



Effect of exercise in reducing breast and chest-wall pain in patients with breast cancer: a pilot study

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ABSTRACT

Background

Breast or chest-wall pain (BCP) is prevalent in 20%–50% of breast cancer survivors, and it affects quality of life (QOL). To determine the feasibility and potential efficacy of an exercise program to improve patient QOL and BCP, such a program was offered to breast cancer patients suffering from BCP.

Methods

The study enrolled 10 breast cancer patients with moderate-to-severe BCP at 3–6 months after completion of all adjuvant treatments. These patients participated in a 12-week comprehensive health improvement program (CHIP). Intensity was adjusted to reach 65%–85% of the patient's maximal heart rate. Before the CHIP and at 1 and 6 months after completion of the CHIP, QOL and pain were measured using questionnaires [European Organisation for Research and Treatment of Cancer Quality of Life core and breast cancer modules (QLQ-C30, -BR23) and the McGill Pain Questionnaire short form] completed by the patients. Results were compared with those from case-matched control subjects from another study at McGill University.

Results

After the CHIP, patients reported significant and clinically important improvements in QOL and symptoms. At 1 and 6 months post-CHIP, patients in the study felt, on average, better in overall QOL than did historical control subjects.

Conclusions

Our study suggests that patients who experience chronic BCP may benefit from an exercise program. A randomized controlled trial is warranted.

KEY WORDS

Breast cancer, exercise, pain, quality of life, rehabilitation, chest wall, chronic, survivorship

1. INTRODUCTION

After adjuvant therapies, the 5-year survival of breast cancer patients with localized and locoregional breast cancer is estimated to be 98% and 83% respectively¹. Because many patients become long-term survivors, concerns about the medium- and long-term consequences of their treatment regimens have led to multiple quality-of-life (QOL) studies that have demonstrated significant emotional, cognitive, and physical deterioration after treatment^{2,3}. Those studies showed that symptoms such as muscle stiffness, breast sensitivity, tendency to take naps, and difficulty concentrating were common and associated with poor physical functioning and emotional well-being^{3–6}.

Surgery and radiotherapy are thought to cause acute and chronic breast pain, tenderness, and shoulder impairments in up to 50% of patients who complete breast-conserving therapy^{7–12}. The U.K. START (Standardisation of Breast Radiotherapy) trial, which compared hypofractionation with conventional fractionation of adjuvant radiotherapy for breast cancer, assessed the QOL of 2208 of the patients over 5 years¹³. It was observed that 20% and 30% of the patients from both arms of the study experienced breast and arm pain respectively at 5 years of follow-up¹³.

Randomized controlled studies have shown that, compared with control patients who received no interventions, breast cancer patients directed to exercise more frequently after their diagnosis experienced improvements in physical functioning, overall QOL, and cardiopulmonary functioning^{14,15}. In 2006, the McGill Comprehensive Health Improvement Program (CHIP), which was originally developed for patients with cardiovascular disease, started to include an exercise rehabilitation program to help cancer survivors

recover and reach their full health potential once they had completed their cancer treatments. The CHIP team consists of an internist, an oncologist or palliative care physician, a psychologist, a nurse, a physiotherapist, a dietician, and a clinic manager, who together provide the patient with information, treatment, and support. The program emphasizes adapting exercise routines that help patients recover from treatment-induced symptoms, educating patients on how to improve their ongoing state of health, and forming a long-term exercise plan for health maintenance.

To our knowledge, no studies have examined the role of a rehabilitation program focused primarily on exercise training in reducing cancer therapy-induced breast and chest-wall pain (BCP) and shoulder mobility impairments—symptoms that affect the physical and biopsychosocial functioning of patients and, ultimately, their QOL. The pilot study reported here focuses on women with nonmetastatic breast cancer who had completed their adjuvant treatment or treatments 3–6 months before enrollment and who had chronic BCP.

