Axillary node dissection in patients with breast cancer diagnosed through the Ontario Breast Screening Program: a need for minimally invasive techniques

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Objective: To determine the role of axillary node dissection by studying patient and tumour characteristics of invasive breast cancer through the Ontario Breast Screening Program (OBSP) .

Design: A retrospective evaluation.

Setting: The London, Ont., branch of the OBSP.

Patients: Three groups of women seen were studied: 50 women with screen-detected breast cancers, which were palpable and detected by the nurse-examiner, 62 women with occult screen-detected breast cancers and 353 age-matched women with invasive breast cancer from the LRCC prospective database, who served as controls.

Main outcome measure: The proportion of involved axillary nodes within the 3 groups based on patient and tumour characteristics.

Results: Twenty-five (22.3%) of the 112 women had screen-detected tumours less than 1 cm in dimension, but only 1 had an involved axillary node. Twelve (19%) of the 62 women with occult screen-detected tumours had involved lymph nodes compared with 17 (34%) of the 50 women with palpable screen-detected cancers (NS). In the control group tumour dimension less than 1 cm versus 1 cm or larger had a marked effect on the probability of axillary node involvement (12.5% v. 40.7%, $p = 0.001$). In the palpable screen-detected group 3 times as many women with outer quadrant or central lesions had involved nodes as those with inner quadrant lesions (38% v. 12%) and for those with a family history of breast cancer almost twice as many had involved axillary nodes. In occult screen-detected patients there was more nodal involvement in patients aged 60 years or less than in those older than 60 years (35% v. 10%, $p = 0.042$); only 4 of 41 patients older than 60 years had involved nodes at surgery. A significant difference in nodal involvement was found with respect to high or intermediate grade versus low grade lesions in the occult group (44% v. 12%, $p = 0.033$). In the control group, tumour grade (intermediate and high [45.3%] v. low [20.0%]) and hormone replacement therapy (HRT) (current or recent use [56.5%] v. no use [34.5%]) were significant findings ($p < 0.001$ and $p = 0.005$ respectively).

Conclusions: Women older than 60 years with tumours smaller than 1 cm had a low probability of nodal positivity (0% to 8.7%), but there is insufficient information in this group to give a 95% or better prediction of nodal status at the time of surgery. Studies of minimally invasive techniques such as sentinel node biopsy are needed in this group to minimize surgical morbidity in these women who, as a result of early diagnosis, have an excellent long-term outlook.

Objectif : Déterminer le rôle de la dissection de ganglions axillaires en étudiant les caractéristiques des patientes et des tumeurs dans les cas de cancer du sein de type envahissant, dans le cadre du Programme ontarien de dépistage du cancer du sein (PODCS).

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CONCEPTION : Évaluation rétrospective.

CONTEXTE : Section de London (Ontario) du PODCS.

PATIENTES : On a étudié trois groupes de femmes : 50 femmes atteintes d'un cancer du sein dépisté, qui était palpable et a été décelé par une infirmière examinatrice, 62 femmes atteintes d'un cancer du sein occulte dépisté et 353 femmes jumelées selon l'âge et atteintes d'un cancer du sein de type envahissant, tirées de la base de données prospectives du LRCC, qui ont servi de sujets témoins.

PRINCIPALE MESURE DES RÉSULTATS : La proportion des ganglions axillaires atteints dans les 3 groupes, fondée sur les caractéristiques des patientes et des tumeurs.

