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Review Article
Published: 26 Jan, 2018

Journal of Surgery Forecast

Current Approach to Axilla in Breast Cancer

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Abstract

The characteristics of the axillary lymph node are one of the most important prognostic factors determining the prognosis in breast cancer.Until the beginning of 1990s staging and survival were evaluated only with axillary lymph node dissection, but the introduction of the path-breaking sentinel lymph node biopsy enabled the prevention of many unnecessary morbidities. In this article, we will discuss current approaches to axilla in breast cancer.

Keywords: Axilla; Breast cancer; Sentinel lymph node biopsy

Introduction

The goal of the breast cancer surgery is to increase the survival, remove the tumor, decrease the relapse rate with the establishment of the local control and increase the quality of life of patients [1]. At the beginning of 1990s, William S. Halsted was the first author, who defined the complete removal of the lymph nodes in breast surgery with the radical mastectomy method [2]. Halsted believed that breast cancer was a local disease and suggested that the cure of the disease might be achieved with a radical excision [3]. While surgeons considered the breast cancer as a local disease, which could be controlled with lymph node dissection, oncologists believed that it was a systemic disorder as a result of the nature of cancer. Today, according to the spectrum hypothesis, it is well known that the regional lymphatics have a very important role in the relation of the host and the tumor and that invasive tumors at the early stage may be systemic while certain non-invasive tumors at the advanced stage may remain local for a long time [4]. With the development of the radiotherapy during and after lumpectomy, mastectomy was avoided especially in the early-stage breast cancer. As the comparison of the survival rates did not show any superiority according to the mastectomy, this cleared the way of the wide usage of the sentinel lymph node biopsy (SLNB) [5-7]. SLNB is not only a safe method for the axillary lymph nodes in breast cancer but it also decreases the complications, which may emerge after the unnecessary conventional axillary lymph node dissection [8,9]. Although axillary lymph node dissection (ALND) is still recommended in SLNB-positive cases, the complications such as lymphedema, paresthesia, pain, seroma, loss of mobility and strength in the upper extremities and post-operative infection are more common in ALND than SLNB (38-72% and 20% respectively) [10,11]. Vieni et al. [12] showed in their study that the sensitivity of SLNB was approximately 92% in breast cancer. Therefore, in order to avoid the complications of ALND caused by the unnecessary false positivity, partial axillary lymph node dissection was defined [13]. While in the conventional ALND, the lymph nodes at level 1-2 are dissected, in partial ALND, the upper limit is defined at the intercostobrachial nerve, the medial limit at the nervus thoracicus longus and the posterior limit at the thorocadorsal nerve. The comparison of the partial and total ALND showed that morbidity rate is significantly lower in partial ALND [14].

In the last years, the majority of the surgeons started routinely to use the SLNB method. Thus, unnecessary complications of partial and total ALND will be avoided.

Sentinel Lymph Node Biopsy

SLNB, which was introduced at the beginning of 1990s, is a suggestive method about the involvement of the axillary lymph nodes in the breast cancer [15]. The size, stage of the tumor, lymphovascular invasion are all known as independent risk factors for lymph node metastasis [16]. Although a prediction can be done with all these risk factors, the most appropriate approach for the determination of the lymph node metastasis is the histopathological examination with SLNB. So unnecessary ALND will be avoided in the light of the findings, which indicate that in 70% of the T1 and T2 tumors there is no metastasis in the lymph nodes [17].

Systemic studies have shown that breast cancer, spreads to a few lymph nodes, which are called as sentinel lymph node(s), before infiltrating other axillary lymph nodes. These nodes are usually at

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Received Date: *30 Nov 2017*
Accepted Date: *15 Jan 2018*
Published Date: *26 Jan 2018*

Citation: *Yılmaz EM, Demirkıran AE. Current Approach to Axilla in Breast Cancer. J Surg Forecast. 2018; 1(1): 1005.*

level 1 and sentinel lymph node marking/mapping may be done with colloid injection labeled with blue stain or radioactive material.

