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RESEARCH REPORT

AXILLARY WEB SYNDROME AFTER LYMPH NODE DISSECTION: RESULTS OF 1,004 BREAST CANCER PATIENTS

Bergmann, A; PT, PhD [1]; Mattos, IE; MD, PhD [2]; Pedrosa, E; PT [1]; Nogueira, EA; PT [1]; Koifman, RJ; MD, PhD [2].

[1] National Cancer Institute / Cancer Hospital III; [2] National School of Public Health / FIOCRUZ

Author's address
Anke Bergmann
Av. Lineu de Paula Machado, 905 apto 906
Jardim Botânico Zip code: 22470-040
Rio de Janeiro – RJ Brazil
e-mail: ankebergmann@terra.com.br or abergmann@inca.gov.br
Phone: (21) 3874-9535

Abstract

Introduction: Axillary web syndrome (AWS) occurs in patients submitted to surgical treatment for breast cancer due to injury of superficial lymphatic vessels during lymph node dissection. Its incidence and risk factors are unknown. The purpose of this study was to evaluate the incidence and risk factors of AWS in breast cancer patients. **Methods:** Prospective cohort of 1,004 breast cancer patients submitted to axillary clearance at the National Cancer Institute (INCA), between August 2002 and November 2002. Women with prior conditions of the upper arm were excluded. The following variables were collected: age at operation, body mass index (BMI); marital status; years of schooling; neoadjuvant radiotherapy, chemotherapy or tamoxifen; number of lymph nodes removed; number of metastatic lymph nodes; type of axillary surgery; total days with closed suction drainage; TNM stage (pathology); type of surgery; early arm edema (volume > 200 ml). Univariate analysis was performed for describing population profile. Bivariate analysis and logistic regression were performed in order to identify risk factors involved in the development of AWS. This study was approved by the Ethics and Research Committees of INCA and FIOCRUZ. **Results:** The follow-up period was 24 months. The sample comprised 1,004 women, with a mean age of 55 years, 48% were married, 53% had not completed elementary school and 70% were obese. Mastectomy was performed in 65%, the mean number of lymph nodes removed was 17. As for staging, 47% of the cases were considered in an advanced stage (higher than IIB). The incidence of AWS was 38.2%. The variables that showed significant statistical association with AWS (logistic regression) were: early arm edema (RR=2.27 IC 1.10-4.65) and number (continuous) of lymph nodes removed (RR=1.01 IC 1.00 – 1.03). **Conclusion**: AWS is a common condition after axillary lymphadenectomy for breast cancer and was statistically associated with the number of lymph nodes removed and with early arm edema.

Keywords: Axillary web syndrome, breast cancer, complications, lymphadenectomy

Introduction

The most important factor for survival in breast cancer is the presence of lymph node metastasis. Axillary clearance (AC) or sentinel node biopsy (SNB), depending on the characteristics of the tumor, are recommended for its appropriate staging [1].

Axillary web syndrome (AWS) is a condition that occurs in the early postoperative period after AC and SNB, characterized by axillary pain irradiation down the ipsilateral arm, shoulder range-of-motion limitation and axillary web of tissue most obvius during the abduction of the arm [2].

This syndrome is rarely described in the literature. Hoffman and Rolff [3] observed three patients who developed painful bands across the axilla after breast surgery and AC, suggesting thrombosis, obstruction and inflammation of lymphatic channels as the probable pathogenesis. Similar observation after AC was described recently in four studies [4-6]. Morkovitz et al [2] in a retrospective study of 750 women, found a prevalence of 6% of AWS after AC. Leidenius et al [7] observed a prevalence of 72% after AC and 20% after SNB, in 85 patients submitted to breast cancer surgery. Pappo et al [8] described three cases after SNB.

The factors associated with AWS following breast cancer surgery are still not clear. After performing biopsies of axillary webs, Markowitz *et al* [2] suggested that the pathogenesis of AWS was related to a lymphovenous injury that might occur in the retraction of tissue and patient positioning during AC; stasis of lymphovenous channels induced by removal of axillary lymphatics draining to the arm; and a hypercoagulability in surrounding tissues due to tissue injury during operation and releasing of tissue factor.

