Supplementary material

Appendix 1: PRISMA-P 2015 checklist (16)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Appendix 2: Search Strategy

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Strategy:

1 Biomarkers/bl [blood] (98759)
2 Natriuretic Peptide, Brain/ (12407)
3 Nerve Tissue Proteins/ (82365)
4 Peptide Fragments/bl [blood] (9649)
5 ((biomarker* or marker*) adj2 (myocardial adj1 (strain* or stretch*))).tw,kf. (15)
6 ((biomarker* or marker*) and (PVR or vascular resistance*)).tw,kf. (846)
7 ((biomarker* or marker*) and (RV strain* or ventricular strain*)).tw,kf. (73)
8 BNP*.tw,kf. (9471)
9 (NT-proBNP* or NTproBNP*).tw,kf. (5278)
10 N terminal proBNP*.tw,kf. (251)
11 natriuretic peptide*.tw,kf. (26604)
12 nerve tissue protein*.tw,kf. (150)
13 or/1-12 [Combined MeSH & text words for BNP] (210406)
14 Ventilator Weaning/ (3444)
15 (extubat* adj2 (fail* or succe* or unsuccessful*)).tw,kf. (1436)
16 CPAP trial*.tw,kf. (59)
17 (pressure support ventilation adj3 trial*).tw,kf. (12)
18 SBT*.tw,kf. (2697)
19 (spontaneous breathing adj3 trial*).tw,kf. (485)
20 ((T-piece* or T-tube*) adj3 trial*).tw,kf. (103)
21 or/14-20 [Combined MeSH & text words for breathing trials] (7134)
22 Airway Management/ (2129)
23 Respiration, Artificial/ (44154)
24 ((airway* or air way*) adj3 (control* or manage*)).tw,kf. (9111)
25 ((artificial* or mechanical*) adj1 (respir* or ventilat*)).tw,kf. (51467)
26 respirator*.tw,kf. (387837)
27 ventilator*.tw,kf. (47662)
28 or/22-27 [Combined MeSH & text words for artificial respiration] (465447)
29 Airway Extubation/ (923)
30 Tidal Volume/ (9135)
31 extubat*.tw,kf. (11474)
32 liberat*.tw,kf. (22840)
33 postextubat*.tw,kf. (490)
34 tidal volume*.tw,kf. (13308)
35 wean*.tw,kf. (42743)
36 or/29-35 [Combined text words for weaning] (92605)
37 and/28,36 [Combined concept for weaning from artificial respiration] (24471)
38 or/21,37 [Combined concepts for breathing trials or weaning from artificial respiration] (28432)
39 and/13,38 [Combined index test & condition concepts] (186)
40 exp Animals/ not Humans/ (4428797)
41 (animal model* or bovine or canine or capra or cat or cats or cattle or cow or cows or dog or dogs or equine or ewe or ewes or feline or goat or goats or horse or hamster* or horses or macaque or macaques or mare or mares or mice or monkey or monkeys or mouse or murine or nonhuman or non-human or ovine or pig or pigs or porcine or primate or primates or rabbit or rabbits or rat or rats or rattus or rhesus or rodent* or sheep or simian or sow or sows or vertebrate or vertebrates).ti. (2162123)
42 39 not (40 or 41) [Excluded animal studies] (155)
43 remove duplicates from 42 (155)

Appendix 3: Data extraction parameters

Authors (first two)
Title
Journal
Year
DOI
Library
PMID
PDF availability
Setting
Academic setting
Age range
% males
Weight
Height
BMI
EF
Diastolic function (presence, severity)
Valvular dysfunction (type, severity)
Organ failure scores
Acuity of illness scores
Fluid balance at time of SBT
Atrial fibrillation
Pulmonary emboli
Pulmonary hypertension
Chronic kidney disease
Renal replacement therapy
Diagnosis
Intubation status
Duration of intubation
SBT type
Duration of SBT
Respiratory Rate at end of SBT
PS at end of SBT
PEEP at end of SBT
PaO2/FiO2
% Successful SBT
% failure extubation
Time to reintubation
Ventilator free days
Mortality at 30 days
Total ICU admission days
Post-extubation ICU days
Hospitalization days
% Tracheostomy
ICU-acquired weakness rate
BNP type
BNP pre-SBT
BNP post-SBT
% BNP change

