**Additional file 3:** Characteristics of included studies.

**Asfar2017**

**Hyperoxia and hypertonic saline in patients with septic shock (HYPERS2S): a two-by-two factorial, multicentre, randomised, clinical trial**

|  |  |
| --- | --- |
| **Participants** | **Sample size:** 223 assigned to conservative group (217 included in analysis);  219 assigned to liberal group (217 included in analysis). |
|  | **Sex (male):** conservative group 140 (65%); liberal group 137 (63%). |
|  | **Age (mean):** conservative group 66·3±14·6; liberal group 67·8±12·7. |
|  | **Country:** France. |
|  | **Setting:** Patients aged 18 years and older if they were mechanically ventilated, and exhibited septic shock refractory to fluid resuscitation. |
|  | **Follow-up duration:** 90 days. |
|  | **Inclusion criteria：** |
|  | 1. Patients aged 18 years and older if they were mechanically ventilated, and exhibited septic shock refractory to fluid resuscitation. |
|  | 2. They also had to have been assessed within 6 h after the initiation of vasopressors. |
|  | **Exclusion criteria：** |
|  | 1. Severe hypoxaemia defined as PaO2:FiO2 ratio of less than 100 mm Hg for a minimum positive end­expiratory pressure of 5 cm H2O. |
|  | 2. Plasma sodium concentration of less than 130 mmol/L or more than 145 mmol/L. |
|  | 3. Intracranial hypertension. |
|  | 4. Patient admitted for cardiac arrest, overt cardiac failure. |
|  | 5. Under legal guardianship, no affiliation with the French health­care system. |
|  | 6. Pregnancy |
|  | 7. Recent participation in another biomedical study or another interventional study with mortality as the primary endpoint. |
|  | 8. Investigator’s decision not to resuscitate. |
| **Interventions** | **Liberal group:** the hyperoxia group (mechanical ventilation with FiO2 of 1·0 for 24 h after inclusion; thereafter FiO2 as in the normoxia group). |
|  | **Conservative group:** mechanical ventilation with FiO2 set to achieve an arterial haemoglobin oxygen saturation between 88% and 95%. |
|  | **Duration:** 24 hours. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was death from any cause at day 28 after inclusion |
|  | **Secondary outcomes：** |
|  | 1. 90-day mortality. |
|  | 2. Daily sequential organ failure score (SOFA) from inclusion to day 7. |
|  | 3. Days alive and free from organ dysfunction at day 28. |
|  | 4. Alive at day 28 without organ support (defined as days alive without vasopressor infusion, mechanical ventilation, or renal replacement treatment). |
|  | 5. All prespecified serious adverse events potentially related to hyperoxia or hypertonic saline, or both. |
| **Conclusions** | In patients with septic shock, hyperoxia did not reduce the mortality at either 28 days or 90 days. Setting FiO2 to 1·0 to induce hyperoxia might increase mortality. |

