

Flavia Swan, PhD
 Wolfson Palliative Care Research Centre
 Hull York Medical School, University of Hull
 Hull, UK
 E-mail: flavia.swan@hyms.ac.uk

Anne English, MSc
 Dove House Hospice, Hull, UK

Victoria Allgar, PhD
 Hull York Medical School
 Department of Health Sciences
 University of York
 Heslington, UK

Simon P. Hart, PhD
 Hull York Medical School, University of Hull,
 Hull, UK

Miriam J. Johnson, MD
 Wolfson Palliative Care Research Centre
 Hull York Medical School, University of Hull
 Hull, UK

<https://doi.org/10.1016/j.jpainsymman.2019.03.009>

References

1. Swan F, English A, Allgar V, Hart SP, Johnson M. The hand-held fan and the Calming Hand for people with chronic breathlessness: a feasibility trial. *J Pain Symptom Manage* 2019;57:1051–1061.e1.
2. Johnson MJ, Bland JM, Oxberry SG, Abernethy AP, Currow DC. Clinically important differences in the intensity of chronic refractory breathlessness. *J Pain Symptom Manage* 2013;46:957–963.
3. Fletcher C. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). *BMJ* 1960;2:1665.
4. Farquhar MC, Prevost AT, McCrone P, et al. Is a specialist breathlessness service more effective and cost-effective for patients with advanced cancer and their carers than standard care? Findings of a mixed-method randomised controlled trial. *BMC Med* 2014;12:194.
5. Gysels MH, Higginson IJ. Caring for a person in advanced illness and suffering from breathlessness at home: threats and resources. *Palliat Support Care* 2009;7:153–162.
6. Booth S, Farquhar M, Gysels M, Bausewein C, Higginson IJ. The impact of a breathlessness intervention service (BIS) on the lives of patients with intractable dyspnea: a qualitative phase 1 study. *Palliat Support Care* 2006;4:287–293.
7. Booth S, Silvester S, Todd C. Breathlessness in cancer and chronic obstructive pulmonary disease: using a qualitative approach to describe the experience of patients and carers. *Palliat Support Care* 2003;1:337–344.

The Use of Continuous Positive Airway Pressure Ventilation in the Palliative Management of Stridor in a Head and Neck Cancer Patient



Introduction

Upper airway obstruction and stridor are common symptoms faced by head and neck cancer patients.

Progression of cancers of the head and neck region often results in an audible stridor when the primary tumor occupies an already anatomically restricted space in the upper airway. Management of upper airway obstruction includes nonpharmacological maneuvers such as head tilt, chin lift, and jaw thrust.¹ Pharmacological measures are usually limited to the relief of symptoms associated with the airway obstruction such as breathlessness and stridor. These include steroids, opioids, and benzodiazepines. The distressing symptom of stridor may be challenging to manage at the end of life with clinicians facing the potential development of terminal asphyxiation. In these patients, alternative methods of relieving stridor and its resulting complication of respiratory failure are required.^{2–5} Discussions regarding prophylactic tracheostomy should be conducted with patients and their family as part of a management strategy. We report the use of continuous positive airway pressure (CPAP) as a means of noninvasive ventilation in the palliative management of stridor at the end of life.

Case Description

Mdm. Chan, a 91-year-old lady, was diagnosed with metastatic cricopharyngeal cancer before her referral to our home hospice care service. The primary tumor had metastasized to surrounding lymph nodes and her disease continued to progress despite her being placed on immunotherapy. Radiological investigations revealed a large posterior pharyngeal mass sitting above the laryngeal inlet and obscuring the view of the vocal cords. In view of the high risk of complete laryngeal obstruction, radiotherapy was offered which both family and patient declined (partly due to risk of potential worsening of stridor because of inflammation as well as the advanced age of the patient).

Subsequently, Mdm. Chan received palliative care at home. As her disease progressed, she developed a loud audible stridor which could be heard in both inspiratory and expiratory phases of respiration. This greatly distressed her family members although she was comfortable. An attempt to reposition her head and neck while lying down improved the stridor, limiting it only to the expiratory phase. As Mdm. Chan deteriorated further, she developed dyspnea and insomnia, which was accompanied with restlessness. Pharmacological agents such as subcutaneous fentanyl (average of 75 mcg a day in three divided doses of 25 mcg) and subcutaneous midazolam (average of 5 mg a day in two divided doses of 2.5 mg) were given for palliation of her dyspnea and restlessness. These agents provided temporary relief but her audible stridor continued to worsen.

