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Lymphedema and Axillary Sentinel Lymph Node Biopsy (SLNB) in Node-Negative Patients with Breast Cancer

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Abstract

Background: Breast cancer (BC) poses a significant health concern for females, often resulting in complications such as lymphedema due to treatment effects.
Objectives: This study examines the link between lymphedema and the number of removed negative axillary lymph nodes (LNs) after sentinel lymph node biopsy (SLNB) in BC patients.
Methods: A prospective study from 2016 to 2019 included 150 eligible women out of 1 600 BC patients who underwent axillary sentinel node biopsy (SNB). The prognostic value of isolated negative nodes and BMI in predicting lymphedema post-SLNB was analyzed.
Results: Among 950 women receiving radiotherapy, 4% developed lymphedema. Notably, patients with lymphedema were younger (average age 53.34 years). BMI didn't differ significantly, but the number of removed sentinel LN-negatives was crucial. Patients with 4 - 5 nodes removed had an 89.47% likelihood, while those with 1 - 3 nodes had zero incidence.
Conclusions: BC-related lymphedema significantly impacts patient well-being. Our study establishes a direct correlation between the number of removed negative LNs and the severity of edema, emphasizing the need for further research.

Keywords: Breast Cancer, Axillary Sentinel Lymph Node Biopsy, Lymphedema

1. Background

Breast cancer (BC) is the most common cancer and a significant health concern in females, causing cancer-related deaths worldwide (1, 2). According to the American Cancer Society, approximately 287,850 new cases of BC were reported in 2022, with 530 men and 43,250 women expected to die in 2022 (3). In 2018, BC accounted for 10% of all cancer types in Asia, with 845,400 patients (1). It is predicted that the number of new patients in Asia will reach 1.34 million by 2040 (4). In a 2018 study, BC constituted 16% of all reported cancers in Iran, with more than 40% of patients aged between 40 - 50 years (5). Lifestyle changes, smoking, alcohol, obesity, delay in childbearing, and reduced breastfeeding contribute to the increase of BC in low and middle-income countries, accounting for more than 55% of BC deaths (6, 7).

Common medical treatments for BC include a combination of surgeries (such as breast removal and axillary lymph node dissection (ALND), radiation therapy, chemotherapy, and hormone therapy (8) Since there are about 10 - 30 lymph nodes (LNs) below the axillary vein, to which the breast lymph drains (9), in the past, all of them were removed during breast surgery. Later, it was found that according to the surgeon's opinion, the removal of 10 - 12 LNs is sufficient (10). Of course, later, instead of removing all or most of the axillary LNs, the first lymph node that exists after the breast tissue and is called the sentinel lymph node (SLND) was removed and examined. The condition of this LNs indicates the condition of the other LNs, and if it is involved, the axillary LNs must be removed completely (11). Therefore, recently in surgery, the process of local treatment of BC has changed from removing a large number of axillary lymph nodes (ALND) to sentinel lymph node biopsy (SLNB) in people who are clinically negative in the axilla (12). As a result of BC treatment (removal and surgery of LNs, radiation therapy followed by lymphatic system destruction), complications

occur (13).

Lymphedema is a significant cause of morbidity in BC patients undergoing axillary surgery (8), resulting from the long-term accumulation of fluid rich in protein due to lymphatic injury during surgery (14). Symptoms include swelling, heaviness, and stiffness in the affected extremity, impacting the overall quality of life (8, 14). Recognizing associated risk factors is essential to decrease the incidence of lymphedema (15).

Sentinel lymph node biopsy is widely accepted for axillary staging in early BC, even in patients positive for axillary lymph nodes (16). Increased use of SLNB has reduced the incidence of lymphedema, but some cases still develop it following SLNB (15). The number of retrieved sentinel lymph nodes during SLNB can influence its accuracy, and a higher count may lead to a higher prevalence of lymphedema in the ipsilateral arm (17, 18). Recent studies suggest that lymphedema might be a morbidity in SLNB-negative patients (19).

