Non-invasive respiratory support in the hypoxemic perioperative/periprocedural patient: a joint ESA/ESICM guideline

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Abbreviation list

CI: Confidence Interval
COT: Conventional Oxygen Therapy
CPAP: Continuous Positive Airway Pressure
ESA: European Society of Anaesthesiology
ESICM: European Society of Intensive Care Medicine
GRADE: Grading of Recommendations, Assessment, Development, and Evaluation
HFNC: High Flow Nasal Cannula
ICU: Intensive Care Unit
NIPPV: Non-Invasive Positive Pressure Ventilation
OR: Odds Ratio
PaO_2:FiO_2 ratios: Ratio Between Arterial Oxygen Pressure and Inspired Fraction of Oxygen
PEEP: Positive End-Expiratory Pressure
PICO: Population/Intervention/Comparison/Outcome
RCT: Randomised Clinical Trial
RR: Relative Risk
SpO_2: Arterial Oxygen Saturation

Abstract

Hypoxemia is a potential life-threatening yet common complication in the perioperative and periprocedural patient (ie. during invasive procedure at risk of deterioration of gas exchange like bronchoscopy). The European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM) developed guidelines for the use of non-invasive respiratory support techniques in the hypoxemic patient in the perioperative and periprocedural period. The panel outlined five clinical questions regarding treatment with non-invasive respiratory support techniques (*i.e.* Conventional Oxygen Therapy (COT), High Flow Nasal Cannula [HFNC], Non-Invasive Positive Pressure Ventilation [NIPPV] and Continuous Positive Airway Pressure [CPAP]) for hypoxemic patients with acute perioperative/periprocedural respiratory failure. The goal was to assess the available literature on the various non-invasive respiratory support techniques, provided these were studies which included adult participants with hypoxemia in the perioperative/periprocedural period. The literature search strategy was developed by a Cochrane Anaesthesia and Intensive Care trial search specialist in close collaboration with the panel members and the ESA group methodologist. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to assess the level of evidence and to grade recommendations. The final process was then validated by both ESA and ESICM scientific committees. **Among 19 recommendations**, **the two grade 1B** recommendations state that *(1)* **in the perioperative/periprocedural hypoxemic patient, the use of either NIPPV or CPAP (based on local expertise) is preferred to COT for improvement of oxygenation**, and (2) that member panel suggest using NIPPV or CPAP immediately post-extubation for hypoxemic patients at risk of developing acute respiratory failure after abdominal surgery.

Key words: ventilation; perioperative; periprocedural; hypoxemia

Summary of recommendations

What goals of therapy can be achieved with each type of non-invasive respiratory support techniques in the postoperative/periprocedural hypoxemic patient with acute respiratory failure?		
Number	Recommendation	Grade
R1	**In the perioperative/periprocedural hypoxemic patient, the use of either NIPPV or CPAP (based on local expertise) is preferred to COT for improvement of oxygenation**	1B
R2	**In the postoperative hypoxemic patient after cardiac surgery, we suggest using NIPPV rather than CPAP for reducing the risk of atelectasis**	2C
R3	**In the postoperative hypoxemic patient after upper abdominal surgery, we suggest CPAP or NIPPV rather than COT to reduce the risk of hospital acquired pneumonia and its associated complications**	2A
R4	**In the perioperative/periprocedural hypoxemic patient, either NIPPV or CPAP are preferred over COT for prevention of reintubation**	2B
R5	**In the perioperative/periprocedural hypoxemic patient, we suggest the use of NIPPV rather than COT to reduce mortality**	2C
Which patient populations may benefit from the use of non-invasive respiratory support techniques for the hypoxemic patients with acute respiratory failure?		
R6	**We suggest using NIPPV or CPAP immediately post-extubation for hypoxemic patients at risk of developing acute respiratory failure after abdominal surgery**	1B
R7	**We suggest that either NIPPV or CPAP may be considered for prevention of further respiratory deterioration in hypoxemic patients after cardiac surgery**	2B
R8	**We suggest that use of the HFNC may be considered for hypoxemic patients after cardiac surgery**	2C
R9	**We suggest that NIPPV may be considered for prevention of atelectasis in hypoxemic patients after lung resection**	2C
R10	**We suggest the use of NIPPV in hypoxemic patients after solid organ transplantation**	2C
R11	**In the hypoxemic patient requiring bronchoscopy, we suggest using non-invasive respiratory support techniques rather than COT**	2B
What minimal standards of hemodynamic and respiratory monitoring and what laboratory and radiological tests are required during the support period?		
R12	**We suggest that perioperative/periprocedural hypoxemic patients undergoing NIPPV be treated by clinicians with recognized competence and**	2C

	skill in airway management and ventilation of patients with lung injury	
R13	**We suggest that perioperative/periprocedural patients treated with non-invasive respiratory support techniques be examined periodically for signs of respiratory distress, neurological deterioration, and interface intolerance by a clinician with recognized competence and skill in airway management and ventilation of patients with lung injury**	2C
R14	**We suggest that perioperative/periprocedural hypoxemic patients undergoing NIPPV undergo continuous physiological monitoring including pulse oximetry, blood pressure measurement and electrocardiography. When a closed NIPPV technique is being used, we suggest adding monitoring of flow and pressure ventilation waveforms**	2C
R15	**In perioperative/periprocedural hypoxemic patients treated with a non-invasive respiratory support technique, we suggest periodic arterial blood gas sampling after the first hour of treatment, at least every six hours during the first 24 hours and daily until the end of the treatment**	2C
R16	**We cannot provide a recommendation regarding the need for routine imaging. However in the presence of an appropriate clinical indication, lung imaging should be considered during NIPPV treatment in hypoxemic perioperative/periprocedural patients**	
What are the (way to prevent) avoidable complications in patients receiving various types of non-invasive respiratory support?		
R17	**The expert panel identified no studies addressing means of prevention of complications and therefore decided to refrain from issuing a recommendation on this topic**	
R18	**We suggest using a HFNC rather than conventional oxygen therapy in perioperative/periprocedural hypoxemic patients with low tolerance to other forms of non-invasive respiratory support techniques**	2B
How and where to initiate non-invasive respiratory support?		
R19	**The expert panel identified no studies addressing this query and therefore decided to refrain from issuing a recommendation on this topic**	

COT: Conventional oxygen therapy; CPAP: Continuous positive airway pressure; HFNC: high flow nasal cannula; NIPPV: non-invasive positive pressure ventilation

Introduction

Hypoxemia is a potential life-threatening yet common complication after surgery. In observational studies, hypoxemia was reported in 21% to 55% of patients during the initial 48 postoperative hours,[1,2] and was reported even after mini-invasive surgery.[3] Routine use of supplemental oxygen does not prevent hypoxemic episodes.[2] Therefore, several non-invasive ventilation supports have been proposed for provision of oxygen supplementation in this setting.[4] However, to date no guidelines exist regarding their use. To the purpose of this guideline, hypoxemia was defined as a ratio between the arterial oxygen pressure and the inspired fraction of oxygen (PaO_2:FiO_2 ratio) below 300 mmHg.[5,6]

