Dyspnea and ASCO guidelines

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Objectives

- Apply appropriate tools for assessment of dyspnea in palliative/oncology populations
- Identify and assess modulating factors and related symptoms that compound the burden of dyspnea and impact prognosis
- Describe recommended approaches for treatment and management of dyspnea, including pharmacologic and non-pharmacologic strategies and interventions

Case 1

- 62 yo severe pulmonary HTN, OSA
- Exacerbation of Pulmonary HTN → RVF → Acute on chronic hypoxic RF.
- Was on Lasix gtt, Dobutamine gtt, Sildenafil, Nitric oxide Letairis (Ambrisentan),Treprostinil and Midodrine.
- The patient is alert, interactive, anxious needed BiPAP at night, high flow nasal cannula oxygen and also non-rebreather intermittently.
- Patient was transferred to PCU with goals to wean high flow nasal cannula oxygen as patient wishes to go home with hospice care.
- Patient was apprehensive about using opioids.
- Patient's vitals T 36.5 HR 105 RR 22 BP 98/61
- O2 sat 88% on 50 L Flow / 90 % Fio2 HFNC
- Respiratory effort was labored
- Reported last 24-hour RASS of +1 to 0

Case 2

- 69 yo CAD s/p CABG, CVA, HTN
- Stroke alert was found to have right M1 occlusion.
- Was not a candidate for thrombectomy.
- Repeat CT showed worsening edema and hemorrhagic conversion.
- Patient continued to be somnolent, afebrile, CXR shows atelectasis, continues to be tachypneic.
- Patient was transferred to PCU with comfort care goals and for end-of-life care.
- Patient was already started on Fentanyl nebs and basal infusion.
- Patient's vitals were T 36.5 HR 106 RR 26 BP 99/68
- O2 sat 99% on 2L NC
- Respiratory effort was nonlabored
- Reported last 24-hour RASS of -2 to -1

Case 1

The patient is alert, interactive needed BiPAP at night. HFNC oxygen and nonrebreather intermittently.

Patient was transferred to PCU with goals to wean high flow nasal cannula oxygen and go home with hospice.

Patient was apprehensive about using opioids.

Patient's vitals T 36.5 HR 105 RR 22 BP 98/61

O2 sat 88% on 50L Flow / 90 % Fio2 HFNC

Respiratory effort was labored

Reported last 24-hour RASS of +1 to 0

Case 2

Patient continued to be somnolent, afebrile. CXR shows atelectasis, continues to be tachypneic.

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Reported last 24-hour RASS of -2 to -1

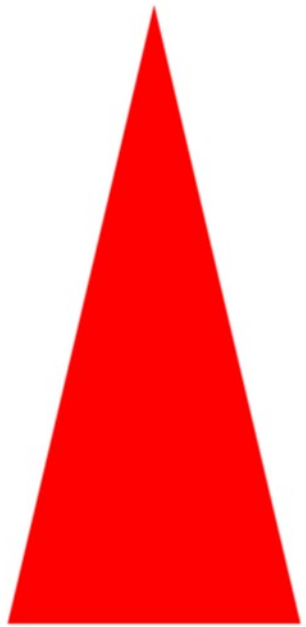
Hierarchy of evidence

based on quality

STUDY DESIGN

- Randomized Controlled Trials
- Cohort Studies and Case Control Studies
- Case Reports and Case Series, Non-systematic observations
- Expert Opinion

BIAS



Interpretation of grades of evidence

- ⊕⊕⊕⊕/A/High: We are very confident that the true effect lies close to that of the estimate of the effect.
- ⊕⊕⊕◯/B/Moderate: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- ⊕⊕◯◯/C/Low: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- ⊕◯◯◯/D/Very low: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

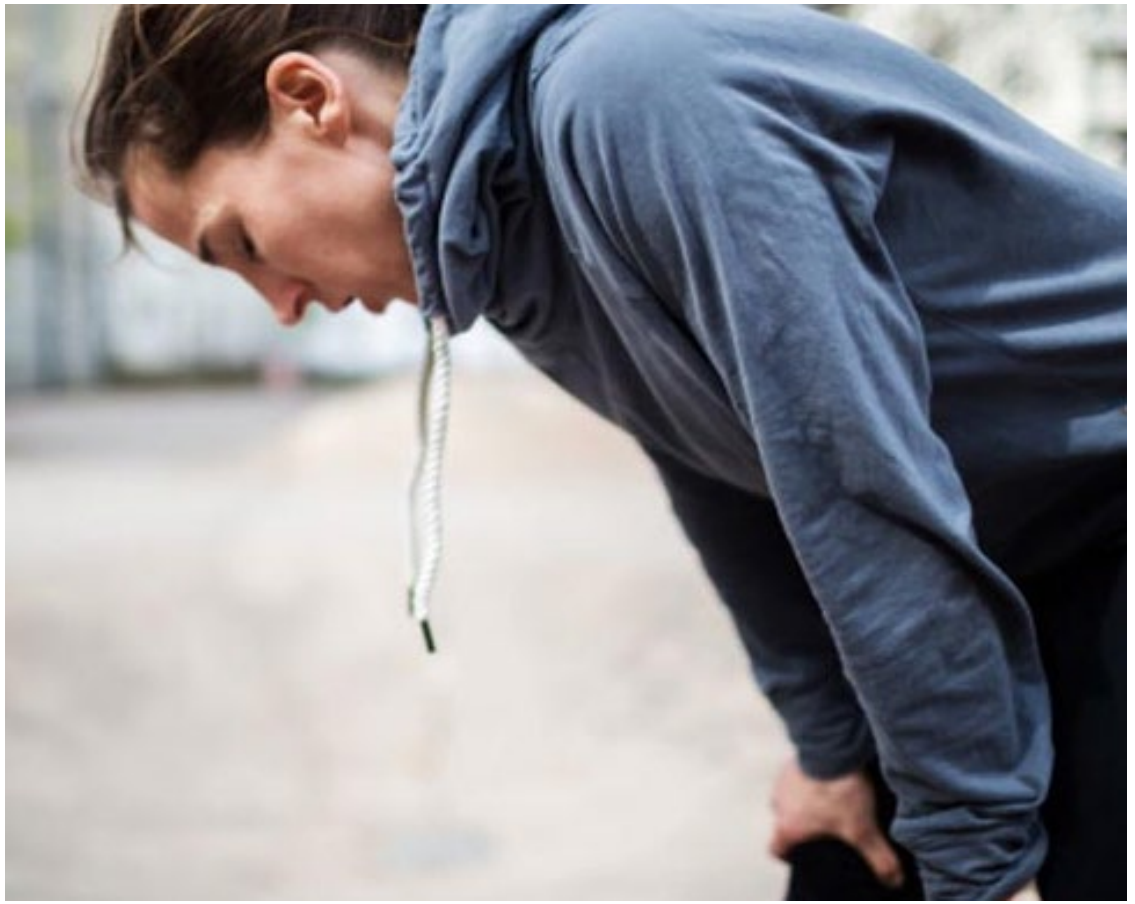
Strength of recommendation

"The strength of a recommendation reflects the extent to which we can, across the range of patients for whom the recommendations are intended, be confident that desirable effects of a management strategy outweigh undesirable effects."

- Strong or conditional

What is Dyspnea ?

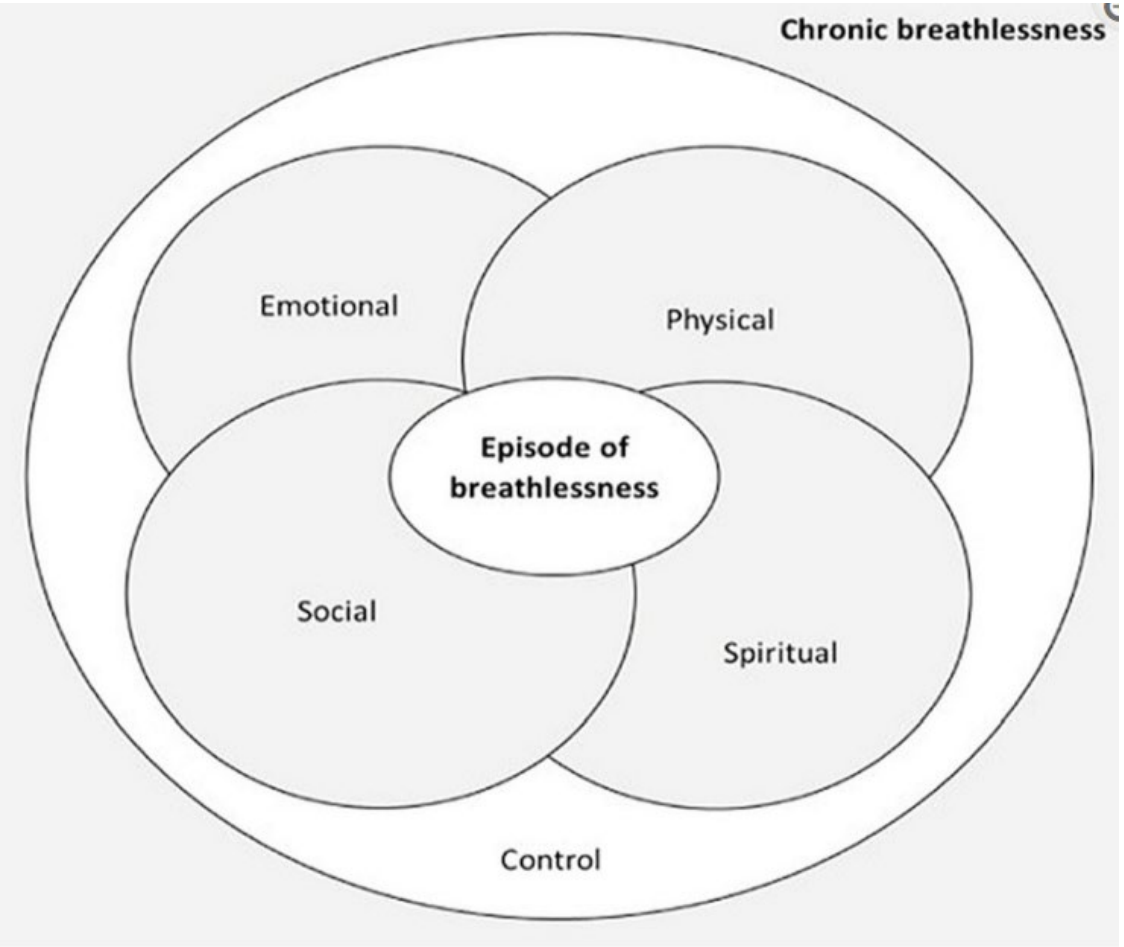
- Shortness of breath
- Air Hunger
- Difficulty breathing
- Feeling of suffocation
- Running out of the air
- Chest tightness
- Inability to breathe
- Not able to breathe fast enough
- Not able to breathe deep enough



