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Morning breathing exercises prolong lifespan by improving hyperventilation in people living with respiratory cancer

Wei-Jie Wu, MB[a], Shan-Huan Wang, MB[a,b], Wei Ling, MD[a], Li-Jun Geng, MPhil[a], Xiao-Xi Zhang, PhD[a], Lan Yu, MPhil[a,c], Jun Chen, MPhil[a,c], Jiang-Xi Luo, MD[a,c], Hai-Lu Zhao, PhD[a,*]

Abstract

Disturbance of oxygen–carbon dioxide homeostasis has an impact on cancer. Little is known about the effect of breath training on cancer patients. Here we report our 10-year experience with morning breathing exercises (MBE) in peer-support programs for cancer survivors.

We performed a cohort study to investigate long-term surviving patients with lung cancer (LC) and nasopharyngeal cancer (NPC) who practiced MBE on a daily basis. End-tidal breath holding time (ETBHT) after MBE was measured to reflect improvement in alveolar O_2 pressure and alveolar CO_2 pressure capacity.

Patients (female, 57) with a diagnosis of LC (90 patients) and NPC (32 patients) were included. Seventy-six of them were MBE trainees. Average survival years were higher in MBE trainees (9.8 ± 9.5) than nontrainees (3.3 ± 2.8). The 5-year survival rate was 56.6% for MBE trainees and 19.6% for nontrainees (RR = 5.371, 95% CI = 2.271–12.636, $P < 0.001$). Survival probability of the trainees further increased 17.9-fold for the 10-year survival rate. Compared with the nontrainees, the MBE trainees shows no significant differences in ETBHT (baseline, $P = 0.795$; 1–2 years, $P = 0.301$; 3–4 years, $P = 0.059$) at baseline and within the first 4 years. From the 5th year onwards, significant improvements were observed in ETBHT, aCO_2%, $PaCO_2$, and PaO_2 ($P = 0.028$). In total, 18 trainees (40.9%) and 20 nontrainees (74.1%) developed new metastasis (RR = 0.315, 95% CI = 0.108–0.919, $P = 0.031$).

MBE might benefit for the long-term survival in patients with LC and NPC due to improvement in hyperventilation.

Abbreviations: ETBHT = end-tidal breath holding time, LC = lung cancer, MBE = morning breathing exercises, NPC = nasopharyngeal carcinoma.

Keywords: hyperventilation, lung cancer, morning breathing exercises, nasopharyngeal cancer

1. Introduction

All diseases, particularly cancer, are dependent on oxygen utilization.[1,2] Hypoxia plays a critical role in the pathobiology of all cancers,[3–5] and cancer is the second leading cause of death all over the world.[6] Correspondingly, lung cancer (LC) and nasopharyngeal carcinoma (NPC) are fatal respiratory diseases compromising aerobic respiration.[7,8] Prior studies have demonstrated the causation between cancers and oxygen utilization.[9,10] However, there are unmet clinical needs since applicable regiments with sustained effects are rare. By using a breath training program, would it be possible to improve probabilities of overall long-term survival?

Morning breathing exercises (MBE) are one of the most famous and effective peer-support cancer programs originating from traditional Chinese medical approaches.[11] The impact of breathing exercises on oxygen–carbon dioxide homeostasis improves hyperventilation in both healthy people and cancer patients. Many Chinese cancer patients nowadays practice MBE in addition to conventional therapies to prolong their survival.[12,13] However, the value of MBE has rarely been recognized because of the Chinese language barrier and the absence of published clinical observations.

In this study, we document our 10-year experience working with several peer-support groups of patients living with cancer and persistently practicing MBE, to explore the impact of MBE on hyperventilation in patients with LC and patients with NPC.

2. Methods

2.1. Study design

We performed a longitudinal cohort study of patients with LC and patients with NPC who had practiced MBE on a daily basis for at least 6 months. Nontrainees who did not practice MBE served as the control group. The Ethics Committee of the

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W-JW, S-HW, and WL contributed equally to this study.

