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Papers

Late Effects of Adjuvant Chemotherapy and Postoperative Radiotherapy on Quality of Life among Breast Cancer Patients

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Late effects of adjuvant treatment on perceived health and quality of life were assessed through a questionnaire mailed to 448 premenopausal and postmenopausal breast cancer patients, free from recurrence 2–10 years after primary therapy. The patients had been randomised to postoperative radiotherapy or adjuvant chemotherapy as adjuncts to primary surgery. The differences between the two treatments were generally small. However, the radiotherapy patients had significantly greater problems with decreased stamina, symptoms related to the operation scar and anxiety. The chemotherapy patients had significantly more problems with smell aversion. Activity level inside and outside the home, anxiousness and depressive symptoms were similar in both groups. The chemotherapy patients scored their overall quality of life higher than the radiotherapy patients.
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INTRODUCTION

POSTOPERATIVE RADIOTHERAPY and adjuvant chemotherapy as adjuncts to primary surgery for early breast cancer are both claimed to be beneficial for patients with an unfavourable prognosis. Radiotherapy significantly prolongs the relapse-free interval, mainly because of a reduction of locoregional recurrences, but the effect on overall survival is uncertain [1–3]. Chemotherapy may prolong survival [4] among premenopausal women [5, 6], polychemotherapy more so than single agent chemotherapy [6], while the effect among postmenopausal women appears to be only marginal. Chemotherapy seems to have less efficacy than radiotherapy in reducing locoregional recurrences [3, 6].

According to several studies, the impact of a breast cancer diagnosis and the subsequent surgery (mastectomy) is a persisting problem for many patients. Psychic distress occurs in 20–25%, sexual problems in about 30% [7] and many patients have persisting body-image problems [8]. As indicated by several studies, adjuvant chemotherapy influences many aspects of the quality of life during the period of treatment [9–12]. A few authors have compared radiotherapy and 12 months of chemotherapy, and have concluded that chemotherapy influences various quality of life aspects to a greater extent than radiotherapy [9, 13–15]. The differences between patients treated with radiotherapy compared to chemotherapy have been reported to persist more than 1 year after the completion of treatment [10].

There are, as far as we know, no comparative studies of late effects of radiotherapy and chemotherapy, i.e. more than 1 year after treatment. Craig *et al.* [16] compared breast cancer patients diagnosed 5 or more years prior to the study with healthy controls and found the patients to be more physically disabled, but there were no differences in psychosocial disability. Vinokur *et al.* [17] also studied differences between breast cancer patients and matched healthy controls. Of the breast cancer patients, 55% were diagnosed more than 5 years prior to the study. The breast cancer patients had more medical problems that limited their activities and they also consumed more drugs. However, there were no differences between the groups with respect to mental health and social and mental well-being.

Most quality of life studies of breast cancer patients comparing radiotherapy and chemotherapy have dealt with the immediate impact of treatment or the impact during the rehabilitation phase. The present study was done 2–10 years after treatment. The aim was to investigate differences in aspects of quality of life, e.g. functional status and physical and mental symptoms that could be late consequences of treatment. Furthermore, to increase the probability for outcome to be an effect of treatment, it was decided to study the effect of age, since many of the dependent variables were assumed to be age-dependent.

Our hypothesis was that chemotherapy would be associated with late consequences in the form of more physical, mental and social problems compared to radiotherapy.

PATIENTS AND METHODS

The patients were originally entered in a controlled clinical trial which was initiated in 1976. Details of the trial design and preliminary results have been reported elsewhere [3]. After primary surgery for breast cancer (modified radical

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mastectomy), patients aged below 71 years with lymph-node metastases and/or a tumour diameter exceeding 30 mm were randomised to postoperative radiotherapy to the chest wall and regional nodes (46 Gy/4–5 weeks) or to 12 courses of chemotherapy (CMF: cyclophosphamide, methotrexate and 5-fluorouracil). In addition, the postmenopausal patients were included in a concurrent randomised comparison of adjuvant tamoxifen (40 mg daily for 2 years) versus no adjuvant endocrine therapy. They were thus randomised between radiotherapy, radiotherapy plus tamoxifen, or chemotherapy. From 1976 to 1985, a total of 849 patients were included in the trial.

