New set of indicators with consensus definition for anaesthesia-related severe morbidity: A scoping review followed by a Delphi study

Marie-Pierre Bonnet, Perrine Guckert, Cécile Boccara, Chafia Daoui, Hélène Beloeil

Journal of Clinical Anesthesia 99 (2024) 111626

Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

journal homepage: www.elsevier.com/locate/jclinane

Original Contribution

New set of indicators with consensus definition for anaesthesia-related severe morbidity: A scoping review followed by a Delphi study

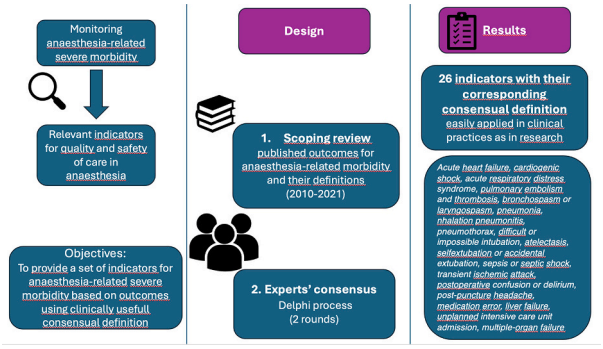
Marie-Pierre Bonnet [a,f,*], Perrine Guckert [b], Cécile Boccara [c], Chafia Daoui [d], Hélène Beloeil [e], on behalf of the SFAR research network[1]

[a] Sorbonne University, Department of Anaesthesia and Critical Care Medicine, Armand Trousseau Hospital, DMU DREAM, GRC 29, AP-HP, 75012 Paris, France;
[b] Department of Anaesthesia and Intensive Care, Rennes University Hospital, University Rennes 1, 35000 Rennes, France
[c] Department of Anaesthesia and Critical Care Medicine, Armand Trousseau Hospital, DMU DREAM, AP-HP, 75012 Paris, France
[d] Chef de projets - Réseau Recherche SFAR, Société Française d'Anesthésie et de Réanimation, 75016 Paris, France
[e] Univ Rennes, CHU Rennes, Inserm, COSS 12142, CIC 1414, Anaesthesia and Intensive Care Department, F-35000 Rennes, France
[f] Université Paris Cité, Centre for Epidemiology and Statistics (CRESS), Obstetrical Perinatal and Paediatric Epidemiology Research Team, EPOPé, INSERM, INRA, 75014 Paris, France

HIGHLIGHTS

- Monitoring anaesthesia-related severe morbidity is essential for assessing quality and safety of care in anaesthesia.
- First we identifies the outcomes used in the literature to characterize anaesthesia-related severe morbidity by conducting a scoping review.
- Then a set of indicators for anaesthesia-related severe morbidity with specific definitions was obtained by experts' consensus.
- This consensual set of 26 indicators for anaesthesia-related severe morbidity is useful for clinical practice as for research.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Anaesthesia
Perioperative medicine
Severe morbidity
Core outcome
Indicators

ABSTRACT

Study objective: Monitoring anaesthesia-related severe morbidity constitutes a good opportunity for assessing quality and safety of care in anaesthesia. Several recent studies attempted to describe and define indicators for anaesthesia-related severe morbidity with limitations: no formal experts' consensus process, overlap with surgical complications, no consensual definitions, inapplicability in clinical practice. The aim of this study was to provide a set of indicators for anaesthesia-related severe morbidity based on outcomes and using clinically useful consensual definitions.

Design: 1/ scoping review of studies published in 2010–2021 on outcomes of anaesthesia-related severe morbidity with different definitions;

* Corresponding author at: Department of Anaesthesia and Critical Care Medicine, Armand Trousseau Hospital, 26, avenue du Docteur Arnold Netter, 75,012 PARIS, France.
E-mail address: marie-pierre.bonnet@aphp.fr (M.-P. Bonnet).

[1] Members of the SFAR Research Network: Raphael Cinotti, Aurélien Mazeraud, Stephanie Sigaut, Amelie Yavchitz, Alice Jacquens, Elodie Lang, Amelie Rolle, Lucillia Bezu, Jean-Noel Evain, Maxime Léger, Marwan Bouras, François Dépret, Céline Monard

https://doi.org/10.1016/j.jclinane.2024.111626
Received 26 October 2023; Received in revised form 11 July 2024; Accepted 10 September 2024
Available online 17 September 2024

