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

Wei-Jie Wu, MB; Shan-Huan Wang, MB; Wei Ling, MD; Li-Jun Geng, MPhil; Xiao-Xi Zhang, PhD; Lan Yu, MPhil; Jun Chen, MPhil; Jiang-Xi Luo, MD; Hai-Lu Zhao, PhD

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 O₂ pressure and alveolar CO₂ 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, aCO₂, PaCO₂, and PaO₂ (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,[3,4] cancer is the second leading cause of death all over the world.[5] 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] 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.[10] 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.[11,12,13] 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
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.

2.2. 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.

2.3. 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 exhalation. ETBHT could indirectly reflect alveolar CO2 (aCO2) pressure and alveolar O2 (aO2) 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 CO2 percent (aCO2%), aCO2 pressure and aO2 pressure were calculated using the following formulae:

\[
\text{(1) aCO2\% = } 3.5\% + 0.05 \times \text{BHT\%}
\]

\[
\text{(2) aCO2 \text{ pressure} = 760 \times aCO2 \text{ mm Hg}}
\]

\[
\text{(3) aO2 \text{ pressure} = -1.25 \times aCO2 \text{ pressure} + 137.1 } \text{ (mm Hg)}
\]

2.6. Statistical 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 37 participants (73%) 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/m² | 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 (50.0/45.2) | 22 (47.8/30.9) |
| 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 (69.6) |
| 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.
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 non-trainees 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 non-trainees in the control group. The 5-year survival rate of the trainees were 56.6%, significantly higher than 19.6% of the 46 non-trainees (RR = 5.371, 95% CI = 2.271–12.636, P < 0.001).

A total of 37 non-trainees (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 aCO2 pressure and aO2 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 non-trainees (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 non-trainees 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, 95.0% CI for Exp (B)

| B       | SE      | Wald | df | Sig.  | Exp (B) | Lower | Upper |
|---------|---------|------|----|-------|---------|-------|-------|
| Age     | 0.072   | 0.014| 26.216 | 1  | <0.001 | 0.930 | 0.905 | 0.956 |
| 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.
PaCO2, mm Hg 33.25
aCO2, % 4.38
ETBHT, second 17.5
PaO2, mm Hg 95.41
RR, per minute 24.2
Cases, no. 76 46 76 46 56 24 43 9

MBA group: 44 cases, 57.9%; non-MBA group: 27 cases,
while the remaining patients had early- or middle-clinical stage
subsequently were labeled as patients with late clinical stage.

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
(MBA group: 44 cases, 57.9%; non-MBA group: 27 cases,
58.7%). After starting MBA, 18 MBA 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.

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 MBA on long-term survival rates. MBA
practitioners might likely survive LC and NPC for 5 more years
after the diagnosis through improved hyperventilation defined by
aCO2%, aCO2 pressure, and PaO2 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 MBA in the
management of LC and NPC. MBA could improve hyperventilation
to sustain the MBA 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 breaths
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 MBA trainees
demonstrated an improvement in ETBHT, aO2 pressure, and
aCO2 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 MBA to
minimize hyperventilation and prolong survival probably links
to psychological factors. Researchers have suggested that
psychological symptoms such as tension, hallucination, lack of

---

**Table 3**

Differences of ETBHT, alveolar O2, and CO2 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 |
| RR, per minute| 24.2±5.65 | 24.1±4.69 | 22.5±5.25 | 23.5±3.78 | 20.7±5.10 | 23.6±4.09 | 18.6±5.05 | 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±8.68 | 18.0±6.25 |
| aCO2%, %      | 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±0.44 | 4.40±0.41 |
| PaCO2, 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±3.34 | 33.44±3.12 |
| PaO2, 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±6.96 | 95.30±6.17 |

*aCO2% = alveolar CO2 percent, ETBHT = end-tidal breathe holding time, MBA = morning breathing exercises, PaCO2 = aCO2 pressure, PaO2 = O2 pressure, RR = respiratory rate.

<0.05, *P*-value of Student’s *t* test between MBA trainees versus non-MBA trainees.
<0.01, †*P*-value of comparisons between baseline versus 5 to 10 years or 3 to 4 years.

---

**Figure 3**

Trends of ETBHT and respiratory rate after different survival years between MBA-trainees and nontrainees. Solid line (MBA trainees) and dashed lines (non-MBA trainees). *P* < 0.05 MBA versus non-MBA.
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.\(^{35}\) 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.\(^{39,40}\) \(^{a}\)

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 \(\text{aO}_{2}\) pressure and \(\text{aCO}_{2}\) 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 with cancer.

