 0.01-0.23/p<0.0001) indicated a significant association with worse survival outcomes.

Conclusion: The findings demonstrated that time intervals of 60 days or longer between biopsy and surgery adversely impact overall patient survival. The presence of comorbidities and metastasis is likely to reduce the overall survival during the specified intervals.

Keywords: Biopsy, Breast neoplasms, Clergy, Humans, Proportional hazards models, Retrospective studies, Time-to-treatment

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Introduction

Breast cancer is considered as one of the most prevalent malignant diseases worldwide, with an 11.7% proportion among different types of cancers (1). Based on the stage of the breast cancer from I-IV and the types, namely, lobular and ductal carcinoma, different treatments are utilized (2). It is noteworthy that the treatment protocol for breast cancer varies from non-invasive to surgical interventions, depending on the stage and type of the breast cancer (3). Breast cancer was responsible for the highest mortality rate of malignant cancers among female patients which was estimated to be more than 150,000 patients in 2018 (4). The 5-year and 10-year relative survival rates of women with breast cancer were also estimated to be 73% and 61%, respectively (5). Hence, previous findings showed that the 5-year survival rate of breast cancer in Iran (67.6%) is lower compared to other developed countries (6).

Despite the lack of a standard medical definition for the interval between diagnosis and treatment initiation, studies have revealed that a time interval of approximately 90 days from diagnosis to surgery can significantly impact the survival outcomes of breast cancer patients (7,8). Moreover, it was reported that the delay in initiating treatment was more prominent in developing countries (9). However, previous studies revealed inconsistency in the association between delayed treatment and survival outcomes (10-16). Although some studies have found a significant positive association between the risk of mortality and longer treatment delays (10,11,13,14,16), others showed that shorter periods between diagnosis and treatment of breast cancer did not affect the survival outcomes (12,15). Notably, prior studies emphasized more the possible correlation of treatment delay between the tumor size and stage than its survival (8). Considering the controversial results of the related studies, understanding the possible relationship between treatment delay and survival outcome can lead us to launch more efficient treatment protocols, leading to a higher survival rate. Furthermore, to the best of authors' knowledge, no previous study has been conducted to assess the mentioned association in Iran. Accordingly, the study was aimed at exploring the effect of delay in the initiation of cancer treatment (the time from diagnosis to surgery) and its effect on patient survival outcomes (1,3,5 and 10-year survival) with an Iranian population.

Materials and Methods

Eligibility criteria

This retrospective cross-sectional study was conducted on patients with stage I-III breast cancer referred to Imam Hossein Hospital in Tehran between September 2011 and February 2013. Medical records of 93 patients were studied. All the patients had filled the informed consent form at admission in the hospital and before any diagnostic workup or treatment. They agreed to have their medical information used anonymously for research purposes.

Patients whose diagnosis time was unknown, had undergone palliative treatments, had metastasis at the time of diagnosis (using pathology report or imaging modality), or had not undergone surgical treatment, were excluded from the study. Patients who mentioned a previous history of cancer in their history were excluded. Patients who experienced a delay of over 6 months from the time of biopsy to surgery were excluded from the study to minimize the influence of non-medical factors, such as family refusal or financial problems, which could confound the analysis of treatment delays and their impact on survival. Basic clinical, pathological, and survival data of the patients were extracted from the patients' medical records. In cases where the information was incomplete, additional information was requested by calling the patients. Patients whose pathological diagnosis date was known were included in the study.

Data extraction

The interval between the diagnosis and the start of treatment was defined as the time between the date of the pathological diagnosis of the cancer and the start of treatment (surgery). Pathological diagnosis was performed with core needle biopsy or surgery (excisional biopsy). The patients' social and demographic variables including age at the time of diagnosis, comorbidity, and family history of cancer were extracted. Tumor-specific characteristics were extracted from the patient's medical records: tumor size, metastasis status, cancer stage (TNM staging), tumor hormone receptor status, and the status of the human epidermal growth factor receptor 2 (HER2).

Overall Survival (OS) is defined as the date of initiation of treatment until the date of death of any reason or the date of the last visit on medical file.