Methods

In a collaborative effort, the European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM) nominated a joint panel of experts to develop guidelines for the use of non-invasive respiratory support techniques in the hypoxemic patient in the perioperative and periprocedural period. Following discussions and votes conducted during several professional meetings under the auspices of ESICM and ESA (2018), the expert panel outlined five clinical questions regarding treatment with non-invasive respiratory support techniques (*i.e.* Conventional Oxygen Therapy (COT), High Flow Nasal Cannula [HFNC], Non-Invasive Positive Pressure Ventilation [NIPPV] and Continuous Positive Airway Pressure [CPAP]) for hypoxemic patients with acute perioperative/periprocedural respiratory failure:

1. What (realistic) goals of therapy (*i.e.* outcomes) are to be expected when using these types of support?
2. Which patient populations may benefit from the use of these types of support?
3. What minimal standards of hemodynamic and respiratory monitoring and what laboratory and radiological tests are required during the support period?
4. How can the complications of these types of support be prevented?
5. Where should treatment with these types of support be initiated (*i.e.* location) and using what device settings?

These clinical questions were developed into five PICO queries (Population/Intervention/Comparison/Outcome) (PICO) and then developed further into 27 elements for the search strategy (Supplemental Material 1).

Objective

The objective of the panel was to evaluate the available literature on the various non-invasive respiratory support techniques, provided these were studies which included adult participants with hypoxemia in the perioperative or periprocedural period. The panel compared the efficacy and safety and of treatment with HFNC, NIPPV and CPAP, comparing them to each other and to COT (*i.e.* low flow nasal cannula and/or face mask) for all outcomes (see below). This objective, put forward by the authors initiating the process (ML and SE), was approved by both ESA and ESICM leaderships.

Definitions

COT: low-flow oxygen (≤ 15 l/min) delivered either by nasal cannula or face mask.

Hypoxemia: a ratio between the PaO_2:FiO_2 ratio below 300 mmHg – based on a consensus of the panel.[5,6]

Non-invasive respiratory support techniques: HFNC, CPAP, or NIPPV defined as such by the authors.

Criteria for considering studies for data analysis

Types of studies: Data analysis included all randomised, parallel, and quasi-randomised studies (including cross-over studies) and observational studies performed in adult humans that compared any of the above types of non-invasive respiratory support techniques either to each other or to COT for any outcome. Prior meta-analyses were considered when available and meeting the inclusion criteria. Data from quasi-randomised and observational studies were included due to the small number of RCTs. Retrospective studies, reviews, case series and case reports were excluded unless data was lacking altogether, in which case retrospective data and experience were used to derive an expert opinion. Similarly, when perioperative/periprocedural data was lacking, information was extrapolated from data in other settings.

Types of participants: The qualitative and quantitative analysis of the literature was confined to adult hypoxemic patients (16 years of age or older) requiring non-invasive respiratory support with any of the techniques detailed above in the perioperative or periprocedural period. Studies relating solely to paediatric patients were excluded due to the differences between adults and children in physiology, disease progression, diagnosis and overall clinical approach. Studies including a mix of paediatric and adult populations were reviewed if they included mostly adult patients.

Types of interventions

We included the following (as described by the authors) as the experimental interventions:

- HFNC
- CPAP

- NIPPV

Types of comparators

We included the following as comparators:

- COT
- Any of the above interventions when compared with another intervention.

Types of outcomes: Following discussion within the panel a decision was reached that other than PaO_2:FiO_2, physiological data is not sufficiently strong. Focus was therefore placed preferably on clinical outcomes (*i.e.* all clinical outcomes found were included) and among the physiological parameters only PaO_2:FiO_2 was included.

Search methods for identification of studies

The panel was divided to five subgroups and each was allocated one query. Each subgroup formulated their query into relevant PICO questions (Supplemental Material 1) and suggested keywords for their literature search. The list of PICO questions and the accompanying keywords were sent to the entire panel for discussion, amendment and approval. The final list of keywords framed the literature search (Supplemental Material 2).

Electronic searches

The literature search strategy was developed by a Cochrane Anaesthesia and Intensive Care trial search specialist (Janne Vendt, Copenhagen, Denmark) in close collaboration with the panel of members, the ESA group methodologist and Cochrane editor (AA).[7] The literature search was conducted in MEDLINE (OvidSP), EMBASE (OvidSP), CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL). All searches were restricted to the English, French, Italian and Spanish languages and from 1980 to 2018. A similar search strategy was used for all the databases. The electronic database searches were run twice in 2018. The members of panel were also encouraged to add any missing paper of interest that they were aware of and to conduct a "snow-balling" search themselves.

After removal of all duplicates, the authors screened the abstracts and titles and all relevant papers were retrieved for full-text assessment and data extraction. For a detailed description of the PICO questions and the search strategy, the readers are referred to the Supplement Material 1. More details on additional resources are available in Supplemental Material 2.

Data collection and analysis

Selection of studies

All papers meeting inclusion criteria were included. At least two authors within each of the five PICO subgroups independently examined the titles and abstracts of the articles identified during the search and screened them for suitability (PICO 1 (AC, LB, SE, YH); PICO 2 (PP, CG, SE, YH); PICO 3 (DC, MG); PICO 4 (EDR, SMM, SJ); PICO 5 (MS, JM, JMC)). Disagreements were resolved by third party adjudication (ML and AA). If relevant, the article full-text was assessed. The number of hits responding to key words for each PICO are reported in Table 1.

Data extraction and management

Each pair of review authors extracted data from relevant studies onto a predesigned Excel data extraction table. All authors extracted data in a similar manner in relation to study design, population characteristics, interventions, and outcome measures. Review authors reached consensus regarding extracted data through discussion.

Assessment of risk of bias in included studies

Review authors first underwent training for assessment of risk of bias by a trained methodologist (AA), then assessed the risk of bias of each of the studies selected for their PICO question. Risk of bias assessment was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions source.[7] The risk of bias was assessed for the following domains -

- Random sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of outcome assessors (performance and detection bias)
- Incomplete outcome data, intention-to-treat (attrition bias)
- Selective reporting

Trials were assessed as having a low risk of bias if all of the domains were considered adequate and as having high risk of bias if one or more of these domains were considered inadequate or unclear. Review authors reported no disagreements regarding assessment of risk of bias.

Assessment of quality of the evidence

In accordance with ESA policy,[8] GRADE methodology (Grading of Recommendations, Assessment, Development, and Evaluation) was used for assessing the methodological quality of the included studies and for formulating the recommendations.[9]

Decisions to downgrade the level of evidence for a recommendation were based on the quality and type of the included literature, observed inconsistencies, indirectness or directness of the evidence, overall impression and the presence of publication bias as proposed by GRADE. Decisions to upgrade

the level of evidence for recommendations were based on study quality and magnitude of effect ratio, dose-response gradient, and plausible confounding. A more detailed account of GRADE ((https://www.uptodate.com/home/grading-guide) is available elsewhere.[9] The systematic reviews were performed, reviewed and approved by all the panel members (June 1st, 2019, Vienna, Austria). No meta-analyses were carried out due to extensive clinical heterogeneity among the included trials.