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[a] Center for Systems Medicine, Guangxi Key Laboratory of Excellence, Guilin Medical University, [b] Department of Pathology, the Affiliated Hospital of Guilin Medical University, [c] College of Basic Medical Sciences, Guilin Medical University, Guilin, China.

[*] Correspondence: Hai-Lu Zhao, Center for Systems Medicine, Guangxi Key Laboratory of Excellence, Guilin Medical University, Guilin 541004, China (e-mail: zhaohailu9@126.com; zhaohailu@glmc.edu.cn).

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Affiliated Hospital of Guilin Medical University approved the study protocol.

2.2. Study participants

Participants were patients living with LC and patients living with NPC in Guilin. All the patients had a clinical and pathological diagnosis of LC or NPC, regardless of histopathological classifications, sex, race, age, duration of diagnosis, clinical stage, and therapeutics. It was the patients themselves who decided to practice MBE or not. The MBE trainees were given a thorough understanding of the study and gave written informed consent. Once patients were enrolled in the MBE program, a face-to-face interview was performed on a weekly basis. Time of dropout and death was recorded. The control group comprised of LC patients and NPC patients who did not practice MBE though they had similar baseline demographic characteristics. Individuals enrolled after 2003 had the end-tidal breath holding time (ETBHT) measured before and after MBE.

2.3. Morning breathing exercises

The aim of MBE focused on relaxing normal breathing and shifting anxiety and panic to a stress-free mind. All MBE trainees followed a standardized protocol (Supplementary Appendix, http://links.lww.com/MD/B510) and professional instruction by a team of qualified MBE coaches. The protocol of MBE consisted of 3 main steps: the preparatory exercises, the breathing exercises, and the walking exercises (Supplementary Figs. 1 and 2, http://links.lww.com/MD/B510). All the trainees practiced MBE at least 1 hour a day every morning.

2.4. Follow-up assessments and outcomes evaluation

Since 2003, our research staff followed up on both MBE trainees and nontrainees in the control group with face-to-face interviews. Information including sex, age, body mass index, diagnosis, metastasis, invasion, therapeutics, years of survival, and MBE-practicing time were collected. For patients who dropped-out, the latest interview data were used. The primary outcome was cancer-related death. The second outcome was ETBHT between MBE trainees and nontrainees. Recurrences or new metastases after the onset of the study were also recorded in both groups.

2.5. End-tidal breath holding time test

ETBHT refers to the normal breath holding time after a normal peaceful exhalation. ETBHT could indirectly reflect alveolar CO_2 (aCO_2) pressure and alveolar O_2 (aO_2) pressure. An ETBHT test was performed to measure improvement in respiration function between MBE-trainees and nontrainees. Before the ETBHT test, baseline data were collected to avoid bias. All the tests were performed by qualified staff. Alveolar CO_2 percent ($aCO_2\%$), aCO_2 pressure and aO_2 pressure were calculated using the following formulae:

(1) $aCO_2\% = 3.5\% + 0.05 \times BHT\%$
(2) aCO_2 pressure $= 760 \times aCO_2$ (mm Hg)
(3) aO_2 pressure $= -1.25$ aCO_2 pressure $+ 137.1$ (mm Hg)

2.6. Statistic analysis

Data are expressed as mean ± standard deviation (SD), absolute number, or percentage. Independent Student *t* test was used to calculate differences between MBE trainees and nontrainees, followed by 1-way ANOVA with Bonferroni comparison to detect within-group and between-group differences, Cox regression was performed to estimate cumulative survival function after adjusting for age, gender, cointervention, and duration of disease at the baseline. All the statistic analyses were done by using the SPSS 18.0. Relative risk (RR) and 95% confidence interval (95% CI) demonstrated the probability of survival and recurrence rate between the MBE trainees and nontrainees. A 2-tailed $P < 0.05$ was considered significant.