**Barrot2020**

**Liberal or Conservative Oxygen Therapy for** **Acute Respiratory Distress Syndrome**

|  |  |
| --- | --- |
| **Participants** | **Sample size:** 103 assigned to conservative group (99 included in analysis);  102 assigned to liberal group (102 included in analysis). |
|  | **Sex (male):** conservative group 65 (65.7%); liberal group 64 (62.7%). |
|  | **Age (mean):** conservative group 63.0±15.5; liberal group 63.5±14.5. |
|  | **Country:** France. |
|  | **Setting:** Patients with ARDS had been receiving mechanical ventilation. |
|  | **Follow-up duration:** 90 days. |
|  | **Inclusion criteria：** |
|  | 1. Patients had undergone intubation and had been receiving mechanical ventilation for less than 12 hours for ARDS and new or worsening respiratory symptoms, and if they had bilateral opacities on chest imaging and respiratory failure that was not fully explained by heart failure or fluid over-load. |
|  | **Exclusion criteria：** |
|  | 1. The use of long-term oxygen therapy or noninvasive ventilation at home and cardiac arrest. |
|  | 2. Cardiac arrest, traumatic brain injury, or cranial hypertension as the reason for hospitalization in the ICU. |
|  | 3. Pregnancy, patients less than 18 years old, sickle cell disease, patient deprived of freedom, under a legal protective measure. |
|  | 4. Hemoptysis with the need for embolization or surgery, extracorporeal life support or extracorporeal membrane oxygenation before randomization. |
|  | 5. Patient with very high risk of death during following hours, indication for hyperbaric oxygen therapy, cyanide intoxication, methemoglobinemia, untreated pneumothorax, lymphangitic carcinomatosis, eosininophilic pneumonia, intensive care management for organ donation. |
|  | 6. No affiliation with the French health care system. |
|  | 7. Recent participation in another biomedical study or another interventional study with mortality as the primary endpoint. |
|  | 8. Investigator’s decision not to resuscitate. |
| **Interventions** | **Liberal group:** Pao2 target between 90 and 105 mmHg over the first 7 days of invasive mechanical ventilation or until  extubation. During the 6-hour interval between the two measurements of levels of arterial blood gases, the Spo2 was maintained at a level of at least 96%. |
|  | **Conservative group:** Pao2 target between 55 and 70 mmHg over the first 7 days of invasive mechanical ventilation or until  extubation. During the 6-hour interval between the two measurements of levels of arterial blood gases, the Spo2 was maintained at a level between 88 and 92%. |
|  | **Duration:** Seven days or until extubation, if the latter was performed earlier. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was death from any cause at 28 days after randomization among the patients. |
|  | **Secondary outcomes：** |
|  | 1. Death in the ICU and at day 90. |
|  | 2. The Sequential Organ Failure Assessment score calculated without the respiratory component at days 0, 3, and 7. |
|  | 3. Ventilator-associated pneumonia during the first 28 days. |
|  | 4. Septicemia during the first 28 days. |
|  | 5. Cardiovascular complications, defined as new-onset arrhythmia or a cardiac ischemic event and the use of vasopressors over the first 7 days. |
|  | 6. Respiratory weaning success was determined at days 28 and 90. |
|  | 7. Neurologic status. |
|  | 8. Seizures, new cerebral stroke on imaging, administration of neuroleptics, and delirium. |
| **Conclusions** | Among patients with ARDS, early exposure to a conservative-oxygenation strategy with a Pao2 between 55 and 70 mmHg  did not increase survival at 28 days. A worrisome safety signal was observed in the group assigned to a lower oxygen exposure. |

**Girardis2016**

**Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit The Oxygen-ICU Randomized Clinical Trial**

|  |  |
| --- | --- |
| **Participants** | **Sample size:** 236 assigned to conservative group (216 included in analysis);  244 assigned to liberal group (218 included in analysis). |
|  | **Sex (male):** conservative group 121 (66%); liberal group 125 (57.3%). |
|  | **Age (IQR):** conservative group 63 (51-74); liberal group 65 (52-76). |
|  | **Country:** Italy. |
|  | **Setting:** All patients aged 18 years or older and admitted to the ICU. |
|  | **Follow-up duration:** 60 days. |
|  | **Inclusion criteria：** |
|  | 1. All patients aged 18 years or older and admitted to the ICU with an expected length of stay of 72 hours or longer were considered for inclusion. |
|  | **Exclusion criteria：** |
|  | 1. Age younger than 18 years. |
|  | 2. Pregnancy. |
|  | 3. ICU readmission. |
|  | 4. A decision to withhold life-sustaining treatment. |
|  | 5. Immunosuppression or neutropenia. |
|  | 6. Enrolment in another study. |
|  | 7. Patients with acute decompensation of COPD and ARDS with a PaO2:FiO2 ratio of less than 150. |
| **Interventions** | **Liberal group:** Oxygen therapy was administered according to standard ICU practice, in which each patient received an FiO2 of at least 0.4, allowing PaO2values up to 150 mm Hg and an SpO2 between 97% and 100%. If the SpO2decreased below 95% to 97%, the FiO2 was increased to reach the target value of SpO2. |
|  | **Conservative group:** Oxygen therapy was administered at the lowest possible FiO2to maintain the PaO2between 70 and  100mmHg or SpO2 values between 94% and 98%. |
|  | **Duration:** Until patient death or ICU discharge. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was ICU mortality. |
|  | **Secondary outcomes：** |
|  | 1. New-onset respiratory, cardiovascular, liver, and renal failure (defined as a SOFA score ≥3 for the corresponding organ) occurring 48 hours or more after ICU admission. |
|  | 2. Need for reoperation in surgical patients. |
|  | 3. Bloodstream, respiratory, and surgical site infections. |
|  | 4. Hospital mortality. |
|  | 5. Ventilation-free hours during the ICU stay. |
| **Conclusions** | Among critically ill patients with an ICU length of stay of 72 hours or longer, a conservative protocol for oxygen therapy vs conventional therapy resulted in lower ICU mortality. |