2/ International experts' consensus on indicators for anaesthesia-related severe morbidity with specific definitions using a Delphi process.
Main results: After including 142 studies, 68 outcomes for anaesthesia-related severe morbidity were identified and organized in 34 indicators divided into 8 categories (cardiovascular, respiratory, sepsis, renal, neurological, medication error, digestive and others). The indicators were then submitted to the experts. After 2 Delphi rounds, the 26 indicators retained by the experts with their corresponding consensual definition were: acute heart failure, cardiogenic shock, acute respiratory distress syndrome, pulmonary embolism and thrombosis, bronchospasm or laryngospasm, pneumonia, inhalation pneumonitis, pneumothorax, difficult or impossible intubation, atelectasis, self-extubation or accidental extubation, sepsis or septic shock, transient ischemic attack, postoperative confusion or delirium, post-puncture headache, medication error, liver failure, unplanned intensive care unit admission, multiple-organ failure.
Conclusions: This study provides a new consensual set of indicators for anaesthesia-related severe morbidity with specific definitions, that could be easily applied in clinical practice as in research.

1. Introduction

Mortality and severe morbidity are considered as essential indicators for quality and safety of anaesthesia care, and broadly of a care system, whether at the scale of a hospital structure, a region, or a country [1]. In the research field, the study of mortality and severe morbidity related to anaesthesia are mostly based on clinical outcomes [2]. Mortality related to anaesthesia has drastically dropped in the last 50 years and is considered as the extreme part of the spectrum of severe morbidity. Thus, the study of anaesthesia safety and quality of care is now focused on severe morbidity.

Anaesthesia-related severe morbidity is difficult to define. It includes all severe critical events resulting from an anaesthetic procedure, whether general or regional. However, there is no unique consensual definition of anaesthesia-related severe morbidity. Various definitions have been previously proposed, with different objectives. In Germany, the "Perioperative anaesthesia outcome database" systematically records any adverse effect related to anaesthesia and its severity, defined by the intervention of an anaesthetist or a damage for the patient [3]. Since 2021, in the United Kingdom, any event related to anaesthesia, defined by a prejudice for the patient and its severity, is collected in "The National Patient Safety Agency" (NPSA) [4]. Studies from the US Veterans Health administration provide data on perioperative morbidity, mortality and quality of surgical care using morbidity defined by pneumonia, urinary tract infection, and failure to wean from the ventilator at 48 h postoperatively [5]. In 2015, the European Society of Anesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM) created a joint task force to propose standards for the definition and outcome measures in clinical effectiveness research in perioperative medicine [6]. Similarly, two recent studies have focused on perioperative medicine: Haller et al. identified eight clinical indicators measuring quality and safety in perioperative care [7], while The StEP-COMPAC initiative developed a core outcome set for trials in perioperative medicine and anaesthetic care [8]. These proposed indicators were not specifically dedicated to anaesthesia-related morbidity and the definitions of the indicators were not consensual. Finally, these indicators were mainly dedicated to research and not designed for clinical routine practice.

However, standardized consensual indicators based on clinical outcomes and with detailed definitions would allow to assess anaesthesia-related severe morbidity in a reproducible and comparable way in future clinical audits, as well as in research, or in daily practice.

The objective of the study was to identify, using an experts' consensus after a scoping review of the literature, a set of indicators for anaesthesia-related severe morbidity based on clinical outcomes with their definitions.

2. Materials and methods

2.1. Scoping review of the literature

We first performed a scoping review to identify all the outcomes used in the literature to characterize anaesthesia-related severe morbidity, according to the Cochrane recommendation and the PRISMA declaration.

We included randomized controlled trials and observational studies (cohort studies or case-control studies), published between January 2010 and September 2021, in French or English language, that explored anaesthesia-related severe morbidity as a primary outcome. Non-inclusion criteria were studies that included paediatrics or obstetrical population, focused on non-severe morbidity or non-potentially life-threatening complications (i.e., postoperative nausea or vomiting), assessed surgery-related or patient-related morbidity, and studies with pain as primary outcome.

The Medline database was searched for the following terms: "morbidity", OR "complication", OR "threatening", OR "sequelae", OR "adverse", OR "disability", OR "injury", OR "damage", OR "mortality", OR "death ", AND "anaesthesia" OR "anesthesia", OR "anesthesiology" to identify the relevant references. The computer search was completed with a manual search based on the references and citations of selected studies to identify any additional studies. After removing duplicates, a stepwise approach was used. The process of study selection was undertaken by two junior reviewers (CB and PG) who independently screened titles and abstracts. Full texts were then reviewed, and irrelevant papers were excluded. At any stage, in the event of disagreement between the two reviewers, the opinion of two senior reviewers (HB and MPB) was taken.