RÉSULTATS : Vingt-cinq (22,3 %) des 112 femmes avaient une tumeur dépistée de moins de 1 cm de diamètre, mais une seulement avait un ganglion axillaire atteint. Douze (19 %) des 62 femmes atteintes d'une tumeur occulte dépistée avaient des ganglions lymphatiques atteints, comparativement à 17 (34 %) des 50 femmes atteintes d'un cancer palpable dépisté. Chez les sujets témoins, les tumeurs dont le diamètre était inférieur à 1 cm par rapport à celles qui avaient 1 cm ou plus avaient un effet marqué sur la probabilité d'atteinte de ganglions axillaires (12,5 % c. 40,7 %, $p = 0,001$). Chez les sujets atteintes d'une tumeur palpable dépistée, trois fois plus de lésions du quadrant extérieur ou de lésions centrales que de lésions du quadrant intérieur (38 % c. 12 %) avaient atteint des ganglions, et chez les sujets qui avaient des antécédents familiaux de cancer du sein, presque deux fois plus avaient des ganglions axillaires atteints. Chez les sujets atteintes d'une tumeur occulte dépistée, il y avait plus de ganglions atteints chez les patientes âgées de 60 ans ou moins que chez celles de plus de 60 ans (35 % c. 10 %, $p = 0,042$); 4 patientes seulement sur 41 qui avaient plus de 60 ans avaient des ganglions atteints au moment de l'intervention chirurgicale. On a constaté une différence importante dans l'atteinte des ganglions en ce qui concerne les lésions de grade élevé ou intermédiaire par rapport aux lésions de grade inférieur chez les sujets atteintes d'une lésion occulte (44 % c. 12 %, $p = 0,033$). Chez les sujets du groupe témoin, le grade de la tumeur (intermédiaire et élevé [45,3 %] c. inférieur [20,0 %]) et l'hormonothérapie de remplacement (HTR) (utilisation courante ou récente [56,5 %] c. aucune utilisation [34,5 %]) ont représenté des constatations significatives ($p < 0,001$ et $p = 0,005$ respectivement).

CONCLUSIONS : Les femmes de plus de 60 ans qui avaient des tumeurs de moins de 1 cm présentaient une faible probabilité d'atteinte des ganglions (0 % à 8,7 %), mais on n'a pas suffisamment de renseignements sur ce groupe pour établir une prédiction à 95 % ou mieux de l'état des ganglions au moment de la chirurgie. Des études réalisées au moyen de techniques d'effraction minimale comme la biopsie du ganglion de Troisier s'imposent dans ce groupe si l'on veut réduire au minimum la morbidité chirurgicale chez ces femmes dont les perspectives à long terme sont excellentes à la suite d'un diagnostic précoce.

The results of randomized clinical trials[1–3] and an overview of data from several Swedish studies of breast screening support the concept that population screening for breast cancer reduces the death rate from the disease by up to 30%.[4–7] The major effect of breast cancer screening is appropriately judged by a reduction in mortality (Dr. Susan Aitken, Head, Ontario Breast Screening Program [OBSP]: Personal communication, 1997).[8] In addition, increased diagnosis of early stage disease should also lead to improvements in therapy and should encourage the use of newer surgical techniques like sentinel node biopsy[9,10] rather than the reliance on formal axillary node dissection for staging the cancer in such patients. This would be a major advance in treatment and would limit the surgical morbidity of early stage breast cancer.

The OBSP was initiated in 1990. All women in Ontario aged 50 years or over are offered biennial physical examination by specially trained nurses and 2-view mammography.[11,12] The province-wide screening rate is only 13%, although the rate of cancer detection is high at 9.3 per 1000 initial screening examinations performed, when compared with other programs in Canada, the United Kingdom and Sweden, which have reported prevalence screening of 5 to 6.9 cancers per 1000 women screened (Dr. Susan Aitken: personal communication, July 1997). Of cancers detected in the first 5 years of the program (1990 to 1995), 89.4% were invasive and 68.5% were less than 2 cm in diameter; in 71.4% of cases in which the nodal status was available, the nodes were not involved (node-negative disease) (Dr. Susan Aitken: personal communication, July 1997).

From the inception of the OSBP in July 1990 until December 1993, the London Branch screened a total of 13 000 women of whom 11 000 were a prevalence cohort. This included 25% of eligible clients living within a 72 km radius of the screening centre.

The purpose of this report is to determine if features of the primary tumour or patient demographics could be used prospectively to select a group of patients with a low probability of having involved axillary nodes (positive nodes). If these women could be identified, they could be spared a formal axillary node dissection.

