

RESPIRATORY FAILURE

Supporting information

This guideline has been produced with reference to the following:

NICE. Extracorporeal carbon dioxide removal for acute respiratory failure. 2023. London. NICE

<https://www.nice.org.uk/guidance/ipg776>

O'Driscoll BR, Howard LS, Earis J et al. BTS guideline for oxygen use in adults in healthcare and emergency settings. Thorax. 2017;72(Suppl 1):ii1-ii90

<https://bmjopenrespres.bmj.com/content/4/1/e000170>

Fan E, Del Sorbo L, Goligher EC et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2017;195:1253-63

<http://www.thoracic.org/statements/resources/cc/ards-guidelines.pdf>

Rochwerg B, Brochard L, Elliott MW et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50. pii: 1602426

<https://erj.ersjournals.com/content/50/2/1602426.long>

The dividing line between high and low survival rates in respiratory failure is 6.5 kPa of PaO₂?

It has been proposed (Hutchison, 1964) that one aim of controlled oxygen therapy should be to provide a PaO₂ of at least 50 mm Hg (equivalent to 6.6 kPa) as this “will prevent immediate death from hypoxia”.

A prospective study in 586 patients with acute respiratory distress syndrome (Squara, 1998) noted that low PaO₂ (< 6.6 kPa) was a negative prognostic indicator.

In a study of 239 episodes of respiratory failure (Asmundsson, 1969), 57/159 episodes (35%) in patients with PaO₂ < 6.6 kPa ended in death, compared to 20/80 episodes (25%) in patients with PaO₂ > 6.6 kPa.

A study in 154 patients with hypoxic COPD (MacNee, 1992) found that a PaO₂ of < 7.0 kPa when breathing air produced a significant decrease in survival.

A study in 140 patients (Kanner, 1983) calculated that an exercise PaO₂ of <= 50 mm Hg was associated with a 12-year death risk ratio of 2.7. A resting PaO₂ of <= 55 mm Hg gave a figure of 1.8.

Asmundsson T, Kilburn KH. Survival of acute respiratory failure: a study of 239 episodes. Ann Intern Med 1969;70:471-85

Hutchison DC, Flenley DC, Donald KW. Controlled oxygen therapy in respiratory failure. BMJ 1964;ii:1159-66
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1816743/pdf/brmedj02575-0014.pdf>

Kanner RE, Renzetti AD, Stanish WM, et al. Predictors of survival in subjects with chronic airflow limitation. Am J Med 1983;74:249-55

MacNee W. Predictors of survival in patients treated with long-term oxygen therapy. Respiration 1992;59(Suppl 2):5-7

Squara P, Dhainaut JF, Artigas A, et al. Hemodynamic profile in severe ARDS: results of the European Collaborative ARDS Study. Intens Care Med 1998;24:1018-28

Evidence Level: III

Achieving a PO₂> 6.5 kPa gives adequate tissue oxygenation?

As stated in the previous question, it has been proposed (Hutchison, 1964) that one aim of controlled oxygen therapy should be to provide a PO₂ of at least 50 mm Hg (equivalent to 6.6 kPa) as this “will prevent immediate death from hypoxia”.

Not found an answer to your question? Wish to suggest an edit to this document?

Please contact the BCGP Clinical Effectiveness Librarian at bedsideclinicalguidelines@uhnm.nhs.uk

Haemoglobin saturation is 90% complete at a PaO_2 of 60 mm Hg and large increments in PaO_2 are necessary to achieve minimal increments in O_2 content (Snider, 1980).

A study in 139 episodes of type 2 respiratory failure in 95 patients (Jeffrey, 1992) established that maintaining PaO_2 above 6.6 kPa successfully treated most patients without recourse to assisted ventilation.

Hutchison DC, Flenley DC, Donald KW. Controlled oxygen therapy in respiratory failure. *BMJ* 1964;ii:1159-66
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1816743/pdf/brmedj02575-0014.pdf>

Jeffrey AA, Warren PM, Flenley DC. Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. *Thorax* 1992;47:34-40
<http://thorax.bmjjournals.org/content/47/1/34.full.pdf+html>

Snider GL, Rinaldo JE. Oxygen therapy: oxygen therapy in medical patients hospitalized outside of the intensive care unit. *Am Rev Respir Dis* 1980;122(Suppl):29-36

Evidence Level: III

High concentrations of oxygen given to patients with type 2 respiratory failure can cause arterial acidosis?

