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 PaO_2?
It has been proposed (Hutchison, 1964) that one aim of controlled oxygen therapy should be to provide a PaO_2 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 PaO_2 (< 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 PaO_2 < 6.6 kPa ended in death, compared to 20/80 episodes (25%) in patients with PaO_2 > 6.6 kPa.
A study in 154 patients with hypoxic COPD (MacNee, 1992) found that a PaO_2 of < 7.0 kPa when breathing air produced a significant decrease in survival.
A study in 140 patients (Kanner, 1983) calculated that an exercise PaO_2 of </= 50 mm Hg was associated with a 12-year death risk ratio of 2.7. A resting PaO_2 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 PO_2 > 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 PO_2 of at least 50 mm Hg (equivalent to 6.6 kPa) as this "will prevent immediate death from hypoxia".
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).

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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.bmj.com/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 (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 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 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 (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 (Tinits, 1983; Aubier, 1980), but more recent editorials (Tobin, 1995; Stradling, 1986) support the theory.

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

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.bmj.com/content/41/12/897.full.pdf+html

Tinits 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 $PaCO_2$ 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.bmj.com/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, Karetsky MS. Response of the arterial Po_2 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

CO_2 narcosis (respiratory acidosis) may occur several hours after the start of O_2 therapy in type 2 respiratory failure?

In a small study in 9 patients (Hutchison, 1964), one patient developed a serious rise in PCO_2 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 $PaCO_2$ 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 Co_2 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

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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 (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.bmj.com/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

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