Statistical analysis

Using IBM SPSS version 27, the Kaplan-Meier survival analysis and -log rank tests were used to evaluate the effect of the length of diagnosis until the start of treatment on (overall survival) OS. Multivariate survival analysis was performed using the Cox proportional hazards regression model. For subgroup analyses, the time interval from diagnosis to surgery was divided into different categories (<15 days *vs.* ≥15 days, <30 days *vs.* ≥30 days, <45 days *vs.* ≥45 days, and <60 days *vs.* ≥60 days). The descriptive statistics were presented as mean±SD or median with Inter-Quartile Range (IQR) for continuous variables and frequency (percent %) for categorical variables. p-value less than 0.05 was considered as significant.

Results

A total of 93 patients were treated between September 2011 and February 2013 at Imam Hossein Hospital in Tehran. The mean age of the patients was 51.24 years (range 23-87 years). Comorbidities of the patients included diabetes (N=12), hypertension (N=12), heart disease (N=1), and other diseases (N=3). Four patients had several comorbidities at the same time. Among 93 patients, 58 patients were treated with Modified Radical Mastectomy (MRM), and 35 patients were treated with Breast-Conserving Surgery (BCS). In addition to surgery, some patients underwent neoadjuvant chemotherapy (N=24), adjuvant chemotherapy (N=45), radiotherapy (N=82), and hormone therapy (N=70). Types of hormone therapies used to treat patients included:
tamoxifen (61.5%), letrozole (32.8%), and combination therapy of tamoxifen and letrozole (5.7%). Most of the patients were in stage II (N=43, 46.2%) and stage III (N=38, 40.9%) of the disease at the time of diagnosis. During the follow-up, 17 patients progressed to metastasis (by using imaging modality). The median and IQR of the time between diagnosis and surgery were 4 [0-24] days (range: 0-180 days). In the studied cases, 69 patients (74.1%) underwent surgery within 30 days after biopsy and 19 patients (20.4%) underwent surgical treatment over 60 days after diagnosis. Table 1 shows the descriptive

Table 1. Descriptive statistics of the patients' clinical information

Factor	Descriptive summary (N=93)	Factor	Descriptive summary (N=93)
Age (years)	51.24±11.85	HER2	-
<40	16(17.2%)	Positive	49(52.7%)
40-49	29(31.2%)	Negative	44(47.3%)
50-59	26(28%)	Progesterone receptor	-
60-69	14(15.1%)	Positive	61(65.6%)
>70	8(8.6%)	Negative	32(34.4%)
Comorbidity	-	Estrogen receptor	-
Yes	24(25.8%)	Positive	68(73.1%)
No	69(74.2%)	Negative	25(26.9%)
Family history	-	Adjuvant chemotherapy	-
Yes	17(18.3%)	Yes	45(48.39%)
No	76(81.7%)	No	48(51.61%)

Contd. table 1.

N (At the time of diagnosis)		Neoadjuvant chemotherapy	-
N0	28(30.1%)	Yes	24(25.8%)
N1	31(33.3%)	No	69(74.2%)
N2	16(17.2%)	Radiotherapy	-
N3	18(19.4%)	Yes	82(88.2%)
T (At the time of diagnosis)		No	11(11.8%)
T1	26(28%)	Hormone therapy	-
T2	53(57%)	Yes	70(75.3%)
T3	14(15.1%)	No	23(24.7%)
M (At the time of diagnosis)	-	Recurrence	-
M0	93(100%)	Yes	11(11.8%)
M1	0(0%)	No	82(88.2%)
Stage (TMN)		Progression to Metastasis during the follow-up	
Stage I	12(12.9%)	Yes	17(18.3%)
Stage II	43(46.2%)	No	76(81.7%)
Stage III	38(40.9%)	-	-

characteristics of the patients' clinical information.

