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GUIDELINES

European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium

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The purpose of this guideline is to present evidence-based and consensus-based recommendations for the prevention and treatment of postoperative delirium. The cornerstones of the guideline are the preoperative identification and handling of patients at risk, adequate intraoperative care, postoperative detection of delirium and management of delirious patients. The scope of this guideline is not to cover ICU delirium. Considering that many medical disciplines are involved in the treatment of surgical patients, a team-based approach should be implemented into daily practice. This guideline is aimed to promote knowledge and education in the preoperative, intraoperative and postoperative setting not only among anaesthesiologists but also among all other healthcare professionals involved in the care of surgical patients.

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Introduction

The European Society of Anaesthesiology (ESA) is committed to develop evidence-based clinical guidelines of high quality. The ESA Guidelines Committee selected the 'Reduction of Postoperative Delirium' as a topic of interest and dedicated a Task Force – established in March 2013 – to cover this matter. The ESA Guidelines Committee chose the members of the Task Force (CDS, CA, GB, FB and RDS) based on their clinical and methodological expertise. The Task Force elected its chairperson, by common consent, at their first telephone conference on 15 March 2013, and the ESA formally confirmed this election during the first constitutional meeting at the European Anaesthesiology Congress in Barcelona on 2 June 2013. Following the first Task Force meeting, members of the Advisory Board were chosen by the Guidelines Committee and the Task Force based on their clinical and methodological expertise in regard to the key questions as agreed by the Task Force in Barcelona in June 2013 (Table 1). The Task Force received its entire financial support from the ESA, without any

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Table 1 Key questions as agreed by the Task Force in Barcelona, June 2013

Key question	Statements
What is postoperative and what is postinterventional delirium	7/7
What is emergence delirium (inadequate emergence)?	7/7
• What are risk factors for POD?	6/8
○ Predisposing (pre-intra-postoperative)	
○ Precipitating (pre-intra-postoperative)	
What measures can be taken to determine the individual risk of patients?	6/8
When should a risk evaluation be performed?	8/8
• Preoperative phase	7/8
○ Which pharmacological interventions can be recommended for which subgroup of patients?	
○ Which medication/actions should be avoided?	
○ Which nonpharmacological interventions can be recommended?	
■ Which supportive strategies are beneficial?	
■ Is the use of checklists/algorithms useful and does it affect incidence, severity or duration of POD?	
• Intraoperative phase	8/8
○ Which pharmacological interventions can be recommended for which subgroup of patients?	
○ Which medication/actions should be avoided?	
○ Which nonpharmacological interventions can be recommended?	
■ Which supportive strategies are beneficial?	
■ How should anaesthesia be conducted to avoid POD?	
• Postoperative phase	8/8
○ Which pharmacological interventions can be recommended for which subgroup of patients?	
■ Which medication/actions should be avoided?	
○ How should pain management be conducted in the postoperative phase to prevent delirium?	
○ Is there evidence for an algorithm (like the Pain-Agitation-Delirium Management on ICUs) that can be applied?	
Which tools should be used to monitor for POD?	8/8
Which tool should be used to monitor postoperative pain?	7/8
When should POD be monitored?	7/8
How often should POD be monitored?	8/8
What are reversible causes of POD?	7/8
How can symptoms be evaluated objectively?	8/8
When should pharmacological interventions be conducted?	8/8
Which pharmacological treatment can be used?	7/7
Where should POD be treated?	7/7
Which nonpharmacological treatment can be conducted?	7/7
■ Geriatric patients	
Are there differences in the management of POD in geriatric patients?	8/8
Is there evidence for a beneficial pre-, peri-, and postoperative treatment algorithm regarding POD?	7/7
How to manage delirium superimposed on a preexisting dementia/cognitive disorder?	8/8

POD, postoperative delirium.

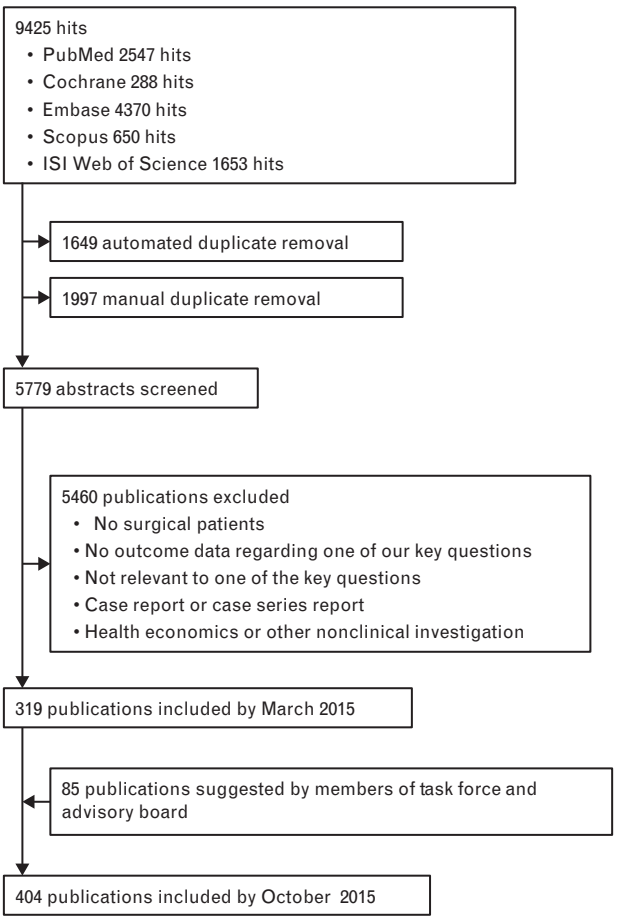
involvement from the healthcare industry. Sub-committees were established to address the questions of interest.