Development of recommendations

Each subgroup developed recommendations relevant to their PICO questions. These were then discussed and re-discussed as required with the panel members in light of the data synthesis (when available), the risk of bias and the quality of the evidence. Each draft and its revisions were reviewed by the entire panel and the final version was approved by all members of the panel in a modified delphi approach in Vienna (June 2019) during the Euroanaesthesia conference. After agreeing on the final terminology the recommendations were merged into a shared document by the lead author (ML). The final version of the document was composed by the lead authors (ML, AA, SE) and endorsed by all of the expert panel.

Management of Conflicts of Interests and Expert Panel Selection

Conflicts of Interest Policy

To reduce the impact of conflicts of interests (COIs), the guideline panel developed a strategy adhering to ESA guideline policy requirements. Conflicts of interests of each panel member were assessed from the point of inclusion into the guideline panel and were disclosed at the point of submission of our manuscript. The extent and type of COIs are reported at the end of the manuscript (acknowledgment). During the process of this guideline creation, the chair of the panel and the methodologist have organized and undertaken several lectures and electronic-communications for the panel members on how to grade and assess evidence and adequately address the risk of bias. All recommendations have been reviewed and monitored from the infant stages until the final steps by our methodologist and chair of the guideline committee. These recommendations have been subject to voting and discussions by all members of the panel until full agreement was reached for every single recommendation. When in doubt and in cases of disagreement, as it is ESA guideline committee policy, the methodologist and chair of the guideline committee (AA) had the final saying in regards to grading. His assessment has been subject to an "external" review by another methodologist (MH). None of the methodologists have any conflicts of interests. The chair of the guideline panel (ML) had no conflict of interest in relation to this guideline.

The member panel selection details are found in Supplemental Material 2.

Query 1

What goals of therapy can be achieved with each type of non-invasive respiratory support technique in the perioperative/periprocedural hypoxemic patient with acute respiratory failure?

Based on available literature, the panel identified the following goals of therapy that should be considered when delivering respiratory support in perioperative/periprocedural hypoxemic patient with acute respiratory failure:

- Improvement of oxygenation
- Reducing the risk of pulmonary complications – atelectasis and pneumonia
- Avoiding reintubation
- Reducing mortality

1.1 Improvement of oxygenation

Recommendation 1 - Strong recommendation, moderate-quality evidence (1B)

In the perioperative/periprocedural hypoxemic patient, the use of either non-invasive positive pressure ventilation or continuous positive airway pressure (based on local expertise) is preferred to conventional oxygen therapy for improvement of oxygenation

Evidence Summary: Four RCTs compared postoperative patients treated with non-invasive respiratory support techniques to those treated with COT.[10-13] The use of non-invasive respiratory support techniques was superior to COT for improvement of oxygenation in two RCTs.[10,11] After lung resection, patients randomised to NIPPV developed less severe hypoxemia than those randomised to COT.[11] After solid organ transplantation, patients randomised to NIPPV and COT had improved PaO_2:FiO_2 ratios in 70% and 25% of cases respectively (p=0.03).[10] During and after major vascular surgery when NIPPV was compared with COT, the arterial partial pressure of oxygen was increased in the patients receiving NIPPV at 1 h, 6 h and at the end of intervention (p<0.01 for all).[13] Conversely, after abdominal surgery, patients randomised to either NIPPV or COT had similar gas exchange on postsurgical day-1 (p=0.6).[12]

Rationale for the Recommendation. The recommendation is based on four RCTs with different case-mixes.[9-12] Three were unrelated single-centre RCTs, yet they all describe similar findings.[10,11,13] However, this similarity provides only moderate certainty since the only multicentre study did not confirm their findings.[12]

Of note, one RCT comparing CPAP to COT after abdominal surgery could not be included in this

analysis because oxygenation levels were not reported.[14] Two more studies that compared two non-invasive respiratory support techniques were also not included because they included no comparison with COT.[15,16] One of these also noted better oxygenation with NIPPV than with CPAP in patients after cardiac surgery.[15]

Our findings are aligned with those of a previous meta-analysis that focused on adult patients with planned extubation following mechanical ventilation rather than with hypoxemia. These authors found that HFNC was superior to COT in terms of partial pressure of oxygen in the arterial blood (standardized mean difference 0.30; 95% CI 0.04, 0.56; p=0.03).[17]

1.2.1. Reducing the risk of atelectasis

Recommendation 2 - Weak recommendation, low-quality evidence (2C)

In the postoperative hypoxemic patient after cardiac surgery, we suggest using non-invasive positive pressure ventilation rather than continuous positive airway pressure for reducing the risk of atelectasis

Evidence Summary. In one multicentre non-inferiority trial where patients after cardiothoracic surgery were randomized to either NIPPV or HFNC, the radiological score at day 1 was better with NIPPV.[16] In a study that randomised patients with a body mass index above 30 after cardiac surgery to either HFNC or COT, no differences were reported in the radiological atelectasis score of days 1 and 5 (median scores = 2, p=0.7 and p=0.15 respectively).[18] In a single-centre study where patients after vascular surgery were randomised to either HFNC or COT, the reported rates of atelectasis were also similar in the two groups.[13]

Rationale for the Recommendation. Although this recommendation is based on a low level of evidence, it is supported by a potential positive effect of NIPPV without any reported detrimental effect.[16] However, equipoise still exists regarding the choice of HFNC or NIPPV for improving oxygenation since the largest RCT found no difference between the two. Furthermore, the efficacy of HFNC seems similar to that of COT for prevention of atelectasis.[18]

Of note – The expert panel found no RCT comparing hypoxemic patients treated with NIPPV to those treated with CPAP. An additional RCT that randomised patients with an "Atelectasis Score" equal or greater than two after tracheal extubation to either CPAP or NIPPV was excluded because the patients enrolled were not hypoxemic (PaO_2:FiO_2 ratios at 338 and 345 mmHg in the two groups respectively). This study found that patients in the NIPPV group developed less atelectasis (p=0.02).[19]

1.2.2 Reducing the risk of pneumonia and its associated complications

Recommendation 3 - Weak recommendation, high-quality evidence (2A)

In the postoperative hypoxemic patient after upper abdominal surgery, we suggest continuous positive airway pressure or non-invasive positive pressure ventilation rather than conventional oxygen therapy to reduce the risk hospital acquired pneumonia and its associated complications