Patients and methods

The worksheets from the London branch of the OBSP were used to identify women with a diagnosis of carcinoma of the breast. A total of 125 patients with unilateral carcinoma of the breast with no history of carcinoma in the contralateral breast were identified. Hospital charts and, where available, London Regional Cancer Centre (LRCC) records were used to complete the clinical information reported in this study. Seven of the 125 women had known clinical breast abnormalities and were referred to the OBSP for further evaluation, not for screening; another 6 women did not have an axillary dissection or the nodal status was unknown, leaving 112 women with screen-detected cancer for study. The policy of performing both physical examination and mammography allowed us to identify 2 groups of screen-detected tumours: palpable lesions (50 women) documented by the nurse examiner and occult lesions (62 women) detected only by mammography.

A control group was identified from the LRCC prospective database. Excluding women under 50 years of age, who are not offered breast cancer screening, and using the same study period (July 1990 until December 1993), we identified 353 control patients.

Results

Of the 112 women in the study, 103 (92.0%) were postmenopausal (mean age 63.3 years [range from 50 to 89 years]). The majority of women had stage I (53.6%) or II disease (32.1%) and the commonest site of tumours was the upper or lower outer quadrant of the breast (42.0%) (Table I).

Twenty-five (22.3%) of the 112 women had screen-detected tumours less than 1 cm in diameter; only 1 of these women had axillary node involvement. Although only 12 (19%) of 62 women with occult screen-detected tumours had positive lymph nodes compared with 17 (34%) of 50 women with palpable screen-detected cancer, this finding was not statistically significant ($p = 0.079$, χ^2 analysis), probably because of the small sample size. In the LRCC control group, tumour diameter less than 1 cm versus 1 cm or larger had a marked effect on the probability of axillary node positivity (12.5% v. 40.7%, $p = 0.001$, χ^2 analysis).

Tumour and patient demographic variables were examined in relation to nodal positivity (Table II). The percentage of women with positive nodes is documented in relation to each variable for the 3 groups studied, namely, women with occult and women with palpable screen-detected cancers and LRCC controls. In the palpable screen-detected group, there were no statistically significant differences in nodal positivity in respect of the variables studied. However, 3 times as many outer quadrant or central lesions were associated with positive nodes than inner quadrant lesions (38% v. 12%). Similarly, twice as many node-positive patients had estrogen (ER)- or progesterone-receptor (PR)- positive lesions (40% v. 22% and 44% v. 22%). ER and PR status was reported in only 72 (64.3%) of the 112 women, which may lead to a bias in conclusions based on findings in this subgroup. Family history was documented as significant if there was a mother or sister with breast cancer, regardless of the age at the time of diagnosis. There were almost twice as many women with positive axillary nodes for those with a significant family history of breast cancer in the palpable screen-detected group (57% v. 31%). These differences were not statistically significant likely due to the small numbers in each group.

In the occult screen-detected group there was a significantly greater percentage of women aged 60 years or younger with positive nodes than those older than 60 years ($p = 0.042$, Fisher's exact test); only 4 (10%) women older than 60 years had positive nodes at the time of surgery. A similarly significant difference in nodal positivity was found with respect to high or intermediate grade versus low grade lesions in the occult screen-detected group ($p = 0.033$, Fisher's exact test).

In the LRCC control group there were 2 significant variables with respect to nodal positivity. These were tumour grade ($p < 0.001$, Fisher's exact test) and a history of current or recent use of HRT, where users had significantly greater nodal positivity ($p = 0.005$, Fisher's exact test). The numbers of patients in each group is too small to reliably determine the role of each variable using a multiple logistic regression model.

Having examined the association of tumour and patient demographic

Table I

Stage and Location of Breast Cancers in 112 Women From the Ontario Breast Screening Program (OBSP)

Stage/location	No. (%) of women
Stage	
In situ	11 (9.8)
I	60 (53.6)
II	36 (32.1)
III and IV	5 (4.5)
Location	
Upper and lower outer quadrants	47 (42.0)
Central	29 (25.9)
Upper and lower inner quadrants	36 (32.1)

parameters with respect to nodal positivity within the group of patients with palpable and occult screen-detected tumours separately, we then documented differences between the 2 patient groups and the control group. When the effect of a particular parameter on nodal positivity was different for occult than for palpable screen-detected cancers, there was said to be an interaction. The interaction of each patient demographic and tumour-related variable in the 3 groups was tested statistically. The interactions of palpability with ER and PR status and grade (low v. intermediate and high) were statistically significant ($p = 0.05$, 0.04 and 0.02 respectively) whereas the interaction with benign breast disease tended toward significance ($p = 0.06$). The interactions of palpability with age, family history of breast cancer in a mother or sister, history of HRT use, tumour size and location were not significant in the group of women whose cancers were diagnosed through the OBSP. With only 112 patients, this may represent low statistical power for detecting an effect.

