STRATEGIES FOR MORBIDITY CONTROL OF AXILLARY DISSECTION FOR BREAST CANCER

Cover design:	Robbert Zweegman; *'Bust of reclining woman'*; ©1998, Pablo Picasso, c/o Beeldrecht, Amstelveen
Lay-out:	Els Zwartendijk
ISBN:	90 - 9011877 - 2
Copyright 1998	J.Bonnema
Printed by	Thela Thesis Amsterdam

Strategies for morbidity control of axillary dissection for breast cancer

Strategieën voor de controle van
morbiditeit van okselklierdissectie
bij borstkanker

PROEFSCHRIFT

Ter verkrijging van de graad van doctor aan
de Erasmus Universiteit van Rotterdam op gezag van de
Rector Magnificus

Prof. dr P.W.C. Akkermans M.A.

en volgens het besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op
woensdag 16 september 1998 om 11.45 uur

door

Jorien Bonnema

geboren te Amsterdam

Promotiecommissie

Promotor:	Prof.Dr J.Jeekel
Co-promotor:	Dr Th.Wiggers
Overige leden:	Prof.Dr F.F.H.Rutten
	Prof.Dr G.Stoter
	Prof.Dr C.J.H.van de Velde

The investigations presented in this thesis were performed at the Department of Surgery of the Zuider hospital Rotterdam and the Department of Surgical Oncology of the Daniel den Hoed Cancer Centre, Rotterdam, in collaboration with the Institute of Health and Environmental Issues (IGO), Willemstad (Chapter 5,6,7), the Netherlands Institute for Care and Welfare (NIZW), Utrecht (Chapter 7) and the National Organisation of Breast Cancer Patients (LCBB), the Netherlands (Chapter 7).

The studies described in Chapter 5 and 6 were financially supported by the Ministry of Welfare, Health and Sports, the Netherlands. The study described in Chapter 7 was supported by the Dutch Foundation for Preventive Medicine (Preventiefonds). Financial support for this thesis was given by Glaxo Wellcome, Astra Tech, Van Straten, Zeneca Farma and VVAA.

In nagedachtenis aan mijn vader

Contents

Chapter 1

General introduction

Introduction

Breast cancer accounts for one third of all cancers in females in the Netherlands [1] and the incidence has been increasing world-wide in the past decades [2]. For the majority of patients, surgery forms the primary treatment of choice [3]. Dissection of the axillary lymph nodes has been part of the surgical treatment since the introduction of radical mastectomy at the end of the nineteenth century [4] and has remained an important element in the management of breast cancer up until the present day [5]. Initially, lymph node dissection was considered to be essential for the cure of breast cancer, but over the last decades it has been primarily regarded as a staging procedure, with the secondary purpose of maintaining local control in the axilla [6,7]. In the absence of reliable, non-invasive techniques, axillary lymph node dissection remains the most important method for determining axillary node status.
A number of studies have reported the adverse effects of axillary lymph node dissection, which include seroma formation [8], edema of the arm and breast [9,10], shoulder dysfunction [11,12] and loss of sensation in the distribution area of the intercostobrachial nerves [11,13]. The length of hospital stay after axillary lymphadenectomy for breast cancer is usually determined by the need for wound and drain management of the patient [14-16]. Recently, clinicians have begun to explore the possibilities of earlier discharge of the patient, and the conclusion has been made that this offers safe and cost-effective management [17-20] and may be of psychological benefit for the patient [21,22].
Changes related to the indications and sequelae of axillary lymph node dissection and to the postoperative care need have major implications, as they affect the well-being of many women.

The role of axillary lymph node dissection in the treatment of breast cancer

Axillary lymph node status is the most important prognostic factor in patients with breast cancer [23,24]. Numerous studies have correlated increasing nodal positivity with decreasing prognosis [25,26]. Survival of patients with lymph node metastasis can be prolonged by using adjuvant chemotherapy and hormonal treatment [27].
Complete dissection of axillary nodes is recommended as the standard procedure for assessing lymph node involvement [7,28-31]. A positive correlation between the number of nodes dissected and recurrence-free and overall survival has been found [32,33]. A minimum of ten nodes need to be removed in order to achieve a 93 % predictive value that the remaining nodes are tumor free [34]. Dissection of level I, II and III nodes (respectively lateral, behind and medial of the pectoralis minor muscle)

is advocated as the procedure of choice in the Netherlands [35]. However, in other countries management of the axilla is far from uniform. Alternatives to complete axillary dissection include node sampling [36,37], lower axillary dissection [38] and radiotherapy to the regional nodes alone or in combination with a surgical staging procedure [39-41].
Complete axillary dissection is highly effective in preventing axillary failure (0-3%) [42-44]. The axillary failure rate increases when a less extensive surgical technique is used [45,46]. The influence of the routine use of axillary treatment in the asymptomatic patient on survival rates, compared with 'delayed' axillary treatment (i.e. used only when patients develop clinically axillary recurrence), remains a controversial issue but is calculated to be low [47].

Morbidity of axillary dissection

Serous fluid formation

Dissection of the axillary nodes is always followed by the formation of a serous fluid in the wound, the collection of it usually called 'seroma'. Although the origin of the fluid is unknown, it has been suggested that it originates from disruption of the lymphatic channels [48]. Other explanations are that it is an ultrafiltrate of blood, or a wound exudate [49]. The formation of seroma is associated with an increased risk of wound infection [50] and delayed wound healing [51,52].
About 25 years ago, closed suction drains were introduced as a method to evacuate serous fluid following radical mastectomy [53,54], and these drains are now generally used after surgery for breast cancer [54]. Closed wound suction is expected to reduce serous fluid formation by obliterating the space beneath skin flaps [55,56] or quicker closure of lymph vessels [57]. Although it is generally assumed that closed suction drainage prevents wound infection, support for this hypothesis is weak as the two randomised studies on this subject have several methodological shortcomings [58,59]. Infection following axillary dissection is observed in 5-13 % of patients [38,60,61] and may be related to prolonged drainage [62].
Throughout the decades surgeons have attempted to prevent the formation of serous fluid. Closing the dead space of the axilla by suturing skin flaps to underlying muscle [63] or suturing of the pectoral flaps and latissimus dorsi to the chest wall [52,64] have been associated with a reduced incidence of serous fluid formation. Other techniques attempted for prevention of serous fluid formation include sclerotherapy with tetracycline [65], the use of fibrin adhesives [66-68], and the use of laser [69,70] or electrocautery [71] for preparation of skin flaps.

Long term morbidity

In addition to short term morbidity experienced directly after the operation, axillary

dissection is associated with several long term complications. Morbidity of the arm is common, with one study reporting numbness in 70 % of patients, pain in 33 %, weakness in 25 %, arm swelling in 10%, stiffness in 10% and effects upon daily life in 39 % of patients [11]. The 'intercostalbrachial nerve syndrome' is responsible for some of the complaints and is characterized by paresthesia of the upper arm, shoulder and axilla, and occasionally of the more anterior portion of the chest wall [72]. Pain is another symptom resulting from lesions of the intercostobrachial nerves [13] and one recommendation is to preserve the nerve when performing an axillary dissection [73]. The risk of impaired shoulder mobility is significant: in one series 42 % of patients had subjective or objective impairment of arm function one year after surgery [74]. The risk increases when surgery of the axilla is combined with radiotherapy [12].
Edema of the arm is one of the most distressing complications of treating breast cancer and causes psychological and functional morbidity. It predisposes patients to develop cellulitis [75] and may lead to lymphangiosarcoma [9]. The reported overall incidence of arm swelling after axillary surgery varies widely, and depends on the definition of edema used, the extent of surgery, the intensity of radiotherapy, and the length of follow-up. In present surgical series the incidence ranges from 8-20 % [10,11,76], and the risk is significantly increased when axillary clearance is followed by radiotherapy [9].

Diagnostic procedures for assessment of axillary lymph node metastases

Several modalities have been developed to determine the presence of pathological axillary nodes prior to axillary dissection. Physical examination has an impressive inaccuracy with a false negative rate of 39 - 45 % [77,78]. Imaging modalities that have been used are: mammography [79,80], ultrasonography [81-83], computed axial tomography (CT) [84], magnetic resonance imaging (MRI) [85-87], radionuclide lymphography [88,89], radionuclide immunoscintigraphy [90], single-photon emission tomography [91] and positron emission tomography (PET) [92,93]. The problem with imaging methods such as CT, MRI and ultrasound, is the correlation between abnormal patterns, like enlargement of nodes or contrast enhancement, and the histological diagnosis of cancer. The predictability of diagnosis of metastatic involvement, therefore, is low. However, the combination of imaging modalities with biopsy methods may improve the possibility of presurgical staging of the axilla [94]. A new technique which employs this concept is the biopsy of the 'sentinel-node', located by immunoscintigraphy and gamma-probe guided surgery [95].

Postoperative care and hospital stay

International and national trends in length of hospital stay

In the last 20 years, the length of hospital stay for any diagnosis has become shorter [96] and this trend is also being observed in various fields of surgery [97-99]. The shift of intramural to extramural care is partly due to the availability of new diagnostic and therapeutic modalities available to outpatients and home treatment [100]. Cost containment and increasing demand on beds are other contributing factors [101]. Moreover, the attitudes towards the need of hospital care following surgical procedures have changed [100]. Day surgery is now the procedure of choice for the majority of surgical procedures in the United Kingdom [100] and is also steadily increasing in the Netherlands [102]. Governmental organisations have reacted to this development by offering advice about the organisation, conditions and availability of day-surgery and home care facilities [103-105]. The hospitalisation of cancer patients shows the same trend: hospital stay for any cancer diagnosis has been reduced from four weeks in 1970 to 10 days in the Netherlands [106].

Hospital stay after surgery for breast cancer

As with other categories of patients, the length of stay after surgery for breast cancer has gradually become shorter. The mean length of stay in the Netherlands after breast conserving therapy is now 8,7 days and after modified radical mastectomy 11,2 days (see table on page 15).

Patients usually remain in hospital after axillary dissection until the amount of drainage from the axilla is minimal (< 30-50 ml per day) and the drains are removed [14,19]. Shorter hospital stays are possible if patients are discharged with their drain in situ or if drains are removed early. Experiences with early hospital discharge after surgery for breast cancer were firstly described in 1984 in the United States (US) [16]. Several other US publications on shorter hospitalisation have followed [14,15,17-19,21,107-110]. These studies report on the complication rates, patient satisfaction and savings of hospital charges. In Europe, experiences with short stay surgery for diagnostic procedures of the breast have been reported [111-113], but studies about short stay procedures following axillary dissection have only been published recently and are in limited in number [20,114,115].

The current post-operative procedures after axillary dissection for breast cancer in the Netherlands were evaluated in 1995 by means of a national survey among 146 hospitals conducted by the author. The response rate was 78 % (114 hospitals). Complete axillary dissection (Level I,II and III) was the standard procedure in nearly all clinics (97%) and vacuum drainage (high vacuum (74%) and low vacuum (26%)) was used to evacuate serous fluid. In 73 hospitals (64%) the length of postoperative hospitalisation was dependent on the axillary drainage production,

	Mean total length of stay after surgery for breast cancer in days (length of pre-operative stay)					
Type of surgery	1980	1986	1991	1994	1995	1996
lumpectomy with axillary dissection			10,8 (1,2)	9,5 (1)	9,3 (1)	8,7 (1)
modified radical mastectomy	19,7 (2,3)	16,6 (2,0)	13,6 (1,7)	11,6 (1,5)	11,6 (1,4)	11,2 (1,3)

Source: SIG Health Care Information, Utrecht 1998

and patients were discharged after drain removal; in fifteen clinics (15%) patients were discharged standardly after more than seven days. Fourteen clinics had experience with early discharge within one week with drains in situ, but in only six clinics this was an accepted procedure.

Relevant aspects of early hospital discharge

Complication rates, patient satisfaction and psychosocial rehabilitation

Early discharge from the hospital after surgery for breast cancer is found to have no adverse effects on complication rates including wound infection and seroma formation [15,17,18,20,21,107,115]. Patient satisfaction with a short length of stay after surgery for breast cancer is reported to be high [17,20,109,114,116]. This is in agreement with studies on satisfaction of patients with one day admission for a variety of surgical specialties [117].

The influence of early hospital discharge on psychosocial rehabilitation after surgery for breast cancer is unknown. It has been suggested, though not confirmed, that recovery in the patient's own environment results in an improved psychosocial adjustment, due to enhanced patient comfort, control and independence, and better interaction with family members [22].

Substitution of care and costs

The shift of intra- to extramural care for cancer patients increases the demand for professional home care [106]. It is also expected that the promotion of home care will lead to an increased need for informal care [105]. The extent of substituting intramural care for home care in patients discharged early after surgical treatment for breast cancer is unknown. In most studies on early discharge, there is little or no information on the number of control visits needed in the outpatient department or on the

amount of professional or informal home care used [17-19,109,110]. Some studies state that district nurses visit breast cancer patients but do not quantify the amount or type of care given [15,20,21,115].
Implementing short hospital stays or outpatient procedures is one of the measures expected to reduce health care expenses. The economic effects of early discharge after breast cancer surgery as measured by calculation of savings of hospital charges have been reported in several studies [16,17,19,21,109]. Although these calculations may be relevant from the perspective of health care insurers, it gives no insight in the costs of introducing short stay policies for 'society as a whole' [118]. The shift of care and the costs for society are important effects of early hospital discharge that should be considered if this management would be introduced on a larger scale.

Continuity of care and information

Discharge planning is an integral part of the care process. It includes the assessments of needs and coordination of appropriate resources for patients as they move through the health care system [119]. It has been found that breast cancer patients experience shortcomings in this coordination and are poorly informed about the possibilities for receiving help and guidance following discharge from hospital [120,121]. Early hospital discharge reduces the time needed for assessment and discharge planning and increases the demand for attuning intra- and extramural care [122].
In order to provide the patient with quality of care, continuity of information and psychosocial support should be guaranteed throughout the disease process [123]. However, a great deal of information and guidance is provided by a variety of individuals attending the patient. Patients sometimes experience the information process as being discontinuous and psychosocial guidance is often not guaranteed [124,125]. There has been no consistent effort made to compile essential information into one comprehensive document, thereby limiting access to vital information for patients and their families [126].

Scope of the thesis

Axillary lymph node dissection plays a central role in the treatment of breast cancer patients. It provides accurate prognostic information, helps guide the use of adjuvant systemic therapy, provides effective local control, and probably results in an improved survival rate in some sub-groups of patients. However, the surgical treatment of the axilla is not a trivial matter. It results in short term as well as long term morbidity and over-treatment of node negative patients. There are several ways to control morbidity after axillary dissection. These include considering alternative diagnostic procedures for detection of axillary lymph node metastases, the reduction of serous fluid formation, and improvement of postoperative care management.

In Chapter 2 the chemical composition of the serous fluid formed after axillary lymph node dissection has been described. In Chapter 3, a study on the influence of the negative pressure in the closed suction drainage system on the amount of serous fluid production in the axilla, duration of drainage and complication rates is presented. In Chapter 4 we examined the accuracy of ultrasound guided aspiration biopsy for detection of axillary lymph node metastases in clinically node negative patients.
Serous fluid production formed after axillary dissection prolongs hospital stay. There exists an increasing trend in reducing the length of hospital stay after axillary dissection. These policies are considered feasible and probably of benefit for the patient. Chapter 5 describes a randomised trial exploring the medical and psychosocial effects of early hospital discharge after axillary lymph node dissection and patient satisfaction with this form of treatment.
The consequences of the introduction of short stay care from societal perspective with regard to substitution of care and costs are relatively unknown. However, these aspects should be addressed if this treatment will be introduced on a large scale. Therefore, we provided an estimation of substitution of care and of societal costs following the short and long hospital stay treatment (Chapter 6).
For the patient with breast cancer continuity and care of information after surgical treatment should be guaranteed. In Chapter 7 the development and implementation of a multidisciplinary care-protocol has been described integrating medical, nursing, and extramural activities in order to enhance continuity of care and information.

References

1 Netherlands Cancer Registry, General results. In: *Incidence of Cancer in the Netherlands 1993*, Utrecht: Vereniging Integrale Kankercentra, 1996, p. 13-19.

2 Kelsey JL, Horn-Ross PL. Breast cancer: magnitude of the problem and descriptive epidemiology. *Epidemiol Rev* 1993;15:7-16.

3 Netherlands Cancer Registry, *Incidence of cancer in the Netherlands 1991*, Utrecht:SIG Health Care Information, 1992.

4 Halsted WS. The results of operations for the cure of cancer of the breast performed at the John Hopkins Hospital from June,1889 to January, 1894. *Johns Hopkins Hosp Bull* 1894;4:297.

5 Morrow M. Axillary dissection:when and how radical? *Semin Surg Oncol* 1996;12:321-327.

6 Hellman S, Harris JR. The appropriate breast cancer paradigm. *Cancer Research* 1987;47:339-342.

7 Fentiman IS, Mansel RE. The axilla:not a no-go zone. *Lancet* 1991;337:221-223.

8 Tejler G, Aspegren K. Complications and hospital stay after surgery for breast cancer: a prospective study of 385 patients. *Br J Surg* 1985;72:542-544.

9 Kissin MW, Querci della Rovere G, Easton D, Westbury G. Risk of lymphoedema following the treatment of breast cancer. *Br J Surg* 1986;73:580-584.

10 Hoe AL, Iven D, Royle GT, Taylor I. Incidence of arm swelling following axillary clearance for breast cancer. *Br J Surg* 1992;79:261-262.

11 Ivens D, Hoe AL, Podd TJ, Hamilton CR, Taylor I, Royle GT. Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992;66:136-138.

12 Aitken RJ, Gaze MN, Rodger A, Chetty U, Forrest APM. Arm morbidity within a trial of mastectomy and either nodal sample with selective radiotherapy or axillary clearance. *Br J Surg* 1989;76:568-571.

13 Vecht CJ, van de Brand HJ, Wajer OJM. Post-axillary dissection pain in breast cancer due to a lesion of the intercostobrachial nerve. *Pain* 1989;38:171-176.

14 Litvak S, Borrero E, Katz R, Munoz E, Wise L. Early discharge of the postmastectomy patient: unbundling of hospital services to improve profitability under DRGs. *Am Surgeon* 1987;53:577-579.

15 Wagman LD, Terz JJ, Hill LR, Beatty JD, Kokal WA, Rihimaki DU, et al. Evaluation of a short-stay program for patients undergoing mastectomy. *J Surg Oncol* 1989;41:98-102.

16 Tarazi R, Esselstyn CB, Kuivila T, Hardesty I. Early hospital discharge following mastectomy. *Cleve Clin Q* 1984;51:579-584.

17 Clark JA, Kent RB. One-day hospitalization following modified radical mastectomy. *Am Surg* 1992;58:239-242.

18 Orr RK, Ketcham AS, Robinson DS, Moffat FL, Tennant ND. Early discharge after mastectomy. A safe way of diminishing hospital costs. *Am Surgeon* 1987;53:161-163.

19 Edwards MJ, Broadwater JR, Bell JL, Ames FC, Balch CM. Economic impact of reducing hospitalization for mastectomy patients. *Ann Surg* 1988;208:330-336.

20 Holcombe C, West N, Mansel RE, Horgan K. The satisfaction and savings of early discharge with drain in situ following axillary lymphadenectomy in the treatment of breast cancer. *Eur J Surg Oncol* 1995;21:604-606.

21 Goodman AA, Mendez AL. Definitive surgery for breast cancer performed on an outpatient basis. *Arch Surg* 1993;128:1149-1152.

22 Kambouris A. Physical, psychological, and economic advantages of accelerated discharge after surgical treatment for breast cancer. *Am Surg* 1996;62:123-127.

23 Nemoto T, Vana J, Bedwani RN, Baker HW, McGregor FH, Murphy GP. Management and survival of female breast cancer: results of a national survey by the American College of Surgeons. *Cancer* 1980;45:2917-2924.

24 Fisher B, Slack N, Katrych D, Wolmark N. Ten-year follow-up results of patients with carcinoma of the breast in a cooperative clinical trial evaluating surgical adjuvant chemotherapy. *Surg Gynecol Obstet* 1975;140:528-534.

25 Smith JA, Gamez-Araujo JJ, Gallager HS, White EC, McBride CM. Carcinoma of the breast. Analysis of total lymph node involvement versus level of metastasis. *Cancer* 1977;39:527-532.

26 Fisher B, Bauer M, Wickerham D, Redmond CK, Fisher ER. Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update.
Cancer 1983;52:1551-1557.

27 Early Breast Cancer Trialists' Collaborative Group . Systemic treatment of early breast cancer by hormonal,cytotoxic,or immune therapy. *Lancet* 1992;339:1-15.

28 Cabanes pA, Salmon RJ, Vilcocq JR, Durand JC, Fourquet A, Gautier C, et al. Value of axillary dissection in addition to lumpectomy and radiotherapy in early breast cancer. *Lancet* 1992;339:1245-1248.

29 Sacks NPM, Barr LC, Allan SM, Baum M. The role of axillary dissection in operable breast cancer. *Breast* 1992;1:41-49.

30 Senofsky GM, Moffat FL, Davis K, Masri MM, Clark K, Robinson DS, et al. Total axillary lymphadenectomy in the management of breast cancer. *Arch Surg* 1991;126:1336-1342.

31 Sacre RA. Modern thoughts on lymph nodes in breast cancer. *Semin Surg Oncol* 1989;5:118-125.

32 Axelsson CK, Moudridsen HT, Zedeler K. Axillary dissection of level I and II lymph nodes is important in breast cancer classification. *Eur J Cancer* 1992;28A:1415-1418.

33 Wilking N, Rutqvist LE, Carstensen J, Mattsson A, Skoog L. Prognostic significance of axillary nodal status in primary breast cancer in relation to the number of resected nodes. *Acta Oncol* 1992;31:29-35.

34 Kiricuta CI, Tausch J. A mathematical model of axillary lymph node involvement based on 1446 complete axillary dissections in patients with breast carcinoma. *Cancer* 1992;69:2496-2501.

35 Rutgers EJTh, Peterse JL, Bartelink H, van Dongen JA. Surgical treatment and deciding definitive management policy in a premenopausal patient with early breast cancer. *Eur J Surg Oncol* 1994;20:607-610.

36 Steele RJC, Forrest APM, Gibson T, Stewart HJ, Chetty U. The efficacy of lower axillary sampling in obtaining lymph node status in breast cancer: a controlled randomized trial. *Br J Surg* 1985;72:368-369.

37 Hadiminas DJ, Burke M. Intraoperative assessment of nodal status in the selection of patients with breast cancer for axillary clearance. *Br J Surg* 1994;81:1615-1616.

38 Siegel BM, Mayzel KA, Love SM. Level I and II axillary dissection in the treatment of early-stage breast cancer. *Arch Surg* 1990;125:1144-1147.

39 Schwartz GF, Rosenberg AL, Danoff BF, Mansfield CM, Feig SA. Lumpectomy and level I axillary dissection prior to irradiation for operable breast cancer. *Ann Surg* 1984;200:554-600.

40 Haffty BG, McKhann C, Beinfield M, Fischer D, Fischer JJ. Breast conservation therapy

without axillary dissection. *Arch Surg* 1993;128:1315-1319.

41 Forrest APM, Stewart HJ, Roberts MM, Steele RJC. Simple mastectomy and axillary node sampling(pectoral node biopsy)in the management of primary breast cancer. *Ann Surg* 1982;196:371-378.

42 Recht A, Pierce SM, Abner A, Vicini F, Osteen RT, Love SM, et al. Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. *J Clin Oncol* 1991;9:988-996.

43 Vicini FA, Horwitz EM, Lacerna MD, Brown DM, White J, Dmuchowski CF, et al. The role of regional nodal irradiation in the management of patients with early stage breast cancer treated with breast conserving therapy. *Int J Radiation Oncology Biol Phys* 1997;39:1069-1076.

44 Fisher B, Redmond C, Fisher ER, Bauer M, Wolmark N, Wickerham DL, et al. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985;312:674-681.

45 Graversen HP, Blichert-Toft M, Andersen JA, Zedeler K, Danish Breast Cancer Co-operative Group . Breast cancer:risk of axillary recurrence in node-negative patients following partial dissection of the axilla. *Eur J of Surg Oncol* 1988;14:407-412.

46 Benson EA, Thorogood J. The effect of surgical technique on local recurrence rates following mastectomy. *Eur J Surg Oncol* 1986;12:267-271.

47 Recht A, Houlihan MJ. Axillary lymph nodes and breast cancer. *Cancer* 1995;76:1491-1512.

48 Tadych K, Donegan WL. Postmastecomy seromas and wound drainage. *Surg Gynecol Obstet* 1987;165:483-487.

49. Watt-Boolsen S, Nielsen VB, Jensen J, Bak S. Postmastectomy seroma. A study of the nature and origin of seroma after mastectomy. *Dan Med Bull* 1989;36:487-489.

50 Hayes JA, Bryan RM. Wound healing following mastectomy. *Aust N Z J Surg* 1984;54:25-27.

51 Say CC, Donegan W. A biostatistical evaluation of complications from mastectomy. *Surg Gynecol Obstet* 1974;138:370-376.

52 Aitken DR, Hunsaker R, James AG. Prevention of seromas following mastectomy and axillary dissection. *Surg Gynecol Obstet* 1984;158:327-330.

53 Raffl AB. The use of negative pressure under skin flaps after radical mastectomy. *Ann Surg* 1952;136:1048.

54 Moss JP. Hisorical and surrent perspectives on surgical drainage. *Surg Gynecol Obstet* 1981;152:517-527.

55 Terrel GS, Singer JA. Axillary versus combined axillary and pectoral drainage after modified radical mastectomy. *Surg Gynecol Obstet* 1991;175:437-440.

56 Brottin BJ, Gilmore OJA, Lumley JSP, Castleden WM. A comparison between disposable and non-disposable suction drainage units: a report of a controlled trial. *Br J Surg* 1979;66:279-280.

57 Petrek JA, Peters MM, Cirrincione C, Thaler HT. A prospective randomized trial of single versus multiple drains in the axilla after lymphadenectomy. *Surg Gynecol Obstet* 1992;175:405-409.

58 Bourke JF, Balfour TW, Hardcastle JD. A comparison between suction and corrugated drainage after simple mastectomy: A report of a controlled trial. *Br J Surg* 1976;63:67-69.

59 Morris AM. A controlled trial of closed wound suction. *Br J Surg* 1973;60:357-359.

60 Vinton AL, Traverso LW, Jolly PC. Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection. *Am J Surg* 1991;161:584-588.

61 Shaw JHF, Rumball EM. Complications and local recurrence following lymhadenectomy. *Br J Surg* 1990;77:760-764.

62 Rotstein C, Ferguson R, Cummings KM, Piedmonte MR, Lucey J, Banish A. Determinants of clean surgical wound infections for breast procedures at an oncology center. *Infect Control Hosp Epidemiol* 1992;13:207-214.

63 Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy. A prospective randomized clinical trial. *Eur J Surg Oncol* 1993;19:143-146.

64 Chilson TR, Chan FD, Lonser RR, Wu TM, Aitken DR. Seroma prevention after modified radical mastectomy. *Am Surgeon* 1992;58:750-754.

65 McCarthy PM, Kirk Martin J,Jr., Wells DC, Welch JS, Ilstrup DM. An aborted, prospective, randomized trial of sclerotherapy for prolonged drainage after mastectomy. *Surg Gynecol Obstet* 1986;162:418-420.

66 Gilly FN, Carry PY, Brachet A, Curtil A, Burgard G, Buisson L, et al. Efficacité d'une colle de fibrine sur la lymphostase au cours des curages ganglionnaires. *Ann Chir* 1994;48:194-196.

67 Uden P, Aspegren K, Balldin G, Garne JP, Larsson SA. Fibrin adhesive in radical mastectomy. *Eur J Surg* 1993;159:263-265.

68 Waclawiczek HW, Pimpl W. Lymphfisteln nach Lymphknotendissektionen - Verhütung und Behandlung mit Hilfe der Fibrinverklebung. *Chirurg* 1986;57:330-331.

69 Ansanelli VW. The CO2 laser in axillary dissection for breast cancer. *Lasers Surg Med* 1987;7:87. (Abstract)

70 Wyman A, Rogers K. Radical breast surgery with a contact Nd:YAG laser scalpel. *Eur J Surg Oncol* 1992;18:322-326.

71 Miller E, Paull DE, Morrisey K, Cortese A, Nowak E. Scalpel versus electrocautery in modified radical mastectomy. *Am Surgeon* 1994;

72 Assa J. The intercostobrachial nerve in radical mastectomy. *J Surg Oncol* 1974;6:123-126.

73 Temple WJ, Ketcham AS. Preservation of the intercostobrachial nerve during axillary dissection for breast cancer. *Am J Surg* 1985;150:585-588.

74 Hladiuk M, Huchcroft S, Temple W, Schnurr BE. Arm function after axillary dissection for breast cancer: a pilot study to provide parameter estimates. *J Surg Oncol* 1992;50:47-52.

75 Tobin MB, Lacey HJ, Meyer L, Mortimer PS. The psychological morbidity of breast cancer-related arm swelling. *Cancer* 1993;72:3248-3252.

76 Werner RS, McCormick B, Petrek J, et al. . Arm edema in conservatively managed breast cancer: obesity is a major predictive factor. *Radiology* 1991;180:177-184.

77 Sacre RA. Clinical evaluation of axillary lymph nodes compared to surgical and pathological findings. *Eur J of Surg Oncol* 1986;12:169-173.

78 Davies GC, Millis RR, Path MRC, Hayward JL. Assessment of axillary lymph node status. *Ann Surg* 1980;192:148-151.

79 Pamilo M, Soiva M, Lavast EM. Real-time ultrasound, axillary mammography, and clinical examination in the detection of axillary lymph node metastases in breast cancer patients. *J Ultrasound Med* 1989;8:115-120.

80 Dershaw DD, Panicek DM, Osborne MP. Significance of lymph nodes visualized by the mammographic axillary view. *Breast Dis* 1991;4:271-280.

81 Mustonen P, Farin P, Kosunen O. Ultrasonographic detection of metastatic axillary lymph nodes in breast cancer. *Ann Chir Gynaecol* 1990;79:15-18.

82 Tate JJT, Lewis V, Archer T, Guyer PG, Royle GT, Taylor I. Ultrasound detection of axillary lymph node metastases in breast cancer. *Eur J Surg Oncol* 1989;15:139-141.

83 de Freitas RJr, Costa MV, Schneider SV, Nicolau MA, Marussi E. Accuracy of ultrasound and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. *Eur J Surg Oncol* 1991;17:240-244.