3. Results

3.1. Demographics and characteristics of included participants

By the end of August 2015, a total of 160 respiration cancer patients were recruited for eligibility. Among them, 38 patients were excluded due to difficulties in practicing MBE (n = 10), lack of interest (n = 20), and poor compliance (n = 8). Eventually, 122 participants (male, 65; female, 57; LC, 90 patients, and NPC, 32 patients) were included for analysis. Among them, 46 patients did not practice MBE (mean age, 56.1 ± 10.0 years). Hereby they were labeled as nontrainees. The other 76 patients had practiced MBE. Hence they were defined as MBE trainees (mean age, 60.9 ± 11.5 years). Baseline demographic variables such as sex, age, clinical stage, and body mass index were similar between the 2 groups (Table 1).

There were 12 patients practicing the MBE program before 2003. The duration of the cancers at the enrollment was 3.3 ± 2.5 years in MBE trainees and 0.6 ± 0.3 years in nontrainees. Overall, the trainees annually had practiced MBE for 279 ± 48 days (range, 215–355 days); a total of 57 participants (75%) had attended the MBE program for 300 or more days per year. There were no significant differences in participants' lifestyle or medications before starting the program.

Table 1

Demographic and clinical characteristics of included participants at baseline.

	MBE	Non-MBE
Cancer cases, no. (%)	76	46
Lung cancer	52	38
Nasopharynx cancer	24	8
Gender, M/F	42/34	23/23
Age, y	60.9 ± 11.5	56.1 ± 10.0
Body mass index, kg/m^2	22.8 ± 2.9	22.7 ± 3.7
Clinical stage, no. (%)		
Early	19 (25.0)	12 (26.1)
Middle	25 (32.9)	15 (32.6)
Late	32 (42.1)	19 (41.3)
Age at initial diagnosis, y	54.1 ± 10.5	53.0 ± 8.9
Smoking (current/former), no. (%)	38 (50.0)/4 (5.2)	22 (47.8)/3 (3.9)
Betel nut eating (current/former), no. (%)	3 (3.9)/0 (0)	1 (4.5)/0 (0)
Duration of disease before the study, y	3.3 ± 2.5	0.6 ± 0.3
Therapeutics, no. (%)		
Surgery	40 (52.6)	20 (43.5)
Chemo or radio	64 (84.2)	39 (84.7)
Other	52 (68.4)	31 (59.6)
Metastasis, no. (%)	32 (42.1)	19 (41.3)

Clinical stage: early, without metastasis; middle, with regional lymph nodes metastasis; late, with distal metastasis.
MBE = morning breathing exercises.

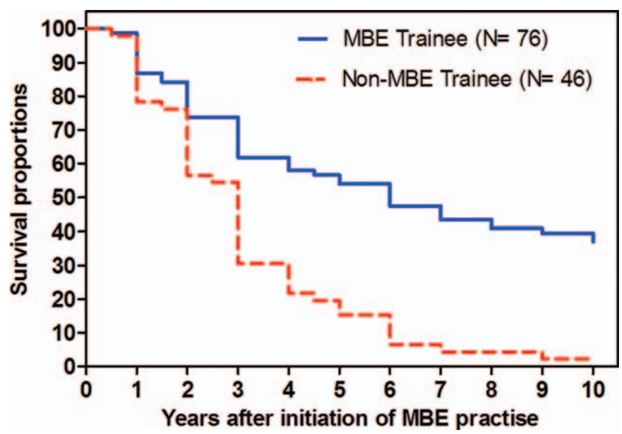

Figure 1. Cumulative survival curves of included patients alive relating to the duration of the MBE. The solid line (MBE trainees) and dashed lines (non-MBE trainees) are derived from Cox regression analysis.