Mdm. Chan developed breakthrough seizures and was admitted to an acute hospital for workup and management. A CT scan of the brain did not reveal any metastasis, and the seizure was attributed to recurrent chronic cerebral hypoxia. Oxygen supplementation was administered, and subcutaneous midazolam and morphine were given for palliation of symptoms. Owing to the persistence of symptoms, the primary medical team in charge decided to put Mdm. Chan on a trial of CPAP ventilation as a noninvasive method of keeping her airway open. This greatly improved her stridor and she subsequently required minimal subcutaneous fentanyl (2 doses of 25 mcg in a week) with no need for subcutaneous midazolam for symptom relief. The treatment was continued successfully and she remained comfortable until she passed away two weeks from the date of admission into hospital.

Discussion

The mechanism of stridor is due to the presence of a supraglottic tumor arising from the posterior pharyngeal wall resulting in obstruction of smooth flow of air via the laryngeal inlet producing the characteristic stridor. The upper airway is a complex structure comprising muscles and soft tissue and is involved in a variety of functions such as passage of air, swallowing, as well as phonation. The lack of a rigid cartilaginous/bony structure predisposes the structure to collapse.

During inspiration, intrathoracic volume increases with reciprocal decrease in intrathoracic pressure, drawing air in via the upper airway. The presence of a cricopharyngeal tumor greatly narrows an already easily collapsible airway. Pharyngeal patency is known to be influenced by lung volume.⁶ Higher lung volumes are associated with a decrease in upper airway resistance to airflow and vice versa. When lung volume is reduced, there is a displacement of the diaphragm and thorax toward the head. This results in a loss of caudal traction on the upper airway, yielding a more collapsible airway.

CPAP hence may potentially splint the upper airway and relieve stridor and dyspnea by 1) maintaining a high level alveolar partial pressure O₂, 2) improving ventilation by saturating dead space with higher FiO₂, 3) decreasing the work of breathing through pressure support, and 4) increasing airway compliance and positive distending pressure. The resulting increase in lung volume also reduces the collapsibility of the upper airway.^{6–9}

Extrapolating this concept, CPAP does not aim to displace a solid tumor but to increase pharyngeal patency. This positive distending pressure may be able to explain the improvement of stridor and subsequent

effective palliation of this symptom.⁵ It has been observed in a previous study¹⁰ that positive pressure ventilation can provide significant improvement in dyspnea as it not only assists with ventilation, it corrects hypoventilation, increases inspiratory flow rate, and also reduces the work of breathing in cancer patients with dyspnea. In another study by Abernathy et al.,⁸ findings reveal that movement of air near nasal passages rather than oxygen itself can improve dyspnea. As such, CPAP with room air may be just as beneficial as CPAP with a higher FiO₂.

Although this experience is only limited to one patient and has limited generalizability, it opens up the possibility of an alternative when other therapeutic options may have failed. A therapeutic trial of CPAP may be justified when a patient has symptomatic stridor and dyspnea and has less than ideal outcome from the usage of commonly used drugs such as opioids and benzodiazepines. Further research is necessary to learn more about the effectiveness of noninvasive ventilation in head and neck cancers.

Jasvin Lee, MD
Kyaw Naing, MD
Zhi Zheng Yeo, BA
Poh Heng Chong, MD
HCA Hospice Care
Kwong Wai Shiu Hospital
Singapore, Singapore
E-mail: jasvinl@hcahospicecare.org.sg

<https://doi.org/10.1016/j.jpainsymman.2019.04.025>

Disclosures and Acknowledgments

The authors thank Dr. Mervyn Koh and Dr. Wu Huei Yaw for their input and guidance.

References

1. Meier S, Geiduschek J, Paganoni R, Fuehrmeyer F, Reber A. The effect of chin lift, jaw thrust, and continuous positive airway pressure on the size of the glottic opening and on stridor score in anesthetized, spontaneously breathing children. *Anesth Analg* 2002;94:494–499.
2. Meert AP, Berghmans T, Hardy M, Markiewicz E, Sculier JP. Non-invasive ventilation for cancer patients with life-support techniques limitation. *Support Care Cancer* 2006;14:167–171.
3. Meduri GU, Fox RC, Abou-Shala N, Leeper KV, Wunderink RG. Noninvasive mechanical ventilation via face mask in patients with acute respiratory failure who refused endotracheal intubation. *Crit Care Med* 1994;22:1584–1590.
4. Cuomo A, Delmastro M, Ceriana P, et al. Noninvasive mechanical ventilation as a palliative treatment of acute respiratory failure in patients with end-stage solid cancer. *Palliat Med* 2004;18:602–610.

5. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. *Respir Med* 2009;103:1400–1405.

6. Squier SB, Patil SP, Schneider H, et al. Effect of end-expiratory lung volume on upper airway collapsibility in sleeping men and women. *J Appl Physiol* (1985) 2010;109:977–985.

7. Bruera E, de Stoutz N, Velasco-Leiva A, Schoeller T, Hanson J. Effects of oxygen on dyspnoea in hypoxaemic terminal-cancer patients. *Lancet* 1993;342:13–14.

8. Abernethy AP, McDonald CF, Frith PA, et al. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. *Lancet* 2010;376:784–793.

9. Nava S, Cuomo AM. Acute respiratory failure in the cancer patient: the role of non-invasive mechanical ventilation. *Crit Rev Oncol Hematol* 2004;51:91–103.

10. Hui D, Morgado M, Chisholm G, et al. High-flow oxygen and bilevel positive airway pressure for persistent dyspnea in patients with advanced cancer: a phase II randomized trial. *J Pain Symptom Manage* 2013;46:463–473.

Nearly Half of Metastatic Brain Disease Patients Prescribed 10 Fractions of Whole-Brain Radiation Therapy Die Without Completing Treatment



To the Editor

Since 1954, whole-brain radiation therapy (WBRT) has been an integral palliative treatment modality for brain metastases.¹ For over 40 years, the standard palliative WBRT regimen in the U.S. has been 30 Gy in 10 fractions over two weeks, although shorter regimens have been reported.^{2–4} Although prolonged (≥ 10 fractions) WBRT regimens have historically been favored owing to a perceived improvement in neurocognitive side effect profile, hypofractionated WBRT is equally effective for disease control^{2,3} and reduces the burden of prolonged treatment on patients and caregivers near the end of life. In addition, some patients cannot finish planned WBRT owing to declining performance status; however, the likelihood of failing to complete standard-fractionation WBRT has not been rigorously evaluated. To address this void, the following analysis was performed to allow for improved objective quantifying of this commonly used palliative modality.

Methods

An IRB-approved prospective institutional database identified 52 patients receiving WBRT (30 Gy/10 fractions) for brain metastases between April 2015 and December 2018. Functional independence was defined as Karnofsky Performance Status (KPS) ≥ 70 ; 30-day

Table 1
Clinical Characteristics of Patients Who Did Versus Did Not Complete WBRT

Patient Demographic	Failed WBRT Completion (n = 23)	Completed WBRT (n = 29)	P-value
Age (mean)	58.0	58.2	0.966
Male	11 (47.8%)	11 (37.9%)	0.576
Female	12 (52.2%)	18 (62.1%)	
Inpatient	14 (60.1%)	12 (41.4%)	0.264
Outpatient	9 (29.9%)	17 (58.6%)	
KPS ≥ 70	4 (17.4%)	13 (44.8%)	0.043
Death within 30 days of final fraction	16 (69.6%)	9 (31.0%)	0.011

WBRT = whole-brain radiation therapy; KPS = Karnofsky Performance Status.

mortality was defined as death within 30 days immediately after final radiation treatment. Statistical analyses were performed in SPSS version 24 (IBM Corp., Armonk, NY). $P < 0.05$ was considered statistically significant.

Results

Of 52 patients who began WBRT, 29 (55.8%) completed prescribed therapy; demographics are depicted in Table 1. Patients completing WBRT were significantly more likely to be functionally independent at baseline and had lower 30-day mortality. Mean treatment duration for patients completing WBRT was 15.3 days. Of the 23 patients failing to complete standard WBRT, 30-day mortality was nearly 70%.

Discussion

Brain metastases carry a poor prognosis; median survival after WBRT is three to four months.^{2,3,5} However, this relatively long anticipated survival after WBRT has historically provided practitioners with confidence that prolonged treatment regimens will not adversely affect QOL. Our results indicate this widespread presumption may be incorrect. The large minority (nearly 50%) of patients prescribed standard 10-fraction WBRT who died without completing treatment suggests that a large subset of this patient population may not live as long as generally presumed. Consequently, adjustments to clinical practice of both prescribing and requesting WBRT should be considered, particularly because the data originally establishing 10-fraction WBRT as the standard of care demonstrated no significant difference in survival or local control between 30 Gy in 10 fractions, 20 Gy in five fractions, and 10 Gy in one fraction.^{2–3} In addition, Level I evidence has demonstrated no neurocognitive advantage of prolonged WBRT.⁶ For the significant proportion of WBRT patients with less than four weeks to live, any reduction in treatment time represents a meaningful reduction in the rigors of