84 Meyer JE, Munzenrider JE. Computer tomographic demonstration of lymph node metastases in patients with recurrent breast cancer. *Radiology* 1991;139:661-663.

85 Allan SM, McVicar D, Sacks NPM. Prospects for axillary staging in breast cancer by magnetic resonance imaging. *Br J Radiol* 1993;66 (suppl):15-16. (Abstract)

86 Mumtaz H, Hall-Craggs MA, Davidson T, Walmsley K, Thurell W, Kissin MW, et al. Staging of symptomatic primary breast cancer with MR imaging. *Am J Roentgenol* 1997;169:417-424.

87 Mussurakis S, Buckley DL, Horsman A. Prediction of axillary lymph node status in invasive bresat cancer with dynamic contrast-enhanced MR imaging. *Radiology* 1997;203:317-321.

88 McClean RG, Ege GN. Prognostic value of axillary lymphoscintigraphy in breast carcinoma patients. *J Nucl Med* 1986;27:1116-1124.

89 Black RB, Taylor TV, Merrick MV, Forrest APM. Prediction of axillary metastases in breast cancer by lymphoscintigraphy. *Lancet* 1980;2:15-17.

90 Tjandra JJ, Sacks NPM, Thompson CH, Leyden MJ, Stacker SA, Lichtenstein M, et al. The detection of axillary lymph node metastases from breast cancer by radiolabelled monoclonal antibodies: a prospective study. *Br J Cancer* 1989;59:296-302.

91 Chiti A, Agresti R, Maffioli LS, Tomasic G, Savelli G, Crippa F, et al. Breast cancer staging using technetium-99m sestamibi and indium-111 pentetreotide single-photon emission tomography. *Eur J Nucl Med* 1997;24:192-196.

92 Avril N, Dose J, Janicke F, Ziegler S, Romer W, Weber W, et al. Assessment of axillary lymph node involvement in breast cancer patients with positron emission tomography using radiolabeled 2-(fluorine-18)-fluoro-2-deoxy-D-glucose. *J Natl Cancer Inst* 1996;88:1204-1209.

93 Nieweg, O.E., Wong, W., Singletary, S.E., Hortobagyi, G.N. and Kim, E.E. Positron emission tomography of glucose metabolism in breast cancer. In: *Breast cancer: from biology to therapy*, Annals of the New York Academy of Sciences, 1993, p. 423-428.

94 Ceci G, Pescarenico MG, Di Sarra S, Manotti L, Cocconi G. Ultrasound (US) examination of axillary nodes with fine needle aspiration biopsy (FNAB). A new non invasive diagnostic method improving the presurgical staging of breast carcinoma. *Proc Am Soc Clin Oncol* 1995;14:109. (Abstract)

95 Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet* 1997;349:1864-1867.

96 Casparie AF, Hoogendoorn D. Effects of budgeting on health care services in Dutch hospitals. *Am J Public Health* 1991;81:1442-1447.

97 Engelman RM. Mechanisms to reduce hospital stays. *Ann Thorac Surg* 1996;61:26-29.

98 Hackman B, Navaneethan N. Early discharge after gynaecological surgery. *Eur J Obstet Gynecol Reprod Biol* 1993;52:57-61.

99 *Trends in surgery 1984-1993*, Utrecht:SIG Health Care Information, 1995.

100 Maddern GJ. The changing pattern of surgery. *Br J Surg* 1996;83:145-146.

101 Waghorn A, McKee M, Thompson J. Surgical outpatients:challenges and responses. *Br J Surg* 1997;84:300-307.

102 *Dagverpleging.Advies over de ontwikkelingen van dagverpleging in ziekenhuizen*, Zoetermeer:Nationale Raad voor de Volksgezondheid, 1993.

103 *Discussienota Thuiszorg*, Zoetermeer:Nationale Raad voor de Volksgezondheid, 1989.

104 *Advies,kwaliteit,organisatie en financiering thuiszorg*, Zoetermeer:Nationale Raad voor de Volksgezondheid, 1990.

105 Gezondheidsraad:Commissie Thuiszorg voor patiënten met kanker, *Thuiszorg voor patiënten met kanker*, Den Haag:Gezondheidsraad, 1991.

106 Stuurgroep Toekomstscenario's Gezondheidszorg, *Kanker Signaleringsrapport 3 1992*, Rijswijk:STG, 1992.

107 Cohen AM, Schaeffer N, Chen Z, Wood WC. Early discharge after modified radical mastectomy. *Am J Surg* 1986;151:465-466.

108 Parikh HK, Badwe RA, Ash CM, Hamed H, Freitas RJr, Chaudary MA, et al. Early drain removal following modified radical mastectomy: a randomized trial. *J Surg Oncol* 1992;51,4:266-269.

109 Pedersen SH, Douville LM, Eberlein TJ. Accelerated surgical stay programs. A mechanism to reduce health costs. *Ann Surg* 1994;219:374-381.

110 Sesto ME, Hall RM, Esselstyn CB, Hardesty IJ. Early discharge following mastectomy: 239 consecutive patients over three years. *Contemp Surg* 1989;35:38-40.

111 Cappel J, Luders K. Ambulante mammachirurgie. *Fortschr Med* 1980;3:105-107.

112 Jacobsen U, Karesen R, Skaane A, Skjorten F,. Out-patient surgical biopsy for nonpalpable breast lesions. *Acta Chir Scand* 1989;155:313-316.

113 Calderoli H, Rohr S, Keiling R, Hollender LF. La chirurgie ambulatoire en pathologie mammaire. *Chirurgie* 1987;113:344-352.

114 Boman L, Björvell H, Cedermark B, Theve NO, Wilking N. Effects of early discharge from hospital after surgery for primary breast cancer. *Eur J Surg* 1993;159:67-73.

115 Yii M, Murphy C, Orr N. Early removal of drains and discharge of breast cancer surgery patients: a controlled prospective clinical trial. *Ann R Coll Surg Engl* 1995;77:377-379.

116 Burke CC, Zabka CL, McCarver KJ, Singletary SE. Patient satisfaction with 23-hour 'short-stay' observation following breast cancer surgery. *Oncol Nurs Forum* 1997;24:645-651.

117 Ghosh S, Sallam S. Patient satisfaction and postoperative demands on hospital and community services after day surgery. *Br J Surg* 1994;81:1635-1638.

118 Williams C, Coyle D, Gray A, Hutton J, Jefferson T, Karlsson G, et al. Cost-effectiveness in cancer care. Report of a Working Party from the European School of Oncology. *Eur J Cancer* 1995;31A:1410-1424.

119 O'Hare PA, Yost LS, McCorkle R. Strategies to improve continuity of care and decrease rehospitalization of cancer patients: a review. *Cancer Invest* 1993;11:140-158.

120 van den Borne HW, Pruyn JFA, van den Heuvel WJA. Effects of contacts between cancer patients on their psychosocial problems. *Patient Educ Couns* 1987;9:33-38.

121 van den Borne, H.W. and Pruyn, J.F.A. *Lotgenotencontact bij kankerpatiënten (Contact between fellow-cancer patients). Thesis*, Assen/Maastricht:van Gorcum, 1985.

122 Feather BL, Wainstock JM, Remington A, Ringenberg QS. Postmastectomy educational needs and social support. *J Cancer Education* 1988;3:135-144.

123 Lauria MM. Continuity of cancer care. *Cancer* 1991;67:1759-1766.

124 Mandemaker, T., Pruyn, J.F.A. and Jonkers-Kuiper, L. *Continuiteit in de patiënten-voorlichting.Een verkennende studie*, Tilburg/Utrecht:IVA/NIZW, 1990.

125 Vleeshouwers, E.M. *De ontwikkeling, introductie en evaluatie van een voorlichtingsmodel*, Maastricht:Comprehensive Cancer Centre Limburg, 1993.

126 Conkling VK. Continuity of care issues for cancer patients and families. *Cancer* 1989;64;suppl.:290-294.

Chapter 2

The composition of serous fluid after axillary dissection

Jorien Bonnema, David A. Ligtenstein, Theo Wiggers, Albert N. van Geel

Eur J Surg, in press

Abstract

Objective. To analyse the composition of the serous fluid formed after axillary dissection
Design. Descriptive study
Setting. University hospital and teaching hospital, The Netherlands
Subjects. 16 Patients whose axillas were dissected as part of a modified radical mastectomy for stage I or II breast cancer
Main outcome measures. Chemical and cellular composition of axillary drainage fluid on the first, fifth, and tenth postoperative days compared with the same constituents in blood and with reported data on the composition of peripheral lymph.
Results and conclusion. On the first postoperative day the drainage fluid contains blood contents and a high concentration of creatine phosphokinase (CPK). After day one it changes to a peripheral lymph-like fluid but containing different cells, more protein, and no fibrinogen, making coagulation impossible. The reduction in the fluid production must be caused by other wound healing processes, such as formation of scars and connective tissue.

Introduction

Non-haemorrhagic fluid commonly forms in wounds after the dissection of axillary nodes and the collection is known as seroma. The origin of this fluid is not well understood and studies on its origin and composition are scarce [1]. The name suggests that the fluid originates from ultrafiltration of blood. Other explanations for its formation are leakage of lymph from disrupted lymphatics in the axilla [2,3] and the production of a wound exudate as part of the inflammatory phase of wound healing [1].

We studied the composition of the fluid formed in the axilla after dissection of axillary lymph nodes and compared the results with the composition of blood of the same patients and with reported data on the composition of peripheral lymph. To distinguish it from chyle, as it can be sampled from the thoracic duct, we have used the term peripheral lymph, which is lymph produced in the extremities and has not yet passed through a node or come into contact with other lymphoid structures [4]. The aim of the study was to analyse the chemical and cellular composition of serous fluid from the axilla to shed some light on the processes involved in its formation.

Patients en methods

Sixteen patients with breast cancer patients underwent axillary dissection as part of a modified radical mastectomy done as prescribed by Madden [5]. Criteria for exclusion were the use of corticosteroids or anticoagulants, preoperative radiotherapy or chemotherapy, and postoperative hematoma or infection. Level I, II and III nodes were resected. Low-dose heparin was used for prophylaxis of deep venous thrombosis. The axilla was drained with a closed suction drainage system. A separate drain was used for the skin flaps of the mastectomy wound. Drains were removed if less than 30 ml of fluid was produced on two consecutive days. Samples of the axillary drainage fluid were obtained on the first, fifth, and tenth postoperative days. On the first postoperative day a blood sample was also taken. The fluids were assayed in the clinical laboratory of the Zuider Hospital. Concentrations of the following substances were measured: electrolytes - sodium, potassium, calcium, magnesium, phosphate and iron; proteins - total protein and albumin; electrophoresis - α-1 globulins, α-2 globulins, ß globulins and gamma globulins; haemoglobin, transferrin, IgG, and fibrinogen; lipids - triglycerides and cholesterol; cells - platelets, red cells and leucocytes; and glucose, osmolality and creatine phosphokinase (CPK).

The mean values of the variables in blood and drainage fluid were compared by independent group analysis using a Tukey non-parametric multiple comparison test. Statistical analyses were done on a personal computer using the Kwikstat version 4.1 statistical data analysis package (TexaSoft, Cedar Hill, Texas, USA).

Results

Results of the analyses are shown in Table 1. No patients had intermittent fluid formation, and no patients had to be excluded because they produced too little or no fluid.
The values of electrolytes in serous fluid were lower for calcium compared with blood. The calcium:albumin ratio was 0.080 for serous fluid and 0.067 for blood. The iron content was high on day 1 in serous fluid which was also iso-osmotic (290 mOsm). Concentrations of CPK in serous fluid were extremely high on day 1. Concentrations of all proteins were significantly lower in serous fluid compared with blood with the exception of ß globulin, which did not differ on day 1. Only very small amounts of fibrinogen were found in the serous fluid. Red cells, platelets and leucocytes were present in the fluid on day 1, but had nearly gone on days 5 and 10. The serous fluid:blood ratio on day 1 was similar for red cells and platelets (0.26), but was much higher for leucocytes (1.05). Differentiation of the leucocytes on day 1 showed 93 % neutrophils, 6 % lymphocytes, and 1 % monocytes.

Discussion

Obviously during the first days the drainage fluid is contaminated with blood from the surgical wound, so iron, triglycerides, haemoglobin, and blood cells are present in the fluid on day 1. They disappear rapidly thereafter. The same goes for CPK, the presence of which may be attributed to tissue destruction as a direct result of the operation. In addition, the fluid is iso-osmotic. The presence of fibrinogen from blood may lead to the formation of some clots early in the wound healing process, but later on, when the fibrinogen originating from blood has been used up, this ceases.
Once constituents of blood have disappeared concentrations of electrolytes and glucose in the serous fluid are similar to those in serum, with the exception of calcium. For sodium, potassium, magnesium, phosphate, and calcium the reported concentrations in lymph [4,6-9] are similar to those we found in serous fluid. Iron is present in large quantities on the first day, probably as a result of decomposition of haemoglobin.
Concentrations of protein in the serous fluid are lower than those in plasma, but somewhat higher than in peripheral lymph [7,10-14]. There is no relation with the molecular weight of the proteins, and there is no development over time.
What is striking about the fluid formed in the axilla is the almost complete absence of fibrinogen. As a consequence of this, it does not clot spontaneously so clotting cannot be the cause of the reduced production of fluid over time. This must, therefore, be caused by other processes such as the formation of collagen and connective

Table 1 Mean (SEM) concentrations of constituents of axillary drainage fluid

Variable	Blood (n=16)	Serous fluid Day 1 (n=16)	Serous fluid Day 5 (n=14)	Serous fluid Day 10 (n=5)	Comment*
Electrolytes					
Sodium (mmol/L)	141.3 (0.7)	140.1 (0.6)	141.3 (0.5)	140.2 (1.4)	No differences
Potassium (mmol/L)	3.9 (0.1)	4.3 (0.1)	4.2 (0.1)	4.3 (0.1)	No differences
Calcium (mmol/L)	2.26 (0.03)	1.87 (0.04)	1.90 (0.03)	1.94 (0.04)	Serous fluid lower than blood
Magnesium (mmol/L)	0.75 (0.02)	0.80 (0.03)	0.74 (0.01)	0.78 (0.02)	No differences
Phosphate (mmol/L)	0.95 (0.05)	1.23 (0.12)	1.13 (0.06)	1.15 (0.08)	No differences
Iron (µmol/L)	10.9 (1.0)	25.4 (2.9)	13.1 (1.2)	14.4 (2.7)	Serous fluid day 1 higher than other values
Proteins					
Total protein (g/L)	57.7 (1.3)	42.8 (2.5)	37.0 (1.2)	39.2 (1.6)	Serous fluid lower than blood
Albumin (g/L)	33.8 (1.0)	23.2 (1.1)	24.6 (1.0)	26.0 (1.7)	Serous fluid lower than blood
Alpha-1 globulins (g/L)	3.17 (0.18)	1.51 (0.15)	1.53 (0.15)	1.48 (0.10)	Serous fluid lower than blood
Alpha-2 globulins (g/L)	5.8 (0.2)	2.6 (0.3)	2.4 (0.2)	2.3 (0.3)	Serous fluid lower than blood
Beta globulins (g/L)	7.3 (0.3)	8.3 (1.5)	3.5 (0.3)	4.5 (0.4)	No difference serous fluid day 1 and blood
Gamma globulins (g/L)	8.1 (0.5)	5.2 (0.3)	4.1 (0.3)	5.0 (0.5)	Serous fluid lower than blood
Immunoglobulins G (g/L)	8.5 (0.6)	4.9 (0.3)	4.6 (0.3)	5.2 (0.6)	Serous fluid lower than blood
Haemoglobin (mmol/L)	7.79 (0.24)	1.74 (0.40)	0.25 (0.09)	Trace	Serous fluid lower than blood. Rapid decline
Transferrin (µmol/L)	54.1 (2.9)	32.5 (2.0)	32.0 (2.0)	31.4 (1.7)	Serous fluid lower than blood
Fibrinogen (g/L)	3.07 (0.21)	0.15 (0.02)	0.13 (0.02)	Trace	Serous fluid lower than blood
Lipids					
Triglycerides (mmol/L)	1.92 (0.50)	1.42 (0.21)	0.60 (0.06)	0.46 (0.05)	No difference serous fluid day 1 and blood
Cholesterol (mmol/L)	4.6 (0.4)	2.4 (0.2)	1.8 (0.1)	2.1 (0.3)	Serous fluid lower than blood
Cells					
Platelets ($x10^9$/L)	248 (15)	64 (10)	21 (5)	16 (4)	Serous fluid lower than blood. Rapid decline
Red cells ($x10^{12}$/L)	4.1 (0.1)	1.1 (0.2)	0.1 (0.04)	Trace	Serous fluid lower than blood. Rapid decline
Leucocytes ($x10^9$/L)	10.1 (1.0)	10.6 (1.5)	1.3 (0.3)	0.3 (0.2)	No difference serous fluid day 1 and blood
Differentiation					
Neutrophils (%)	72.2 (3.2)	93 (1.8)	Not measurable	Not measurable	
Lymphocytes (%)	22.2 (2.9)	6 (1.6)	Not measurable	Not measurable	
Monocytes (%)	5.6 (1.2)	1 (0.6)	Not measurable	Not measurable	
Eosinophils and basophils(%)	0.8 (0.05)	0.1 (0.02)	Not measurable	Not measurable	
Other					
Glucose (mmol/L)	4.0 (0.05)	4.2 (0.3)	3.9 (0.1)	4.2 (0.2)	No differences
Osmolality (mOsm/L)	296 (3)	290 (2)	292 (2)	302 (10)	No differences
CPK (E/L)	223 (62)	22600 (3800)	2750 (1800)	75 (13)	Extreme increase after operation, then rapid decline

All differences statistical significant with $p<0.001$, Tukey multiple comparison test

tissue. This accords with the low concentration of coagulation factors that is found in peripheral lymph in animal studies [15,16]. In humans fibrinogen can be measured only in thoracic duct lymph, in which concentrations vary [17].
It has been suggested that the sealing of ruptured lymphatics by the coagulation of lymph is an important factor in the eventual cessation of leakage of lymph after pelvic lymphadenectomy. This process may be slowed down by the use of low-dose heparin [18]. The absence of fibrinogen in fluid from the axilla makes such a mechanism for the cessation of the production of fluid unlikely. The mechanism by which tranexamic acid acts in reducing the volume of axillary fluid production, as reported recently [19], therefore remains obscure [20].
The fluid in the axilla is a cell-deficient product. It contains mainly leucocytes on day one, but the concentration of cells rapidly declines with time. Granulocytes were the dominant leucocytes, but we saw no shift to lymphocytes such as was reported in a previous study to be and associated with the exudative phase of wound healing [1]. Peripheral lymph contains appreciable counts of lymphocytes [4,9,14,21,22], no platelets [23] and, like serous fluid only few red cells [4,9,22].
Some aspects on the composition of serous fluid need further investigation, such as its role in wound healing and the problem of protracted seroma formation after removal of the drain. The presence of seroma is considered to be a risk factor for wound infection. Wound fluid collected from patients after modified radical mastectomy impaired the neutrophil-dependent killing of bacteria because of a deficiency in the normal humoral factors such as complement factors and fibronectin [24]. The loss of opsonic activity of plasma proteins in wound fluids progresses over time [25]. We found low concentrations of albumin and transferrin in the drainage fluid, which may contribute to the inability of the fluid to support lymphocyte blastogenesis to the same extent as serum, a process necessary for wound healing. This topic needs further elucidation in future studies.
The development of seroma fluid around a prosthetic graft in reconstructive vascular surgery is associated with the presence of a fibroblast inhibitor in serum [26], recently identified as a protein with a molecular weight of 2000 Da. [27]. Fibroblast inhibitors with low molecular weights are also found in wound fluids and may very well be part of a physiological regulatory mechanism in wound healing [28]. Macrophages have a role in the production of these inhibitors [29]. It is still to early to speculate about the role of inhibition of fibroblast growth as a factor in protracted seroma production as happens in some patients after surgery for breast cancer.
In conclusion, the serous fluid formed in the axilla after lymph node dissection seems to be a peripheral lymph-like fluid. However, the cell content is somewhat different from that of lymph, and it contains no fibrinogen. Initially postoperatively the composition of the fluid includes blood components, but these disappear rapidly thereafter. The absence of fibrinogen, precluding the coagulation of the fluid, has

important consequences for the process responsible for the ultimate cessation of seroma production. The fluid shares little resemblance with a wound exudate, because of the low concentration of cells, absence of fibrinogen, and the low protein content.

References

1 Watt-Boolsen S, Nielsen VB, Jensen J, Bak S. Postmastectomy seroma. A study of the nature and origin of seroma after mastectomy. *Dan Med Bull* 1989;36:487-489.

2 Tadych K, Donegan WL. Postmastecomy seromas and wound drainage. *Surg Gynecol Obstet* 1987;165:483-487.

3 Sitzmann JV, Dufresne C, Zuidema GD. The use of sclerotherapy for treatment of postmastectomy seromas. *Surgery* 1983;93:345-347.

4 Yoffey, J.M. and Courtice, F.C. *Lymphatics, lymph and lymphoid tissue*, Cambridge:Harvard University Press, 1956.

5 Madden JL. Modified radical mastectomy. *Surg Gynecol Obstet* 1965;121:1221-1230.

6 Keyl MJ, Dowell RT, Yunice AA. Comparison of renal and cardiac lymph constituents. *Lymphology* 1980;13:158-160.

7 Physical properties and chemical composition of lymph. In: *Mammals, Blood and Other Body Fluids*, edited by Altman, P.L. and Dittmer, D.S. Bethesda: Federation of American Societies for Experimental Biology, 1971, p. 307-312.

8 Braun WE, Banowsky LH, Straffon RA, Nakamoto S, Kiser WS, Popwniak KL, et al. Lymphoceles associated with renal transplantation. *Am J Med* 1974;57:714-729.

9 Robinson CLN. The management of chylothorax. *Ann Thorac Surg* 1985;39:90-95.

10 Engeset A, Olszelwski W, Jaeger PM, Sokolowski J, Theodorsen L. Twenty-four hour variation in flow and composition of leg lymph in normal men. *Acta physiol scand* 1977;99:140-148.

11 Coates G, O'Brodovich H, Goeree G. Hindlimb and lung lymph flows during prolonged exercise. *J Appl Physiol* 1993;75:633-638.

12 Sloop CH, Castle CK, Lefevre M, Wong L. Comparison of the lipid and lipoprotein composition of skeletal muscle and peripheral lymph in control dogs and in dogs fed with a high fat, high cholesterol, hypothyroid diet. *Biochim Biophys Acta* 1993;1169:196-201.

13 Lewis GP, Winsey NJP. The action of pharmacologically active substances on the flow and composition of cat hind limb lymph. *Br J Pharmacol* 1970;40:446-460.

14 Smith JB, McIntosh GH, Morris B. The traffic of cells through tissues: a study of peripheral lymph in sheep. *J Anat* 1970;107:87-100.

15 Brinkhous KM, Walker SA. Prothrombin and fibrinogen in lymph. *Am J Physiol* 1941;132:666-669.

16 Kaulla KN, Pratt EB. Influence of intravenously administered heparin on clotting of

lymph in the dog. *Am J Physiol* 1956;187:89-93.

17 Chrobak L, Bartos V, Brzek V, Hnizdora D. Coagulation properties of human thoracic duct lymph. *Am J Med Sci* 1967;253:69.

18 Catalona WL, Kadmon D, Crane DB. Effect of mini-dose heparin on lymphocele formation following extraperitoneal pelvic lymphadenectomy. *J Urol* 1980;123:890-892.

19 Oertli D, Laffer U, Haberthuer F, Kreuter U, Harder F. Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer. *Br J Surg* 1994;81:856-859.

20 Bonnema J, van Geel AN, Wiggers T, Ligtenstein DA. Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer (Letter). *Br J Surg* 1994;81:1693.

21 Engeset A, Hager B, Nesheim A, Kolbenstvedt A. Studies on human peripheral lymph. *Lymphology* 1973;6:1-5.

22 de Hert S, Heytens L, van Hee R, Adriaensen H. Current management of traumatic chylothorax. *Acta Anaesth Belg* 1988;39:101-107.

23 Fantl P, Nelson JF. Coagulation in lymph. *J Physiol* 1953;122:33-37.

24 Bridges M, Morris D, Hall JR, Deitch EA. Effects of wound exudates on in vitro immune parameters. *J Surg Res* 1987;43:133-138.

25 Alexander JW, Korelitz J, Alexander NS. Prevention of wound infections: A case for closed suction drainage to remove wound fluids deficient in opsonic proteins. *Am J Surg* 1976;132:59-63.

26 Ahn SS, Machleder HI, Gupta R, et al. . Perigraft seroma: clinical, histological and serologic correlates. *Am J Surg* 1987;154:173-178.

27 Ahn SS, Williams DE, Thye DA, Cheng KQ, Lee DA. The isolation of a fibroblast growth inhibitor associated with perigraft seroma. *J Vasc Surg* 1994;20:202-208.

28 Pricolo VE, Caldwell MD, Mastrofrancesco B, Mills CD. Modulatory activities of wound fluid on fibroblast proliferation and collagen synthesis. *J Surg Res* 1990;48:534-538.

29 Concannon MJ, Barrett BB, Adelstein EH, Thornton WH, Puckett CL. The inhibition of fibroblast proliferation by a novel monokine: an in vitro and in vivo study. *J Burn Care Rehab* 1993;14:141-147.

Chapter 3

A prospective randomized trial of high versus low vacuum drainage after axillary dissection for breast cancer

Jorien Bonnema, Albert N. van Geel, David A. Ligtenstein,
Paul I.M. Schmitz, Theo Wiggers

Am J Surg 1997;173:76-79

Abstract

Background and methods. The influence of negative pressure on fluid production and complication rates after axillary dissection for breast cancer was studied in a prospective randomized trial. Patients were randomized for either a high or a low vacuum drainage system. Drainage volumes and complication rates were recorded.

Results. No statistically significant differences were found between the low vacuum group (n=68) and the high vacuum group (n=73) in volume (728 ml versus 780 ml) and duration (9.5 days versus 10 days) of seroma production, number of wound complications (5 versus 6) or infections (3 versus 2). There was a significant positive relationship between body mass index and seroma production, independent of the drainage system (P=0.002). The drainage volume of the separately drained breast wound after mastectomy and lumpectomy was larger for the high vacuum system (55 ml versus 100 ml; P=0.02). Vacuum loss was more frequent in the high vacuum drain group (11 versus 2, P=0.01), where as leakage around the drain occurred more often in the low vacuum group (18 versus 6, P=0.004).

Conclusion. There are no differences in axillary fluid production or wound complication rates after axillary dissection and subsequent drainage between high and low vacuum drainage systems.

Introduction

Axillary lymph node dissection is typically followed by secretion of a non haemorrhagic fluid from the wound. To remove this fluid, some form of closed suction drainage is usually applied [1-4]. Suction drainage obliterates the axillary cavity as it results from the dissection, thereby causing apposition of wound surfaces. It has been suggested that this might facilitate wound healing and counteract fluid production [3,5], although dispute exists on the optimal suction pressure [6,7].
We studied the influence of negative pressure on fluid production and complication rates after axillary dissection in a prospective randomized trial comparing high and low vacuum drainage systems.

Patients and methods

The low vacuum drain was the Bellovac R (Astra Tech, The Netherlands), a bellow-type drain with a negative pressure of 115 mm Hg (15.3 kPa). The drain gradually looses its vacuum pressure with increasing filling of the bellow. The vacuum can be restored by emptying the bellow into a changeable collecting sac. The maximum effective collecting volume is 220 ml. Backflow in the system is prevented by valves. The high vacuum system was the Medinorm R (Van Straten, The Netherlands), a bottle drain with a negative pressure of 720 mm Hg (95.9 kPa) without valves. Here the vacuum with increasing filling of the container remains largely unchanged [8]. The effective volume is 600 ml. The size of the drain tubes for both types was 14 Charriere (4.6 mm).

Patient selection

From April 1992 to June 1993 all patients that underwent a modified radical mastectomy, a lumpectomy with axillary dissection, or an axillary dissection after a previous diagnostic lumpectomy were included in the study. Excluded were patients undergoing iridium implantation, patients who used corticosteroids or anticoagulants, and those who underwent pre-operative radiotherapy or chemotherapy. With informed consent patients were randomized for high or low vacuum drainage during the operation after the axillary dissection was completed. Randomization was performed by the trial bureau of the hospital according to a predefined randomization table. The ethical committees of both hospitals involved approved the study.

Operative procedures

The modified radical mastectomy was performed according to Madden [9] but with a transverse incision. The axillary dissection was conducted between standard anato-

mic borders: the axillary vein, the latissimus dorsi muscle, the medial border of the pectoralis minor muscle, the serratus anterior muscle, and subscapular muscle. Level I,II and III nodes were resected. The long thoracic nerve and the thoracodorsal nerve were preserved. The intercostobrachial nerves were spared when possible. In case of a lumpectomy, two separate incisions were made. The end of the axillary drain was placed in the top of the axilla. If a drain for the breast wound was required, it was of the same type and size as the axillary drain. Both drains were brought out through separate stab wounds. No attempts were made to close the dead space in the axilla or the breast wound by additional measures. Low-dose heparin was used for prophylaxis of perioperative thrombosis.

Postoperative procedures

Drainage volumes were registered daily. All drains were removed either if the fluid production was less than 30 ml on two consecutive days, or after a maximum of 14 days regardless of the drainage volume. Each patient was seen 1 week after discharge, and weekly thereafter or more frequently as needed. After drain removal, a clinically apparent fluid collection in the axilla was removed by percutaneous aspiration. The total drainage volume and the number of aspirations were recorded. Shoulder exercises were standardized and performed without limitations from the first postoperative day.

Wound complications recorded were infection, necrosis, hematoma and dehiscence. Wound infection was defined according to the Centers for Disease Control and Prevention (CDC) definitions [10]. Necrosis was defined as any visible necrosis along the edge of the wound. A blood collection under the skin, removable by puncture, was considered a hematoma. Drain complications such as obstruction of the drain, loss of vacuum, leakage and drain loss were also recorded. Radiotherapy was not given before the sixth postoperative week. Other parameters recorded were age, axillary lymph node status and body mass index (body weight divided by body length square in $kg.m^{-2}$.