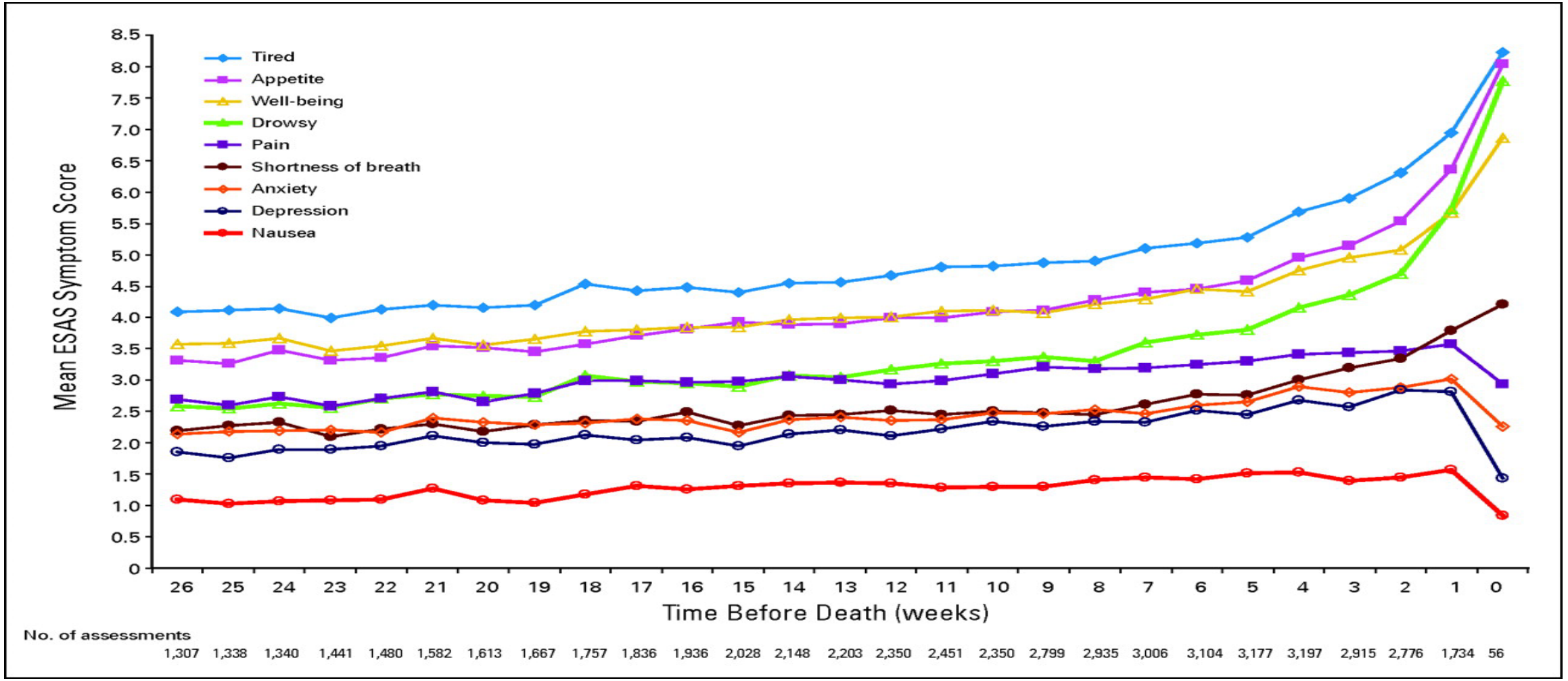
Definition

A consensus statement of American Thoracic Society has defined dyspnea as

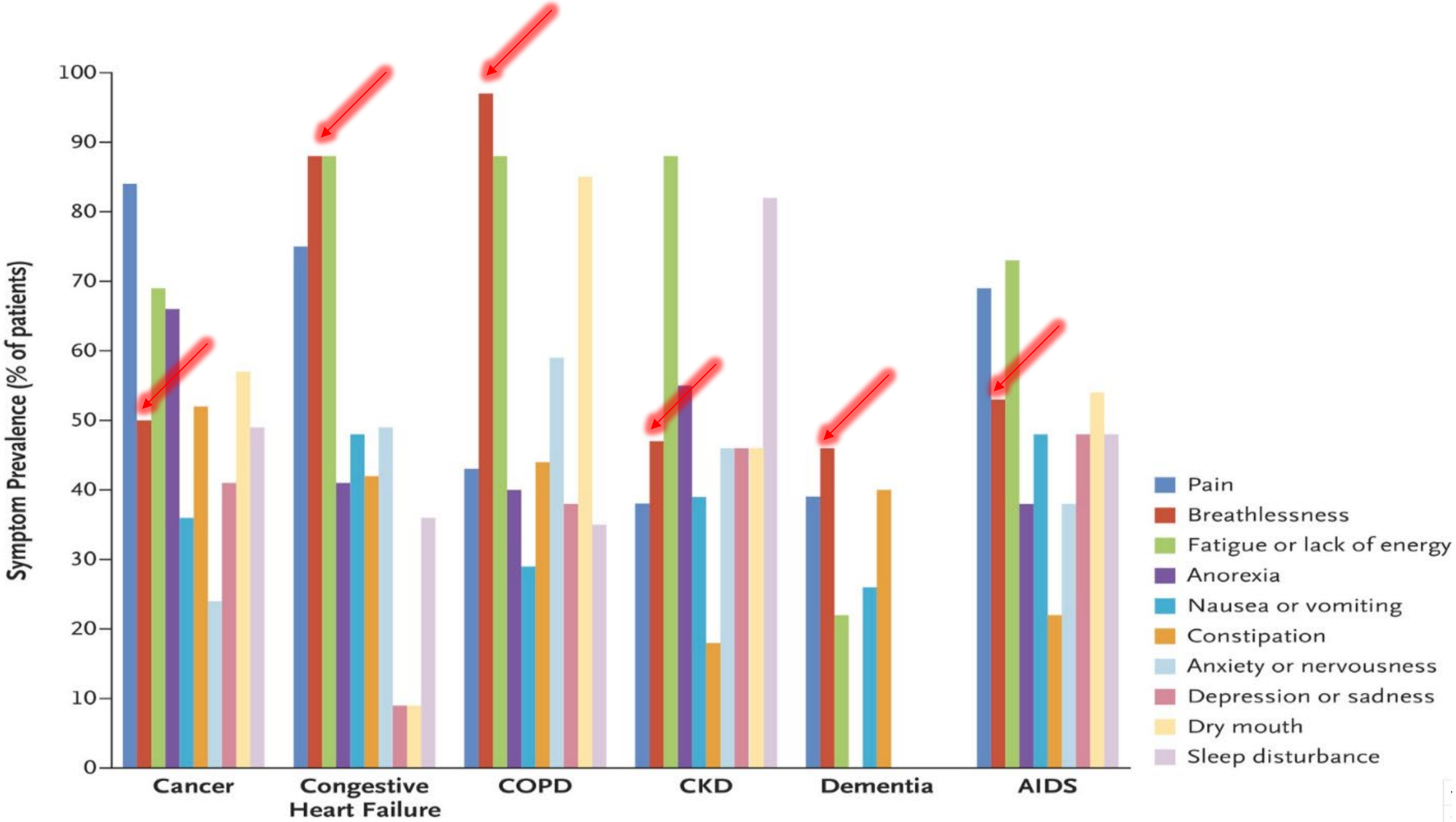
"a term used to characterize **a subjective experience of breathing discomfort that comprises qualitatively distinct sensation that vary in intensity.** Experience derives from interactions among multiple physiological, psychological, social and environmental factors, and may induce secondary physiologic and behavioral response."



Mean Edmonton Symptom Assessment System (ESAS) symptom scores over time (10752 patients)



Hsien Seow et al. JCO 2011;29:1151-1158


Symptom Prevalence (% of patients)
100
90
80
70
60
50
40
30
20
10
0
Cancer
Congestive Heart Failure
COPD
CKD
Dementia
AIDS
Pain
Breathlessness
Fatigue or lack of energy
Anorexia
Nausea or vomiting
Constipation
Anxiety or nervousness
Depression or sadness
Dry mouth
Sleep disturbance

One of the most common and distressing symptoms affecting patients with advanced cancer.[2]

In a meta-analysis that included more than 10,000 patients with advanced cancer, 10%-70% of patients reported dyspnea.[2]

Dyspnea typically increases in prevalence and intensity as patients approach the last weeks to days of life.[3-6]

In a longitudinal observational study of patients with lung cancer, dyspnea was consistently ranked as the most distressing symptom.[7]

The burden of dyspnea is further compounded by other related symptoms such as fatigue, anxiety, and depression, resulting in functional limitation, compromised quality of life, and increased informal (family) caregiver burden.[8]

In the advanced cancer setting, the presence of dyspnea, particularly at rest, indicates a poor prognosis (typically less than a few months) and has important clinical implications.[9]

2. Solano JP, Gomes B, Higginson IJ: A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 31:58-69, 2006

3. Seow H, Barbera L, Sutradhar R, et al: Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. J Clin Oncol 29:1151-1158, 2011

4. Hui D, dos Santos R, Chisholm GB, et al: Symptom expression in the last seven days of life among cancer patients admitted to acute palliative care units. J Pain Symptom Manage 50:488-494, 2015

5. Campbell ML, Kiernan JM, Strandmark J, et al: Trajectory of dyspnea and respiratory distress among patients in the last month of life. J Palliat Med 21:194-199, 2018

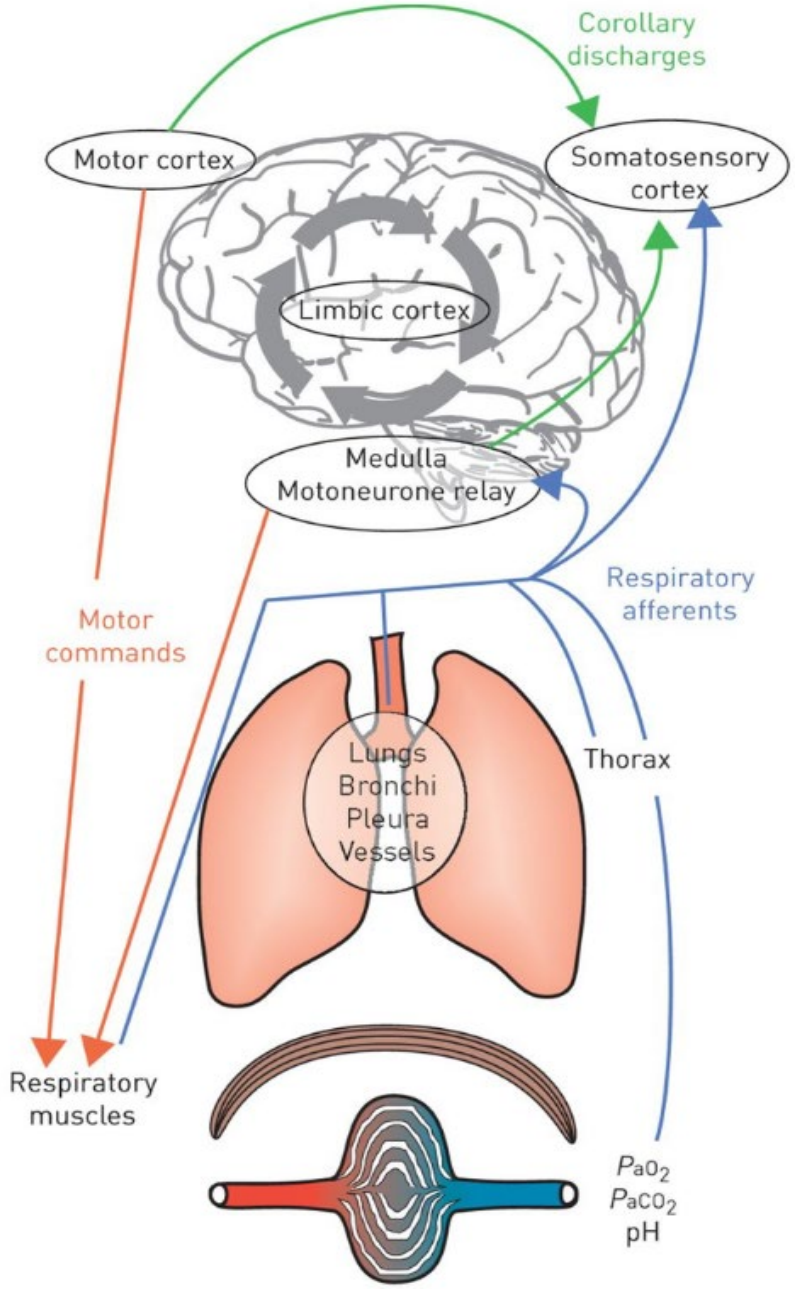
6. Currow DC, Smith J, Davidson PM, et al: Do the trajectories of dyspnea differ in prevalence and intensity by diagnosis at the end of life? A consecutive cohort study. J Pain Symptom Manage 39:680-690, 2010