Evidence-based and consensus-based methods

The guideline was designed following the 'Appraisal of Guidelines for Research and Evaluation (AGREE II)'.[1–3]

During its meetings, the Task Force agreed on several key questions (Table 1). To answer these questions and to develop evidence-based recommendations, search strategies included PubMed, Cochrane, Scopus, ISI Web of knowledge and Embase up to March 2015. Afterwards, only selected new published articles in respect of current clinical practice were considered. Search terms were (delirium OR confusion OR confusion* OR disorientation OR bewilderment) AND (postoperative OR postoperative period OR postoperative period* OR post surgical OR postsurgical OR anesthesia recovery period OR anesthesia recovery period* OR postanesthesia). The searches were performed between January 2014 and March 2015. These searches led to 9425 hits. After automated and manual removal of duplicates, 5779 hits were screened for relevance. Relevant articles included existing systematic and narrative reviews, editorials, meta-analyses, randomised controlled trials (RCTs), cohort studies, case–control studies and cross-sectional studies. Case (series) reports were not included but screened for relevant references. We additionally used the 'Cited by xx PubMed Central articles' function in PubMed to identify potentially

Fig. 1



Flow chart of the study selection process.

overlooked but relevant articles. We also screened the reference lists of relevant articles for further publications and included references suggested by the members of the Task Force and the advisory board. Overall, 405 articles were included in the guideline (Fig. 1). Relevant articles were graded according to their level of evidence (LoE) using the Critical Appraisal Worksheets from the Centre for Evidence-Based Medicine of the University of Oxford.[4] The grade of recommendation (GoR) was obtained on the basis of the LoE of the literature (Table 2) and the consensus expert opinions by the majority (≥75%) of the Task Force and the advisory board. Experts had to disclose a conflict of interest before participating in the consensus-based voting on any recommendation. Experts were excluded from voting if a conflict of interest relating to any recommendation was possible. *For all statements, the strength of the recommendation is prefaced by the GRADE phrase 'we recommend' for strong recommendations (GoR A) or by the GRADE phrase 'we suggest' for conditional recommendations (GoR B).*

The final draft of the guideline was peer-reviewed by the relevant sub-committees of the ESA's Scientific Committee. The reviewed draft was made available between 8 October 2015 and 7 November 2015 on the ESA website for critical appraisal by ESA members. The final manuscript of the guideline was approved by the Guidelines Committee and Board of the ESA before publication. The guidelines expire after 5 years unless updated earlier.

Background

Postoperative delirium (POD) is an adverse postoperative complication that can occur in patients of any age, from children to the elderly. Its incidence varies in the various age groups and is substantially influenced by patient-related risk factors that are variably distributed and differentially accumulate in the different age groups. Elderly patients are generally thought to be at higher risk because predisposing risk factors such as cognitive impairment, comorbidity, sensorial deficits, malnutrition, polymedication, impaired functional status and frailty (a condition that can only be observed among aged patients) accumulate and overlap with ageing.

Moreover, POD (refer to the specific definition in the 'Paediatric patients' section) is a common complication in children of pre-school age (5 to 7 years): whether this is due to age-related psychological issues or to additional inflammatory effects on the brain cannot currently be determined. There is a limited number of studies on cognitive outcomes in children.[7] For the USA, the Food and Drug Administration (FDA) recently recommended cautious indications for anaesthesia and surgery in children aged less than 3 years.[8] In Europe, the ESA launched an initiative, the EUROpean Safe Tots Anaesthesia Research (Eurostar) Initiative Task Force to promote translational research on anaesthesia neurotoxicity and long-term outcomes after paediatric anaesthesia and surgery.[9]

In addition, POD is more common in all age groups if precipitating risk factors such as major surgery[10–13] or emergency surgery[14–19] are present. The incidence increases with a high burden of comorbidities presenting as multiorgan dysfunction before surgery, for example low haemoglobin concentration,[20–23] low ejection fraction,[16] carotid artery stenosis,[24] or high serum creatinine concentration.[25–28] POD is associated with several negative clinical consequences, including major postoperative complications, cognitive decline, distress, longer hospitalisation with increased costs and higher mortality.[17,20,29–36] Therefore, prevention of POD should be the aim in all patients; if it cannot be prevented, it is essential to intervene immediately.[29,37–39]

Definition

Delirium is defined by either the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)[40] or by the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD 10, Table 3).[41] Delirium is an acute and fluctuating alteration of mental state of reduced awareness and disturbance of attention. POD often starts in the recovery room and occurs up to 5 days after surgery.[42–44] One investigation[43] found that many patients with POD on the peripheral ward already had POD in the recovery room.

Table 2 From evidence to recommendations (modified from GRADE[5] and The European Council Recommendation[6])

LoE	GoR	Wording of the statements
Level of Evidence (LoE) from the Centre for Evidence-Based Medicine of the University of Oxford	Considered judgement – group decision	
High	A – strong recommendation	We recommend
Data derived from multiple randomised clinical trials or meta-analyses	Evidence and/or general agreement that a given treatment or procedure is beneficial/useful/effective	
Moderate	B – recommendation	We suggest
Data derived from a single randomised clinical trial or large nonrandomised studies	Conflicting evidence and/or a divergence of opinion about the treatment or procedure, however evidence/opinion is in favour of usefulness/efficacy	
Weak	Not considered[a]	
Consensus of opinion of the experts and/or small studies, retrospective studies and registries		

[a] If evidence or general agreement that the given treatment or procedure is not useful/effective or in some cases may even be harmful, the information is included in the manuscript, but no statements are given.

Table 3 Definition of delirium Gold standard according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,[40] or the 10th revision of the International Statistical Classification of Diseases and Related Health Problems[41]

ICD-10 criteria (F05.0) Delirium, not induced by alcohol and other psychoactive drugs and not superimposed on dementia	DSM-5 criteria
An aetiologically nonspecific organic cerebral syndrome characterised by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behaviour, emotion and the sleep–wake schedule. The duration is variable and the degree of severity ranges from mild to very severe	A disturbance in attention (i.e. reduced ability to direct, focus, sustain and shift attention) and awareness (reduced orientation to the environment)
Diagnostic criteria:	The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
A. Clouding of consciousness, that is reduced clarity of awareness of the environment, with reduced ability to focus, sustain or shift attention	An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability or perception
B. Disturbance of cognition, manifest by both:	The disturbances in criteria a and c are not better explained by another preexisting, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma
(1) Impairment of immediate recall and recent memory, with relatively intact remote memory; and	There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies
(2) Disorientation in time, place or person	
C. At least one of the following psychomotor disturbances:	
(1) Rapid, unpredictable shifts from hypoactivity to hyperactivity	
(2) Increased reaction time;	
(3) Increased or decreased flow of speech	
(4) Enhanced startle reaction	
D. Disturbance of sleep or the sleep–wake cycle, manifest by at least one of the following:	
(1) Insomnia, which in severe cases may involve total sleep loss, with or without daytime drowsiness, or reversal of the sleep–wake cycle	
(2) Nocturnal worsening of symptoms	
(3) Disturbing dreams and nightmares which may continue as hallucinations or illusions after awakening	
E. Rapid onset and fluctuations of the symptoms over the course of the day	
F. Objective evidence from history, physical and neurological examination or laboratory tests of an underlying cerebral or systemic disease (other than psychoactive substance–related) that can be presumed to be responsible for the clinical manifestations in A to D	

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ICD-10, 10th revision of the International Statistical Classification of Diseases and Related Health Problems.