1.1. Hypothesis

We hypothesize that patients who undergo the removal of less than 5 sentinel nodes are at a lower risk of developing lymphedema.

2. Objectives

This study aims to explore the relationship between lymphedema and the number of removed negative axillary lymph nodes in SLNB after negative SLNB in females with BC.

3. Methods

3.1. Study Design

This study, conducted from 2016 to 2019, included 1150 women meeting the study inclusion criteria out of 1 600 BC patients who underwent axillary SLNB at the Cancer Research Center, Shahid Beheshti University of Medical Sciences. The study had a fundamental-applied design, measuring lymphedema after SLNB surgery.

3.2. Sampling

In this cross-sectional research, 950 women with BC who had breast-conserving surgery and underwent sentinel lymph node surgery at least 3 years before the study were selected as study samples. Excluded were 200 patients who underwent simpler subcutaneous mastectomy without radiotherapy.

Inclusion criteria was as follow: (1) Patients must have a history of BC; (2) referral to Cancer Research Center, Shahid Beheshti University of Medical Sciences; (3) the age of the women was between 30 and 60 years; (4) all patients had a negative SLNB result; (5) at least 3 years have passed since treatment; (6) he patient's consent to participate in the research was obtained; (7) all patients had Breast Conserving surgery; (8) none of the patients had previously been treated for postoperative lymphedema, had no history of preoperative lymphedema, orthopedic disorders, neurological problems on the affected side; (9) have secondary edema of the upper limb on the side of the affected breast; (10) have a difference in circumference of $>$ 2 cm compared to that of the contralateral extremity for either the forearm or the upper arm.

Exclusion criteria was as follow: (1) Patients unwilling to participate in the research for any reason; (2) had a history of axillary lymph node removal; (3) patients who exhibited a positive result in their sentinel lymph node biopsy (SLNB); (4) patients who did not undergo radiotherapy.

3.3. Methods

All eligible patients after sentinel lymph node biopsy were contacted to obtain their medical history and pathology documents. A questionnaire related to background information and clinical evaluation, including body mass volume and lymphedema measurement, was completed. The evaluation included a clinical examination by a cancer surgeon and lymphotherapist at the center's lymphedema clinic. A demographic information questionnaire with 20 questions was completed for each patient.

Lymphedema was evaluated by objective assessment of the upper limbs and subjective measurement of symptoms. Using non-stretch tape, an experienced researcher measured the difference in circumference between two affected organs and healthy organs in four parts: Palm, wrist, 10 cm below, and 10 cm above the first cranial appendage of the elbow. A lymphedema patient had a difference in circumference of more than 2 cm compared to that of the contralateral extremity for either the forearm or the upper arm.

3.4. Statistical Analysis

Quantitative variables were described using mean and standard deviation, while qualitative variables were reported as numbers (percentages). *t*-test and chi-square tests were used to analyze the correlation between different variables and the number of lymph nodes after the removal of sentinel lymph node-negatives in women with breast cancer. Data were analyzed using Stata software (version 14), and $P < 0.05$ was considered statistically significant.

4. Results

In this study, 950 women with breast cancer (BC) having axillary sentinel LN-negatives and undergoing radiotherapy were recruited. 4% of patients (38 individuals) experienced lymphedema. The patients' average age was 56.74 ± 7.68 years (age range: 39 to 71 years), and the average age in patients with lymphedema was significantly lower compared to patients without lymphedema (53.34 years vs. 56.88 years) (P = 0.005). The mean body mass index (BMI) was 27.43 ± 4.14 kg/m^2, and its average did not show a significant difference between the two groups with lymphedema and without edema (P = 0.577). Additionally, the average number of sentinel LN-negatives removed was 1.64 ± 0.97 (ranging from 1 to 5 nodes) in patients. The average number of LN-negatives in patients with edema was significantly higher than in patients without edema (4.89 ± 0.31 vs. 1.51 ± 0.73) (P < 0.001) (Table 1).