Evidence Summary. One multicentre study showed that patients with hypoxemia after abdominal surgery that were randomised to either preventive CPAP or COT had lower rates of pneumonia (2% *vs.* 10% respectively, p=0.02), infection (3% *vs.* 10%, p=0.03) and sepsis (2% *vs.* 9%, p=0.03) with CPAP.[14] Another multicentre study that randomised patients who developed hypoxemic respiratory failure after upper abdominal surgery to either NIPPV or COT had lower rates of hospital-acquired pneumonia on days 7 (10.1% *vs.* 22.1%, (p=0.005) and 30 (14.6% *vs.* 29.7% (p=0.003) with NIPPV but similar ICU and hospital lengths of stay.[12]

Also a case-control series of 36 consecutive patients undergoing esophagectomy found a similar rate of pneumonia in patients treated with NIPPV *vs*. COT (p=1.0), but NIPPV was associated with less respiratory distress syndrome (19% *vs.* 53%, p=0.015).[20]

These findings contrast with a multicentre study that randomised patients "at risk for postoperative pulmonary complications" to either HFNC or COT which showed no difference in the absolute risk reduction of postoperative hypoxemia 1 h after extubation (21% *vs.* 24%, -3 (-14 to 8), p=0.62).[21]

Rationale for the Recommendation. For this recommendation the level of evidence was considered high because two unrelated RCTs have reported a significant decrease in complications with CPAP or NIPPV compared with COT. The two studies are dissimilar in the type of support provided (CPAP in one[14] and NIPPV in the other[12]) and in the indication for NIPPV (therapeutic in one[12] and prophylactic in the other[14]), which likely explains the difference in the rate of complications observed in the two trials.[12,14] Taken together, the results of these two trials support the use of non-invasive respiratory support techniques in a large group of patients after upper abdominal surgery.

In contrast, caution is advised with regards to selecting HFNC rather than COT for treatment of this patient population; the only RCT comparing the use of these two types of support was negative.[21] This note of caution is somewhat tempered by the fact that this study included only patients at risk for developing postoperative pulmonary complications and hypoxemia was not an inclusion criteria but rather its primary endpoint.

This conclusion is in line with a Cochrane systematic review[22] of non-invasive respiratory support techniques in acute respiratory failure after upper abdominal surgery that also reported reduced complication rates with CPAP or NIPPV, as compared with COT. The complications noted were

pneumonia (relative risk (RR) 0.19; 95% CI 0.04, 0.88; p=0.02), sepsis (RR 0.22; 95% CI 0.04, 0.99; p=0.03) and infection (RR 0.27; 95% CI 0.07, 0.94; p=0.03).

Although the use of a non-invasive respiratory support technique seems supported by evidence, the role of different devices requires further elucidation. The panel could not comment on the choice of non-invasive respiratory support technique since no study directly compared the use of HFNC and CPAP in postoperative hypoxemic patients after upper abdominal surgery.

1.3 Avoiding reintubation

Recommendation 4 - Weak recommendation, moderate-quality evidence (2B)

In the perioperative/periprocedural hypoxemic patient, either non-invasive positive pressure ventilation or continuous positive airway pressure are preferred over conventional oxygen therapy for prevention of reintubation

Evidence Summary. In a single-centre study that randomised lung resection patients to either NIPPV or COT decreased the rate of tracheal reintubation during the ICU stay (from 50% to 21%, p=0.035).[11] Significant differences in reintubation rates between non-invasive respiratory support technique including NIPPV or CPAP and control groups were also reported in three RCTs including patients after solid organ transplantation (single centre, *vs.* COT)[10], after cardiac surgery (single centre, *vs.* COT)[13] and after abdominal surgery (multicentre, *vs.* COT)[12]. The multicentre study found less reintubations by day-7 and day-30 in the NIPPV group than in the COT group (33.1% *vs.* 45.5%, p=0.03 and 38.5% *vs.* 49.7%, p=0.06, respectively).[12]

Another multicentre study that randomised patients after abdominal surgery to either CPAP or COT found significantly lower 7-day reintubation rates were with CPAP (1% and 10% respectively, p=0.005).[14]

A case-control study also showed less reintubations with NIPPV than with COT in patients undergoing esophagectomy (25% *vs.* 64%, p=0.008).[20]

Rationale for the Recommendation. The panel assessed firstly the available RCTs and concluded that COT use was associated with an increased risk of reintubation, based on relatively homogeneous findings. The caveats to this determination are that several RCTs were single-centre studies including a small number of patients and that the time frame defining the need for reintubation varies between studies.

1.5 Reducing mortality

Recommendation 5 - Weak recommendation, low-quality evidence (2C)

In the perioperative/periprocedural hypoxemic patient, we suggest the use of non-invasive

positive pressure ventilation rather than conventional oxygen therapy to reduce mortality

Evidence Summary. The panel identified no studies designed to assess mortality as the primary end-point. However, a reduction in mortality was found as a secondary endpoint in several studies which compared the use of non-invasive respiratory support techniques to COT in perioperative/periprocedural patients with hypoxemia. In a single-centre study that randomised patients after lung resection to NIPPV or COT, NIPPV was superior to COT in reducing mortality; both short-term (12.5% *vs.* 37.5%, p=0.045) and long-term (12.5% *vs.* 37.5%, p=0.045).[11] This study was stopped after interim analysis because of this finding. In another single-centre study that randomised patients undergoing solid organ transplantation to either NIPPV or COT, ICU survival was higher with NIPPV (50% *vs*. 20%, p=0.05), but in-hospital mortality was similar (p=0.17).[10] A third multicentre study randomised patients after abdominal surgery to either NIPPV or COT and found higher 30- and 90-day survival with NIPPV (10.1 *vs*. 15.3, p=0.2, and 14.9 *vs*. 21.5, p=0.15) in patients randomised.[12] Conversely, in a study which randomised postoperative cardiac surgery patients to either NIPPV or COT ICU and hospital mortality rates were similar.[13]

With regards to CPAP and NIPPV – the findings were somewhat more consistent. A multicentre study in which patients after major elective surgery were randomised to either CPAP or COT found no association with mortality either way (3% *vs.* 0%, p=0.12).[14] A case-control single-centre study comparing NIPPV and COT after esophagectomy also found no significant differences in mortality.[20] Finally, a single-centre study that randomised cardiac surgery patients to either CPAP or COT also reported no difference in 30-day mortality (p=0.99).[23]

Rationale for the Recommendation. The panel considered four RCTs which reported measures of effect for NIPPV *vs.* COT in terms of survival.[10,12,13,20] As in all of these studies, survival was a secondary outcome, none was powered to detect differences in survival. Three of the studies included a very small number of patients.[10,13,20] Furthermore, one of the studies was terminated prematurely which further limits any ability to draw conclusions from its data.[11] Hence the level of recommendation was downgraded.

There are additional caveats with regards to the data comparing CPAP with COT. In one study the patients were less severely ill than in other studies[12,13] and mortality was very low.[14] In the second study patients were admitted to a conventional ward which raises questions regarding either their severity or the quality of care provided.[23] The resultant effect estimates were very unstable and insignificant.