Selected articles were independently analysed by the two junior reviewers, and outcomes of anaesthesia-related severe morbidity were extracted. Studies were then classified according to the study design, the surgical settings, the type of anaesthesia, the timing of evaluation in the postoperative period, and finally the type of anaesthesia-related severe morbidity explored.

From the results of the scoping review, the coordination team (PG, CB, HB and MPB) constructed an initial set of indicators. These indicators were then classified into categories corresponding to organs. Additionally, different definitions retrieved from the literature were proposed for each indicator.

2.2. Delphi method

The second part of the study consisted of a Delphi process to achieve consensus from international experts on anaesthesia-related severe morbidity. The Delphi method is a process framework based on the results of multiple rounds of questionnaires sent to an experts panel. It is notably used to develop quality indicators [9]. The research coordination team identifies a problematic, analyses the available evidence,

develops questionnaire statements submitted to selected experts who rate them, and feedback results (statistical, qualitative, or both) between rounds until a consensus statement is obtained [10].

To get an international expert panel, including anaesthesiologists specialized in all sub-specialties and involved in research and scientific publication, we invited to participate all the 57 members of the editorial board of the *Anaesthesia Critical Care and Pain Medicine journal,* and all the 10 members of the French Society of Anaesthesia and Intensive Care (SFAR) research network. In addition, one patient representative was invited to participate. Clear instructions were given to the expert panel (Appendix A). In few words, experts were asked to select indicators with the following characteristics: Precisely defined, with significant level of severity corresponding to a life-threatening event, independent of care practices and organizations, applicable to the entire population (except obstetric and paediatric patients) and not only related to a subgroup of individuals according to surgical settings, easily identifiable from hospital databases, applicable together or separately.

In the First Delphi round, the initial list of indicators with corresponding proposed definitions was submitted to the experts. They were asked to score each of the listed indicators with definitions using a scale graded from 1 to 5 ("1" = "Strongly disagree" with the indicator and the proposed definition, "2" = "disagree", "3" = "Need precision", "4 = "agree", "5″ = "Strongly agree"). Up to three definitions could be proposed for each indicator. Participants were also invited to add plain text comments and suggestions for modifications. They had one month to answer before reminders were sent, for a total period of three months given to answer the first-round questionnaire online.

Then the coordination team (PG, CB, HB and MPB) analysed the percentage of responses for each indicator and its definition after the first round, discussed experts' comments and suggestions and finally prepared the questionnaire for the second Delphi round. The results of the Delphi round 1 was analysed as follows: Indicators with ≥70 % of experts' answers in one of the categories "strongly agree", "agree", "disagree" or "strongly disagree" were validated. Indicators with ≥70 % of experts' answers in the category "need precision" were systematically submitted to the second Delphi round. Indicators for which the combination of the categories "strongly agree" and "agree" was ≥70 % of the expert's answers were included in the second Delphi round without any modification and identified as such. Indicators for which the combination of "strongly disagree" and "disagree" was ≥70 % of the experts' answers were not included in the second round. After this selection, indicators and definitions that needed revision were modified by the authors according to expert's suggestions. Finally, a modified list of outcome indicators with definitions was built and submitted to the experts for the second Delphi round. Experts were asked to score the items using the same rating procedure as in round 1. The former questionnaire with the distribution of the answers (round 1) and additional notes of the experts, was also provided for information. Once again, the experts had to score every proposed item and the definitions associated. There was room for additional note. The experts had 3 months to answer, and reminder emails were sent to prompt completion of the survey.

Analysing the answers of questionnaire 2, indicators with ≥70 % of consensus in one of the categories "strongly agree" or "agree" were validated without modification in the final core outcome set of anaesthesia-related severe morbidity. Indicators with ≥70 % of experts' answers in the categories "strongly disagree", or "disagree", or the indicators with <70 % of experts' answers in the categories "agree" or "strongly agree" were definitively excluded. When several definitions were proposed, the one with the strongest consensus was chosen.

Each Delphi round was coordinated by the SFAR Research network project director (CD). Participants' answers to the Delphi rounds were recorded and analysed using Redcap® (Vanderbilt University, Tennessee, USA).

3. Results

3.1. Scoping review

Between January 2021 and July 2021, we identified 2557 studies based on titles and abstracts. Finally, after selection, 142 were included in the analysis (see flow chart, Appendix Fig. A).