2. METHODS

2.1 Patient Population

Our study was approved by the McGill University Health Centre Institutional Review Board at McGill University. After providing informed consent, 10 patients agreed to participate in the study, which was conducted between November 2008 and June 2009. Eligible patients had to have completed their adjuvant treatments between 3 and 6 months before enrollment. All patients answered “occasionally” or “frequently” to two screening questions adapted from Whelan *et al.*¹²:

- During the past 2 weeks, have you been troubled by pain or discomfort of the skin of your chest?
- During the past 2 weeks, have you been troubled or inconvenienced as a result of pain in the breast that was operated on?

2.2 Cardiovascular Risk Factors and Fitness Assessment

At baseline, all subjects performed a maximal graded exercise stress test on a treadmill to determine their level of fitness. During the test, measurements were taken for heart rate, heart rhythm, blood pressure, and maximal metabolic equivalent (MET) capacity using the ramp/Bruce protocol¹⁶. Blood samples taken immediately after completion of the questionnaires for assessment of cardiovascular risk factors were analyzed for B-type natriuretic peptide, C-reactive protein, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, and ratio of total cholesterol to HDL.

2.3 Exercise Intervention

The exercise program was individualized according to each patient’s fitness level while following guidelines from the American College of Sports Medicine for the development and maintenance of cardiorespiratory fitness^{17,18}. Each participant was supervised by an exercise physiologist twice weekly for 12 weeks (total of 24 sessions). In addition, patients were taught to exercise once weekly at home using a routine similar to the one at the CHIP.

Programs were individually tailored, but included at least 30 minutes of cardiovascular exercise (for example, walking or cycling), 20 minutes of strength training, and 10 minutes of stretching concentrated to the upper body. Intensity was adjusted to reach 65%–85% of the patient’s maximal heart rate as measured during an initial stress test before the CHIP and was not to exceed a score of 13–14 on the Borg Rating of Perceived Exertion scale. Physiotherapeutic interventions and teaching focused on stretching exercises to induce connective tissue and myofascial mobilization. At baseline, at completion of the CHIP, and 6 months after completion of the CHIP, shoulder range of motion was evaluated using a goniometer to measure the angle of arm abduction until the patients felt pain or discomfort. Attendance for the exercise sessions was recorded.

2.4 Pain and QOL Questionnaires

Validated questionnaires were used to evaluate pain and QOL. The Short Form McGill Pain Questionnaire (SF-MPQ) was used to measure BCP¹⁹. This validated questionnaire uses 15 pain descriptors to form the pain rating index, a pain index scale, and a visual analog scale. Patient QOL, functioning, and symptoms were measured using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire core module (QLQ-C30) and breast cancer-specific module (-BR23)^{20,21}. Questionnaires were completed by the patients immediately before their baseline stress test evaluation, at completion of the CHIP, and at 6 months after completion of the CHIP. Participants were asked to evaluate pain related to the chest wall or breasts when answering the SF-MPQ.

2.5 Activity Level

Patient activity levels were assessed using the validated International Physical Activity Questionnaire, which was administered to the patient by telephone before initiation of the CHIP, 1 month after completion of the CHIP, and at 6 months after completion of the CHIP. The International Physical Activity Questionnaire measures a patient’s MET during the preceding week, and thus the assessment was made 1 month after completion of the CHIP to exclude the CHIP from the measurement.

2.6 Data Analysis

Because this study was a prospective pilot feasibility study, the sample size was arbitrarily set at 10 patients. The analysis of QOL and pain was a pre-versus-post treatment comparison using a paired Student *t*-test (2-tailed) with level of significance set at $p < 0.05$. Significant results were re-analyzed using the Wilcoxon (2-tailed) signed rank test with level of significance set at $p < 0.05$. A minimum change of 10 points on the EORTC scales is considered clinically relevant²². The QOL data from enrolled patients were compared with QOL data from control patients matched²³ for age, axillary surgical extent, and use of chemotherapy and radiotherapy. The QOL data of matched control subjects were collected 856 days (mean) after breast surgery.

3. RESULTS

3.1 Patient Compliance

The study recruited 10 patients (Table 1), and 8 patients completed all the CHIP sessions. One patient was unable to undergo fitness training because she was diagnosed with brain metastasis just before commencing the CHIP. One patient aggravated a foot injury after the first CHIP session. Of the remaining 8 patients, 7 returned all their QOL and pain questionnaires, and 6 attended the 6-month post-CHIP follow-up physical examination. At 6-months post-CHIP, the mean time from breast surgery was 565 days.