Based on BMI levels, 28.11% of patients were in the normal group, 43.79% in the overweight group, and 28.11% in the obese group. Regarding marital status, most women, both in general and among patients with and without lymphedema, were married. In terms of education level, the majority had primary and middle school education. Among all patients, 52.11% (495 individuals) had a history of underlying diseases. In 52.11% of all patients, the affected limb was on the right side. No statistically significant relationship was found between the mentioned variables and the occurrence of lymphedema (P > 0.05) (Table 2).

There was a significant relationship between the number of removed LN-negatives and the occurrence of lymphedema, so that with the increase in the number of LNsto 4 and 5 nodes, the occurrence of lymphedema in patients was 10.53% and 89.47%, respectively, but in patients with 1-3 LNs, the percentage of lymphedema was zero (Table 3).

5. Discussion

The sentinel lymph node biopsy (SLNB), introduced over 15 years ago in clinically node-negative BC patients, serves to assess their LN status for diagnostic purposes (20). In cases of a negative SLN, an axillary lymph node dissection (ALND) is omitted. The SLN is negative in about 74% of patients in the general BC population (21). Lymphedema is a non-negligible complication in cases of SLNB-negative BC (22), observed in one of five cases with BC, following radiation therapy, breast surgery, and chemotherapy (23). SLNB stages the clinically negative axilla (19), and the prevalence of lymphedema (LE) following SLNB is nearly 5% (24). Patients receiving axillary excision of more than five LNs are more prone to develop LE (25, 26). Risk factors for LE include LN dissection, high BMI, mastectomy, the number of affected LNs, lack of regular physical activity, and receiving radiation therapy and chemotherapy. However, in our study, no significant difference in average BMI was observed between the two groups (with and without edema) (27-29).

We investigated the association between lymphedema and the number of removed axillary LN-negatives in SLNB in BC patients. The patients' average age was 56.74 ± 7.68, and the average BMI was 27.43 ± 4.14 kg/m^2, with an average follow-up period after surgery of 3 years. Based on BMI, 43.42% of the group were overweight. The number of retrieved LN-negatives can be considered a risk factor for LE development. Lymphedema occurs after surgery in some patients and affects their quality of life (30). We found a significant relationship between the number of isolated LN-negatives and LE (4.89 ± 0.31 versus 1.51 ± 0.73) (P < 0.001). The relationship between the number of removed LN-negatives and the occurrence of lymphedema was significant, with 10.53% and 89.47% occurrence rates in patients with 4 and 5 nodes, respectively, and zero incidence in patients with 1 - 3 LNs. In Gebruers's study, the general incidence of lymphedema after SLNB in nodes-negative cases was reported broadly (0% to 63.4%) (22).

We found an association between the number of removed LN-negatives had a significant relationship with the occurrence of lymphedema, so that with the increase in the number of LNs to 4 and 5 nodes, the occurrence of lymphedema in patients was 10.53% and 89.47%, respectively, but in patients with 1 - 3 LNs, the percentage of lymphedema was zero (Table 3).

Isik et al. reported in 2022, in a retrospective study of the BC database from 2013 to 2017, that patients with removal of more than 5 LNs were more likely to develop lymphedema (25). A 2022 study by Yaghoobi Notash et al., aiming to determine factors influencing lymphedema which was done on 970 patients with BC, the percentage of influencing variables was reported as follows: The number of LNs/the number of LNs isolated ratio (68%), the feeling of heaviness (67%), number of LNs isolated (64%), receiving radiotherapy (63%), surgery type (62%), number of involved LNs (61%), BMI (61%) (31). So both of these studies showed a significant association between the number of isolated LN-negatives and Lymphedema in patients same our study.