When oxygen is administered to these patients, PaCO_2 commonly increases, risking acidosis. This may be due to:

- a) a decrease in ventilation caused by removal of the hypoxic stimulus
- b) increased V_A/Q inequality in the lung
- c) the effect of O_2 on the CO_2 dissociation curve of blood ("Haldane effect")
(Aubier, 1980).

Aubier M, Murciano D, Milic-Emili J, et al. Effects of the administration of O_2 on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. *Am Rev Respir Dis* 1980;122:747-54

Evidence Level: IV

Respiratory acidosis ($\text{pH} < 7.26$) is predictive of a poor outcome?

In a study of 157 admissions in 135 patients with type 2 respiratory failure (Warren, 1980), 19/54 deaths (35%) occurred in patients with $\text{pH} < 7.26$, whilst 7/54 (13%) occurred in those whose pH remained above 7.26.

In a study of 239 episodes of acute respiratory failure (Asmundsson, 1969), 33/64 episodes (51%) in patients with $\text{pH} < 7.30$ ended in death, compared to 44/175 episodes (25%) in patients with a pH above this level.

Asmundsson T, Kilburn KH. Survival of acute respiratory failure: a study of 239 episodes. *Ann Intern Med* 1969;70:471-85

Warren PM, Flenley DC, Millar JS, et al. Respiratory failure revisited: acute exacerbations of chronic bronchitis between 1961-68 and 1970-76. *Lancet* 1980;i:467-71

Evidence Level: IV

The use of low concentrations (24-28%) of oxygen elevates the arterial oxygen tension (PaO_2) to acceptable levels ($\text{PaO}_2 > 6.5$ kPa) in patients with hypercapnic respiratory failure without producing a dangerous fall in pH (acidosis) or rise in PaCO_2 ?

A small physiological study in 4 patients (Campbell, 1960i) demonstrated that continuous oxygen therapy within a range 24-35% provided adequate tissue oxygenation without causing acidosis or raising PaCO_2 . This avoided the risk of severe anoxia that attended intermittent oxygen therapy. A further paper by the same author (Campbell, 1960ii) established the use of high-flow air with controlled oxygen enrichment, delivered via the Venturi mask.

A study in 50 patients (Bone, 1978) successfully used 24-28% oxygen to maintain PaO_2 between 50-60 mm Hg.

The belief that hypoventilation is the main cause of hypercapnia in these patients has been challenged (Tintis, 1983; Aubier, 1980), but more recent editorials (Tobin, 1995; Stradling, 1986) support the theory.

Not found an answer to your question? Wish to suggest an edit to this document?

Please contact the BCGP Clinical Effectiveness Librarian at bedsideclinicalguidelines@uhnm.nhs.uk

Aubier M, Murciano D, Milic-Emili J, et al. Effects of the administration of O₂ on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. *Am Rev Respir Dis* 1980;122:747-54

Bone RC, Pierce AK, Johnson RL. Controlled oxygen administration in acute respiratory failure in chronic obstructive pulmonary disease: a reappraisal. *Am J Med* 1978;65:896-902

Campbell EJ. Respiratory failure: the relation between oxygen concentrations of inspired air and arterial blood. *Lancet* 1960;ii:10-1

Campbell EJ. A method of controlled oxygen administration which reduces the risk of carbon-dioxide retention. *Lancet* 1960;ii:12-4

Stradling JR. Hypercapnia during oxygen therapy in airways obstruction: a reappraisal. *Thorax* 1986;41:897-902
<http://thorax.bmjjournals.org/content/41/12/897.full.pdf+html>

Tintis P. Oxygen therapy and oxygen toxicity. *Ann Emerg Ther* 1983;12:321-8

Tobin MJ. Oxygen takes the breath away: old sting, new setting. *Mayo Clin Proc* 1995;70:403-4

Evidence Level: IV

Each patient with hypercapnic respiratory failure responds differently to breathing the same concentration of oxygen. All patients must therefore be individually monitored by blood gases as soon as possible?

Linear regressions have been described (Mithoefer, 1971) that allow estimation of individual response to oxygen administration, based on measurements during air breathing.

In acute cases, however, prompt individual monitoring of blood gases is essential (MacNee, 2000). A study in 139 episodes of type 2 respiratory failure in 95 patients (Jeffrey, 1992) showed that about one-third showed a rise in PaCO₂ of > 0.5 kPa (3.75 mmHg) when given controlled oxygen therapy (24-28%), one-third showed no change, and one-third showed a fall.