3.2 Control Comparison

The QOL data collected from matched control subjects were gathered, on average, 856 days from the date of surgery (Table 1). By comparison, baseline, 1-month post-CHIP, and 6-month post-CHIP QOL data were collected from the CHIP patients 293, 414, and 565 days from surgery respectively. Compared with the case-matched control subjects, CHIP patients had similar overall QOL at baseline and better overall QOL at 1 and 6 months post-CHIP ($p < 0.05$; mean difference: >10 points). Although not statistically significant, the average scores of the CHIP patients were more than 10 points better than those of the control subjects in all of the other key QOL subscales at 6 months (Figure 1, Tables II and III).

3.3 QOL Over Time

3.3.1 Clinical Results

Baseline QOL functional and symptom scores were compared with QOL scores at 1 and 6 months after completion of the CHIP (Tables II and III). Figure 1 shows key QOL subscales pertaining to the potential efficacy of the CHIP. In comparing pre-CHIP QOL with 1-month post-CHIP QOL, physical functioning and arm symptoms had improved significantly. Key QOL

TABLE 1 Characteristics of patients participating in the Comprehensive Health Improvement Program (CHIP) and of matched control subjects

Variable	Group	
	CHIP	Control
Patients (n)	8	8
Age (years)		
Mean	51	52.5
Range	42–58	43–59
Disease stage		
0(is)	2	1
I	3	5
II	2	2
III	2	
Breast surgery (%)		
Breast-conserving	62.5	100
Mastectomy	37.5	
Axillary surgery (%)		
None	12.5	12.5
Sentinel node	50	50
Node dissection	37.5	37.5
Adjuvant radiotherapy dose (n)		
42.4 Gy	4	8
50 Gy	4	
Radiation boost		
Patients receiving (%)	67.5	75
Median dose (Gy)	10	10
Adjuvant therapy (%)		
Chemotherapy	50	62.5
Hormone therapy	100	75
Mean time of QOL data collection (days from surgery)		
Baseline	293	856
1 Month after CHIP	414	
6 Months after CHIP	565	

QOL = quality of life.

subscales either continued to improve or were maintained during the subsequent 5 months. By 6 months post-CHIP, cognitive, physical, and role functioning scores were improved ($p < 0.05$). Symptomatically, fatigue, arm, and breast symptoms lessened compared with baseline ($p < 0.05$). Overall QOL was also better post-CHIP. Most of these improvements were clinically important (mean difference in scores: >10 points).

3.3.2 Breast and Chest-Wall Pain

The pain rating index and pain index scale both demonstrated improvement at 1 month post-CHIP

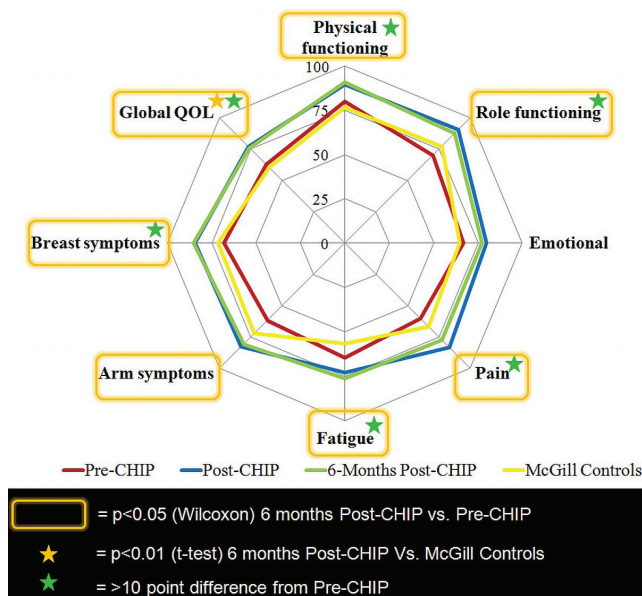


FIGURE 1 Key European Organisation for Research and Treatment of Cancer quality-of-life (QOL) subscales in Comprehensive Health Improvement Program (CHIP) and control patients. Symptoms are scored out of 100. Higher scores and larger circles indicate better QOL.