The mean of survival time was 9.20±0.43 (95% CI: 8.34-10.07) years. Overall survival of 1,3,5,10-years was 91%, 80%, 74% and 67%, respectively. Using Kaplan-Meier survival curve and Log-ranked test, duration with cut-off of 15, 30, and 45 days had no effect on OS (p=0.436, p=0.143, p=0.107, respectively). A longer duration with cut-off of 60 days had significant impact on OS (p=0.017) (Figure 1). Comparison of the impact of different categories

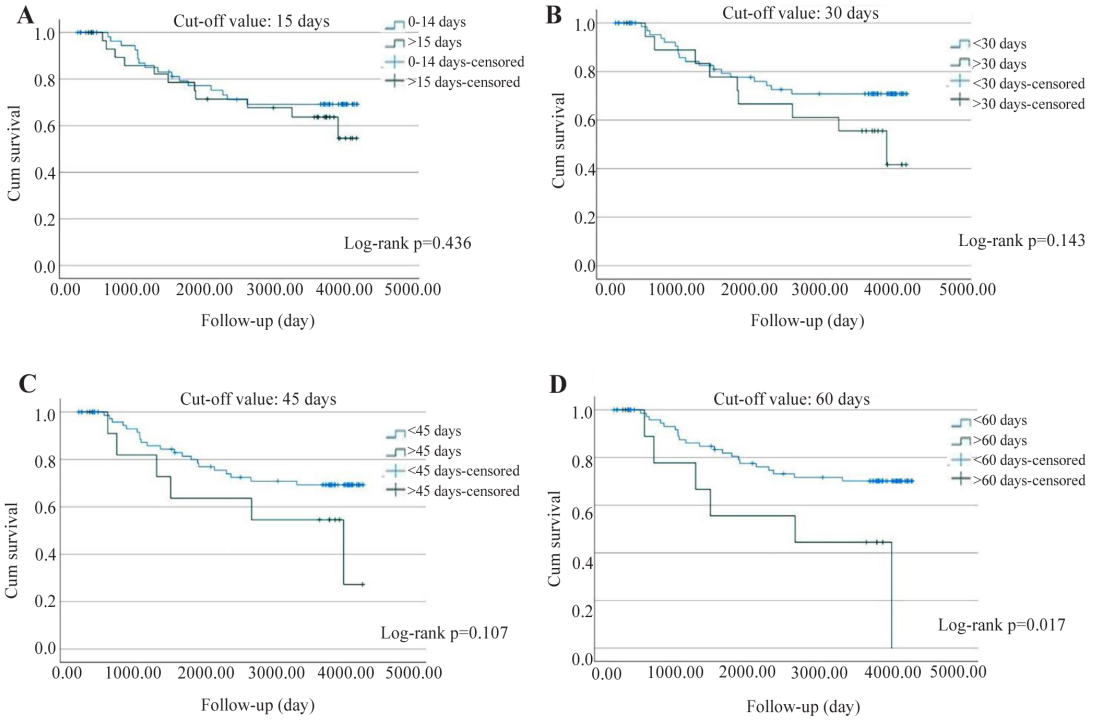

Figure 1. Kaplan-Meier survival curves of Overall Survival (OS) by interval between diagnosis and surgery. (A) OS by interval of <15 days versus ≥15 days. (B) OS by interval of <30 days versus ≥30 days. (C) OS by interval of <45 days versus ≥45 days. (D) OS by interval of <60 days versus ≥60 days.

of biopsy time to surgery on survival outcomes in different stages of the disease shows no effect on OS, except in stage II of the disease with a cut-off value of 60 days (p=0.011).

In general, Cox regression analysis demonstrated that OS is significantly related to having comorbidity [Hazard Ratio (HR); 95%CI:4.17; 1.42-13.41, p-value: 0.043], higher grade of lymph node involvement (N3 *vs.* N1=HR; 95%CI:14.58; 1.97-84.28, p value: 0.003), and the presence of metastasis (HR; 95%CI:10.87; 4.06-29.88, p<0.0001). However, age, neoadjuvant chemotherapy, adjuvant chemotherapy, radiotherapy, and hormone therapy revealed no significant association with risk of death. Also, the time from biopsy to surgery as an independent variable showed no significant relationship with OS (HR; 95%CI:1.04; 1.0-1.12, p-value: 0.758). Therefore, Cox analysis was also performed considering the comparison of two-time stratifications, the results of which are presented in table 2. As it is shown in Table 2, multivariate analysis for two subgroup intervals between diagnosis to surgery indicated that the absence of comorbidity might significantly have about 80% less risk of mortality in breast cancer patients (HR and 95%CI:0.2; 0.02-0.8, p<0.05). Also, the absence of metastasis had a significant association with longer OS (HR and 95%CI:0.07; 0.01-0.23/p< 0.0001).