Appendix 4: Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) Tool Checklist (22) (available at: https://www.bristol.ac.uk/media-library/sites/quadas/migrated/documents/quadas2.pdf)

QUADAS-2

Phase 1: State the review question:

Patients (setting, intended use of index test, presentation, prior testing):
Index test(s):
Reference standard and target condition:

Phase 2: Draw a flow diagram for the primary study

Phase 3: Risk of bias and applicability judgments

QUADAS-2 is structured so that 4 key domains are each rated in terms of the risk of bias and the concern regarding applicability to the research question (as defined above). Each key domain has a set of signalling questions to help reach the judgments regarding bias and applicability.

DOMAIN 1: PATIENT SELECTION

A. Risk of Bias

Describe methods of patient selection:

- ❖ Was a consecutive or random sample of patients enrolled? Yes/No/Unclear
- ❖ Was a case-control design avoided? Yes/No/Unclear
- ❖ Did the study avoid inappropriate exclusions? Yes/No/Unclear

Could the selection of patients have introduced bias? **RISK: LOW/HIGH/UNCLEAR**

B. Concerns regarding applicability

Describe included patients (prior testing, presentation, intended use of index test and setting):

Is there concern that the included patients do not match the review question? **CONCERN: LOW/HIGH/UNCLEAR**

DOMAIN 2: INDEX TEST(S)

If more than one index test was used, please complete for each test.

A. Risk of Bias

Describe the index test and how it was conducted and interpreted:

- ❖ Were the index test results interpreted without knowledge of the results of the reference standard? Yes/No/Unclear
- ❖ If a threshold was used, was it pre-specified? Yes/No/Unclear

Could the conduct or interpretation of the index test have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

B. Concerns regarding applicability

Is there concern that the index test, its conduct, or interpretation differ from the review question? **CONCERN: LOW /HIGH/UNCLEAR**

DOMAIN 3: REFERENCE STANDARD

A. Risk of Bias

Describe the reference standard and how it was conducted and interpreted:

- ❖ Is the reference standard likely to correctly classify the target condition? Yes/No/Unclear
- ❖ Were the reference standard results interpreted without knowledge of the results of the index test? Yes/No/Unclear

Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

B. Concerns regarding applicability

Is there concern that the target condition as defined by the reference standard does not match the review question? **CONCERN: LOW /HIGH/UNCLEAR**

DOMAIN 4: FLOW AND TIMING

A. Risk of Bias

Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram):
Describe the time interval and any interventions between index test(s) and reference standard:

- ❖ Was there an appropriate interval between index test(s) and reference standard? Yes/No/Unclear
- ❖ Did all patients receive a reference standard? Yes/No/Unclear
- ❖ Did patients receive the same reference standard? Yes/No/Unclear
- ❖ Were all patients included in the analysis? Yes/No/Unclear

Could the patient flow have introduced bias? **RISK: LOW /HIGH/UNCLEAR**

Appendix 5: Quality assessment criteria (23)

Study Design	Quality of Evidence	Lower if	Higher if
Randomized trial →	High	Risk of bias -1 Serious -2 Very serious	Large effect +1 Large +2 Very large
	Moderate	Inconsistency -1 Serious -2 Very serious	Dose response +1 Evidence of a gradient
Observational study →	Low	Indirectness -1 Serious -2 Very serious	All plausible confounding +1 Would reduce a demonstrated effect or
	Very low	Imprecision -1 Serious -2 Very serious	+1 Would suggest a spurious effect when results show no effect
		Publication bias -1 Likely -2 Very likely	

Appendix 6: Schematic view of GRADE's process for developing recommendations. (23)