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Obesity Doesn't Make Breast Hot or Blue

Anne Marie Wallace

S.T. Anthony Kaviratne

Sang-Joon Lee

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Anne Marie Wallace, MD
Assistant Professor of Surgery
Cancer Research and Treatment Center
University of New Mexico

S. T. Anthony Kaviratne
Medical student
School of Medicine
University of New Mexico

Sang-Joon Lee, PhD
Assistant Professor
Division of Epidemiology and Biostatistics
Department of Internal Medicine
University of New Mexico

Abstract

Background: Sentinel lymph node (SLN) mapping and biopsy have become the standard of care for axillary staging of a breast cancer patient. Higher rate of use has led to the identification of an absolute failure rate and a subset of patients who fail lymph node mapping due to causes independent of the procedure. Failure of lymph node mapping leads to more invasive procedures with higher morbidity. Body mass index has been associated with higher SLN failure rate.

Methods: Retrospective study of patients who underwent Sentinel lymph node procedures between October 2003 to June 2008 at University of New Mexico. After internal board review, electronic medical database was used to identify patients within study parameters, and to collect data needed for BMI calculation and SLN procedure details.

Results: BMI of greater than 30 had a failure rate of 44.83% with blue dye and 13.33% with technetium collide tracer (p value 0.05 and 0.04). BMI less than 30 had a failure rate of 30.56% for blue dye and 4.63 for technetium. Odds of success for blue dye were 0.5 and 0.3 for technetium for patients with BMI greater than 30. Failure rates for palpation of sentinel node 41.47% and 50% for BMI less than 30 and greater than 30 respectively.

Discussion: Study identified higher failure rate in obese patients compared to overweight to normal weight patients. Study indicates higher failure rates in obese patients than the reported absolute failure rate of SLN mapping.

Conclusion: Obesity increases the failure rate of both blue dye and technetium colloid. Obesity does not contribute to the failure to palpate a sentinel node. Obesity alone is not a contraindication for SLN mapping suing Technetium or blue dye, but surgeon must be aware of higher failure rate in obese patients and change their procedural methods to accommodate.

Introduction

Axillary staging is important because it influences overall staging and future decisions regarding adjuvant treatments. However, Axillary dissection can lead to significant side effects, such as lymphedema, nerve injury, chronic pain, neuromas, seroma formation, and increase susceptibility to infections.[1]Further, self-breast exams, screening mammography and access to good healthcare maintenance have led to a decrease in the number of advanced invasive breast cancers that involve the lymph node basins. Therefore, those patients who are early stage and/or without detectable lymph node involvement will not clinically benefit from an axillary lymph node dissection, but may suffer the adverse effects.[1-3]

A sentinel lymph node is defined as the first lymph node or nodes to which a cancer might metastasize from the primary tumor. In order to identify the sentinel lymph node(s), the surgeon injects a radioactive substance (technetium sulfur-labeled colloid) and/or blue dye peritumorally or in the subareolar/dermal lymphatic plexus.[2]Once the SLN is located, the surgeon removes the lymph node(s). In addition to a decrease in morbidity, SLNB procedures have reported successful lymph node identification rates between 65%-94% [2, 4] with false negative rates between 0%-11% and an absolute failure rate that has been reported to be between 1% to 2%. [1, 2, 5, 6]The efficacy of sentinel lymph node identification is reported as 94% using Isosulfan blue dye technique. [4]

Many factors have been associated with SLNB mapping failure. For example, injection methods, inadequate volume of tracer, dispersion of the tracer, and time of massage are considered as extrinsic factors that may influence the ability of the mapping dyes or colloids to reach the lymphatic basin. In addition, inflammation around the biopsy site, compression of the lymhatics by the tumor, affects of neoadjuvant chemotherapy treatments, localized edema dye to