Although our findings are mostly aligned with those published by the European Respiratory Society guidelines for post-operative acute respiratory failure (conditional recommendation, moderate

certainty of evidence),[24] one should keep in mind that two RCTs found no benefit for either NIPPV or CPAP in patients after cardiac surgery.[13,23]

QUERY 2

Which patient populations may benefit from perioperative/periprocedural use of non-invasive respiratory support (including high flow nasal cannula, non-invasive positive pressure ventilation and continuous positive airway pressure) when presenting with hypoxemia and acute respiratory failure?

The panel identified relevant literature on the following adult patient populations:

- Post abdominal surgery
- Post cardiac surgery
- Post lung resection
- Post transplant
- During fiberoptic bronchoscopy

2.1 Post-abdominal surgery

Recommendation 6 - Strong recommendation, moderate-quality evidence (1B)

We suggest using non-invasive positive pressure ventilation or continuous positive airway pressure immediately post-extubation for hypoxemic patients at risk of developing acute respiratory failure after abdominal surgery

Evidence Summary. Two RCTs suggested that non-invasive respiratory support techniques are preferable COT after upper abdominal surgery.[12,14] In a multicentre study, postoperative patients with a PaO_2:FiO_2 ratio below 300 mmHg 1h post-extubation were randomised to either helmet CPAP or COT.[14] The rate of reintubation within 7 days of surgery was lower (1% *vs.* 10% respectively, p=0.005; RR 0.099; 95% CI 0.01, 0.76), ICU lengths of stay were shorter (1.4±1.6 *vs.*2.6±4.2 days respectively, p=0.09) and infection rates were lower (3% *vs.* 10% respectively) yet hospital lengths of stay did not differ.[14] In a multicentre trial, hypoxemic patients after major elective abdominal surgery were randomised to either NIPPV or COT.[12] The proportion of patients reintubated within 7 days of randomisation was 33.1% with NIPPV and 45.5% with COT (absolute difference, −12.4%; 95%CI, −23.5%to −1.3%; p=0.03). NIPPV was also associated with more invasive ventilation–free days than COT (25.4 *vs.* 23.2 days; absolute difference, −2.2 days; 95%CI, −0.1to 4.6 days; p=0.04), less healthcare-associated infections (31.4% *vs.* 49.2%; absolute difference, −17.8%; 95%CI, −30.2% to

−5.4%; p=0.003) and lower 90-day mortality (14.9% vs. 21.5%, absolute difference, −6.5%; 95%CI, −16.0% to 3.0%; p=0.15).[12]

In contrast, patients at risk of postoperative pulmonary complications randomised to either HFNC or COT fared similarly in terms of hypoxemia 1 h after extubation (21% *vs.* 24%, p=0.62) and at study treatment discontinuation (27% *vs.* 30%, p=0.57).[21]

Rationale for the Recommendation. The recommendation is based on two RCTs that included patients with different levels of severity.[12,14] Both showed clear benefit with the use of non-invasive respiratory support techniques compared with COT. The caveat to this recommendation is that these studies contain no data regarding potential abdominal complications. The only RCT assessing HFNC showed no superiority over COT.[21]

2.2 Post Cardiac surgery

Recommendation 7 - Weak recommendation, moderate-quality evidence (2B)

We suggest that either non-invasive positive pressure ventilation or continuous positive airway pressure may be considered for prevention of further respiratory deterioration in hypoxemic patients after cardiac surgery

Evidence Summary. Two RCTs compared non-invasive respiratory support techniques in patients after cardiac surgery.[15,23] In one single-centre trial, hypoxemic patients after cardiac surgery were randomised to either CPAP (n=33) or COT (n=31). The use of CPAP was associated with the primary endpoint of less patients developing a PaO_2:FiO_2 ratio below 200 mmHg (12% *vs.* 45%, p=0.003).[23] In another single-centre trial hypoxemic patients with acute respiratory failure were randomised to either NIPPV (n=75) or CPAP (n=75). Resolution of the clinical signs and symptoms of acute respiratory failure within 72 h occurred at a similar rate in the two groups (57.9% *vs.* 47.3%, p=0.5).[15]

Rationale for the Recommendation. The recommendation is based on two single-centre trials in which some patients with a trajectory of worsening hypoxemia showed improvement with non-invasive respiratory support techniques.[15,23] However, the evidence supporting this recommendation is weak since both studies were conducted in only one centre, one included few patients[23] and the other has important limitations (*e.g.* no power calculation for the primary study endpoint[15]).

Recommendation 8 - Weak recommendation, low-quality evidence (2C)

We suggest that use of the high flow nasal cannula may be considered for hypoxemic patients after cardiac surgery

Evidence Summary. Stephan *et al.* conducted a multicentre noninferiority RCT in post-cardiac hypoxemic surgery patients with or at risk of respiratory failure. The patients were randomly assigned to treatment with either HFNC (n=414) (flow 50 l/min at FiO_2 0.5) or NIPPV (n=416) delivered through a full-face mask for at least 4 hours daily (pressure support 8 cmH_2O; PEEP 4 cmH_2O; FiO_2 0.5).[16] The primary outcome was treatment failure, defined as reintubation, crossover, or premature treatment discontinuation (patient request or adverse effects), skin breakdown and mortality. The treatment failed in 87 (21.0%) patients with HFNC and 91 (21.9%) patients with NIPPV (absolute difference, 0.9%; 95%CI, −4.9%, 6.6%; p=0.003). ICU mortality rates were similar in the two groups (5.5% *vs.* 6.8%, p=0.66) (absolute difference, 1.2%; 95%CI, 2.3%, 4.8%). Skin breakdown was significantly more common with NIPPV after 24 hours (p<0.001). The authors concluded that HFNC was not inferior to NIPPV.

Rationale for the Recommendation. For this query one large non-inferiority RCT comparing HFNC to NIPPV, was evaluated.[16] The side effects associated with the use of NIPPV (skin breakdown) and the simplicity of the user interface with the HFNC led the expert panel to recommend the HFNC.

2.3 Post Lung resection

Recommendation 9 - Weak recommendation, low-quality evidence (2C)

We suggest that non-invasive positive pressure ventilation may be considered for prevention of atelectasis in hypoxemic patients after lung resection

Evidence Summary. One single-centre study randomised hypoxemic patients after lung resection to either NIPPV (n=48) or COT (n=48).[11] The study was terminated early after interim data analysis showed significantly higher rates of endotracheal intubation (the primary outcome) (50.0% *vs*. 20.8% respectively, p=0.035) and 120-day mortality (37.5% *vs.* 12.5% respectively, p=0.045) with COT.