After this procedure, unnecessary ALND and its complications will be avoided. ACOSOG (American College of Surgeons Oncology Group) reported in Z0011 study, that the development rate of the lymphedema after one year was 3% in the SLNB, while the same rate was 13% in the ALND group. They also stated that ALND had a higher risk regarding other complications [18]. In this ACOSOG Z0011 study, in respect of survival rate and disease-free survival rate, ALND and SLNB were compared and after a 6.3 years follow-up period, the local recurrence rate was determined as 2.8% in the SLNB group and 4.1% in the ALND group and it was reported that SLNB could be safely used [19].

Although physical examination of the axillae is very important, SLNB has still the priority. Even though, in the conventional approach, the physical examination of the axillae is important, at the present time most of the surgeons prefer SLNB as the standard approach. The positivity rate of SLNB is approx. 30% in patients with clinically negative axilla findings and sentinel lymph node metastasis rate is reported as 25% in patients with palpable lymph nodes [20].

With the implementation of SLNB, unnecessary ALND will be avoided, staging is correctly done, the duration of the anesthesia and of the hospitalization are shortened, the cost is reduced and psychological compliance is easily achieved.

Who Should Undergo Sentinel Lymph Node Biopsy?

SLNB should be carried out in patients with no clinical findings or microinvasion [21]. In patients, who have clinically axillary irregularity, axillary ultrasound examination or fine needle aspiration biopsy (FNAB) should be first carried out and ALND should be performed instead of SLNB if any metastasis is determined [22]. Moreover, in patients, who had ductal carcinoma *in situ* (DCIS) and underwent mastectomy, SLNB should be performed [21]. In cases, in whom SLNB does not provide definitive results and clinically status is unclear, ALND should be carried out. The large size of the tumor, its multicentric shape and the age should not be a contraindication for SLNB [23,24]. Previous surgery, obesity, large tumors, previous axillary trauma or infection, pregnancy and lactation are not contraindications but factors, which make the technique more difficult to implement.

SLNB and Treatment Management

According to the classification of AJCC (The American Joint Committee on Cancer), in respect of the dimension of the SLNB metastasis, three groups are defined as isolated tumor cells, micrometastasis and macrometastasis [25].

Isolated tumor cells

If the size of the metastatic lymph node is less than 0.2mm, they are called isolated tumor cells and the survival rate of these patients is comparable with the SLNB negative patients. Therefore no additional surgical intervention and adjuvant treatment are recommended [20].

Micrometastasis

If the size of the tumor deposit in metastatic lymph node is between 0.2mm and 2mm, it is called as micromestasis [25]. Although in several studies nodal micrometastasis are reported as a prognostic factor, in the study [26], which was conducted by Mittendorf et al. with 8,000 women, who were followed up for 10 years, it was reported that there was no significant difference between two groups consisting of patients with micrometastasis and without micrometastasis regarding the survival rate.

Macrometastasis

is considered if the size of the metastatic lymph node is greater than 2mm. Although, routine axillary dissection is recommended in the 2010 NCCN guideline, it became nowadays a debatable topic. The implementation of ALND, if the number of the micro- and macrometastasis is less than three, is a controversial issue currently in the literature. Although, in the 2014 guideline, American Society of Clinical Oncology (ASCO) recommended ALND in the SLNB-positive early-stage breast cancer patients considering the evidence-based data, in the meta-analysis-3 published by Huang et al., no significant difference was determined between the long-term survival rate results in a limited number of macrometastasis patients and it was recommended that the usage of ALND had limited usage in these patients and should be used cautiously if necessary [27,28].

Is ALND Definitively Necessary in SLNB-positive Patients?

Following the development of the technique of the sentinel lymph node biopsy, implementation of the dissection

was waived in the patients with negative axilla findings. In patients with no SLNB involvement, morbidities may be prevented with the avoidance of ALND, if the involvement of the non-sentinel lymph node (NSLN) is known. As SLN involvement indicates that other axillary lymph nodes are also affected, axillary dissection is implemented. However, other lymph nodes are not involved in some patients, although SLN is involved. NSLN involvement is changing between 20% to 70% among the patients with SLN involvement [29-31]. Therefore, many ALNDs are performed unnecessarily.