**Jakkula2018**

**Targeting two different levels of both arterial carbon dioxide and arterial oxygen after cardiac arrest and resuscitation: a**

**randomised pilot trial**

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| --- | --- |
| **Participants** | **Sample size:** 63 assigned to conservative group (61 included in analysis);  60 assigned to liberal group (59 included in analysis). |
|  | **Sex (male):** conservative group 50 (82%); liberal group 48 (81%). |
|  | **Age (mean):** conservative group 59 ±13; liberal group 60 ±14. |
|  | **Country:** Finland and Denmark. |
|  | **Setting:** Adults admitted to the ICU after out-of-hospital cardiac arrest (OHCA). |
|  | **Follow-up duration:** 6 months. |
|  | **Inclusion criteria：** |
|  | 1. Adult patients resuscitated from witnessed out-of-hospital cardiac arrest (OHCA) with ventricular fibrillation (VF) or ventricular tachycardia (VT) as the initial rhythm. In addition, all of the following inclusion criteria had to be met:  (1) return of spontaneous circulation (ROSC) 10-45 minutes from the onset of cardiac arrest;  (2) confirmed or suspected cardiac origin of the arrest;  (3) **mechanical ventilation** upon ICU arrival;  (4) markedly impaired level of consciousness defined as no response to verbal commands and Glasgow coma scale (GCS)  motor score < 5 (withdrawal to painful stimuli at best);  (5) deferred consent from next of kin possible or likely;  (6) active intensive care and targeted temperature management (TTM) initiated. |
|  | **Exclusion criteria：** |
|  | 1. Patients with confirmed or suspected acute or pre-existing intracranial pathology and/or suspicion of increased intracranial pressure. |
|  | 2. Patients with severe oxygenation failure defined as PaO2/FiO2 (fraction of inspired oxygen) < 100 mmHg upon arrival to ICU and no improvement in oxygenation after adding sufficient PEEP level. |
|  | 3. Severe chronic obstructive pulmonary disease. |
|  | 4. Age < 18 or > 80 years. |
|  | 5. Pregnancy. |
| **Interventions** | **Liberal group:** Target PaO2of 20 to 25 kPa (150 to 187.5 mmHg). |
|  | **Conservative group:** Target PaO2 of 10 to 15 kPa (75 to 112.5 mmHg) or target SpO2 of 95% to 98%. |
|  | **Duration:** During the first 36 h in the ICU. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was the neuron-specific enolase (NSE) serum concentration at 48 h after cardiac arrest. |
|  | **Secondary outcomes：** |
|  | 1. NSE serum concentrations at 24 and 72 h after cardiac arrest. |
|  | 2. S100B protein (a biomarker of glial injury) serum concentrations at 24, 48 and 72 h after cardiac arrest. |
|  | 3. Cardiac troponin (TnT) plasma concentrations at 24, 48 and 72 h after cardiac arrest. |
|  | 4. Regional frontal cerebral oxygenation (rSO2) measured by continuous near-infrared spectroscopy (NIRS) monitoring during the first 48 h after admission to the ICU. |
|  | 5. Results of continuous EEG monitoring for the first 48 h after admission to the ICU. |
|  | 6. Neurological recovery assessed with Cerebral Performance Category (CPC) at 6 months after cardiac arrest. |
|  | 7. Total duration of intensive care. |
|  | 8. Total duration of mechanical ventilation. |
|  | 9. Length of hospital stay. |
|  | 10. Discharge destination and vital status at 30 days after cardiac arrest (dead or alive). |
| **Conclusions** | Both high-normal PaCO2 and moderate hyperoxia increased NIRS values, but the NSE concentration was unaffected. |