A few changes were made of the study design during the period of patient entry. These included: (1) from 1978 onward, the upper age limit was lowered to 65 years, because it was found that many old patients could not complete the protocol chemotherapy due to toxicity; (2) in 1978, the chemotherapy course interval was changed from 6 to 4 weeks. This shortened the total treatment time from 1.5 years to 1 year; (3) in 1985, the chemotherapy regimen was changed from 12 to 6 courses. The reason was that data from other studies indicated that adjuvant CMF for 6 months was as efficient as CMF for 12 months [18]; and (4) due to restricted radiotherapy resources, a 2:1 randomisation design in favour of chemotherapy was performed from March 1982 to May 1985. The total number of randomised patients was thus higher in the chemotherapy group than in the radiotherapy group (475 vs. 374 patients).

The quality of life study only included relapse-free survivors: 245 chemotherapy and 203 radiotherapy patients, since well-being of patients with recurrent disease is more influenced by their recurrence and salvage treatment than by their adjuvant therapy. Furthermore, many patients who received postoperative radiotherapy were treated with chemotherapy because of their recurrence and vice versa, making it impossible to distinguish between treatment arms.

In January 1987, a total of 215 recurrence-free survivors were identified who received their adjuvant treatment during November 1976 to August 1981. Among these patients, the period from randomisation to inclusion in the current study was 5–10 years. In January 1988, an additional 233 recurrence-free survivors randomised from September 1981 to 1985, i.e. 2–5 years previously were identified. Thus, a total of 448 patients were identified, which corresponded to 53% of those initially randomised. All patients received the questionnaire by mail. Patients who did not return their first questionnaire were reminded by letter—if necessary, twice. The final number of returned completed questionnaires was 382 (83%), 201 (82%) in the chemotherapy group and 172 (85%) in the radiotherapy group.

Of the 66 patients who did not return the questionnaire, 33 were interviewed by telephone about the reasons. They represent all patients from one of the hospitals. Of the 18 chemotherapy patients, 11 (61%) and of the 15 radiotherapy patients 6 (40%) chose not to answer the questionnaire because of negative thoughts and feelings associated with their treatment. This difference was not significant (χ^2 test).

Some patients did not receive their allocated treatment. Of the 203 patients randomised to radiotherapy, 1 patient did not receive that treatment. Of the 245 patients randomised to chemotherapy, 22 (9%) were not so treated. The most frequent reason for these protocol deviations was patient refusal. The analyses presented in this paper were based on "intention to treat". In the analysis of subjective symptoms, however, we chose to exclude patients with protocol deviations.

The mean age, at the time of responding to the questionnaire, was 59.8 years in the radiotherapy group (range 33–79) and 57.6 in the chemotherapy group (range 34–77) [t (380) = 2.05, $P < 0.05$]. The age difference occurred only in the postmenopausal group (premenopausal radiotherapy: 49.5, chemotherapy: 49.6, postmenopausal radiotherapy: 66.8, chemotherapy: 64.7). At the time of randomisation, there was only a slight difference between groups, radiotherapy = 53.5 and chemotherapy = 53.0, respectively. The explanation of the age difference was the lowering of the upper age limit from 71 years to 65 years and the unbalanced randomisation in favour of chemotherapy.

Quality of life measurements

After reviewing the literature in the field, quality of life was operationalised into physical symptoms (of disease and treatment), psychic well-being, physical and social activities and quality of life. This operationalisation agrees with most quality of life studies [19]. A discussion was held with the involved clinicians (physicians and nurses) to elaborate important aspects of the variables. A Swedish questionnaire with these criteria, and a confirmed high reliability and validity, was not available. Therefore, a questionnaire with 56 items was constructed. A pilot study, including 10 patients, was done and patients were asked if the questionnaire described their situation or if something should be changed or added. As a result, some corrections were made.