Sentinel lymph node biopsy-negative patients may exhibit mild lymphedema, but if untreated, it can become more severe. However, in our study, severe lymphedema was diagnosed in 4% of patients, which falls within the recorded range of 0.2% to 9% in SLNB patients with

Table 1. Description of the Variables of Age, BMI, and the Number of Lymph Node-Negatives According to the Occurrence of Lymphedema in Patients with Breast Cancer [a]

Different Variables	Total: 950	Yes: 38	No: 912	P-Value [b]
Age (y)	56.74 ± 7.68	53.34 ± 7.85	56.88 ± 7.64	0.005
BMI (Kg/m^2)	27.43 ± 4.11	27.07 ± 3.69	27.45 ± 4.13	0.577
Number of removed sentinel lymph node-negatives	1.64 ± 0.97	4.89 ± 0.31	1.51 ± 0.73	> 0.001

[a] Values are expressed as mean ± SD.
[b] Using the chi-square test.

Table 2. Frequency of Demographic and Disease-related Variables According to the Occurrence of Lymphedema in Breast Cancer Patients [a]

Variables	Total: 950	Yes: 38	No: 912	P-Value [b]
BMI				0.484
Normal	264 (28.11)	10 (26.32)	257 (28.18)	
Overweight	416 (43.79)	20 (52.63)	396 (43.42)	
Obesity	267 (28.11)	8 (21.05)	259 (28.40)	
Marital status				0.166
Single	58 (5.11)	5 (13.16)	53 (5.81)	
Madrid	851 (89.58)	31 (81.58)	820 (89.91)	
Divorce	41 (4.32)	2 (5.26)	39 (4.28)	
Level of education				0.178
Elementary school	382 (40.21)	15 (39.47)	367 (40.24)	
High school	296 (31.16)	7 (18.42)	289 (31.69)	
Diploma and sub-diploma	217 (22.84)	12 (31.58)	205 (22.48)	
University	55 (5.79)	4 (10.53)	51 (5.59)	
Underlying disease				0.947
Yes	495 (52.11)	20 (52.63)	475 (52)	
No	455 (47.89)	18 (47.37)	437 (47.92)	
Affected organ				0.947
Right	495 (52.11)	20 (52.63)	475 (52)	
Left	455 (47.8)	18 (47.37)	437 (47.92)	

[a] Values are expressed as No. (%).
[b] Using the chi-square test.

Table 3. The Frequency of the Number of Lymph nodes According to the Occurrence of Lymphedema in Patients with Breast Cancer [a]

Number of Removed Sentinel Lymph Node-Negatives	Total: 950	Yes: 38	No: 912	P-Value [b]
1	572 (60.21)	0 (0)	62.72 (572)	> 0.001
2	211 (22.21)	0 (0)	23.14 (211)	
3	129 (13.58)	0 (0)	14.14 (129)	
4	4 (0.42)	4 (10.53)	0 (0)	
5	34 (3.58)	34 (89.47)	0 (0)	

[a] Values are expressed as No. (%).
[b] Using the chi-square test.

lymphedema in some studies (15, 32-35). Therapists and clinicians should consider lymphedema as a complication when evaluating patients who have had SLNB. Although our study evaluated lymphedema over a period of at least 3 years, some studies suggest a critical follow-up period of 6 - 12 months following surgery to assess the presence of lymphedema in such cases (36, 37).

5.1. Conclusions

Lymphedema is a morbid and chronic complication resulting from BC treatment using axillary surgery and/or radiation treatment which causes psychological and functional problems affecting patients' quality of life. For this reason, prognostic factors help a lot in treating and reducing complications. In our study, a positive association was reported between the number of removed LN-negative in axillary SNB and the degree of lymphedema in patients, although more studies are needed in this field to obtain more accurate results.

Footnotes

Authors' Contribution: All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interests: The authors declare no conflict of interest. One of the authors is the editor-in-chief of the journal (Mohammad Esmaeil Akbari).

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: The study was approved by the Shahid Beheshti University of Medical Sciences and the respective ethics committees in the participating institution and patient information confidentiality were upheld (ethics number: IR.SBMU.CRC.REC.1401.024).