Very early onset of POD in the immediate postanaesthesia period before or on arrival at the recovery room is referred to as 'emergence delirium'.[45–49] In children, paediatric emergence delirium (paedED) may present with purposeless agitation with kicking, absence of eye contact with caregivers or parents (with eyes staring or averting), inconsolability and absence of awareness of the surroundings.[50]

Delirium can present as hypoactive (decreased alertness, motor activity and anhedonia), as hyperactive (agitated and combative) or as mixed forms.[51,52] Increased age seems to be a predisposing factor for the hypoactive form.[51,53] The prognosis may be worse with hypoactive delirium, possibly due to relative under-detection by staff and consequently delayed treatment.[51]

Relevance

More than 230 million surgical procedures are performed each year worldwide, of which more than 80 million are in Europe.[54–56] In Europe, the in-hospital mortality rate up to a maximum of 60 days is 3% after elective surgery and nearly 10% after emergency surgery.[55] In addition to mortality, postoperative cognitive impairments such as POD and postoperative cognitive dysfunction (POCD) impose a huge burden on individuals and society.[39]

The incidence of POD is dependent on perioperative and intraoperative risk factors.[57] Therefore, the incidence of POD varies within a broad range.[58,59] For example, a meta-analysis of 26 studies of POD reported an incidence of 4.0 to 53.3% in hip fracture patients and 3.6 to 28.3% in elective patients.[60]

POD, and delirium in general, is often regarded as a temporary attenuation of brain function, usually followed by a full remission. However, strong evidence exists that POD is linked with longer term cognitive and noncognitive morbidity as well as reduced quality of life. It is also associated with increased mortality in the short term and long term. The impact of POD on mortality has been found across different surgical disciplines, in elective and emergency surgery.[17,20,23,24,29,31–33,36,61–71] Only a few

studies, some of them after adjustment for preoperative cognitive status, found no[72–77] or only borderline[78] association between POD and mortality.

There is evidence that POD is associated with deteriorating cognition in both the short term (months) and long term (≥1 year) after its occurrence.[39,79–81] Often referred to as postoperative cognitive dysfunction (POCD), altered cognition has been found shortly after POD in the ICU setting.[82–84] Some investigators have found POD to be associated with POCD up to 12 months postsurgery[30,78,85,86] and even associated with dementia up to 5 years after POD.[68] In addition, POD has been associated with posttraumatic stress disorder 3 months after surgery.[87]

POD increases total hospital length of stay (LOS).[13,15,20,23,31,34,84,88–96] POD on day 1 after surgery is most predictive of hospital LOS.[13] In addition, even POD in the recovery room has been associated with increased total hospital LOS.[13] After discharge, patients with POD have an increased level of care dependency[20,23,30,32,34–36,61,89,92] or limitations in basic activities of daily living up to 12 months.[31]

Because patients can present with both delirium and cognitive impairment before surgery, preoperative evaluation of patients for the presence of delirium and cognitive impairment should be considered. Of note, studies that evaluated delirium on admission, that is before surgery, reported prevalence rates between 4.4 and 35.6%.[92,97–104] Cognitive impairment at any time during surgical stay, including preoperative delirium, was a risk factor in hip fracture patients for poor functional outcome 12 months later.[104] Any cognitive impairment before hospital admission was an independent risk factor for worse longer term cognitive impairment.[104,105]

Risk factors

A widely accepted model of delirium differentiates predisposing factors (that are related to the patient) and precipitating factors (that trigger the onset of delirium).[106] The risk of developing delirium can be seen as the product of predisposing and precipitating factors. Risk assessment is considered as the responsibility of different disciplines and should be implemented in the perioperative clinical pathway.

The evidence-based and consensus statements and their GoR for preoperative, intraoperative and postoperative risk factors for POD are listed in Table 4. As many studies identified advanced age as a risk factor for POD both in univariate and in multivariate analysis, we show the evidence in two columns (all adults vs. elderly ≥65 years of age) according to the inclusion criteria of the cited studies. In the medical literature, elderly patients are often defined as aged at least 65 years.[105] However, chronological age may be an insufficient proxy to capture the complex underlying pathological mechanism leading to increased vulnerability to POD.

In addition to the above statements, emergency surgery[14–19,155] and postoperative complications[156] increase the risk of higher rates and prolonged duration of POD as well as long-term cognitive impairment.[157] Protocols are required to identify these risk factors and to implement risk reduction strategies (e.g. fast track).[105,158,159]

Hypothermia on admission to the recovery room has also been reported to be a risk factor for hypoactive emergence.[49] In addition, preoperative fasting glucose concentrations are associated with more delirium after cardiac surgery.[128,160] Despite existing evidence on biomarkers for the detection and monitoring of POD from both the ICU setting[93,161,162] and the non-ICU setting,[14,116,163–169] their use in clinical routine cannot currently be recommended; further research is required.

Monitoring of postoperative delirium

Early diagnosis of POD is critical to trigger focussed and effective treatment.[29,37–39,79,80] Patients should not leave the recovery room without being screened for POD. Current reference standards for diagnosing delirium, including POD, are the DSM-5[40] or the ICD 10[41] (Table 3). Extensive training is required to use these reference standards.[105] In addition, the new definition of DSM-5 compared with DSM IV-TR decreases the sensitivity to diagnose delirium because the disturbances do not occur in the context of a severely reduced level of arousal.[170,171] However, the DSM-5 guidance notes clarify this, stating that patients with a severely reduced level of arousal (of acute onset) above the level of coma should be considered as having 'severe inattention' and hence as having delirium.[40,172] As this is relevant in the postoperative and ICU setting, it is important that both a sedation/agitation tool such as the Richmond Agitation-Sedation Scale[173] (RASS; Table 5) and a delirium screening tool are used.