Table 2. Multivariate analysis of the variables affecting overall survival for interval between diagnosis and surgery.

Variable	Interval <15 days *vs.* ≥15 days		Interval <60 days *vs.* ≥60 days	
	HR (95%CI)	p-value	HR (95%CI)	p-value
Age (year) ≥50 *vs.* <50	1.18(0.35-4.12)	0.566	1.03(0.30-3.65)	0.746
Comorbidity No *vs.* yes	0.23(0.02-0.84)	**0.034**	0.27(0.05-0.856)	**0.029**
N3 *vs.* N0,1,2	4.85 (0.37-39)	0.285	4.15(0.34-45.6)	0.298
T3 *vs.* T1,2	0.40(0.05-3.67)	0.432	0.34(0.05-3.43)	0.459
Stage III *vs.* stage I, II	4.41(0.18-160.2)	0.469	4.38(0.17-199.25)	0.427
HER2 Negative *vs.* positive	2.10(0.76-6.01)	0.187	1.39(0.53-5.45)	0.206
Progesterone receptor Negative *vs.* positive	0.72(0.23-2.86)	0.559	0.77(0.22-3.16)	0.524
Estrogen receptor Negative *vs.* positive	1.61(0.33-7.72)	0.656	1.57(0.42-7.02)	0.630
Recurrence No *vs.* Yes	1.86(0.28-8.06)	0.781	1.65(1.0-9.32)	0.654
Metastasis No *vs.* Yes.	0.074(0.015-0.23)	**<0.001**	0.08(0.02-0.23)	**<0.001**
Neoadjuvant chemotherapy Yes *vs.* No	1.041(0.22-5.24)	0.674	1.22(0.23-6.36)	0.752
Adjuvant chemotherapy Yes *vs.* No	0.98(0.19-5.04)	0.347	1.17(0.19-7.24)	0.385
Radiotherapy Yes *vs.* No	1.32(0.21-8.22)	0.491	2.10(0.29-15.48)	0.503
Hormone therapy Yes *vs.* No	0.88(0.16-5.04)	0.232	1.15(0.18-7.14)	0.268

Hazard Ratio (HR) and p-values are from Cox proportional hazard models.

Discussion

In this retrospective study, it was found that a longer duration of more than 60 days between diagnosis of breast cancer and the start of treatment significantly affected the overall survival rate. However, other treatment initiation intervals demonstrated no significant relationship with OS. Regarding the staging features, the study indicated no significant differences between various stages of breast cancer with OS, except in stage II of the disease with a cut-off value of 60 days (p=0.011). In addition, it was found that a time interval of more than 60 days between biopsy and surgery had a negative effect on overall survival. It should be noted that a positive significant association was observed between the absence of metastasis and OS.

A number of studies have investigated the potential relationship between delay in treatment initiation, namely, curative surgery and its impact on survival outcomes in various societies, including American, Asian, and European ones (9,12,15). However, these reports showed differing results.

In terms of OS, in a systematic review conducted in 2019, the global survival rates of breast cancer in one, three, five, and ten-year were reported as 0.92, 0.75, 0.73, and 0.61, which are lower than the findings of the current study (5). However, patients with metastases at baseline were not included in the present study. Another systematic review and meta-analysis conducted by Rezaianzadeh *et al* showed an overall pool-estimated 5-year survival rate of 67.6% among Iranian women (6). The present study determined a overall 5-year survival rate of 74%, respectively. To note, previous papers in the last decade demonstrated that the awareness about breast cancer among Iranian people, particularly in rural areas was inadequate (17-19). Stages II and III showed a remarkable proportion of the stages of patients at the time of diagnosis, which supports the data from previous literature (20-22). It has been well understood that the OS in other developing countries tends to be lower compared to the high-income societies (9).