The most frequently represented settings of surgery were digestive or general (37 %, 52/142 studies), orthopaedic (33 %, 47/142 studies) and cardiac surgery (29 %, 41/142 studies) (Appendix Tables A and B). Overall, 127 studies (89 %) concerned general anaesthesia, 17 studies (12 %) peripheral regional anaesthesia, 23 studies (16 %) sedation and 36 (25 %) neuraxial anaesthesia. The great majority of the studies included patients who had scheduled surgery (88 %). Sixty-eight criteria of severe morbidity related to anaesthesia were extracted. Cardiovascular morbidity, respiratory morbidity, and mortality were the 3 most represented categories (Appendix Fig. B). Myocardial infarction (36 %), stroke (35 %) and pneumonia (33 %) were the most frequently assessed severe anaesthesia-related morbidities. Most of the studies assessed anaesthesia-related morbidity during the first 30 days after the surgery ($n = 100$ studies, 70 %), with a follow-up after 30 days in 22 studies (15 %). Mortality was assessed after 30 days in 58 % of the studies, and only during hospital stay in 12 %.

This review retrieved 68 indicators. After exclusion of indicators directly related to clinical practices and after grouping indicators of similar conditions, the authors constructed a first set of 34 indicators with several potential definitions, classified in 8 categories (mortality, cardiovascular morbidity, respiratory morbidity, neurological morbidity, renal morbidity, infectious morbidity, characteristics of the hospital admission, and surgical complications involving anaesthesia) (Table 1).

3.2. Delphi round 1

Overall, 42 experts from Australia, Belgium, China, Egypt, France, India, Israel, Italy, Japan, Poland, Saudi Arabia, South Africa, Spain, Switzerland, United Kingdom, and Unites States of America agreed to participate (see the list of experts panel). Among them, 37 answered, and one of them did not completely fulfil the questionnaire (response rate 85.7 %). One French patient also participated.

After round 1, 6 out of the 34 proposed indicators (18 %) presented at least 70 % of strong agreement and were consequently selected: "cardiac arrest", "mortality", "infarction, myocardial injury", "acute respiratory failure", "acute renal failure, acute kidney injury, dialysis" and "stroke" (Appendix Table C, round 1). Among them, only cardiac arrest had a consensual definition definitively accepted after round 1. Mortality was accepted without any definition. Nine indicators (9/34 = 26 %) were definitively excluded "hypotension, collapses"; "bradycardia, atrial fibrillation, arrhythmia, pacemaker implantation"; "bleeding, anaemia, transfusion"; "pleural effusion"; "seizure"; "coma"; "ileus"; "extension of expected length of stay"; "unscheduled revision surgery". Finally, 19 indicators and their modified definitions, as well as definitions of 4 indicators already accepted were carried forward to be revised in the Delphi round 2.

3.3. Delphi Round 2

In the second round, 37 experts received the questionnaire and 34 answered (response rate 92 %). At the end of Delphi round 2, 21 indicators and their definitions were definitively included and validated (Appendix Table C, round 2). It should be noticed that three criteria were split in two different indicators for clarity improvement as suggested by the experts: "cardiogenic shock, acute heart failure" was split into 'acute heart failure' and 'cardiogenic shock', 'acute respiratory failure: hypoxemia, hypoxia, ARDS, need for non-invasive ventilation, post-operative mechanical ventilation, desaturation' was split into

Table 1
Severe anaesthesia-related morbidity indicators extracted from the literature ($N = 142$ studies).

Category	Indicators							
Mortality	Study Period for mortality							
	During hospital stay	D30		3 months	6 months		1 year	
Total 84 studies (59 %)	10 (12 %)	49 (58 %)		8 (9 %)	3 (4 %)		3 (4 %)	
Cardio-vascular	**Cardiac Arrest**	**SVRD**	**Myocardial infarction**		**Myocardial Injury**	**Hypotension**		**Acute heart failure**
Total: 90 studies (63 %)	36 (25 %)	32 (23 %)	51 (36 %)		20 (14 %)	28 (20 %)		25 (18 %)
Respiratory	**Unplanned reintubation**	**Bronchospasm**	**Hypoxemia**	**Pneumonia**	**Atelectasis**	**Aspiration pneumonia**	**Acute respiratory failure**	**Pulmonary embolism**
Total: 85 studies (60 %)	23 (16 %)	13 (9 %)	15 (11 %)	47 (33 %)	18 (12 %)	17 (12 %)	30 (21 %)	22 (16 %)
Neurological	**Stroke**	**Transient cerebrovascular accident**	**Coma**		**Delirium**	**Cognitive disorder**		**Neurological deficit**
Total: 74 studies (52 %)	50 (35 %)	7 (5 %)	6 (4 %)		22 (16 %)	15 (11 %)		7 (5 %)
Renal	**Acute Renal Failure**				**Dialysis**			
Total: 49 studies (35 %)	45 (32 %)				12 (9 %)			
Infectious	**Septic Shock**		**Abscess**			**SIRS**		
Total: 33 studies (23 %)	23 (16 %)		20 (14 %)			6 (4 %)		
Characteristics of hospital admission	**Intensive care admission**				**Extension of length of stay**			
Total: 49 studies (35 %)	39 (28 %)				34 (24 %)			
Surgical complications involving anaesthesia	**Bleeding**				**Revision Surgery**			
Total: 25 studies (18 %)	17 (12 %)				15 (11 %)			