7. Tishelman C, Petersson LM, Degner LF, et al: Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death. J Clin Oncol 25:5381-5389, 2007

8. Reddy SK, Parsons HA, Elsayem A, et al: Characteristics and correlates of dyspnea in patients with advanced cancer. J Palliat Med 12:29-36, 2009

9. Cuervo Pinna MA, Mota Vargas R, Redondo Moralo MJ, et al: Dyspnea: A bad prognosis symptom at the end of life. Am J Hosp Palliat Care 26:89-97, 2009

Mechanism



Approach to Tachypnea in the ED SettingAuthor: Dorian Alexander, MD (Associate Program Director, Director of Critical Care in Emergency Medicine, Brookdale University Hospital, Brooklyn, NY) // Edited by: Alex Koyfman, MD (@EMHighAK, EM Attending Physician, UTSW / Parkland Memorial Hospital) and Brit Long, MD (@long_brit)

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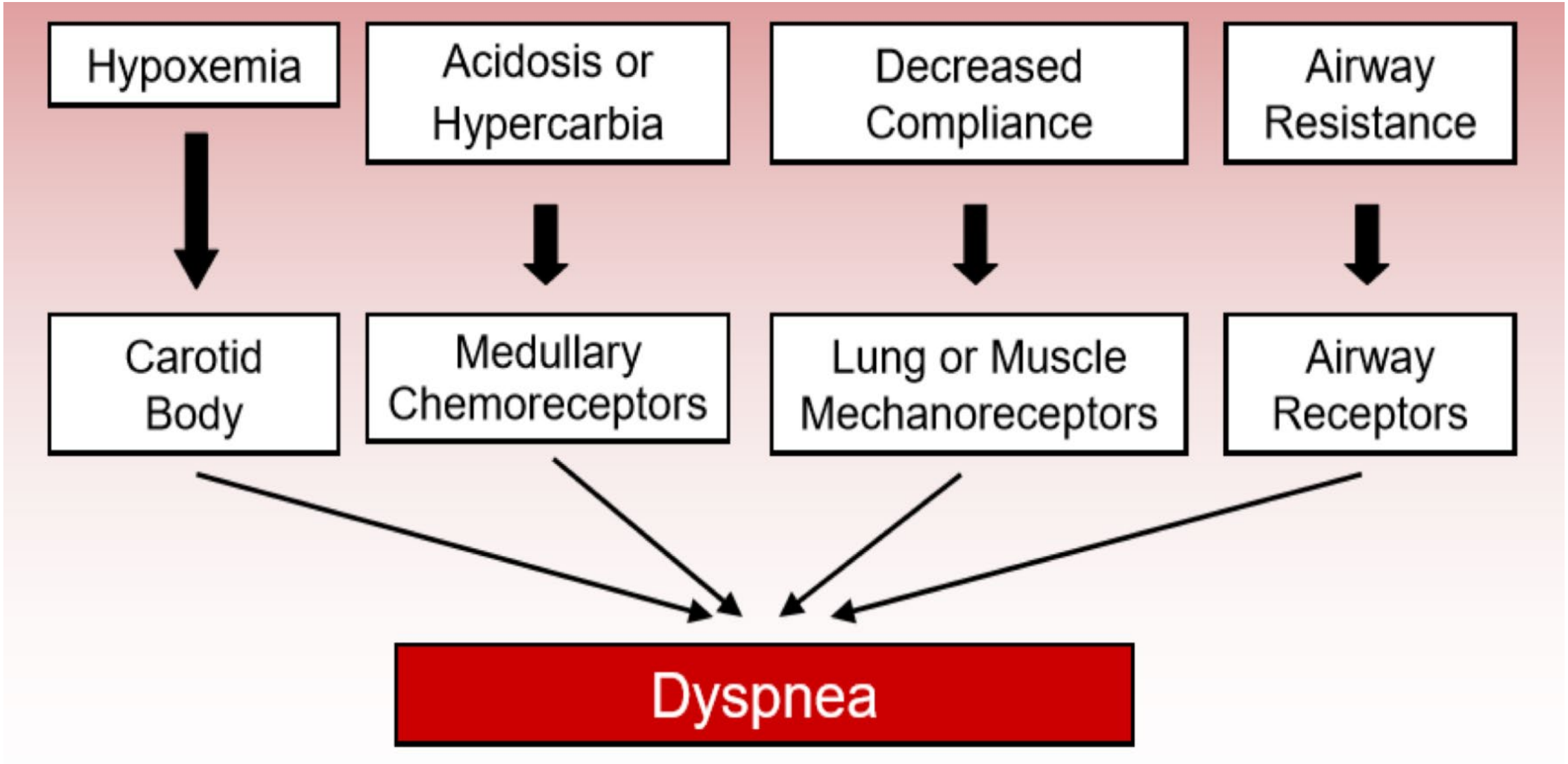


Approach to Tachypnea in the ED SettingAuthor: Dorian Alexander, MD (Associate Program Director, Director of Critical Care in Emergency Medicine, Brookdale University Hospital, Brooklyn, NY) // Edited by: Alex Koyfman, MD (@EMHighAK, EM Attending Physician, UTSW / Parkland Memorial Hospital) and Brit Long, MD (@long_brit)

What starts production of dyspnea ?

- Increase in respiratory effort to overcome a certain load
  - e.g. obstructive, restrictive lung disease, pleural effusion
- Increase in the proportion of the respiratory muscle requirement to maintain a normal workload
  - e.g. malnutrition, cachexia
- Increase in ventilatory requirement
  - e.g. hypoxemia, hypercapnia, acidosis, anemia

In cancer patients these abnormalities may co exist and therefore the pathophysiologic interpretation of the intensity of dyspnea can be more complex.

Types of breathing

A. Forebrain

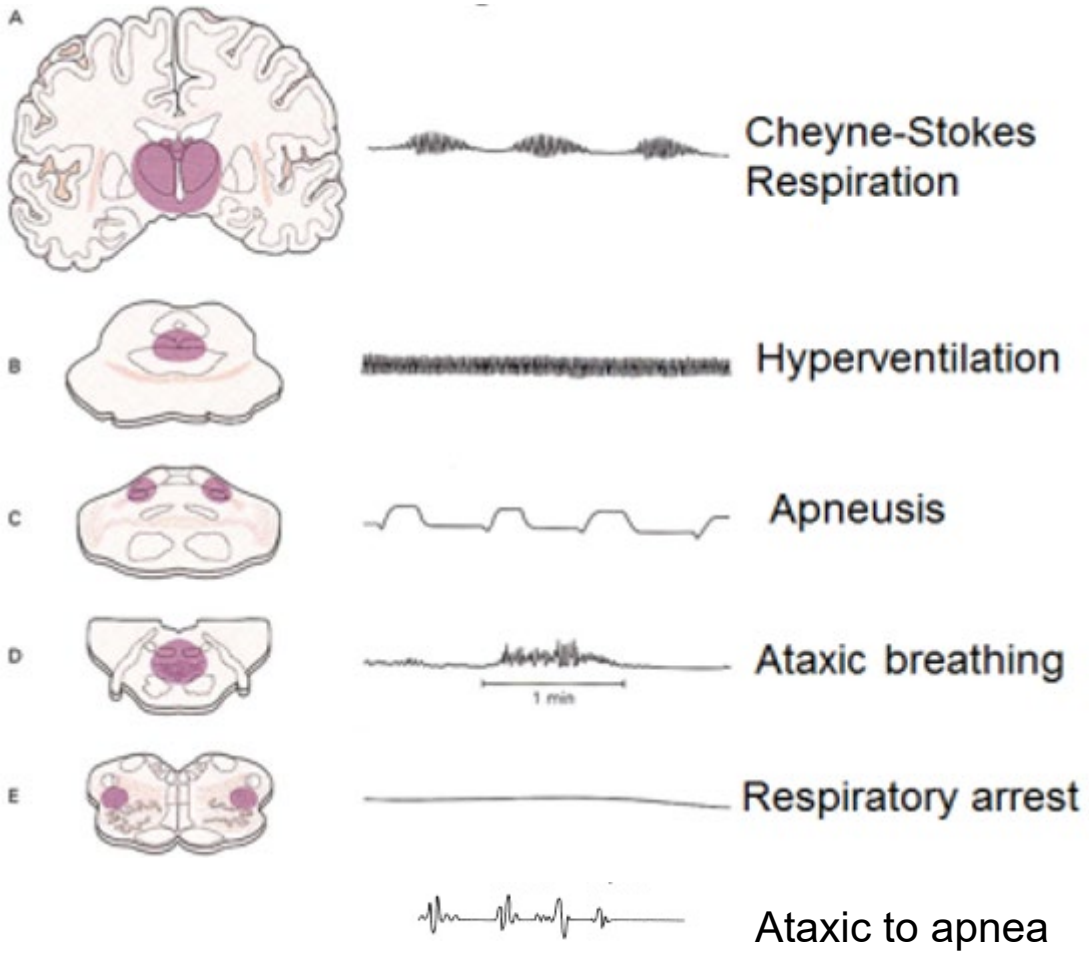
B. Midbrain

C. Upper Pons

D. Lower Pons

E. Upper medulla

F. Medulla



Upper Diencephalon- Sighing, Yawning

Lower Diencephalon – Cheyne- Stokes

Cheyne- Stokes

OR

Central Neurogenic Hyperventilation

Plum and Posner's Diagnosis of Stupor and Coma: 4th Edition 1980

Common cancer related causes

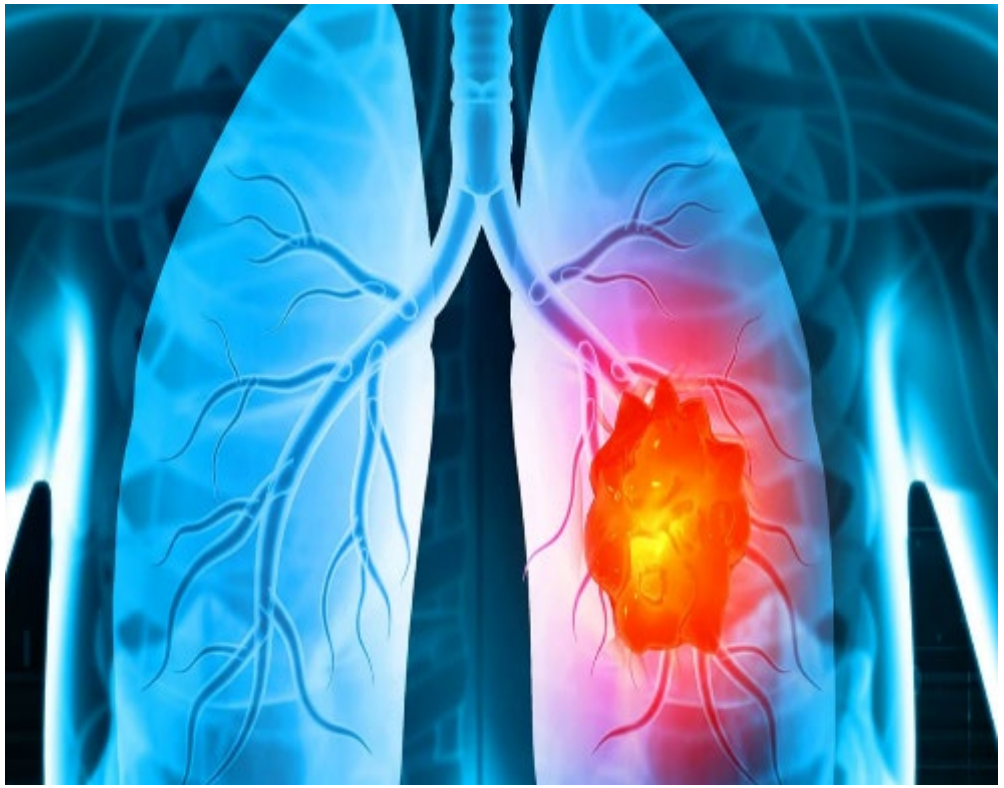
Direct involvement

Primary Tumor

- Bronchial or tracheal obstruction
- Pulmonary Mass
- Mediastinal Obstruction (SVC)
- Pleural thickening (Mesothelioma)

