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Reducing breathlessness, fatigue, and anxiety in Chinese patients undergoing lung cancer radiotherapy in Hong Kong

Key Messages

1. Levels of breathlessness, fatigue, and anxiety are moderately correlated, supporting the notion of viewing these three symptoms as a cluster.
2. An intervention combining patient education and progressive muscle relaxation is effective for combating the breathlessness, fatigue, and anxiety symptom cluster over a 6-week period.
3. The combined intervention is also effective for improving patients' overall functional ability over a 6-week period.
4. Progressive muscle relaxation alone does not produce a significant effect on the symptom cluster and functional ability.

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Introduction

Lung cancer is the leading cancer diagnosis for both genders in Hong Kong.[1] The majority of patients with lung cancer present with either advanced disease or develop metastases soon after the initial diagnosis. Patients undergoing lung cancer radiation therapy (RT) experience many different types of symptoms, of which breathlessness, fatigue, and anxiety have a higher prevalence.[2]

Breathlessness was reported by 65% of lung cancer patients.[2] The use of opiates and steroids to treat breathlessness only partially relieves the symptoms, as the emotional distress caused by this component of lung cancer is not addressed. Fatigue is another distressing symptom experienced by nearly all lung cancer patients (93%) during RT or in the months that follow.[3] Stress is considered a major cause of fatigue and recommended interventions include preparatory information and relaxation techniques. Anxiety is the most common psychological symptom seen in patients with lung cancer as they are facing a rapidly progressive fatal disease and a myriad of stressors. Anxiety and fear of suffocation increase in lung cancer patients (74%) who experience breathlessness and lack knowledge about the possible symptoms.[4]

Functional ability has been associated with breathlessness, fatigue, and anxiety in patients with lung cancer[2] and is often evaluated as a secondary outcome measure in interventional studies.[2] Interventions directed at assisting patients with these debilitating symptoms focus on education and relaxation therapies such as progressive muscle relaxation (PMR). Short and structured preparatory education reinforced by repeated sessions and written material, is generally recommended, however, psycho-educational interventions to reduce breathlessness and fatigue have seldom been tested.

Aims

This study aimed to examine the effectiveness of two interventions—PMR alone and a combination of education and PMR—on anxiety, breathlessness, and fatigue experienced by patients with lung cancer receiving radiotherapy. We hypothesised that there would be a significant difference over time between the three groups in the study—PMR alone (intervention group I); education combined with PMR (intervention group II); and usual care (control group)—in levels of anxiety, breathlessness, and fatigue.

Methods

This study was conducted from April 2002 to September 2004. A pre-test/post-test three-group randomised controlled trial was conducted in an out-patient RT unit of a public-funded hospital in Hong Kong. Subjects were asked to complete all instruments before (T0) and after the commencement of RT and the psycho-educational intervention at 3 weeks (T1), 6 weeks (T2), 3 months (T3), and 6 months (T4). A total of 183 subjects were recruited and consented to the study. Four subjects in the intervention group II withdrew before the baseline data collection due to fatigue and other discomfort.

Table 1. Disease and treatment characteristics of the participants in the intervention and control groups*

Demographic characteristic	Total sample (n=179)	Control group (n=61)	Intervention group I (n= 61)	Intervention group II (n=57)	P value
Stage of cancer illness					
Stage 3	100 (56%)	25 (41%)	40 (66%)	35 (61%)	0.01
Stage 4	79 (44%)	36 (59%)	21 (34%)	22 (39%)	
Duration of disease (months)	4.32±6.79	3.68±5.93	4.80±9.13	4.50±4.39	0.66
Radiotherapy dose (Grays)	28.79±8.67	28.03±7.82	30.69±10.19	27.57±7.48	0.10
Fractionation (Gy/fraction)	4.34±1.51	4.43±1.33	4.42±1.76	4.18±1.39	0.59
Days of radiation therapy (days)	7.49±3.38	7.00±3.07	8.11±3.76	7.35±3.23	0.18
Radiotherapy field size (cm^2)	134.86±52.31	134.95±44.74	145.88±72.62	122.95±25.01	0.06