TABLE II Function scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core (C30) and breast cancer (BR23) modules for patients participating in the Comprehensive Health Improvement Program (CHIP) and for matched control subjects^a

Domain	Scores by group and time interval			
	Pre (mean)	CHIP		Control subjects (mean)
		1 Month (mean)	6 Months (mean)	
Physical functioning	80	89.5 ^b	90.8^b	76.5
Role functioning	70	90.5	87.5^b	77.1
Emotional functioning	66.7	79.76	77.1	64.6
Social functioning	83.3	88.1	89.6	72.9
Financial functioning	26.7	19	25.0	23.8
Sexual functioning	72.2	75.0	72.9	72.9
Sexual enjoyment	50.0	58.3	NA	66.7
Global quality of life	62.9	77^c	76.0^{b,c}	60.4
Time since surgery (days)	293	414	572	843

^a Higher scores indicate better quality of life. Scores in boldface type show a difference of more than 10 points from pre-CHIP scores.
^b $p < 0.05$ compared with pre-CHIP by the Student paired *t*-test and the (2-tailed) Wilcoxon signed rank test.
^c $p < 0.05$ compared with controls by the Student paired *t*-test and the (2-tailed) Wilcoxon signed rank test.

TABLE III Symptom scores on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core (C30) and breast cancer (BR23) modules for patients participating in the Comprehensive Health Improvement Program (CHIP) and for matched control subjects^a

Domain	Scores by group			
	Pre (mean)	CHIP		Control subjects (mean)
		1 Month (mean)	6 Months (mean)	
Dyspnea	16.7	9.5	12.5	29.2
Pain	40	16.7	22.9	33.3
Fatigue	35.5	27 ^b	23.6^b	43.1
Appetite loss	0 ^c	9.5	0.0 ^c	20.8
Nausea and vomiting	3.33	4.8	4.2	6.3
Constipation	6.67	9.5	12.5	20.8
Diarrhea	3.33	4.76	4.2	20.8
Systemic therapy	22.2	14.0	15.9	36.2
Hair loss	41.7	22.2	NA	0.0
Body image	66.7	78.6	80.2	86.5
Future perspective	40.7	61.1	62.5	52.4
Arm symptoms	38.3	17.4^b	19.4^b	27.8
Breast symptoms	31.9	15.5	14.6^b	28.5

^a Lower scores indicate fewer symptoms. Scores in boldface type show a difference of more than 10 points from pre-CHIP scores.
^b $p < 0.05$ compared with pre-CHIP by the Student paired *t*-test and the (2-tailed) Wilcoxon signed rank test.
^c $p < 0.05$ compared with controls by the Student paired *t*-test and the (2-tailed) Wilcoxon signed rank test.

($p = 0.016$). Although no further improvements were observed after the first month post-CHIP, 6 of the 7 women who responded to the SF-MPQ sustained the decline in the pain rating index and pain index scale at 6 months (Figure 2). Scores on the visual analog scale are not shown because only 3 of 8 patients completed that section of the SF-MPQ. Improvements in the pain rating index were both secondary to improvements in affective and sensory pain elements.

3.3.3 Shoulder Range of Motion

The mean range of motion (to a sensation of discomfort) was improved by 45 degrees (*t*-test $p = 0.009$) after completion of the CHIP. Despite having a similar mean improvement in range of motion (42 degrees) at 6 months, the result was no longer significant ($p = 0.07$). Mean shoulder range of motion to the sensation of pain was not significantly improved.