Statistical analysis

Percentages in the two study groups were compared by a chi-square test without correction for continuity. For continuous variables the median and the 95 interpercentile range were calculated. The mean values of these variables in the two study groups were compared by the Mann-Whitney U Test. The null hypothesis was rejected if $P < 0.05$. Analyses were performed on a personal computer by STATA, version 3.10 (Computing Resource Center, Santa Monica, California, USA).

Results

One hundred and forty-one patients participated in the study: 68 patients were randomized to low vacuum and 73 to high vacuum drainage (Table I). In the low vacuum group 35 and in the high vacuum group 37 patients required a separate breast wound drain. There were no statistically significant differences between the two groups regarding patient characteristics. The quantitative results of drainage and complications are summarized in Tables II and III (next page). There were no differences between low and high vacuum drainage groups for total drainage volume of the axillary drain, duration of drainage, number of aspirations performed, or number of wound complications. The nonaxillary wound drain production was higher for the high vacuum drain (P = 0.02). Drain related complications differed only for vacuum loss and leakage. The high vacuum drain irreversibly loses its vacuum after the tubing system is accidentally disconnected. In the low vacuum drain group there were more leakages along the skin insertion site of the drain.
There was no statistical difference in total drainage volume between patients that required needle aspirations and those who did not (1046 ml versus 782 ml; P = 0.16), neither was there a significant relationship between the total drainage volume and the number of aspirations (P = 0.17). Also the drainage volume of the first 5 post-operative days was not indicative for seroma formed after the drain was removed. There was no influence of the type of surgical procedure performed on the drainage volume, neither for the axillary nor for the wound drain. There was a significant linear relationship with a low correlation between body mass index and seroma production, independent of the drainage system (Pearson's correlation coefficient 0.28; P = 0.002). The number of nodes removed from the axilla and the

Table I Type of surgical intervention and patient characteristics

	high vacuum drain group (n = 68)	low vacuum drain group (n = 73)
mastectomy and axillary dissection*	37	42
lumpectomy and axillary dissection*	26	24
axillary dissection*	5	7
age (years)**	59 (37 - 86)	55 (31 - 83)
body mass index (kg/m²)**	24.3 (17.8 - 32.1)	25.7 (17.8 - 35.8)
no. of patients with pos. nodes*	28 (43)	29 (40)
no. of nodes removed**	14 (3 - 25)	13 (6 - 29)
percentage of positive nodes**	0 (0 - 100)	0 (0 - 90)

** Values are numbers (percentage).** Values are median (95 inter-percentile range). There were no statistically significant differences between the groups.*

Table II Values of drainage and aspirations

	low vacuum drain group (n = 68)	high vacuum drain group (n = 73)	P'''
total volume axillary drain''	728 ml (144 - 3065)	780 ml (78 - 2192)	n.s.
total volume breast wound drain''#	55 ml (0 - 730)	100 ml (10-1090)	0.02
duration of drainage axillary drain''	9.5 days (3 - 22)	10 days (3 - 17)	n.s.
duration of drainage breast wound drain''#	3 days (1 - 9)	3 days (1 - 9)	n.s.
no. of patients with aspirations'	18 (27)	11 (15)	n.s.
no. of aspirations per patient(if done)''	1 (1 - 4)	1 (1 - 4)	n.s.
aspiration day (post-operative day)''	19 (7 - 35)	19 (8 - 29)	n.s.
total volume aspirated''	212 ml (60-600)	140 ml (17-635)	n.s.

' Values are numbers (percentage). '' Values are median (95 inter-percentile range).
 # Number of breast wound drains in low vacuum group 35 and high vacuum group 37.
''' Mann-Whitney U Test; n.s., not significant.

Table III Numbers of complications

	low vacuum drain group (n = 68) '	high vacuum drain group (n = 73)	P'
Wound complications			
hematoma	2 (3)	1 (1)	n.s.
necrosis	0 (0)	3 (4)	n.s.
infection	3 (4)	2 (3)	n.s.
dehiscence	0 (0)	0 (0)	---
Drain complications			
obstruction	6 (9)	5 (7)	n.s.
vacuum loss	2 (3)	11(15)	0.01
leakage	18(27)	6 (8)	0.004
drain loss	4 (6)	3 (4)	n.s

Values in parentheses are percentages. ' Chi-square test; n.s., not significant.

number of positive nodes in the specimen had no relation with the total drainage volume.

Discussion

Several techniques have been advocated to reduce seroma formation by minimizing axillary dead space. The use of closed suction drainage can reduce seroma for-

mation, as compared to no drainage [2], drainage by punctures only [3], or corrugated drainage [1]. Seroma production was successfully reduced by suturing skin flaps to the underlying muscles following mastectomy with axillary node clearance [4]. Sclerotherapy with tetracycline, effective in eliminating persistent seroma productions after mastectomy [11], has the disadvantage of causing severe pain reactions after administration [12]. Fibrin adhesive has been tested after axillary and inguinal node dissections with inconsistent effects on seroma formation [13,14]. Immobilization of the affected arm in the post-operative period did not affect seroma production in two prospective studies [15,16]. Recently a significant reduction in postoperative drainage volume after mastectomy by perioperative and postoperative administration of tranexamic acid was reported [17], although the mechanism of action of the drug is not clear [18].

We compared a high vacuum drainage system with a pressure of 720 mm Hg (95.9 kPa) with a low vacuum system with a pressure of 115 mm Hg (15.3 kPa) for draining fluid after an axillary dissection to test the null hypothesis that there is no difference in fluid production between the two systems. We found no indication that suction pressure has any influence on axillary fluid production. For the breast wound, high vacuum drainage increased fluid production but the level of vacuum did not influence the duration of drainage. The higher incidence of seromas after modified radical mastectomy compared with lumpectomy and axillary node dissection, reported in two studies [19,20], was not found in our study. Seroma production was found to be positively correlated with body mass index, confirming the observations in previous studies [21,22].

In the high vacuum drain group a higher incidence of vacuum loss was seen as a result of disconnecting the tubing system. Leakage around the drain was more frequently seen in the low vacuum drain group although there were no differences in the insertion technique used. In animal experiments draining by high vacuum drain systems suffered from early obstruction of the drains by muscle fibers [23]. In our study we did not observe any difference in obstruction between the two drainage systems. Tissue damage by high vacuum pressure was demonstrated by histological methods in two animal studies [23,24]. Skin flap necrosis is a complication with an incidence of 3.7 to 7.1 % in modified radical mastectomy [20,22]. We did not see differences in the incidence of necrosis between the low and high vacuum drain group. Infection was seen in 2.9% of the population and the frequency was equally distributed among the groups. The infection rate is similar to the rate of 3.6 % found in another study [20]. It is not proven that closed suction drainage has any value in preventing infection in clean wounds compared with open drainage [25], but compared to no drainage the incidence of infections is reduced by closed suction drainage [3].

We conclude that there are no differences in axillary fluid production or wound

complication rates after axillary dissection and subsequent drainage between high and low vacuum drainage systems. The high vacuum drain results in a statistically lower incidence of leakage around the drain, which is more convenient for the patient. Preference for using low or high vacuum drainage systems may be also determined by factors such as cost, nursing manageability and patient comfort.

References

1 Bourke JF, Balfour TW, Hardcastle JD. A comparison between suction and corrugated drainage after simple mastectomy: A report of a controlled trial. *Br J Surg* 1976;63:67-69.

2 Cameron AEP, Ebbs SR, Wylie F, Baum M. Suction drainage of the axilla: a prospective randomized trial. *Br J Surg* 1988;75:1211.

3 Somers RG, Jablon LK, Kaplan MJ, et al. The use of closed suction drainage after lumpectomy and axillary node dissection for breast cancer. *Ann Surg* 1992;215:146-149.

4 Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy. A prospective randomized clinical trial. *Eur J Surg Oncol* 1993;19:143-146.

5 Aitken DR, Hunsaker R, James AG. Prevention of seromas following mastectomy and axillary dissection. *Surg Gynecol Obstet* 1984;158:327-330.

6 Brottin BJ, Gilmore OJA, Lumley JSP, Castleden WM. A comparison between disposable and non-disposable suction drainage units: a report of a controlled trial. *Br J Surg* 1979;66:279-280.

7 Whitfield PC, Rainsbury RM. Suction versus siphon drainage after axillary surgery for breast cancer: a prospective randomized trial. *Br J Surg* 1994;81:546-547.

8 Rudberg C, Tera H. How does the increasing filling of the vacuum source diminish the suction in modern portable drainage systems? *Acta Chir Scand* 1988;154:1-8.

9 Madden JL. Modified radical mastectomy. *Surg Gynecol Obstet* 1965;121:1221-1230.

10 Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections,1988. *Am J Inf Contr* 1988;16:128-140.

11 Nichter LS, Morgan RF, Dufresne CR. Rapid management of persistent seromas by sclerotherapy. *Ann Plast Surg* 1983;11:233-236.

12 McCarthy PM, Kirk Martin J,Jr., Wells DC, et al. An aborted, prospective, randomized trial of sclerotherapy for prolonged drainage after mastectomy. *Surg Gynecol Obstet* 1986;162:418-420.

13 Uden P, Aspegren K, Balldin G, et al. Fibrin adhesive in radical mastectomy. *Eur J Surg* 1993;159:263-265.

14 Waclawiczek HW, Pimpl W. Lymphfisteln nach Lymphknotendissektionen - Verhütung und Behandlung mit Hilfe der Fibrinverklebung. *Chirurg* 1986;57:330-331.

15 Petrek JA, Peters MM, Nori S, et al. Axillary lymphadenectomy.A prospective randomized trial of 13 factors influencing drainage,including early or delayed arm mobilization. *Arch*

Surg 1990;125:378-382.

16 Jansen RFM, van Geel AN, de Groot HGW, et al. Immediate versus delayed shoulder exercises after axillary lymph node dissection. *Am J Surg* 1990;160:481-484.

17 Oertli D, Laffer U, Haberthuer F, et al. Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer. *Br J Surg* 1994;81:856-859.

18 Bonnema J, van Geel AN, Wiggers T, Ligtenstein DA. Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer (Letter). *Br J Surg* 1994;81:1693.

19 Vinton AL, Traverso LW, Jolly PC. Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection. *Am J Surg* 1991;161:584-588.

20 Tejler G, Aspegren K. Complications and hospital stay after surgery for breast cancer: a prospective study of 385 patients. *Br J Surg* 1985;72:542-544.

21 Wyman A, Rogers K. Radical breast surgery with a contact Nd:YAG laser scalpel. *Eur J Surg Oncol* 1992;18:322-326.

22. Say CC, Donegan W. A biostatistical evaluation of complications from mastectomy. *Surg Gynecol Obstet* 1974;138:370-376.

23 Graf J, Stofft E, Tittel K. Muskelveränderungen durch Saugdrainagen. *Unfallchirurgie* 1983;9:223-228.

24 Cherry G, McClatchey K. Wound drainage: effects of negative pressure on healing. *Infections in Surgery* 1983;1:243-247.

25 Dougerthy SH, Simmons RL. The biology and practice of surgical drains: Part II. *Curr Probl Surg* 1990;29:637-727.

Chapter 4

Ultrasound-guided aspiration biopsy for detection of nonpalpable axillary node metastases in breast cancer patients: new diagnostic method

Jorien Bonnema, Albert N. van Geel, Bart van Ooijen, Sybrand P M Mali,
Swanny L. Tjiam, Sonja C. Henzen-Logmans,
Paul I. M. Schmitz, Theo Wiggers

World J Surg 1997;21:270-274

Abstract

This study was designed to evaluate the accuracy of ultrasonography alone and in combination with fine needle aspiration biopsy (FNAB) for detection of axillary metastases of nonpalpable lymph nodes in breast cancer patients. Ultrasonography was carried out in 150 axillas of 148 patients (mean age 57 years, range 30-80 years); and in 93 axillas lymph nodes were detected. Nodes were described according to dimension and echo patterns and compared with histopathologic results. FNAB was carried out in 81 axillas (122 nodes). The sensitivity of ultrasonography was highest (87 %) when size (length > 5 mm) was used as criterion for malignancy, but specificity was rather low (56%). When nodes with a malignant pattern (echopoor or inhomogeneous) were visualized, specificity was 95 %. Ultrasound guided FNAB had a sensitivity of 80 % and a specificity of 100 % and detected metastases in 63 % of node positive patients. It is concluded that FNAB is an easy, reliable and inexpensive method for identifying patients with positive nodes. In the case of negative findings other diagnostic procedures to exclude lymph node metastases, such as sentinel node mapping, could be performed.

Introduction

In breast cancer patients the number and level of axillary lymph node metastases are important prognostic indicators and determinants for selecting patients who should receive adjuvant treatment [1]. Complete axillary dissection with histologic examination of nodes provides the most accurate information about nodal status [2-4]. However, node-negative patients who are not selected for adjuvant treatment probably do not benefit by this procedure, which causes morbidity [5] and prolongs hospital stay [6]. Efforts have been made to avoid complete axillary dissection by preoperative evaluation with imaging techniques [7] or intraoperative assessment by axillary node sampling [8].

Ultrasonography is used as an imaging method to detect axillary nodes of breast cancer patients in several studies [9-13]. Patients with and without clinically positive nodes were included in these studies, and ultrasonographic enlargement of a node was used as only criterion for malignancy. The results may differ for patients with clinically negative nodes, and nodal size alone is reported to be of limited value for ultrasonographic differentiation between benign and malignant disease [14]. Better results can be obtained with high resolution ultrasonography using ultrasonomorphologic features as criterion for malignancy [14]. Combining ultrasonography with fine-needle aspiration biopsy (FNAB) may further improve the presurgical staging of the axilla in breast cancer patients [15].

The purpose of this prospective study was to assess the accuracy of ultrasonography (using ultrasonomorphologic criteria for malignancy) and of ultrasound-guided FNAB for detection of axillary lymph node metastases in breast cancer patients without palpable nodes at clinical examination.

Methods

During a 15-month period all patients with proved breast cancer without palpable axillary nodes and amenable to axillary dissection were included in the study. The absence of clinical enlarged nodes was confirmed by two experienced clinicians. Excluded were patients who underwent preoperative radiotherapy or chemotherapy. The day before surgery ultrasound examination of the ipsilateral axilla was carried out by two experienced radiologists using a 7.5M MHz linear array transducer (Acuson 128). The area between the axillary vein, latissimus dorsi muscle, and medial border of the pectoralis minor muscle was carefully inspected. Any definable mass within the axilla was considered to be a lymph node.

The echopatterns of axillas without visible nodes and axillas with nodes with an echo-rich or homogeneous aspect, so called benign characteristics [14,16], were considered as not suspect for malignancy. Echo-poor and inhomogeneous nodes

were considered suspect for metastatic deposit [14,16]. The length of the node, defined as the largest diameter on ultrasonography (US) in millimeters, was scored. An ultrasound guided FNAB was obtained with a 21-gauge needle from at least one visible node, regardless of the echo pattern, with a maximum of four biopsies per axilla. The aspirated node was marked by leaving 0.5 cm of a guide wire to make comparison with histological findings possible. The aspiration biopsies were analyzed for cytologic features and classified as benign or malignant. After FNAB all patients underwent complete axillary dissection and resection of the primary tumor either by segmental or total mastectomy. The standard anatomic borders of the axillary dissection were the axillary vein, latissimus dorsi muscle, medial border of the pectoralis minor muscle, serratus anterior muscle, and subscapular muscle. Level I, II and III nodes were resected. The specimen was examined by radiology and the marked nodes were indicated with needles for easy localization by the pathologist. All axillary specimens were processed for histologic examination using hematoxylin and eosin (H&E) and examined by the pathologist.
The results were analyzed with descriptive statistical methods. Sensitivity, specificity, overall accuracy, and positive and negative predictive values were calculated by comparing the results of ultrasonography and FNAB with histologic findings, according to the following matrix:

	Histology	
	Positive	Negative
Examination method		
Positive	A	B
Negative	C	D

Sensitivity: A/A+C, specificity: D/D+B, overall accuracy: A+D/A+B+C+D, positive predictive value: A/A+B, negative predictive value: D/D+C.

Results

Ultrasonography was performed in 150 axillas of 148 patients. Two patients with synchronous bilateral breast cancer underwent bilateral examination and axillary dissection. The age range was 30-80 years (mean 57 years). The histology of the primary tumor was invasive ductal carcinoma in 135 patients (91 %), invasive lobular carcinoma in 6 patients (4%) and other histologic types of breast cancer in 7 patients. There were 78 T1 tumors (51%), 66 T2 tumors (43%) and 6 T3 tumors

(6%). The mean number of nodes in the axillary specimen was 14 (range 4-32). Lymph node metastases were present in 62 axillas (41 %), 40 of these having fewer than four positive nodes (26 axillas one node, 7 two nodes, 7 three nodes), 22 axillas having four or more positive nodes. The ultrasound examination detected axillary nodes in 93 axillas (62 %); no nodes could be detected in 57 axillas (38 %). A total of 143 nodes could be visualized, of which 122 were aspirated. In 47 axillas one, in 29 axillas two, in 3 axillas three and in 2 axillas four successful biopsies could be performed. In 12 axillas with 21 visualized nodes FNAB was not possible because the position of the node was too difficult, the node was too small, or no adequate material could be obtained. The mean length of the nodes was 14 mm (range 6-25 mm). The results of ultrasonography, cytology, and histology of the lymph nodes are summarized in Table 1. The aspects of the lymph nodes detected by ultrasonography were categorized as not suspect for malignancy, suspect for malignancy, or no classification possible, as described above, and compared with the gold standard: the results of the histologic examination. The sensitivity was 36 %, specificity 95 %, overall accuracy 67 %, positive predictive value 86 %, and negative predictive value 63 % (Table 2).

In previous studies all axillary nodes visualized with ultrasonography [10-12] or nodes with a diameter of at least 5 mm [9] were considered as involved with metastasis. The diameter of the smallest node detected in our study was 6 mm. When any visible node was defined as malignant, sensitivity was 87 %, specificity 56 %, overall

Table 1 Ultrasonography and cytologic and histologic results

Echo pattern	No cytology	Benign cytology	Malignant cytology	Total number	Malignant histology
Benign					
target	9	39	10	58	25
homogenous	2	10	18	30	21
Malignant					
hypoechogenic	7	6	16	29	25
inhomogeneous	0	3	4	7	6
No classification	3	7	9	19	14
Total	21	65	57	143	91

(n=number of nodes)

Table 2
Ultrasonography and FNAB of axillary nodes

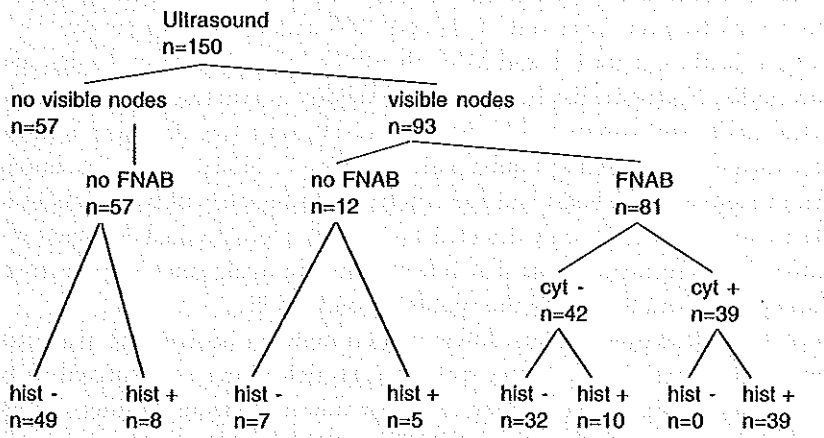
Parameter (%)	Ultrasonography by criterion for malignancy: Echo pattern of node	Ultrasonography by criterion for malignancy: Node size > 5 mm	FNAB
Sensitivity	36 %	87 %	80 %
Specificity	95 %	56 %	100 %
Overall accuracy	67 %	68 %	88 %
Positive predictive value	86 %	58 %	100 %
Negative predictive value	63 %	86 %	76 %

accuracy 68 %, and positive and negative predictive values 58 % and 86 %, respectively (Table 2).
The results of FNAB versus histologic outcome are summarized in Figure 1. Positive cytologic analysis (one or more nodes positive) was found in 39 axillas. All the positive cytologies were confirmed to be metastatic by light microscopic examination. Of the cytologic negative axillas, 10 of 42 (24%) were positive for malignancy with histologic examination. The number of positive nodes per axilla clearly influenced the chance of detection: only 11 of 26 axillas with one positive node were detected by FNAB, in contrast to 19 of 22 axillas with 4 or more positive nodes. It was possible to detect 39 (63%) of the 62 positive axillas in 26 % of the total patient population. The sensitivity of FNAB was 80 %, the specificity 100 %, the overall accuracy 88 %, and the positive and negative predictive value 100 % and 76 %, respectively (Table 2).

Discussion

Axillary dissection has a central place in breast cancer treatment, although debate exists about the extent of dissection necessary for adequate staging [17]. Complete axillary dissection can be considered overtreatment for those patients whose nodes do not contain metastases with histologic examination [18]. Most of these patients will have T1 and T2 tumors, as it is well established that the incidence of lymph node involvement increases with increasing diameter of the tumor [19]. This correlation is already seen for small (T1) tumors [18]. In our study T1 and T2 tumors were found in 94 % of the patients, and lymph node metastases were present in 41 %. As the number of patients presenting with early stage breast cancer without axillary metastases will increase as a result of breast screening activities, the need to look for alternatives

Figure 1 FNAB and cytologic and histologic results



LEGEND to figure 1
n = number of axillas
cyt - = cytologic outcome benign
cyt + = cytologic outcome malignant
hist - = histologic outcome benign
hist + = histologic outcome malignant

for axillary dissection becomes more compelling [20]. The use of neoadjuvant chemotherapy necessitates alternative techniques for assessment of metastatic status of axillary nodes [21]: first to select patients with positive nodes and second because of lack of histopathologic control of treatment results during chemotherapy.

Clinical examination for assessment of axillary metastases is notoriously unreliable, with an overall error rate of 39 % and false-negative rate up to 45 % [22]. No imaging technique until now has been successfully enough to replace the histologic examination. One should realize that it will be almost impossible to reach a sensitivity higher than 90 % with any imaging technique because occult micrometastases are found in at least 9 % of patients [23]. The results of radionuclide lymphography [24] or immunoscintigraphy [25] do not differ from those of the clinical examination. CT scan and MRI are limited to diagnosing enlargement of lymph nodes without being able to differentiate between those infiltrated with cancer from hyperplastic glands [26,27]. Other drawbacks of CT and MRI are the high cost and the difficulty of obtaining material for pathologic analysis. New techniques as positron emission tomography are even costlier than CT and MRI, and experiences with this method are limited [28]. Ultrasonography, a frequently used technique for lymph node imaging, is characterized by low cost and the possibility of obtaining biopsy specimens. Several studies have shown that ultrasonography has value for the detection of enlarged lymph

nodes in breast cancer [9-13], head and neck cancer [29-31], and gastrointestinal cancer [32]. For the detection of axillary node metastases in breast cancer the sensitivity and the specificity varied between 56% and 72 % and 70% and 90 %, respectively [9-13]. A problem is, as in the case of CT and MRI, the differentiation between benign and malignant nodes. Nodal size has been tested for validity as criterion for malignancy. For cervical nodes the minimal axial diameter (2-30 mm) was the most accurate parameter to use for predicting tumor-positive nodes [31]. Nodal size varies among the different regions in the body, and size criteria for malignancy of lymph nodes in the axilla are not known. We only detected nodes with a longitudinal diameter of 6 mm or more. If enlargement was used as only criterion for malignancy, the sensitivity of ultrasonography was 87 % and the specificity only 56 %.

High-resolution ultrasound enables differentiation between benign and malignant echo pattern characteristics [14]. Nodes with an echo-rich center are expected to be benign, and nodes with an echo-poor center or inhomogeneous architecture are more suspect for tumor infiltration [14,16,33]. We used this technique in our study. Sensitivity was low (36%) and specificity high (95%), which means that ultrasonography of axillary nodes is more accurate for the diagnosis of metastatic than for nonmetastatic lymph nodes. However, the accuracy of ultrasonography is too low to rely on this technique for selection of node-negative or node-positive patients. Therefore, we combined ultrasonography with FNAB of visualized nodes. The latter is a reliable method for diagnosing primary carcinoma of the breast [34]. In our study, FNAB could not improve the sensitivity of ultrasound alone, because of a false-negative rate of 12 %. Analysis of the false negative findings showed that 7 of the 10 false negative axillas contained only one metastatic node, which makes it more difficult to aspirate the right node. Ultrasound-guided FNAB therefore cannot be used for selection of patients with negative nodes in whom an axillary dissection can be omitted for this reason. The specificity of the technique, however, was 100 %, as there were no cases of positive cytology that proved to be negative on histology. In our study population of 148 patients with 62 node positive axillas, 39 of these patients (63 %) could be accurately detected by ultrasound-guided FNAB. The high specificity makes the technique valuable for staging of patients entering neoadjuvant chemotherapy protocols and other patients who are not selected for surgery as primary treatment.

Experiments with sentinel node resection have successfully identified node- positive breast cancer patients [35,36]. Although the technique is more conservative than axillary dissection, surgical resection of the sentinel node with some form of anaesthesia is still needed. Ultrasound-guided FNAB is minimally invasive, needs no anaesthesia, and is easier to perform than the sentinel node biopsy. It can detect 63 % of positive axillas in patients with small breast tumors. In our opinion, the sequence of diagnostic procedures in the future to detect axillary node metastases could be to

perform first FNAB and, in case of negative findings, a sentinel node biopsy. The technical ease of the procedures and the major reduction in morbidity and costs that can be expected justify larger clinical trials to verify the feasibility and accuracy of these new diagnostic methods.

In conclusion, ultrasound-guided FNAB has a high sensitivity and specificity for detecting axillary lymph node metastases in patients with T1 and T2 tumors. In this study 63 % of node-positive patients could be identified as having metastases. In these patients other, more invasive diagnostic methods can be avoided.

References

1 Fisher B, Bauer M, Wickerham D, Redmond CK, Fisher ER. Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. *Cancer* 1983;52:1551-1557.

2 Fentiman IS, Mansel RE. The axilla:not a no-go zone. *Lancet* 1991;337:221-223.

3 Axelsson CK, Moudridsen HT, Zedeler K. Axillary dissection of level I and II lymph nodes is important in breast cancer classification. *Eur J Cancer* 1992;28A:1415-1418.

4 Senofsky GM, Moffat FL, Davis K, Masri MM, Clark K, Robinson DS, et al. Total axillary lymphadenectomy in the management of breast cancer. *Arch Surg* 1991;126:1336-1342.

5 Recht A, Houlihan MJ. Axillary lymph nodes and breast cancer. *Cancer* 1995;76:1491-1512.

6 Ivens D, Hoe AL, Podd TJ, Hamilton CR, Taylor I, Royle GT. Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992;66:136-138.

7 Maisey MN. Imaging techniques in breast cancer. What is new? What is useful? - A review. *Eur J Cancer Clin Oncol* 1988;24:61-68.

8 Hadiminas DJ, Burke M. Intraoperative assessment of nodal status in the selection of patients with breast cancer for axillary clearance. *Br J Surg* 1994;81:1615-1616.

9 Bruneton JN, Caramella E, Hery M, Aubanel D, Manzino JJ, Picard JL. Axillary lymph node metastases in breast cancer:preoperative detection with ultrasound. *Radiology* 1986;158:325-326.

10 Mustonen P, Farin P, Kosunen O. Ultrasonographic detection of metastatic axillary lymph nodes in breast cancer. *Ann Chir Gynaecol* 1990;79:15-18.

11 Tate JJT, Lewis V, Archer T, Guyer PG, Royle GT, Taylor I. Ultrasound detection of axillary lymph node metastases in breast cancer. *Eur J Surg Oncol* 1989;15:139-141.

12 de Freitas RJr, Costa MV, Schneider SV, Nicolau MA, Marussi E. Accuracy of ultrasound and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. *Eur J Surg Oncol* 1991;17:240-244.

13 Pamilo M, Soiva M, Lavast EM. Real-time ultrasound, axillary mammography, and clinical examination in the detection of axillary lymph node metastases in breast cancer patients. *J Ultrasound Med* 1989;8:115-120.

14 Vassallo P, Wernecke K, Roos N, Peters PE. Differentiation between benign from malignant superficial lymphadenopathy:the role of high resolution US. *Radiology* 1992;183:215-220.

15 Ceci G, Pescarenico MG, Di Sarra S, Manotti L, Cocconi G. Ultrasound (US) examination of axillary nodes with fine needle aspiration biopsy (FNAB). A new non invasive diagnostic method improving the presurgical staging of breast carcinoma. *Proc Am Soc Clin Oncol* 1995;14:109. (Abstract)

16 Sakai F, Kiyono K, Sone S, et al. . Ultrasonic evaluation of cervical metastatic lymphadenopathy. *J Ultrasound Med* 1988;7:305-310.

17 Greenall MJ, Davidson T. How should the axilla be treated in breast cancer? *Eur J Surg Oncol* 1995;21:2-7.

18 Silverstein MJ, Glerson ED, Waisman JR, Senotsky GM, Colburn WJ, Gamagani P. Axillary lymph node dissection for T1a breast carcinoma: is it indicated? *Cancer* 1994;73:664-667.

19 Hartveit F. Axillary metastasis in breast cancer: when, how, and why? *Semin Surg Oncol* 1989;5:126-136.

20 Walls J, Boggis CRM, Wilson M, Asbury DL, Roberts JV, Bundred NJ, et al. Treatment of the axilla in patients with screen-detected breast cancer. *Br J Surg* 1993;80:436-438.

21 Belembaogo E, Feillel V, Chollet P, Cure H, Verrelle P, Kwiatkowski F, et al. Neoadjuvant chemotherapy in 126 operable breast cancers. *Eur J Cancer* 1992;28A:896-900.

22 Sacre RA. Clinical evaluation of axillary lymph nodes compared to surgical and pathological findings. *Eur J of Surg Oncol* 1986;12:169-173.

23 International (Ludwig) Breast Cancer Study Group . Prognostic importance of occult axillary lymph node micrometastases from breast cancers. *Lancet* 1990;335:1565-1568.

24. McClean RG, Ege GN. Prognostic value of axillary lymphoscintigraphy in breast carcinoma patients. *J Nucl Med* 1986;27:1116-1124.

25 Tjandra JJ, Sacks NPM, Thompson CH, Leyden MJ, Stacker SA, Lichtenstein M, et al. The detection of axillary lymph node metastases from breast cancer by radiolabelled monoclonal antibodies: a prospective study. *Br J Cancer* 1989;59:296-302.