Metastatic Tumor

- Pulmonary metastases
- Pleural / Pericardial effusion
- Lymphangitis carcinomatosis
- Tumor emboli
- Ascites, hepatomegaly (diaphragmatic splinting)
- Rib metastases
- En cuirasse disease (Skin involvement)



Due to treatments

Radiotherapy

- Pulmonary fibrosis

Surgery

- Pneumectomy
- Lobectomy
- Pneumothorax

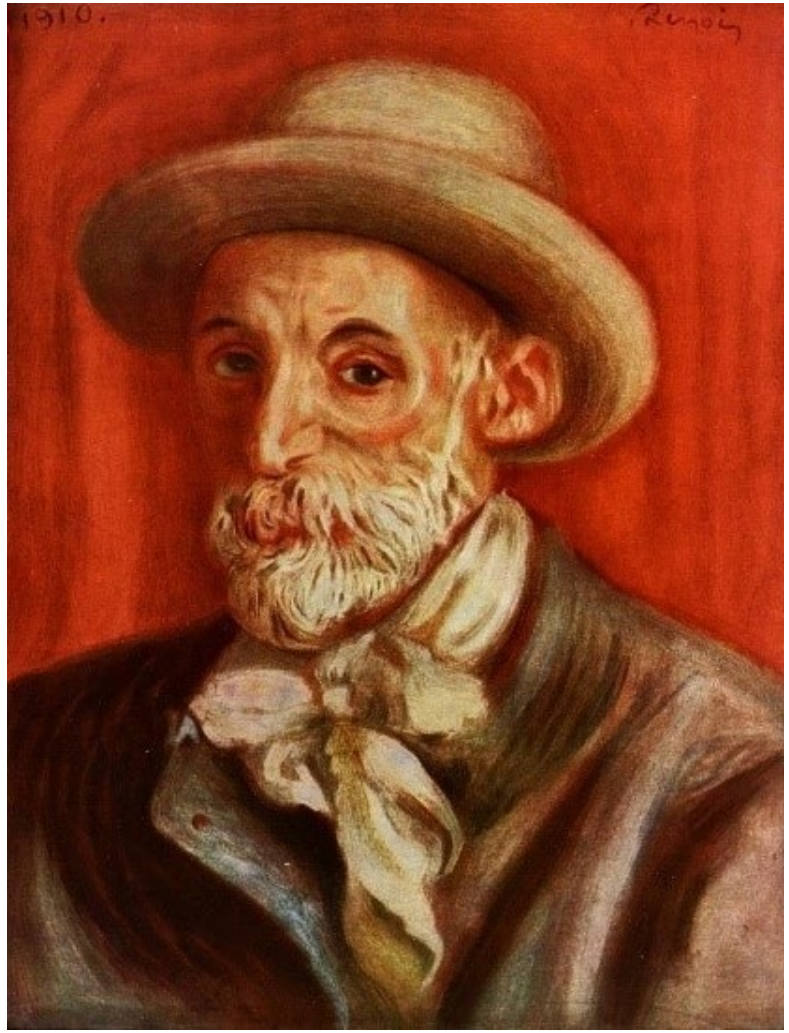
Systemic Therapy

- Pulmonary toxicity (Bleomycin, Busulfan)
- Cardiotoxicity (Anthracyclines)
- Anemia or infection secondary to myelosuppression
- Fluid retention (Progestogens, Docetaxel)

Not directly related to cancer

- Anemia of chronic disease
- Cachexia
- Metabolic acidosis
- Muscle weakness

  (e.g Myasthenia gravis, Eaton-Lambert syndrome)
- Chest wall deformity
- COPD
- Pulmonary embolism
- Pneumonia
- Anxiety



Assessment of Dyspnea

Gold standard - Patient self report

Multiple studies have demonstrated that objective measurement of physiologic changes such

- Tachypnea
- Tachycardia
- Decreased oxygen saturation
- Pulmonary function test abnormalities

only have low correlations with the intensity of dyspnea.

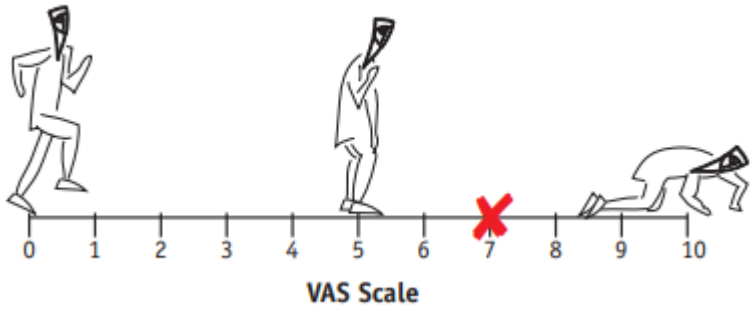
Stoller JK, Ferranti R, Feinstein AR. Further specification and evaluation of a new clinical index for dyspnea. Am Rev Respir Dis 1986; 134: 1129-1134.

Bums BH, Howell JBL. Disproportionately severe breathlessness in chronic bronchi&Q&t J Med 1969; 151: 277-294.

Burdon IGW. Pain MCE Rubinfeld AR. Nana A. Chronic lung disease'and the perception of breathlessless: a clinical perspective. Eur Respir J 1994; 7: 1342-1349.

Do we have any tools ?

VAS



Modified Borg scale

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe (almost maximal)
10	Maximal

Can we assess and solve…..

Multidimensional problem with a Linear assessment and plan ?

Do we have any tools ?

- ESAS
- Cancer dyspnea scale
  - Multidimensional
    - Assess sense of effort
    - Sense of anxiety
    - Sense of discomfort

Table 1. The Original Cancer Dyspnea Scale

We would like to ask you about your breathlessness or difficulty in breathing. Please answer each question by circling only the numbers that best describe the breathing difficulty that you felt *during the past few days*. Base your response on your first impression.

		Not At All	A Little	Somewhat	Considerably	Very Much
1	Can you inhale easily?	1	2	3	4	5
2	Can you exhale easily?	1	2	3	4	5
3	Can you breathe slowly?	1	2	3	4	5
4	Do you feel short of breath?	1	2	3	4	5
5	Do you feel breathing difficulty accompanied by palpitations and sweating?	1	2	3	4	5
6	Do you feel as if you are panting?	1	2	3	4	5
7	Do you feel such breathing difficulty that you do not know what to do about it?	1	2	3	4	5
8	Do you feel your breath is shallow?	1	2	3	4	5
9	Do you feel your breathing may stop?	1	2	3	4	5
10	Do you feel your airway has become narrower?	1	2	3	4	5
11	Do you feel as if you are drowning?	1	2	3	4	5
12	Do you feel as if something is stuck in your airway?	1	2	3	4	5

Reprinted with permission from Tanaka K. Development and validation of the Cancer Dyspnoea Scale: a multidimensional, brief, self-rating scale. Br J Cancer 2000;82:800–805.

What if patient cannot self report ?

RDOS

Variable	0 Points	1 Point	2 Points	Sub-Total
Heart rate per min (beats / min = bpm)	less than 90 bpm	90 – 109 bpm	greater than or equal to 110 bpm	
Respiratory rate per minute (auscultated) (breaths / min)	less than 19 breaths	19 – 30 breaths	greater than 30 breaths	
Restlessness: non-purposeful movements	No	Yes - Occasional, slight movements	Yes - Frequent movements	
Paradoxical breathing pattern: abdomen moves in on inspiration	No		Yes	
Accessory muscle use: rise in clavicle during inspiration	No	Yes - Slight rise	Yes - Pronounced rise	
Grunting at end-expiration: guttural sounds	No		Yes	
Nasal flaring: involuntary movement of nares	No		Yes	
Look of fear: ☐ Eyes wide open ☐ Facial muscles tense ☐ Brow furrowed ☐ Mouth open ☐ Teeth together	No		Yes	

RDOS ≥ 4 predicted patients with moderate and severe dyspnea with a Sensitivity of 76.6%, Specificity of 86.2%, Positive Predictive Value of 86.0%, Negative Predictive Value of 76.9%.

Count respiratory and heart rates for one full minute;

Grunting may be audible with or without auscultation;

An RDOS score of less than 3 indicates respiratory comfort[2];

An RDOS score greater than or equal to 3 signifies respiratory distress and need for palliation[2,3];

Higher RDOS scores signify a worsening condition[2,3].

1. Campbell, M. L. (2008b). Psychometric testing of a respiratory distress observation scale. J Palliative Care Medicine, 11(1), 48.
2. Campbell, ML and Templin TN. (2015). Intensity cut-points for the Respiratory Distress Observation Scale. Palliat Med. 29(5): 436–442
3. Zhang et al. (2019). Validity, Reliability, and Diagnostic Accuracy of the Respiratory Distress Observation Scale for Assessment of Dyspnea Adult Palliative Care Patients. J Pain Symptom Manage;57(2):304-310.

GUIDELINES

Management of Dyspnea in Advanced Cancer : ASCO Guideline

DOI: 10.1200/JCO.20.03465 *Journal of Clinical Oncology* 39, no. 12 (April 20, 2021) 1389-1411. Published online February 22, 2021.