Parts of the instrument were taken from existing questionnaires (P.O.S. and Ref. 20) and the rest were developed specifically for the current study. The activity scale (physical and social activities) was developed in collaboration with the Department of Clinical Psychology and the Department of Oncology, Uppsala Akademiska Hospital (P.O.S.). The symptom list of 16 items used in 1987 consisted of items thought to be a consequence of treatment or disease or concerned complaints frequently reported by patients during follow-up visits. In 1988, the same instrument was used, but 16 symptoms were added.

Anxiety and depressive signs were assessed by a modification of the Hospital Anxiety and Depression (HAD) scale developed by Snaith [20]. The three weakest items, one in the depressive symptom scale and two in the anxiety symptom scale, were deleted to increase the internal consistency determined by calculating correlations between each item and the total score of the remaining items in the subscale. Zigmond and Snaith [21] have reported that the number of items composing the scales could vary between four and ten without changing the performance of the scales. A global measure used in many studies is the question "How is your quality of life today?". In our pilot study, this question was not understood by the patients and was therefore replaced by two statements: "I feel fine" and "I am satisfied with my daily life".

Patients were asked to rate on a scale from 0 to 4 to what extent specific activities, physical sequelae and mood states applied to them during the previous week. Zero indicated absence of problems or activity performed every day and 1–4 indicated the degree of problem, intensity of symptoms or frequency of activity. The HAD questions were used with five response categories: never, seldom, sometimes, often and always, coded from 0–4 depending on whether the statement was positive or negative. The reason for using five categories in the HAD scale was to maintain the response format used in previous questions.

The following questions were included in the questionnaire:

Activities (12 *items*). At home how often did you: do easy work like washing up or cooking, talk on the telephone, read a book or magazine, listen to the radio or watch television, do heavy household duties such as gardening or floor cleaning and receive guests? In the community how often did you: go shopping or visit a bank or post office, travel by bus or car, take a walk, do physical exercises, visit friends or relatives, and attend organised activities such as church or club meetings and/or social activities such as restaurant visits?

Symptom list (32 *items*). Score your intensity of: fatigue, decreased stamina, pain, changes in physical appearance, joint problems, problems with the scar, infections, hair loss, sleeping problems, memory problems, concentration problems, nausea, smell aversion, food aversion, worries about health, and anxiousness. Added in 1988 were: weight increase, weight loss, decreased appetite, gastritis, diarrhoea, dysphagia, urinary tract problems, cystitis (urinary), decrease in sexual desire, decrease in sexual ability, irritation of mouth and throat, skin irritation, dry skin, headache, dizziness and irritability.

Anxiety signs (5 *items*). How often is the following statement true for you: I feel tense or wound up, worrying thoughts go through my mind, I can sit at ease and feel relaxed, I feel restless as if I have to be on the move, and I get sudden feelings of panic?

Depressive signs (6 *items*). How often is the following statement true for you: I can laugh and see the funny side of things, I feel cheerful, I have lost interest in my appearance, I look forward with enjoyment to things, I feel as if I am slowed down, and I can enjoy a good book or a good radio or television programme?

Quality of life (2 *items*). How often is the following statement true for you: I feel satisfied with my daily life and I feel fine?

Validity of the constructed instrument

The method for constructing the instrument used in this study (reviewing the literature and interviewing staff and patients) implies a certain face validity. Also, questions concerning presence and degree of certain symptoms, frequency of activities and other specific events can be assumed to have a high criterion-related validity.

Statistical methods

χ^2 tests were used for evaluating differences in intensity and frequency counts of physical symptoms and activities in the two treatment groups in different age strata. The five grade scales were transformed to two or three levels. In the symptom list, the two levels were: none (0) and some degree of symptom (1–4) categorised as a little, fairly much, much and very much. In the activity list, the three levels were: every day of the week (0), at least 1 day per week (1–3) categorised as once, two to three times and four to six times, and never (4) categorised as no time during the week.