**Lång2018**

**A pilot study of hyperoxemia on neurological injury, inflammation and oxidative stress**

|  |  |
| --- | --- |
| **Participants** | **Sample size:** 27 assigned to conservative group (27 included in analysis);  38 assigned to liberal group (38 included in analysis). |
|  | **Sex (male):** conservative group 23 (85.2%); liberal group 31 (81.6%). |
|  | **Age (mean):** conservative group 43 ±17; liberal group 45 ±13. |
|  | **Country:** Finland. |
|  | **Setting:** Mechanically ventilated adults with traumatic brain disease admitted to the ICU. |
|  | **Follow-up duration:** 6 months. |
|  | **Inclusion criteria：** |
|  | 1. Isolated non-penetrating TBI or multiple trauma patient with TBI with Glasgow coma scale (GCS) eight or less |
|  | 2. Recruitment within 18 h after admission to ICU and time from TBI<36 h. |
|  | 3. Informed consent from next of kin. |
|  | **Exclusion criteria：** |
|  | 1. Age<18 or >65 years. |
|  | 2. Anticipated brain death in 12 h or otherwise moribund patient expected to die in 24 h. |
|  | 3. Expected need for mechanical ventilation <24 h. |
|  | 4. Insufficient oxygenation assessed by a clinician or multiple trauma patients with brain injury and severe abdominal, thoracic or pelvic injury possibly affecting oxygenation. |
|  | 5. No consent. |
|  | 6. Insufficient oxygenation with the treatment modality of the lower oxygenation group (PaO2 < 13 kPa or SpO2 < 95% with FiO2 of 0.40 and PEEP of 10) or oxygenation failure probable during ICU care. |
|  | 7. Penetrating TBI. |
|  | 8. Suspected pregnancy. |
| **Interventions** | **Liberal group:** Receiving FiO2 0.70 of inspired oxygen. |
|  | **Conservative group:** Receiving FiO2 0.40 of inspired oxygen. |
|  | **Duration:** During the period of mechanical ventilation for a maximum time of 14 days. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was laboratory markers during the first 3 days. |
|  | **Secondary outcomes：** |
|  | 1. Arterial blood gases. |
|  | 2. Pulmonary function. |
|  | 3. Length of mechanical ventilation. |
|  | 4. Length of ICU stay. |
|  | 5. Length of hospital stay. |
|  | 6. Death. |
|  | 7. eGOSE at 6 months. |
| **Conclusions** | Higher fraction of inspired oxygen did not increase blood concentrations of markers of oxidative stress, inflammation  Or neurological injury or the incidence of pulmonary complications in severe TBI patients on mechanical ventilation. |