TABLE A1. Management of Dyspnea in Advanced Cancer: ASCO Guideline Expert Panel Membership

Name	Affiliation or Institution	Area of Expertise
David Hui, MD (cochair)	MD Anderson Cancer Center, Houston, TX	Medical oncology and palliative care
Margaret L. Campbell, PhD, RN (cochair)	Wayne State University, Detroit, MI	Palliative care
Ting Bao, MD	Memorial Sloan Kettering Cancer Center, New York, NY	Breast oncology and integrative medicine
Toby C. Campbell, MD, MS	University of Wisconsin-Madison, Madison, WI	Medical oncology and palliative care
Patrick J. Coyne, MSN, ACHPN, ACNS-BC	Medical University of South Carolina, Charleston, SC	Palliative care
David C. Currow, BMed, MPH, PhD	University of Technology Sydney, Sydney, Australia	Palliative care
Arjun Gupta, MD	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD	Medical oncology
Aliza L. Leiser, MD	Rutgers RWJ Cancer Institute of New Jersey, New Brunswick, NJ	Gynecologic oncology, PGIN representative
Masanori Mori, MD	Seirei Mikatahara General Hospital, Hamamatsu, Shizuoka, Japan	Palliative care
Stefano Nava, MD	IRCCS Azienda Ospedaliera University of Bologna, S. Orsola-Malpighi Hospital, Alma Mater University, Bologna, Italy	Respiratory medicine
Lynn F. Reinke, PhD, ARNP	VA Puget Sound Health Care System, Seattle, WA	Palliative care and respiratory medicine
Eric J. Roeland, MD	Massachusetts General Hospital Cancer Center, Boston, MA	Medical oncology and palliative care
Carole Seigel	Brookline, MA	Advocacy
Declan Walsh, MD, MSc	Levine Cancer Institute, Charlotte, NC	Medical oncology and palliative care
Kari Bohlke, ScD	ASCO	ASCO practice guideline staff (health research methods)

First three clinical questions

1. Assessment of dyspnea
2. Management of reversible causes of dyspnea
3. Referral to palliative care and/or specialty breathlessness services

Included six publications

4 systematic reviews and 2 guidelines

1. Bausewein C, Farquhar M, Booth S, et al: Measurement of breathlessness in advanced disease: A systematic review. Respir Med 101:399-410, 2007
2. Brighton LJ, Miller S, Farquhar M, et al: Holistic services for people with advanced disease and chronic breathlessness: A systematic review and meta-analysis. Thorax 74:270-281, 2019
3. Dorman S, Byrne A, Edwards A: Which measurement scales should we use to measure breathlessness in palliative care? A systematic review. Palliat Med 21:177-191, 2007
4. Elliott-Button HL, Johnson MJ, Nwulu U, et al: Identification and assessment of breathlessness in clinical practice: A systematic review and narrative synthesis. J Pain Symptom Manage 59:724-733.e19, 2020

1. Parshall MB, Schwartzstein RM, Adams L, et al: An official American Thoracic Society statement: Update on the mechanisms, assessment, and management of dyspnea. Am J Respir Crit Care Med 185:435-452, 2012
2. Hui D, Maddocks M, Johnson J, et al: Management of breathlessness in patients with cancer: ESMO clinical practice guidelines. ESMO Open 5:e001038, 2020

Screening and Assessment

1. Screening and assessment

    1.1. Clinicians should perform systematic assessment of dyspnea at every inpatient and outpatient encounter in patients with advanced cancer using validated patient-reported outcome measures (good practice statement).

    1.2. For patients who are unable to self-report, clinicians should use a validated observation measure (good practice statement).

    1.3. Whenever possible, patients with dyspnea should undergo a comprehensive evaluation for the severity, chronicity, potential causes, triggers, and associated symptoms, as well as emotional and functional impact (good practice statement).

Approach

- Treat any underlying cause
- Palliative measure to reduce any sensation of dyspnea
- Manage any modulating factors

2.Treatment of underlying causes

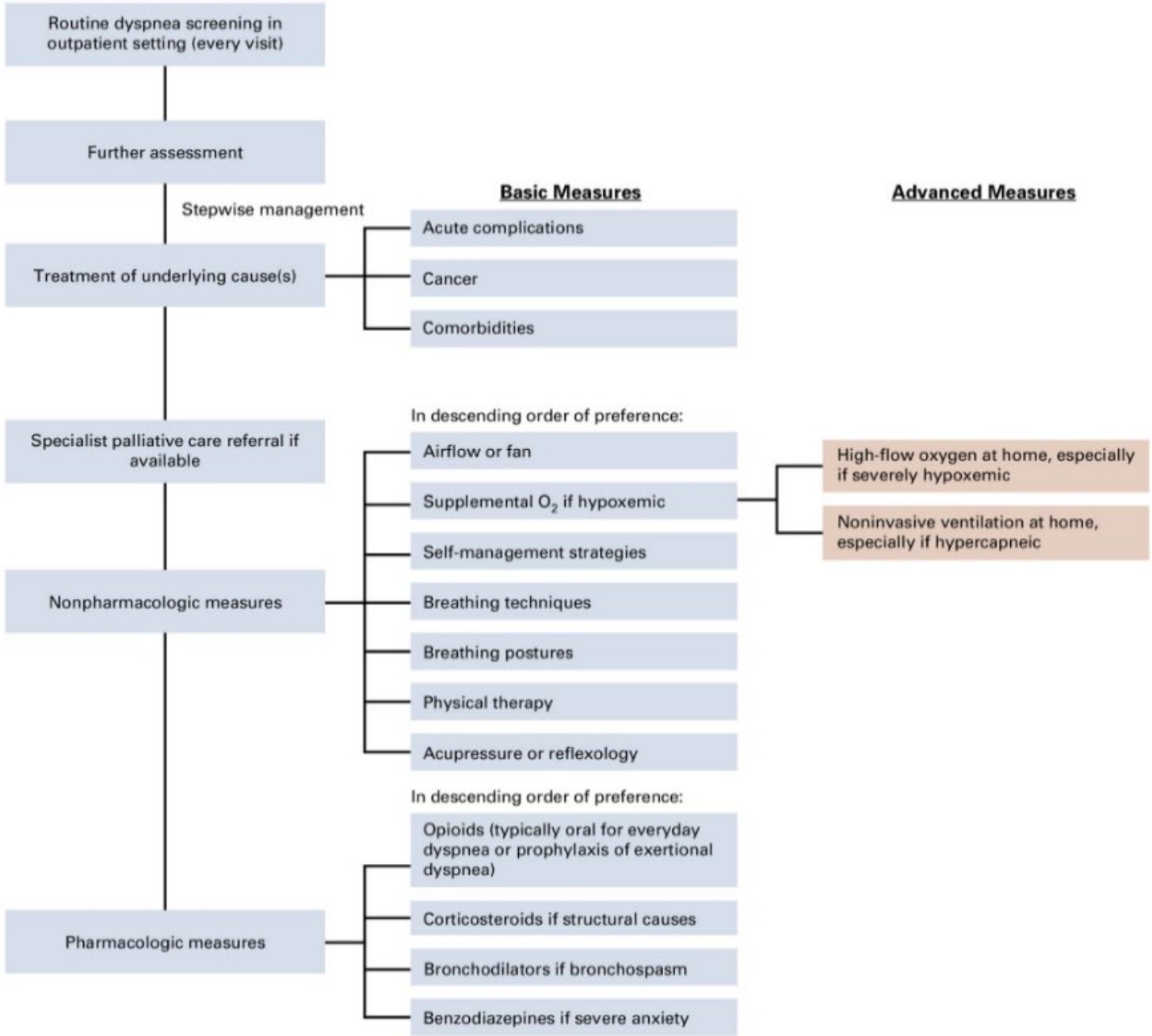
2.1. Patients with potentially reversible, common etiologies of dyspnea such as pleural effusion, pneumonia, airway obstruction, anemia, asthma, chronic obstructive pulmonary disease (COPD) exacerbation, pulmonary embolism, or treatment-induced pneumonitis should be given goal-concordant treatment(s) consistent with their wishes, prognosis, and overall health status (good practice statement).

2.2. Patients with dyspnea because of underlying malignancy (eg, lymphangitic carcinomatosis, atelectasis because of large pulmonary mass, malignant pleural effusion) may benefit from cancer-directed treatments if consistent with their wishes, prognosis, and overall health status (good practice statement).

2.3. Patients with underlying comorbidities such as COPD or heart failure should have the management of these conditions optimized (good practice statement).

3.Referral to palliative care

3.1. Patients with advanced cancer and dyspnea should be referred to an interprofessional palliative care team where available (type: evidence based; evidence quality: intermediate; strength of recommendation: strong).


Routine dyspnea screening in outpatient setting (every visit)
Further assessment
Stepwise management
Basic Measures
Advanced Measures
Treatment of underlying cause(s)
Acute complications
Cancer
Comorbidities
Specialist palliative care referral if available
In descending order of preference:
Nonpharmacologic measures
Airflow or fan
Supplemental O_2 if hypoxemic
High-flow oxygen at home, especially if severely hypoxemic
Noninvasive ventilation at home, especially if hypercapneic
Self-management strategies
Breathing techniques
Breathing postures
Physical therapy
Acupressure or reflexology
In descending order of preference:
Pharmacologic measures
Opioids (typically oral for everyday dyspnea or prophylaxis of exertional dyspnea)
Corticosteroids if structural causes
Bronchodilators if bronchospasm
Benzodiazepines if severe anxiety

Agency for Healthcare Research and Quality (AHRQ) systematic review on the treatment of dyspnea

4. Nonpharmacologic interventions
5. Pharmacologic interventions

Included 48 RCTs and two retrospective cohort studies.

29 RCTs (2,423 patients) addressed the comparative benefits of nonpharmacologic interventions

17 RCTs and 1 retrospective cohort study (1,224 patients) addressed the comparative benefits of pharmacologic interventions

2 RCTs (287 patients) addressed the comparative benefits of nonpharmacologic, pharmacologic, and multimodal interventions..

ROLE OF OPIOIDS

Original Article

Effects of Morphine on the Dyspnea of Terminal Cancer Patients

Eduardo Bruera, MD, Karen Macmillan, RN, Jim Pither, RT, and R. Neil MacDonald, MD
Palliative Care Unit, Edmonton General Hospital, Edmonton, Canada

Abstract
We report an open, uncontrolled study designed to assess the effects of subcutaneous (SC) morphine on dyspnea of terminal cancer. Twenty patients with dyspnea caused by restrictive respiratory failure received an SC dose of morphine of 5 mg (5 patients who were not receiving narcotics), or equivalent to 2.5 times their regular dose (15 patients who were receiving narcotics for pain). Dyspnea (D) and pain (15 cases) were measured before the dose and every 15 min for 150 min after the injection using a visual analog scale 0–100. Respiratory rate (RR), respiratory effort (RE) (score 1–6), arterial saturation of O_2 (SO_2) and end-tidal $PACO_2$ were determined before and 45 min after SC morphine. D, RR, RE, SO_2, and $PACO_2$ were 68 ± 32, 32 ± 7; 3.5 ± 1.8, 87 ± 10, and 31 ± 12, respectively, before SC morphine, and 34 ± 25 ($P < 0.001$), 31 ± 9 (P:NS), 3.2 ± 1.9 (P:NS), 86 ± 11 (P:NS), and 33 ± 9 (P:NS), respectively, 45 min after SC morphine. Nineteen of 20 patients (95%) reported improved dyspnea after morphine. We conclude that morphine appears to improve dyspnea without causing a significant deterioration in respiratory function in terminal cancer patients. Double-blind placebo controlled studies are needed in this population. J Pain Symptom Manage *1990;5:341–344.*

VCU Health

Bruera et al. Journal of Pain and Symptom Management 1990

Impact Factor 4.7

How do opioids help ?

- Relieve dyspnea without inducing respiratory depression
- Decrease neuromechanical dissociation in the respiratory center
- Modulate sensitivity of chemoreceptors
- Increase peripheral vasodilation
- ? Reduce anxiety

Journal of Pain & Palliative Care Pharmacotherapy. 2015;29:341–352.
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DOI: 10.3109/15360288.2015.1082005

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ARTICLE

Opioids for the Management of Dyspnea in Cancer Patients: Evidence of the Last 15 Years—A Systematic Review

Alejandro Vargas-Bermúdez, Felipe Cardenal, and Josep Porta-Sales

ABSTRACT

The objective of this study was to review the evidence on the use of opioids for treatment of the dyspnea in adult cancer patients. A systematic literature review was conducted in the databases MEDLINE, CINAHL (EBSCO), ScienceDirect, and Cochrane Library of trials testing the effect of opioids in relieving dyspnea in cancer patients. Fourteen trials met the criteria for inclusion in the review. Eight randomized trials and six nonrandomized trials. All randomized clinical trials analyzed present risks of bias. Morphine has been the most studied strong opioid showing efficacy in alleviating dyspnea when administered, either orally or subcutaneously, in cancer patients. The potential benefit of the strong opioids in the alleviation of dyspnea in cancer patients is modest and limited to some opioids. More studies are needed to sufficiently support the role of opioids in dyspnea at rest, at exertion, and for breakthrough dyspnea and to clarify the safety issues.