A delirium screening system suitable for use in the recovery room should be easily applicable and fast to perform.[44] A high sensitivity (to detect POD as early as possible) may be achieved with two scores – the Nursing Delirium Screening Scale[174] (Nu-DESC) and the Confusion Assessment Method (CAM).[44,176] However, in a recent study, the sensitivities of both of these tests were lower than expected,[177] and it is to be noted that the CAM has a low sensitivity when not used by staff specially trained in its use. In the latter study reporting lower sensitivities despite a high methodological standard, the measurements were performed in a prolonged time frame of 60 min, that is too slow to assess the sudden changes in the recovery room seen in this patient population.[177] The study reporting a higher sensitivity was embedded in an accreditation process in which all team members – nurses and physicians – were educated

Table 4 Evidence-based and consensus-based statements regarding risk factors

Statements	LoE	Age group (inclusion criteria) All adults	Elderly ≥65 years	GoR
We suggest evaluating the following preoperative risk factors for POD				
• Advanced age	[10], 1b; [14], 2b; [17], 4; [18], 2b; [20], 2b; [34], 2b; [35], 2b; [76], 2b; [105], 5	[10,14,17,20, 34,107,108,112, 113,116,118]	[18,35,76,105,111–113, 114,117,119,119]	B
	[107], 2b; [108], 2b			
	[109], 2b; [110], 2b			
	[111], 2b; [112], 2b			
	[113], 2b; [114], 2b			
	[115], 2b; [116], 2b			
	[117], 2b; [118], 2b			
	[119], 2b			
• Comorbidities (e.g. cerebrovascular including stroke, cardiovascular, peripheral vascular diseases, diabetes, anaemia, Parkinson's disease, depression, chronic pain and anxiety disorders)	[17], 4; [20], 2b; [21], 2b; [71], 4; [103], 2b	[17,20,110,112, 121,124,127,128]	[21,103,123,125,126,130,132]	B
	[108], 1b; [112], 2b			
	[121], 2b; [122], 1b			
	[123], 2b; [124], 3b			
	[125], 2b; [126], 4			
	[127], 2b; [128], 2b			
	[130], 1b; [131], 2b			
	[132], 2b			
• The results of comorbidity scores such as the American Society of Anesthesiologists' physical status classification system (ASA-PS) or the Charlson Comorbidity Index (CCI) or the Clinical Impairment Assessment Score (CIAS) before surgery	[28], 2b; [34], 2b; [89], 2b; [96], 4; [122], 4; [133], 2b; [134], 4; [135], 4	[28,34,135]	[89,94,122,133,134]	B
• Preoperative fluid fasting and dehydration	[13], 2b; [112], 2b	[13]	[112], Incl. ≥18 years, obsvd. 66 ± 11 years, range 58 to 72 years	B
• Hyponatraemia or hypernatraemia	[34], 2b; [110], 1b	[34,135,136]	[110], Incl. ≥60 years, obsvd. 75 years	B
	[135], 4; [136], 4			
• Drugs with anticholinergic effects (e.g. measured by an anticholinergic drug scale)	[92], 4; [109], 2b	[137,139,140]	[92,109,113], Incl. ≥50 years, obsvd. 67 ± 9 years; [115,138], Incl. ≥18 years, obsvd. 68 ± 8 years, range 46 to 88 years	B
	[113], 2b; [117], 2b			
	[137], 4; [138], 4			
	[139], 4; [140], 4			
We recommend evaluating alcohol-related disorders (ICD-10)/alcohol use disorders (DSM-5) as a further preoperative risk factor	[20], 2b; [23], 2b; [34], 2b; [71], 4; [105], 5; [116], 2b; [138], 2b; [141], 2b	[20,34,116], Incl. none, mean 63 years, range 24 to 90 years	[23], Incl. ≥50 years, obsvd. 64 ± 9 years, POD+, 69 ± 9 years, POD−, 61 ± 6 years; [71,105,138,141], Incl. ≥18 years, obsvd. 68 ± 8 years, range 46 to 88 years	A
	[142], no full text			
We suggest considering the following intraoperative risk factors for POD				
• Site of surgery (abdominal and cardiothoracic)	[13], 2b; [23], 2b; [34], 2b	[13,34]	[23], Incl. none, obsvd. POD+, 69 years, POD−, 61 years	B
• Intraoperative bleeding	[42], 2b; [128], 2b	[128,143–145]	[42], Incl. none, obsvd. POD+71 years, POD−, 61 years	B
	[143], 2b; [144], 2b			
	[145], 4			
We recommend considering duration of surgery as a further intraoperative risk factor	[16], 2b; [116], 2b	[16,116,136,149]	[147], Incl. ≥60 years, obsvd. 72 years; [148], Incl. >60 years, obsvd. POD+, 76.1 ± 6.1 years, POD−, 69.8 ± 6.0 years; [144], Incl. ≥60 years, obsvd. 72 years	A
	[136], 4; [146], 4			
	[147], 2b; [148], 2b			
	[149], 2b			
We recommend evaluating pain as a postoperative risk factor for POD	[13], 2b; [49], 2b; [93], 2b; [103], 2b; [129], 2b	[13,49]	[93], Incl. ≥60 years, obsvd. 72 years; [103,129,150], Incl. ≥60 years, obsvd. 75 years; [152], Incl. ≥50 years, obsvd. 66 years; [153]; [154]	A
	[150], 4; [151], no full text; [152], 2b; [153], 1b; [154], 2b			

Data presented as reference number, GoR, grade of recommendation (strong = A, conditional = B); LoE, level of evidence; Incl., inclusion criterion; obsvd., observed; POD, postoperative delirium.

Table 5 Richmond Agitation-Sedation Scale to assess sedation depths[169]

+4	Combative	Violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube (tubes) or catheter (catheters); aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious, apprehensive but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert, but has sustained awakening to voice (eye opening and contact for more than or exactly 10 s)
−2	Light sedation	Briefly awakens to voice (eye opening and contact for <10 s)
−3	Moderate sedation	Movement or eye opening to voice (but no eye contact)
−4	Deep sedation	No response to voice but movement or eye opening to physical stimulation
−5	Unrousable	No response to voice or physical stimulation

The usual target/aim of alertness is within the grey rectangle.

before implementing quality indicators for delirium, pain and postoperative nausea and vomiting assessment in the recovery room.[44] More research is needed regarding the optimal tools for detection of delirium in the recovery room.