Results are presented in number of studies (%). SVRD: supraventricular rhythm disorders, SIRS: Systemic Inflammatory Response Syndrome, D30: First 30 Days.

'ARDS' and 'Acute respiratory failure'; 'pneumonia' was split in 'pneumonia' and"aspiration pneumonia". Twenty-one definitions were validated after Delphi round 2, including the 4 definitions already validated after round 1 (Table 2). Seven definitions were excluded: one of the definitions for "bronchospasm and laryngospasm", "pneumonia", "aspiration pneumonia", "sepsis", "septic shock", "transient ischemic attack" and "anaphylaxis". Overall, the final set includes 26 indicators with their corresponding consensual definition (excepting for mortality and self-extubation).

4. Discussion

The study identified a set of 26 consensual indicators with their corresponding definitions to assess anaesthesia-related severe morbidity. This set of indicators, based on patients' outcomes, results from a rigorous process: a review of the literature, followed by an experts' consensus obtained by a Delphi method.

Indicators for anaesthesia-related severe morbidity have already been proposed previously. The Step-COMPAC group developed a consensus-based definition for endpoints in perioperative clinical trials

Table 2
Final outcome set to be considered as indicators in the evaluation of anaesthesia-related severe morbidity.

1	Indicator 1	CARDIAC ARREST	An absence of cardiac rhythm or presence of chaotic rhythm requiring any component of basic or advanced cardiac life support
2	Indicator 2	MORTALITY	
3	Indicator 3	MYOCARDIAL INJURY	Clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cTn values with at least 1 value above the 99th percentile and at least 1 of the following: - Symptoms of myocardial ischemia - New ischemic ECG changes - Development of pathological Q waves - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic aetiology. dentification of a coronary thrombus by angiography or autopsy (not for types 2 or 3 myocardial infarction)
4	Indicator 4	ACUTE HEART FAILURE	New onset in-hospital signs or symptoms of dyspnoea or fatigue, orthopnoea, paroxysmal nocturnal dyspnoea, increased jugular venous pressure, pulmonary rales on physical examination, cardiomegaly, or pulmonary vascular engorgement
5	Indicator 4bis	CARDIOGENIC SHOCK	Acute heart failure in association with clinical and biological sign of hypoperfusion, and need for vasopressor
6	Indicator 8	ARDS	ARDS was defined according to Berlin criterion
7	Indicator 8bis	ACUTE RESPIRATORY FAILURE	PaO2 < 60 mmHg (kPa) on room air, or PaO2 / FiO2 ratio < 300 or arterial oxyhemoglobin saturation measured with pulse oximetry <90 % and requiring oxygen therapy
8	Indicator 9	PULMONARY EMBOLISM AND THROMBOSIS	A venous blood clot diagnosed with a duplex ultrasonography, venogram, or CT scan and treated with anticoagulation or vena cava filter
9	Indicator 10	BRONCHOSPASM, LARYNGOSPASM	Bronchospasm is defined as newly detected expiratory wheeze treated with bronchodilators. Laryngospasm is defined as an audible stridor or silent auscultation secondary to upper airway obstruction
10	Indicator 11	PNEUMONIAE	New infiltrate on CXR combined with two of the following: temperature > 38.8C, leucocytosis, and positive sputum or bronchial culture
11	Indicator 11bis	ASPIRATION PNEUMONIAE	Respiratory failure and/or pneumonia after the inhalation of regurgitated gastric contents
12	Indicator 12	PNEUMOTHORAX	Air in the pleural space with no vascular bed surrounding the visceral pleural
13	Indicator 15	ATELECTASIS	Lung opacification with a shift of the mediastinum, hilum, or hemidiaphragm toward the affected area, and compensatory overinflation in the adjacent non-atelectatic lung
14	Indicator 16	SELF EXTUBATION	
15	Indicator 18	SEPSIS, SEPTIC SHOCK (RELATED TO ANAESTHESIA)	Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia
16	Indicator 19	ACUTE RENAL FAILURE, ACUTE KIDNEY INJURY, DIALYSIS	Applying the AKIN classification over the course of five postoperative days
17	Indicator 20	STROKE	New neurologic deficit persisting for 24 h or longer, confirmed by assessment by a neurologist or computed tomography or magnetic resonance imaging
18	Indicator 21	TRANSIENT ISCHEMIC ATTACK	Transient episode of focal neurological dysfunction caused by focal brain ischemia without acute infarction in the clinically relevant area of the brain or transient monocular visual loss due to retinal ischemia. Symptoms should resolve completely within 24 h
19	Indicator 22	PERIPHERAL NERVE DAMAGE, MEDULLAR DAMAGE	New onset of sensory and/or motor deficit with clinical and/or electrophysiological abnormalities and/or computed tomography or magnetic resonance imaging abnormalities
20	Indicator 23	POCD OR DELIRIUM	POCD can be assessed by the Confusion Assessment Method (CAM– ICU), and is positive if criteria 1 and 2 + 3 or 4 are reunited. 1- acute change or fluctuating course of mental status 2- inattention 3- altered level of consciousness 4- Disorganized thinking
21	Indicator 26	POST-DURAL PUNCTURE HEADACHE	Headache occurring within 5 days of a lumbar puncture, caused by CSF leakage through the dural puncture. It is usually accompanied by neck stiffness and/or subjective hearing symptoms
22	Indicator 27	MEDICATION ERROR	Unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient. It concerns mistakes in the prescribing, dispensing, storing, preparation and administration of a medicine
23	Indicator 29	HEPATIC FAILURE	Onset of coagulopathy and/or hepatic encephalopathy within 8 weeks of onset of symptoms
24	Indicator 31	UNPLANNED STAY IN ICU	Any admission that was not previously planned in the plan of care
25	Indicator 33	ANAPHYLAXIS	Anaphylaxis is highly likely when any of the following three criteria is fulfilled: Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal

(*continued on next page*)

Table 2 (*continued*)

1	Indicator 1	CARDIAC ARREST	An absence of cardiac rhythm or presence of chaotic rhythm requiring any component of basic or advanced cardiac life support
			tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips–tongue–uvula) And at least one of the following: • Respiratory compromise (e.g., dyspnoea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia) • Reduced BP or associated symptoms of end-organ dysfunction (e.g., hypotonia -collapse-, syncope, incontinence) Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): • Involvement of the skin–mucosal tissue (e.g., generalized hives, itch-flush, swollen lips–tongue–uvula) • Respiratory compromise (e.g., dyspnoea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia) • Reduced BP or associated symptoms (e.g., hypotension-collapse, syncope, incontinence) • Persistent gastrointestinal symptoms (e.g., abdominal pain, vomiting).
26	Indicator 34	MULTIPLE ORGAN FAILURE	Critical illness characterized by reversible physiological abnormalities with the dysfunction of two or more organs that occurs simultaneously leading to longer stays in the ICU and, in severe conditions, results in higher mortality

cTn: Troponin c, ARDS: acute respiratory distress syndrome, CT: Computed tomography, CXR: chest radiography, AKIN: AKIN-network, POCD: post operative cognitive dysfunction, ICU: intensive care unit, BP: blood pressure, CSF: cerebrospinal fluid, ECG: electrocardiogram.

using a similar method (systematic reviews followed by a Delphi process). Some of our final indicators are consistent with those retained by the Step-COMPAC group, such as mortality, admission in the intensive care unit, myocardial infarction, sepsis and septic shock [11–14]. Contrastingly with the step-COMPAC studies, our study aimed on providing a set of indicators with consensual definitions for severe peri-operative complications specifically focused on anaesthesia and not on the global perioperative management of the patient, mixing surgery, and anaesthesia related morbidity, as in the Step-COMPAC group core outcome set. Haller et al. also identified indicators for anaesthesia-related severe morbidity after a systematic review of the literature and a Delphi process, followed by an expert assessment of the validity, reliability, feasibility, and clarity of the indicators [7]. In this study, eight indicators were retained by a panel of clinicians-researchers: surgical site infection, stroke within 30 days of surgery, 30-day mortality after coronary artery bypass grafting, operative mortality, ICU admission within 14 days of surgery, need fort patient readmission to hospital, length of stay. Among these indicators, some were not consensually validated. Moreover, the consensus was weaker than in our study as it required at least 50 % of the experts' agreement. In Haller et al., characteristics of the indicators evaluated by the experts (validity, reliability, feasibility, clarity) were broad concepts without any consensual definition, and not necessarily usable in clinical practice. Finally, two of these eight indicators were related to mortality, and several were dependent of local practices, limiting their external validity. The members of the European Perioperative Clinical Outcome (EPCO) definitions from the ESA-ESICM also proposed a core outcome set for perioperative severe morbidity, but the indicators were selected through discussion and informal consensus between experts [6]. Overall, 22 indicators were identified, including single organ failure outcome and thrombo-embolic event, with severity grading, and composite outcome measures, such as major adverse cardiac events or postoperative pulmonary complications. In the EPCO, most of the indicators were related to both surgery and anaesthesia, or to patient characteristics.