KEYWORDS breathlessness, dyspnea, morphine, neoplasm, opioids, palliative care

Journal of Pain and Palliative Care 2015
Impact factor 1

Opioids for the management of dyspnea in cancer patients: a systematic review and meta-analysis

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Abstract

Dyspnea is a prevalent symptom that significantly reduces quality of life of cancer patients. Palliative treatment is necessary when the symptoms do not respond to treatment for their cause. Opioids are widely used as pharmacological therapy, but evidence for individual agents is inconsistent. The purpose of this study was to evaluate the efficacy and safety of opioids for dyspnea in cancer patients. We searched the CENTRAL, MEDLINE, EMBASE, and ICHUSHI for studies using opioids for dyspnea in adult cancer patients reported by September 2019. Screening of the retrieved literature and assessment of risk of bias and outcomes were performed by two independent authors. A meta-analysis was performed on the primary endpoint, relief of dyspnea, and secondary endpoints including quality of life, somnolence as a side effect, and serious adverse events. Twelve randomized controlled trials were evaluated regarding relief of dyspnea. Somnolence and serious adverse events were evaluated in seven and four randomized controlled trials, respectively, but no randomized controlled trials were evaluable for quality of life. Overall, opioids were more effective than placebo for dyspnea (standardized mean difference − 0.43, 95% confidence interval [CI] − 0.75 to − 0.12). Although significant difference was found between systemic morphine and placebo in the drug-specific analysis, no significant difference could be detected in the other analyses. Systemic administration of opioids is more effective than placebo in relieving dyspnea in cancer patients. Robust evidence on the efficacy and safety of opioids on dyspnea in cancer patients is lacking, and further studies are needed.

Keywords Opioid · Dyspnea · Cancer · Systematic review · Meta-analysis

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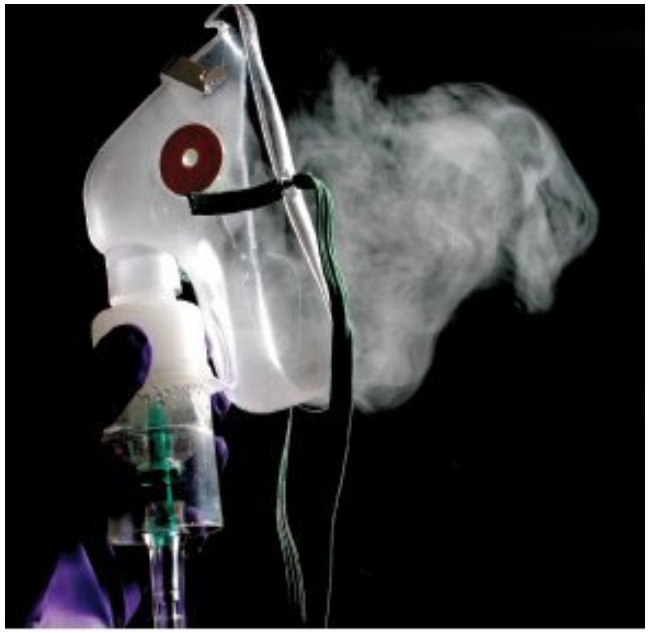
Impact Factor 3.85

ROLE OF OTHER OPIOIDS AND ROUTES



Clinical Note

Nebulized Fentanyl Citrate Improves Patients' Perception of Breathing, Respiratory Rate, and Oxygen Saturation in Dyspnea

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Abstract

Dyspnea, a subjective symptom of impaired breathing, occurs in 70% of terminally ill cancer patients. Current treatments are suboptimal and little is known about the patient's perception of effect. We tested nebulized inhaled fentanyl citrate on patient perceptions, respiratory rate, and oxygen saturation. The study was conducted using a convenience sample of 35 cancer patients on a dedicated oncology unit. We assessed patient perception (did breathing stay the same, worsen, or improve), respiratory rate, and oxygen saturation by pulse oximetry at baseline, 5 minutes, and 60 minutes. Twenty-six of 32 (81%) patients reported improvement in breathing, 3 (9%) were unsure, and 3 (9%) reported no improvement. Oxygen saturation improved from 94.6% at baseline to 96.8% at 5 minutes and 96.7% at 60 minutes (P = 0.0069 compared to baseline). Respiratory rates improved from a baseline of 28.4/min to 25.9/min at 5 minutes and 24.1/min at 60 minutes (P = 0.0251 compared to baseline). No side effects were observed. Inhaled nebulized fentanyl citrate significantly improved patient perception of breathing, respiratory rate, and oxygen saturation. This inexpensive and readily available treatment may offer substantial relief of end-of-life dyspnea. Randomized trials, dose, and length of effect trials are underway. J Pain Symptom Manage 2002;23:157–160.

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A systematic review of the use of opioids in the management of dyspnoea

A Jennings, A Davies, J Higgins, J Gibbs, and K Broadley

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Abstract

Background: Opioids are commonly used to treat dyspnoea in palliative medicine but there has been no formal evaluation of the evidence for their effectiveness in the treatment of dyspnoea. A systematic review was therefore carried out to examine this.

Methods: The criteria for inclusion required that studies were double blind, randomised, placebo controlled trials of opioids for the treatment of dyspnoea secondary to any cause. The methods used to identify suitable studies included electronic searching of the literature, hand searching of the literature, and personal contact with relevant individuals and organisations. Random effects meta-analyses were performed on all included studies and on various subgroups (studies involving nebulised opioids or patients with chronic obstructive pulmonary disease (COPD)). Subgroups were compared using meta-regression. Some studies included in the systematic review could not be included in the meta-analysis because insufficient data were presented.

Results: Eighteen studies fulfilled the criteria for the review. The meta-analysis showed a statistically significant positive effect of opioids on the sensation of breathlessness ($p=0.0008$). Meta-regression indicated a greater effect for studies using oral or parenteral opioids than for studies using nebulised opioids ($p=0.02$). The subgroup analysis failed to show a positive effect of nebulised opioids on the sensation of breathlessness. The results of the subgroup analysis of the COPD studies were essentially similar to the results of the main analysis.

Conclusion: This review supports the continued use of oral and parenteral opioids to treat dyspnoea in patients with advanced disease. There are insufficient data from the meta-analysis to conclude whether nebulised opioids are effective, but the results from included studies that did not contribute to the meta-analysis suggest that they are no better than nebulised normal saline.

Thorax. 2002 Nov; 57(11): 939–944.
Impact Factor 9.2

Clinical Note

Nebulized Versus Subcutaneous Morphine for Patients with Cancer Dyspnea: A Preliminary Study

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Abstract

This study compared the effects of nebulized versus subcutaneous morphine on the intensity of dyspnea in cancer patients. Patients with a resting dyspnea intensity ≥3 on a 0–10 scale (0 = no dyspnea, 10 = worst possible dyspnea) who received regular oral or parenteral opioids were included. On day 1, patients received either subcutaneous (SC) morphine plus nebulized placebo or nebulized morphine plus SC placebo. On day 2, a crossover was made. Dyspnea intensity, side effects, and blinded preference of treatment were assessed. Eleven patients completed the study. Dyspnea decreased from a median of 5 (range, 3–8) to 3 (range, 0–7) after SC morphine (P = 0.025) and from 4 (range, 3–9) to 2 (range, 0–9) after nebulized morphine (P = 0.007). There was no significant difference in dyspnea intensity between nebulized and subcutaneous morphine at 60 minutes. Unfortunately, due to limited sample size, there was insufficient power to rule out a significant difference between both routes of administration. Nebulized morphine offered dyspnea relief similar to that of SC morphine. Larger randomized controlled trials in patients with both continuous dyspnea and earlier stages of dyspnea are justified.

J Pain Symptom Manage 2005;29:613–618. *© 2005 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Fentanyl treatment for end-of-life dyspnoea relief in advanced cancer patients

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Abstract

Purpose We assessed the effects of subcutaneous-endovenous fentanyl on dyspnoea in a cohort of advanced cancer patients.

Methods We performed a retrospective study in a cohort of advanced cancer patients with dyspnoea at rest who received subcutaneous or intravenous fentanyl. Patients with no shortness of breath at rest or at minimal exertion, no rescue doses per 24 h, were deemed to be responders to fentanyl. The period of assessment was 6 days from the beginning of fentanyl treatment.

Results Seventy-two patients were evaluated: 65% males, 50% ≥ 75 years, Palliative Performance Scale (PPS) median of 30%. Seventy-six percent of the patients were responders to fentanyl. Fentanyl efficacy was not statistically related to age, gender, cancer type, previous opioid treatment, steroid and midazolam doses and PPS. The median fentanyl dose in responders was 25 mcg/h (interquartile range 12–70). It was significantly related to age (37 vs 12 mcg/h, for ≤ 75 vs > 75 years, respectively; $p = 0.02$). There was not a significant difference between fentanyl doses of responders and non-responder patients. Thirty-six, 23 and 15 patients had sustained improvements in dyspnoea over 48, 72 and 96 h. Fentanyl had no significant toxicity. The length of inclusion in the study and exclusion were related to low performance status (hazard ratio 0.961; $_{95\%}$CI 0.927–0.996; Cox-regression) but not to fentanyl doses (hazard ratio 0.875; $_{95\%}$CI 0.620–1.234; Cox-regression).

Conclusion Our preliminary data suggest that subcutaneous-endovenous fentanyl may be associated with dyspnoea relief in dying patients. Further research is needed to confirm these findings.

Supportive Care in Cancer (2019) 27:157–164
Impact factor 3.6

ROLE OF OXYGEN

Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial

Amy P Abernethy, Christine F McDonald, Peter A Frith, Katherine Clark, James E Herndon II, Jennifer Marcello, Iven H Young, Janet Bull, Andrew Wilcock, Sara Booth, Jane L Wheeler, James A Tulsky, Alan J Crockett, David C Currow

Summary

Background Palliative oxygen therapy is widely used for treatment of dyspnoea in individuals with life-limiting illness who are ineligible for long-term oxygen therapy. We assessed the effectiveness of oxygen compared with room air delivered by nasal cannula for relief of breathlessness in this population of patients.

Methods Adults from outpatient clinics at nine sites in Australia, the USA, and the UK were eligible for enrolment in this double-blind, randomised controlled trial if they had life-limiting illness, refractory dyspnoea, and partial pressure of oxygen in arterial blood (PaO_2) more than 7·3 kPa. Participants were randomly assigned in a 1:1 ratio by a central computer-generated system to receive oxygen or room air via a concentrator through a nasal cannula at 2 L per min for 7 days. Participants were instructed to use the concentrator for at least 15 h per day. The randomisation sequence was stratified by baseline PaO_2 with balanced blocks of four patients. The primary outcome measure was breathlessness (0–10 numerical rating scale [NRS]), measured twice a day (morning and evening). All randomised patients who completed an assessment were included in the primary analysis for that data point (no data were imputed). This study is registered, numbers NCT00327873 and ISRCTN67448752.