Rationale for the Recommendation. Development of pulmonary complications (including atelectasis) after lung resection is accompanied by increased morbidity, hospital length of stays and death.[25] It is reasonable to assume that as reintubation and mortality overlapped in the only study on the topic,[11] at least some of the mortality is attributable to pulmonary complications However, study interruption by the safety committee precluded recruitment of the number of patients required to support the assumption of superiority of CPAP over COT. The panel found no evidence to support the use of any type of support other than NIPPV. An additional non-inferiority trial that randomised patients to either HFNC or NIPPV and found similar rates of reintubation, crossover and premature

study-treatment discontinuation (at the request of the patient or for medical reasons, was not included in the analysis since only 7.7% of the patients were after lung resection.[16]

2.4 Post transplant

Recommendation 10 - Weak recommendation, low-quality evidence (2C)

We suggest the use of non-invasive positive pressure ventilation in hypoxemic patients after solid organ transplantation

Evidence Summary. In a single-centre study that randomised hypoxemic patients after solid organ transplantation either NIPPV (n=20) or COT (n=20),[10] less patients underwent endotracheal intubation (the primary outcome) with NIPPV (20% *vs.* 70%, p=0.002). Similarly, the patients treated with NIPPV had less fatal complications (20% *vs.* 50%, p=0.05), briefer length of ICU stays for survivors (5.5 [3.0] *vs.* 9.0 [4.0] days, p=0.03), and lower mortality rates (20% *vs.* 50%) (all secondary outcomes).

Rationale for the Recommendation. The recommendation is based on the result of a single-centre RCT which included a small number of patients.[10] The expert panel could not draw any meaningful conclusions since the dataset was small and also somewhat dated given the dynamics of innovation in transplantation.

2.5 During fiberoptic bronchoscopy

Recommendation 11 - Weak recommendation, moderate-quality evidence (2B)

In the hypoxemic patient requiring bronchoscopy, we suggest using non-invasive respiratory support techniques rather than conventional oxygen therapy

Evidence Summary. Two RCTs assessed non-invasive respiratory support techniques in hypoxemic patients undergoing bronchoscopy.[26,27] In one single-centre trial, patients undergoing fibreoptic bronchoscopy (n=30) were randomised to either CPAP or COT during the procedure. Those treated with CPAP had higher SpO_2 values within 30 minutes of procedure termination (95.7±1.9% *vs.* 92.6±3.1% respectively, p=0.02) and less respiratory failure within 6 hours (none *vs.* five respectively, p=0.03).[26] In another single-centre trial hypoxemic patients requiring bronchoscopy in the ICU (n=40) were randomised to either NIPPV or HFNC. The rate of intubation within 24 h of procedure termination was lower with HFNC but this finding was not statistically significant (three *vs.* one respectively, p=0.29).[27]

Rationale for the Recommendation. The recommendation is based on two single-centre RCTs[26,27] and on expert opinion. Both studies included a small number of patients, albeit the sample sizes did meet their a-priori power calculation for proving the primary end-points. Furthermore, the studies compare different devices. Thus information could not be derived regarding the preferred type of support. However, as time is of the essence during airway management, the experts decided that during the brief periprocedural period there may be more to gain than to lose by ensuring higher saturations.

QUERY 3

What minimal standards of hemodynamic and respiratory monitoring and what laboratory and radiological tests are required during the support period?

The panel sought direct and indirect evidence to support standards of monitoring and testing on the following topics:

- **Competence and skill**
- **Clinical examination**
- **Physiological monitoring**
- **Blood sampling**
- **Radiological testing**

3.1 Competence and skill

Recommendation 12 - Moderate recommendation, weak evidence (2C)

We suggest that perioperative/periprocedural hypoxemic patients undergoing non-invasive positive pressure ventilation be treated by clinicians with recognized competence and skill in airway management and ventilation of patients with lung injury

Evidence Summary. More often than not, hypoxemia is the reason for use of NIPPV. Postoperative hypoxemic patients are highly likely to ultimately require intubation. Predicting progression to respiratory failure is clinically challenging and failure is not always directly attributable to respiratory issues alone.[28] Several studies have shown a median time from initiation of NIPPV treatment to reintubation approximating one day.[16,28]

Delayed escalation to invasive mechanical ventilation may be detrimental to patient outcome. In one single-centre study, which did not specifically include perioperative patients, early intubation was associated with significantly less ICU mortality (propensity-adjusted OR=0.317, p=0.005, matched

OR=0.369, p=0.046).[29] In a prospective multicentre trial that randomised patients after elective extubation with subsequent respiratory failure to NIPPV (n=114) *vs.* COT (n=107), reintubation rates were similar in the two groups but the median time from acute respiratory failure to reintubation was significantly longer with NIPPV (12 h *vs.* 2.5 h respectively, p=0.02) as was ICU mortality (25 % *vs.* 14% respectively; RR 1.78 (1.03 to 3.20) p=0.048).[30] Most patients that improve with NIPPV will do so within an hour of treatment initiation.[31-33]

Rationale for the Recommendation. Unsurprisingly, no RCTs have compared the outcomes of patients treated by clinicians untrained or poorly trained in airway management and ventilation of patients with lung injury to those treated by clinicians who are well trained. Yet treatment by staff members that lack appropriate training may occur in certain settings. Untrained clinicians may view non-invasive respiratory support, like HFNC, as less demanding than invasive ventilation since requires setting and adaptation of less parameters.

Conversely this system has no alarms. Therefore, treatment with these techniques does not ensure patient safety. The recommendation does not rely on RCTs showing benefit, but rather on clinical judgment. Given the high likelihood of treatment failure and the potentially great consequences to the patient stemming from delayed intubation, such patients are likely to benefit from treatment by expert caregivers.

3.2 Clinical examination

Recommendation 13 - Weak recommendation, very low-quality evidence (2C)

We suggest that perioperative/periprocedural patients treated with non-invasive respiratory support techniques be examined periodically for signs of respiratory distress, neurological deterioration, and interface intolerance by a clinician with recognized competence and skill in airway management and ventilation of patients with lung injury

Evidence Summary. No RCTs have studied the impact of periodic clinical assessment of hypoxemic patients requiring non-invasive respiratory support techniques. However, at least three randomised controlled trials described periodic clinical assessment in their monitoring protocol, likely because the authors viewed such assessment as useful for detection of patient deterioration. Gaszynski *et al.* sought clinical signs of increased work of breathing work such as substernal retraction, sternocleidomastoid activity and paradoxical abdominal wall motion in obese postoperative patients non-responsive to treatment.[34] Clinical assessment also included patient activity, arousal, and tolerance to the method of oxygen delivery used but the times of assessment were not reported. Corley *et al.* measured respiratory rate hourly and subjective dyspnea 1 hand 8 h post-extubation in

patients after cardiac surgery.[18] Stephan *et al.* documented respiratory rate 1 h and then 6-12 h after treatment initiation and daily quantified the treatment effects of HFNC and NIPPV on dyspnea.[16]

Rationale for the Recommendation. Despite the low level of evidence to support this recommendation, the panel viewed assessment by a skilled clinician as an important aspect of care for patients requiring non-invasive respiratory support. More data is needed to assess the actual impact of clinical assessment (including its details and timing) on patients treated with various non-invasive respiratory support techniques

3.3 Physiological monitoring

Recommendation 14 - Weak recommendation, low-quality evidence (2C)

We suggest that perioperative/periprocedural hypoxemic patients undergoing non-invasive positive pressure ventilation undergo continuous physiological monitoring including pulse oximetry, non-invasive or invasive blood pressure measurement, respiratory rate and electrocardiography. When a closed non-invasive positive pressure ventilation technique is being used, we suggest adding monitoring of flow and pressure ventilation waveforms

Evidence Summary. There is no evidence to support any level of monitoring (or lack thereof) in patients treated with non-invasive respiratory support techniques.