If POD is detected, patients should not be discharged from the recovery room to the ward without having started aetiology-based and symptom-based treatment.[179] This is because the longer the duration of delirium and the later the treatment is started, the more cognitive decline may be expected.[39,79] On the postoperative ward, POD should be monitored at least once per shift due to the fluctuating course of POD.[175] The evidence-based and consensus-based statements regarding POD monitoring are listed in Table 6.

POD screening is recommended by using standardised rating scales validated for the postoperative setting. The scales usually take less than 1 min to complete. Only those scores that are validated for the recovery room or the peripheral ward with an adequate sensitivity are listed below. Scores validated only for the ICU or other settings are not listed.

For *emergence delirium* immediately after surgery, agitation scales such as the RASS[173] were used in all studies,[47–49,180] whereas the Pediatric Anesthesia Emergence Delirium (PAED) scale (Table 7) was used in children.[181]

In the *recovery room* setting, the following delirium scores have undergone validation against the criteria according to the DSM:

(1) Nu-DESC[44,174,177] reported sensitivity between 32 and 95% and reported specificity up to 87%.[44] If sensitivity in the different recovery room setting is in the lower range, it may be advisable to use a threshold of at least 1 point to increase sensitivity to 80%.[177]
(2) CAM[43,44,105,176] or the CAM-ICU.[178] In a post-anaesthesia care unit (PACU), sensitivity has been reported between 28 and 43%, with a specificity of 98%.[45,177]

In special patient populations, other scores have been used, and diagnostic validity has been assessed. Although, these scores might be applicable and have been validated regarding standards (not necessarily DSM), they have either been assessed in special patient populations or in settings different from the postoperative setting. Some of these scores, such as the Delirium Rating Scale-98[182] or the Memorial Delirium Assessment Scale,[183] might be useful to evaluate postoperative patients, but they might take longer to perform in a busy recovery room setting. Several scores can be used as alternatives: the Bedside Confusion Scale,[184] Clinical Assessment of Confusion,[139] Confusion Rating Scale,[186] the Delirium-O-Meter,[187] Delirium Observation Screening,[188] the delirium symptom interview (DSI),[189] the Neelon and Champagne Confusion Scale[190] or the 4 'A's Test.[191]

In general, the team (including nurses and physicians) should be involved in the choice of which score to use. For routine implementation, it is mandatory to train the team on the basic features of delirium as well as the features of any tools that will be used. This is not only because scores such as CAM require training, whereas the NuDesc does not, but also because the team needs to have a common understanding of delirium and to be able to communicate consistently on the results of tools used.[105,192]

Table 6 Evidence-based and consensus-based statements regarding monitoring of postoperative delirium

Statements	LoE	Age group (inclusion criteria)		GoR
		All adults	≥65 years	
We recommend screening for POD in all patients starting in the recovery room and in each shift up to postoperative day 5	[42], 2b; [44], 2b; [178], 2b	[44,178]	[42]	A
We recommend using a validated delirium score for POD screening	[44], 2b; [172], 2b	[44,172,178]	[175]	A
	[175], 2b; [178], 2b			

Data presented as reference number, GoR, grade of recommendation (strong = A, conditional = B); LoE. LoE, level of evidence; POD, postoperative delirium.

Table 7 The Pediatric Anesthesia Emergence Delirium scale[179]

Item	
1	The child makes eye contact with the caregiver
2	The child's actions are purposeful
3	The child is aware of his/her surroundings
4	The child is restless
5	The child is inconsolable

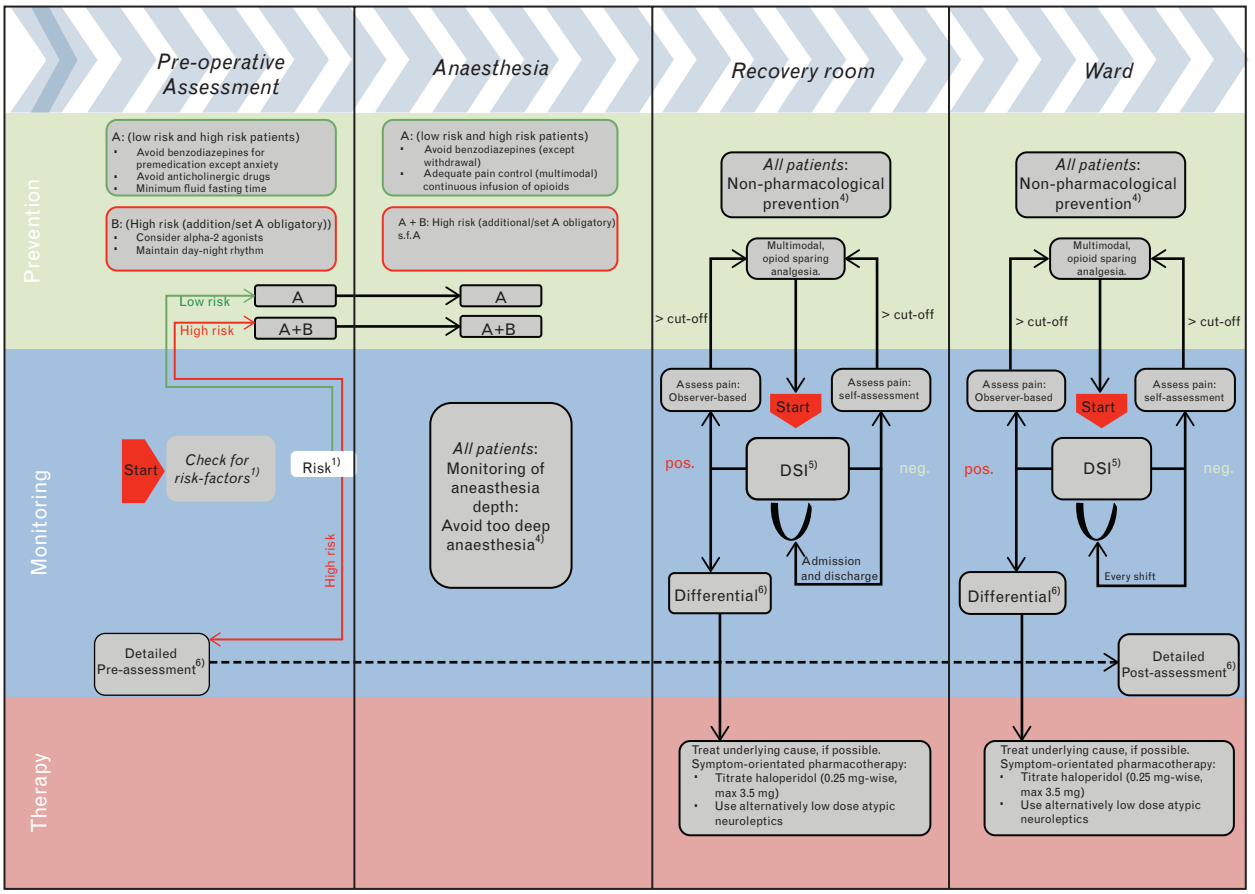
Items 1, 2 and 3 are reverse scored as follows: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Items 4 and 5 are scored as follows: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely. The scores of each item were summed to obtain a total Pediatric Anesthesia Emergence Delirium scale score. The degree of emergence delirium increased directly with the total score.