Jeffrey AA, Warren PM, Flenley DC. Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. *Thorax* 1992;47:34-40
<http://thorax.bmjjournals.org/content/47/1/34.full.pdf+html>

MacNee W. Respiratory failure. In: Seaton A, Seaton D, Leitch AG, (eds). *Crofton and Douglas's Respiratory diseases*, 5th ed. Oxford: Blackwell Science, 2000. p701

Mithoefer JC, Keighley JF, Karetzky MS. Response of the arterial Po₂ to oxygen administration in chronic pulmonary disease: interpretation of findings in a study of 46 patients and 14 normal subjects. *Ann Intern Med* 1971;74:328-35

Evidence Level: IV

CO₂ narcosis (respiratory acidosis) may occur several hours after the start of O₂ therapy in type 2 respiratory failure?

In a small study in 9 patients (Hutchison, 1964), one patient developed a serious rise in PCO₂ to 94 (pH 7.25) when given 52% oxygen after 24 hours' controlled oxygen therapy. Others experienced similar problems up to 3 days after the start of controlled oxygen therapy.

Hutchison DC, Flenley DC, Donald KW. Controlled oxygen therapy in respiratory failure. *BMJ* 1964;ii:1159-66
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1816743/pdf/brmedj02575-0014.pdf>

Evidence Level: IV

Doxapram hydrochloride stimulates breathing and lowers PaCO₂ in patients with type 2 respiratory failure?

A global statement from the American Thoracic Society (Vestbo, 2013) explicitly does not recommend the use of Doxapram. This contradicts earlier guidance given in a Cochrane review of 4 trials involving 176 patients (Greenstone, 2002) which concluded that doxapram improved blood gas exchange over the first few hours of treatment. However, the 2002 trial data was limited and largely based on extrapolation from the anaesthetic literature where doxapram has an established role in reversing CO₂

Not found an answer to your question? Wish to suggest an edit to this document?

Please contact the BCGP Clinical Effectiveness Librarian at bedsideclinicalguidelines@uhnm.nhs.uk

narcosis. In the last 10 years, Doxapram use has diminished as non-invasive ventilation has become much more widely used.

Greenstone M, Lasserson TJ. Doxapram for ventilatory failure due to exacerbations of chronic obstructive pulmonary disease. The Cochrane Database of Systematic Reviews 2002, Issue 3. Art. No.: CD000223
<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000223/full>

Vestbo, J, Hurd, SS, Agustí, AG et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary Am J Respir Crit Care Med.2013; 187 (4):347-365

Evidence Level: I

Noninvasive positive pressure ventilation (NIPPV) is indicated for patients with type 2 respiratory failure and a pH <= 7.35?

A meta-analysis of 15 randomised trials on NIPPV in respiratory failure (Peter, 2002) included 8 on type 2. NIPPV was associated with reduced mortality (13%, $p = .001$), reduced need for mechanical ventilation (18%, $p = .02$) and shortened hospital length of stay (5.66 days, $p = .01$).

Two systematic reviews and meta-analyses (Hess, 2004; Lightowler, 2003) came to similar conclusions and recommended that NIPPV should be the first line intervention in type 2 respiratory failure, in addition to standard treatment.

NIPPV should be considered in patients “even with mild acidosis ($\text{pH}<7.35$)” and is of benefit when introduced earlier in the course of the illness than would be the case for invasive ventilation (Brochard, 2002).

Brochard L, Mancebo J, Elliott MW. Noninvasive ventilation for acute respiratory failure. Eur Respir J 2002;19:712-21

<http://erj.ersjournals.com/content/19/4/712.long>

Hess DR. The evidence for noninvasive positive-pressure ventilation in the care of patients in acute respiratory failure: a systematic review of the literature. Respir Care 2004;49:810-29

<http://rc.rcjournal.com/content/49/7/810.full.pdf+html>

Lightowler JV, Wedzicha JA, Elliott MW, et al. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. BMJ 2003;326:185

<http://www.bmjjournals.org/content/326/7382/185>

Peter JV, Moran JL, Phillips-Hughes J, et al. Noninvasive ventilation in acute respiratory failure: a meta-analysis update. Crit Care Med 2002;30:555-62

Evidence Level: I

Last amended August 2024
Last reviewed January 2026