blue dye allergy, and other issues such as degree of fatty tissue content have been postulated as possible causes for the failure of SLNB[7-9]. A potential serious side-effect of blue dye injection is the possibility of severe anaphylactic allergic reaction at the rate of about 0.7% to 1.9% among patient who undergo SLNB [5, 10-12]. In addition, there are observed corollaries which hypothesize that complete replacement of lymph node by tumor cells can hinder dye or colloid penetration into the lymph node that may contribute to failure of proper lymph mapping. Lymph congestion by tumor cells hypothesis has been made largely by observing large dilated lymphatic channels that terminate abruptly at lymph glands later found to be completely replaced by tumor. Furthermore, even with surgeons experienced in SNLB procedure and progressive accumulation of procedural knowledge, there still remains an absolute failure rate that indicates there might be inherent patient factors that contribute to lymphatic mapping failure in a subset of the patients. Identifying this subset of patients ahead of time can potentially benefit the patient by foregoing a lengthy sampling procedure that may lead to increased operative time and/or yield poor quality information in this particular population. Identifying a group of patients who specifically fail to demonstrate blue dye as a means of sentinel lymph node detection can allow this group of patients to forgo exposure to an additional potential allergen that can have serious side effects in some patients.

It is important to identify factors that contribute to the failure of the SLNB procedure, as this can add operative time to a patient's procedure and expose them to potential serious allergens with the use of vital blue dyes. Recent data on SNLB procedural outcomes shows that with an increased use of SLNB procedure, the rate of failure has increased reflexively [2, 4-6]. In addition, various side effects, such as anaphylactic reactions, [9, 11-13] interference with pulse oximeter[12], and adverse skin reactions[14] rates will become more prominent. If it is possible to

identify the subset of patients or characteristics in patients that would correlate to a higher degree of failure, surgical oncologists may be able to avoid subjecting patients to unnecessary procedures and better inform the patients of the benefits versus the drawbacks, which will help promote the autonomy of the patient and increase the overall quality of care that is offered.

We believe that there is a subgroup of breast cancer patients in whom Technetium or blue dyes are unlikely to be efficacious in determining accurate sentinel nodes using standard SLNB techniques. If we can reproducibly identify these patients with preoperative screening criteria, we can potentially save these patients' increased length in operative time and exposure to possible severe allergens.[18, 19] Our main objective is to retrospectively investigate the failure rates of SLNB patients who used blue dye with a BMI greater than 30. SNLB procedural outcomes will be ascertained compared to reported "absolute" failure rate to see if there is a statistically significant difference between our population of interest and reported absolute failure rates with respect to the blue dye, technetium, and the ability of the surgeon to palpate a sentinel node.

Methods

A retrospective review will be conducted of female breast cancer patients who underwent lymphatic mapping for sentinel node biopsy at the University of New Mexico Hospital from Sep 2003 to June 2008. The data was captured in the University of New Mexico Main Operating Room and Outpatient Surgery and Imaging Services (OSIS) Operating Room operative log database. All patients eligible for our study include those who (1) are female; (2) were 18 years of age or older at the time of treatment; (3) required surgical treatment for diagnosed or suspected invasive malignant breast cancer and also required axillary staging as part of their standard of care treatment, and/or had elected to have therapeutic mastectomy for DCIS, and/or prophylactic mastectomy due to risk factors and had risk of occult invasive malignancy. Patients

who were pregnant or who did not qualify for SLNB under current National Comprehensive Cancer Network (NCCN) treatment guidelines were excluded from the study.

Lymphatic mapping and SLNB were performed at UNM Hospital or OSIS in the standard fashion by surgeons who had met the usual required training and experience with SLNB techniques. Lymph nodes were considered sentinel nodes if they met the following criteria either alone or in combination: (1) blue stained, (2) had a blue lymphatic leading up to the node, (3) had a 10:1 ex vivo ratio of colloid uptake, or (4) were palpable. The axilla was carefully examined at the end of the SLNB procedure, and any additional lymph nodes that were palpable were also removed and sent as additional sentinel nodes. The characteristics of the sentinel nodes were collected from dictated procedure note, operation work sheet, and the finalized pathology report. The data will be used to determine the failure rates between patients whose BMI is less than 30 to patients with BMI greater than 30. The rates will then be compared to reported absolute failure rate to determine if a higher BMI corresponds with higher failure rate in sentinel lymph node mapping.