3.3.4 International Physical Activity Questionnaire

Compared with the baseline daily MET, physical activity levels in the patients increased 1 month after completion of the CHIP by a mean of 13.3 MET-hours

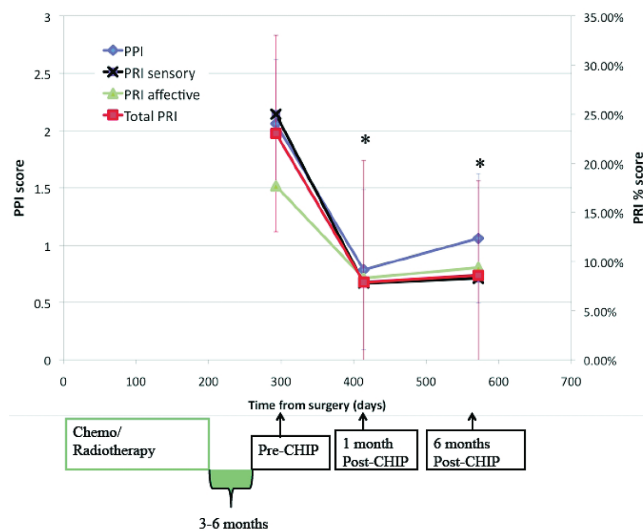


FIGURE 2 Scores on the Short Form McGill Pain Questionnaire (SF-MPQ) from patients in the Comprehensive Health Improvement Program (CHIP). * $p < 0.05$ by Student paired t -test and (2-tailed) Wilcoxon signed rank test, compared with pre-CHIP score. PRI = pain rating index; PPI = pain index scale.

per day (t -test $p < 0.05$). At 6 months, study patients continued, on average, to be more active than at baseline, but the mean active MET was no longer significantly different (Table IV).

3.3.5 Blood Tests

No significant changes in B-type natriuretic peptide, C-reactive protein, total cholesterol, triglycerides, HDL, LDL, or ratio of total cholesterol to HDL were found (Table V). Qualitatively, mean B-type natriuretic peptide and C-reactive protein were more elevated at completion of the CHIP than at baseline. However, those values recovered to baseline by 6 months post-CHIP. Total cholesterol, triglycerides, LDL, and ratio of total cholesterol to HDL trended lower at 6 months post-CHIP compared with baseline values. The inverse was observed for HDL.

4. DISCUSSION

With improved detection and care, an increasing number of breast cancer patients will survive their disease to face the long-term side effects of their cancer treatments. In particular, breast and shoulder pain affect 20%–50% of breast cancer survivors^{7–13}. A recent meta-analysis from the Cochrane Collaboration examined the role of exercise interventions for upper-limb dysfunction resulting from breast cancer treatment²⁴. That analysis observed that exercise interventions administered during adjuvant therapies did not improve QOL^{25–27} or pain^{26,28} at the upper limbs. On the other hand, when the intervention was given after completion of adjuvant treatments, QOL improved^{29,30}. The influence of exercise on pain of

TABLE IV Activity level of patients participating in the Comprehensive Health Improvement Program (CHIP), excluding resting maximal metabolic equivalent capacity (MET)

	Pre-CHIP	Post-CHIP	
		6 Months	1 Month
Mean active MET hours per day	4.6	17.9 ^a	11.4

^a $p = 0.04$ compared with pre-CHIP score.

TABLE V Blood assays in patients participating in the Comprehensive Health Improvement Program (CHIP)

Variable	Pre-CHIP (mean)	Post-CHIP	
		1 Month (mean)	6 Months (mean)
BNP (pg/mL)	19.3	35	21.4
CRP (mg/L)	1.3	3.0	1.0
TC (mmol/L)	5.3	5.0	5.2
TG (mmol/L)	0.96	0.89	0.76
HDL (mmol/L)	1.8	1.7	2.1
LDL (mmol/L)	3.0	2.9	2.8
TC/HDL ratio	3.0	3.2	2.6

BNP = B-type natriuretic peptide; CRP = C-reactive protein; TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol.

the upper limbs or breast area after completion of treatments was, however, never investigated.

Currently, no specific treatment is known to help patients recover from chronic BCP, a symptom that affects patient QOL. The present pilot study used a multidisciplinary program, the CHIP, to examine the feasibility and potential efficacy of exercise to reduce chronic BCP. Realizing that exercise interventions may be more beneficial when offered after the completion of all treatments (reviewed in Spence *et al.*³¹), the CHIP was offered to symptomatic patients 3–6 months after completion of their treatments for breast cancer.