In several studies, a large number of factors such as tumor size, lymphovascular invasion, multifocality, receptor positivity, which are independent of SLNB and may affect survival rate, were defined [32,33]. In 2003, Van Zee and his colleagues had developed the normogram method for the determination of the effect of the SLN metastasis with the help of these factors. An estimated risk can be calculated with the normogram and the same investigator group showed in 2007 that the ALND rate had dropped from 69% to 62% [34,35]. In such studies, normogram scales were used and they tried to decide, which SLNB-positive patients should undergo ALND. However, routine usage of normogram did not become a common implementation in the clinics [36].

SLNB Method in Specific Cases

Locally advanced breast cancer

In the guideline of American Society of Clinical Oncology (ASCO), published in the year 2005, SLNB was not recommended in the locally advanced breast cancer [20]. In these patients, ALND is recommended in order to prevent the locoregional recurrence [37].

Inflammatory breast cancer

In a statement, issued by ASCO in 2005, routine use of SLNB was not recommended for the patients with the inflammatory breast cancer and it was suggested that ALND might be useful to prevent recurrence. In the 2010 consensus of the international experts panel, SLNB was considered as a contraindication in these patients [37,38].

Ductal carcinoma *In situ* (DCIS)

If DCIS was determined in many women especially during the breast-conserving surgery, axillary evaluation is not necessary. However, if these patients need mastectomy due to the large-scaled DCIS, planning of a simultaneous SLNB is recommended, as there is no chance of a further evaluation in case of the determination of the invasive focus [37].

After the Neoadjuvant Chemotherapy

Neoadjuvant chemotherapy is recommended in patients with a large primary breast cancer and a locally advanced breast cancer. The optimal timing of SLNB is controversial in these patients [21]. In the 2011 NCCN guideline, SLNB prior to the neoadjuvant chemotherapy was recommended for these patients [20].

Presence of a previous mammal and axillary intervention

In patients, who underwent previously a cosmetic intervention such as breast implant or reduction mammoplasty, SLNB is still under discussion. ASCO could not provide a consensus on this topic. It was recommended, that it was better to perform a preoperative lymphoscintigraphy, if SLNB was considered [37].

Multicentric focus

According to the opinion of Harlow et al. [21], which is in line with the report of ASCO, the studies, which evaluated the functional anatomy of the breast, confirm the theory that all quadrants of the breast are drained into the same lymph node(s). Therefore, as stated in the ASCO report, SLNB is not contraindicated in the multicentric tumors [39,40].

Pregnancy and lactation

According to the 2014 report of ASCO, SLNB is not recommended in the pregnancy and lactation periods. As studies focused on the teratogenic effects of the isosulfane blue stain are limited, the use of SLNB is restricted in this group of patients [21]. In a study on this subject, retrospective data of 25 pregnant women, who were followed up approx. 2.5 years, showed that 7 of them received injections of methylene blue, 16 of them Tc 99m and 2 of them other substances. All of these women gave live birth and 24 of these patients had no complaints during the follow-up period and only one patient had a baby with a cleft-lip [41]. As only a very limited number of studies were focused on this topic in the literature, 2014 ASCO report restricted the use of SLNB in pregnancyand lactation [21,28].