When age and tumour size alone were considered, women older than 60 years with tumours less than 1 cm in diameter were least likely to have positive axillary lymph nodes either screen-detected or found by routine clinical means (range from 0% to 8.7%) (Table III). Only 12% of patients with occult screen-detected lesions 1 cm or larger in diameter and older than 60 years had positive nodes. With small numbers in each subgroup, however, there is low statistical power to detect clinically relevant differences for these parameters. The results of axillary node dissection, tumour size and pathological grade, and ER status were used individually to determine the role for adjuvant systemic treatment. All node-positive patients were given therapy as well as those with high-risk node-negative disease. Determination of this category is based on a risk of relapse equivalent to patients with 1 to 3 positive nodes.

Table II

The Percentage of Women With Positive Axillary Nodes in Relation to Variables Expected to Have an Impact on Nodal Status

Variable	Screen detected		Control, $n = 353$
	Occult, $n = 62$	Palpable, $n = 50$	
Age, yr			
≤ 60	35*	40	41.5
> 60	10	30	34.9
Tumour location			
Inner quadrant	19	12	29.7
Outer quadrant/central	20	38	37.5
Estrogen-receptor status			
Negative	67	22	41.4
Positive	26	40	41.0
Progesterone-receptor status			
Negative	57	22	46.6
Positive	22	44	39.8
Tumour grade			
Low	12†	50	20.0‡
Intermediate/high	44	34	45.3
History of benign disease			
No	14	35	37.5
Yes	33	12	42.6
Current or recent use of hormone replacement therapy			
No	20	37	34.5§
Yes	18	22	56.5
Family history of breast cancer (mother, sister)			
No	20	31	41.5
Yes	17	57	27.3

*$p = 0.042$
†$p = 0.033$
‡$p < 0.001$
§ = 0.005

Discussion

The role of axillary lymph node dissection in patients with invasive carcinoma of the breast has been established as a staging procedure[13] and to obtain locoregional control.[14] Its effect on overall survival remains controversial although the presence and extent of nodal metastases remain strong prognostic indicators in relation to outcome.[14–17] The role of minimally invasive techniques such as sen-

tinel node biopsy is especially relevant in women with screen-detected breast cancer at an early stage as they could be spared the morbidity of formal axillary dissection.[18–21] The main aim of population screening is to promote early diagnosis. Minimizing surgical intervention would extend the value of early diagnosis by decreasing therapy-related morbidity in addition to its impact on long-term survival.

The risk of axillary node positivity has been reported to depend largely but not exclusively on tumour-related factors such as size, grade and ER and PR status.[22] Although it is established that some women with pure noninvasive ductal carcinoma in situ have such a low incidence of nodal metastases that axillary dissection is generally not recommended, there are no validated criteria for omitting a lymph node dissection in women with invasive carcinoma of the breast.[23–26] Physical examination is unreliable, because of the high rate of false-positive and false-negative results.[27,28] Prognostic factors including tumour size, number of positive nodes, age, ER and PR levels, ploidy and S-phase fraction have been used to determine risk of relapse, and in a recent large retrospective report[29] they were evaluated to define risk estimates of nodal positivity. No patient subset could be identified as having a greater than 95% chance of being either node negative or node positive.

Despite examining extensive patient and tumour-related demographic information in our group of screen-detected tumours, we could not identify any group in whom there was a 95% chance of being either node negative or node positive. Although women over 60 years of age, especially those with tumours less than 1 cm in diameter, have a very low probability of nodal positivity in our data set (0% to 8.7%), this is insufficient evidence to recommend a change in current surgical practice.