Differences between the two main treatment arms, radiotherapy and chemotherapy, and between different menopausal strata, with respect to anxiety, depression and quality of life were evaluated with *t* tests (pooled variance estimate). Menopausal status was considered important when analysing data since it is a stratified variable in the clinical design and medical outcome differs according to the menopausal state.

Since age is known to influence many of the mentioned variables, significant differences between the radiotherapy and chemotherapy groups were further analysed using multiple regression to correct for possible confounding from the mentioned difference in age distribution.

Correlations between the data (intensity of problems) and time (time since treatment and age) were checked by use of Pearson's correlation coefficients.

Factor analysis was applied to test whether the HAD anxiety and depression items formed internally consistent scales [22], or if it was preferable to form other scales able to distinguish treatment groups more clearly. Factor analyses were based on a matrix of interitem correlations. The factors extracted accounted for a major part of the correlations between the original variables. Factor loadings for included items were at least 0.40. To test the homogeneity of the factor-analytically derived scales (worry and positive affect), internal consistency was measured using Cronbach's α [23].

Table 1. Daily activities during past week

How often did you . . ?	Every day		At least once		Never	
	RT	CT	RT	CT	RT	CT
At home						
Wash up, cook	84	84	15	15	1	1
Read a good book	83	84	16	13	1	3
Listen to radio or watch TV†	83	81	16	18	1	1
Talk over the telephone*	71	60	29	39	0	1
Do heavy household duties	8	6	68	80	24	14
Have guests	6	3	70	72	24	26
In the community						
Go shopping	24	20	75	78	1	2
Travel by bus or car†	25	31	52	48	23	22
Take a walk	17	22	61	60	21	19
Do physical training	13	6	46	42	42	53
Visit friends or relatives	5	1	75	78	20	20
Do organised activities like church or club meetings†	2	2	37	45	61	53

RT = radiotherapy (n = 144–168), CT = chemotherapy (n = 184–199).

*χ^2: 6.08, df 2, $P < 0.05$.

† The difference between age strata was significant.

RESULTS

Present work situation

The present work situation did not differ significantly between the radiotherapy (n = 172) and chemotherapy (n = 201) groups (χ^2 = 2.39, P = 0.18). All patients below 65 years (the age for retirement in Sweden), who were fully employed (radiotherapy: 31%, chemotherapy: 41%), half employed (radiotherapy: 26%, chemotherapy: 21%) and not employed (radiotherapy: 5%, chemotherapy: 7%) were included in this analysis.

Home activities

There were few differences in activity level between the treatment and age groups (premenopausal vs. postmenopausal). Most women dedicated themselves every day to easy activities at home while heavy household duties were less frequently performed by the majority of patients. There were some small differences with respect to treatment and age strata. Patients treated with radiotherapy talked more over the telephone than

Table 2. Percentage of patients rating some degree of symptoms and problems

	Total group		Premenopausal		Postmenopausal	
Problems and symptoms	RT (n = 153–172)	CT (n = 173–184)	RT (n = 63–69)	CT (n = 82–86)*	RT (n = 89–103)	CT (n = 88–98)
Fatigue‡	76	68	72	72	80	64
Decreased stamina*‡	75	61	67	57	79	65
Pain	46	40	38	38	52	42
Changes in physical appearance	38	30	35	33	40	28
Joint problems	39	40	26	38	48	41
Operation scar*	24	14	23	13	24	16
Infections	20	24	20	29	20	19
Hair loss	17	17	5	14	25	19
Sleeping†	47	50	34	52	55	48
Memory	37	36	26	32	45	41
Concentration	30	30	27	32	33	28
Nausea	17	11	11	9	22	12
Smell aversion*	10	18	6	19	13	17
Food aversion	10	9	8	7	11	11
Worrying about health	59	53	50	50	66	55
Anxiousness*§	41	38	28	30	49	46

$P < 0.05$ for * total group, † premenopausal group and ‡ postmenopausal group.
§ Three levels: no problems, light and severe problems. $\chi^2 = 6.53$, df = 2.

did chemotherapy-treated patients ($\chi^2 = 6.08$, $P < 0.05$, df = 2). Postmenopausal women listened more to the radio and watched TV more than did premenopausal women ($\chi^2 = 6.22$, $P < 0.05$, df = 2).