3.2. Survival rates

Cox regression analysis demonstrated the cumulative survival proportion of enrolled patients (Fig. 1). Results of independent variables are shown in Table 2. The MBE-trainees contrasting nontrainees showed an increased probability of survival rates: 2-year survival rate by 1.2-fold, 3-year survival rate by 1.5-fold, 4-year survival rate by 2.2-fold, 5-year survival rate by 2.9-fold, and impressively 10-year survival rate by 17.9-fold. By the end of August 2015, the 76 trainees had survived an average of 9.8 ± 9.5 years, significantly longer than the 3.3 ± 2.8 years for the nontrainees in the control group. The 5-year survival rate of the trainees were 56.6%, significantly higher than 19.6% of the 46 nontrainees (RR = 5.371, 95% CI = 2.271–12.636, $P < 0.001$).

A total of 37 nontrainees (80.4%) and 33 trainees (43.4%) died within 5 years after the diagnosis of cancer. Interestingly, most of the deaths in the MBE group occurred in the first 5 years after diagnosis (Fig. 2), the mortality rate largely decreased after practicing MBE for more than 5 years. By the end of August 2015, normal life was achieved by 22 trainees in MBE group (29.2%), far more than the 1 patient (2.2%) of the control group (RR = 13.16, 95% CI = 1.86–95.56, $P < 0.0001$).

3.3. Secondary outcomes

ETBHT and respiratory rate were measured to demonstrate improvement of aCO_2 pressure and aO_2 pressure between the 2 groups (Table 3). Interestingly, ETBHT continued to increase in parallel to the cumulative MBE-practice time. In contrast, no significant improvement was seen in the nontrainees (Fig. 3A). By contrast, the respiratory rate slowed along with the continued training of MBE (Fig. 3B). In the first 4 years, improvement between MBE and nontrainees was not significant in ETBHT (baseline, $P = 0.795$; 1–2 years, $P = 0.301$; 3–4 years, $P = 0.059$) and respiratory rate (baseline, $P = 0.849$; 1–2 years, $P = 0.375$). From the fifth year and onwards, significant improvement due to MBE was seen in respiratory rates (5–10 years, 3–4 years,