26 Meyer JE, Munzenrider JE. Computer tomographic demonstration of lymph node metastases in patients with recurrent breast cancer. *Radiology* 1991;139:661-663.

27 Allan SM, McVicar D, Sacks NPM. Prospects for axillary staging in breast cancer by magnetic resonance imaging. *Br J Radiol* 1993;66 (suppl):15-16. (Abstract)

28 Adler LP, Crowe JP, Al-Kaisi NK, Sunshine JL. Evaluation of breast masses and axillary lymph nodes with [F-18] 2-deoxy-2-fluoro-D-glucose PET. *Radiology* 1993;187:743-750.

29 Sutton RT, Reading CC, Charboneau JW, et al. . US-guided biopsy of neck masses in post-operative management of patients with thyroid cancer. *Radiology* 1988;168:769-772.

30 Bruneton JN, Roux P, Caramello E, Demard F, Vallicioni J, Chauvel P. Ear,nose and throat cancer:ultrasound diagnosis of metastatis to cervical lymph nodes. *Radiology* 1984;152:771-773.

31 van den Brekel MWM, Castelijns JA, Snow B. Detection of lymph node metastases in the neck: radiologic criteria. *Radiology* 1994;192:617-618.

32 Lok Tio T, Coene PPLO, Schouwink MH, Tijtgat GN. Esophagogastric carcinoma:preoperative TNM classification with endosonography. *Radiology* 1989;173:411-417.

33 Kruyt RH, van Putten WLJ,, Levendag PC, de Boer MF, Oudkerk M. Biopsy of nonpalpable cervical lymph nodes: selection criteria for ultrasound guided biopsy in patients with head and neck squamous cell carcinoma. *Ultrasound Med Biol* 1996;22:413-419.

34 Patell JJ, Gartell PC, Smallwood JA, et al. . Fine needle aspiration cytology of breast masses: an evaluation of its accuracy and reasons for diagnostic failure. *Ann R Coll Surg Engl* 1987;69:156-169.

35 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;2:335-340.

36 Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg* 1994;220:391-398.

Chapter 5

Medical and psychosocial effects of early discharge after surgery for breast cancer: randomised trial

Jorien Bonnema, Anneke M. E. A. van Wersch, Albert N. van Geel, Jean F. A. Pruyn, Paul I. M. Schmitz, Marinus A. Paul, Theo Wiggers

BMJ 1998;316:1267-1271

Abstract

Objective. To assess the medical and psychosocial effects of early hospital discharge after surgery for breast cancer on complication rate, patient satisfaction, and psychosocial outcomes.
Design. Randomised trial comparing discharge from hospital 4 days after surgery (with drain in situ) with discharge after drain removal (mean 9 days in hospital). Psychosocial measurements performed before surgery and 1 and 4 months after.
Setting. A general hospital and cancer clinic in Rotterdam with a socioeconomically diverse population.
Subjects. 125 women with operable breast cancer.
Main outcome measures. Incidence of complications after surgery for breast cancer, patient satisfaction with treatment, and psychosocial effects of short stay or long stay in hospital.
Results. Patient satisfaction with the short stay in hospital was high; only 4% (2/56 at 1 month after surgery and 2/52 at 4 months after surgery) of patients indicated that they would have preferred a longer stay. There were no significant differences in duration of drainage from the axilla between the short stay and long stay groups (median 8 *v* 9 days respectively, P=0.45) or the incidence of wound complications (10 patients *v* 9 patients). The median number of seroma aspirations per patient was higher for the long stay group (1 *v* 3.5, P=0.04). Leakage along the drain occurred more frequently in short stay patients (21 *v* 10 patients, P=0.04). The two groups did not differ in scores for psychosocial problems (uncertainty, anxiety, loneliness, disturbed sleep, loss of control, threat to self esteem), physical or psychological complaints, or in the coping strategies used. Before surgery, short stay patients scored higher on scales of depression (P=0.03) and after surgery they were more likely to discuss their disease with their families (at 1 month P=0.004, at 4 months P=0.04).
Conclusions. Early discharge from hospital after surgery for breast cancer is safe and is well received by patients. Early discharge seems to enhance the opportunity for social support within the family.

Introduction

The length of time patients spend in hospital after surgical procedures has been decreasing.[1,2] Patients having surgery for breast cancer are considered especially suitable for shorter stays in hospital because recovery after surgery is usually rapid. These patients usually remain in hospital for 9 to 12 days, until the serous fluid produced by the axilla is minimal and the closed suction drain is removed.[3] Shorter hospital stays are possible if patients are discharged with their drains in situ[4] or if drains are removed early.[5] Several studies have claimed that these procedures are safe.[4,5,6,7,8] However, these studies have been retrospective,[6] have given little information about the selection of controls,[4, 5] or have used self selected patients.[8] These factors make the results difficult to interpret.

Patient satisfaction with early discharge is reported to be high.[4,7,8,9] Recovery in the patient's own environment may result in better psychosocial adjustment as a result of enhanced patient comfort, control, independence, and better interaction with family members.[10] In the only study of the psychological effects of early discharge, no adverse effects were found, but patients in this study decided for themselves that they would leave hospital early.[8]

We conducted a randomised trial to compare short and long postoperative stays in hospital after surgery for breast cancer to determine the effect of early discharge on complication rate, patient satisfaction, and psychosocial outcome. We hypothesised that there would be no differences between the two interventions.

Subjects and methods

Patients

Patients were eligible for inclusion in the study if they had stage I or II breast cancer, had been referred to the Daniel den Hoed Cancer Centre and Zuider hospital, and had been selected for treatment by either modified radical mastectomy or lumpectomy with axillary dissection. Patients were excluded if they had received preoperative radiotherapy or chemotherapy, were at high risk of complications (category III or higher of the American Society of Anesthesiologists classification), or were mentally incompetent; patients who had difficulties with the Dutch language or an inappropriate home situation were also excluded.

Between October 1993 and April 1995, 139 out of 173 (80%) women with operable breast cancer were enrolled in the study: 69 were assigned to short stay treatment and 70 to long stay treatment. Women randomised to short stay treatment were discharged on the morning of the fourth day after surgery with the axillary drain in situ. Women randomised to long stay treatment were discharged after their drain

had been removed.
Of the 34 women who were not entered into the study, 22 declined to participate, 10 had an unsatisfactory home situation, and two were not asked to participate. Fourteen more women were excluded after randomisation: two long stay patients received preoperative chemotherapy, one long stay patient was treated in another hospital, one short stay patient had no malignancy, and 10 patients withdrew from the study. Reasons given for short stay patients withdrawing from the study were: questionnaires too difficult (2), refusing home care (2), dissatisfaction with randomisation outcome (1), and unknown reason (1). Reasons for long stay patients withdrawing from the study were: dissatisfaction with randomisation outcome (1), unwillingness to fill out forms (2), and unknown reason (1). Thus, the final group consisted of 125 patients: 62 short stay and 63 long stay.

Randomisation and study design
Approval from the ethics committees of both hospitals was obtained before the start of the study. Written informed consent was obtained from all patients.
A randomisation list was prepared by the statistician (PIMS) using a program for the generation of random numbers and assignment into two groups with a prespecified size of blocks. The size of the blocks (8 patients) was not known by the investigators, and no stratification was applied. The randomisation list was accessible only to the data managers of the central trial office at the Daniel den Hoed Cancer Centre. The patient was informed of her diagnosis, treatment plan, and the design of the study by her surgeon. The patient's home situation was subsequently assessed by a breast cancer nurse. Surgeons telephoned the trial office to discover each eligible patient's randomisation before admission.
An early discharge protocol was developed to guarantee continuity of care. It included structured patient education provided by the breast cancer nurse and also available in written form, referral to a community health nurse, provision of an emergency telephone number, the scheduling of follow up visits, and an information letter being sent to the general practitioner. The development and implementation of this protocol have been described.[11] For women assigned to short stay treatment, drain removal was performed at home or in the outpatient clinic. For both groups drains were removed when the production of serous fluid was less than 30 ml per day or after 14 days. Nursing care of the wound and drain, and the provision of arm exercises, protheses, and psychosocial guidance were standardised for both groups. Patients were followed up for 4 months. At admission, patients were given a daily diary, to be used for one month, and a weekly diary, to be used for the following 3 months. The length of stay in hospital was recorded in the diaries. Clinical study end points were recorded in the diaries and patients' files by the doctors and nurses. Three questionnaires were used to assess psychosocial variables and record

demographic characteristics. The first was distributed at admission and completed the same day; the second questionnaire was distributed 1 month after surgery, and the third 3 months later, during outpatient visits.

Study end points

Complications

Complications recorded included infection, necrosis, haematoma, and dehiscence. Wound infection was defined according to the standards of the Centers for Disease Control and Prevention.[12] Necrosis was defined as any visible necrosis along the edge of the wound. Blood that had collected under the skin, and that was removed by puncture or opening of the wound, was considered to be a haematoma. Drain complications were also recorded. After the drain was removed, fluid collection in the axilla that was clinically apparent was defined as seroma and removed by percutaneous aspiration.

Patient satisfaction

Patient satisfaction with the length of stay was assessed with questions about preferences for a shorter or longer stay. Patients were also asked if they would recommend short stay treatment to other patients. Satisfaction with the care provided by the community health nurse was also assessed.

Psychosocial variables

The psychosocial functioning of patients was evaluated using validated scales based on a theoretical model of coping with cancer developed by van den Borne and Pruyn.[13,14] Some specific items concerning breast cancer were added. Scale structures were made by factor analyses and were similar to those found in previous research.[14] The reliability indices of the scales, assessed for each of the three questionnaires, were evaluated using Cronbach's α.[15] Scores varied between 0.62 and 0.95 with most >0.70. Three out of 57 scores were excluded from analysis because the reliability of the scale was too low (α <0.60). The following variables were measured: uncertainty,[14,16,17,18] state and trait anxiety,[19] object anxiety,[14,16,17,18] loneliness,[14,16,17,18] depression,[14,16,17,18] sleep disturbances,[14,18] feelings of loss of control,[14,16,18] self esteem,[14,16,18] and the cancer locus of control.[20] Locus of control refers to whether patients attribute the cause of their cancer to personal or situational factors. The Rotterdam symptom checklist was used to assess physical and psychosocial complaints.[21]

Coping strategies were assessed with scales constructed previously.[14] Communication about the disease in the home was evaluated with a scale that assesses the openness of discussion within the family, with the patient's partner, and with the patient's children.[17]

Statistical considerations

A primary objective in this trial was to calculate a degree of patient satisfaction in the short stay group that would be about equal to the satisfaction found in long stay patients. We hypothesised that at 1 month after surgery, 5% of long stay patients at most would have preferred a longer stay in hospital. We also supposed that if the percentage of patients satisfied with their stay in hospital was equal the upper 95% confidence limit for the difference in satisfaction should not exceed 10% with a probability of 80% (α=5% one tailed, β=20%) [22]. For these specifications 2∞57=114 patients were necessary. To allow for withdrawals we decided to randomly allocate interventions to 140-150 patients.

For the 125 patients who were studied the power for comparing several outcomes can be calculated (all comparisons with α=0.05). The statistical power was 99% (SD 400 ml within groups) for detecting a difference of 300 ml in total volume of axillary drainage between the groups. A difference between groups in the duration of axillary drainage of 1.5 days was detectable with a power of 80% (SD 3 days within groups). The sample size was inadequate to detect small but clinically significant wound complications (5%, power about 50%).

Data analysis

Psychosocial variables were analysed with the SPSS package. All other analyses were performed using STATA release 5.0 (StatCorp, College Station, TX). The X^2 test was used to compare data between categories without correction for continuity. Fisher's test of exact probability was applied in 2∞2 tables with small expected numbers. Student's *t* test was used to analyse continuous variables in the psychosocial part of the study. The Mann-Whitney U test was used to compare data on drainage between the two groups. Significance was defined as P <0.05.

Results

The two groups were comparable in tumour stage, type of treatment, age, marital status, family income, and educational level (Table 1). Women in the short stay group were in hospital a median of 4 days (mean 4.1 including day of discharge, range 3-5); women in the long stay group had a median length of stay of 9 days (mean 9.0 including day of discharge, range 4-14).

Complications

There were no significant differences between short and long stay patients in drainage volume or duration of drainage, but the mean number of aspirations required per patient was higher in the long stay group (P=0.04) (Table 2). Clinically significant wound infection occurred in eight patients in the short stay group and in seven

Table 1 Characteristics of patients randomised to short or long stay in hospital after surgery for breast cancer.

	Short stay (n=62)*	Long stay (n=63)**
Operative procedure		
Axillary dissection (after previous lumpectomy)	10(16%)	21 (33%)
Breast conserving therapy	20(32%)	14 (22%)
Modified radical mastectomy	21(34%)	21 (33%)
Mastectomy and direct breast reconstruction	11(18%)	7 (11%)
Tumour size		
0-2 cm	33(53%)	39 (62%)
>2-5 cm	19(31%)	17 (27%)
>5 cm	3 (5%)	4 (6%)
unknown	7 (11%)	3 (5%)
Nodal status		
Negative nodes	40 (65%)	41 (65%)
Positive nodes	21 (34%)	21 (33%)
Unknown	1	1
Adjuvant treatment		
No treatment	45 (73%)	40 (64%)
Radiotherapy nodal regions	2 (3%)	2 (3%)
Chemotherapy	3 (5%)	7 (11%)
Hormonal therapy	7 (11%)	3 (5%)
Combination	5 (8%)	11 (18%)
Median age (range)	55 (29-80)	58 (30-75)
Marital status		
Married or cohabiting	51(82%)	47 (75%)
Single	4 (7%)	9 (14%)
Divorced	2 (3%)	2 (3%)
Widowed	5 (8%)	1 (2%)
Unknown	0	4 (6%)
Monthly family income (US $)		
600-1100	13 (21%)	7 (11%)
>1100-2000	20 (32%)	25 (40%)
>2000	20 (32%)	16 (25%)
unknown	9 (15%)	15 (24%)
Education		
Primary school	12 (19%)	10 (16%)
Secondary school	40 (65%)	43 (68%)
University	10 (16%)	5 (8%)
unknown	0	5 (8%)

Values are numbers (%) of patients

** Discharged 4 days after surgery **Discharged after drain removal (median 9 days after surgery)*

Table 2 Complications among patients after surgery for breast cancer according to length of stay in hospital

	Short stay (n=61)*	Long stay (n=59)†	P value
Drainage			
Total median volume (range) (ml):			
From axillary drain	515 (400-3000)	685 (30-2130)	0.19
From drain in breast wound	175 (5-885)	80 (10-1070)	0.51
Duration (days):			
From axillary drain	8 (1-15)	9 (2-14)	0.45
From drain in breast wound	3 (1-12)	2 (1-9)	0.27
Aspiration			
No (%) of patients who had aspiration	10 (16)	8 (14)	0.80
Median No (range) aspirations per patient	1 (1-3)	3.5 (1-7)	0.04
Median total volume (range) (ml) aspirated	105 (5-650)	400 (150-880)	0.01
Wound complications			
No (%) of patients with:			
Haematoma	2 (3)	1 (2)	1.00
Necrosis	0	1 (2)	0.49
Infection	8 (13)	7 (12)	1.00
Dehiscence	1 (2)	1 (2)	1.00
Any type of wound complication	10 (16)	9 (15)	1.00
Drainage complications			
No (%) of patients with:			
Obstruction	20 (33)	15 (25)	0.42
Loss of vacuum	24 (39)	16 (27)	0.18
Leakage	21 (34)	10 (17)	0.04
Loss of drain	5 (8)	2 (3)	0.44
Any type of drain complication	38 (62)	27 (46)	0.10

**Discharged 4 days after surgery.*
†Discharged after drain removal (median 9 days after surgery).

patients in the long stay group; all were treated with antibiotics. One short stay and two long stay patients also required abscess drainage. Two short stay patients were readmitted for removal of a persistent haematoma. Leakage of drainage fluid alongside the drain occurred more often in the short stay group (in 21 *v* 10 patients, P=0.04). One short stay patient died of unsuspected distant metastases during the study.

Patient satisfaction

Table 3 shows patients satisfaction with their length of stay. Most of the women in the short stay group indicated that they would recommend early discharge to other patients, as did 37% of the long stay patients at 1 month and 42% of long stay patients at 4 months, despite the fact that they had no experience of early discharge

Table 3 Patient satisfaction with short stay or long stay in hospital after surgery for breast cancer.

	Short stay (n=62)*	Long stay (n=63)†	Mean difference (%) (95% CI)	P value
Patient would have preferred longer hospital stay:				
1 month after surgery	2/56 (4)	7/52 (14)	-10 (-20 to 0.6)	0.08
4 months after surgery	2/52 (4)	4/44 (9)	-5 (-15 to 5)	0.41
Patient would have preferred shorter hospital stay:				
1 month after surgery	8/55 (15)	16/53 (30)	-16 (-31 to -0.2)	0.05
4 months after surgery	7/51 (14)	15/46 (33)	-19 (-35 to -2)	0.03
Patient would recommend short stay to other patients:				
1 month after surgery	51/55 (93)	17/46 (37)	67 (40 to 71)	<0.001
4 months after surgery	50/52 (96)	19/45 (42)	54 (39 to 69)	<0.001

Values are numbers (percentages) of patients
**Discharged 4 days after surgery.*
†Discharged after drain removal (median 9 days after surgery).

(Table 3).
Evaluation of the nursing care provided at home showed that 42 out of 45 (93%) short stay patients were satisfied that they had received enough attention and that 30 out of 42 (71%) felt as secure at home as in hospital.

Psychosocial variables

There was no difference between the two groups in scores on scales measuring uncertainty, anxiety, loneliness, disturbed sleep, loss of control, or threats to self esteem (Table 4, next page). Before surgery short stay patients scored higher than long stay patients on scales measuring depression (score 10.3 *v* 8.9, P=0.03; minimum score 6, maximum score 24).[14,18] This difference disappeared after surgery. There were no differences in physical or psychological complaints, as measured by the Rotterdam symptom checklist, or in coping strategies used.
A shorter stay in hospital seemed to influence the extent to which the disease could be discussed within the patient's family. Before surgery there were no differences between the two groups, but at 1 and 4 months after surgery short stay patients were more likely to discuss their disease with their family (score 1 month after surgery 23.2 *v* 21.5, P=0.004; score 4 months after surgery 23.5 *v* 21.9, P=0.04; minimum score 7, maximum score 28).[17]

Table 4 Review of scales of psychosocial variables

Scale	Mm[1]	No.item	Minimum score	Maximum score	Mean short stay (SD)	Mean long stay (SD)	Cronbach's alpha
Psychosocial problems							
uncertainty	1	10	10	40	31.3 (8.3)	31.1 (8.5)	0.91
	2				27.3 (9.4)	28.4 (10.1)	0.95
	3				26.8 (9.6)	26.8 (9.1)	0.95
'state' anxiety	1	13	13	52	37.7 (8.7)	38.5 (7.1)	0.74
	2				30.2 (9.3)	31.3 (8.6)	0.84
	3				29.0 (8.2)	29.5 (8.7)	0.81
'trait' anxiety	1	10	10	40	24.6 (7.1)	26.9 (7.0)	0.83
	2				23.0 (6.8)	24.1 (6.8)	0.88
	3				22.8 (6.2)	23.0 (5.7)	0.86
'object' anxiety	1	15	15	60	27.7 (7.9)	29.2 (8.6)	0.89
	2				27.5 (8.2)	27.5 (7.0)	0.89
	3				27.3 (7.8)	27.5 (9.8)	0.92
depression	1	6	6	24	10.3 (2.9)*	8.9 (2.0)	0.71
	2				9.4 (2.9)	8.8 (2.3)	0.80
	3				9.6 (2.8)	9.5 (2.8)	0.71
loneliness	1	5	5	20	14.1 (2.7)	14.8 (2.2)	0.65
	2				10.4 (2.6)	10.5 (2.3)	0.70
	3				11.2 (2.7)	11.1 (2.4)	0.69
sleep disturbances	1	4	4	16	7.9 (2.8)	7.3 (2.9)	0.85
	2				7.9 (3.1)	7.7 (2.7)	0.84
	3				7.8 (1.4)	8.0 (1.8)	0.84
loss of control	1	6	6	24	9.8 (3.4)	10.1 (2.5)	0.71
	2				11.2 (3.6)	10.9 (3.5)	0.79
	3				9.8 (2.8)	9.8 (3.4)	0.74
threat to self-esteem	1	3	3	12	9.1 (1.5)	9.5 (1.6)	0.64
	2				9.3 (1.4)	9.4 (1.3)	0.72
	3				9.1 (1.7)	9.4 (1.3)	0.64
RSCL: psychological complaints	1	12	12	28	21.9 (6.7)	20.4 (6.6)	0.91
	2				18.3 (6.9)	17.1 (4.6)	0.93
	3				17.6 (5.5)	17.5 (5.3)	0.90
RSCL: physical complaints	1	12	12	28	16.0 (3.4)	15.5 (3.9)	0.80
	2				16.5 (.52)	16.8 (3.5)	0.73
	3				15.6 (2.9)	17.0 (4.2)	0.74
Coping strategies							
Denial	1	5	5	20	11.8 (1.8)	11.8 (2.6)	0.68
	2				11.7 (2.5)	11.6 (2.6)	0.76
	3				11.1 (2.9)	11.4 (2.3)	0.74
Cognitive control	1	3	3	12	α too low	α too low	0.50
	2				6.9 (1.6)	6.9 (1.8)	0.63
	3				7.0 (1.7)	7.4 (1.4)	0.66
Search for support in religion	1	2	2	8	3.9 (1.6)	4.2 (1.5)	0.94
	2				4.4 (1.3)	4.1 (1.3)	0.89
	3				4.3 (1.4)	4.0 (1.5)	0.86
Psychosocial release	1	5	5	20	α too low	α too low	0.52
	2				α too low	α too low	0.57
	3				8.0 (2.1)	7.8 (2.2)	0.63
Search for information and support	1	5	5	20	8.6 (2.7)	8.6 (2.8)	0.75
	2				6.9 (2.2)	7.2 (2.5)	0.79
	3				6.9 (2.0)	7.5 (2.6)	0.71
Acceptance	1	6	6	24	12.8 (2.7)	12.7 (2.8)	0.66
	2				12.7 (3.1)	12.7 (2.6)	0.71
	3				12.2 (3.1)	12.3 (2.2)	0.62
Locus of control	1	6	6	24	10.8 (2.9)	10.2 (3.1)	0.82
	2				10.5 (2.9)	9.4 (3.1)	0.87
	3				10.2 (2.9)	10.2 (3.0)	0.87
Openness to discuss illness in the family	1	7	7	28	22.9 (3.5)	22.7 (3.6)	0.74
	2				23.2 (2.9)**	21.5 (2.8)	0.78
	3				23.5 (3.5)***	21.9 (3.5)	0.83

[1]*Mm, measure moment: 1:pre-operative; 2: one month post-operative; 3: four months post-operative*

Discussion

This paper presents the results of a randomised trial evaluating the medical and psychosocial effects of short and long hospital stays after surgery for breast cancer. Comparison between the two groups found no significant differences in wound complications, duration of drainage, patient satisfaction, or psychosocial outcomes. In fact there seemed to be an increase in social support within the family among patients in the short stay group.

The high scores for treatment satisfaction among the short stay patients are in accordance with the results of other studies.[4,7,8,9] Short stay patients were highly satisfied with their community based nursing care. Support from a specialist nurse considerably reduces psychological morbidity.[23] In the home, community nurses take on the role of breast cancer nurses. We considered it important to continue this care after a short stay in hospital.

There were no adverse effects of a shorter stay in hospital on the rate of complications or the incidence of seroma formation. However, the number of patients in this study was too small to detect a difference of 5% in rates of wound complication; a sample size of more than 800 patients would have been necessary to do this. This is not feasible in this type of research. We decided to discharge patients with drains in situ and to remove drains when production of serous fluid was minimal. This practice leads to a low incidence of seroma aspiration[24,25] and fewer outpatient visits. The alternatives are to remove the drain after a fixed number of days regardless of fluid production[5,26,27] or not to place a drain in the axilla.[27,28] Seromas have been reported in as few as 10% of patients after early drain removal,[5] but others have reported seromas in as many as 40%[3] and 73%[27] of patients, albeit without affecting the risk of infection. The length of time the drain was in situ was equal for both groups and is consistent with previous findings from our own clinic.[29]

Before surgery those randomly allocated to a short hospital stay scored higher on scales measuring depression than did those randomly allocated to a long stay. The uncertainty about the experimental treatment after surgery may have contributed to these feelings. A shorter stay in hospital seems to make it easier for a patient to discuss the disease with her family; however, the data should be interpreted carefully as this was the only significant difference in psychosocial variables found between the two groups after surgery. The positive effects of social support in psychosocial adjustment for patients with breast cancer have been discussed.[30,31] The ability to express emotions within the family is associated with less mood disturbance.[32] In our study there was no decrease in mood disturbance in the short stay group; our follow up was 4 months, but the positive effects may have become evident later.

In the United States patients having surgery for breast cancer often stay in hospital only one or two days[4,10] or are treated as outpatients.[6] These changes were initially

financially motivated but have gradually become accepted by surgeons.[10] In most European hospitals, however, these types of early discharge policies are not the normal practice. Our randomised study has proved that shortening the length of time a patient spends in hospital after surgery for breast cancer has no adverse effects. It would be interesting to evaluate the American practice in a European setting, paying special attention to the psychosocial effects of this policy, especially since there have been no data available on these aspects until now.

References

1 McAleese P, Odling-Smee W. The effect of complications on length of stay. *Ann Surg* 1994;220:740-4.

2 Maddern GJ. The changing pattern of surgery. *Br J Surg* 1996;83:145-6.

3 Inwang R, Hamed H, Chaudary MA, Fentiman IS. A controlled trial of short-term versus standard axillary drainage after axillary clearance and iridium implant treatment of early breast cancer. *Ann R Coll Surg Engl* 1991;73:326-8.

4 Clark JA, Kent RB. One-day hospitalization following modified radical mastectomy. *Am Surg* 1992;58:239-42.

5 Yii M, Murphy C, Orr N. Early removal of drains and discharge of breast cancer surgery patients: a controlled prospective clinical trial. *Ann R Coll Surg Engl* 1995;77:377-9.

6 Goodman AA, Mendez AL. Definitive surgery for breast cancer performed on an outpatient basis. *Arch Surg* 1993;128:1149-52.

7 Holcombe C, West N, Mansel RE, Horgan K. The satisfaction and savings of early discharge with drain in situ following axillary lymphadenectomy in the treatment of breast cancer. *Eur J Surg Oncol* 1995;21:604-6.

8 Boman L, Björvell H, Cedermark B, Theve NO, Wilking N. Effects of early discharge from hospital after surgery for primary breast cancer. *Eur J Surg* 1993;159:67-73.

9 Pedersen SH, Douville LM, Eberlein TJ. Accelerated surgical stay programs. A mechanism to reduce health costs. *Ann Surg* 1994;219:374-81.

10 Kambouris A. Physical, psychological, and economic advantages of accelerated discharge after surgical treatment for breast cancer. *Am Surg* 1996;62:123-7.

11 Van Wersch AMEA, Bonnema J, van Geel AN, Prinsen B, Pruyn JFA, Wiggers T. Continuity of information for breast cancer patients: the development, use and evaluation of a multidisciplinary care protocol.
Patient Education and Counseling 1997;30:175-86.

12 Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Inf Control* 1988;16:128-40.

13 Pruyn JFA. Coping with stress in cancer patients. *Patient Education and Counseling* 1983;5:57-62.

14 Van den Borne HW, Pruyn JFA. *Lotgenotencontact bij kankerpatiënten.* [Contacts between

fellow cancer patients.] Maastricht: van Gorcum, 1985.

15 Cronbach LJ. *Essentials of psychological testing.* New York: Harper and Row, 1990.

16 De Boer MF, Pruyn JFA, van den Borne HW, Knegt PP, Ryckman RM, Verwoerd CDA. Rehabilitation outcomes of long-term survivors treated for head and neck cancer. *Head Neck* 1995;17:503-15.

17 Mesters I, van den Borne HW, McCormick L, Pruyn JFA, de Boer MF, Imbos I. Openness to discuss cancer in the nuclear family scale: development and validation. *Psychosom Med* 1997;59:269-79.

18 Van den Borne HW, Pruyn JFA, van den Heuvel WJA. Effects of contacts between cancer patients on their psychosocial problems. *Patient Education and Counseling* 1987;9:33-51.

19 Spielberger CD, Gorsuch RL, Lushene RE. *STAI manual for the state-trait anxiety inventory.* Palo Alto: Consulting Psychologists Press, 1970

20 Watson M, Greer S, Pruyn JFA, van den Borne HW. Locus of control and adjustment to cancer. *Psychol Rep* 1990;66:39-48.

21 De Haes JCJM, van Knippenberg FCE, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. *Br J Cancer* 1990;62:1034-8.

22 Makuch R, Simon R. Sample size requirements for evaluating a conservative therapy. *Cancer Treat Rep* 1978;62:1037-40.

23 McArdle JMC, George WD, McArdle CS, Smith DC, Moodie AR, Hughson AVM, et al. Psychological support for patients undergoing breast cancer surgery: a randomised study. *BMJ* 1996;312:813-6.

24 Tadych K, Donegan WL. Postmastecomy seromas and wound drainage. *Surg Gynecol Obstet* 1987;165:483-7.

25 Vinton AL, Traverso LW, Jolly PC. Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection. *Am J Surg* 1991;161:584-8.

26 Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy. A prospective randomized clinical trial. *Eur J Surg Oncol* 1993;19:143-6.

27 Somers RG, Jablon LK, Kaplan MJ, Sandler GL, Rosenblatt NK. The use of closed suction drainage after lumpectomy and axillary node dissection for breast cancer. *Ann Surg* 1992;215:146-9.

28 Jeffrey SS, Goodson WH, Ikeda DM, Birdwell RL, Bogetz MS. Axillary lymphadenectomy for breast cancer without axillary drainage. *Arch Surg* 1995;130:909-13.

29 Bonnema J, van Geel AN, Ligtenstein DA, Schmitz PIM, Wiggers Th. A prospective randomized trial of high versus low vacuum drainage after axillary dissection for breast cancer. *Am J Surg* 1997;173:76-9.

30 Nelles WB, McCaffrey RJ, Blanchard CG, Ruckdeschel JC. Social support and breast cancer: a review. *J Psychosoc Oncol* 1991;9:21-35.