In addition, it is important to note that not all scores are available in different languages. Therefore, national societies might consider validating the scores in the language in which it is to be applied.

Prevention and treatment

Prevention and treatment options are available to reduce the incidence and duration of POD. If POD occurs, immediate treatment of both causative factors and symptoms has a major impact in reducing its duration[29,37–39] (Fig. 2). The evidence-based and consensus-based statements regarding prevention and treatment are listed in Table 8.

Fig. 2



Algorithm for pre-operative, intra-operative and post-operative management of post-operative delirium in adult patients. The algorithm shows the different time stages of surgery (left to right) and, in a different axis, preventive (top), diagnostic (middle) and therapeutically (lower) actions that should be taken. The red 'start button' helps the user to start at the first step in the different time stages. (1) Risk estimation (clinical assessment taking into consideration predisposing and precipitating risk factors); risk factors can be found in detail in the guideline recommendation, determination of risk into a high and a low-risk group can be made as a clinical decision (2) Neuromonitoring (EEG/EMG-based) recommended if available; (3) DSI, Delirium Screening Instrument (should be validated in the applied language); (4) nonpharmacological measures to reduce postoperative delirium should include orientation (clock, communication, etc.); visual/hearing aids; noise reduction and facilitation of sleep; avoidance of useless indwelling catheters; early mobilisation; early nutrition; pharmacological treatment should be instituted to improve patient safety if nonpharmacological measures fail; (5) differential includes the assessment and possible modification of underlying causes for delirium: use, for example, the 'I WATCH DEATH'-acronym: Infectious (e.g. UTI and pneumonia); Withdrawal (e.g. alcohol, opioids and benzodiazepines); Acute metabolic disorder (electrolyte imbalance and renal dysfunction); trauma (operative trauma); CNS pathology (e.g. stroke and perfusion); hypoxia (e.g. anaemia, cardiac failure and pulmonary failure); deficiencies (e.g. vitamin B 12, folic acid and thiamine); endocrine pathologies (e.g. T3/T4 and glucose); acute vascular (e.g. hyper-/hypotension); toxins (e.g. anaesthetics, drugs with anticholinergic side-effects); heavy metals (rare cause); (6) detailed pre/post-surgical assessment of cognitive function with validated tools. EEG, Electroencephalograph; EMG, Electromyography; UTI, urinary tract infection; CNS, central nervous system.

Table 8 Evidence-based and consensus-based statements regarding prevention and treatment

Statement	LoE	Age group (inclusion criteria)		GoR
		All adults	≥65 years	
We suggest implementing fast-track surgery to prevent POD	[158], 1b; [159], 2b; [193], 2b; [193], 2b	[159,193]	[158,194]	B
We suggest avoiding routine premedication with benzodiazepines except for patients with severe anxiety	[10], 2b; [105], 5; [195], 2b; [196], 3b; [197], NR; [198], 2b; [204], 2b		[10], Incl. none, POD+, 67.7 years, POD−, 50 years; [105,195,196], >60% were ≥65 years; [197]; [199] mean age 66.8 years and range 43–87 years	B
We recommend monitoring depth of anaesthesia	[105], 5; [199], 1b; [200], 1b; [201], 1b; [202], 1b	[199–201]	[105,202]	A
We recommend adequate pain assessment and treatment	[103], 2b; [153], 1b; [197], NR; [203], 4; [205], 2b; [206], (SR)	[202]	[103,153,197,199,205]	A
We suggest using a continuous intraoperative analgesia regimen (e.g. with remifentanil)	[13], 2b; [207], 2b	[13,207]		B
We recommend promptly diagnosing POD, establishing a differential diagnosis, and instituting treatment	[37], 2b; [38], 2b; [179], 2b; [208], Consensus review	[37]	[38,179,208]	A
We suggest using low-dose haloperidol[a] or low-dose atypical neuroleptics to treat POD	[208], 5; [209], SR; [210], 2b; [211], 2b	[208,209]	[211,212]	B

Data presented as reference number, LoE. Incl. inclusion criteria; obsvd., observed; LoE, level of evidence; GoR, grade of recommendation (strong = A, conditional = B); POD, postoperative delirium. [a] Low-dose haloperidol means 0.25 mg stepwise titrated up to maximum of 3.5 mg.[213] An excessive dose of haloperidol of more than 6 mg a day should not be used.[214] Long-term use in dementia patients may increase harm.[215]

Pharmacological premedication (in particular benzodiazepines) is not always needed, and its routine use has been questioned.[208] However, for highly anxious patients or patients with alcohol or benzodiazepine use disorders, careful use of premedication for prevention and treatment can be considered.[107,216,217]

Prevention of POD in patients with alcohol use disorders (e.g. measured by the Alcohol Use Disorders Identification Test ≥8 points) may include long-acting benzodiazepines, neuroleptics, α_2-agonists and alcohol.[218] In the subset of patients with alcohol withdrawal-induced delirium, benzodiazepines should be one of the first-line medications.[105] As second-line medication, α_2-agonists or neuroleptics can be used. For emergence delirium, benzodiazepines might be a precipitating factor,[48,107,219] although this remains controversial.[180]

Data on melatonin for premedication on the evening before surgery are insufficient to draw final conclusions, and currently no clear recommendation can be given.[220–223] Perioperative α_2-agonists, for example dexmedetomidine or clonidine, might be considered to decrease the incidence of POD after cardiac or vascular surgery.[224–228]

There are conflicting results regarding the incidence and severity of POD through prophylactic administration of haloperidol[35,229–231] or atypical neuroleptics.[122,232–234] Although there is some evidence that preventive low-dose haloperidol[35,229–231] or preventive low-dose atypical neuroleptics[122,233,234] reduce the incidence of POD[231] or reduce its severity and duration,[229] these findings remain uncertain due to inconsistent results of aggregated evidence.[232,235] Therefore, their routine use is currently not advisable.