In the current study, the indicators included in the final core outcome set are relevant for practical use as they focus on clinical outcomes in multiple fields of anaesthesia-related morbidity. Another strength of this study is that these indicators are provided with specific headings and precise definitions, also based on a review involving a wide range of surgeries, both urgent and elective, in adult patients of all types (with or without comorbidity). Thus, the external validity of these indicators is high. The indicators provided by the current study are based on pathologies and not on procedures that often depend on local practices. In addition, definitions of indicators have been selected through a Delphi process and are therefore consensual within the experts' group, composed of an international panel of experts of all specialties and of a representative patient. The Delphi process is a standardized process. It has been developed and validated by the University of California and the American Institute of research and development [10]. This process allowed the selection of indicators with a strong consensus, creating an easy-to-use tool, standardizing endpoint measures for trials. Finally, the set of indicators also included morbidity related to regional anaesthesia, which was rarely previously assessed in the above-mentioned studies.

Our study has several limitations. First, the literature search was limited to Medline and to articles in French and English, restricting the screening. However, the objective of the study was to create a first proposition of set of indicators based on literature review, not to be exhaustive. In addition, experts could propose an indicator that was not retrieve in the search. Secondly, although the experts were clearly asked to focus on anaesthesia-related severe morbidity, some indicators could still be related to surgery and/or to patient's comorbidities, in particular mortality, ~~and~~ multiple organ failure, or pulmonary embolism and thrombosis. However, the severity and/or iatrogenicity of these indicators justified their inclusion in the final set, as shown by their definitive selection by the experts at round 1. It also highlights that the extend of anaesthesia involvement is sometimes difficult to established. Third, the panel was predominantly anesthesiologists. A more diverse panel, including data managers, quality and safety experts, patient advocates, and lawyers, could have provided a broader and more balanced perspective on severe morbidity. Fourth, non-severe anaesthesia-related morbidity, such as "shivering and vomiting", was not considered in the core outcome set. We suggest that this morbidity related to anaesthesia deserves a specific set. Finally, we endeavoured to propose indicators independent from local practices, but some of them still depend on local organization (i.e., "transfusion" or "unplanned ICU admission"). These are however classic indicators of quality of care, considered by the experts as necessary to include in the final set, even if they were instructed to avoid event related to practice. It is remarkable that two indicators were not provided with definition: mortality and self-extubation. Indeed, the definition of mortality is universally shared in the medical field; no definition for self-extubation was available in the literature and none of the definitions proposed to the expert's obtained consensus.

In conclusion, this study provides a set of indicators for severe anaesthesia-related morbidity with their specific definitions based on experts' consensus. It provides reproductible and valuable clinical endpoints to evaluate in future trials studying severe anaesthesia-related morbidity. Before implementation, new studies are probably needed to test the feasibility, validity, and consensus among a more general set of

participants.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Contribution of authors

MPB and HB contributed to the conception and design of the research protocol. PG and CC performed the research and wrote the initial draft of the manuscript. All authors participated in the analysis of the results of the review, the answers of the Delphi survey, and the revisions of the manuscript. MPB and HB gave a critical input in the writing of the manuscript. All authors approved the final version of the manuscript. CD coordinated the Delphi survey.

Presentation: This work has been selected for oral presentation during the congress of the French Society of Anaesthesia and Intensive Care, September 20–22, 2023.

List of the expert panel:

Sylvain Ausset, Osama Abou Arab, Dan Benhamou, Matthieu Biais, Alice Blet, Matthieu Boisson, Fanny Bounes, Lionel Bouvet, Sorin J. Brull, Anais Caillard, Aude Carillon, Thomas Clavier, Philippe Cuvillon, Jean-Stéphane David, Marc-Olivier Fischer, Patrice Forget, Denis Frasca, Anne Godier, Sophie Hamada, Ahmed Mohamed Hasanin, Arthur James, Olivier Joannes-Boyau, Eric Kipnis, Kerstin Kolodzie, Ruth Landau-Cahana, Arthur Le Gall, Morgan Le Guen, Mathieu Legrand, Nicolas Mongardon, Armelle Nicolas Robin, Romain Pirracchio, Philippe Richebé, Sacha Rozencwajg, Stephanie Sigaut, Françis Veyckemans, Paul Zetlaoui, Marzena Zielinska.