Rationale for the Recommendation. Several studies have shown that respiratory rate is a good predictor of impending patient collapse.[35-37] Similarly, the use of early warning scores integrating several physiological parameters has proven its worth in identification of patient deterioration.[35,36] There is seemingly little support for the recommendation to monitor these parameters in a continuous manner. However, it is nearly impossible to tie between the intensity of monitoring and patient outcome since the timeliness and appropriateness of the medical response to the monitoring signal will ultimately determine outcome. Given the high stakes in this patient population (see previous recommendations) the panel chose to exercise clinical logic with regards to this recommendation.

3.4 Blood sampling

Recommendation 15 - Weak recommendation, low-quality evidence (2C)

In perioperative/periprocedural hypoxemic patients treated with a non-invasive respiratory support technique, we suggest periodic arterial blood gas sampling after the first hour of

treatment, at least every six hours during the first 24 hours and daily until the end of the treatment

Evidence Summary. In a study that randomised morbidly obese patients (n=19) after open Roux-en-Y gastric bypass to either CPAP with the Boussignac device or COT, arterial blood gases were measured 30 min, 4 h and 8 h after treatment initiation.[34] In another study that randomised patients with an intermediate to high risk for postoperative complications after planned thoracoscopic lobectomy to either HFNC (n=56) or COT (n=54), arterial blood gases were sampled 1, 2, 6, 12, 24, 48, and 72 h after extubation.[37] In a third study that randomised patients admitted to a cardiac ward to either CPAP or COT, arterial blood was sampled for gas analyses 2 hours after each CPAP cycle and after 30 minutes of breathing through a Venturi mask with a known FiO_2.[23] Finally, in a trial that randomised patients after solid organ transplantation to either NIPPV (n=20) or COT (n=20) arterial blood was sampled for gas analysis at baseline, at 1 h and then regularly at 4 h-intervals.[10]

Rationale for the Recommendation. The current recommendation is based on the commonly reported time frame for clinical deterioration in prior studies (see recommendation 11) and practice when monitoring this patient group in randomised clinical trials where concerns exist regarding possible respiratory failure. Blood gases best reflect the possible effect (or lack thereof) of respiratory intervention in the hypoxemic patient.

3.5 Radiological testing

Recommendation 16

We cannot provide a recommendation regarding the need for routine imaging. However, in the presence of an appropriate clinical indication, lung imaging should be considered during non-invasive positive pressure ventilation treatment in hypoxemic perioperative/periprocedural patients

Evidence Summary. The Radiological Atelectasis Score which was developed by Richter *et al*.[39] is a 5-point score describing: clear lung fields = 0, plate-like atelectasis or slight infiltration = 1, partial atelectasis = 2, lobar atelectasis = 3 and bilateral lobar atelectasis = 4. In a single-centre RCT, Corley *et al.* applied the Radiological Atelectasis Score to patients with a body mass index above 30 after cardiac surgery who were being treated with either HFNC or COT.[17] No differences were found on days 1 and 5 (median score = 2, p=0.70 and p=0.15, respectively). Similarly, Parke *et al.* scored atelectasis observed in chest X-rays to determine whether routine administration of HFNC *vs.* COT improved pulmonary function after cardiac surgery. No differences were observed at baseline or on

post-extubation days 1 and 3.[40] In a randomised controlled trial comparing the effect of HFNC *vs.* COT in obese patients after cardiac surgery on the rate of atelectasis (primary outcome). Chest radiography was performed on days 1 and 5 post-operatively, and the Radiological Atelectasis Score was assessed.[18] In all of these studies only some of the patients included were actually hypoxemic.

Rationale for the Recommendation. Lung imaging may be indicated in some patients treated with non-invasive respiratory support techniques. Few studies have reported imaging results during the use of non-invasive respiratory support techniques in hypoxemic patients after surgery.[18] Lung ultrasound is radiation-free and is currently accepted as a useful tool for assessing aeration, congestion and consolidation in acute respiratory failure.[41] Studies are required on the role of ultrasound in the hypoxemic postoperative patient.

QUERY 4

What are the (ways to prevent) avoidable complications in perioperative/periprocedural hypoxemic patients receiving various types of non-invasive respiratory support?

Recommendation 17

The expert panel identified no studies addressing means of prevention of complications and therefore decided to refrain from issuing a recommendation on this topic

Recommendation 18 - Weak recommendation, moderate-quality evidence (2B)

We suggest using a high flow nasal cannula rather than conventional oxygen therapy in perioperative/periprocedural hypoxemic patients with low tolerance to other forms of non-invasive respiratory support techniques

Evidence Summary. Mild complications of HFNC are reported in 0-6% of postoperative patient.[16,42,43] These mainly include discomfort related to flows and/or heating, focal erythema, and skin damage. A study that randomised hypoxemic patients after cardiothoracic surgery to either NIPPV or HFNC found more skin lacerations with NIPPV after 24 h of treatment (10% *vs.* 3%; 95%CI, 7.3%-13.4% *vs.* 1.8%-5.6%; p<0.001).[16] Another noninferiority trial that randomised patients (38% of them surgical) at high risk for post-extubation respiratory failure to either HFNC or NIPPV via a facemask found more damage to the nasal mucosa and skin with NIPPV (42.9% *vs.* 0%, p<0.001). These complications required discontinuation for 25% or more of the per-protocol time (18 h).[28] A two-centre study that randomised patients with PaO_2:FiO_2 ratio less than or equal to 300 immediately before extubation to either COT or HFNC noted that with HFNC the rate of interface displacement was lower (32% *vs.*

56%; p=0.01) and there were less oxygen desaturations (40% *vs.* 75%; p<0.001).[44] Conversely, a trial which randomised patients at high risk for post-operative pulmonary complications undergoing major abdominal surgery to either COT or HFNC found no difference between the two in terms of discomfort between groups.[21]

Mild complications have been reported in 0.2%-43% of postoperative patients with acute respiratory failure.[13,16,28,45] These include conjunctivitis, sinusitis, eye irritation, air leaks, mask discomfort, skin breakdown, drying of the oro-nasal mucosa, gastric insufflation, claustrophobia, vomiting and patient-ventilator asynchrony. Severe complications have been reported in 0-10% in the general population of patients.[46,47] There are no specific reports in postoperative patients but there is nothing to suggest the rates of such complications should be different in this patient population. These complications include amongst others pneumothorax, pulmonary aspiration of stomach content, hypotension, arrhythmias and gastrointestinal bleeding.