References

1. Marrazzo A, Damiano G, Taormina P, Buscemi S, Lo Monte AI, Marrazzo E. Does Conservative Surgery for Breast Carcinoma Still Require Axillary Lymph Node Evaluation? A Retrospective Analysis of 1156 Consecutive Women With Early Breast Cancer. Clin Breast Cancer. 2016; 17: 53-57.
2. Kilkenny JW 3rd, Bland KI. Surgery of breast cancer. Curr Opin Oncol. 1997; 9: 520- 526.
3. Donegan W. History of Breastcancer. In: Winchesters DJ, Winchesters DP, eds. Breast Cancer. 2nd ed. Ontorio: BC Decker. 2006: 1-13.
4. Noguchi MM, Taniya T. Biology and surgical management of breast cancer. Breast Cancer. 2001; 8: 16-22.
5. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plusir radiation for the treatment of invasive breast cancer. N Engl J Med. 2002; 347: 1233–1241.
6. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year followup of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002; 347: 1227–1232.
7. Guiliano AE, Dale PS, Turner RR, Morton DL, Evans SW, Krasne DL. Improved axillary staging of breast cancer with sentinel lymp had enectomy. Ann Surg. 1995; 222: 394-399.
8. Sugie T, Ikeda T, Kawaguchi A, Shimizu A, Toi M. Sentinel lymphnode biopsy using indocyanine green fluorescence in early-stage breast cancer: a meta-analysis. Int J ClinOncol. 2016; 22: 11-17.
9. Parada D, Peña KB, Riu FF, Aguilar AE, Cohan S. Intraoperative molecular analysis of sentinel lymphnodes following neoadjuvant chemotherapy in patients with clinical node negative breast cancer: An institutional study. MolClinOncol. 2016; 5: 507- 510.
10. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, et al. Randomized multicentertrial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC trial. J NatlCancerInst. 2006; 98: 599-609.
11. Wariss BR, Costa RM, Pereira AC, Koifman RJ, Bergmann A. Axillary web syndrome is not a risk factor for lymphoedema after 10 years of follow-up. Support Care Cancer. 2017; 25: 465-470.
12. Vieni S, Graceffa G, La Mendola R, Latteri S, Cordova A, Latteri MA, et al. Application of a predictive model of axillary lymphnode status in patients with sentinel node metastasis from breast cancer. A retrospective cohort study. Int J Surg. 2016; 35: 58-63.
13. Li J, Jia S, Zhang W, Qiu F, Zhang Y, Gu X, et al. Partial axillary lymph node dissection inferior to the inter cost obrachial nerves complements sentinel node biopsy in patients with clinically node-negative breast cancer. BMC Surg. 2015; 30: 15: 79.
14. Schunemann H, Willich N. Lymphedema after breast carcinoma. A study of 5868 cases. Dtsch Med Wochenschr. 1997; 122: 536-541.
15. Li CZ, Zhang P, Li RW, Wu CT, Zhang XP, Zhu HC. Axillary lymphnode dissection versus entinel lymphnode biopsy alone for early breast cancer with sentinel node metastasis: a meta-analysis. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2015; 41: 958- 966.
16. He Z, Wu S, Yang Q, Sun J, Li F, Lin Q, et al. Breast cancer subtype is associated with axillary lymphnode metastasis: a retrospective cohort study. Medicine. 2015; 94: e2213.
17. Pijpers R, Meijer S, Hoekstra OS, Collet GJ, Comans EF, Boom RP, et al. Impact of lympho scintigraphy on sentinel node identification with technetium-99m-colloidal albumin in breast cancer. J Nucl Med. 1997; 38: 366-368.
18. Wiatrek R, Kruper L. Sentinel lymphnode biopsy indications and controversies in breast cancer. Maturitas. 2011; 69: 7-10.
19. Verheuvel NC, Voogd AC, Tjan-Heijnen VC, Roumen RM. Potential impact of application of Z0011 derived criteria to omitaxillary lymphnode dissection in node positive breast cancer patients. Eur J Surg Oncol. 2016; 42: 1162-1168.
20. Kapkaç M, Cantürk NZ. Meme Kanserinde Aksillaya Güncel Yaklaşımlar. Turkiye Klinikleri J Gen Surg-Special Topics. 2013; 6: 77-83.
21. Harlow SP, Weaver DL. Diagnosis, stagingand the role of sentinel lymphnode biopsy in the nodale valuation of breast cancer. Up To Date. 2016.
22. Hinson JL, McGrath P, Moore A, Davis JT, Brill YM, Samoilova E, et al. The critical role of axillary ultrasound and aspiration biopsy in the management of breast cancer patients with clinically negative axilla. Ann Surg Oncol. 2008; 15: 250.
23. Wiatrek R, Kruper L. Sentinel lymphnode biopsy indications and controversies in breast cancer. Maturitas. 2011; 69: 7-10.
24. Pepels MJ, Vestjens JHMJ, de Boer M, Smidt M, vanDiest PJ, Borm GF, et

al. Safety of avoiding routine use of axillary dissection in early stage breast cancer: a systematic review. Breast Cancer Res Treat. 2011; 125: 301-313.