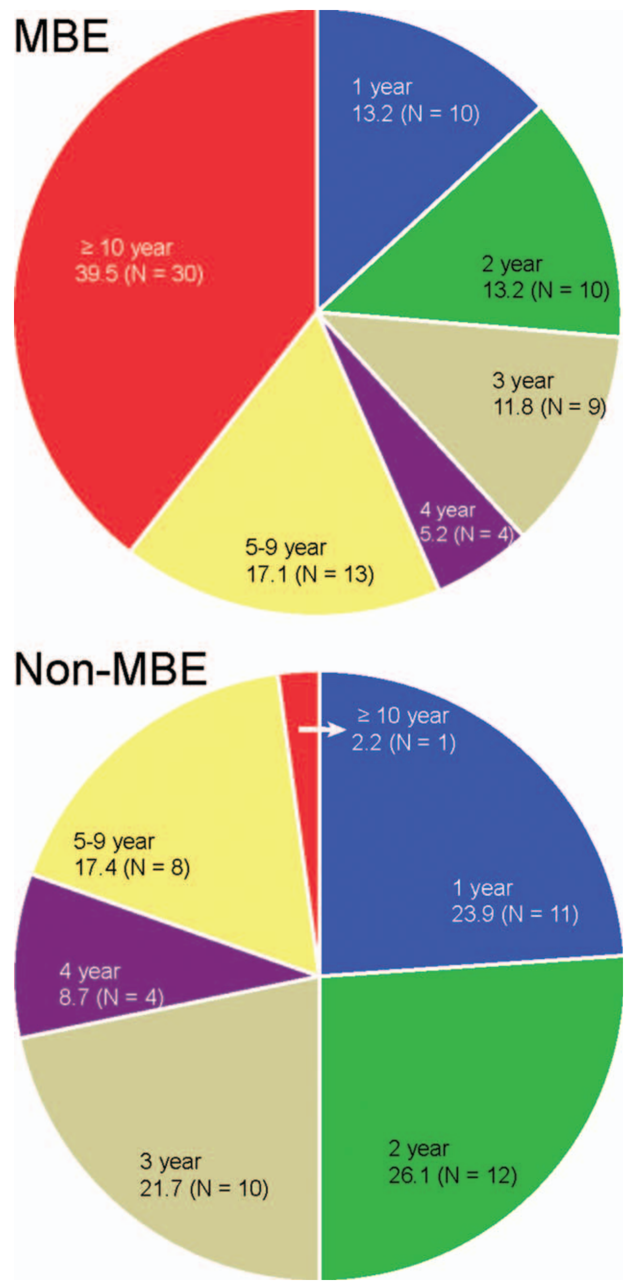

Figure 2. Survival rate between MBE trainees and nontrainees at different follow-up years.

Table 2

Results of independent variables.

	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B) Lower	Upper
Age	−0.072	0.014	26.216	1	<0.001	0.930	0.905	.956
Sex	−0.398	0.313	1.610	1	0.204	0.672	0.364	1.242
Stage	0.181	0.332	0.297	1	0.586	1.199	0.625	2.300
Cointervention	0.810	0.351	5.327	1	0.021	2.247	1.130	4.468

CI = confidence interval; SE = standard error.

Table 3

Differences of ETBHT, alveolar O_2, and CO_2 pressure after different survival years.

	Baseline		1–2 y		3–4 y		5–10 y	
	MBE	Non-MBE	MBE	Non-MBE	MBE	Non-MBE	MBE	Non-MBE
Cases, no.	76	46	76	46	56	24	43	9
RR, per minute	24.2 ± 5.65	24.1 ± 4.69	22.5 ± 5.25	23.5 ± 3.78	$20.7 \pm 5.19^{*,\dagger}$	23.6 ± 4.09	$18.6 \pm 5.95^{*,\dagger}$	23.0 ± 3.21
ETBHT, second	17.5 ± 6.98	17.8 ± 7.39	19.2 ± 7.18	17.9 ± 6.85	20.5 ± 6.19	18.1 ± 6.83	$21.3 \pm 8.88^{*,\dagger}$	18.0 ± 6.25
aCO_2,%	4.38 ± 0.35	4.39 ± 0.37	4.46 ± 0.36	4.38 ± 0.32	4.53 ± 0.36	4.41 ± 0.35	$4.57 \pm 0.44^{*,\dagger}$	4.40 ± 0.41
$PaCO_2$, mm Hg	33.25 ± 2.65	33.36 ± 2.81	33.90 ± 2.73	33.25 ± 2.43	34.39 ± 2.74	33.48 ± 2.66	$34.69 \pm 3.34^{*,\dagger}$	33.44 ± 3.12
PaO_2, mm Hg	95.41 ± 7.71	95.40 ± 7.23	94.73 ± 5.95	95.54 ± 5.42	94.11 ± 6.75	95.25 ± 7.51	$93.06 \pm 6.96^{*,\dagger}$	95.30 ± 6.17

aCO_2% = alveolar CO_2 percent, ETBHT = end-tidal breathe holding time, MBE = morning breathing exercises, $PaCO_2$ = aCO_2 pressure, PaO_2 = O_2 pressure, RR = respiratory rate.
* <0.05, *P*-value of Student *t* test between MBE trainees versus non-MBE trainees.
† <0.05, *P*-value of comparisons between baseline versus 5 to 10 years or 3 to 4 years.

$P = 0.038$; 5–10 years, $P = 0.0003$), ETBHT, aCO_2%, $PaCO_2$, and PaO_2 ($P = 0.028$). The results of the independent Student *t* test and 1-way ANOVA with Bonferroni for multiple comparisons are shown in Tables 4 and 5, respectively.

3.4. Metastasis after morning breathing exercises

In total, 51 patients (41.8%) developed new metastasis and subsequently were labeled as patients with late clinical stage, while the remaining patients had early- or middle-clinical stage (MBE group: 44 cases, 57.9%; non-MBE group: 27 cases, 58.7%). After starting MBE, 18 MBE trainees (40.9%) and 20 nontrainees (74.1%) had new metastasis (RR = 0.315, 95% CI = 0.108–0.919, $P = 0.031$). Most of the trainees complained that stressful social relations and fear of sudden death were responsible for their new metastasis.