Women with only 1 to 3 positive nodes and high-risk women having node-negative disease are usually offered the same adjuvant chemotherapy regimen (most commonly adriamycin and cyclophosphamide [AC] or cyclophosphamide, methotrexate and 5-fluorouracil [CMF]). Those with 4 or more positive nodes are usually offered more aggressive anthracycline-based chemotherapy and women with 10 or more positive nodes may be given an opportunity to participate in a clinical trial to determine the role of high-dose chemotherapy with stem cell or autologous bone marrow transplantation.

The role of axillary dissection, even in women with screen-detected invasive breast cancer, is pivotal in determining prognosis. It remains a crucial element in determining the need for, and recommendations regarding, the type of adjuvant systemic therapy and should continue to be performed outside the setting of a clinical trial.

If formal axillary dissection is to be avoided in the future, newer approaches such as sentinel node biopsy must be evaluated in the context of a clinical trial. At present, there is insufficient patient and tumour-related information to accurately determine the need for axillary node dissection in this population of patients. The impact of node dissection on therapy has been reported previously[30] and has been shown to benefit as few as 15% of women. The accurate identification of the potential 85% of women who do not apparently benefit from axillary node dissection remains to be undertaken using newer less invasive techniques such as sentinel node biopsy.

Breast screening will almost inevitably expand with the recent National Cancer Institute-US recommendation that women between the ages of 40 and 49 should have annual or biennial mammography. This will, as already documented, lead to more surgical procedures being performed for mammographically detected abnormalities.[31] There is therefore an urgent economic need to undertake clinical trials of appropriate minimally invasive surgical strategies for this ever-expanding group of women.

Table III

Effect of Patient Age and Tumour Size on Lymph Node Positivity

	Positive lymph nodes, no./total no. (%)		
	Screen detected		
Tumour size/age,yr	Occult, *n* = 62	Palpable, *n* = 50	Control, *n* = 353
< 1 cm			
50–60	0/11 (0)	0/1 (0)	3/17 (17.6)
> 60	1/12 (8)	0/1 (0)	2/23 (8.7)
≥ 1 cm			
50–60	7/11 (64)	7/17 (41)	53/116 (45.7)
> 60	3/24 (12)	9/27 (33)	72/191 (37.7)

Tumour size was not available in 4 patients in each of the occult and palpable groups and in 6 patients in the control group.