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Informed Consent: The patient's consent to participate in the research was obtained.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;**68**(6):394–424. [PubMed ID: 30207593]. https://doi.org/10.3322/caac.21492.
2. Jeibouei S, Akbari ME, Kalbasi A, Aref AR, Ajoudanian M, Rezvani A, et al. Personalized medicine in breast cancer: Pharmacogenomics approaches. *Pharmgenomics Pers Med*. 2019;**12**:59–73. [PubMed ID: 31213877]. [PubMed Central ID: PMC6549747]. https://doi.org/10.2147/PGPM.S167886.
3. American Cancer Society. *Cancer Facts and Figured 2022*. American Cancer Society; 2022.
4. *GLOBOCAN: Estimated number of new breast cancer cases, Asia in 2040*. Global Cancer Observatory; 2022. Available from: https://gco.iarc.fr/tomorrow/en/dataviz/tables.
5. Farhood B, Geraily G, Alizadeh A. Incidence and Mortality of Various Cancers in Iran and Compare to Other Countries: A Review Article. *Iran J Public Health*. 2018;**47**(3):309–16. [PubMed ID: 29845017]. [PubMed Central ID: PMC5971166].
6. Heidarirad F, Yarahmadi M, Heidarirad H, Shafiei M. [Evaluation of Prevalence of Depression and Its Related Factors among Women with Breast Cancer Referred to the Radiotherapy Center of Tawhid Hospital of Sanandaj, Iran in 2017]. *Sci J Nurs Midwifery Paramed Faculty*. 2018;**4**(2):39–49. Persian.
7. Isfahani P, Hossieni Zare SM, Shamsaii M. The Prevalence of Depression in Iranian Women With Breast Cancer: A Meta-Analysis. *Q Horizon Med Sci*. 2020;**26**(2):170–81. https://doi.org/10.32598/hms.26.2.3207.1.
8. Hayes SC, Janda M, Cornish B, Battistutta D, Newman B. Lymphedema after breast cancer: incidence, risk factors, and effect on upper body function. *J Clin Oncol*. 2008;**26**(21):3536–42. [PubMed ID: 18640935]. https://doi.org/10.1200/JCO.2007.14.4899.
9. Safaeei Keshtgar MR, Austin R, Barzegar M, Akbari A, Akbari ME. *[General informarion for prevention and clinical drawings for women with breast cancer]*. **25**. Cancer Research Center of Shahid Beheshti University; 2010. Persian.
10. Ebrahimi M, Olfat Bakhsh A, Ansari M, Habibi M. *[A comprehensive guide of breast diseases]*. **2**. Cancer Research Center of academic Jahad of Tehran University; 2011. p. 110–2. Persian.
11. Ebrahimi M, Olfat Bakhsh A, Omidari S, Anbiai R, Ongooti Oshnari L, Haghighat S, et al. *[An introduction to diseases of the Breast]*. Varsity Jahad Publication; 2014. 258 p. Persian.
12. Zahoor S, Haji A, Battoo A, Qurieshi M, Mir W, Shah M. Sentinel Lymph Node Biopsy in Breast Cancer: A Clinical Review and Update. *J Breast Cancer*. 2017;**20**(3):217–27. [PubMed ID: 28970846]. [PubMed Central ID: PMC5620435]. https://doi.org/10.4048/jbc.2017.20.3.217.
13. Moffat C, Doherty D, Morgan P. Best practice for the management of lymphoedema. *International Consensus*. 2006;**12**(2):125–32.
14. McLaughlin SA, Staley AC, Vicini F, Thiruchelvam P, Hutchison NA, Mendez J, et al. Considerations for clinicians in the diagnosis, prevention, and treatment of breast cancer-related lymphedema: Recommendations from a multidisciplinary expert asbrs panel : Part 1: Definitions, assessments, education, and future directions. *Ann Surg Oncol*. 2017;**24**(10):2818–26. https://doi.org/10.1245/s10434-017-5964-6.
15. Goldberg JI, Wiechmann LI, Riedel ER, Morrow M, Van Zee KJ. Morbidity of sentinel node biopsy in breast cancer: the relationship between the number of excised lymph nodes and lymphedema. *Ann Surg Oncol*. 2010;**17**(12):3278–86. [PubMed ID: 20574774]. https://doi.org/10.1245/s10434-010-1155-4.
16. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. *JAMA*. 2017;**318**(10):918–26. [PubMed ID: 28898379]. [PubMed Central ID: PMC5672806]. https://doi.org/10.1001/jama.2017.11470.
17. Chagpar AB, Scoggins CR, Martin RC, Carlson DJ, Laidley AL, El-Eid SE, et al. Are 3 sentinel nodes sufficient? *Arch Surg*. 2007;**142**(5):456–9. discussion 459-60. [PubMed ID: 17515487]. https://doi.org/10.1001/archsurg.142.5.456.
18. Zakaria S, Degnim AC, Kleer CG, Diehl KA, Cimmino VM, Chang AE, et al. Sentinel lymph node biopsy for breast cancer: how many nodes are enough? *J Surg Oncol*. 2007;**96**(7):554–9. [PubMed ID: 17685432]. https://doi.org/10.1002/jso.20878.