It remains unclear whether different regimens of anaesthesia influence the development of POD. Cohort studies, retrospective or secondary analyses[185,236,237] and RCTs[88,126,238–242] have shown mixed results and do not imply a role in adults. However, an important factor in managing POD is adequate stress reduction with sufficient analgesia, an appropriate choice of analgesia and the use of intraoperative opioids.[13,180] Currently, it remains unclear if intraoperative administration of short-acting analgesia impacts on POD. Some observational data are available suggesting that analgesia provided with continuous administration of remifentanil might reduce the incidence of POD compared with a bolus-driven regimen with fentanyl,[207] but to draw convincing conclusions, evidence from RCTs is required.

To standardise the assessment and treatment of postoperative pain, we refer to the American Society of Anesthesiologists' guideline on acute pain management in the perioperative setting.[243] Although high preoperative[129] and postoperative pain[244] are risk factors for delirium, opioid analgesics may also be a risk factor in respect of side effects and organ dysfunction.[115,180,197,245,246] Patient-controlled analgesia (PCA)

could be one option if the patient is able to titrate the medication and find the right balance between analgesia and the minimum dose of opioids.[247] POD does not limit PCA use.[247] Regional anaesthesia and regional analgesia have not shown any benefit in respect of POD.[248]

A healing environment should be considered for the prevention of POD. Apart from the consensual statements on nonpharmacological treatment, this should be embedded in an environment for cognitive,[249] functional, social and emotional enhancement.[250] Further research is required to optimise the use of self-healing competencies of patients.

Special patient groups

Geriatric patients

A 'threshold theory of cognitive decline' was postulated to explain a situation of diminished brain reserve capacity occurring in older age, the genesis of which coincides with the degenerative phenomena occurring with ageing.[251] Due to this reduced brain capacity, older patients are on a 'functional cliff' for developing POD when undergoing a major physiological stress.

In Europe, the percentage of people aged at least 65 years currently ranges from 12% in 'young' countries such as Ireland to 21% in 'old' countries such as Germany and Italy.[252] With the passage of time, this will have a major impact on the demand for healthcare services, especially surgery. There are higher rates per population of both inpatient and outpatient surgical and nonsurgical procedures among the elderly compared with other age groups.[253] Patients older than 80 years are the most rapidly increasing group among surgical admissions.[254] In Italy, 38% of patients who undergo surgery are at least 65 years old.[255] In the USA, approximately half of operations are performed in patients aged at least 65 years.[254,256] Thus, the demand for surgery by older and sicker patients is increasing,[257] and POD is regarded as a major problem.

Risk factors and preoperative evaluation

Ageing involves a continuum of changes in biological and functional parameters that increase vulnerability and reduce functional reserve.[258] Ageing is often accompanied by chronic multiple diseases, disability and frailty.

Although chronological age plays a role in predisposing to POD, it probably acts as a surrogate variable for the accumulation of age-related risk factors that are differentially expressed among individuals; it is almost certainly the sum of these risk factors that is most important in determining the probability of POD.

Dementia is a main predisposing factor for POD. This condition is very rare among patients under 60 years of age and becomes increasingly frequent as age increases. Data provided by the WHO for Western Europe report a prevalence of 1.6% in patients aged 60 to 64 years and up to 43.1% in patients older than 90 years.[259] Previous dementia,[23,67,146] cognitive impairment[11,12,15,18,34,71,90,93,108–110,113,115,116,125,169,260,261] and depression[20,22,71,91,110,112,123,143] are associated with development of POD.

Other chronic diseases are often reported to be present in more than 50% of patients aged 65 to 70 years. In 30% of these patients, more than one single chronic disease is present. Cardiovascular[14,16,17,24,28,77,95,103,125,127,148,260,262] and metabolic[15,34,131,135,136] risk factors/diseases were found to be most frequently associated with POD.

Multimorbidity consists of a situation in which clinical patterns, evolution and treatment become more complicated than the simple sum of the different illnesses. Multimorbidity reduces the capability to cope with stress and increases global vulnerability – including the risk for POD.[257,263] Functional status, also called the sixth vital sign, is defined as the sum of behaviours that are needed to maintain daily activities, including social and cognitive functions.[264] Impaired functional status (i.e. reduced levels of independence, abilities and socialisation) is common among the elderly as a result of gait alteration, loss of coordination, reduced or abolished sphincter control, malnutrition, associated illnesses and/or cognitive deterioration. Impaired functional status is associated with surgical site infection, increased mortality and complication rate. In the preoperative setting, performance measures such as the timed 'Up & Go' Test[265] and other forms of Comprehensive Geriatric Assessment[266] have often been used. Impaired functional status has been reported as a predisposing factor for POD.[23,34,89,169,267–271]

The term 'frailty' indicates a situation of critically reduced functional reserves, involving multiple organ systems. It manifests with impaired capability to cope with intrinsic and environmental stressors and limited capability to maintain physiological and psychosocial homeostasis. Currently, 5.8 to 27.3% of the elderly (≥65 years of age) in the general European population are reported to be frail.[272] However, studies examining older patients undergoing elective cardiac and noncardiac surgery quote prevalences of frailty between 41.8 and 50.3%[273,274]; this highlights the great vulnerability of this patient age group. Hypoalbuminaemia, hypocholesterolaemia and high levels of inflammation together with muscular atrophy are specific markers. Frailty has been found to be a predisposing factor for POD among elderly surgical patients.[75,123,133,275]

Hearing loss was found to be a predisposing factor for POD in three studies[276–278] and mentioned in three reviews[58,270,279]; the last two of these reviews and one additional study on internal medicine patients[120]

additionally mention visual impairment as a risk factor for POD.