The results were inconsistent with the findings of some related previous studies in which cut-off intervals between diagnosis to surgical treatment do not affect the OS. Although the present study indicated no significant impact of time intervals of less than 45 days on OS, the time gap of more than 60 days between diagnosis and initiation of treatment was negatively associated with OS. In a South Korean epidemiological study conducted in 2016, the interval between diagnosis and initiation of treatment among breast cancer patients more than 60 days or shorter had no impact on overall survival rate and outcomes (12). In 2013, another population-based study in Malaysia showed no significant association between primary treatment delay and overall survival rate (23). Moreover, in another retrospective study, Brazda *et al* found that time to treatment delay >90 days was not significantly associated with OS. Nevertheless, this research literature assessed the effect of treatment delays, including surgery, chemotherapy, or radiation treatment on OS (24). In line with the results, data from an American study indicated that with each 60-day interval delay, the mortality rate of breast cancer significantly increased (14). Shin *et al* also reported that delay in surgical treatment initiation of more than 12 weeks increased the breast cancer-specific mortality rate (25). Another South Korean study in 2012 also indicated that delays in surgical intervention of breast cancer could lead to decreased survival outcomes (26).

It is important to mention that neoadjuvant chemotherapy, which is necessary in patients with stages IIb and III can lead to delays of curative surgery (27). Nevertheless, in the present study, neoadjuvant chemotherapy had no significant impact on mortality. In line with the study, Gajdos *et al* determined that neoadjuvant chemotherapy had no remarkable benefit on OS in patients with locally advanced breast cancer (28). A retrospective study conducted by Al-Masri *et al* also reported that surgical delays >8 weeks was negatively associated with OS (29). Furthermore, a recent systematic review indicated that the effectiveness of neoadjuvant chemotherapy on survival outcomes, mostly depends on the chemotherapy regimens (30).

The current study showed that the presence of comorbidity adversely affected the overall survival rate, which can also be interpreted from previous studies (31-33). To be noted, the observed finding can be interpreted across two different subgroups of time-intervals of treatment initiation. The possible reason is that only less than 20% of the

study population consisted of patients younger than 40, which can lead to higher rates of comorbidities and potential outcomes of cancer survival. Although comorbidities are recognized to play a crucial role in the mortality rates of breast cancer, the specific impact of each comorbidity across different stages of the disease and also the effect of the comorbidity management on OS should be further investigated in future studies. In the current study, no significant associations were found in the subgroup analysis of other possible variables affecting overall survival and delays in treatment initiation, namely, age, tumor size, hormone receptor, and recurrence status.

Focusing on metastasis status, 17 of the patients progressed to metastatic disease. The findings also indicated that patients without metastatic breast cancer have approximately 93% higher chance of survival, which was similar to the results of previous studies (HR and 95%CI:0.06; 0.01-0.23 /p<0.0001) (34,35). Nevertheless, it should be noted that compared to prior decades, the 5-year survival rate of metastatic breast cancer had steadily risen from 10 to 27%. This can be explained as a result of the availability of adjuvant therapies (36).

The present study had some limitations. The low number of participants and the unavailability of a more accurate follow-up system need to be considered. Moreover, the findings were limited by missing and incomplete data due to the retrospective design of the study. However, a reasonably satisfactory survival rate was reported for the patients with breast cancer despite the limitations previously mentioned. Continued investigations are required to further determine this association and the possible causes of this relationship. In this study, the emphasis was on surgery delay. Hence, chemotherapy and hormonal agents are confounding factors for survival, as they can influence the effectiveness of treatment. Understanding their impact is crucial for assessing survival outcomes in the study.

Conclusion

The results showed that the time intervals of 60 days or more from the time of biopsy to surgery have a negative effect on the overall survival of patients. Additionally, presence of comorbidities and metastasis is more likely to decrease the overall survival in the mentioned intervals. These findings highlight the critical need for timely surgical interventions. Further studies are required to accurately determine optimal timing of surgery, specific reasons for delays in surgery, and the role of comorbidities in delay of breast cancer treatment.

Ethical considerations

This study was confirmed by the local committee of medical ethics, Shahid Beheshti University of Medical Science with Approval Code: IR.SBMU.RETECH.REC.1402.305. Also, written informed consent were obtained from the patients.