19. Verbelen H, Gebruers N, Eeckhout FM, Verlinden K, Tjalma W. Shoulder and arm morbidity in sentinel node-negative breast cancer patients: a systematic review. *Breast Cancer Res Treat*. 2014;**144**(1):21–31. [PubMed ID: 24496928]. https://doi.org/10.1007/s10549-014-2846-5.
20. Voogd AC, Coebergh JW, Repelaer van Driel OJ, Roumen RM, van Beek MW, Vreugdenhil A, et al. The risk of nodal metastases in breast cancer patients with clinically negative lymph nodes: a population-based analysis. *Breast Cancer Res Treat*. 2000;**62**(1):63–9. [PubMed ID: 10989986]. https://doi.org/10.1023/a:1006447825160.
21. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Ashikaga T, et al. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol*. 2007;**8**(10):881–8. [PubMed ID: 17851130]. https://doi.org/10.1016/S1470-2045(07)70278-4.
22. Gebruers N, Verbelen H, De Vrieze T, Coeck D, Tjalma W. Incidence and time path of lymphedema in sentinel node negative breast cancer patients: a systematic review. *Arch Phys Med Rehabil*. 2015;**96**(6):1131–9. [PubMed ID: 25637862]. https://doi.org/10.1016/j.apmr.2015.01.014.
23. Borman P, Yaman A, Yasrebi S, Ozdemir O. The Importance of Awareness and Education in Patients with Breast Cancer-Related Lymphedema. *J Cancer Educ*. 2017;**32**(3):629–33. [PubMed ID: 27048148]. https://doi.org/10.1007/s13187-016-1026-1.
24. O'Donnell TF, Rasmussen JC, Sevick-Muraca EM. New diagnostic modalities in the evaluation of lymphedema. *J Vasc Surg Venous Lymphat Disord*. 2017;**5**(2):261–73. [PubMed ID: 28214496]. [PubMed Central ID: PMC5325714]. https://doi.org/10.1016/j.jvsv.2016.10.083.
25. Isik A, Soran A, Grasi A, Barry N, Sezgin E. Lymphedema After Sentinel Lymph Node Biopsy: Who Is at Risk? *Lymphat Res Biol*. 2022;**20**(2):160–3. [PubMed ID: 34191608]. https://doi.org/10.1089/lrb.2020.0093.
26. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol*. 2013;**14**(6):500–15. [PubMed ID: 23540561]. https://doi.org/10.1016/S1470-2045(13)70076-7.
27. Tsai RJ, Dennis LK, Lynch CF, Snetselaar LG, Zamba GK, Scott-Conner C. The risk of developing arm lymphedema among breast cancer survivors: a meta-analysis of treatment factors. *Ann Surg Oncol*. 2009;**16**(7):1959–72. [PubMed ID: 19365624]. https://doi.org/10.1245/s10434-009-0452-2.
28. Greene AK, Zurakowski D, Goss JA. Body Mass Index and Lymphedema Morbidity: Comparison of Obese versus Normal-Weight Patients. *Plast Reconstr Surg*. 2020;**146**(2):402–7. [PubMed ID: 32740596]. https://doi.org/10.1097/PRS.0000000000007021.