31 Bloom JR. Social support, accommodation to stress and adjustment to breast cancer. *Soc Sci Med* 1982;16:1329-38.

32 Spiegel D, Bloom JR, Gottheil E. Family environment as a predictor of adjustment to metastatic breast carcinoma. *J Psychosoc Oncol* 1983;1:33-44.

Chapter 6

Costs of care in randomised trial of early hospital discharge after surgery for breast cancer

Jorien Bonnema, Anneke M. E. A. van Wersch, Albert N. van Geel, Jean F. A. Pruyn, Paul I. M. Schmitz, Carin A. Uyl-de Groot, Theo Wiggers

Eur J Cancer, in press

Abstract

The aim of the study was to determine the effect of reduction of length of hospital stay after surgery for breast cancer on the rate of care consumption and the costs of care. Patients with operable breast cancer were randomised to a short or long postoperative hospital stay. Data on care consumption were collected for a period of 4 months in diaries administered by patients and socioeconomic status was evaluated by questionnaires. A cost-minimisation analysis using the 'societal' perspective was performed and savings were compared with the savings of hospital charges. The use of professional home care was higher for the short stay group during the first month (7.2 vs. 1.3 hrs.,$p<0.0001$). The number of outpatient consultations, the intensity of informal home care and patient's expenses did not increase after early discharge. The total cost of care was reduced with US $ 1320 by introducing the short stay program ($p=0.0007$), but the savings were substantially lower than the savings in hospital charges ($2680).

Introduction

Inpatient hospital care constitutes the major expense in the initial treatment of cancer [1]. Shifting treatment to short stay in hospital or outpatient procedures is one of the measures expected to reduce the expenses of cancer care. Breast cancer is the most frequent newly diagnosed cancer in women. The savings realized by shortening hospitalization after initial surgical treatment may be substantial [2].

Most breast cancer patients require surgery for treatment of the primary tumor and for staging of the disease by axillary dissection. Postoperatively, some form of care is necessary for wound and drain management and psychosocial support. Early discharge from hospital is realized by shifting hospital care to outpatient care and to professional and informal home care. In the Netherlands professional home care is delivered by general practitioners, physiotherapists, district nurses and home helps. Informal care is defined as care provided by relatives, neighbors, friends and relatives [3]. The extent of substitution between intramural care and home care, and the care intensity used by this category of patients in the different settings, are unknown. Studies of the economic effects of early discharge after breast cancer surgery have mainly focused on savings of hospital charges without taking into account additional costs of outpatient care and home care [4-8]. A shift in costs may counteract the savings achieved by shortening hospitalisation.

We conducted a randomised trial to assess the medical, psychosocial and economic effects of early hospital discharge after surgery for breast cancer. The results of the medical and psychosocial evaluation have been described [9]. There were no statistical significant differences between the two groups in the incidence of wound complications, seroma formation, or physical or psychological complaints, in the experience of psychosocial problems, or in coping strategies used. In this paper we want to present the results of the economic evaluation. The aim of the economic evaluation was to determine the effect of the reduction of length of hospital stay after breast cancer surgery on the rate of care consumption and the costs of professional and informal care, both inside and outside the hospital.

Patients and methods

Design of the trial

Patients

The sample comprised a consecutive series of patients with stage I or II breast cancer who had surgery of the primary tumor in the breast and axillary dissection between October 1993 and April 1995. Patients were excluded if they had received preoperative radiotherapy or chemotherapy, were at high risk for complications (ASA classification 3 and higher), or were mentally incompetent; patients who had difficulty with the

Dutch language or an inappropriate home situation were also excluded. The study was carried out in two hospitals, a cancer center and a middle sized general hospital, in Rotterdam. Approval from the ethics committees of both hospitals was obtained before the start of the study and written consent was obtained from all participants.

Study design

The study design was a prospective randomised trial. Patients were randomised to either a short postoperative stay with discharge in the morning of the fourth postoperative day with drain in situ or a long postoperative stay, i.e. discharge after drain removal. Randomisation took place in the outpatient clinic after the patient had been informed of the diagnosis of her cancer. Operative procedures performed included modified radical mastectomy and lumpectomy with axillary dissection. For both groups drains were removed when the production of serous fluid had decreased to less than 30 cc per day or after 14 days regardless of the drainage volume. For women assigned to short stay treatment drain removal was performed in the outpatient clinic or at home. A comprehensive early discharge protocol was developed to guarantee continuity of care and information [10]. Community nursing care was offered to all short stay patients. The community nurse scheduled a number of home visits after discharge, with a minimum of two. This schedule was flexible to the needs of the patient. The general practitioner was informed by letter about the early discharge of the patient. Telephone support from the hospital was available 24 hours a day. Home help was arranged for patients of both groups according to their needs.

Data collecting procedures

The study period started on the first postoperative day and continued during the 4 following months. At admission, patients were given a daily diary, to be used for one month, and a weekly diary, to be used for the following 3 months. The weekly diary was introduced after initiation of the study and distributed to 90 patients. In the diaries the length of stay in hospital, the number of outpatient visits and the amount of time the care-professionals and informal carers had spent directly on the patient in hospital and at home were recorded. Demographic characteristics were collected by questionnaires and clinical data were recorded in the diaries and patient files. Clinical study end points were recorded in the diaries and patient files by the doctors and nurses and included wound and drain complications, duration and amount of axillary drainage, incidence of seroma's and number of aspirations.

Economic analysis

For the determination of costs a cost-minimisation analysis was performed by analysing the total costs of both postoperative regimens [11,12]. This means that the two alternatives are compared on the basis of minimum cost; an approach useful for comparing different

treatment techniques with similar patient outcome. The choice of perspective was that of 'societal level', which means that all costs and benefits for all parties in society were accounted for [13]. The cost-analysis was carried out in three phases. The resources were tabulated in appropriate units and the use of the resources was measured. After valuation of the resources the volumina were multiplied by the unit costs. Resources measured were: (1) postoperative days in hospital (2) use of professional care in the hospital of the following disciplines: surgeons, residents, nurses, breast cancer nurses, and physiotherapists (3) number of outpatient visits and use of professional care in the outpatient departments (4) use of professional home care (5) use of informal home care (6) transport to hospital and costs incurred by the patient. The costs of these units were determined. The costs of a hospital day and outpatient visit were based on the economic administration of the hospital and included direct costs (manpower and materials) and indirect costs (overhead). A hospital day amounted to US $ 287 and a consultation to US $ 106. The costs of professional care used in the hospital measured at patient level were determined in terms of hourly wages based on salary costs of the financial department of the hospital including employers costs.

Costs per hour of care by professional workers outside the hospital were calculated taking into account the costs not directly related to patient care such as costs of overhead and transport. Informal care was valued according to the market value approach. In this approach, the price of professional care is used as the shadow-price for informal care, with the reasoning that if informal care is not available, it has to be substituted by professional care [3]. Because informal care-takers have a lower productivity and carry out less complicated tasks, the market price of the cheapest home help, household service, was used. Costs of materials and transport were recorded by the patients. Transport by car was recorded in kilometers and multiplied by a fixed price of 31 $ ct per km.

Prices of 1994 were used (1.00 US $ = approximately 1.78 Dfl). Average total costs and medians with 95 interpercentile range were calculated.

A cost analysis from a financial perspective was also carried out. This perspective implies that the charges of the Dutch tariff system have been used.

Statistical analysis

Comparison of patient characteristics and complications was done with the SPSS package. Cost analysis was performed using STATA. Categorical data were compared by the chi-square test without correction of continuity. Continuous variables were compared by the Mann-Whitney U test. Statistical significance is defined for P values <0.05.

The sample size of the economic part of the study was based on the main endpoint in the medical and psychosocial part of the trial [9]. It was not possible to calculate the required sample size for the economic analysis before the start of the study because

the deviation of costs was unknown. Nevertheless, for the final 36 patients in the short stay group and 39 patients in the long stay group the standard deviation of the total costs of treatment can be obtained.
Using mean total costs of 4226 $ in the long stay group and 3062 $ in the short stay group (so a reduction of 30 %) it can be shown that the power to detect this difference as significant (alpha one-sided 0.05) is 98 %. The mean and standard deviations on a log scale are of 8.30 and 0.42 log $ in the long stay group and 7.96 and 0.37 log $ in the short stay group.

Results

Patient groups

During the study period 173 women were operated on for breast cancer, of whom 139 were randomised. Reasons for non randomisation were: refusal to participate (n=22), an unsatisfactory home situation (n=10) and not having been asked to participate (n=2). Fourteen more women were excluded after randomisation because they were allocated to another form of treatment (n=4), or withdrew from participation (n=10) for several reasons. Data from the daily diary (first month) were available for 120 (61 short and 59 long stay) patients and from the weekly diary (month 2-4) for 79 (37 short and 42 long stay) patients. There were no differences in the reasons for noncompliance of the diaries between the two groups. Total costs over the 4 month study period were calculated for the subset of patients who had returned the daily diary as well as the weekly diary (n=75). Data on tumour stage, type of treatment, age, marital status, educational level and family income are detailed in Table 1.

Complications

There were no significant differences between short and long stay patients in median values of drainage volume from the axillary drain (515 ml versus 685 ml), the median duration of drainage (8 versus 9 days), number of patients with aspirations (10 versus 8), or number of patients with wound (10 versus 9) or drain complications (38 versus 27). The mean number of aspirations required per patient was higher in the long stay group (3,5 versus 1 in the short stay group, P=0.04).

Care intensity

Table 2 presents the data on the intensity of postoperative care per patient.
In accordance with the protocol inpatient hospital care was longer for the patient randomised for discharge after drain removal: the median length of stay was 4 days for the short stay group and 9 days for the long stay group. The use of professional home care following discharge, especially district nursing and home help, was higher for the short stay group than for the long stay group: respectively 7.2 and 1.3 hours

Table 1 Patient characteristics

	Short stay* n=62	Long stay n=63
Operative procedures		
Axillary dissection (after previous lumpectomy)	10 (16%)	21 (33%)
Breast conserving therapy	20 (32%)	14 (22%)
Modified radical mastectomy	21 (34%)	21 (33%)
Mastectomy and direct breast reconstruction	11 (18%)	7 (11%)
Tumor size		
0-2 cm	33 (53%)	39 (62%)
> 2-5 cm	19 (31%)	17 (27%)
> 5 cm	3 (5%)	4 (6%)
unknown	7 (11%)	3 (5%)
Nodal status		
Negative nodes	40 (65%)	41 (65%)
Positive nodes	21 (34%)	21 (34%)
Unknown	1	1
Adjuvant treatment		
No treatment	45 (73%)	40 (63%)
Radiotherapy nodal regions	2 (3%)	2 (3%)
Chemotherapy	3 (5%)	7 (11%)
Hormonal therapy	7 (11%)	3 (5%)
Combinations	5 (8%)	11 (17%)
Demographics		
Median age (yrs) †	55 (29-80)	58 (30-75)
Marital status		
Married or living together	51 (82%)	47 (75%)
Single	4 (6%)	9 (14%)
Divorced	2 (3%)	2 (3%)
Widowed	5 (8%)	1 (2%)
Unknown	-	4 (6%)
Monthly family income		
US $ 600-1100	13 (21%)	7 (11%)
US $ > 1100-2000	20 (32%)	25 (40%)
US $ > 2000	20 (32%)	16 (25%)
unknown	9 (15%)	15 (24%)
Educational level		
Primary school	12 (19%)	10 (16%)
Secondary school	40 (64%)	43 (68%)
University	10 (16%)	5 (8%)
unknown	-	5 (8%)

Values are numbers of patients. † *Median (95-interpercentile range)*
* *No significant differences between study groups*

($p<0.0001$).
There was no statistically significant difference between the two groups in the number of outpatient visits, or the amount of informal care used. As is shown in Table 2, the variance in use of care in the home situation was highly skewed to the left as indicated by the value of the median which is much smaller than the mean. This pattern is a quite common phenomenon in health care consumption: many 'modest' consumers and relatively few 'large' consumers [3].

Cost analysis

The overall total cost of care amounted to US $ 3062 for the short stay treatment and US $ 4382 for the long stay treatment, leading to a potential saving of US $ 1320 (95

Table 2 Intensity of care per patient

	week 1-4		week 5-17	
	short stay n=61	long stay n=59	short stay n=37	long stay n=42
Hospital care				
Hospital stay (days)	4.1 (4)	9.0 (9)		
Professional care in hospital (hrs)	2.7 (2.6)	4.8 (3.0)		
Number of outpatient visits	2.7 (2)	2.4 (2)	1.2 (1)	1.2 (1)
Home care				
Professional care				
community nurse (hrs)	2.3* (1.75)	0.3 (0.0)	0.6 (0.0)	0.05 (0.0)
general practitioner (hrs)	0.5 (0.4)	0.3 (0.1)	0.1 (0.0)	0.3 (0.0)
physiotherapist (hrs)	0.3 (0.0)	0.2 (0.0)	1.1 (0.0)	1.3 (0.0)
home help (hrs)	4.1 (0.0)	0.5 (0.0)	7.7 (0.0)	9.3 (0.0)
Total (hrs)	7.2* (2.9)	1.3 (0.25)	9.6 (0.5)	10.9 (0.3)
Informal care (hrs)	29.7 (10.6)	20.1 (5.7)	24.7 (1.0)	24.5 (6.5)
Total home care (hrs)	37** (17.7)	21.4 (10.0)	34.4 (9.5)	35.4 (12.0)

Numbers are means (median)
**p<0.0001, **p=0.006*

% confidence interval 580-2056) by introducing short stay for this category of patients (Table 3). The mean total cost excluding informal care and patient expenditures was US $ 2253 for the short stay group (median 1929, range 1367-4793) and US $ 3603 (median 3466, range 1736-6817) for the long stay group. The mean difference was $ 1350 (95 % confidence interval 747-1876).
For the short stay group the costs of hospitalisation amounted to 41 % of the total costs and the costs of home care to 35 % of total costs. For the long stay group these percentages were 64 % and 19 % respectively. The extent of substitution between hospital care and home care was limited. Cost reduction was only slightly influenced by an increase in home care costs because of the much higher costs of hospital care compared to home care.

Financial perspective

The average cost per hospital day charged was US $ 547, resulting in mean total hospital costs of US $ 2243 for a patient in the short stay group and US $ 4923 for a patient in the long stay group.

Sensitivity analysis

Sensitivity analyses were performed to assess the effect of changes in the number of

Table 3 Costs of care (in US $)

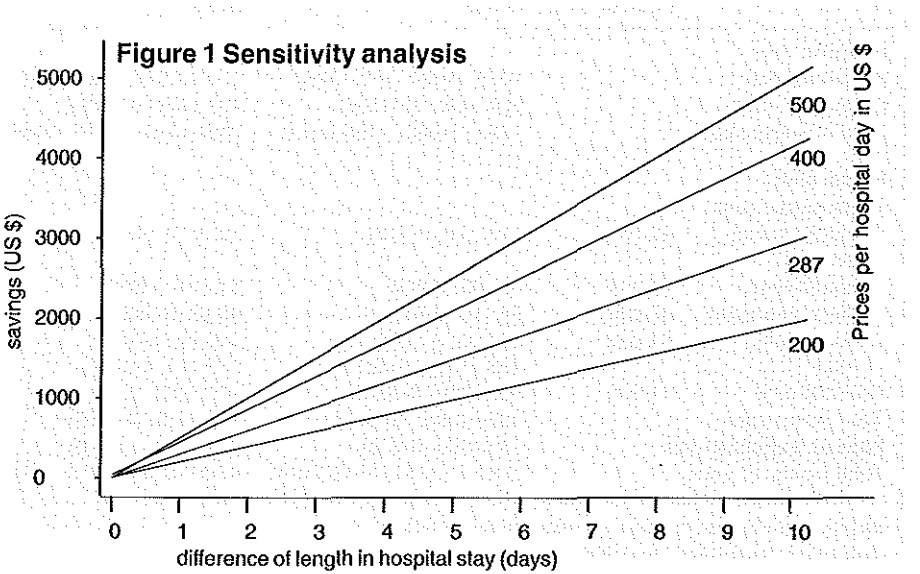
	costs per hour of care	short stay n=36	long stay n=39
Hospital care			
Hospitalisation		1256* (1224, 853-1525)	2787 (2657, 1160-4280)
Outpatient visits		504 (440, 90-1530)	437 (322, 0-1337)
Total hospital care		1760** (1683, 1199-2911)	3224 (3101, 1445 -5133)
Home care			
Professional care			
district nurse	45 p/hr	115* (76, 0-449)	18 (0, 0-143)
general practitioner	75 p/hr	46 (35, 0-209)	54 (19, 0-260)
physiotherapist	42 p/hr	64 (12, 0-331)	66 (0, 0-332)
home help	24 p/hr	267 (0, 0-1765)	240 (0, 0-2073)
total		493 (186, 10-2215)	379 (75, 0-2181)
Informal care	11 p/hr	563 (259, 0-2376)	470 (223, 0-1896)
Total home care		1057 (886, 76-3716)	849 (619, 0-2983)
Patient expenditures		246 (160; 0-888)	309 (142; 0-1510)
Total costs of care		*3062*** *(2640, 1646-5599)*	*4382 (4226, 1870-7524)*

Values are means (median, 95-interpercentile range)
**p=0.0001, **p<0.0001 ***p=0.0007*

days in hospital and the cost per hospital day (Figure 1). The cost per hospital day used in the study was $ 287. For the sensitivity analysis it was varied from US $ 200 to US $ 500. Because hospital stay is the main cost determinator, reduction of length of stay always resulted in cost reduction, independent of the cost per hospital day.

Discussion

In this study the effect of shortening the stay in hospital after surgery for breast cancer on the consumption and the cost of care was studied by means of a prospective randomised trial. The shortening of hospitalisation resulted in a potential cost reduction of 30 % of the total cost of postoperative care. We analysed costs from the 'societal' perspective. This implies that not only costs made within the health care system are taken into account, but also the costs of informal care and costs incurred by the patient [11]. Exclusion of these indirect costs may lead to an underestimation of the total costs of health care [14] and to an overestimation of savings. In our study, there was a significant increase in use of professional home care by the short stay patients during the first postoperative weeks, but there was no increase in ambulatory hospital care nor in the use of informal care. Care substitution was limited to nursing care and home help, which have much lower costs than traditional care in hospital.
Costs were calculated by means of units based on the real use of resources, multiplied by unit costs. This method has been recommended for costing diseases in a surgical ward [15,16] and evaluating the cost of cancer treatment [12]. In other studies on early



hospital discharge after surgery for breast cancer, the savings of hospital charges were calculated [4-8]. In our study the savings based on a calculation of real costs were substantially lower than the savings of hospital charges (US $ 1320 and US $ 2680 respectively).

There are some methodological limitations to our study design. Unit prices were based on local or national data, making generalisation of the results to other countries difficult. However, in the sensitivity analysis the price per hospital day was varied and it was demonstrated that there is a linear function between the costs of a hospital day and total costs. The highest savings can be achieved when hospital stay is reduced considerably and costs per hospital day are high.

In our study protocol, standard care of the community nurse was provided for the short stay patients to guarantee continuity of care. In many countries however, patients and their families are instructed in wound and drain care and professional home care is not a common practice. Because the costs of community care were rather low in proportion to the high hospital costs, the use of the district nursing care only slightly influences the results. Our economic analysis was conducted alongside a prospective randomised trial into the effects of shortened hospital stay on complication rate, patient satisfaction and psychosocial outcome [9]. One may object that the rigorous protocol design gives no insight into real costs in general practice and that in our study the home care may have been improved by the protocol, in particular the use of the patient diary. Nevertheless, we think that the treatment in our long stay condition represents a realistic situation: patients in this group had no predetermined length of stay or home care procedures. The postoperative care of the long stay group is similar to that used in many European countries: discharge after drain removal [17,18].

The study population used for the cost analysis was smaller than for the clinical study due to a later start of the economic evaluation. We compared the group who had received a daily diary (n=125) with the group who completed as well a daily diary as a weekly dairy (n=75) with regard to total cost of hospitalisation, outpatient care and home care during the first month and found no statistical significant differences between the groups. The diaries that were not used for the cost analysis were not centre related and randomly distributed among the two study arms so it is very unlikely that as a consequence of this a bias would have been introduced.

Early discharge can be implemented on condition that there is no increase in complications and that the quality of care is guaranteed. In our randomised trial, it was demonstrated that the wound complication rate remained unchanged, that there were only minor drain complications for both groups and that patient satisfaction with a short length of stay was high [9]. In our opinion, it is the task of the hospital to arrange home care facilities. It is widely recognized that intensive post-discharge care leads to higher outpatient costs but lower inpatient costs, due to shorter hospital stays and fewer readmissions [19]. Our results demonstrate the same trend.

In conclusion, early discharge after breast cancer surgery increases the use of professional nursing care and home help, but does not lead to an increase of consumption of outpatient medical care. Informal home care is used frequently by both groups. The shifting of care results in a potential cost saving; but these savings are not as high as would expected from a calculation of the savings in hospital charges. This study can be used as a model for estimating the savings achieved by substituting hospital care for home care.

References

1. Koopmanschap MA, van Roijen L, Bonneux L, Barendregt JJ. Current and future costs of cancer. *Eur J Cancer* 1994;30A:60-65.
2. Kambouris A. Physical, psychological, and economic advantages of accelerated discharge after surgical treatment for breast cancer. *Am Surg* 1996;62:123-127.
3. Koopmanschap MA, Ineveld BM, Miltenburg TEM. Costs of home care for advanced breast and cervical cancer in relation to cost-effectiveness of screening. *Soc Sci Med* 1992;35:979-985.
4. Clark JA, Kent RB. One-day hospitalization following modified radical mastectomy. *Am Surg* 1992;58:239-242.
5. Tarazi R, Esselstyn CB, Kuivila T, Hardesty I. Early hospital discharge following mastectomy. *Cleve Clin Q* 1984;51:579-584.
6. Pedersen SH, Douville LM, Eberlein TJ. Accelerated surgical stay programs. A mechanism to reduce health costs. *Ann Surg* 1994;219:374-381.
7. Goodman AA, Mendez AL. Definitive surgery for breast cancer performed on an outpatient basis. *Arch Surg* 1993;128:1149-1152.
8. Edwards MJ, Broadwater JR, Bell JL, Ames FC, Balch CM. Economic impact of reducing hospitalization for mastectomy patients. *Ann Surg* 1988;208:330-336.
9. Bonnema J, van Wersch AMEA, van Geel AN, Pruyn JFA, Schmitz PIM, Paul MA, et al. Randomised trial of early hospital discharge after surgery for breast cancer: medical and psychosocial effects. *B M J* 1998;316:1267-1271.
10. van Wersch AMEA, Bonnema J, van Geel AN, Prinsen B, Pruyn JFA, Wiggers T. Continuity of information for breast cancer patients: the development, use and evaluation of a multidisciplinary care protocol. *Patient Educ Couns* 1997;30:175-186.
11. Williams C, Coyle D, Gray A, Hutton J, Jefferson T, Karlsson G, et al. Cost-effectiveness in cancer care. Report of a Working Party from the European School of Oncology. *Eur J Cancer* 1995;31A:1410-1424.
12. Uyl-de Groot, C.A. *Economic evaluation of cancer treatments (Thesis)*, Rotterdam:Erasmus University Rotterdam, 1995.
13. Bonsel GJ, Rutten FFH, Uyl-de Groot CA. Economic evaluation alongside cancer trials; methodological and practical aspects. *Eur J Cancer* 1993;29A:S10-S14.

14 Rhodes RS. Ambulatory surgery and the societal cost of surgery. *Surgery* 1994;116:938-940.

15 Harper DR. Disease cost in a surgical ward. *B M J* 1979;1:647-649.

16 Hardy KJ, Miller H, McNeil J, Shulkes A. Measurement of surgical costs: a clinical analysis. *Aust N Z J Surg* 1994;64:607-611.

17 Holcombe C, West N, Mansel RE, Horgan K. The satisfaction and savings of early discharge with drain in situ following axillary lymphadenectomy in the treatment of breast cancer. *Eur J Surg Oncol* 1995;21:604-606.

18 Boman L, Björvell H, Cedermark B, Theve NO, Wilking N. Effects of early discharge from hospital after surgery for primary breast cancer. *Eur J Surg* 1993;159:67-73.

19 Weinberger M, Smith DM, Katz BP, Moore PS. The cost-effectiveness of intensive postdischarge care. *Med Care* 1988;26:1092-1101.

Chapter 7

Continuity of information for breast cancer patients: the development, use and evaluation of a multidisciplinary care-protocol

Anneke M. E. A van Wersch, Jorien Bonnema, Bert Prinsen, Jean F. A. Pruyn, Theo Wiggers, Albert N. van Geel

Patient Educ Couns 1997;30:175-186

Abstract

The multidisciplinary nature of much patient-care may lead to gaps in the continuity of information which they receive, as well as to different care-professionals giving them contradictory information. As a counter-measure, a protocol has been developed which integrates medical, nursing, and a variety of extra-mural events and activities into a comprehensive description of 15 'moments' in the care of breast cancer surgery-patients. Among innovations, the protocol includes information about psychosocial guidance following diagnosis, and about the discharge procedure and contact with fellow-sufferers. The protocol was implemented in Rotterdam in 1994, in two hospitals and in the community; and evaluated formatively on the basis of reactions from 53 patients and 81 care-professionals. Both groups found its form and content to be successful and informative.

Introduction

Breast cancer is the most frequently diagnosed form of cancer among women in the Western world. A number of issues have been identified in the literature which focus on the patient's need for information about her treatment and care. However, although she can benefit from receiving more information about both her illness and its treatment, throughout their various stages, she often experiences shortcomings in the information which she actually receives. These have to do with the multidisciplinary nature of the care-regime - different professionals not knowing what others are doing to, or telling, the patient; and, more specifically, with their unfamiliarity with patients' psychological and psychosocial needs. There is considerable scope for improving the 'continuity of information' which patients receive.

The optimal delivery of information depends on the fulfilment of the 4 functions of information as distinguished by Dekkers [1]: (i) *Information* about the disease and its treatment; (ii) *Instructions* dealing, for example, with care of the wound; (iii) *Education*, to stimulate increases in the patient's independence and self-reliance (cf. Bokma's emancipation model [2]; and (iv) *Guidance*, whereby psycho-social support is offered to enable patients to cope as well as possible with the disease and its consequences. The findings of several studies indicate how patients can benefit from being informed about their illness. A patient's insight into the treatment process enables her to devise changes in her life-style and to develop self-care activities [3-5]. Information-seeking is a coping strategy which may be used in order to gain control of her situation [4,6,7]. However, several other studies have shown that patients experience shortcomings in the information which they receive. They want more information than that provided, about what they should expect in hospital and what is involved in rehabilitation at home [8-12]. They experience difficulties in communicating with the medical team [13]. They have too little opportunity to ask questions of the doctor [9,14]; and there is a discrepancy between patients' desire for knowledge and their ability to ask pertinent questions [15]. Doctors may underestimate patients' knowledge of their illness: those who most seriously underestimate patients' knowledge tend to communicate the least information [15]. Patients' desire for information is often underestimated, while their wish to participate in decision-making is over-estimated [16-18]. There is a need for a more active role in the interaction between patients and care-professionals, because of its positive relation to patient-satisfaction [19], hopefulness [3] and a sense of control over the disease [20]. It has been found that a majority of breast cancer patients believe that they are poorly informed about the possibilities for receiving help and guidance following discharge from hospital: for example, from community nurses, the family doctor, a psychologist, fellow-patients or a self-help group [21-23].

Breast cancer patients, like many others, are treated in a multidisciplinary approach , with a large number of different professionals being involved [24]. This raises questions of who does what, where and when, and who or what guarantees that the most appropriate information is given. In order to provide the patient with quality care, information should exhibit continuity throughout the course of the disease - i.e. at diagnosis, during initial treatment, after discharge, during follow-up and at time of recurrence [25]. But the complex pattern of care, provided in a variety of settings, with the involvement of many disciplines, makes it difficult to give the patient continuity of information. This depends on each professional knowing that there are colleagues involved in the treatment process, who will also ensure that the patient is informed, instructed, educated and emotionally guided in areas outside that particular professional's disciplinary competence; and their knowing that other care-professionals are not giving information to the patient which is contradictory to that which they themselves give. In other words, care-activities, and the information about them which is given, need to be attuned to one another.

However, it does seem from the literature that different care-professionals often do not know what the other is doing. Communication between carers is not found to be optimal. Nurses, for example, are uncertain about their role [4,8,16,26]. They may consider that the giving of information is the duty of doctors; while patients expect to receive it from nurses as well [16]. This ambiguity may be a major limiting factor upon the extension of breast cancer prevention-activities [27]. The activities of care-professionals from different disciplines, both inside and outside the hospital, are frequently fragmented and uncoordinated [28]. Patients, too, experience the giving of information by the care-professionals who are involved in their care as discontinuous [9]. Communication channels between disciplines are difficult to establish and professionals often do not know what care, information and support their colleagues are giving to a patient [29]. Because information for inpatients and outpatients is not integrated, the use of, for example, community resources is determined more by the resourcefulness of the patient and her family than by any organisational arrangements [28]. Formal arrangements for information exchange between surgeon and family doctor are undeveloped: it usually occurs in writing and is rarely attuned; and the family doctor frequently receives information too late [30,31].

Two recent studies into information for patients, found that more attention was given to information and instruction for patients than to their psychosocial guidance [9,32]. The majority of doctors and nurses did not consider it their job to give cancer patients emotional support and guidance, unless they explicitly asked for it.

The importance of patient education in increasing the patient's independence and responsibility for self has been highlighted in an 'emancipation' model of the former concept [2]. The effectiveness of patient education can be enhanced by care-providers understanding both the psychological adaptation process which is initiated by the

diagnosis of cancer and its impact on the motivation to learn and on the need for information [16,33,34]. However, they often have inaccurate perceptions of how patients feel: they expect patients to feel worse than they actually do [35], or underrate the extent of their distress [36]. The way in which the cancer diagnosis is disclosed to the patient has been found to be important for their psychological adaptation [34,37]: the doctor has to be aware of the emotional impact of the diagnosis and give an opportunity to the patient to express her feelings and ask questions. Patients prefer a caring attitude to the provision of information as such [34].

Aim of the study

Against the background of the informational needs and constraints identified in the literature, the present study aimed to develop a multidisciplinary care-protocol, combining a continuous flow of information on medical and nursing matters with information about psychosocial aspects of the disease and its treatment, contact with fellow-patients and with other helpers in the community. The protocol was intended to achieve continuity and integration of information, in the sense that it should make clear in an uniform way, to both patients and a wide variety of professionals, who is providing the patient with what form of care and information, and at what moment in time.