**Mackle2020**

**Conservative Oxygen Therapy during Mechanical Ventilation in the ICU**

|  |  |
| --- | --- |
| **Participants** | **Sample size:** 499 assigned to conservative group (484 included in analysis);  501 assigned to liberal group (481 included in analysis). |
|  | **Sex (male):** conservative group 306 (63.2%); liberal group 302 (62.8%). |
|  | **Age (mean):** conservative group 58.1 ±16.2; liberal group 57.5 ±16.1. |
|  | **Country:** Australian and New Zealand. |
|  | **Setting:** Adults undergoing mechanical ventilation in the ICU. |
|  | **Follow-up duration:** 6 months. |
|  | **Inclusion criteria：** |
|  | 1. All adults (≥18 years of age) who were expected to receive mechanical ventilation in the ICU beyond the day after recruitment were eligible for inclusion in the trial. |
|  | **Exclusion criteria：** |
|  | 1. In the view of the treating clinician, hyperoxia is clinically indicated for reasons including (but not limited to) carbon monoxide poisoning or a requirement for hyperbaric oxygen therapy. |
|  | 2. In the view of the treating clinician, avoidance of hyperoxia is clinically indicated for reasons including (but not limited to) chronic obstructive pulmonary disease paraquat poisoning, previous exposure to bleomycin, or chronic hypercapnic respiratory failure. |
|  | 3. Pregnancy. |
|  | 4. Death is deemed to be inevitable as a result of the current acute illness and either the treating clinician, the patient or the substitute decision maker are not committed to full active treatment. |
|  | 5. Patients with a life expectancy < 90 days due to a chronic or underlying medical condition. |
|  | 6. Patients admitted after a drug overdose (including alcohol intoxication). |
|  | 7. Long term dependence on invasive ventilation prior to this acute illness. |
|  | 8. Confirmed or suspected diagnosis of any of the following: Guillain–Barré syndrome, cervical cord injury above C5, muscular dystrophy, or motor neurone disease. |
|  | 9. Enrolment not considered in the patient’s best interests. |
|  | 10. Enrolled in any other trial of targeted oxygen therapy. |
|  | 11. Previously enrolled in the ICU-ROX study. |
| **Interventions** | **Liberal group:** There were no specific measures limiting the Fio2 or the Spo2. |
|  | **Conservative group:** The upper limit of the Spo2 alarm was set to sound when the level  reached 97%, and the Fio2 was decreased to 0.21 if the Spo2 was above the acceptable lower limit (Spo2 90%). |
|  | **Duration:** Until discharge from the ICU or 28 days after randomization, whichever was earlier. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was the number of ventilator-free days from randomization to day 28. |
|  | **Secondary outcomes：** |
|  | 1. Death from any cause at day 90 and day 180 after randomization. |
|  | 2. The duration of survival. |
|  | 3. The proportion of patients in paid employment at baseline who were unemployed at day 180. |
|  | 4. Cognitive function and health-related quality of life at day 180. |
|  | 5. The patients’ quality of life was assessed with the use of the five-level EuroQol five dimensions (EQ-5D-5L) questionnaire. |
| **Conclusions** | In adults undergoing mechanical ventilation in the ICU, the use of conservative oxygen therapy, as compared with usual oxygen therapy, did not significantly affect the number of ventilator-free days. |

**Mazdeh2015**

**Effects of Normobaric Hyperoxia in Severe Acute Stroke: a Randomized Controlled Clinical Trial Study**

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| --- | --- |
| **Participants** | **Sample size:** 25 assigned to conservative group (25 included in analysis);  26 assigned to liberal group (26 included in analysis). |
|  | **Sex (male):** conservative group 14 (56 %); liberal group 14 (53.8%). |
|  | **Age (mean):** Not available. |
|  | **Country:** Iran. |
|  | **Setting:** Patients with severe acute stroke admitted to the ICU. |
|  | **Follow-up duration:** 6 months. |
|  | **Inclusion criteria：** |
|  | 1. Age between 40 and 70 years. |
|  | 2. GCS >12 and patients with isolated brain damage and intact airway control. |
|  | 3. Ischemic and hemorrhagic stroke with no need for surgical intervention. |
|  | 4. Less than 12 hours have passed from the accident. |
|  | 5. NIHSS square between 7 and 9. |
|  | **Exclusion criteria：** |
|  | 1. Patients under 40 and older than 70 years. |
|  | 2. Patients with diabetes mellitus, and ischemic heart disease, renal failure, acute pulmonary edema, history of massive myocardial infarction and heart failure. |
|  | 3. Patients who need intubation on arrival to the hospital. |
|  | 4. Patients with a baseline blood pressure of less than 90/60, or hypoxia. |
|  | 5. Patients requiring surgical intervention (i.e. acute subdural hematoma and cerebral hemorrhage). |
|  | 6. Patients with blood pressure greater than 170/90 in the first 12 hours of the incident. |
|  | 7. Patients with successful Cardiopulmonary resuscitation (CPR) within 12 hours. |
|  | 8. History of previous stroke or unconsciousness, resulting in the need for intubation and mechanical ventilation. |
|  | 9. Death or lost to follow-up. |
|  | 10. Patients of the control group which oxygen therapy were inevitable for them were also excluded from this study. |
| **Interventions** | **Liberal group:** FiO2 of 0.5 - oxygen therapy with Venturi mask. |
|  | **Conservative group:** No supplemental oxygen was administered. |
|  | **Duration:** Oxygen administration was given in the first 12 hours of admission. |
| **Outcomes** | **Primary outcome：** |
|  | 1. Good recovery and lower number of complications in the first day of admission, before discharge, and  6 months after discharge using ranking scale and Barthel Index. |
|  | **Secondary outcomes：** |
|  | 1. Death. |
| **Conclusions** | Normobaric oxygen therapy in the first 12 hours of accident could improve long time outcome of the patients with either ischemic or hemorrhagic stroke. |