Results

Search of University of New Mexico electronic medical data base during the period of September 2003 to June 25, 2008 yielded 560 entries. From the 560 possible entries 198 individual patient records were identified that fit the study parameters. Entries that were rejected were largely due to patient record duplication and Sentinel node mapping other than breast (i.e. skin). Patient age ranged from 24 to 84 with mean age of 55. BMI ranged from 17 to 47 with mean BMI of 29. The ethnic distribution among the patient population reflected Caucasian and Hispanic predominance (Table 1).

Figure 1 shows the success and failure rates of sentinel node identification using blue dye, radioactive tracer and palpation for patients with BMI less than 30 and BMI greater than 30. Our analysis showed that patients who have a BMI less than 30 showed a SLN mapping failure by blue dye to be 30.56% while patient with BMI greater than 30 showed a failure rate of 44.83%. The failure rate showed to be marginally significant with p value of 0.05. The patients with BMI of greater than 30 seem more likely to fail with 0.5 odds of success (table 2). Technetium use showed a failure rate of 4.63% in patients with BMI of less than 30, however, showed a failure rate of 13.33% with failure rate difference being statistically significant ($p = 0.0404$). The odds of a surgeon finding a hot node with success with the use of technetium tracer in a patient with BMI greater than 30 were shown to be 0.3 (table 2).

The failure of the surgeon to palpate a sentinel node is 41.47% and 50% in patients whose BMI is less than 30 and greater than 30 respectively. The difference in rates is statistically insignificant ($p = 0.2547$). The odds of success to palpate seem likely to fail with the odds of success of 0.7. Table 2 shows as the BMI cut off increases from 25 to 30 the efficacy of the tracer to detect a sentinel node decreases on all three detection methods.

Discussion

Patients' BMI has been considered to be a risk factor for development of breast carcinoma. Further, higher BMIs have been linked to poorer prognosis and more invasive carcinoma at the time of detection.[20] Recently there have been three well designed published studies that have tried to establish a correlation among increases in BMI and SLNB procedural outcomes. [2, 6, 13] Cox et al's studied 1356 SNLB patients with mean BMI of 29.54 and an age range of 20-81. Even though Cox's study indicated that with an increase of one year or 1 unit of BMI decrease the success rate by almost 5%, they concluded that there is only a general trend

which suggests a decrease in the success rate with increasing BMI and age, but this was not found to have statistical significance. Therefore, it is suggested, but not confirmed, that SLNB may be unsuccessful in this patient population[6]. However, Hughes et al who looked at a large spectrum of BMIs similar to the Cox et al study (BMI of 18-54.1) with approximately equal distribution between normal, overweight, and obese patients' concluded that obesity alone does not affect sentinel node identification or contribute to the false negative rate.[2] In addition, another study similar done by Derossis et al looked at BMI and age and concluded that SLNB cannot be contraindicated in patients with increasing weight and age[13].

Our study which looked at BMI of 30, which demarcates normal to overweight from obese individuals, showed that obesity itself seems to be a significant variable that contributes to failure of sentinel node mapping using both blue dye (methylene blue and lymphazurin). The odds of success using blue dye in an obese patient were approximated to be 0.5 or almost a fifty percent chance of failure, while the normal to overweight patient showed a higher success rate. Our study's Sentinel Node mapping failure rate seems to be at a higher rate and statistically significant compared to Cox study. However, our study has less power. Further, our study showed there is a significant effect on the failure of lymph mapping using technetium colloid. However, the ability to palpate a sentinel node seem not be affected by obesity. While the reported overall failure in sentinel lymph node detection approximately 1-2%, our study seem to indicate it would be higher in obese patients.

It is unclear why failure increases with increasing BMI, but the increase adiposity might contribute to slower lymphatic flow. This might be the reason why the obese patients have higher failure rates in both blue dyes and technetium colloids. As our study's trend indicate, as patients BMI increase, a surgical oncologist must be aware that the chances of failure of both technetium

colloid and blue dye have a higher chance of failure with current practice guidelines. Therefore, surgeon might want to consider employing other methods such as longer massage or more time for lymph drainage to ensure lymph spread before interrogating for sentinel nodes. We anticipate more reliable and increased success rates for sentinel lymph mapping will reduce morbidity associated with sentinel node procedures.

Obesity alone might not contribute to failure of sentinel nodes because our study still shows considerable failure rate even among normal to overweight category. Therefore, other characteristics inherent to the patient might contribute to failure.