The use of such a protocol implies a degree of standardisation in the care-process. A protocol clarifies the role of each professional, facilitates communication between the different disciplines involved in the process and makes auditing possible. It provides an alternative to fragmented patient- management in mono-disciplinary terms, which tends to focus primarily on medical treatment and has little to say about the wider informational, educational and psychological needs of patients [38].

The protocol was intended for the use, equally, of patients and care-professionals. Given the anticipated level of knowledge and lack of information on the part of patients about what to expect in their treatment, it was important that the protocol should be drawn up in language which was intelligible to lay people. In the United States, it has been found that reading materials for patients about cancer have a higher reading level than the average for adults [39,40]. Care-professionals may underestimate the reading-skills of their patients [41].

The protocol was to be implemented in both in-patient and out-patient settings. It would be evaluated on the basis of the reactions both of patients and a variety of care-professionals. At this developmental stage, the evaluation would be formative, rather than one of impact. Attention would be paid to the use and utility of the protocol, the continuity of the information offered, the status of 'patient education' as perceived both by the patients themselves and by care-professionals, and the psychosocial guidance offered.

Methods

Development of the care-protocol

Multidisciplinary working group

Development of the protocol, as well as its later implementation, were assisted at all stages by a steering and a working group. These groups consisted of representatives of the various health professionals involved in breast cancer treatment, information and education experts, and researchers and ex-patients.

Inventory

Initially, an inventory of existing informational materials for cancer patients in the Netherlands was drawn up. For this purpose, contact was sought with the coordinators of patient-information in all academic hospitals and comprehensive cancer centres, and with researchers, information-experts and care-professionals who were engaged in comparable initiatives. Surgical, medical, nursing and radiotherapeutic protocols, as well as any available patient information were exchanged. Although separate protocols or guidelines for each function (surgery, nursing,etc.) were found, there was no multidisciplinary example for a single disease as such. Furthermore, protocol content consisted mainly of details of the treatment which was to be carried out, without relating it to patient information and social support. None of the documents was written in such a way as to be readily accessible to the patient.

After the inventory had been completed, the current state of treatment, care and information for breast cancer patients in the two participating hospitals was mapped by means of interviews with 60 health professionals and 40 patients. The informational needs of patients were recorded.

Changes to existing care

In order to make the information process as comprehensive and continuous as possible, several innovations were built into the existing line of care and were incorporated into the protocol. These included psychosocial guidance after the cancer diagnosis, information about discharge planning and the possibility of structured contact with fellow-patients. Directly after the 'bad news' of the cancer diagnosis has been given by the surgeon, the patient and her family have the chance to talk with an oncological nurse. An opportunity is given for emotions to be expressed; and the treatment which has been agreed upon with the surgeon is discussed. To make sure that everything is clear, a list is made of any questions which the patient wishes to ask the surgeon during the next consultation. A psychosocial case-history is taken, to determine whether the patient has adequate support and help in her immediate environment. Discharge is planned and additional measures for home-care support are taken. Patients are given the opportunity of leaving hospital on the

fourth day after the operation ('short stay'); or following removal of the suction drain, usually on the 8-10th day ('long stay'). Information leaflets about breast cancer and the organization for fellow-patients are given to the patient, together with some explanation. During the hospital stay, and with the patient's consent, contact with a fellow-patient is arranged by the oncological nurse. The fellow-patient visits the patient in the hospital and offers information and the possibility of continuing the contact.

Uniformity

One problem in the development of a multidisciplinary care-protocol - particularly with a view to its implementation nationally - is that there is rarely a uniform provision of care for any category of patient. Care-professionals often work on the basis of their own knowledge, perspective and ideas. These may not be shared by all care-professionals from a single discipline in any one hospital, and frequently vary between professionals from the same discipline in different hospitals. For this reason, care was taken to draw up a protocol with the content of which care-professionals participating in its implementation could agree.

Implementation and evaluation

The protocol was implemented in Rotterdam in 1994, in two hospitals (University Hospital Dijkzigt/Dr. Daniel den Hoed Cancer Centre and Zuider Hospital) and with the collaboration of the local home-nursing and care organisation. It was offered to 61 patients treated for primary breast cancer in the period January-June. It was also distributed to 152 care-professionals from disciplines involved in breast cancer treatment: to surgeons, oncologists, radiotherapists, radiologists, anaesthetists, pathologists (cytologists), physiotherapists, nurses and laboratory staff inside the hospital; and to family doctors and community nurses outside the hospital. Members of the working group explained the aims of the protocol to those professionals from their own discipline.

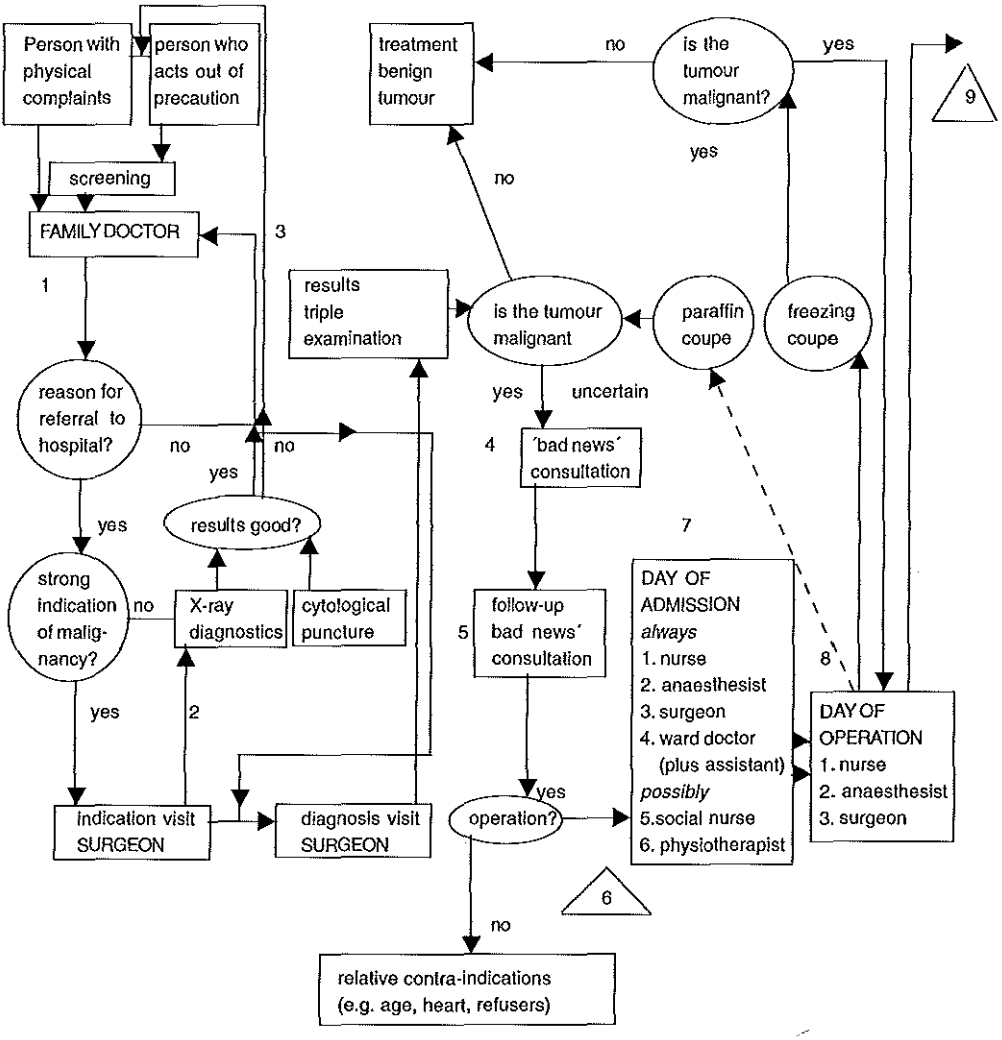
About six months after the introduction of the protocol, all patients and care-professionals were sent an evaluation questionnaire. Questions were included on the use and utility of the protocol, continuity of information, patient education, and psychosocial guidance. Some, but not all, of the questions were identical for both care-professionals and patients [42].

Results

The protocol: flow-diagram of breast cancer care

The developed protocol's description of the important moments in the care process can be represented by means of a flow-diagram (Figure 1, next page). The 15 moments

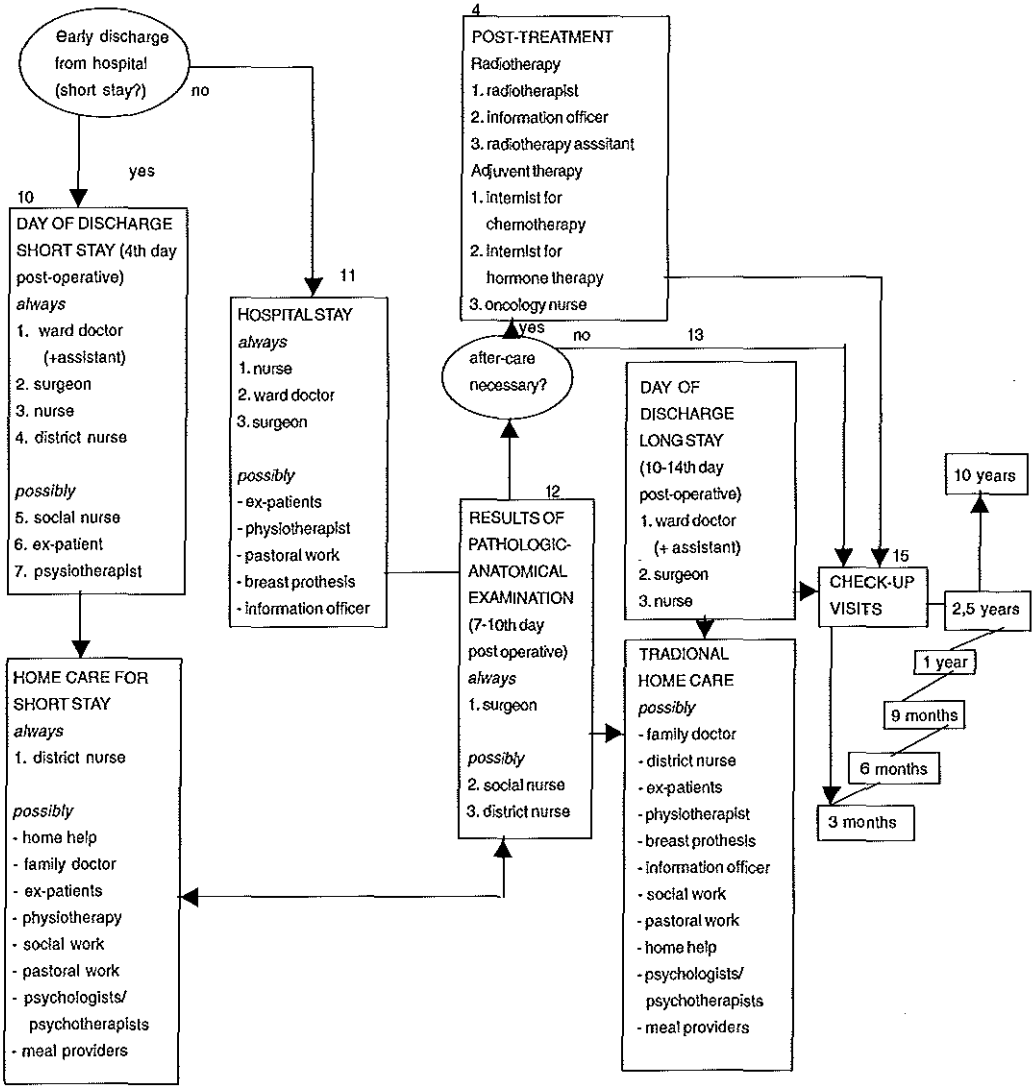
Figure 1a Flow-diagram of care of breast cancer patients



in the flow-diagram are each covered by a section of the protocol. They are: (1) indication of abnormality and family doctor's diagnosis, (2) visit to surgeon, (3) diagnostic process, (4) 'bad news' consultation, (5) follow-up of 'bad news' consultation by oncological nurse, (6) waiting for the operation, (7) admission, (8) operation, (9) first 3 days after operation, (10) 'short stay' discharge and home-care, (11) 'long stay', (12) results of pathologic anatomical examination, (13) 'long stay' discharge, (14) adjuvant therapy, and (15) check-up visits .

Each part of the protocol describes, in general terms, the state of affairs of treatment

Figure 1b



and care at that particular moment, what the current goals are, what actions should be taken and what information should be given by which care-professional. For the patient, this means that she is given concrete information, in a continuous process through the various critical moments, about whom she is going to see, what the professionals are going to do, and what they will talk about. A model for the psychosocial guidance of cancer-patients is included in the protocol. Information delivery is to be adapted to the coping strategy used by the patient.

Implementation and evaluation

Questionnaires were returned by 53 patients (P) and 81 care-professionals (C) (Table 1). The response of extra-mural care-professionals was considerably lower than that of hospital staff. This was due in particular to the fact that many of the family doctors and community nurses had not handled a breast cancer patient during the 6-month experimental period.

Use and utility of the protocol

Three-quarters of each group had read the care-protocol in its entirety; and a majority of the remaining one-quarter had read at least some part of it. More than half of each group (P:62% C:62%) had subsequently used it for reference purposes. One-third of each group had discussed it with fellow-professionals or -patients.

Seventy-five percent of care-professionals confirmed the utility of the protocol. Although most of them had some years of experience caring for breast cancer patients, more than 70% disagreed with the view that it would be more useful for less experienced or younger colleagues. Almost all thought an integrated protocol important for successful treatment where several disciplines were involved; and 60% believed that all care should be laid out in protocol form. For 21% of care-professionals, the use of the protocol led to a greater time-investment in their care-activities; it meant a saving of time for only 6%. In the opinion of 90%, the present protocol was suitable for use in other hospitals.

The great majority (88%) of the care-professionals thought it a good idea to offer patients the care-protocol. However, in answer to an open question about possible changes in the procedure followed, several care-professionals indicated that the content should be altered for patients. For example, one care-professional said: 'The content of the protocol seems to me to be too complicated for some patients'. And another said: 'It is too much for the patient, too remote and too unfeeling'.

The patients had fewer problems with the protocol than the care-professionals' response might suggest: only a small minority (13%) of patients seemed to find the protocol difficult to read or had the idea that it had been written for care-professionals (23%). One patient said: 'I read the protocol from beginning to end, leafed through it several times and used it to look up what I wanted to read more about. The more I read, the clearer it became'. One-third (34%) of the patients wanted to see a separate version of the protocol for patients; two-thirds thought it unnecessary.

Group differences

No items in the evaluation questionnaire, which were common to patients and care-professionals, produced a statistically significant difference in response between these groups.

However, there were some differences in response between nurses (intra- and

Table 1 Evaluation questionnaires: distribution and response rates

	Questionnaires distributed	Questionnaires returned	Response rate (%)
Intramural			
Specialists	21	15	
Physiotherapists	4	4	
Nurses	55	28	
Laboratory staff	10	10	
Total	90	57	63
Extramural			
Family doctors	15	5	
Community nurses	47	19	
Total	62	24	35
Patients			
Total	61	53	87

extramural) and other care-professionals (specialists, family doctors and paramedics). These are summarised in Table 2. (In order to calculate a chi-square statistic, it was necessary to form just these two groups of respondents. In addition, the four response-categories used were collapsed into a simple 'yes-no' distinction.) The first five of the items, as listed in the table, on which there were significant differences, refer to the professional's own care-activities; the next three to observations of patient behaviour, in relation to the protocol; two to interaction between patient and professional; and one to an aspect of inter-professional activity. The final distinguishing item refers to the content of the protocol itself. The results presented in this table show that nurses have a more positive attitude to the protocol's utility, in the interests of both the patients and themselves and of the interaction between the two parties than the other care-professionals.

Continuity of information

Almost all the patients and care-professionals found that the care-protocol was a good means of improving patient information (P:100% C:96%), and attuning the care-activities of various care-professionals (P:96% C:90%). In addition, almost all the care-professionals (96%) reported having learned something from the care-protocol about the care which others provide for breast cancer patients. Half of them said that since reading the protocol they had a better idea than before of

whom they could refer patients to. More than half (59%) said that they actually made more referrals to other care-professionals since going through the protocol. The great majority of care-professionals (90%) said that they were better able to fit the care which they gave to that which was given by others; and 81% found that the transfer of patients to other care-professionals proceeded more smoothly as a result. One in five observed patients having less contradictory information since its use.

Patient-education

The expectation that offering the care-protocol to patients would give them a basis for increased independence and responsibility for self was supported by the responses of both the care-professionals and the patients.

More than half of the care-professionals remarked that patients were more independent (52%) and better informed (57%) than before. They posed different (70%) and more direct questions (59%); and they showed that they had read the protocol (84%). Only a small minority (15%) thought that the protocol was anxiety-provoking or misleading for the patient. Most care-professionals believed that the protocol gave the patient a better preparation for (89%), and more involvement in (94%), the treatment. Nearly two-thirds thought that the protocol made the patient less dependent on the doctor for information.

The above results were echoed by the patients. Nearly three-quarters (73%) of them had read what was to happen, before they saw a care-professional.On that basis, they (72%) asked more focussed questions. Most patients (74%) confirmed that the care-professionals had asked whether they had read in the care-protocol what they could expect. One in three (36%) indicated that they had pointed out to the care-professionals one or more departures from the protocol. However, according to nearly all patients (98%), care generally followed its description in the protocol.

Psychosocial guidance

As regards support and psychosocial guidance for patients, 38% of our care-professionals said that they paid more attention to patients' psychosocial functioning as a result of the protocol. Moreover, 70 % indicated that in practice they increasingly took account of patients' problems and coping strategies; and somewhat more than half (55%) said that they provided patients with more support since reading the protocol. This was confirmed by the patients: the great majority (93%) reported an impression that they had had more support and help from care-professionals as a result of the protocol being used.

The protocol indicates which care-professionals should notify patients about the possibility of contacting fellow-sufferers, and at which moment in the care-process. Information is offered to the patient about the scheme for contacting fellow-sufferers and about how they can be reached by telephone. Sixty-one percent of the care-

Table 2 Significant (p<.05) differences in response to evaluation questionnaire items

Item	% agreeing	
	Nurses	Other care-professionals
Professional's own care-activities		
Reading the protocol has changed my care of breast cancer patients	32	7
Since I've read the care-protocol I give breast cancer patients more information	94	30
Since I've read the care-protocol I give breast cancer patients more support	71	32
Since the introduction of the protocol I have adapted the information which I give, to what other care-professionals say	81	43
Observations of patient behaviour		
Since I've had the protocol, I find that patients have less contradictory information	31	0
Because of the protocol, patients ask more carefully selected questions	78	26
Patients show that they have read the protocol	94	67
Interaction between patient and professional		
Before I give information to breast cancer patients I ask whether they have read the protocol	81	16
During my care-activities I ask the patient whether she has read in the protocol what she can expect	78	22
Since the introduction of the protocol the transfer of patients to other care-professionals works better	93	61
Inter-professional activity:		
Would you like to see the content of the integrated care-protocol changed?	17	40

professionals said that, since reading the protocol, they had given the scheme's telephone-number to more patients. Almost one in three (30%) reported giving more information than before about contact with fellow-sufferers. This is confirmed by answers in the patients' questionnaires: 81% indicated that they had received the telephone number for contact with fellow-patients from a care-professional; and almost all (96%) the patients said that a care-professional had pointed them in that direction. More than two-thirds of them had actually made contact with a fellow-patient; in one in six cases through the organisation which serves that purpose.

Discussion

This study was intended to develop, implement and evaluate a multidisciplinary care-protocol for breast cancer patients. The protocol describes the sequential steps of the care-process during the initial treatment of breast cancer and recommends which information should be given to patients at various points of the disease continuum. It builds on the expertise and experience of a multidisciplinary team, as well as of (ex-) patients [43]. The protocol contains no guidelines for medical treatment and offers no recommendations for clinical decision-making.

The protocol was positively evaluated by care-professionals and patients, both for its content and its form. It proved possible to use it as an informational instrument which acquainted both care-professionals and patients in a full and detailed manner about the entire line of care. It formed a good basis for continuity of information, both for care-professionals, because it enabled them to attune their various care, information and guidance activities to those of their colleagues, throughout the care-process; and for patients, by offering them, from 'day-one', a complete, coherent and valid scenario of the treatment and care which they could expect.

However, changes in the actual performance of the care-professionals during use of the protocol were not investigated. It seems that compliance with medical treatment protocols is low [44-46]. Attuning standards of care and information across care-givers by means of a protocol is only one of the numerous factors influencing their behaviour. There seem to be no studies which explore the compliance of care-givers with informational or care-protocols. Nor was any attempt made in this study to examine possible effects of making the protocol available exclusively, either to patients or to care-professionals.

Health professionals noticed that patients who used the protocol were more prepared for and involved in their treatment, and reported being able to pose different and more focussed questions than the patients who did not receive a protocol. How far this more active role in the interaction with professionals is related to patient satisfaction or other positive outcomes, as reported in the literature, was beyond the scope of this study.

A small sub-group of patients was identified who were not interested in information about the care-process, as laid out in the protocol. Further study is needed to facilitate the recognition and consequent assistance of patients who are not helped by the provision of such extensive information.

A majority of the patients was satisfied with the readability of the protocol and did not think that a separate version for patients was necessary. In the present study, as in other research [41], care-professionals underestimated the reading skills of their patients and proposed that a separate patient protocol should be written. Further study is needed to find out whether a patient's version of the protocol - together

with the present care-professionals' protocol - would form a better instrument for enabling the two parties to share responsibility for treatment.
The introduction of the protocol gave rise to the introduction of some changes in the existing line of care. In particular, the way the cancer diagnosis was disclosed to the patient received more attention; and the protocol successfully encouraged more attention to the psycho-social aspects of treatment.
Another change in care was the structural inclusion of contact with fellow-patients in the care-process, by offering written information about their organisation and relevant telephone numbers, and drawing attention to the possibility of contact with a fellow-patient during hospitalisation. Most patients reported that they had been made aware of the existence of fellow- sufferers' groups and that they did know how to contact them. The activities of care-professionals in informing patients about the fellow-sufferers' organization had increased. It is clear that care-professionals can have a significant and positive effect on the initiative of breast cancer patients to seek contact with fellow-patients [21].
Equally interesting are the differences in response beween nurses and other professionals. In general, it can be said that nurses have a more positive attitude to the protocol's utility, in the interests of both the patients and themselves and of the interaction between the two parties. Why this might be so cannot be explained here. It may be that the finding represents a positive response-set or a socially desirable response on the part of the nurses. One should also bear in mind that the two groups differ in respect of age, experience and gender: the nurses are significantly younger, have fewer years of experience with breast cancer patients; and almost all are female, as opposed to somewhat under one-half of the other care-professionals. They may be more open to the information and assistance which a protocol can give them in carrying out their caring duties, and to its patient-centred approach. Specialists and others may be reluctant to admit that their care-activities are open to significant change; or that patients could ever be in the possession of contradictory information, for example.

Practical implications

The implementation and evaluation of the breast-cancer treatment and care- protocol suggests that it:

1 enables care-professionals to attune their various care-, information- and guidance-activities to those of their colleagues. Once introduced, it gives direction to their activities.
2 is an effective informational instrument. It acquaints both care-professionals and patients in a full and detailed manner about the entire line of care.
3 forms a good basis for continuity of information for women who have been

operated on for breast cancer.

4 leads to more balanced attention to the four functions of patient information.

5 when used by patients, leads to a strengthening of the patient's position. A patient's version of the protocol - together with the present care-professionals' protocol - should form a viable instrument for bringing about a sharing by care-professionals and patient of responsibility for treatment.

Working with the protocol was positively evaluated, both with regard to its content and its form, and by both patients and care-professionals. It contributed to an improvement in the continuity of information. The use of a multidisciplinary protocol was thought to be a good idea, with lessons for the way in which the care-process could be better integrated across disciplines. Since using the protocol, patients were better prepared for, and more involved in, their treatment; and were able to pose different, and more focused, questions. The fact that the opinions of patients and care-professionals are very similar is an interesting finding in itself, which is not consistent with other research results [16,17,35,36]. This may be due to the fruitful collaboration of care-professionals and patients in the steering and working-groups which supported the development and integration of the protocol.

References

1 Dekkers, F. *Patiëntenvoorlichting:De onmacht en de pijn*, Baarn:Ambo, 1981.

2 Bokma J. Patiëntenvoorlichting: kiezen in vierstromenland.
Het Ziekenhuis 1984;14:750-753.

3 Cassileth BR, Zupkis KV, Sutton-Smith K, March V. Information and participation preferences among cancer patients.
Ann Int Med 1980;92:832-836.

4 Fredette SL. A model for improving cancer patient education. *Cancer Nurs* 1990;13:207-215.

5 Williams PD, Valderrama DM, Gloria MD, Pascoguin LG, Saavedra LD, De La Rama DT, et al. Effects of preparation for mastectomy/hysterectomy on women's post-operative self-care behaviors. *Int J Nurs Stud* 1988;25:191-206.

6 Derdiarian A. Informational needs of recently diagnosed cancer patients. A theoretical framework. *Cancer Nurs* 1987;10:107-115.

7 Cunningham AJ, Lockwood GA, Cunningham JA. A relationship between self-perceived self-efficacy and quality of life in cancer patients. *Patient Educ Couns* 1991;17:71-78.

8 Suominen T, Leino-Kipli H, Laippala P. Nurses' role in informing breast cancer patients: a comparison between patients' and nurses' opinions. *J Adv Nurs* 1994;19:6-11.

9 Mandemaker, T., Pruyn, J.F.A. and Jonkers-Kuiper, L. *Continuiteit in de patiëntenvoorlichting.Een verkennende studie*, Tilburg/Utrecht:IVA/NIZW, 1990.

10 Grahn G, Johnson J. Learning to cope and living with cancer. *Scand J Caring Sci* 1990;4:173-181.

11 Cuisinier MCJ, van Eijk JTM, Jonkers R, Dokter HJ. Psychosocial care and education of the cancer patient: strengthening the physician's role. *Patient Educ Couns* 1986;8:5-16.

12 Rimer B, Keintz MK, Glassman B. Cancer patient education: reality and potential. *Prev Med* 1985;14:801-818.

13 Lerman C, Daly M, Walsh WP, Resch N, Seay J, Barsevick RN, et al. Communication between patients with breast cancer and health care providers. Determinants and implications. *Cancer* 1993;72:2612-2620.

14 Borehan P, Gibson D. The informative process in private medical consultations: a preliminary investigation. *Soc Sci Med* 1978;12:409-416.

15 Waitzkin H, Stoeckle JD. Information control and the micropolitics of health care: summary of an ongoing research project. *Soc Sci Med* 1976;10:263-276.

16 Suominen T. How do nurses assess the information received by breast cancer patients? *J Adv Nurs* 1993;18:64-68.

17 Strull WM, Lo B, Charles G. Do patients want to participate in medical decision making? *The Journal of the American Medical Association* 1984;21:2990-2994.

18 Thornton HM. Breast cancer trials: a patient's viewpoint. *Lancet* 1992;339:44-45.

19 Damian D, Tattersall MHN. Letters to patients: improving communication in cancer care. *Lancet* 1991;338:923-926.

20 Greenfield S, Kaplan S, Ware JE. Expanding patient involvement in care. Effects on patient outcomes. *Ann Int Med* 1985;102:520-528.

21 Borne, H.W.van den, and Pruyn, J.F.A. *Lotgenotencontact bij kankerpatiënten. Dissertatie,* Assen/Maastricht:Van Gorcum, 1985.

22 Borne HWvan den,, Pruyn JFA, van Dam-de Mey K. Self-help in cancer patients: A review of studies on the effect of contacts between fellow-patients. *Patient Educ Couns* 1986;4:367-385.

23 Borne HWvan den,, Pruyn JFA, van den Heuvel WJA. Effects of contacts between cancer patients on their psychosocial problems. *Patient Educ Couns* 1987;9:33-38.

24 Eberlein TJ. Current management of carcinoma of the breast. *Ann Surg* 1994;220:121-136.

25 Conkling VK. Continuity of care issues for cancer patients and families. *Cancer* 1989;64;suppl.:290-294.

26 Tilley JD. The nurse's role in patient education: incongruent perceptions among nurses and patients. *J Adv Nurs* 1987;12:291-301.

27 Lillington LB, Padilla GV, Sayre JW, Chlebowski RT. Factors influencing nurses' breast control activity. *Cancer Practice* 1993;1:307-314.

28 Wolfe LC. A model system. Integration of services for cancer treatment. *Cancer* 1993;72:3525-3530.

29 Klop R, Wijmen FCBvan, Philipsen H. Patients' rights and the admission and discharge process. *J Adv Nurs* 1991;16:408-412.

30 Wouden, J.C.van der *Samenwerking tussen huisartsen en specialisten bij mensen die lijden aan kanker;verslag van de eerste onderzoeksfase*, Rotterdam:University of Rotterdam, 1985.

31 Schadée, E. *Overleden patiënten*, Amsterdam:University of Amsterdam, 1986.

32 Vleeshouwers, E.M. *De ontwikkeling, introductie en evaluatie van een voorlichtingsmodel*, Maastricht:Comprehensive Cancer Centre Limburg, 1993.

33 Pruyn JFA. Coping with stress in cancer patients. *Patient Educ Couns* 1983;5:57-62.

34 Roberts CS, Cox CE, Reintgen DS, Baile WF, Gibertini M. Influence of physician communication on newly diagnosed breast patients' psychologic adjustment and decision-making. *Cancer* 1994;74:336-341.

35 Jennings BM, Muhlenkamp AF. Systematic misperception: oncology patients' self-reported affective states and their care-givers' perceptions. *Cancer Nurs* 1981;12:485-489.

36 Ford S, Fallowfoeld L, Lewis S. Can oncologists detect distress in their out-patients and how satisfied are they with their performance during bad news consultations? *Br J Cancer* 1994;70:767-770.

37 Fallowfield L. Giving sad and bad news. *Lancet* 1993;341:476-478.

38 Bartlett EE. Quality improvement,practice guidelines and patient education (Editorial). *Patient Educ Couns* 1991;18:1-2.

39 Meade CD, Diekmann J, Thornhill DG. Readability of American Cancer Society patient education literature. *Oncol Nurs Forum* 1992;19:51-55.