Activities in the community

These activities were not as frequent as the home-based activities, though the majority of patients performed most of them at least once a week.

Premenopausal women travelled more by bus or car ($\chi^2 = 17.19$, $P < 0.0005$, df = 2) and had more organised activities ($\chi^2 = 10.09$, $P < 0.01$, df = 2).

Symptoms and problems in the total group

The 16 questions on symptoms in Table 2 were responded to by all patients. The symptom level was generally below 1, which means that most patients did not suffer from the symptom. Less than 10% reported a severe degree of symptoms. Only fatigue and decreased stamina reached mean values above 1.0 (1.38 and 1.26 in the radiotherapy group and 1.12 and 0.94 in the chemotherapy group). Of the total patient group, 61–76% perceived these two symptoms. When two levels were used in the analysis: not present (0) [not at all] and some degree of symptom [a little (1), fairly much (2), much (3) and very much (4)] (Table 2), three symptoms differed significantly between the treatment arms: decreased stamina ($\chi^2 = 6.90$, $P < 0.05$, df = 1), smell aversion ($\chi^2 = 4.28$, $P < 0.05$, df = 1) and problems with the operation scar ($\chi^2 = 4.95$, $P < 0.05$, df = 1). The radiotherapy patients (75%, n = 162) more frequently reported loss of stamina than did chemotherapy patients (61%, n = 173). Persistent smell aversion was reported by 10% (n = 154) of the radiotherapy patients and 18% (n = 173) of the chemotherapy patients. Of the radiotherapy patients, 24% (n = 155) experienced problems with their operation scar while the corresponding number among the chemotherapy patients was 14% (n = 175). Since there was a slight age difference between the groups, a multiple regression analysis was used to evaluate the relation of treatment and age on the one hand and decreased stamina and smell aversion on the other. Age did not contribute significantly to the difference between the treatment arms.

Another symptom, anxiousness, was found to differ significantly between treatment arms ($\chi^2 = 6.53$, $P < 0.05$, df = 2) when the χ^2 analysis was based on three levels: no symptoms (0), light [a little (1) and fairly much (2)] and severe [much (3) and very much (4)]. The distribution over the three levels was 93, 49 and 15 in the radiotherapy group and 107, 61 and 5 in the chemotherapy group i.e. more patients in the radiotherapy condition recorded severe problems. Using multiple regression analysis, we found that neither age nor time since treatment had any significant relation to problems with the operation scar or anxiousness.

All other problems were experienced by patients in both treatment arms in some frequency varying from 50% to 10%, but there were no significant differences between the groups (Table 2).

Menopausal status

Some of the symptoms differed significantly between menopausal strata i.e. the postmenopausal women experienced them to a higher extent than premenopausal women. That was the case for decreased stamina ($\chi^2 = 7.82$, $P = 0.02$), memory problems ($\chi^2 = 8.14$, $P = 0.02$), hair loss ($\chi^2 = 10.4$, $P < 0.01$), nausea ($\chi^2 = 6.7$, $P < 0.05$) and anxiousness ($\chi^2 = 11.78$, $P < 0.005$).

When analysing results for the treatment arms within each menopausal stratum, we found that in the premenopausal stratum significantly more chemotherapy patients than radiotherapy patients had sleeping problems ($\chi^2 = 4.85$, $P < 0.05$) and smell aversions ($\chi^2 = 4.51$, $P < 0.05$) (Table 2).

In the postmenopausal stratum, significantly more radiotherapy patients than chemotherapy patients experienced fatigue ($\chi^2 = 5.9$, $P < 0.05$) and a decrease in stamina ($\chi^2 = 4.4$, $P < 0.05$). There was a tendency for higher frequencies of

Table 3. Correlations between age and symptoms and time since treatment and symptoms.