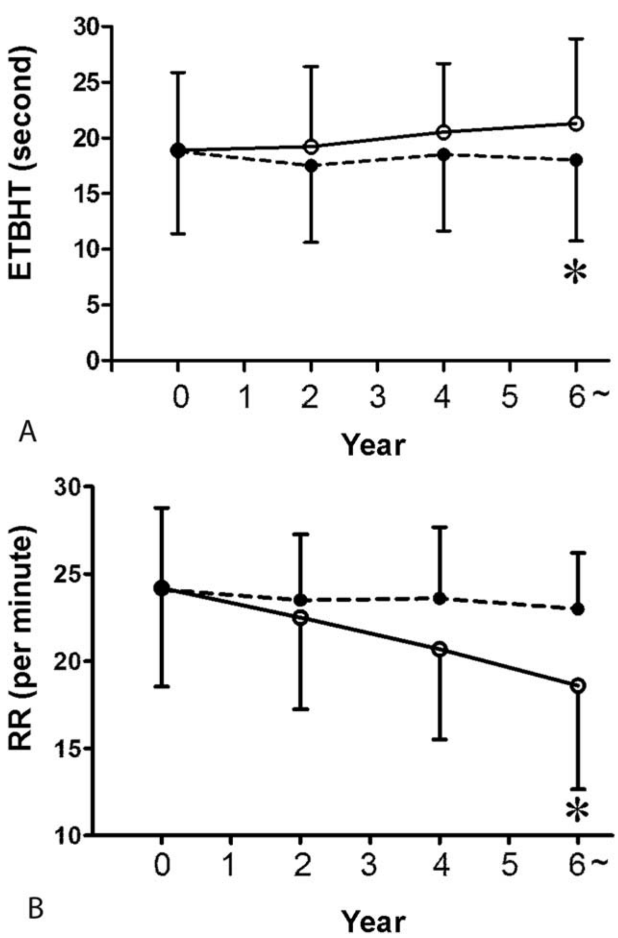

Figure 3. Trends of ETBHT and respiratory rate after different survival years between MBE-trainees and nontrainees. Solid line (MBE trainees) and dashed lines (non-MBE trainees). $^*P < 0.05$ MBE versus non-MBE.

4. Discussion

In our 10-year working experience with the peer-support programs for patients with LC and patients with NPC, we can report the benefit of MBE on long-term survival rates. MBE practitioners might likely survive LC and NPC for 5 more years after the diagnosis through improved hyperventilation defined by aCO_2%, aCO_2 pressure and aO_2 pressure.

Without doubt, physical exercise is important for cancer patients. Several studies have validated the necessity of appropriate exercise for cancer patients.[14–18] Inactivity and sedentary lifestyles are strongly associated with obesity, a risk factor for cancer of the breast, colon, endometrium, kidney, and pancreas.[19–21] This study highlights the benefits of MBE in the management of LC and NPC. MBE could improve hyperventilation to sustain the MBE trainees' survival and maintain a disease-free life in patients living with cancer.

Oxygen–carbon dioxide homeostasis via normal breathing is crucial for health while disturbance of the homeostasis may cause many disorders, especially cancers. Kunz and Ibrahim[22] have proposed that tissue hypoxia may serve as a central factor for carcinogenesis, invasion, aggressiveness, and metastasis. Distant metastases in human soft tissue sarcoma can be predicted by tumor oxygenation.[23] Generally, the difficulty in one's breathes is parallel to the cancer invasion.[24] Moreover, hypoxia can compromise the function of macrophages, enzymes and other cytokines and lymphocytes of the immune system.[25] In addition, hypoxic conditions modulate biological responses including activation of signaling pathways that regulate proliferation, angiogenesis, and death.[26,27] In this study, the MBE trainees demonstrated an improvement in ETBHT, aO_2 pressure, and aCO_2 pressure capacity compared with the nontrainees, suggesting that sustained oxygen–carbon dioxide homeostasis and improved hyperventilation are the explanations of higher survival rates. By contrast, conventional cancer therapies may simultaneously affect one or more components of the oxygen cascade,[28] leading to exacerbated hyperventilation, reduced respiration regulation function and subsequent comorbidities.