* Values are shown in No. (%) or mean±standard deviation

Table 2. Baseline outcome variables*

Variable	Total sample (n=179)	Control group (n=61)	Intervention group I (n= 61)	Intervention group II (n=57)	P value
Abbreviated mental score (0-10)	9.44±0.68	9.36±0.73	9.54±0.57	9.42±0.73	0.33
Karnofsky score (0-100)	82.23±9.80	80.16±9.75	82.95±8.82	83.68±10.63	0.12
Breathing (0-100)	15.81±22.32	17.67±23.59	16.56±24.02	13.02±18.88	0.50
Satisfaction (1-4)	3.08±0.41	2.98±0.43	3.11±0.37	3.16±0.41	0.05
Fatigue (0-10)	3.41±2.12	3.66±2.11	2.98±2.25	3.61±1.95	0.15
Anxiety (20-80)	42.04±10.73	42.84±10.43	41.02±10.76	42.29±11.13	0.63
Physical function (0-100)	66.14±27.32	60±28.87	68.36±27.64	70.35±24.42	0.09
Physical role limitation (0-100)	25.14±38.90	28.28±40.69	25.41±40.95	21.49±34.86	0.64
Emotional role limitation (0-100)	48.23±46.09	51.91±46.95	51.91±46.95	40.35±43.98	0.29
Social function (0-100)	66.41±33.29	69.88±33.73	70.69±33.14	58.11±31.99	0.07

* Values are shown as mean±standard deviation

Study instruments

The study instruments were: (1) breathlessness—patients' subjective experiences of the intensity of breathlessness were assessed with a 100-mm visual analogue scale; (2) fatigue—the revised Piper Fatigue Scale consisting of 23 items was used to measure the duration and intensity of fatigue; (3) functional ability—the functional ability subscale of the Chinese version (HK) of the SF-36 item Health Survey was used; (4) anxiety—the Chinese version of the A-State scale of the State-Trait Anxiety Inventory was used to assess state of anxiety; (5) diary—compliance with the relaxation exercises was recorded by patients in a simple health diary (calendar) for 6 consecutive months; (6) demographic and treatment data—baseline demographic/disease/treatment data were obtained from patients and their medical records; (7) intervention activity log and patients' knowledge—an intervention activity log was set up in which the research assistant recorded at each session the patients' involvement and the problems encountered during implementation of the interventions. Patients in intervention group II were also asked to list three causes of and three solutions for those symptoms in order to assess their knowledge. Each correct answer was given a score of 1, yielding a possible range of 0 to 6; (8) interventions—interventions were given by a research assistant who was a qualified registered nurse with 2 years of clinical experience.

Interventions

Patients in group I were taught PMR within the week prior to commencing their RT course, and this was reinforced in week 3. Patients in group II were given an educational package and taught PMR in the week before commencing their RT course and this was reinforced in week 3. Contents of the educational package included: preparatory information, discussion of symptoms, exploration of the meaning of symptoms, and advice and support for patients on self-care strategies. Chinese leaflets and audiotapes about PMR and educational material were provided to patients according to their intervention groups.

Results

179 subjects completed the baseline data. The overall attrition rate was 8% at 6 weeks (T2), 26% at 3 months (T3), and 53% at 6 months (T4).

Baseline characteristics of the study sample

Most of the study participants were male (83%), had lower educational levels, were married (85%), and retired (53%). Their mean age was 62.84 years (standard deviation, 13.89 years). Disease and treatment characteristics of participants in both groups are shown in Table 1. Participants in the control group had significantly more advanced stage cancer and distant metastases. There was no difference between their baseline variables including breathlessness, fatigue, anxiety, satisfaction, and functional ability (Table 2). Significant moderate positive intercorrelations between breathlessness, fatigue, and anxiety at T0, T1, T2, T3, and T4 were found. Each baseline outcome variable also related significantly to its post-test measurements (r=0.198-0.728). The analyses of outcome variables for T0 to T2 were separated from T3 and T4, as T2 is the primary point for measuring the effect of the intervention, whereas T3 and T4 were used to assess the longer-term effect. To control for the

Table 3. Multivariate test for composite outcome of breathlessness, fatigue, and anxiety from T0 to T2 among the three groups

	P value	Partial eta Squared	Observed power
Group	0.24	0.025	0.520
Time	0.00	0.144	0.978
Time * Group	0.01	0.079	0.946