	Radiotherapy		Chemotherapy	
Problems and symptoms	n = 153–172	n = 153–172	n = 187–201	n = 183–197
	Age	Time	Age	Time
Fatigue	—	—	—	0.22
Decreased stamina	—	—	0.13	—
Pain	0.14	—	—	0.16
Changes in physical appearance	—	—	—	—
Joint problems	0.17	—	—	—
Problems with operation scar	—	−0.14	—	0.12
Infections	—	—	−0.22	—
Hair loss	0.25	0.18	—	—
Sleeping	0.20	—	—	0.15
Memory	0.20	—	—	—
Concentration	—	—	—	—
Nausea	0.27	—	0.17	—
Smell aversion	0.15	—	—	0.16
Food aversion	0.17	—	—	0.17
Worrying about health	—	−0.20	—	−0.18
Anxiousness	—	—	—	—

Only significant correlations ($P < 0.05$) are indicated.

several symptoms among the older radiotherapy patients (Table 2).

Age

In the radiotherapy group, frequency and intensity of many problems correlated positively with age, i.e. problems increased with age. In the chemotherapy group, only decreased stamina and nausea were positively correlated with age (Table 3).

Time since treatment

This was defined as (the year of randomisation) minus (the year of study). In the radiotherapy group, only one problem, hair loss, correlated positively with time since treatment, whereas some problems decreased with time: problems with the scar and worries about health in general (Table 3). In the chemotherapy group, many symptoms increased with time since treatment (Table 3). All correlations, although significant, were low (< 0.28) and the proportion of variance accounted for by age or time since treatment was in no case above 7%.

In 1988, 16 symptoms were added to the original questionnaire. There were no significant differences between treatment arms with respect to these symptoms. Weight increase was the most troublesome problem in both treatment arms (58% of the patients). Most other symptoms were perceived in both treatment groups to an extent of 5–30%. There was a tendency for more radiotherapy patients than chemotherapy patients to experience symptoms such as dysphagia (radiotherapy: 14%, chemotherapy: 8%), headache (radiotherapy: 39%, chemotherapy: 31%) and dizziness (radiotherapy: 24%, chemotherapy: 16%). Less than 10% scored their symptoms at a severe level.

Anxiety signs

There were no significant differences (t test) between treatment groups with regard to anxiety signs (5 items) as determined by the modified HAD scale. The mean value in the radiotherapy group was 1.29 (S.D. 0.73) and in the chemotherapy group 1.23 (0.68). The range was from 0 to 4, thus most patients rated anxiety in the lower part of the scale. Few patients reported high levels of anxiety. 6 patients in the radiotherapy group, and 3 patients in the chemotherapy group, had mean scores above 3.

The radiotherapy group scored higher than the chemotherapy group on most of the included items. "Worrying thoughts go through my mind" was the most frequently experienced symptom in both groups. Mean values for that item were 1.71 (radiotherapy) and 1.51 (chemotherapy), respectively. The symptom perceived least often was "I get sudden feelings of panic". Mean values were 0.71 in the radiotherapy group and 0.67 in the chemotherapy group.

Premenopausal and postmenopausal women rated their anxiety symptoms similarly. Correlations with time since treatment were not significant.

Depressive signs

Mean values of depressive signs (6 items) were 0.95 (S.D. = 0.61) in the radiotherapy group and 0.90 (0.51) in the chemotherapy group. The difference was not significant. Only 1 patient in the radiotherapy group and none in the chemotherapy group had a mean above 3. "I feel as if I am slowed down" was the item with the highest score (mean value in both groups 1.39). "I have lost interest in my appearance" was the least prevalent problem (mean values in the radiotherapy group 0.61 and in the chemotherapy group 0.59).

There were no significant differences between age strata.