Another possible mechanism that could allow MBE to minimize hyperventilation and prolong survival probably links to psychological factors. Researchers have suggested that psychological symptoms such as tension, hallucination, lack of

Table 4

Differences between MBE and non-MBE (Student *t* test).

MBE vs non-MBE	*P*				
	RR	ETBHT	aCO_2	$PaCO_2$	PaO_2
Baseline	0.8492	0.7952	0.7952	0.7952	0.7952
1–2 y	0.3754	0.3008	0.3008	0.3008	0.3008
3–4 y	0.0382*	0.0593	0.0593	0.0593	0.0593
5–10 y	0.0003*	0.0280*	0.0280*	0.0280*	0.0280*

aCO_2% = alveolar CO_2 percent, ETBHT = end-tidal breath holding time, MBE = morning breathing exercises, $PaCO_2$ = aCO_2 pressure, PaO_2 = O_2 pressure, RR = respiratory rate.
* $P < 0.05$.

Table 5

Multiple comparisons derived from 1-way ANOVA in MBE trainees (Bonferroni method).

	P				
	RR	ETBHT	aCO_2	$PaCO_2$	PaO_2
Baseline					
1–2 y	0.2780	1.0000	1.0000	1.0000	1.0000
3–4 y	0.0003*	0.0893	0.0893	0.0893	0.0893
5–10 y	<0.0001*	0.0127*	0.0127*	0.0127*	0.0127*
1–2 y					
Baseline	0.2780	1.0000	1.0000	1.0000	1.0000
3–4 y	0.1978	1.0000	1.0000	1.0000	1.0000
5–10 y	<0.0001*	0.4894	0.4894	0.4894	0.4894
3–4 y					
Baseline	0.0003*	0.0893	0.0893	0.0893	0.0893
1–2 y	0.1978	1.0000	1.0000	1.0000	1.0000
5–10 y	0.0837	1.0000	1.0000	1.0000	1.0000
5–10 y					
Baseline	<0.0001*	0.0127*	0.0127*	0.0127*	0.0127*
1–2 y	<0.0001*	0.4894	0.4894	0.4894	0.4894
3–4 y	0.0837	1.0000	1.0000	1.0000	1.0000

aCO_2% = alveolar CO_2 percent, ETBHT = end-tidal breath holding time, $PaCO_2$ = aCO_2 pressure, PaO_2 = O_2 pressure, RR = respiratory rate.
* $P < 0.05$.

concentration, depression, anxiety, and phobias are strongly associated with hyperventilation.[29–32] Meanwhile, psychological problems are significantly higher among long-term cancer survivors than respondents who are never diagnosed as having cancer.[33,34] Most patients experience extremely stressful reactions at the moment that they are informed they have cancer.[35–37] Compared with individuals without a label of cancer, cancer survivors reported significantly more frequent contact with a mental health provider.[38] In the present study, trainees were guided to practice MBE in a peaceful state on a daily basis to experience a stress-free mind. Additionally, the improvement of hyperventilation might prevent anxiety and restore metabolic and immunological homeostasis.[39,40]

In conclusion, an individualized exercise program such as MBE may be essential in cancer management. Collectively, MBE might be beneficial for long-term survival of LC and NPC. The mechanism of how MBE improves survival probability may be attributed to the attenuation of hyperventilation evidenced by the improvement of aO_2 pressure and aCO_2 pressure. Given the fact that each and every day, thousands of people are diagnosed with cancers, MBE may offer a cost-effective approach to people living cancer.

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