The aim of this study was to evaluate the incidence and risk factors associated with AWS after axillary clearance in patients submitted to breast cancer surgery.

Materials and Methods

We conducted a prospective cohort study of 1,004 breast cancer patients submitted to axillary clearance at the Cancer Hospital III / National Cancer Institute (HCIII/INCA) in Rio de Janeiro, between August 2002 and November 2002. Women with breast cancer submitted to conservative surgery or mastectomy, associated with axillary clearance (level I, II or III) were eligible for the study. Women with prior alterations of the upper arm, bilateral breast cancer, absence of axillary clearance, treated in other hospitals and who were in no condition to answer the questions were excluded. Eligible women gave informed consent and this study was approved by the Committees of Ethics and Research of the National Cancer Institute and of the Oswaldo Cruz Foundation. Women were evaluated in the preoperative, on the first day, and on months 1, 6, 12, 18 and 24 after axillary clearance. Variables related to the characteristics of patients, treatment, the tumor and postoperative complications were studied. The

variables age, body mass index, and the number of removed and metastatic lymph nodes were tested in the regression model as continuous and categorical. AWS was defined as the presence of a visible web in the axilla and/or arm, associated or not with pain and shoulder range-of-motion limitation.

The characteristics of women meeting inclusion criteria were compared and the χ^2 test with a 5% ($p < 0.05$) level of significance was performed in order to determine statistical significance. For continuous variables, we presented the mean and the median, and categorical variables were described through frequency distribution. A bivariate analysis was performed in order to explore the magnitude of the association between AWS and study variables. A model to best represent the risk for lymphedema was searched by unconditional logistic regression using the enter method, adopting as criterion for entrance $p \leq 0.10$ and for exit $p \geq 0.11$ of the tested variables. Epi-Info 2000 and SPSS 10.0 software were used for data analysis.

Results

We studied 1,004 women submitted to axillary clearance. The mean age of the population studied was 56 years (SD ± 13.08). In relation to Body Mass Index (BMI), 28.9% of the patients had adequate weight, 31.9% were overweight and 36.5% were obese. Mastectomy was performed in 65% of the patients, with predominance of the modified radical mastectomy of Madden. Most patients (79%) were submitted to axillary clearance until level III, with a mean of 17 (SD ± 6.77) lymph nodes removed, of which 47% were metastatic. Together, stages IIA and IIB answered for more than half of cases (55.8%). In relation to oncologic treatment, 70% of the women received adjuvant chemotherapy and 63% were submitted to radiotherapy and axillary lymph drainage was necessary in 43% of them.

The incidence of AWS was 38.2%. We observed that women with an increased volume of the arm (> 200 ml) in the first six months after AC (early edema), had 1.54 more risk (IC 95% 1.13 – 2.10) of AWS in comparison with those with a normal volume. Other variables analyzed associated with AWS did not show statistical significance (table 1).

The adjusted model that better predicted the risk for developing AWS after AC consisted of two variables: number of lymph nodes removed (continuous), showing a 1% increase in risk for each lymph node removed (RR 1.01 IC 95% 0.99 – 1.03) and the occurrence of early edema (RR=2.27;IC 95% 1.10 – 4.65).