Table 4. Univariate tests of breathlessness, fatigue, and anxiety from T0 to T2

Measure	P value	Partial eta squared	Observed power (a)
Breathlessness	0.07	0.028	0.631
Fatigue	0.01	0.042	0.834
Anxiety	0.09	0.026	0.591

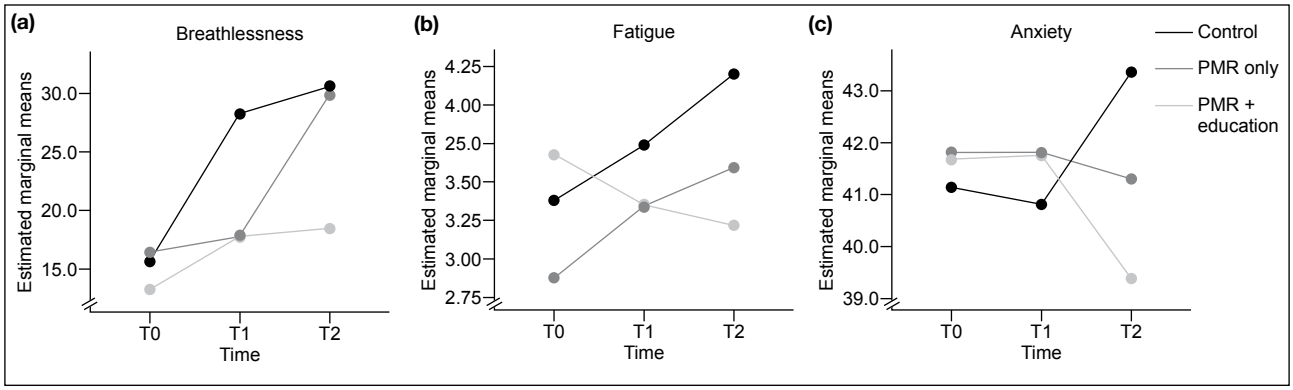

Fig 1. Estimated marginal means of breathlessness, fatigue, and anxiety from T0 to T2

PMR denotes progressive muscle relaxation

Table 5. Multivariate tests of functional ability scores from T0 to T2

	P value	Partial eta squared	Observed power (a)
Group	0.08	0.044	0.763
Time	0.00	0.169	0.987
Time * Group	0.02	0.094	0.962

baseline differences between stages of cancer in the three groups, the stage of cancer was entered into the model for analysis. The results indicated that stage of cancer did not affect the outcome differences between the study groups.

Symptom cluster of breathlessness, fatigue, and anxiety (T0 to T2)

The overall multivariate analysis of variance (MANOVA) showed that the changes in the composite outcome variable across the study period, T0 to T2, were found to be significantly different between the three study groups' time * group interaction effect (Table 3). The control group participants were found to have a greater increase in all symptoms at T2 (Fig 1). The effect size for the interaction was 0.079 (moderate effect). Further two-group MANOVA tests showed a significant difference in the change in composite symptom scores between the control group and intervention group II (P=0.021 and partial eta square=0.14). There was no significant difference between the control group and group I, or between intervention groups I and II. To detect for changes in individual symptoms, Bonferroni's correction was used to protect against a type I error in the three separate analyses, giving a new alpha significance level of 0.017. The only symptom with a significant difference in time * group interaction was fatigue (Table 4).

Functional ability from T0 to T2

Repeated MANOVA testing showed a significant change in the composite function variable over T0 to T2 between the three study groups' time *group interaction effect (Table 5). Control group participants showed a greater decrease in all function variables (Fig 2). Further 2-group MANOVA tests revealed a significant difference in the change in composite functional ability scores across T0 to T2 between the control group and intervention group II (P=0.003, partial eta square=0.213, observed power=0.959). There was no significant difference between the control group and intervention group I, nor between intervention groups I and II. In order to reduce type I errors caused by performing four separate analyses, Bonferroni's correction was used to give a new alpha significance level of 0.0125. There was a significant difference in social function and emotional role limitation between the two study groups across time (Table 6).