Quality of life

Chemotherapy patients rated their quality of life (satisfaction with health and daily life) as more satisfying than did radiotherapy patients [t (357) = 2.63, $P < 0.01$]. The mean value in the radiotherapy group was 1.02 (S.D. 0.94) and in the chemotherapy group 0.79 (0.69). A low value indicates a high quality of life. There were no differences between premenopausal and postmenopausal women. Multiple regression analysis was used to evaluate the relation to age and treatment type. Treatment (chemotherapy or radiotherapy) but not age was related to quality of life ($P < 0.05$) Time since treatment had no significant relationship with the rated quality of life.

Factor analysis

Factor analysis was applied to the combination of HAD items and quality of life questions. Factor loadings of at least 0.40 and high correlations between items (> 0.35) were required. The items arranged themselves in two new variables: worry and positive affect. Of the deleted items, none was excluded because of low factor loadings, but some because of low correlations. The exclusion was done to increase the internal consistency of the variable. Excluded items were: "I have lost interest in my appearance" and "I feel as if I am slowed down".

Worry. The variable involved the following statements: "I feel tense and wound up", "Worrying thoughts go through my mind", "I feel restless as if I have to be on the move" and "I get sudden feelings of panic". The internal consistency was $\alpha = 0.78$. There was no significant difference ($t = 0.63$, $P = 0.53$). In the radiotherapy group, the mean value was 1.29 and in the chemotherapy group 1.23. Both groups showed mean scores on all items of worry < 1.75 (range: 0–4).

Positive affect. The internal consistency of this new variable was high ($\alpha = 0.86$). It contained the following seven questions: "I can laugh and see the funny side of things", "I feel cheerful", "I look forward with enjoyment to things", "I can enjoy a good book or radio or TV programme", "I can sit at ease and feel relaxed", "I feel satisfied with my daily life" and "I feel fine". The new variable "positive affect" thus includes four items from the depression scale, one anxiety item and two quality of life items.

The chemotherapy patients reported a higher positive affect than the radiotherapy patients (radiotherapy mean value: 1.03 and chemotherapy mean value: 0.89; low values correspond to a high degree of satisfaction) [t (347) = 2.19, $P < 0.05$]. This held true for all individual items.

DISCUSSION

We found no support for our hypothesis that chemotherapy would lead to more severe late consequences than radiotherapy. In the chemotherapy group, only smell aversion was a more common complaint than in the radiotherapy group, while the radiotherapy patients more frequently reported problems with stamina, operation scar and anxiousness. Well-being and positive affect was also rated lower by the radiotherapy patients. In general, there were small differences between the two treatment arms. Doubt may be raised if the statistically significant differences also signify clinically relevant differences, particularly since many patients were included in the study. Thus, statistical significance may be easily obtained although absolute differences are small. Some of the mentioned differences may also have occurred by chance in view of the large number of comparisons.

Several symptoms were found to be age-related. The same was true for some activity measures, while the worry and positive affect variables were independent of age. The weak relationship found between time and symptoms (Table 3) could be explained by the fact that most symptoms are over when 2 years have passed since the operation.

The younger chemotherapy group tended to rate a higher frequency of treatment-related symptoms than the younger radiotherapy group. A possible explanation is that the chemotherapy resulted in a chemical castration in many of these patients [24, 25]. In the postmenopausal subgroup the chemotherapy patients perceived less symptoms than the radiotherapy patients. These patterns may be explained by a tendency to push chemotherapy harder (more treatment cycles and higher doses) for the younger than for the older patients [3].

One explanation of the differences between the radiotherapy and chemotherapy groups is the theory of adaptation. In our setting it could imply if a woman has suffered a lot e.g. from chemotherapy and now feels better she tends to overestimate her well-being as compared to a patient who felt better before but now feels exactly the same as the other patient. Positive affect (or satisfaction) may presuppose a process of comparison [26].

The decreased stamina, perceived quality of life and positive affect associated with radiotherapy could perhaps explain why patients treated with lumpectomy followed by radiotherapy have a higher incidence of mental symptoms compared to women who had undergone surgical treatment only [27].