**Panwar2016**

**Conservative versus Liberal Oxygenation Targets for Mechanically Ventilated Patients: A Pilot Multicenter Randomized Controlled Trial**

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| --- | --- |
| **Participants** | **Sample size:** 53 assigned to conservative group (52 included in analysis);  51 assigned to liberal group (51 included in analysis). |
|  | **Sex (male):** conservative group 32 (62%); liberal group 33 (65%). |
|  | **Age (mean):** conservative group 62.4 ±14.9; liberal group 62.4 ±17.4. |
|  | **Country:** Australia, New Zealand, and France. |
|  | **Setting:** ICU patients requiring **invasive mechanical ventilation.** |
|  | **Follow-up duration:** 90 days. |
|  | **Inclusion criteria：** |
|  | 1. ICU patients aged greater than or equal to 18 years were eligible if they had been and their treating clinician expected MV to continue for at least the next 24 hours receiving invasive MV for less than 24 hours. |
|  | **Exclusion criteria：** |
|  | 1. Pregnancy. |
|  | 2. Imminent risk of death. |
|  | 3. The treating clinician lacked equipoise for the patient to be enrolled in this trial. |
| **Interventions** | **Liberal group:** Pulse oximetry (SpO2) greater than or equal to 96%. |
|  | **Conservative group:** Pulse oximetry (SpO2) of 88–92%. |
|  | **Duration:** The study intervention was continued for the entire duration of MV. |
| **Outcomes** | **Primary outcome：** |
|  | 1. Primary endpoints were the mean area under the curve (AUC) for SpO2, SaO2, P aO2, and FIO2on Days 0–7. |
|  | **Secondary outcomes：** |
|  | 1. Change from baseline (▲) Sequential Organ Failure Assessment (SOFA) score, ▲PaO2/FIO2, new-onset ARDS, ▲creatinine. |
|  | 2. Incidence of hemodynamic instability. |
|  | 3. Vasopressor-free days, arrhythmia-free days, and ventilator-free days until Day 28. |
|  | 4. ICU mortality, and 90-day mortality. |
| **Conclusions** | Conservative oxygenation strategy is a feasible alternative to the usual liberal oxygenation strategy, while being effective in reducing exposure to hyperoxia. |