Findings 239 participants were randomly assigned to treatment (oxygen, n=120; room air, n=119). 112 (93%) patients assigned to receive oxygen and 99 (83%) assigned to receive room air completed all 7 days of assessments. From baseline to day 6, mean morning breathlessness changed by –0·9 points (95% CI –1·3 to –0·5) in patients assigned to receive oxygen and by –0·7 points (–1·2 to –0·2) in patients assigned to receive room air (p=0·504). Mean evening breathlessness changed by –0·3 points (–0·7 to 0·1) in the oxygen group and by –0·5 (–0·9 to –0·1) in the room air group (p=0·554). The frequency of side-effects did not differ between groups. Extreme drowsiness was reported by 12 (10%) of 116 patients assigned to receive oxygen compared with 14 (13%) of 108 patients assigned to receive room air. Two (2%) patients in the oxygen group reported extreme symptoms of nasal irritation compared with seven (6%) in the room air group. One patient reported an extremely troublesome nose bleed (oxygen group).

Interpretation Since oxygen delivered by a nasal cannula provides no additional symptomatic benefit for relief of refractory dyspnoea in patients with life-limiting illness compared with room air, less burdensome strategies should be considered after brief assessment of the effect of oxygen therapy on the individual patient.

The Oncologist®

Symptom Management and Supportive Care

High-Flow Oxygen and High-Flow Air for Dyspnea in Hospitalized Patients with Cancer: A Pilot Crossover Randomized Clinical Trial

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Clinical trial • dyspnea • Hospital equipment • Neoplasms • Oxygen

Abstract

Background. The effect of high-flow oxygen (HFOx) and high-flow air (HFAir) on dyspnea in nonhypoxemic patients is not known. We assessed the effect of HFOx, HFAir, low-flow oxygen (LFOx), and low-flow air (LFAir) on dyspnea.

Subjects, Materials, and Methods. This double-blind, 4×4 crossover clinical trial enrolled hospitalized patients with cancer who were dyspneic at rest and nonhypoxemic (oxygen saturation >90% on room air). Patients were randomized to 10 minutes of HFOx, HFAir, LFOx, and LFAir in different orders. The flow rate was titrated between 20–60 L/minute in the high-flow interventions and 2 L/minute in the low-flow interventions. The primary outcome was dyspnea numeric rating scale (NRS) "now" where 0 = none and 10 = worst.

Results. Seventeen patients (mean age 51 years, 58% female) completed 55 interventions in a random order. The absolute change of dyspnea NRS between 0 and 10 minutes was −1.8 (SD 1.7) for HFOx, −1.8 (2.0) for HFAir, −0.5 (0.8) for LFOx, and − 0.6 (1.2) for LFAir. In mixed model analysis, HFOx provided greater dyspnea relief than LFOx (mean difference [95% confidence interval] −0.80 [−1.45, −0.15]; p = .02) and LFAir (−1.24 [−1.90, −0.57]; p < .001). HFAir also provided significantly greater dyspnea relief than LFOx (−0.95 [−1.61, −0.30]; p = .005) and LFAir (−1.39 [−2.05, −0.73]; p < .001). HFOx was well tolerated. Seven (54%) patients who tried all interventions blindly preferred HFOx and four (31%) preferred HFAir.

Conclusion. We found that HFOx and HFAir provided a rapid and clinically significant reduction of dyspnea at rest in hospitalized nonhypoxemic patients with cancer. Larger studies are needed to confirm these findings (Clinicaltrials.gov: NCT02932332). ***The Oncologist*** 2021;26:e883–e892

Implications for Practice: This double-blind, 4×4 crossover trial examined the effect of oxygen or air delivered at high- or low-flow rates on dyspnea in hospitalized nonhypoxemic patients with cancer. High-flow oxygen and high-flow air were significantly better at reducing dyspnea than low-flow oxygen/air, supporting a role for palliation beyond oxygenation.

ROLE OF BENZODIAZEPINES

Original Article

Midazolam as Adjunct Therapy to Morphine in the Alleviation of Severe Dyspnea Perception in Patients with Advanced Cancer

Alfredo H. Navigante, MD, PhD[a], Leandro C.A. Cerchietti, MD[a], Monica A. Castro, MD, Maribel A. Lutteral, MD, and Maria E. Cabalar, MD
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Abstract

The mainstay of dyspnea palliation remains altering its central perception. Morphine is the main drug and anxiolytics have a less established role. This trial assessed the role of midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in terminally ill cancer patients. One hundred and one patients with severe dyspnea were randomized to receive around-the-clock morphine (2.5 mg every 4 hours for opioid-naïve patients or a 25% increment over the daily dose for those receiving baseline opioids) with midazolam rescue doses (5 mg) in case of breakthrough dyspnea (BD) (Group Mo); around-the-clock midazolam (5 mg every 4 hours) with morphine rescues (2.5 mg) in case of BD (Group Mi); or around-the-clock morphine (2.5 mg every 4 hours for opioid-naïve patients or a 25% increment over the daily dose for those receiving baseline opioids) plus midazolam (5 mg every 4 hours) with morphine rescue doses (2.5 mg) in case of BD (Group MM). All drugs were given subcutaneously in a single-blinded way. Thirty-five patients were entered in Group Mo, 33 entered in Mi, and 33 entered in MM. At 24 hours, patients who experienced dyspnea relief were 69%, 46%, and 92% in the Mo, Mi, and MM groups, respectively (P = 0.0004 and P = 0.03 for MM vs. Mi and MM vs. Mo, respectively). At 48 hours, those with no dyspnea relief (no controlled dyspnea) were 12.5%, 26%, and 4% for the Mo, Mi, and MM groups, respectively (P = 0.04 for MM vs. Mi). During the first day, patients with BD for the groups Mo, Mi, and MM were 34.3%, 36.4%, and 21.2%, respectively (P = NS or not significant), whereas during the second day, these percentages were 38%, 38.5%, and 24%, respectively (P = NS). The data demonstrate that the beneficial effects of morphine in controlling baseline levels of dyspnea could be improved with the addition of midazolam to the treatment. J Pain Symptom Manage 2006;31:38–47. *© 2006 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

VCU Health

Navigante et al. Journal of Pain and Symptom Management 2006

Impact Factor 4.7

Original Article

Morphine Versus Midazolam as Upfront Therapy to Control Dyspnea Perception in Cancer Patients While Its Underlying Cause Is Sought or Treated

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Abstract

Context. Cancer patients with dyspnea may be able to have the symptom pharmacologically controlled while its underlying cause is sought or treated.

Objectives. This study was done to determine whether symptom control can be achieved while the cause is evaluated or treated and whether morphine or midazolam would be more suitable in this setting.

Methods. Sixty-three ambulatory patients with advanced cancer and dyspnea were clinically characterized and then randomized to receive either oral morphine or oral midazolam. A fast in-clinic drug titration scheme was implemented followed by an ambulatory five-day period in which the patients received the effective dose that relieved their dyspnea. During this period, the patients were followed daily while the underlying causes of dyspnea were sought out or treated.

Results. Thirty-one patients with dyspnea entered the morphine arm and 32 patients entered the midazolam one. During the initial in-clinic phase, dyspnea was alleviated by at least 50% in all patients, whether they received morphine or midazolam. During the ambulatory phase, midazolam was superior to morphine in controlling baseline and breakthrough dyspnea. Both treatments were well tolerated, with mild somnolence being the most common adverse event. Neither morphine nor midazolam affected the outcome and/or implementation of additional diagnostic and/or therapeutic interventions.

Conclusion. Our results suggest that cancer-related dyspnea in ambulatory patients can be pharmacologically treated while its most probable specific cause is

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Navigante et al. Journal of Pain and Symptom Management 2010

Impact Factor 4.7

ROLE OF PALLIATIVE SEDATION

Palliative Sedation

European Association for Palliative Care (EAPC), Palliative Sedation is the use of sedative medication to relieve intolerable suffering in the last days of life.

For hospitalized patients with refractory dyspnea despite all standard measures, continuous palliative sedation may be considered in select cases.

The goal is to alleviate suffering.

2 studies show palliative sedation does not shorten life.

Some patients "may be reassured" that this option is available if their dyspnea became extremely severe, even if they may never have to use it.

1. Materstvedt LJ, Clark D, Ellershaw J, et al. Euthanasia and physician-assisted suicide: a view from an EAPC Ethics Task Force. *Palliative Medicine*. 2003;17(2):97-101. doi:10.1191/0269216303pm673oa
2. Maltoni M, Scarpi E, Rosati M, et al: Palliative sedation in end-of-life care and survival: A systematic review. J Clin Oncol 30:1378-1383, 2012
3. Maeda I, Morita T, Yamaguchi T, et al: Effect of continuous deep sedation on survival in patients with advanced cancer (J-Proval): A propensity score-weighted analysis of a prospective cohort study. Lancet Oncol 17:115-122, 2016

Palliative Sedation

Specialist palliative care teams

- Facilitating the complex communication
- Medication administration

The most common medication : Midazolam infusion.

Before initiation of palliative sedation, the healthcare team should have an extensive discussion with patients (if able to retain decision-making capacity) and caregivers about the risks and benefits.

Ethics consultation may also be helpful, if available.

1. Materstvedt LJ, Clark D, Ellershaw J, et al. Euthanasia and physician-assisted suicide: a view from an EAPC Ethics Task Force. *Palliative Medicine*. 2003;17(2):97-101. doi:10.1191/0269216303pm673oa

SUMMARY OF MANAGEMENT GUIDELINES

4.Nonpharmacologic interventions

4.1. Airflow interventions such as directing a fan at the cheek (trigeminal nerve distribution) should be offered (type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate).

4.2. Standard supplemental oxygen should be available for patients with hypoxemia who are experiencing dyspnea (ie, $SpO_2 \leq 90\%$ on room air) (type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate).

4.3. Supplemental oxygen is not recommended when $SpO_2 > 90\%$ (type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate).

4.4. A time-limited therapeutic trial of high-flow nasal cannula oxygen therapy, if available, may be offered to patients who have significant dyspnea and hypoxemia despite standard supplemental oxygen (type: evidence-based; evidence quality: low; strength of recommendation: moderate).

4.5. A time-limited therapeutic trial of noninvasive ventilation, if available, may be offered to patients who have significant dyspnea despite standard measures and do not have contraindications (type: evidence-based; evidence quality: low; strength of recommendation: moderate).

4.6. Other nonpharmacologic measures such as breathing techniques, posture, relaxation, distraction, meditation, self-management, physical therapy, and music therapy may be offered (type: evidence-based; evidence quality: low; strength of recommendation: weak).

4.7. Acupressure or reflexology, if available, may be offered (type: evidence-based; evidence quality: low; strength of recommendation: weak).

4.8. Evidence remains insufficient for a recommendation for or against pulmonary rehabilitation in patients with advanced cancer and dyspnea.

5.Pharmacologic interventions

5.1. Systemic opioids should be offered to patients with dyspnea when nonpharmacologic interventions are insufficient to provide dyspnea relief (type: evidence-based; evidence quality: low; strength of recommendation: moderate).

5.2. Short-acting benzodiazepines may be offered to patients who experience dyspnea-related anxiety and continue to experience dyspnea despite opioids and other nonpharmacologic measures (type: evidence-based; evidence quality: low; strength of recommendation: weak).

5.3. Systemic corticosteroids may be offered to select patients with airway obstruction or when inflammation is likely a key contributor of dyspnea (type: evidence-based; evidence quality: low; strength of recommendation: weak).

5.4. Bronchodilators should be used for palliation of dyspnea when patients have established obstructive pulmonary disorders or evidence of bronchospasm (type: evidence-based; evidence quality: low; strength of recommendation: weak).

5.5. Evidence remains insufficient for a recommendation for or against the use of antidepressants, neuroleptics, or inhaled furosemide for dyspnea.