40 Stephens ST. Patient education materials: are they readable? *Oncol Nurs Forum* 1992;19:83-85.

41 Penman DT, Holland JC, Bahna GF, Morrow G, Schmale AH, Derogatis LR, et al. Informed consent for investigational chemotherapy: patients' and physicians' perceptions. *J Clin Oncol* 1984;7:849-855.

42 Wersch, A.van, Bonnema, J., van Geel, A.N., Pruyn, J.F.A. and Wiggers, Th. *Continuiteit van voorlichting bij mammacarcinoompatiënten*, Utrecht/Rotterdam:NIZW, 1995.

43 Wersch, A.van, Prinsen, B., Geel, A.N.van and Wiggers, Th. *Contnuïteit van voorlichting bij borstkanker. Interdisciplinaire samenwerking rond voorlichting, zorg en behandeling. (Continuity of information for breast cancer patients. Interdisciplinary collaboration in patient information, care and treatment)*, Utrecht:NIZW, 1994.

44 Kerner JF, Mortenson LE, Anderson PN, Enck R, Sturgeon SR. Utilization of local patient management guidelines and protocols in CHOP hospitals. *Prog Clin Biol Res* 1986;216:117-129.

45 Sheldon TA, Borowitz M. Changing the measure of quality in the NHS: from purchasing activity to purchasing protocols. *Qual Health Care* 1993;2:149-150.

46 Greco PJ, Eisenberg JM. Changing physicians' practices. *N Engl J Med* 1993;339:1271-1273.

Chapter 8

General discussion

Introduction

The past decades have shown a number of improvements in the local management of primary breast cancer. Surgery continues to play a major role in this treatment, but its scope has changed dramatically in the last decades. Randomised trials have uniformly confirmed that the survival rate after breast conserving therapy is equivalent to that after modified radical mastectomy [1]. Improvements in pre-treatment evaluation and management of early stage breast cancer have emerged including screening mammography, more precise pathological assessment with regard to margin involvement and ductal carcinoma in situ, and an increased used of reexcision [2]. New possibilities have arisen for individualizing local treatment and improvements have been made to prevent morbidity. In addition there is an increased awareness in the need for psychosocial support, postoperative care, and patient and family education.

Axillary lymph node dissection still plays an important role in both the diagnostic and therapeutic approach of primary breast cancer. In this thesis results of studies pertaining to morbidity of axillary dissection, postoperative care, and to a new approach for the diagnosis of axillary lymph node metastases are presented. In this chapter the results will be discussed and recommendations for patient management and future research will be given.

Serous fluid production and drainage

Serous fluid production commonly occurs in axillary wounds following lymph node dissection. Although several techniques have been advocated to reduce fluid production [3-11], the source and composition of the fluid remains unclear. In Chapter 2 the chemical composition of the fluid has been analyzed. We demonstrated that the fluid is similar to peripheral lymph, although it contains higher levels of protein and only few cells. Reliable data on the composition of lymph other than chyle from the thoracic duct are virtually absent especially from man [12-16]. One explanation for this is the difficulty to obtain lymph fluid from the tiny lymphatic vessels with a low flow.

The fluid formed in the axilla contains no fibrinogen which means that the cessation of its production cannot be caused by coagulation but must be provided by other wound healing processes such as collagen formation as it obstructs disrupted lymph channels, or the formation of other components of scar tissue. Fibroblasts invade a wound by the 2nd or 3rd postoperative day and collagen synthesis begins by the 4th or 5th day. By day 10 fibroblasts are the dominant cell population [17]. This is the period in which normally fluid production ceases (Chapter 3 and 5). Fibroblast growth inhibition is associated with protracted seroma formation in reconstructive

vascular surgery [18]. It would be interesting to elucidate if this mechanism is also responsible for protracted seroma formation after axillary dissection as it is observed in some patients. If serous fluid from the axilla does not clot and collagen synthesis in the wound is responsible for the ultimate cessation of its production, it is also understandable why techniques aiming at reduction of fluid formation are ineffective. Although diminishing dead space is considered an important preventive measure for seroma formation [4,5], there is only one randomised trial (n=39) supporting this hypothesis [3]. This makes the results difficult to generalise.

We conducted a randomised trial to study the influence of negative pressure in the drainage system (low vacuum with a negative pressure of 115 mm Hg (15.3 kPa) versus high vacuum 720 mm Hg (95.9 kPa)) on serous fluid formation and duration of drainage (Chapter 3). In theory high vacuum drainage obliterates the wound more adequately, but we found no effect on the amount of fluid production from the axilla compared with low vacuum drainage (Chapter 3). Recent studies have shown that neither immobilization of the shoulder [19] nor sealing of the wound with bovine thrombin [20] or fibrin glue [21] causes a reduction of serous fluid formation. It is not likely that further studies will shortly reveal new mechanisms for the elimination of serous fluid production by which the wound healing process could be accelerated. A meticulous surgical technique avoiding blunt dissection and clipping or ligating of lymphatic channels may reduce the lymphatic leak, but the contribution of this technique to the reduction of fluid formation is difficult to objectivy. In any case, serous fluid production will remain an inevitable result of surgical axillary lymph node dissection. Until the production ceases spontaneously, some form of drainage is necessary. Preference for high or low vacuum drainage systems may be determined by factors such as cost, manageability, and patient comfort. The optimal duration of drainage is unclear. Fluid collections after drain removal, usually referred to as seroma, occur frequently. We found an incidence of seroma formation of 18 and 11 % if drains were removed when production of fluid was less than 30 ml on two consecutive days (Chapter 3) and of 10% and 8 % when drains were removed when production was less than 30 ml for 24 hours (Chapter 5). These results are comparable with studies using the same drainage strategy [22,23]. There are studies that suggest that early drain removal results in a low rate of seroma formation [24,25], while in others high incidences of seroma are reported [26,27], albeit without affecting the rate of infections [27]. Obviously, there is not much difference between short-term or long-term drainage, as in both cases postoperative seroma formation occur. The question of what is more inconvenient for the patient, closed suction drainage or percutaneous aspirations of the fluid, has not been addressed systematically in the studies on early drain removal.

We chose in our study on early discharge to not combine the new discharge policy with changes in our drainage policy. We studied the effects of discharge with a

drain in situ as a way to control the morbidity of serous fluid formation and to possibly enhance the quality of treatment for patients after axillary dissection.

Early hospital discharge after axillary dissection

Feasibility of the procedure

In a randomised trial comparing discharge from hospital 4 days after surgery with drain in situ, with discharge after drain removal (mean 9 days in hospital) it was found that there were no adverse effects of a short stay in hospital on the rate of complications, total volume and duration of axillary drainage, or the incidence of seroma formation (Chapter 5). However, the number of patients in this study was too small to detect a difference less than 5% in rates of wound complication; a sample size of more than 800 patients would than have been necessary. Short stay patients were satisfied with their length of stay: only 4 % would have preferred a longer stay in hospital both after 4 weeks and after 4 months and nearly all patients (93% and 96%) would recommend short stay to other patients. One third of long stay patients would have preferred a shorter stay, indicating that the benefits of short stay may be underestimated by this group of patients.
We conclude that early discharge after surgery for breast cancer is feasible as there are no adverse medical effects of the procedure and patients are highly satisfied with their length of stay.

Psychosocial rehabilitation and social support

One of the aims of our study comparing short and long postoperative hospital stay was to assess the effects of early hospital discharge on psychosocial rehabilitation. We found no adverse effects in the experience of psychosocial problems, physical and psychological complaints, and the coping strategies used (Chapter 5). Prior to surgery, patients in the short stay group scored higher on scales of depression than long stay patients, but these depressive feelings preceding the experimental treatment had no predictive value for mood disturbances following early discharge (Chapter 5). After surgery, patients in the short stay group were more likely to discuss their disease with their families. A possible explanation for this may be that short stay patients were at home earlier in the recuperation phase and still had their drains in situ, enhancing the interaction with the partner, children and other relatives in the direct physical care process. This may facilitate communication over the disease and its consequences and provide more opportunity for social support. Social support is found to be a promoter of better psychosocial adjustment after breast cancer treatment [28-31]. Particularly the emotional support offered by partners, relatives and friends - defined as those who would show empathy and with whom they could talk about their illness - is perceived as very important [32,33]. Both short stay and long stay

patients have a need for family-support, which was measured by the number of hours spent by informal care-givers interacting with the patient during the primary treatment phase (Chapter 6).

Conditions for early hospital discharge at patient level and recommendations for patient management

It has been demonstrated that early discharge following surgery is feasible for breast cancer patients. The benefits of the procedure compared with the traditional long stay are that patient satisfaction with the length of hospital stay is increased and that the early discharge enhances the opportunity for social support within the family. This means that the procedure can be implemented in other centers, provided that continuity of care and information are guaranteed. In our study we took the following measures to fulfill this requirement: district nursing care referral and the development and implementation of a multidisciplinary care-protocol.

All short stay patients were offered district nursing care and 89 % of the short stay population benefited from it. The district nurse spent in total a mean of 2.3 hours with each patient. Patients reported having no problems with the discontinuity in the presence of nursing and were satisfied with this form of care. Before the start of the study, district nurses had no experience with the postoperative care for this category of patients. Two teaching sessions on care of the breast cancer patient were offered by the two hospitals involved. The educational program included courses on surgical treatment of breast cancer, postoperative care, possible complications, and psychosocial concerns of this patient population. If district nurses were confronted with problems in patient care, they consulted with hospital cancer care nurses.

When introducing the early discharge policy in other centers, than the organizational structure of our protocol can be used and part of the care process can be delegated to local affiliates. The hospitals should arrange for district nursing care and offer educational programs to the district nursing staff. If district nurses cannot be utilized for the short stay procedure, than patient care following discharge should be performed in the outpatient department by a trained nurse.

Replacing postoperative hospitalisation with outpatient department activities and extramural care emphasizes the need for attuning intra- and extramural care and information. In this thesis the development, utilization and evaluation of a multidisciplinary care-protocol has been described (Chapter 7). This protocol provides a comprehensive description of the sequential steps of the care process which attunes the various services delivered by health care professionals. It has proven to be an effective informational instrument for both professionals and patients, and contributed to an improvement in the continuity of care and information services (Chapter 7).

The protocol was intended both for health professionals and for patients. More

than 350 copies have been distributed among hospitals, and home care and patient organisations [34]. Whether a different version of the protocol for patients will have more value as an informational instrument is currently under investigation [34].
Although the protocol is an effective instrument for attuning information of the multidisciplinary team, it gives no insight into what is actually communicated to the patient. To ensure continuity in the information services provided to patients, each professional should document his or her role in this process. One could chose to document the information given in a diary that patients carry with them during visits with clinicians and allied personnel [35]. This should assure that all information will be given. In the Netherlands it is the responsibility of the physicians and their organisations to play a pivotal role in developing these patient oriented information services.

Conditions for early discharge: societal level

Although the short stay procedure is feasible from perspective of the patient, successful implementation remains determined by social factors. These are that the costs of this new treatment compared to long stay treatment will not increase for society, and that of extent of substitution of care from intra- to extramural is feasible.
Societal cost of both treatments were calculated and it was demonstrated that the total cost of care was reduced with US $ 1320 per patient by introducing the short stay program (p=0.0007) (Chapter 6). In the Netherlands 80 % new breast cancer patients are treated yearly by breast amputation or breast conserving therapy including axillary lymph node dissection [36]. In 1994 10050 new breast cancer patients were diagnosed [37]. One can estimate from our study that maximally 22 % of this population will not be suitable for early hospital discharge for reasons of an inappropriate home situation or of patient refusal to follow the short stay procedure (in our study out of 173 patients 22 refused participation before randomisation and 6 short stay patients refused participation after randomisation; 10 patients were excluded because of an inappropriate home situation). If the short stay procedure will be introduced nationwide, it can be estimated that a reduction in cost of minimally 78 % x (80 % x 10050) x $1320 = $ 8.277.984 and maximally of $ 10.612.800 can be achieved by replacing hospital care by home care. The savings result from the substitution of expensive in hospital care by the much more inexpensive home nursing care. We found no increase in the number of outpatient or general practitioner consultations after early hospital discharge. The mean total amount of hours of household home help and informal care used during the first month was higher for the short stay group, but the difference was not significant. The variance in use of home help care and informal care in the home situation was highly skewed to the left as indicated by the value of the median which was much smaller than the mean. This means that there are many 'modest' consumers and relatively few 'large' consumers [38]. It is to

be expected that the demand for professional home care may increase if the early discharge policy is introduced on a nation wide scale, while the need for outpatient medical care facilities will not be affected.

Future research

As outlined above, serous fluid is always formed after axillary lymph node dissection and it is not to be expected that new methods will be shortly available that can completely prevent its formation. Some form of evacuation of the fluid from the axilla remains necessary. It is still unclear if early drain removal - before cessation of the fluid production -, or even no drainage, is more convenient for the patient then removal of the drain until fluid production is minimal. Experiences with axillary lymphadenectomy without drainage have been reported with no adverse effects on the incidence of infections [39], but several issues remain to be addressed in future research: (i) are there any advantages for the patient if the drain is removed before cessation of fluid production; (ii) what is the risk for seroma formation after early drain removal; (iii) if seroma formation is increased, what are the effects from the patient perspective of seroma aspirations compared to prolonged closed suction drainage. New studies regarding these subjects should give insight in what procedures are most convenient for the patient in managing the problem of serous fluid formation. Families, relatives and friends play a large role in delivering care to patients and early hospital discharge has an positive influence on social support. This fact requires that more research should be done to identify issues relevant to the role of the family in the care process. These may encompass the role of the family during the initial patient information sessions, awareness of the anticipated physical, psychological and spiritual effects of diagnosis and treatment, the development of coping strategies, stress and pain management techniques, and support to negotiate the health care system.

Worldwide, there is an increasing trend in employing brief periods of hospitalisation following breast cancer surgery, and particulary in the US. Two American studies [39,40] report day surgery for this patient population. Four American [41-44] and two European [24,45] studies, and one study from India [46], describe the results of early discharge on day one or two; and three American [47-49] and one European [50] study discharge after three days. The short stay patients in our study were discharged after three days, that is early in the morning of the fourth day. The studies from other countries suggest that the length of stay in the hospital can be further reduced. However, the effects on psychosocial rehabilitation of breast cancer patients treated on outpatient or very short hospital stay basis, as it is practiced in several centers, is unknown. It would be interesting to evaluate American practice in the European setting paying special attention to the psychosocial effects of this policy and to how the continuity of information can be assured beginning at the time of diagnosis and

ending after full rehabilitation.
Pain control must be optimal when patients are discharged the day of surgery or shortly thereafter. Suboptimal pain management is found to be the main reason to consult general practitioners or hospital staff following day surgery [51]. In our study intravenous opiates were used for the first postoperative days followed by oral pain medication. Although pain management was not experienced to be a problem for short stay patients compared to long stay patients (data not published), it is worthwhile to evaluate innovative analgesic strategies which can avoid postoperative intravenous administration such as the use of long acting local anesthetics administered in the wound and around the nerves of the axilla [40], and locally administrated non-steroidal antiinflammatory agents [52].

The role of axillary dissection

Serous fluid formation has a short term impact on quality of life in breast cancer patients. Long-term sequelae of axillary lymph node dissection are also fairly common, even in contemporary surgical series when conservative surgical techniques are employed [53-55]. Individualizing breast cancer therapy so that axillary lymph node dissection can be limited to women who are most likely to benefit from the procedure is essential.
Recently the new technique of the 'sentinel node' biopsy has been developed [56-58]. It allows the excision of a physiologically representative node to be removed from the axilla that has a predictive value as high as 97.5 % for axillary lymph node metastases [56]. We developed a technique using an ultrasound guided fine needle aspiration biopsy (FNAB) of axillary nodes in clinically node negative patients (Chapter 4). This technique identified 39 of 62 (63%) of node positive patients prior to surgery. Sensitivity was 80% and specificity 100%. The negative predictive value was low (76%) which means that this technique is inferior to the sentinel node biopsy for identifying node negative patients. However, ultrasound guided FNAB has a positive predictive value of 100% making the technique suitable to identify a majority of node positive patients in whom sentinel node biopsy thus can be avoided. Another application of our technique is in a group of patients treated with induction chemotherapy for locally advanced primary breast cancer. Ultrasound guided FNAB can support the clinical estimation of the response for establishing a reliable prognosis and the selection of appropriate therapy.
There are two major developments in the area of breast cancer diagnosis and treatment influencing the decision on which indications should be used for determining when axillary dissection should be performed in clinically node negative patients. They are (i) the increased frequency of detecting very small breast cancers by mammography and (ii) the increased use of adjuvant systemic therapy on basis

of primary tumor characteristics regardless of nodal status.
Screen-detected breast cancers are smaller than those detected in symptomatic populations [59,60] and decreased tumor size is associated with the decreased incidence of nodal metastases [61]. However, tumor size, whether alone or in combination with other prognostic factors, cannot be used to reliably identify a group of breast cancer patients with a very low risk of axillary nodal metastases [62,63]. If the high sensitivity of 'sentinel' node biopsy in patients with small tumors can be reproduced, axillary dissection can be avoided for many breast cancer patients, since the majority of patients is node-negative.
We have come a long way since the time when the decision to treat with adjuvant therapy was based upon the presence or absence of positive lymph nodes. Axillary lymph node status is a strong predictor of outcome, but axillary lymph node involvement is not always a predictor of disseminated disease, since some of the patients in this high risk group will be cured by local therapy alone [64]. On the other hand, about 25 % of axillary node negative patients will have an unfavorable outcome. Other histopathological prognostic factors, such as tumor size, histological subtype and nuclear grade, are being used to predict the biological behavior of breast cancer. The potential utility of newer, molecular prognostic factors is yet to be fully integrated with conventional histopathological and clinical prognostic assessments [65]. In the United States, adjuvant therapy is now routinely recommended for all patients with tumors measuring 1 cm or larger, independent of their nodal status [66,67]. Axillary dissection for the determination of lymph node metastases in this group of patients is only needed if identification of the number of nodes will change the choice of adjuvant therapy, as in the experimental high dose chemotherapy trials, or will determine which patients will benefit from chest wall radiotherapy. Node-positive patients can be identified prior to surgery by ultrasound guided FNAB or sentinel node biopsy.
Although axillary dissection may not be necessary to establish the use of adjuvant chemotherapy, it is a valuable technique for maintaining local control in the axilla [68-71]. An alternative therapy for the clinically node negative axilla is axillary irradiation which has a local failure rate between 0.8 and 4 % [68,72]. In patients with gross nodal disease axillary surgery remains the preferred technique.
In conclusion, the role of axillary dissection is currently being reexamined. In the nearby future, more limited procedures will be available to identify patients who have no added benefit from axillary lymph node dissection. This will prevent the morbidity of axillary lymph node dissection in most patients with early stage breast cancer following their surgery.

Conclusion

The results of the studies reported in this thesis provide several leads for improvement of the integral process of diagnosis, treatment and care of the breast cancer patient in relation to the performance of axillary lymph node dissection. This information contributes to the growing knowledge of the present day patient-centered management of women with breast cancer. The overall objective being to prevent unnecessary physical and psychological morbidity and to increase the quality of life for this patient population.

References

1 Early Breast Cancer Trialists' Collaborative Group . Effects of radiotherapy and surgery in early breast cancer:an overview of the randomized trials. *N Engl J Med* 1995;333:1444-1445.

2 Nixon AJ, Troyan SL, Harris JR. Options in the local management of invasive breast cancer. *Sem Oncol* 1996;23:453-463.

3 Coveney EC, O'Dwyer PJ, Geraghty JG, O'Higgins NJ. Effect of closing dead space on seroma formation after mastectomy. A prospective randomized clinical trial. *Eur J Surg Oncol* 1993;19:143-146.

4 Aitken DR, Hunsaker R, James AG. Prevention of seromas following mastectomy and axillary dissection. *Surg Gynecol Obstet* 1984;158:327-330.

5 Chilson TR, Chan FD, Lonser RR, Wu TM, Aitken DR. Seroma prevention after modified radical mastectomy. *Am Surgeon* 1992;58:750-754.

6 Uden P, Aspegren K, Balldin G, Garne JP, Larsson SA. Fibrin adhesive in radical mastectomy. *Eur J Surg* 1993;159:263-265.

7 Gilly FN, Carry PY, Brachet A, Curtil A, Burgard G, Buisson L, et al. Efficacité d'une colle de fibrine sur la lymphostase au cours des curages ganglionnaires. *Ann Chir* 1994;48:194-196.

8 Waclawiczek HW, Pimpl W. Lymphfisteln nach Lymphknotendissektionen - Verhütung und Behandlung mit Hilfe der Fibrinverklebung. *Chirurg* 1986;57:330-331.

9 Ansanelli VW. The CO2 laser in axillary dissection for breast cancer. *Lasers Surg Med* 1987;7:87. (Abstract)

10 Wyman A, Rogers K. Radical breast surgery with a contact Nd:YAG laser scalpel. *Eur J Surg Oncol* 1992;18:322-326.

11 Miller E, Paull DE, Morrisey K, Cortese A, Nowak E. Scalpel versus electrocautery in modified radical mastectomy. *Am Surgeon* 1994;

12 Engeset A, Olszelwski W, Jaeger PM, Sokolowski J, Theodorsen L. Twenty-four hour variation in flow and composition of leg lymph in normal men. *Acta physiol scand* 1977;99:140-148.

13 Reichl D, Myant NB, Pflug JJ. Concentration of lipoproteins containing apolipoprotein B in human peripheral lymph. *Biochim Biophys Acta* 1977;489:98-105.

14 Reichl D, Pflug JJ. The concentration of apolipoprotein A-I in human peripheral lymph. *Biochim Biophys Acta* 1982;710:456-463.

15 Braun WE, Banowsky LH, Straffon RA, Nakamoto S, Kiser WS, Popwniak KL, et al. Lymphoceles associated with renal transplantation. *Am J Med* 1974;57:714-729.

16 Yoffey, J.M. and Courtice, F.C. *Lymphatics, lymph and lymphoid tissue*, Cambridge:Harvard University Press, 1956.

17 Madden, J.W. and Arem, A.J. Wound healing:biologic and clinical features. In: *Textbook of surgery*, edited by Sabiston, D.C. Philadelphia: W.B.Saunders Company, 1986, p. 193-213.

18 Ahn SS, Williams DE, Thye DA, Cheng KQ, Lee DA. The isolation of a fibroblast growth inhibitor associated with perigraft seroma. *J Vasc Surg* 1994;20:202-208.

19 Browse DJ, Goble D, Jones PA. Axillary node clearance: who wants to immobilize the shoulder? *Eur J Surg Oncol* 1996;22:569-570.

20 Burak WE, Goodman PS, Young DC, Farrar WB. Seroma formation following axillary dissection for breast cancer: risk factors and lack of influence of bovine thrombine. *J Surg Oncol* 1997;64:27-31.

21 Medl M, Mayerhofer K, Peters-Engl C, Mahrhofer P, Huber S, Buxbaum P, et al. The application of fibrin glue after axillary lymphadenectomy in the surgical treatment of human breast cancer. *Anticancer Res* 1995;15:2843-2845.

22 Tadych K, Donegan WL. Postmastecomy seromas and wound drainage. *Surg Gynecol Obstet* 1987;165:483-487.

23 Vinton AL, Traverso LW, Jolly PC. Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection. *Am J Surg* 1991;161:584-588.

24. Yii M, Murphy C, Orr N. Early removal of drains and discharge of breast cancer surgery patients: a controlled prospective clinical trial. *Ann R Coll Surg Engl* 1995;77:377-379.

25 Parikh HK, Badwe RA, Ash CM, Hamed H, Freitas RJr, Chaudary MA, et al. Early drain removal following modified radical mastectomy: a randomized trial. *J Surg Oncol* 1992;51,4:266-269.

26 Inwang R, Hamed H, Chaudary MA, Fentiman IS. A controlled trial of short-term versus standard axillary drainage after axillary clearance and iridium implant treatment of early breast cancer. *Ann R Coll Surg Engl* 1991;73:326-328.

27. Somers RG, Jablon LK, Kaplan MJ, Sandler GL, Rosenblatt NK. The use of closed suction drainage after lumpectomy and axillary node dissection for breast cancer. *Ann Surg* 1992;215:146-149.

28 Nelles WB, McCaffrey RJ, Blanchard CG, Ruckdeschel JC. Social supports and breast cancer:a review. *J Psychosoc Oncol* 1991;9:21-35.

29 Bloom JR. Social support, accommodation to stress and adjustment to breast cancer. *Soc Sci Med* 1982;16:1329-1338.

30 Irvine D, Brown B, Crooks D, Roberts J, Brown G. Psychosocial adjustment in women with breast cancer. *Cancer* 1991;67:1097-1117.

31 Spiegel D, Bloom JR, Gottheil E. Family environment as a predictor of adjustment to metastatic breast carcinoma. *J Psychosoc Oncol* 1983;1:33-44.

32 Smith EM, Redman R, Burns TL, Sagert KM. Perceptions of social support among patients with recently diagnosed breast, endometrial, and ovarian cancer:an exploratory study. *J Psychosoc Oncol* 1985;3:65-81.

33 Friedman LC, Baer PE, Nelson DV, Lane M, Smith FE, Dworkin RJ. Women with breast cancer: perception of family functioning and adjustment to illness. *Psychosom Med* 1988;50:529-540.

34 Prinsen, B., Personal communication. 1998.

35 van Wersch AMEA, de Boer ME, van der Does E, de Jong P, Knegt P, Meeuwis CA, et al. Continuity of information in cancer care:evaluation of a logbook. *Patient Educ Couns* 1997;31:223-236.

36 Results: Breast cancer. In: *Incidence of Cancer in the Netherlands 1991*, edited by Visser, O., Coebergh, J.W.W. and Schouten, L.J. Netherlands Cancer Registry, 1994, p. 26-31.

37 Incidence data. In: *Incidence of Cancer in the Netherlands 1994*, edited by Visser, O., Coebergh, J.W.W., Schouten, L.J. and van Dijck, J.A.A.M. Utrecht: Netherlands Cancer Registry, 1997, p. 31.

38 Koopmanschap MA, Ineveld BM, Miltenburg TEM. Costs of home care for advanced breast and cervical cancer in relation to cost-effectiveness of screening. *Soc Sci Med* 1992;35:979-985.

39 Jeffrey SS, Goodson WH, Ikeda DM, Birdwell RL, Bogetz MS. Axillary lymphadenectomy for breast cancer without axillary drainage. *Arch Surg* 199;130:909-913.

40 Goodman AA, Mendez AL. Definitive surgery for breast cancer performed on an outpatient basis. *Arch Surg* 1993;128:1149-1152.

41 Clark JA, Kent RB. One-day hospitalization following modified radical mastectomy. *Am Surg* 1992;58:239-242.

42 Kambouris A. Physical, psychological, and economic advantages of accelerated discharge after surgical treatment for breast cancer. *Am Surg* 1996;62:123-127.

43 Sesto ME, Hall RM, Esselstyn CB, Hardesty IJ. Early discharge following mastectomy: 239 consecutive patients over three years. *Contemp Surg* 1989;35:38-40.

44 Tarazi R, Esselstyn CB, Kuivila T, Hardesty I. Early hospital discharge following mastectomy. *Cleve Clin Q* 1984;51:579-584.

45 Boman L, Björvell H, Cedermark B, Theve NO, Wilking N. Effects of early discharge from hospital after surgery for primary breast cancer. *Eur J Surg* 1993;159:67-73.

46 Suryanarayana Deo SV, Shukla NK, Arun Kumar Goel , Kishore J. Short stay surgery for breast cancer: an audit of an experience in a regional cancer centre in northern India. *Eur J Surg Oncol* 1997;23:335-338.

47 Orr RK, Ketcham AS, Robinson DS, Moffat FL, Tennant ND. Early discharge after

mastectomy. A safe way of diminishing hospital costs. *Am Surgeon* 1987;53:161-163.

48 Litvak S, Borrero E, Katz R, Munoz E, Wise L. Early discharge of the postmastectomy patient: unbundling of hospital services to improve profitability under DRGs. *Am Surgeon* 1987;53:577-579.

49 Pedersen SH, Douville LM, Eberlein TJ. Accelerated surgical stay programs. A mechanism to reduce health costs. *Ann Surg* 1994;219:374-381.

50 Holcombe C, West N, Mansel RE, Horgan K. The satisfaction and savings of early discharge with drain in situ following axillary lymphadenectomy in the treatment of breast cancer. *Eur J Surg Oncol* 1995;21:604-606.

51 Ghosh S, Sallam S. Patient satisfaction and postoperative demands on hospital and community services after day surgery. *Br J Surg* 1994;81:1635-1638.

52 Bosek V, Cox CE. Comparison of analgesic effect of locally and systemically administered keterolac in mastectomy patients. *Ann Surg Oncol* 1996;3:62-66.

53 Ivens D, Hoe AL, Podd TJ, Hamilton CR, Taylor I, Royle GT. Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992;66:136-138.

54 Hladiuk M, Huchcroft S, Temple W, Schnurr BE. Arm function after axillary dissection for breast cancer: a pilot study to provide parameter estimates. *J Surg Oncol* 1992;50:47-52.

55 Werner RS, McCormick B, Petrek J, et al. . Arm edema in conservatively managed breast cancer: obesity is a major predictive factor. *Radiology* 1991;180:177-184.

56. Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet* 1997;349:1864-1867.

57 Pijpers R, Meijer S, Hoekstra OS, Collet GJ, Emile FI, Comans RP. Impact of lymphoscintigraphy on sentinel node identification with technetium-99m-colloidal albumin in breast cancer. *J Nucl Med* 1997;38:366-368.

58 Borgstein PJ, Meijer S, Pijpers R. Intradermal blue dye to identify sentinel lymph node in breast cancer. *Lancet* 1997;349:1668-1669.

59 Holland PA, walls J, Boggis CR, Knox F, Baildam AD, Bundred NJ. A comparison of axillary node status between cancers detected at the prevalence and first incidence breast screening rounds. *Br J Cancer* 1996;74:1643-1646.

60 Frankel SD, Sickles EA, Curpen BN, Sollitto RA, Ominsky SH, Galvin HB. Initial versus subsequent screening mammography: comparison of findings and their prognostic significance. *Am J Roentgenol* 1995;164:1107-1109.

61 Morrow M. Axillary dissection:when and how radical? *Semin Surg Oncol* 1996;12:321-327.

62 Chadha M, Chabon AB, Friedmann P, Vikram B. Predictors of axillary lymph node matastases in patients with T1 breast cancer. *Cancer* 1994;73:350-353.

63 Ravdin P, DeLaurentis M, Wenger C. Can prognostic factors be used to predict the nodal status of breast cancer patients?
Proc Am Soc Clin Oncol 1994;13:56.