The questions used for eligibility screening in the present study aimed to identify patients who were most likely to be and to remain affected by moderate-to-severe BCP. Because the potential efficacy of the CHIP was unknown, it was hoped that any improvements in BCP and QOL would be more important in patients who were the most symptomatic. We also hoped that, by selecting patients with the most symptoms, a lack of any sign of efficacy of the CHIP in this pilot study would suggest that the potential benefit of the CHIP is small or perhaps unworthy of further evaluation. As applied, the screening method found 20 patients eligible to enter the study, of whom 10 participated. Patients who entered the study were generally young (median age: 51 years) and more likely to have undergone extensive surgeries (mastectomy and axillary node dissections)

or chemotherapy, or both. This patient population parallels those in previous studies that identified patients with similar characteristics as being particularly prone to develop BCP and arm symptoms^{5,7,10,12,32–34}.

The QOL scores of matched control patients were similar to the baseline QOL scores of CHIP patients even though the QOL data for the controls were obtained approximately 600 days later from surgery than the baseline data for the CHIP patients. Assuming that the matched controls had rates and extents of symptoms similar to those in the study patients, spontaneous healing and recovery after treatments would have occurred in the control group by the time their QOL data were obtained. The similarity in QOL scores between the control group and the CHIP patients at baseline suggests that patients with characteristics similar to those of CHIP patients may often have a similar level of symptoms at the breast and chest wall and may not recover spontaneously from those symptoms with time. Amelioration in the QOL of CHIP patients after their exercise program was therefore unlikely to be solely a result of spontaneous healing with time.

Of 10 patients enrolled, 8 completed the CHIP, but only 6 completed all of the questionnaires and follow-up assessments. These rates of accrual and questionnaire return are in keeping with those in most clinical and QOL studies. Nevertheless, lack of total compliance probably reduced the study's ability to detect hints of the efficacy of the CHIP.

Patients felt better after completion of the CHIP. This amelioration in QOL and BCP either continued or persisted at 6 months after CHIP completion. The SF-MPQ detected improvements in sensory and affective pains (Figure 2). Correspondingly, the EORTC questionnaires detected reductions in arm and breast symptoms, together with improved physical functioning. The EORTC pain and emotional functioning scores were significantly improved based on the *t*-test, but not on the Wilcoxon signed rank test.

Our study has multiple limitations because it aimed at determining the feasibility and potential efficacy of the CHIP in reducing BCP. First, although significant improvements in BCP and QOL were obtained, the number of patients is small, and so the results have to be validated in a larger study with more complete follow-up data. Second, case-matched controls from another QOL study at the same treatment centre were used as controls. A control group of this kind is less ideal than control patients accrued randomly during the same time period and followed in a fashion similar to that used with the study patients. Nevertheless, an advantage of the case-matched control group is a lack of interventional contamination, a common confounding factor in lifestyle intervention studies, because no exercise study was available for the controls. Third, a bias in patient selection may be present, because older and less-fit patients may not want to participate in exercise studies despite having similar symptoms. This study's patients were largely young women with relatively few cardiovascular disease risk factors, who

might have been physically active before their breast cancer diagnosis. Finally, compromised compliance from patients resulted in reduced statistical power and an inability to analyze all of the QOL and pain parameters from the questionnaires.

Despite those limitations, our study suggests that there is a population of breast cancer patients that suffers from chronic BCP and that may benefit from a rehabilitation exercise program to improve BCP and QOL. The CHIP is well tolerated. In accord with previously reported studies, an exercise intervention delivered after completion of adjuvant treatments improved patient QOL. In addition, the CHIP reduced BCP in this select patient group. Unlike previously studied exercise programs for breast cancer patients, the CHIP is tailored according to each patient's maximal cardiovascular tolerance and their upper-body limitations, with the aim of reducing pain induced by breast cancer treatments.

The results from this study are encouraging and will feed into the design of a larger validation study. If validated, exercise rehabilitation programs could be integrated into the long-term care of patients who suffer from chronic BCP, a condition that is not uncommon among young and advanced-stage cancer patients whose functioning and QOL are negatively affected.

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6. CONFLICT OF INTEREST DISCLOSURES

The authors have no conflicts of interest to declare.

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