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Conflict of Interest

The authors declare there is no conflict of interest.

References

1. Kashyap D, Pal D, Sharma R, Garg VK, Goel N, Koundal D, et al. Global increase in breast cancer incidence: risk factors and preventive measures. Biomed Res Int 2022;2022:9605439.

2. Maughan KL, Lutterbie MA, Ham PS. Treatment of breast cancer. Am Fam Physician 2010;81(11):1339-46.

3. Trayes KP, Cokenakes SEH. Breast cancer treatment. Am Fam Physician 2021;104(2):171-8.

4. Smolarz B, Nowak AZ, Romanowicz H. Breast cancer-epidemiology, classification, pathogenesis and treatment

(review of literature). Cancers (Basel) 2022;14(10).

5. Maajani K, Jalali A, Alipour S, Khodadost M, Tohidinik HR, Yazdani K. The global and regional survival rate of women with breast cancer: a systematic review and meta-analysis. Clin Breast Cancer 2019;19(3):165-77.

6. Rezaianzadeh A, Jalali M, Maghsoudi A, Mokhtari AM, Azgomi SH, Dehghani SL. The overall 5-year survival rate of breast cancer among Iranian women: a systematic review and meta-analysis of published studies. Breast Dis 2017;37(2):63-8.

7. Bleicher RJ. Timing and delays in breast cancer evaluation and treatment. Ann Surg Oncol 2018;25(10):2829-38.

8. Caplan L. Delay in breast cancer: implications for stage at diagnosis and survival. Front Public Health 2014;2:87.

9. Rivera-Franco MM, Leon-Rodriguez E. Delays in breast cancer detection and treatment in developing countries. Breast Cancer (Auckl) 2018;12:1178223417752677.

10. Gagliato Dde M, Gonzalez-Angulo AM, Lei X, Theriault RL, Giordano SH, Valero V, et al. Clinical impact of delaying initiation of adjuvant chemotherapy in patients with breast cancer. J Clin Oncol 2014;32(8):735-44.

11. Mikeljevic JS, Haward R, Johnston C, Crellin A, Dodwell D, Jones A, et al. Trends in postoperative radiotherapy delay and the effect on survival in breast cancer patients treated with conservation surgery. Br J Cancer 2004;90(7):1343-8.

12. Yoo TK, Han W, Moon HG, Kim J, Lee JW, Kim MK, et al. Delay of Treatment Initiation Does Not Adversely Affect Survival Outcome in Breast Cancer. Cancer Res Treat 2016;48(3):962-9.

13. Yu KD, Fan L, Qiu LX, Ling H, Jiang YZ, Shao ZM. Influence of delayed initiation of adjuvant chemotherapy on breast cancer survival is subtype-dependent. Oncotarget 2017;8(28):46549-56.

14. Bleicher RJ, Ruth K, Sigurdson ER, Beck JR, Ross E, Wong YN, et al. Time to surgery and breast cancer survival in the United States. JAMA Oncol 2016;2(3):330-9.

15. Shafaee MN, Silva LR, Ramalho S, Doria MT, De Andrade Natal R, Cabello V, et al. Breast cancer treatment delay in safetynet health systems, Houston versus southeast Brazil. Oncologist 2022;27(5):344-51.

16. Ho PJ, Cook AR, Binte Mohamed Ri NK, Liu J, Li J, Hartman M. Impact of delayed treatment in women diagnosed with breast cancer: a population-based study. Cancer Med 2020;9(7):2435-44.

17. Akhtari-Zavare M, Ghanbari-Baghestan A, Latiff LA, Matinnia N, Hoseini M. Knowledge of breast cancer and breast self-examination practice among Iranian women in Hamedan, Iran. Asian Pac J Cancer Prev 2014;15(16):6531-4.

18. Tazhibi M, Feizi A. Awareness levels about breast cancer risk factors, early warning signs, and screening and therapeutic approaches among Iranian adult women: a large population based study using latent class analysis. Biomed Res Int 2014;2014:306352.