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Tables and Figures

Table 1: Patient Characteristics

Characteristic		Number	
age (196)			
	Age range	24 - 84	
	mean	55	
	median	56	
Body mass index (n = 197)			
	BMI range	17 - 47	
	mean	29	
	median	29	
Ethnicity (n= 198)			
	White	102	(52%)
	Hispanic	66	(33%)
	Native American	15	(8%)
	African American	10	(5%)
	Other	5	(3%)
Bra Cup size (n= 97)*			
	A	5	(5%)
	B	22	(23%)
	C	33	(34%)
	D	25	(26%)
	>D	7	(7%)
	Breast Augmentation	1	(1%)
	Pendulous breast	4	(4%)
Stage (n = 161)			
	I	89	(55%)
	IIA	44	(27%)
	IIB	11	(7%)
	IIIA	12	(7%)
	IIIB	3	(2%)
	IIIC	1	(1%)
	IV	1	(1%)

**Bra cup size was not consistently reported*

Figure 1: Sentinel lymph identification method success and failure rates

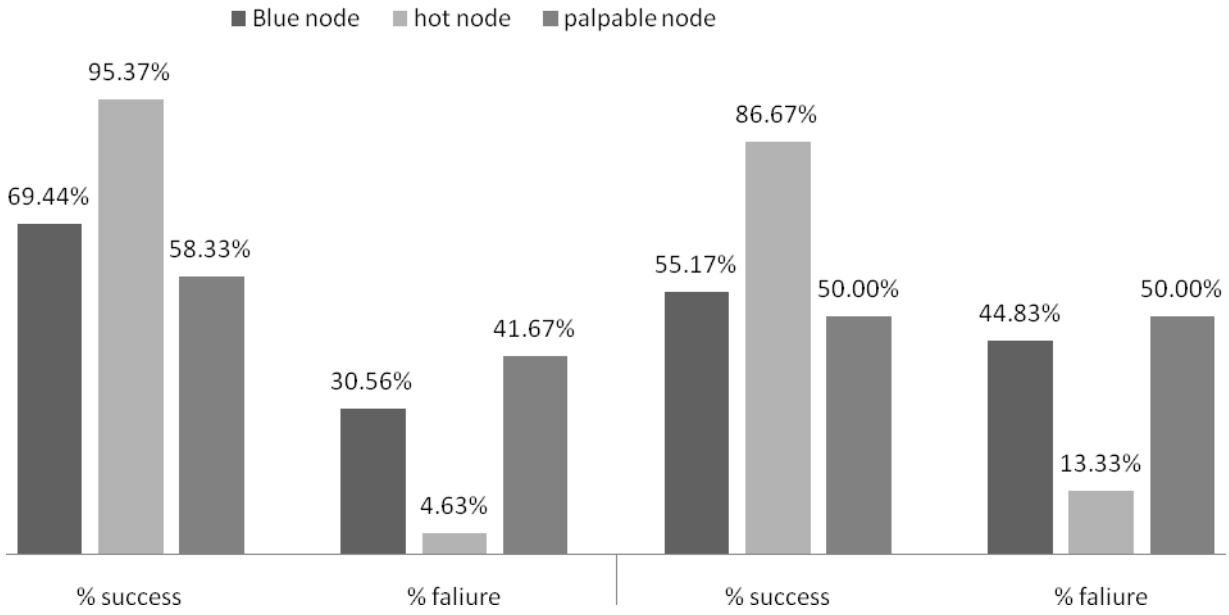

Table 2: - Effect on odds ratio by patient BMI on various sentinel node detection methods

detection method	Variable	odds ratio	95% confidence interval
blue dye	BMI (continuous)	1.04	(1.01 - 1.07)
	BMI 25	0.94	(0.50 - 1.75)
	BMI 30	0.54	(0.30 - 0.98)
Hot Node	BMI (continuous)	0.97	(0.89 - 1.03)
	BMI 25	0.26	(0.06 - 1.16)
	BMI 30	0.32	(0.11 - 0.93)
Palpable node	BMI (continuous)	0.98	(0.941 -1.02)
	BMI 25	0.82	(0.45 - 1.50)
	BMI 30	0.71	(0.41 - 1.25)