References

1. Shapiro S, Strax P, Venet L. Periodic breast screening in reducing mortality from breast cancer. *JAMA* 1971; 215:1777-85.
2. Shapiro S, Venet W, Strax P, Venet L, Roeser R. Selection, follow-up, and analysis in the Health Insurance Plan Study: a randomized trial with breast cancer screening. *NCI Monogr* 1985;67:65-74.
3. Tabar L, Fagerberg CJG, Gad A, Baldetorp L, Holmberg LH, Grontoft O, et al. Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Screening Working Group at the Swedish National Board of Health and Welfare. *Lancet* 1985;1:829-32.
4. Tabar L, Fagerberg G, Duffy SW, Day NE. The Swedish two county trial of mammographic screening for breast cancer: recent results and calculation of benefit. *J Epidemiol Commun Health* 1989;43:107-14.
5. Tabar L, Fagerberg G, Duffy SW, Day NE, Gad A, Grontoft O. Update to the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin North Am* 1992;30:187-210.
6. Rutqvist LE, Miller AB, Andersson I, Hakama M, Hakulinen T, Sigfusson BF, et al. Reduced breast-cancer mortality with mammography screening — an assessment of currently available data [review]. *Int J Cancer Suppl* 1990;5:76-84.
7. Nystrom L, Rutqvist LE, Wall S, Lindgren A, Lundqvist M, Ryden S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials [see comments] [published erratum appears in *Lancet* 1993;342: 1372]. *Lancet* 1993;341:973-8. Comments in: *Lancet* 1993;341:1531-2; *Lancet* 1993;342:549-50.
8. Cole P, Morrison AS. Basic issues in population screening for cancer. *J Natl Cancer Inst* 1980;65:1263-72.
9. Giuliano AE, Dale PS, Turner RR, Morton DL, Evans SW, Krasne DL. Improved axillary staging of breast cancer with sentinel lymphadenectomy [review] [see comment]. *Ann Surg* 1995;222:394-9. Comment in: *Ann Surg* 1997;225:126-7.
10. Statman R, Giuliano AE. The role of the sentinel lymph node in the management of patients with breast cancer. *Adv Surg* 1996;30:209-21.
11. Perrault D, Libstug A, Mercer S, Vayda E. The Ontario Breast Screening Program: the first 18 months. *Ont Med Rev* 1992; December:27-33.
12. Perrault D, Libstug A, Shedden S, Moravan V, Whittick D. The Ontario Breast Screening Program: a progress report. *Ont Med Rev* 1994;June:32-6.
13. Bearhs OH, editor. *Manual for staging of cancer. American Joint Committee on Cancer/ American Cancer Society.* 3rd ed. Philadelphia: J.B. Lippincott, 1988.
14. Fisher B, Redmond C, Fisher ER, Bauer M, Wolmark N, Wickerham DL, et al. Ten-year results of randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985;312:674-81.
15. Fentiman IS. Axillary surgery in breast cancer: What debate? [letter]. *Eur J Cancer* 1993;29:923.
16. Axelsson CK, Mouridsen HT, Zedeler K. Axillary dissection of level I and II lymph nodes is important in breast cancer classification. The Danish Breast Cancer Cooperative Group (DBCG). *Eur J Cancer* 1993;28: 1415-8.
17. Margolese RG. Axillary surgery in breast cancer — there still is a debate [see comment]. *Eur J Cancer* 1993; 29A:801. Comment in: *Eur J Cancer* 1993;29A:923.
18. Krag DN, Weaver DL, Alex JC, Fairbank JT. Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe. *Surg Oncol* 1993;2:335-9.
19. Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer [see comment]. *Ann Surg* 1994;220:391-8. Comment in: *Ann Surg* 1997;225:126-7.
20. Albertini JJ, Lyman GH, Cox C, Yeatman T, Balducci L, Ku N, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer [see comment]. *JAMA* 1996;276:1818-22. Comment in: *JAMA* 1997;277:791-2.
21. Coburn MC, Bland KI. Surgery for early and minimally invasive breast cancer. *Curr Opin Oncol* 1995;7: 506-10.
22. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer* 1989;63:181-7.
23. Deckers PJ. Axillary dissection in breast cancer: when, why, how much, and for how long? Another operation soon to be extinct? [editorial]. *J Surg Oncol* 1991;48:217-9.
24. Moffat FL Jr, Senofsky GM, Davis K, Clark KC, Robinson DS, Ketcham AS. Axillary node dissection for early breast cancer: some is good, but all is better. *J Surg Oncol* 1992;51:8-13.
25. Leborgne F, Leborgne JH, Ortega B, Doldan R, Zubizarreta E. Breast conservation treatment of early stage breast cancer: patterns of failure. *Int J Radiat Oncol Biol Phys* 1995;31: 765-75.
26. Recht A, Houlihan MJ. Axillary lymph nodes and breast cancer: a review. *Cancer* 1995;76:1491-512.
27. Schottenfeld D, Nash AG, Robbins GF, Beattie EJ Jr. Ten-year results of the treatment of primary operable breast cancer: a summary of 304 patients evaluated by the TNM system. *Cancer* 1976;38:1001-7.
28. Butcher HR. Radical mastectomy for mammary carcinoma. *Ann Surg* 1969;170:883-4.
29. Ravdin PM, De Laurentiis M, Vendely T, Clark GM. Prediction of axillary lymph node status in breast cancer patients by use of prognostic indicators. *J Natl Cancer Inst* 1994; 86:1771-5.
30. Lin PP, Allison DC Wainstock J, Miller KD, Dooley WC, Friedman N, et al. Impact of axillary lymph node dissection on the therapy of breast cancer patients. *J Clin Oncol* 1993; 11:1536-44.
31. Cady B, Stone MD, Schuler JG, Thakur R, Wanner MA, Lavin PT. The new era in breast cancer. Invasion, size, and nodal involvement dramatically decreasing as a result of mammographic screening [see comment]. *Arch Surg* 1996;131:301-8. Comment in: *Arch Surg* 1996; 131:788.