In the present study of late consequences, radiotherapy was given to the chest wall and regional nodes which implies that critical organs could be affected and result in late sequelae.

Few patients (8–16%) rated their psychic distress, assessed by questions on psychic symptoms and the HAD-scale, on the extreme values (3 and 4) of the rating scale. In contrast to our results, several studies covering 1–2 years after treatment, report high frequencies of anxiety and depression among breast cancer patients [9, 13–15]. This discrepancy is expected. In our clinical practice, we commonly see how crisis reactions and anxiety subside between 1 and 2 years after treatment. Vinokur [17] has reported problem frequencies similar to ours among breast cancer patients, mostly more than 5 years after diagnosis. On the other hand, Sullivan *et al.* [28], in a survey of patients with a variety of cancer types, found that cancer survivors assessed their mental well-being 2–3 years after diagnosis less positively than did healthy controls.

We conclude that the two studied types of adjuvant treatment, chemotherapy and radiotherapy, do not severely impede life conditions for patients 2–10 years after treatment. The differences between the two treatment types were small.

Our conclusions about the quality of life of radiotherapy and chemotherapy cancer patients should be tempered by considerations of the response rate, instruments used and the quality of the research design. The high rate of response allows us to conclude that the responding patient group probably is representative of the whole patient population i.e. recurrence-free breast cancer patients 2–10 years after mastectomy and adjuvant radiotherapy or chemotherapy. The instrument detected clinically relevant differences. It distinguished between age and treatment groups. The homogeneity of the new worry and satisfaction scales was clearly satisfying.

The reliability and validity of our quality of life instrument should be ascertained. The questionnaire used in this study is currently run in parallel with the Swedish version of the Cancer Inventory of Problem Situations (CIPS) to measure its concurrent validity in an ongoing study of quality of life in breast cancer patients during adjuvant treatment. In this way the reliability and validity of the questionnaire can be more fully evaluated than was possible in the study.

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Efficacy and Safety of Granisetron in the Prevention of Chemotherapy-induced Emesis in Paediatric Patients

Jean Lemerle, Diego Amaral, David P. Southall, James Upward and Robert D. Murdoch

In an open ascending-dose study, granisetron, a specific 5-HT$_3$ receptor antagonist, was admininistered to 24 paediatric patients (17 male, 7 female, mean age 6.2, range 3–15 years) who were receiving moderately or highly emetogenic chemotherapy for malignant disease. Single doses of 10, 20 and 40 μg/kg were administered by intravenous infusion 1 h before chemotherapy. Each dose level was studied in a group of 8 patients. With the 40 μg/kg dose, 5 of 8 patients experienced no nausea or vomiting in the 24 h after granisetron treatment. With 20 μg/kg, a similar response was seen, but with 10 μg/kg only 2 of 8 patients experienced complete antiemetic protection despite additional prophylactic chlorpromazine in this group. Granisetron was very well tolerated, and there were no clinically important changes in pulse rate, blood pressure or Holter electrocardiogram. It is concluded that granisetron was very well tolerated by paediatric patients. In addition, there was clear evidence of a major antiemetic effect for at least 24 h after a single intravenous dose of 20 or 40 μg/kg.
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INTRODUCTION

NAUSEA AND VOMITING are among the most distressing and debilitating side-effects of the chemotherapy regimens used for the treatment of childhood cancers. The currently available antiemetics do afford benefits but none is completely satisfactory: side-effects may be troublesome, particularly sedation and extrapyramidal effects [1], and combination of treatment [2–5] and complex dosing regimens may be required to achieve optimal antiemetic activity [6].

Granisetron is a selective 5-HT$_3$ receptor antagonist. In adult patients it has been found to be well tolerated in single doses of up to 160 μg/kg [9]. Furthermore, a single dose of 40–160 μg/kg has been shown to provide a major degree of antiemetic protection for a full 24 hours, even in patients who have received high doses of cisplatin [7–9].

The present study was the first evaluation of granisetron in paediatric patients. It was undertaken to assess the tolerability and efficacy of the agent in children receiving moderately or