**Acknowledgments**

We would like to thank Miss. Min WANG for her assistance in statistics and Mr. Alan W. Abrams for his professional English editing and proofreading.

**References**

1. Semenza GL. Oxygen sensing, homeostasis, and disease. N Engl J Med 2011;365:537–47.
2. Gatenby RA, Gillies RJ. Why do cancers have high aerobic glycolysis? Nat Rev Cancer 2004;4:891–9.
3. Cook KM, Figg WD. Angiogenesis inhibitors: current strategies and future prospects. CA Cancer J Clin 2010;60:222–43.
4. Lalonde E, Ishikani AS, Sykes J, et al. Tumour genomic and microenvironmental heterogeneity for integrated prediction of 5-year biochemical recurrence of prostate cancer: a retrospective cohort study. Lancet Oncol 2014;15:1521–32.
5. Eltzschig HK, Carmeliet P. Hypoxia and inflammation. N Engl J Med 2011;364:636–45.
6. Seegal RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65:5–29.
7. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995–2010: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 2015;385:977–1010.
8. Wang R, Wu F, Lu H, et al. Definitive intensity-modulated radiation therapy for nasopharyngeal carcinoma: long-term outcome of a multicenter prospective study. J Cancer Res Clin Oncol 2013;139:139–45.
9. Zegers CM, van Elmp Jr, Weym B, et al. In vivo quantification of hypoxic and metabolic status of NSCLC tumors using \([18\text{F}]\text{FDG-PET/CT imaging. Clin Cancer Res 2014;20:6389–97.}\)
10. Hui EP, Chan AT, Pezzella F, et al. Coexpression of hypoxia-inducible factors 1alpha and 2alpha, carbonic anhydrase IX, and vascular endothelial growth factor in nasopharyngeal carcinoma and relationship to survival. Clin Cancer Res 2002;8:595–604.
11. Guolin Qigong for Cancers in China. 2016 (Accessed 30 September, 2015, available at http://www.guolinqigong.cn/main.html).

**Table 4**

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

| MBE vs non-MBE | RR    | ETBHT | \(\text{aCO}_{2}\) | \(\text{PaCO}_{2}\) | \(\text{PaO}_{2}\) |
|---------------|-------|-------|------------------|-------------------|-----------------|
| Baseline      | 0.8492| 0.7952| 0.7952           | 0.7952            | 0.7952          |
| 1–2 y         | 0.3754| 0.3088| 0.3088           | 0.3088            | 0.3088          |
| 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\(*\) |

\(\text{aCO}_{2}\% = \text{alveolar CO}_{2}\text{ percent, ETBHT = end-tidal breath holding time, MBE = morning breathing exercises, PaCO}_{2} = \text{aCO}_{2}\text{ pressure, PaO}_{2} = \text{O}_{2}\text{ pressure, RR = respiratory rate.}\)

\(* P < 0.05.\)

**Table 5**

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

| MBE vs non-MBE | RR    | ETBHT | \(\text{aCO}_{2}\) | \(\text{PaCO}_{2}\) | \(\text{PaO}_{2}\) |
|---------------|-------|-------|------------------|-------------------|-----------------|
| Baseline      | 0.2780| 1.0000| 1.0000           | 1.0000            | 1.0000          |
| 1–2 y         | 0.0003\(*\) | 0.0893| 0.0893           | 0.0893            | 0.0893          |
| 3–4 y         | <0.0001\(*\) | 0.0127\(*\) | 0.0127\(*\) | 0.0127\(*\) | 0.0127\(*\) |
| 5–10 y        | 0.0003\(*\) | 0.4894| 0.4894           | 0.4894            | 0.4894          |
| 1–2 y         | 0.1978| 1.0000| 1.0000           | 1.0000            | 1.0000          |
| 3–4 y         | <0.0001\(*\) | 0.0893| 0.0893           | 0.0893            | 0.0893          |
| 5–10 y        | 0.0837| 1.0000| 1.0000           | 1.0000            | 1.0000          |
| 1–2 y         | 0.0003\(*\) | 0.0127\(*\) | 0.0127\(*\) | 0.0127\(*\) | 0.0127\(*\) |
| 3–4 y         | 0.0837| 1.0000| 1.0000           | 1.0000            | 1.0000          |

\(\text{aCO}_{2}\% = \text{alveolar CO}_{2}\text{ percent, ETBHT = end-tidal breath holding time, PaCO}_{2} = \text{aCO}_{2}\text{ pressure, PaO}_{2} = \text{O}_{2}\text{ pressure, RR = respiratory rate.}\)