Patient: Stephen Lee.

CRediT authorship contribution statement

Marie-Pierre Bonnet: Conceptualization, Formal analysis, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Perrine Guckert:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft. **Cécile Boccara:** Data curation, Formal analysis, Investigation, Methodology. **Chafia Daoui:** Data curation, Investigation, Project administration, Software. **Hélène Beloeil:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank the members of the editorial board of the Anaesthesia Critical Care and Pain medicine, the members of the French Society of Anaesthesia and intensive Care (SFAR) research network, and the patient representative who responded in a timely fashion to the Delphi survey.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2024.111626.

References

[1] Chazapis M, Gilhooly D, Smith AF, Myles PS, Haller G, Grocott MPW, et al. Perioperative structure and process quality and safety indicators: a systematic review. Br J Anaesth 2018;120:51–66. https://doi.org/10.1016/j.bja.2017.10.001.
[2] https://www.aqihq.org n.d.
[3] Bothner U, Georgieff M, Schwilk B. Building a large-scale perioperative anaesthesia outcome-tracking database: methodology, implementation, and experiences from one provider within the German quality project. Br J Anaesth 2000;85:271–80. https://doi.org/10.1093/bja/85.2.271.
[4] https://www.npsa.org.uk/. n.d.
[5] Khuri SF, Daley J, Henderson W, Hur K, Demakis J, Aust JB, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA surgical quality improvement program. Ann Surg 1998;228:491–507. https://doi.org/10.1097/00000658-199810000-00006.
[6] Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Pelosi P, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European perioperative clinical outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. Eur J Anaesthesiol 2015;32:88–105. https://doi.org/10.1097/EJA.0000000000000118.
[7] Haller G, Bampoe S, Cook T, Fleisher LA, Grocott MPW, Neuman M, et al. Systematic review and consensus definitions for the standardised endpoints in perioperative medicine initiative: clinical indicators. Br J Anaesth 2019;123:228–37. https://doi.org/10.1016/j.bja.2019.04.041.
[8] Boney O, Moonesinghe SR, Myles PS, Grocott MPW, StEP-COMPAC group. Core outcome measures for perioperative and Anaesthetic care (COMPAC): a modified Delphi process to develop a core outcome set for trials in perioperative care and anaesthesia. Br J Anaesth 2022;128:174–85. https://doi.org/10.1016/j.bja.2021.09.027.
[9] Graham B, Regehr G, Wright JG. Delphi as a method to establish consensus for diagnostic criteria. J Clin Epidemiol 2003;56:1150–6. https://doi.org/10.1016/s0895-4356(03)00211-7.
[10] Campbell SM, Braspenning J, Hutchinson A, Marshall MN. Research methods used in developing and applying quality indicators in primary care. BMJ 2003;326:816–9. https://doi.org/10.1136/bmj.326.7393.816.
[11] Jackson AIR, Boney O, Pearse RM, Kurz A, Cooper DJ, van Klei WA, et al. Systematic reviews and consensus definitions for the standardised endpoints in perioperative medicine (StEP) initiative: mortality, morbidity, and organ failure. Br J Anaesth 2023;130:404–11. https://doi.org/10.1016/j.bja.2022.12.012.
[12] Buggy DJ, Freeman J, Johnson MZ, Leslie K, Riedel B, Sessler DI, et al. Systematic review and consensus definitions for standardised endpoints in perioperative medicine: postoperative cancer outcomes. Br J Anaesth 2018;121:38–44. https://doi.org/10.1016/j.bja.2018.03.020.
[13] Beattie WS, Lalu M, Bocock M, Feng S, Wijeysundera DN, Nagele P, et al. Systematic review and consensus definitions for the standardized endpoints in perioperative medicine (StEP) initiative: cardiovascular outcomes. Br J Anaesth 2021;126:56–66. https://doi.org/10.1016/j.bja.2020.09.023.
[14] Barnes J, Hunter J, Harris S, Shankar-Hari M, Diouf E, Jammer I, et al. Systematic review and consensus definitions for the standardised endpoints in perioperative medicine (StEP) initiative: infection and sepsis. Br J Anaesth 2019;122:500–8. https://doi.org/10.1016/j.bja.2019.01.009.