25. Iqbal J, Ginsburg O, Giannakeas V, Rochon PA, Semple JL, Narod SA. The impact of nodal micrometastasis on mortality among women with early-stage breast cancer. Breast Cancer Res Treat. 2016; 161: 103-115.

26. Mittendorf EA, Ballman KV, McCall LM, Yi M, Sahin AA, Bedrosian I, et al. Evaluation of the stage IB designation of the American Joint Committee on Cancer staging system in breast cancer. J Clin Oncol. 2015; 33: 1119-1127.

27. Huang TW, Kuo KN, Chen KH, Chen C, Hou WH, Lee WH, et al. Recommendation for axillary lymphnode dissection in women with early breast cancer and sentinel node metastasis: A systematic review and meta-analysis of randomized controlled trials using the GRADE system. Int J Surg. 2016; 34: 73-80.

28. Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, et al. Sentinel lymphnode biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2014; 32: 1365-1383.

29. Yu JC, Hsu GC, Hsieh CB, Sheu LF, Chao TY. Prediction of metastases to non sentinel nodes by sentinel node status and primary tumor characteristics in primary breast cancer in Taiwan. World J Surg. 2005; 29: 813-819.

30. Guenther JM, Hansen NM, DiFronzon LA, Guliano AE, Collins JC, Grube BL, et al. Axillary dissection is not required for all patients with breast cancer and positive sentinel nodes. Arch Surg. 2003; 138: 52-56.

31. Sachdev U, Murphy K, Derzie A, Jaff er S, Bleiweiss U, Brower S. Prediction of nonsentinel lymphnode metastases in breast cancer patients. Am J Surg. 2002; 183: 213-217.

32. Abdessalam SF, Zervos EE, Prasad M, Farrar WB, Yee LD, Walker MJ, et al. Predictors of positive axillary lymphnodes after sentinel lymphnode biopsy in breast cancer. Am J Surg. 2001; 182: 316-320.

33. Weiser M, Montgomery LL, Tan LK, Susnik B, Leunk DYH, Borgen PI, et al. Lymphovascular invasion enhances the prediction of non-sentinel node metastases in breast cancer patients with positive sentinel nodes. Ann Surg Oncol. 2001; 8: 145–149.

34. Fant JS, Grant MD, KnoxSM, Livingston SA, Ridl K, C Ronald, et al. Preliminary outcome analysis in patients with breast cancer and a positive sentinel lymphnode who declined axillary dissection. Ann Surg Oncol. 2003; 10: 126 –130.

35. Katz A, Smith BL, Golshan M. Niemierko A, Kobayashi W, Raad RA, et al. Nomogram for the prediction of having four or more involved nodes for sentinel lymphnode-positive breast cancer. J Clin Oncol. 2008; 26: 2093-2098.

36. Mittendorf EA, Hunt KK, Boughey JC, Bassett R, Degnim AC, Harrell R, et al. Incorporation of sentinel lymphnode metastasis size into a nomogram predicting non-sentinel lymphnode involvement in breast cancer patients with a positive sentinel lymphnode. Ann Surg. 2012; 255: 109-115.

37. Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymphnode biopsy in early-stage breast cancer. J Clin Oncol. 2005; 23: 7703-7720.

38. Kaufmann M, Morrow M, vonMinckwitz G, Harris JR; Biedenkopf Expert Panel Members. Loco regional treatment of primary breast cancer: consensus recommendations from an International Expert Panel. Cancer. 2010; 116: 1184-1191.

39. Borgstein PJ, Meijer S, Pijpers RJ, vanDiest PJ. Functional lymphaticanatomy for sentinel node biopsy in breast cancer: echoes from the past and the periareolar blue method. Ann Surg. 2000; 232: 81-89.

40. Klimberg VS, Rubio IT, Henry R, Cowan C, Colvert M, Korourian S. Subareolar versus peritumoral injection for location of the sentinel lymphnode. Ann Surg. 1999; 229: 860-864.

41. Gropper AB, Calvillo KZ, Dominici L, Troyan S, Rhei E, Economy KE, et al. Sentinel lymphnode biopsy in pregnant women with breast cancer. Ann Surg Oncol. 2014; 21: 2506-2511.