19. Hajian Tilaki K, Auladi S. Awareness, attitude, and practice of breast cancer screening women, and the associated socio-demographic characteristics, in northern Iran. Iran J Cancer Prev 2015;8(4):e3429.

20. Alwan NA, Tawfeeq F, Maallah AS, Sattar SA, Saleh WA. The stage of breast cancer at the time of diagnosis: correlation with the clinicopathological findings among Iraqi patients. J Neoplasm 2017;2(3):22.

21. Ren Z, Li Y, Hameed O, Siegal GP, Wei S. Prognostic factors in patients with metastatic breast cancer at the time of diagnosis. Pathol Res Pract 2014;210(5):301-6.

22. Saadatmand S, Bretveld R, Siesling S, Tilanus-Linthorst MM. Influence of tumour stage at breast cancer detection on survival in modern times: population based study in 173,797 patients. BMJ 2015 Oct 6:351:h4901.

23. Mujar M, Dahlui M, Yip CH, Taib NA. Delays in time to primary treatment after a diagnosis of breast cancer: does it impact survival? Prev Med 2013;56(3-4):222-4.

24. Brazda A, Estroff J, Euhus D, Leitch AM, Huth J, Andrews V, et al. Delays in time to treatment and survival impact in breast cancer. Ann Surg Oncol 2010;17 Suppl 3:291-6.

25. Shin DW, Cho J, Kim SY, Guallar E, Hwang SS, Cho B, et al. Delay to curative surgery greater than 12 weeks is associated with increased mortality in patients with colorectal and breast cancer but not lung or thyroid cancer. Ann Surg Oncol 2013;20(8):2468-76.

26. Yun YH, Kim YA, Min YH, Park S, Won YJ, Kim DY, et al. The influence of hospital volume and surgical treatment delay on long-term survival after cancer surgery. Ann Oncol 2012;23(10):2731-7.

27. Müller C, Juhasz-Böss I, Schmidt G, Jungmann P, Solomayer EF, Breitbach GP, et al. Factors influencing the time to surgery after neoadjuvant chemotherapy in breast cancer patients. Arch Gynecol Obstet 2020;301(4):1055-9.

28. Gajdos C, Tartter PI, Estabrook A, Gistrak MA, Jaffer S, Bleiweiss IJ. Relationship of clinical and pathologic response to neoadjuvant chemotherapy and outcome of locally advanced breast cancer. J Surg Oncol 2002;80(1):4-11.

29. Al-Masri M, Aljalabneh B, Al-Najjar H, Al-Shamaileh T. Effect of time to breast cancer surgery after neoadjuvant chemotherapy on survival outcomes. Breast Cancer Res Treat 2021;186(1):7-13.

30. Cortes J, Haiderali A, Huang M, Pan W, Schmid P, Akers KG, et al. Neoadjuvant immunotherapy and chemotherapy regimens for the treatment of high-risk, early-stage triple-negative breast cancer: a systematic review and network meta-analysis. BMC Cancer 2023;23(1):792.

31. Land LH, Dalton SO, Jørgensen TL, Ewertz M. Comorbidity and survival after early breast cancer. A review. Crit Rev Oncol Hematol 2012;81(2):196-205.

32. Berglund A, Wigertz A, Adolfsson J, Ahlgren J, Fornander T, Wärnberg F, et al. Impact of comorbidity on management and mortality in women diagnosed with breast cancer. Breast Cancer Res Treat 2012;135(1):281-9.

33. Dumas E, Grandal Rejo B, Gougis P, Houzard S, Abécassis J, Jochum F, et al. Concomitant medication, comorbidity and survival in patients with breast cancer. Nat Commun 2024;15(1):2966.

34. Nie Y, Ying B, Lu Z, Sun T, Sun G. Predicting survival and prognosis of postoperative breast cancer brain metastasis: a population-based retrospective analysis. Chin Med J (Engl) 2023;136(14):1699-707.

35. Li S, Li C, Shao W, Liu X, Sun L, Yu Z. Survival analysis and prognosis of patients with breast cancer with pleural metastasis. Front Oncol 2023;13:1104246.

36. Sundquist M, Brudin L, Tejler G. Improved survival in metastatic breast cancer 1985-2016. Breast 2017;31:46-50.