**Schjørring2021**

**Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure**

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| --- | --- |
| **Participants** | **Sample size:** 1462 assigned to conservative group (1441 included in analysis);  1466 assigned to liberal group (1447 included in analysis). |
|  | **Sex (male):** conservative group 925 (63.7%); liberal group 946 (64.9%). |
|  | **Age (IQR):** conservative group 70 (60–77); liberal group 70 (60–77). |
|  | **Country:** Denmark, Switzerland, Finland, the Netherlands, Norway, the United Kingdom, and Iceland. |
|  | **Setting:** Patients with acute hypoxemic respiratory failure in the ICU**.** |
|  | **Follow-up duration:** 90 days. |
|  | **Inclusion criteria：** |
|  | 1. Adult patients (≥18 years of age) who were admitted to the ICU with hypoxemic respiratory failure and who were receiving at least 10 liters of oxygen per minute in an open system or who had an Fio2 of at least 0.50 in a closed system; all the patients had placement of an arterial line and were expected to receive supplementary oxygen therapy for at least 24 hours in the ICU. |
|  | **Exclusion criteria：** |
|  | 1. Cannot be randomized within 12 hours of ICU admission. |
|  | 2. Receives chronic mechanical ventilation (invasive mechanical ventilation, continuous noninvasive ventilation or continuous mask-CPAP) for any reason. |
|  | 3. Use of supplementary oxygen at home. |
|  | 4. Previous treatment with bleomycin. |
|  | 5. Organ transplant. |
|  | 6. Withdrawal from active therapy or brain death deemed imminent. |
|  | 7. Pregnancy confirmed by a positive urine or plasma human chorionic gonadotropin (hCG). |
|  | 8. Carbon monoxide poisoning, cyanide poisoning, or paraquat poisoning. |
|  | 9. Methemoglobinemia, sickle cell disease. |
|  | 10. Any condition expected to involve the use of hyperbaric oxygen (HBO) treatment. |
|  | 11. Consent not obtainable according to national regulations. |
| **Interventions** | **Liberal group:** Receiving oxygen therapy targeting Pao2 of 90 mmHg. |
|  | **Conservative group:** Receiving oxygen therapy targeting Pao2 of 60 mmHg. |
|  | **Duration:** Until a maximum of 90 days after randomization. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was death from any cause within 90 days after randomization. |
|  | **Secondary outcomes：** |
|  | 1. The number of patients with one or more serious adverse events, which were defined as a new episode of shock, myocardial ischemia, cerebral ischemia, or intestinal ischemia. |
|  | 2. The percentage of days that patients were alive without life support, as defined by the absence of mechanical ventilation, renal-replacement therapy, or vasopressor or inotrope infusion. |
|  | 3. The percentage of days that patients were alive after hospital discharge at the 90-day follow-up. |
| **Conclusions** | Among adult patients with acute hypoxemic respiratory failure in the ICU, a lower oxygenation target did not result in lower mortality than a higher target at 90 days. |

**Yang2019**

**Low versus high pulse oxygen saturation directed oxygen therapy in critically ill patients: a randomized controlled pilot study**

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| --- | --- |
| **Participants** | **Sample size:** 100 assigned to conservative group (78 included in analysis);  114 assigned to liberal group (90 included in analysis). |
|  | **Sex (male):** conservative group 52 (66.7%); liberal group 55 (61.1%). |
|  | **Age (IQR):** conservative group 58 (46–72); liberal group 60 (46–68). |
|  | **Country:** China. |
|  | **Setting:** Adult patients with an expected ICU stay of more than 72 hours. |
|  | **Follow-up duration:** 28 days. |
|  | **Inclusion criteria：** |
|  | 1. All patients aged 18 years or older and admitted to the ICU with an expected length of stay of 72 hours or longer. |
|  | **Exclusion criteria：** |
|  | 1. ICU readmission. |
|  | 2. Patients with acute exacerbation of chronic obstruction disease. |
|  | 3. Patients with severe acute respiratory distress syndrome. |
|  | 4. Inclusion in another interventional trial. |
|  | 5. A decision to withhold life-sustaining treatment. |
|  | 6. Pregnancy. |
|  | 7. Paraquat poisoning. |
|  | 8. Not having been screened within 12 hours after admission. |
| **Interventions** | **Liberal group:** The SpO2 target was 96–100%, with FiO2 no lower than 30%. |
|  | **Conservative group:** The SpO2 target was 90–95%, with the FiO2 as low as possible. |
|  | **Duration:** Until 14 days, death or ICU discharge, whichever came first. |
| **Outcomes** | **Primary outcome：** |
|  | 1. The primary outcome was death from any cause within 28 days after randomization. |
|  | **Secondary outcomes：** |
|  | 1. ICU mortality. |
| **Conclusions** | SpO2 directed oxygen therapy in critically ill patients was feasible. |