64 Gardner B, Feldman J. Are positive nodes in breast cancer markers for incurable disease? *Ann Surg* 1993;3:270-278.

65 Dhingra K, Hortobyagi GN. Critical evaluation of prognostic factors. *Sem Oncol* 1996;23:436-445.

66 Glick JH, Gelber RD, Goldhirsch A, Senn HJ. Meeting highlights:Adjuvant therapy for primary breast cancer. *J Natl Cancer Inst* 1992;84:1479-1485.

67 Berlanger D, Moore M, Tannock I. How American oncologists treat breast cancer: an assessment of the influence of clinical trials. *J Clin Oncol* 1991;9:7-16.

68 Recht A, Pierce SM, Abner A, Vicini F, Osteen RT, Love SM, et al. Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. *J Clin Oncol* 1991;9:988-996.

69 Fisher B, Redmond C, Fisher ER, Bauer M, Wolmark N, Wickerham DL, et al. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985;312:674-681.

70 Crowe JP, Gordon NH, Antunez AR, Shenk RR, Hubay CA, Shuck JM. Local-regional breast cancer recurrence following mastectomy. *Arch Surg* 1991;126:429-432.

71 Dewar JA, Sarrazin D, Benhamou E, Petit J, Benhamou S, Arriagada R, et al. Management of the axilla in conservatively treated breast cancer:592 patients treated at institut Gustave-Roussy. *Int J Radiation Oncology Biol Phys* 1987;13:475-481. .

72 Haffty BG, Fischer D, Fischer JJ. Regional nodal irradiation in the conservative treatment of breast cancer. *Int J Radiation Oncology Biol Phys* 1990;19:859-865.

Summary

Summary

The aim of this thesis was to provide several leads for control of morbidity of axillary dissection in patients with breast cancer. These include considering alternative diagnostic procedures for detection of axillary lymph node metastases, the reduction of serous fluid formation, and improvement of postoperative care management.

Chapter 1 is the general introduction of this thesis. The role of axillary lymph node dissection in the treatment of breast cancer and the morbidity related to this operative procedure are discussed. It is established that serous fluid production, one of the short term complications of the operation, is an important determinator of the length of post-operative hospital stay. On the basis of an overview of the studies exploring the possibility of earlier hospital discharge after surgical treatment for primary breast cancer the relevant aspects of early hospital discharge are determined. These are:

- the effects on complication rates
- patient satisfaction and psychosocial rehabilitation
- the extent of substitution of care and costs
- the importance of continuity of care and information

Chapter 2 focuses on the chemical and cellular composition of the non-haemorrhagic fluid formed in the wound after dissection of axillary lymph nodes. The composition of the fuid is compared with the same constituents in blood and with reported data on the composition of peripheral lymph. Samples of axillary drainage fluid were obtained on the first, fifth, and tenth postoperative days of sixteen patients with breast cancer who underwent axillary dissection as part of a modified radical mastectomy. During the first day the drainage fluid is contaminated with blood from the surgical wound. After day one the fluid changes to a peripheral lymph-like fluid but contains only few cells and more protein. The fluid contains no fibrinogen, making coagulation impossible. The reduction in the fluid production over time must be caused by other wound healing processes such as collagen formation as it obstructs disrupted lymph channels, or the formation of other components of scar tissue.

Chapter 3 describes a randomized trial on the influence of the negative pressure in the drainage system on fluid production and complication rates after axillary dissection for breast cancer. Patients were randomized for either a low vacuum (negative pressure of 115 mm Hg (15.3 kPa)) or a high vacuum drainage system (negative pressure of 720 mm Hg (95.9 kPa)). No statistically significant differences were found between the low vacuum group (n=68) and the high vacuum group (n=73) in:

- volume (728 ml versus 780 ml)
- duration (9.5 days versus 10 days) of fluid production
- number of wound complications (5 versus 6)
- number of infections (3 versus 2)
- incidence of seroma formation.

The drainage volume of the separately drained breast wound after mastectomy and lumpectomy was larger for the high vacuum system (100 ml versus 55 ml; P=0.02). Vacuum loss was more frequent in the high vacuum drain group (11 versus 2, P=0.01), where as leakage around the drain occurred more often in the low vacuum group (18 versus 6, P=0.004). As the production of serous fluid cannot be reduced by one of both drainage systems, and there are no differences in wound complication rates, the preference for high or low vacuum drainage systems may be determined by non medical factors such as cost, manageability, and patient comfort.

In Chapter 4 the accuracy of ultrasonography alone and in combination with fine needle aspiration biopsy (FNAB) for detection of axillary metastases in clinically node negative breast cancer was studied in 148 patients. Results of ultrasonography and FNAB were compared with histopathologic data of the lymph node dissection. The sensitivity of ultrasonography alone is highest (87 %) when size (length > 5 mm) is used as criterion for malignancy, but specificity is rather low (56%). When nodes with a malignant pattern (echopoor or inhomogeneous) are visualized, sensitivity is 36 % and specificity 95 %. Ultrasound guided FNAB increases the sensitivity to 80 %. The specificity of FNAB is 100 % and metastases were detected in 63 % of node positive patients. It is concluded that ultrasound guided FNAB is an easy, reliable and inexpensive method for identifying the majority of patients with positive nodes. In these patients more invasive diagnostic procedures can be avoided. The negative predictive value of the technique is low (76%), which means that this technique is inferior to axillary dissection for the identification of node negative patients.

Chapter 5 focuses on the effects of early hospital discharge after surgery for breast cancer on complication rates and psychosocial rehabilitation, as a way to control the morbidity of serous fluid formation and to possibly enhance the quality of life for these patients. In a randomised trial discharge from hospital 4 days after surgery with drain in situ (short stay) was compared with discharge after drain removal (long stay, mean 9 days in hospital). Community nursing care was offered to all short stay patients. Psychosocial measurements were performed before surgery and 1 and 4 months after. It was found that there were no adverse effects of a short stay in hospital on the rate of wound complications (short 10 versus long 9), total volume (515 ml versus 685 ml) and duration (8 versus 9 days) of axillary drainage, or

number of patients with seroma formation (10 versus 8). Short stay patients were highly satisfied with their length of stay: only 4 % would have preferred a longer stay in hospital both after 4 weeks and after 4 months and nearly all patients would recommend short stay to other patients. The two groups did not differ in scores for psychosocial problems (uncertainty, anxiety, loneliness, disturbed sleep, loss of control, threat to self esteem), physical or psychological complaints, or in the coping strategies used. Prior to surgery, patients in the short stay group scored higher on scales of depression than long stay patients, but these depressive feelings preceding the experimental treatment had no predictive value for mood disturbances following early discharge. After surgery, patients in the short stay group were more likely to discuss their disease with their families.
It was concluded that early discharge after surgery for breast cancer is feasible, well received by patients and enhances the opportunity for social support within the family.

In Chapter 6 the results of the economic evaluation of the short hospital stay procedure after axillary dissection are presented. Data on care consumption were collected for a period of 4 months in diaries administered by patients and socioeconomic status was evaluated by questionnaires. A cost-minimisation analysis using the 'societal' perspective was performed and savings were compared with the savings of hospital charges. The use of professional home care following discharge, especially district nursing and home help, was higher for the short stay group than for the long stay group: respectively in total 7.2 and 1.3 hours per patient ($P<0.0001$). The number of outpatient consultations, the intensity of informal home care and patient's expenses did not increase after early discharge. The total cost of care was reduced with US $ 1320 per patient by introducing the short stay program ($P=0.0007$). The savings in hospital charges were $2680 per patient.

Replacing postoperative hospitalisation with outpatient department activities and extramural care emphasizes the need for attuning intra- and extramural care and information.In Chapter 7 the development, utilization and evaluation of a multidisciplinary care-protocol have been described. The protocol was developed by a steering and working group consisting of representatives of the various health professionals involved in breast cancer treatment, education experts, and ex-patients. The development was preceeded by the mapping of the current state of treatment, care and information for breast cancer patients by collecting existing materials and by means of interviews with 60 health professionals and 40 patients. The protocol describes the state of affairs of treatment and care at 15 particular moments of the care process, and what information should be given by which care-professional. The protocol was used by 53 patients and 81 care-professionals. Evaluation by

means of questionnaires showed that the use of the protocol improved the information given to patients, enhanced the continuity of information, and enhanced the attention of care-professionals to patients' psychosocial functioning.

In **Chapter 8** the results of the studies are discussed and recommendations for patient management and future research are given.
Serous fluid formation remains an inevitable result of surgical axillary node dissection and until production ceases spontaneously, some form of evacuation of the fluid from the axilla is necessary. New studies should focus on what is more convenient for the patient, prolonged closed suction drainage or early drain removal followed by aspirations when necessary.
In this thesis it was demonstrated that early hospital discharge following axillary lymph node dissection with the drain in situ is feasible, provided that there is adequate support available in the community. The procedure increases patient satisfaction and enhances social support from the family. When introducing the policy at a larger scale, significant savings will be achieved and the extent of substitution of care from intra- to extramural will be limited. In the future more research should be done to identify issues relevant to the role of the family in the care process, and to evaluate the psychosocial effects of very short hospital stays.
The role of axillary dissection in the treatment of breat cancer is currently being redefined. In the nearby future the indication for axillary lymph node dissection may be limited to node-positive patients identified prior to surgery by ultrasound guided FNAB or the sentinel-node technique. The sentinel-node technique seems to be able to select the truly node-negative patients in whom axillary dissection can be avoided. Patients will benefit of these developments of less aggressive surgery to the axilla, preventing morbidity in most patients with early stage breast cancer.

Samenvatting

Samenvatting

Het doel van dit proefschrift is het in kaart brengen van de mogelijkheden de nadelige gevolgen van de okselklieroperatie bij patiënten met borstkanker te verminderen. Dit houdt in het zoeken naar alternatieve diagnostische methoden voor het aantonen van lymfklieruitzaaiïngen, het verminderen van de seroomproduktie in de oksel, en het verbeteren van de zorg na de operatie.

Hoofdstuk 1 betreft de algemene inleiding op dit proefschrift. De rol van de okselklieroperatie bij de behandeling van borstkanker en de nadelige gevolgen van deze operatie worden besproken. Geconstateerd wordt dat de produktie van sereuze vloeistof in de wond, één van de korte termijn complicaties van de operatie, in belangrijke mate de lengte van de ziekenhuisopname bepaalt. Aan de hand van een overzicht van studies die de mogelijkheden van eerder ontslag uit het ziekenhuis na de chirurgische behandeling van borstkanker onderzoeken, worden de relevante aspecten van het vervroegd ontslag bepaald. De belangrijkste zijn:

- de effecten op het voorkomen van complicaties;
- de tevredenheid van patiënten en het herstel van het psychosociaal functioneren;
- de mate van verschuiving van zorg en kosten;
- het belang van continuïteit van zorg en voorlichting;

In **hoofdstuk 2** wordt de chemische en cellulaire samenstelling van het vocht dat gevormd wordt in de wond na het verwijderen van de lymfklieren in de oksel geanalyseerd. De samenstelling wordt vergeleken met de waarden in het bloed en met gegevens die in de literatuur bekend zijn over de samenstelling van lymfevocht. De analyse werd verricht op monsters van drainvloeistof afgenomen op de eerste, vijfde en tiende postoperatieve dag bij patiënten met borstkanker die een okselklieroperatie ondergingen als onderdeel van een borstamputatie. De eerste dag was de drainagevloeistof gecontamineerd met bloed van de chirurgische wond. Hierna bleek de vloeistof kenmerken van lymfe te hebben, maar met minder cellen en meer eiwit. De vloeistof bevat geen fibrinogeen en stolling is daarom niet mogelijk. Geconstateerd wordt dat de afname van de vloeistofproductie in de tijd daarom veroorzaakt moet worden door andere wondgenezingsprocessen, zoals de vorming van collageen dat de lymfebanen oblitereert, of van andere bestanddelen van littekenweefsel.

Hoofdstuk 3 beschrijft een gerandomiseerde trial naar de invloed van de negatieve druk in het drainsysteem op de hoeveelheid vloeistofproductie en het aantal complicaties na okselklierdissectie. Patiënten werden gerandomiseerd voor een laag vacuüm drain (negatieve druk 115 mm Hg (15.3 kPa)) of een hoog vacuüm drain (negatieve druk 720 mm Hg (95.9 kPa)). Tussen de laag vacuüm (n=68) en de hoog

vacuüm groep (n=73) werden geen statistisch significante verschillen gevonden in:

- drainage volume (728 ml versus resp 780 ml);
- duur van de drainproductie (9.5 dagen versus 10 dagen);
- aantal wondcomplicaties (5 versus 6);
- aantal infecties (3 versus 2);
- de mate van seroomvorming na drainverwijdering.

Het drainage volume van de apart gedraineerde borstwond bleek hoger uit te komen voor de hoog vacuüm groep (100 ml versus 55 ml; P=0.02). Verlies van het vacuüm kwam frequenter voor in de hoog vacuüm drain groep (11 versus 2, P=0.01), terwijl lekkage langs de drain vaker voor kwam bij de laag vacuüm groep (18 versus 6, P=0.004).
Aangezien de seroomproductie in de oksel niet verminderd kan worden door één van beide drains en het aantal wondcomplicaties niet verschilt tussen beide groepen wordt geconcludeerd dat de voorkeur voor een hoog of een laag vacuüm drain kan worden bepaald door niet medische factoren zoals kosten, hanteerbaarheid en comfort voor de patiënt.

In **Hoofdstuk 4** wordt de betrouwbaarheid onderzocht van echografie en van echografie in combinatie met cytologische punctie (dunne naald biopsie, fine needle aspiration biopsy (FNAB)) voor het opsporen van klieruitzaaiïngen in de oksel bij 148 patiënten met borstkanker zonder voelbaar vergrote klieren voorafgaand aan de operatie. De resultaten van echografie en FNAB zijn vergeleken met de histopathologische gegevens van de lymfklieroperatie.
De sensitiviteit van echografie alleen bleek maximaal (87 %) te zijn in geval de grootte van de klier (lengte > 5 mm) werd gebruikt als criterium voor maligniteit, maar de bijbehorende specificiteit was laag (56%).
Indien klieren met een maligne beeld (echo-arm of inhomogeen) werden gevisualiseerd bleek de sensitiviteit 36 % en de specificiteit 95 %. Echogeleide FNAB verhoogde de sensitiviteit naar 80 %. De specificiteit van FNAB bleek 100 % en metastasen werden aangetoond bij 63 % van de patiënten met positieve klieren. Geconcludeerd wordt dat echogeleide FNAB een eenvoudige, betrouwbare en goedkope methode is om het grootste deel van de klierpositieve patiënten te identificeren. Bij deze patiënten kunnen meer invasieve diagnostische procedures achterwege worden gelaten. De negatief voorspellende waarde van de techniek is laag (76%), hetgeen betekent dat deze techniek de okselklierdissectie niet kan vervangen als methode voor de identificatie van patiënten zonder okselkliermetastasen.

Hoofdstuk 5 behandelt de effecten van vervroegd ontslag uit het ziekenhuis van patiënten na een borstkankeroperatie op het aantal complicaties en de psychosociale rehabilitatie. Deze studie kwam voort uit het streven de morbiditeit van de

seroomvorming beter hanteerbaar te maken, en de effecten van het vervroegd ontslag op de kwaliteit van leven van deze patiënten te onderzoeken. In een gerandomiseerd onderzoek werd ontslag uit het ziekenhuis op de vierde dag met de okseldrain in situ en wijkverpleging thuis (kort verblijf) vergeleken met ontslag na drainverwijdering (lang verblijf, gemiddelde opnameduur 9 dagen). Psychosociale metingen werden verricht voor de operatie en 1 en 4 maanden daarna. Er werden geen nadelige gevolgen gevonden van het kort verblijf in het ziekenhuis op het aantal complicaties (kort verblijf 10 versus lang verblijf 9), totaal volume (515 ml versus 685 ml) of duur (8 versus 9 dagen) van de okseldrainage, of het aantal patiënten met seroomvorming (10 versus 8). Kort verblijf patiënten waren zeer tevreden met de opnameduur: slechts 4 % zou langer in het ziekenhuis hebben willen blijven zowel na 4 weken als na 4 maanden en bijna alle kort verblijf patiënten zouden een kort verblijf adviseren aan andere patiënten. De twee groepen verschilden niet in de scores voor psychosociale problemen (onzekerheid, angst, eenzaamheid, slaapstoornissen, controleverlies, verlies van gevoel van eigenwaarde), lichamelijke en psychische klachten, of in het gebruik van afweermechanismen. Voorafgaand aan de operatie scoorden kort verblijf patiënten hoger op de depressieschalen dan lang verblijf patiënten, maar deze depressieve gevoelens voorafgaand aan de experimentele behandeling hadden geen voorspellende waarde voor stemmingsstoornissen na vervroegd ontslag. Na de operatie was de bespreekbaarheid van de ziekte in het gezin hoger voor de kort verblijf patiënten. Geconcludeerd wordt dat een kort verblijf in het ziekenhuis na een borstkanker operatie goed mogelijk is, gewaardeerd wordt door patiënten, en de bespreekbaarheid van de ziekte in de thuissituatie vergroot.

In **hoofdstuk 6** worden de resultaten van de economische evaluatie van de verkorte ziekenhuisprocedure na okselklierdissectie gepresenteerd. Gegevens over de zorgconsumptie werden verzameld gedurende een periode van 4 maanden na de operatie met behulp van door de patiënt zelf ingevulde dagboeken. De sociaaleconomische status werd geëvalueerd met behulp van vragenlijsten. Een kostenberekening vanuit het maatschappelijk perspektief vormde het uitgangspunt voor de kostenanalyse. Besparingen werden tevens vergeleken met de besparing van ligdagprijzen volgens de heersende tarieven. De kort verblijf groep maakte meer gebruik van professionele thuiszorg na ontslag, met name wijkverpleging en gezinszorg, dan de lang verblijf groep: respectievelijk totaal 7.2 en 1.3 uur per patiënt ($P<0.0001$). Het aantal polikliniekbezoeken, de intensiteit van de mantelzorg en de uitgaven van de patiënten zelf verschilden niet of nauwelijks tussen beide groepen. Geconcludeerd wordt dat op basis van een maatschappelijke kostenvergelijking de introductie van het kort verblijf protocol de totale kosten van de zorg per patiënt verminderd met US $ 1320 ($P=0.0007$) in vergelijking met een lang verblijf protocol. De besparing volgens de tarieven van ligdagen in het ziekenhuis komt uit op $ 2680 per patiënt.

Een consequentie van een kort verblijf protocol is dat de klinische zorg wordt vervangen door extramurale zorg of polikliniekactiviteiten. Dit vergroot de noodzaak tot het afstemmen van de intra- en extramurale zorgverlening en de informatievoorziening. In **hoofdstuk 7** worden de ontwikkeling, het gebruik en de evaluatie van een multidisciplinair zorg-protocol beschreven. Het protocol werd in projektverband ontwikkeld met inzet en bijdragen van de verschillende disciplines die betrokken zijn bij de behandeling van borstkanker alsmede voorlichtingsexperts en ex-patiënten. Voorafgaand werden gegevens verzameld over de behandeling, de zorg en informatievoorziening voor borstkankerpatiënten door middel van interviews met 60 professionals en 40 patiënten. Het protocol beschrijft de behandeling en zorg met betrekking tot 15 te onderscheiden momenten in het zorgproces in combinatie met informatieoverdracht inclusief taken en verantwoordelijkheden. Het protocol is in de praktijk getoetst bij 53 patiënten en 81 zorgverleners. Evaluatie door middel van vragenlijsten toonde aan dat het gebruik van het protocol de informatievoorziening aan patiënten verbetert, de continuïteit van voorlichting verhoogt, en de aandacht van de zorgverleners voor het psychosociaal functioneren van de patiënt doet toenemen.

In **hoofdstuk 8** worden de resultaten van de hierboven genoemde studies besproken en worden aanbevelingen gegeven voor de organisatie van de patiëntenzorg en voor toekomstig onderzoek.
De vorming van sereuze vloeistof is een onvermijdelijk gevolg van een okselklierdissectie en enige vorm van drainage blijft noodzakelijk totdat de produktie spontaan tot stilstand komt. Een interessant onderwerp voor een nieuwe studie is een onderzoek vanuit het perspektief van de patient naar het verschil in belasting tussen zuigdrainage totdat de produktie afneemt, versus kortdurende drainage eventueel gevolgd door seroompuncties.
In dit proefschrift werd aangetoond dat vervroegd ontslag uit het ziekenhuis met de drain in situ haalbaar is, mits adequate thuiszorg beschikbaar is. De procedure vergroot de tevredenheid van patiënten en verhoogt de bespreekbaarheid van de ziekte in de eigen omgeving. Door de introductie van het kort verblijf programma op grotere schaal kunnen aanzienlijke besparingen worden bereikt waarbij de mate van substitutie van intra- door extramurale zorg beperkt zal zijn. Onderwerpen voor vervolgstudies zijn de rol van de familie in het zorgproces en de psychosociale effecten van een nog kortere opnameduur.
De rol van okselklierdissectie in de behandeling van borstkanker is de laatste tijd aan veranderingen onderhevig. In de nabije toekomst zal de indicatie voor het verrichten van een okselklierdissectie mogelijk beperkt worden tot die patiënten bij wie met behulp van echogeleide cytologische punctie of de schildwachtklierbiopsie klieruitzaaiïngen zijn aangetoond. De techniek van de schildwachtklierbiopsie lijkt in staat te zijn de werkelijke klier-negatieve patiënten te identificeren bij wie een okselklierdissectie

voorkómen kan worden. Deze ontwikkeling van een minder agressieve chirurgie van de oksel kan voordelen hebben voor patiënten met stadium I en II borstkanker, aangezien voor het grootste deel van deze patiënten de morbiditeit van deze operatie daarmee voorkómen kan worden.

Dankwoord

Dankwoord

In 1991 werd ik als assistent-in-opleiding in het Zuiderziekenhuis benaderd door Bert van Geel met de vraag of ik onderzoek wilde doen naar het gebruik van verschillende drains na okselklierdissectie bij mammacarcinoompatiënten. Dit werd de eerste stap op weg naar dit proefschrift. Hierna volgden al snel ideeën voor andere studies en werd ik uitgenodigd om lid te worden van de werkgroep die de projecten 'Vervangende ziekenhuiszorg voor patiënten met een operabel mammacarcinoom' en 'Continuïteit van voorlichting aan vrouwen die geopereerd worden voor een mammacarcinoom' uitvoerde. Ik ben Bert dankbaar voor het vertrouwen dat hij in mij stelde en voor zijn grote inzet voor de studies voortkomende uit deze projecten, in het bijzonder ook voor het 'computerloos' monnikenwerk dat hij verrichtte voor de echografiestudie.
Theo Wiggers probeerde mij al in een vroeg stadium te overtuigen van de wetenschappelijke waarde van de onderzoeken en de haalbaarheid van een promotie. Zijn scherp inzicht in klinische vraagstukken en belangstelling voor klinisch relevant onderzoek, ook buiten de bekende paden, was een belangrijke stimulans voor het voltooien van dit boekje. Ik prijs zijn geduld met mijn eigenwijsheid, aangezien ik zelf pas definitief werd overtuigd na de toezegging van het BMJ.
In de werkgroep ontmoette ik Anneke van Wersch, de coördinator en de motor van bovengenoemde projecten. Ik raakte al snel onder de indruk van het gemak en de energie waarmee zij vele uiteenlopende zaken ter hand nam. Haar inzet en persoonlijkheid vormden de sleutel tot het succes van de projecten. Ik heb goede herinneringen aan onze 'werkbesprekingen' in haar kamertje in de DDHK, waar wij vele levensonderwerpen bespraken en de schaarse tijd plotseling altijd weer voorbij was. Ik waardeer al haar steun in de afgelopen jaren en ben blij dat zij als paranimf bij mijn promotie aanwezig is.
De multidisciplinaire vergaderingen van de projectwerkgroep werden op efficiënte wijze geleid door Jean Pruyn. Hij liet mij, behalve een andere kijk op de patiëntenzorg, op de racefiets een groot deel van westelijk Brabant zien. Pas toen ik met de blik gefixeerd op zijn kuiten en een gemiddelde snelheid van 32 km/uur 'een rondje Philipsdam' had overleefd, werd ik geaccepteerd als toekomstig vertolker van zijn onderzoek en hebben wij daarna op goede wijze samengewerkt. Dit proefschrift werd uiteindelijk mijn echte rondje Philipsdam. Zijn medewerker Wim Zomer hielp bij de analyse van de medische data van de dagboeken.
Bert van Geel bracht mij in contact met David Ligtenstein, die zich met grote toewijding op het probleem van de seroomvorming stortte en mij inwijdde in de kunst van artikelen schrijven. Zijn gedegen manier van onderzoek doen met een streng wetenschappelijk geweten, en zijn geduld tijdens onze vele avonden achter zijn computer waren onontbeerlijk voor het vervaardigen van de manuscripten en

het formuleren van onze conclusies.
Dr.Mantel en Dr. Wulkan verrichtten de seroomanalyses in het laboratorium van het Zuiderziekenhuis en gaven adviezen bij de interpretatie van de gegevens.
Voor de economische analyse van het project bleek een dermate grote hoeveelheid gegevens bewerkt te moeten worden dat alleen Paul Schmitz en zijn STATA programma nog uitkomst konden bieden. Op indrukwekkende wijze heeft hij de vele duizenden in dag- en weekboeken geregistreerde data statistisch bewerkt. Tijdens de vele sessies groeide de stapel papieren uitdraai met dezelfde snelheid als het kind in mijn buik, maar voor de deadline van het congres -en de bevalling- was dit teruggebracht tot een aantal overzichtelijke tabellen met P-waarden.
Jan Collaris gaf waardevolle adviezen in de beginfase van de kostenanalyse.
Carin Uyl maakt mij wegwijs in de denkwijze van gezondheidseconomen en was gezien haar ervaring de uitgelezen persoon voor verdere begeleiding bij het vervaardigen van het manuscript over de kosten.
Bets van den Sigtenhorst, Sonja Babijn, Nelleke Zoeter, Jeanne Baak, Carla Hillinga en Rob de Vogel waren degenen die de patiënten motiveerden voor al het werk dat zij voor ons moesten verrichten en hen ter zijde stonden. Hetty van Dongen, Elly Berends, Rob Calado, Ellen Brand, en Trees Janssen-van Groesbeek vormden de brug naar de verschillende disciplines en naar de (ex)patiënten en zorgden voor een unieke sfeer in de werkgroep.
De verpleegkundigen van A1 en A3 in de DDHK en van de 3e etage van het Zuiderziekenhuis, en de wijkverpleegkundigen in de regio hebben met hun inzet bijgedragen aan het goede verloop van de projecten en de onderzoeken.
B.Prinsen, A.Kersten-van Beek, M.Kiezenbrink, S.van der Kooy, W.Mellink, E.Taselaar en M.Tepas hebben zich ingezet als leden van de stuurgroep.
Bert Prinsen leverde daarbij in het bijzonder een bijdrage aan het verloop van het voorlichtingsproject.
Rick Paul zorgde voor een goede voortgang van de projecten in het Zuiderziekenhuis en was behulpzaam bij het redigeren van hoofdstuk 5.
Marja van Wijngaarden en Marinka Eijsberg waren onmisbaar voor het verrichten van de vele secretariële werkzaamheden.
Bart van Ooijen, Sybrand Mali, Swanny Tjiam en Sonja Henzen-Logmans verrichtten veel werk voor de echografiestudie.
Prof.Jeekel ben ik erkentelijk voor het optreden als mijn promotor en de beoordeling van het proefschrift en Prof.Rutten, Prof.Stoter en Prof.van de Velde bedank ik voor hun deelname aan de promotiecommissie.
Alle patiënten die participeerden in de onderzoeken ben ik erkentelijk voor hun inzet voor de studies.
Het Engels van de artikelen werd steeds kritisch beoordeeld door Peter Stringer; Diana Batchelor hielp in de laatste fase met de Engelse correctie. Els Zwartendijk

zorgde ervoor dat alles gerangschikt op papier kwam.
Mijn schoonmoeder Mieke Boot bewerkte op bewonderigenswaardige wijze de media van Arnhem zodanig dat de anonieme dief van mijn koffer met onderzoeksmateriaal niets anders meer kon doen dan deze terug te bezorgen op de Waterbergse weg.
Mijn liefsten Michiel en Mirte, mijn allergrootste vreugde, heb ik grotendeels buiten het gebeuren van dit proefschrift kunnen houden. Mirte haar slaapritme werd mijn werkritme; en Michiel had mij al veel eerder met beide benen op de juiste grond gezet en gaf juist daardoor de beste stimulans.
Mijn grootste dank is voor mijn ouders die altijd alle vertrouwen in mijn ambities hebben gehad en mij alle kansen en ruimte hebben geboden om mij te ontwikkelen en daarin mijn eigen weg te gaan. Mijn moeder dank ik voor de steun en liefde in de afgelopen jaren. Mijn vader heeft de aanzet tot mijn specialisatie nog net meegemaakt en hoe bijzonder blij zou hij zijn geweest met dit resultaat. In liefdevolle herinnering draag ik dit boekje aan hem op.

About the author

Jorien Bonnema was born in Amsterdam on October 13, 1962 . She attended high school at the Rijnlands Lyceum in Oegstgeest and began her medical program at the University of Amsterdam in 1980. From 1984 until 1987, she worked as a teaching assistant at the University of Amsterdam in the Department of Physiology. In 1987, she spent 6 months in South America. During this period she worked in a developing-aid project in the Andes uplands of Peru and conducted a study on the abuse of hormonal pregnancy tests in Cusco, Peru. In 1989 she obtained her medical degree (cum laude). Subsequently she began working as a surgical resident at the Free University Hospital, in Amsterdam. The specialist training program in general surgery was started in 1991 at the Zuider hospital in Rotterdam (head Dr. K.J.Brouwer) continuing in 1994 at Dijkzigt University Hospital, Rotterdam (head Prof.Dr H.A.Bruining). During the last 6 months of surgical training she worked in the Daniel den Hoed Cancer Centre in Rotterdam (head Dr.Th.Wiggers). As of 1997, she is working as a surgeon in the Netherlands Cancer Institute/Antoni van Leeuwenhoek hospital in Amsterdam. Her partner is Michiel Boot. They have a daughter called Mirte Lucia, who was born on March 11, 1996.

A word is dead
When it is said
Some say.
I say it just
Begins to live
That day

(E.Dickinson)