Rationale for the Recommendation. Patient ventilator interface may ultimately determine the success of treatment with any NIPPV technique. The HFNC is an open system and therefore may lend itself better to patients who suffer skin abrasion or claustrophobia. Three RCTs noted a higher rate of interface-related complications with CPAP than with HFNC.[16,28,44] The literature regarding some of the outcomes above supports the use of NIPPV over COT in many patients. Therefore, the HFNC is preferred to COT should other NIPPV techniques fail due to interface issues.

QUERY 5

How and where to initiate perioperative/periprocedural non-invasive respiratory support?

Recommendation 19

The expert panel identified no studies addressing this query and therefore decided to refrain from issuing a recommendation on this topic

Discussion

Patients who develop postoperative hypoxemia are at increased risk for postoperative pulmonary complications and death.[48] Most RCTs compared a non-invasive respiratory support technique with the use of COT.[10-12,14,23] Few RCTs compared two non-invasive respiratory support techniques head to head.[15,16] The evidence supporting non-invasive respiratory support techniques (NIPPV, CPAP and HFNC) over COT is therefore more convincing than that supporting one type of support over another. Within the framework of the five queries posed by the expert panel, overall 19 recommendations

were formulated. These are based on the existing literature and thus mostly on low levels of evidence. The first query determined the goals of therapy with each non-invasive respiratory support technique. The panel recommended the use of NIPPV or CPAP to improve oxygenation and to prevent the risk of reintubation.[10-12,14] It was suggested that the use of NIPPV reduced the mortality rate, as compared with COT.[12]

The second query identified populations in which the use of non-invasive respiratory support techniques may be beneficial. NIPPV or CPAP performs better than COT after abdominal surgery and lung resection,[11,12,14] while HFNC may have a role after cardiothoracic surgery.[16] The evidence seems to draw different conclusions for NIPPV and HFNC, particularly after abdominal surgery.

The third query assessed the minimal standards of hemodynamic and respiratory monitoring in patients requiring non-invasive respiratory support techniques. Review of the literature on this topic led the panel to emphasize the importance of avoiding delays in tracheal intubation. For example, among 175 ICU patients receiving HFNC, delay in intubation was associated with increased mortality (39.2 *vs.* 66.7%; p=0.001).[29] Such data suggests that these patients should be managed by clinicians skilled in management of the airway and ventilation. Lacking direct evidence, the recommendations were derived from the monitoring used in various RCTs assessing the non-invasive respiratory support techniques.[10-14,18,21,23,34] Periodic clinical assessment, continuous monitoring (including pulse oximetry, non-invasive blood pressure, electrocardiography) and periodic blood sampling for partial gas pressures were recommended based on indirect evidence. But lacking any evidence, direct or indirect on imaging, no recommendation could be made on this topic

The fourth query sought evidence on methods to prevent avoidable complications. The panel reported on the rate of complications associated with the use of non-invasive respiratory support techniques. The panel also noted that the HFNC may have an advantage in terms of patient tolerance but the evidence on this is only indirect. Furthermore, tolerance to non-invasive respiratory support seems related to the patient ventilator interface and ventilatory settings. Only three studies have addressed this issue. All show that NIPPV delivered with a face mask is associated with greater discomfort and less compliance[49,50] and less treatment failure than with a helmet.[13] One should note that other treatment options may also reduce the incidence of complications, such as semi-recumbent positioning in patients at risk of aspiration. The fifth query focused on the best location to initiate a non-invasive respiratory support technique. No recommendation was made on this topic due to the scarcity of data.

This guideline has several limitations. First, our conclusions are limited to the population selected and based on the literature identified at this time. Second, there is significant heterogeneity in the study populations and the outcomes described in the literature (*e.g.* the time-frame for defining "reintubation"). Thus, assessing the quantitative effects of the interventions with meta-analysis was

not possible. For each recommendation, the evidence was mostly provided by less than a handful of large RCTs. Third, specifically in perioperative/periprocedural patients, outcomes may also be significantly affected by the type and quality of the surgery/procedure. The current recommendations were formulated with no data on this aspect of patient care. Our analyses did not include specific patient subgroups (e.g. asthma, chronic obstructive pulmonary disease). In addition, we had no access to data regarding contraindications to the use of NIPPV or CPAP (hemodynamic instability, decreased level of consciousness, respiratory failure due to neurological failure or asthmaticus status, facial deformities). In addition, the panel unanimously decided that hypoxemia is defined by a PaO_2:FiO_2 ratio below 300 mmHg. To our knowledge, there is no consensual definition of hypoxemia, which could be considered as a limitation. Finally, outcomes may depend on the resources available in a specific clinical environment. There is no standard format for reporting the quality of care. Most of the studies identified were conducted in high-income countries. It is uncertain whether the current findings can be extrapolated to other clinical settings.[51]

Future research should address several gaps. (1) Most studies have compared a non-invasive respiratory support technique (NIPPV, CPAP and HFNC) to COT. Head to head comparisons are scarce. (2) There is also no information regarding surgical complications in peri-operative/periprocedural patients. This is a particularly relevant question after upper abdominal surgery. Non-invasive ventilation with high pressures has traditionally been contraindicated after major gastric and esophageal surgery due to the theoretical risk of gastric dilatation and disruption of surgical anastomoses. Faria *et al.* reported that NIPPV may be considered in patients with acute respiratory failure after esophageal surgery, when the insufflation pressure level was less than 12 cmH_2O and air leaks were absent.[22] However, this statement was based on only three prospective studies.[12,20,52] (3) Another issue that requires further investigation is the use of non-invasive respiratory support techniques outside of the ICU in the periprocedural/perioperative period. Only one RCT compared patients treated with CPAP to those treated with COT on the ward.[23] Yet surveys reveal that non-invasive respiratory support techniques are routinely used in wards[53] and that nurses in such wards feel inadequately informed about the management of non-invasive respiratory support techniques.[54] The decision to use non-invasive ventilation techniques outside of the ICU very much depends on the expertise and means available locally. However, it is important to further study this practice in the context of patient safety. (4) Finally, there is a need to elucidate the means of improving patient and non-invasive respiratory support device interface.

Conclusion

Based on a systematic review of the literature, this joint ESA/ESICM guideline on oxygenation of hypoxemic postoperative patient formulated 19 recommendations for non-invasive ventilation

support in the hypoxemic perioperative/periprocedural patient. These recommendations relate to the goals of therapy, the target populations, clinical assessment and monitoring requirements, prevention of complications and the location of care. Less than a handful of the recommendations could be based on moderate to high-quality evidence. This work also highlights the gaps in the evidence and sets the framework for future research in this area.

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