Table 1 – Relative risks between AWS and selected variables

Variable	AWS			
	Yes	No	RR**	IC*
Patient age				
≤ 55 years	200	321	1.09	0.86 – 1.18
> 55 years	184	299		
Body mass index (BMI)				
≥ 25	265	421	1.04	0.88 – 1.24
< 25	111	189		
Surgery				
Mastectomy	252	400	1.03	0.87 – 1.22
Conservative	132	220		
Immediate reconstruction				
Yes	18	40	0.80	0.54 – 1.19
No	366	580		
Number of lymph nodes dissected				
≥ 18 lymph nodes	179	315	0.90	0.77 – 1.05
< 18 lymph nodes	205	304		
Number of metastatic lymph nodes				
≥ 4	66	103	1.13	0.88 – 1.45
< 4	95	179		
Stage				
II B e III	175	273	1.04	0.89 – 1.22
< II B	206	343		
Early edema				
Yes	18	13	1.54	1.13 – 2.14
No	366	607		
Hematoma				
Yes	10	27	0.70	0.41 – 1.19
No	374	592		
Wound Infection				
Yes	46	81	0.94	0.74 – 1.20
No	336	538		
Seroma				
Yes	227	381	0.91	0.77 – 1.07
No	144	207		

* 95% Confidence interval
** Relative risk

Discussion

The study population, whose origin was a public reference hospital for breast cancer in Rio de Janeiro - Brazil (HCIII/INCA), consisted of a group of women that have routine physiotherapy care and are assessed with standardized instruments, allowing prevention and early identification of complications.

The incidence of AWS in our study (38.2%) was below the one observed by Leidenius et al [7], who found an incidence of 72% by evaluating 36 women submitted to AC. We did not find other studies on the incidence of AWS in the literature reviewed. In both studies, AWS was evaluated by inspection and palpation of the axilla and the arm. The differences observed in the incidence of AWS could probably be due to heterogeneity of the population studied and to different study procedures.

Leidenius et al [7] found that AWS after AC was not associated with shoulder range-of-motion limitation in the preoperative and with axillary metastases. In our study, women with shoulder range-of-motion limitation previous to AC were excluded and we did not find a statistically significant association

with axillary metastases. Our results were different from those of Leidenius et al [7] in relation to BMI, as we did not find an association of this variable (categorical or continuous) and AWS and in their study, women with AWS presented lower BMIs (p=0.01) in relation to those of the ones without such complication. Possibly, the identification of AWS in obese women is difficult, due to poor visualization of lymphatic vessels, and this fact could justify the results observed by these authors.

Moskovitz et al [2] analyzed 750 women submitted to AC for breast cancer between 1980 and 1996, in a retrospective study, and found a 6% prevalence of AWS. Among the cases of AWS observed by these authors, 11% developed lymphedema in the early or late postoperative, 4.5% developed postoperative complications (seroma, necrosis and infection), 64% were submitted to conservative surgery and 49% presented axillary metastasis. The retrospective methodology and the definition of AWS used by the authors do not allow a comparison with the data from our study.

Patients submitted to SNB were not part of our study population. Leidenius et al [7] found an incidence of 10% in this group, which was lower than that observed in the group submitted to AC (74%) (p <0.000). Other authors published reports of cases of AWS after SNB [2,8].

The etiology of AWS after surgical treatment of breast cancer is still not clear. However, published studies agree that AWS occurs because of axillary surgery, as cases after breast surgery only were not observed [2,7,8]. The smaller the axillary surgery, the lower seems to be the occurrence of AWS. In our study the number of lymph nodes removed increased in 1% the risk of AWS for each lymph node removed.

Morkovitz et al [2], observing fibrin clot in superficial veins and lymphatics of biopsied axillary webs in 4 patients, suggested that lymphovenous injury, stasis, and hypercoagulability after axillary surgery in breast cancer could contribute to the development of AWS. Due to surgical trauma, the thrombosis of lymphatic vases could be followed by local coagulation and fibrina deposition, which would induce cellular proliferation along the vase [9]. Our results showed a significant association with early edema and AWS (RR=2.27 IC 95% 1.10 – 4.65) after AC. A possible explanation for these findings could be the common pathophyisiology of those complications, beginning with axillary lymphatic obstruction.

Conclusion

The incidence of AWS AC for breast cancer was 38.6%. The best model to explain the risk of AWS after AC was made up of two variables: number of axillary lymph nodes removed (RR 1.01 IC 95% 0.99 – 1.03) and development of early edema (RR=2.27 IC 95% 1.10 – 4.65).

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