29. Armer JM, Ostby PL, Ginex PK, Beck M, Deng J, Fu MR, et al. ONS Guidelines for Cancer Treatment-Related Lymphedema. *Oncol Nurs Forum*. 2020;**47**(5):518–38. [PubMed ID: 32830794]. https://doi.org/10.1188/20.ONF.518-538.
30. Ma X, Wen S, Liu B, Li D, Wang X, Kong X, et al. Relationship between Upper Extremity Lymphatic Drainage and Sentinel Lymph Nodes in Patients with Breast Cancer. *J Oncol*. 2019;**25**(1):145–52. [PubMed ID: 31057616]. [PubMed Central ID: PMC6463564]. https://doi.org/10.1155/2019/8637895.
31. Yaghoobi Notash A, Yaghoobi Notash A, Omidi Z, Haghighat S. Prediction of lymphedema occurrence in patients with breast cancer using the optimized combination of ensemble learning algorithm and feature selection. *BMC Med Inform Decis Mak*. 2022;**22**(1):195. [PubMed ID: 35879760]. [PubMed Central ID: PMC9310496]. https://doi.org/10.1186/s12911-022-01937-z.
32. Ashikaga T, Krag DN, Land SR, Julian TB, Anderson SJ, Brown AM, et al. Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection versus axillary dissection. *J Surg Oncol*. 2010;**102**(2):111–8. [PubMed ID: 20648579]. [PubMed Central ID: PMC3072246]. https://doi.org/10.1002/jso.21535.
33. Salinas-Huertas S, Luzardo-González A, Vázquez-Gallego S, Pernas S, Falo C, Pla MJ, et al. Risk factors for lymphedema after breast surgery: A prospective cohort study in the era of sentinel lymph node biopsy. *Breast Dis*. 2022;**41**(1):97–108. [PubMed ID: 34542055]. https://doi.org/10.3233/bd-210043.
34. Kim HK, Ju YW, Lee JW, Kim KE, Jung J, Kim Y, et al. Association between Number of Retrieved Sentinel Lymph Nodes and Breast Cancer-related Lymphedema. *J Breast Cancer*. 2021;**24**(1):63–74. [PubMed ID: 33634621]. [PubMed Central ID: PMC7920859]. https://doi.org/10.4048/jbc.2021.24.e9.
35. Shen A, Lu Q, Fu X, Wei X, Zhang L, Bian J, et al. Risk factors of unilateral breast cancer-related lymphedema: an updated systematic review and meta-analysis of 84 cohort studies. *Support Care Cancer*. 2022;**31**(1):18. [PubMed ID: 36513801]. https://doi.org/10.1007/s00520-022-07508-2.
36. Lumachi F, Basso S, Bonamini M, Marino F, Marzano B, Milan E, et al. Incidence of Arm Lymphoedema Following Sentinel Node Biopsy, Axillary Sampling and Axillary Dissection in Patients with Breast Cancer. *In vivo (Athens, Greece)*. 2009;**23**:1017–20.
37. McDuff SGR, Mina AI, Brunelle CL, Salama L, Warren LEG, Abouegylah M, et al. Timing of Lymphedema After Treatment for Breast Cancer: When Are Patients Most At Risk? *Int J Radiat Oncol Biol Phys*. 2019;**103**(1):62–70. [PubMed ID: 30165125]. [PubMed Central ID: PMC6524147]. https://doi.org/10.1016/j.ijrobp.2018.08.036.