Knowledge about symptoms

A paired sample *t*-test found that patients in intervention group II reported significantly higher knowledge scores (t= –5.180, P<0005) after the intervention (mean, 2.34 vs 4.90). MANOVA tests showed no statistically significant group differences in the composite outcome of symptoms and functional ability (group effect) at T3 and T4. Patients in the intervention groups showed a high level of concentration on and participation in the intervention. They were also able to perform the PMR technique competently. More than half of the subjects were accompanied by a relative during the intervention and had the opportunity to read the leaflet and

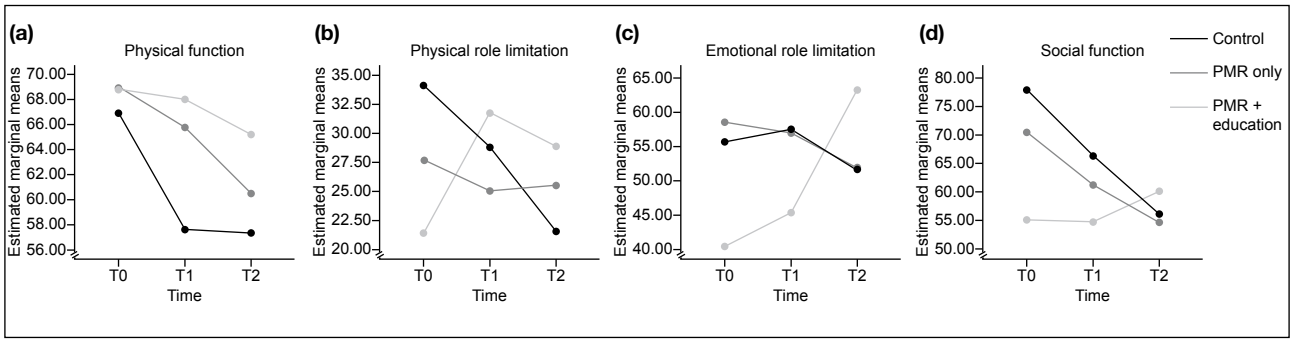

Fig 2. Estimated marginal means of functional ability scores from T0 to T2

PMR denotes progressive muscle relaxation

Table 6. Univariate tests of functional ability scores from T0 to T2

Measure	P value	Partial eta squared	Observed power
Physical function	0.22	0.018	0.437
Physical role limitation	0.15	0.021	0.520
Emotional role limitation	0.01	0.043	0.868
Social function	0.00	0.052	0.918

listen to the tape. The research assistant did not record any problems with delivery of the intervention. Most patients in intervention groups I and II practised PMR 60 to 70 times during the 6-month study period. There was a significant difference in the frequency of use of the relaxation exercise between the three groups ($F=55.203$, $P<0.0005$) with the control group using it least.

Discussion

Patients in intervention group II showed a significant improvement in their composite symptom cluster compared to those in the control group; PMR alone may not produce an effect. Although fatigue was the only symptom showing a statistically significant change, the mean scores for the changes in the three symptoms indicate that patients in the intervention groups had less increase in the intensity of all three symptoms at week 6. These results support the assumption that psycho-educational interventions can improve patients' overall functional ability. However, the results did not indicate that the interventions had long-term effects. A symptom cluster is defined as three or more concurrent symptoms that are moderately related to each other.[5] Whilst a specific cluster of breathlessness, fatigue, and anxiety has not yet been established, this study and several previous ones[6,7] have found that the intensity of the three symptoms positively correlate with one another. Therefore the three symptoms could be viewed as a cluster. Although breathlessness, fatigue, and anxiety are three distinct symptoms, a common psycho-educational intervention package was able to reduce the overall symptom intensity in this study. This makes effective use of nurses' as well as patients' time, and maximises the overall effect of an intervention.

Several limitations of this study should be noted. First, the high attrition rates at 3 and 6 months were mainly due to death. The missing data were not random but were related to outcomes that lead to attrition bias. Second, more of the patients in the control group had more advanced stage cancer and distant metastases. Because of these baseline differences, cancer stage was entered into the model for analysis. Although cancer stage did not significantly affect the outcome, this revealed a failure in the randomisation process.

This study has provided evidence supporting the management of breathlessness, fatigue, and anxiety as a symptom cluster, and explored the use of a common intervention to treat a cluster of symptoms simultaneously. These psycho-educational interventions can be easily adopted by health care professionals to promote optimal patient functioning.

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