5.6. Continuous palliative sedation should be offered to patients with dyspnea that is refractory to all standard treatment options and all applicable palliative options, and who have an expected life expectancy of days (type: informal consensus; evidence quality: low; strength of recommendation: moderate).

Case 1

- 62 y.o. severe pulmonary HTN, OSA
- Exacerbation of Pulm HTN → RVF → acute on chronic hypoxic RF.
- Patient's vitals were T 36.5 HR 95 RR 18 BP 98/61
- O2 sat 90 on 40L HFNC / 90 % Fio2
- Respiratory effort was labored
- Reported last 24 hour RASS of +1 to 0

Case 2

- 69 y.o. CAD s/p CABG, CVA, HTN
- Stroke alert was found to have right M1 occlusion.
- Was not a candidate for thrombectomy.
- Repeat CT showed worsening edema and hemorrhagic conversion.
- 18 RR 26 BP 99/68
- O2 sat 99 on 2L NC
- Respiratory effort was nonlabored
- Reported last 24 hour RASS of -2 to -1

Evaluating with RDOS

Variable	0 Points	1 Point	2 Points	Sub-Total
Heart rate per min (beats / min = bpm)	less than 90 bpm	90 – 109 bpm	greater than or equal to 110 bpm	
Respiratory rate per minute (auscultated) (breaths / min)	less than 19 breaths	19 – 30 breaths	greater than 30 breaths	
Restlessness: non-purposeful movements	No	Yes - Occasional, slight movements	Yes - Frequent movements	
Paradoxical breathing pattern: abdomen moves in on inspiration	No		Yes	
Accessory muscle use: rise in clavicle during inspiration	No	Yes - Slight rise	Yes - Pronounced rise	
Grunting at end-expiration: guttural sounds	No		Yes	
Nasal flaring: involuntary movement of nares	No		Yes	
Look of fear: ☐ Eyes wide open ☐ Facial muscles tense ☐ Brow furrowed ☐ Mouth open ☐ Teeth together	No		Yes	

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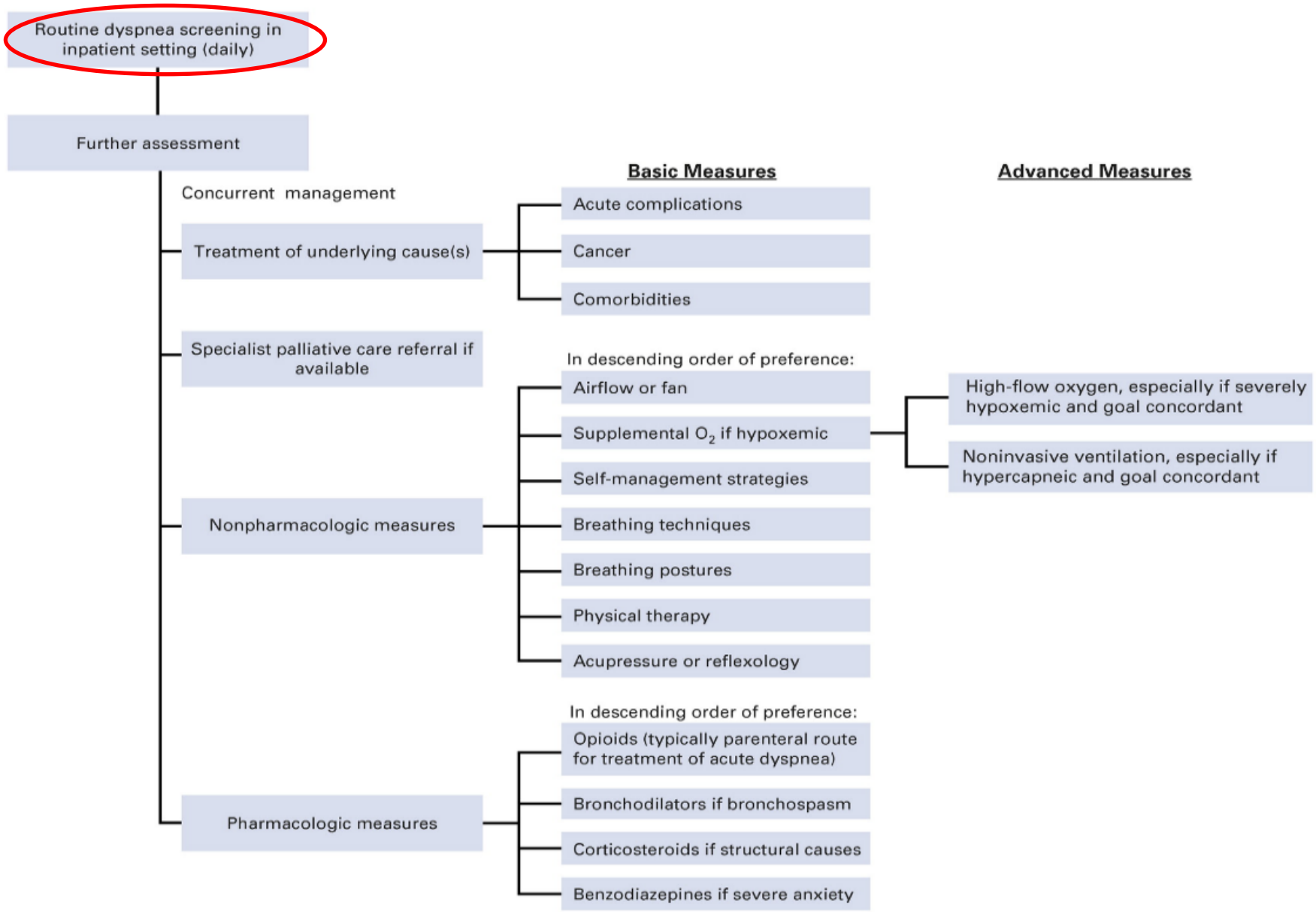
Routine dyspnea screening in inpatient setting (daily)
Further assessment
Concurrent management
Basic Measures
Advanced Measures
Treatment of underlying cause(s)
Acute complications
Cancer
Comorbidities
Specialist palliative care referral if available
In descending order of preference:
Nonpharmacologic measures
Airflow or fan
Supplemental O_2 if hypoxemic
High-flow oxygen, especially if severely hypoxemic and goal concordant
Noninvasive ventilation, especially if hypercapneic and goal concordant
Self-management strategies
Breathing techniques
Breathing postures
Physical therapy
Acupressure or reflexology
In descending order of preference:
Pharmacologic measures
Opioids (typically parenteral route for treatment of acute dyspnea)
Bronchodilators if bronchospasm
Corticosteroids if structural causes
Benzodiazepines if severe anxiety

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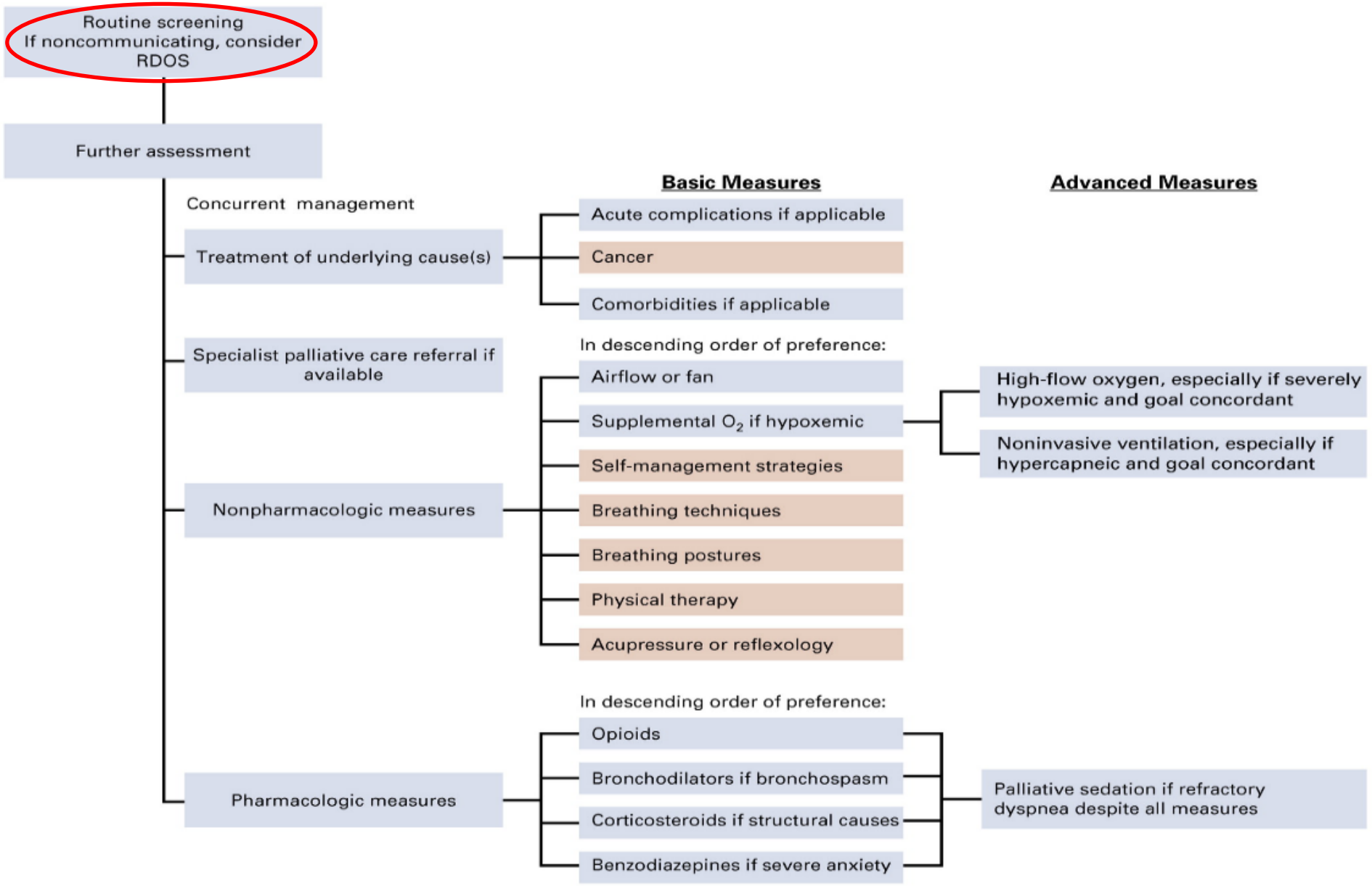
Routine screening
If noncommunicating, consider RDOS
Further assessment
Concurrent management
Basic Measures
Advanced Measures
Treatment of underlying cause(s)
Acute complications if applicable
Cancer
Comorbidities if applicable
Specialist palliative care referral if available
In descending order of preference:
Nonpharmacologic measures
Airflow or fan
Supplemental O_2 if hypoxemic
High-flow oxygen, especially if severely hypoxemic and goal concordant
Noninvasive ventilation, especially if hypercapneic and goal concordant
Self-management strategies
Breathing techniques
Breathing postures
Physical therapy
Acupressure or reflexology
In descending order of preference:
Pharmacologic measures
Opioids
Bronchodilators if bronchospasm
Corticosteroids if structural causes
Benzodiazepines if severe anxiety
Palliative sedation if refractory dyspnea despite all measures

Key Takeaways

Assessment is critical

- Importance of classifying whether patient has hypoxic vs non-hypoxic respiratory failure

Use appropriate assessment tools based on patient status

- Self-report vs RDOS

Consider non-pharmacologic interventions:

- Oxygen if hypoxic
- Airflow or fan
- PT, postures, other self-management techniques

Pharmacologic management

- Systemic opioids or benzodiazepines
- Palliative sedation


Thank You!