\(* P < 0.05.\)
[12] Chen K, Yeung R. Exploratory studies of Qigong therapy for cancer in China. Integr Cancer Ther 2002;1:345–70.
[13] Jones BM. Changes in cytokine production in healthy subjects practicing Guolin Qigong: a pilot study. BMC Complement Altern Med 2001; 1:8. doi: 10.1186/1472-6882-1-8.
[14] Gravitz L. Prevention: tending the gut. Nature 2015;521:86–8.
[15] Turner DP. Advanced glycation end-products: a biological consequence of lifestyle contributing to cancer disparity. Cancer Res 2015;75:1925–9.
[16] Jones LW, Demark-Wahnefried W. Diet, exercise, and complementary therapies after primary treatment for cancer. Lancet Oncol 2006;7:1017–26.
[17] Thune I, Brenn T, Lund E, et al. Physical activity and the risk of breast cancer. N Engl J Med 1997;336:1269–75.
[18] Song M, Garrett WS, Chan AT. Nutrients, foods, and colorectal cancer prevention. Gastroenterology 2015;148:1244.e16–60.e16.
[19] Fontham ET, Thun MJ, Ward E, et al. American Cancer Society perspectives on environmental factors and cancer. CA Cancer J Clin 2009;59:343–51.
[20] Biwas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med 2015;162:123–32.
[21] Arem H, Pfeiffer RM, Engels EA, et al. Pre- and postdiagnosis physical activity, television viewing, and mortality among patients with colorectal cancer in the National Institutes of Health–AARP Diet and Health Study. J Clin Oncol 2015;33:180–8.
[22] Kunz M, Ibrahim SM. Molecular responses to hypoxia in tumor cells. Mol Cancer 2003;2:23. doi:10.1186/1476-4598-2-23.
[23] Brizel DM, Scully SF, Harrelson JM, et al. Tumor oxygenation predicts for the likelihood of distant metastases in human soft tissue sarcoma. Cancer Res 1996;56:941–3.
[24] Normal breathing: the key to vital health (Accessed December 22, 2016, available at http://www.curezone.org/upload/PDF/Books/book_big_ch_1_5.pdf).
[25] Rockwell S. Oxygen delivery: implications for the biology and therapy of solid tumors. Oncol Res 1997;9:383–90.
[26] Chaplin DJ, Durand RE, Olive PL. Acute hypoxia in tumors: implications for modifiers of radiation effects. Int J Radiat Oncol Biol Phys 1986;12:1279–82.
[27] Schmaltz C, Hardenbergh PH, Wells A, et al. Regulation of proliferation-survival decisions during tumor cell hypoxia. Mol Cell Biol 1998;18:2845–54.
[28] Jones LW, Eves ND, Haykowsky M, et al. Exercise intolerance in cancer and the role of exercise therapy to reverse dysfunction. Lancet Oncol 2009;10:658–605.
[29] Cluff RA. Chronic hyperventilation and its treatment by physiotherapy: discussion paper. J R Soc Med 1984;77:853–62.
[30] Magarian GJ, Maddaugh DA, Linz DH. Hyperventilation syndrome: a diagnosis begging for recognition. West J Med 1983;138:733–6.
[31] Wastes TF. Hyperventilation—chronic and acute. Arch Intern Med 1978;138:1700–1.
[32] Lum LC. Hyperventilation: the tip and the iceberg. J Psychosom Res 1975;19:75–83.
[33] Weaver KE, Forzythe LP, Reeve BB, et al. Mental and physical health-related quality of life among U.S. cancer survivors: population estimates from the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev 2012;21:2108–17.
[34] Hoffman KE, McCarthy EP, Recklitis CJ, et al. Psychological distress in long-term survivors of adult-onset cancer: results from a national survey. Arch Intern Med 2009;169:1274–81.
[35] DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin 2014;64:252–71.
[36] Whitney RL, Bell JF, Bold RJ, et al. Mental health needs and service use in a national sample of adult cancer survivors in the USA: has psychosocial care improved? Psycho oncology 2015;24:80–8.
[37] Goodwin PJ, Leszcz M, Ennis M, et al. The effect of group psychosocial support on survival in metastatic breast cancer. N Engl J Med 2001;345:1719–26.
[38] Hewitt M, Rowland JH. Mental health service use among adult cancer survivors: analyses of the National Health Interview Survey. J Clin Oncol 2002;20:4581–90.