Malnutrition affects 2 to 16% of community-dwelling elderly[280] and is frequently undiagnosed in those living at home. Between 20 and 65% of these patients suffer from nutritional deficits.[281,282] The main nutritional deficits concern proteins, minerals and vitamins. The most widely used test to diagnose malnutrition is the Mini-Nutritional Assessment[283] that can be performed at the bedside using a questionnaire. Malnutrition including low serum albumin concentration and/or homeostatic alterations and dehydration have been found to be associated with POD.[112,117,122,132,148,267,284,285]

Preoperative alcohol use disorders are seen in many elderly patients.[286] Many reports indicate that the number of older persons abusing alcohol is increasing in Europe.[287–289] Due to age-related changes, they present increased sensitivity and reduced tolerance to alcohol. POD has been reported as increased in elderly patients with a history of alcohol use disorders.[20,34,71,116,138,141,142]

Other preoperative variables that can influence the level of stress include the admission setting (emergency vs. nonemergency and inpatient vs. outpatient) and the adoption of dedicated perioperative strategies (prehabilitation,[290] fast-track vs. traditional strategy, admission to surgical wards vs. dedicated units). The consensus-based statements regarding risk factors of POD in elderly surgical patients are listed in Table 9.

Intraoperative and postoperative management

Intraoperative neuromonitoring is important to avoid unnecessarily deep anaesthesia,[203–206] often reaching burst suppression in elderly patients.[294] In addition, inflammatory responses due to surgical trauma might be much more relevant for systemic organ dysfunction, including the brain, after surgery. Recently, it was shown that increased blood pressure fluctuation, not absolute or relative hypotension, was predictive of POD in elderly patients after noncardiac surgery.[295] If acute fluid replacement is required, cardiac function,[296] in particular atrial fibrillation,[297–299] should be the focus in respect of perfusion of the brain and all other organs.

Postoperatively, geriatric patients require immediate treatment of POD in the recovery room and on the peripheral ward because of their more vulnerable brain. Additional complications such as respiratory depression and hypoxia (e.g. due to analgesic requirements) should be avoided, and treated if necessary, despite the fact that it remains unclear whether postoperative hypoxia is an independent predictor of POD.[22,267]

POD and cognitive decline are seen more often after surgery and lead to a higher level of care dependency.[36,260] Therefore, monitoring with validated scales (see above) is recommended to detect POD as early as possible. Besides, previous studies evaluating spontaneous eye movements, particularly blinks that appear to be affected in delirious patients, hold promise for delirium detection.[300] In addition, EEG (electroencephalography) monitoring, using the relative δ-power from an eyes-closed EEG recording with two electrodes in a frontal–parietal lead, can distinguish between postoperative cardiac surgery patients who developed POD (mean age 77 years) and those who did not (mean age 74 years).[301]

In patients with dementia, a variety of instruments is available for the measurement of pain, including the Faces Pain Scale and other instruments such as the Pain Assessment in Advanced Dementia Scale[302] or the Non-Communicative Patient's Pain Assessment Instrument.[303] An overview of validated instruments is given by Hadjistavropoulos *et al.*[304] Apart from pain, opioids are also associated with an increased risk of POD[89,245,305,306] and require close monitoring of POD.[180,197,246]

In the elderly, nonpharmacological measures are reported to reduce the incidences of POD and falls.[307–309] Further research should evaluate different multi-component programmes to select the most useful interventions. The consensus-based statement regarding prevention and treatment of POD in elderly surgical patients is listed in Table 10.

Organisational issues

POD is an expensive complication and multi-component interventions can reduce acute and long-term nursing home costs.[312–314] Sufficient evidence supports the idea that organisational measures such as dedicated pathways are preventive.[312] However, dedicated geriatric units aimed to promote co-management and a team-based approach are only (and rarely) present in academic hospitals. In many other small or intermediate hospitals, they are not at hand. In these hospitals, anaesthesiologists and surgeons share the responsibility to establish adequate organisational solutions. Increasing evidence exists that outcomes in geriatric surgery are highly dependent on the level of care that elderly patients receive perioperatively.[315] Both the American Geriatric Association Guidelines on POD[316] and the American College of Surgeons/National Surgical Quality Improvement Program Guidelines[317] emphasise the importance of dedicated pathways as a means to improve quality of care in geriatric surgery. The most important dedicated models of care are Geriatric Consultation Services,[318–321] Acute Care for the Elderly Units[322,323] and co-management based models (Orthogeriatric Units and/or Geriatric Consultation Services).[324,325] These structures were conceived with the aim of reducing complication rates and mortality in geriatric surgery, especially after hip fracture. Team-based approaches, quality of care and, in some cases, hospital design are basic elements. The introduction of proactive multidisciplinary geriatric interventions in

Table 9 Evidence-based and consensus-based statements regarding risk factors in elderly surgical patients

Statements	LoE	Age group (inclusion criteria) All adults	Age group (inclusion criteria) Elderly ≥65 years	GoR
We recommend evaluating the following preoperative risk factors for POD				
• Cognitive impairment	[11], 2b; [12], 2b; [15][15], 2b; [18], 2b; [34], 4; [59], SR		[11,12,15,18,34,71,90,93,105,108], Incl. ≥60 years, obsvd. 74 years; [109,110], Incl. ≥60 years, obsvd. 75 years; [113], Incl. ≥50 years, obsvd. 67 ± 9 years; [115,125], Incl. ≥60 years, obsvd. 72 years; [134,147], Incl. ≥60 years, obsvd. 72 years; [150], Incl. ≥60 years, obsvd. 75 years; [169,260], Incl. ≥60 years, obsvd. 72 (IQR 66 to 77) years; [132,261,291,293]	A
	[71], SR; [90], 4			
	[93], 2b; [105], 5; [108], 4; [109], 2b; [110], 2b; [113], 2b; [115], 2b; [125], 2b; [134], 4; [147], 4; [150], 4; [170], 4; [260], 2b; [261], 2b; [279], SR; [291], 2b; [292], SR; [293], 4			
• Reduced functional status and/or frailty	[23], 2b; [34], 4		[23,34,89,105,113,123,133, 169,267,268,271,275]	A
	[89], 4; [105], 5; [113], 2b; [123], 2b; [133], 2b; [169], 4; [267], 2b; [268], 2b; [269], SR; [270], SR; [271], 2b; [275], 2b			
• Malnutrition (low serum albumin)	[112], 2b; [117], 2b; [122], 2b; [132], 2b; [267], 2b; [284], 2b		[112], No incl. criterion, obsvd. median age 66 (range 58 to 72) years; [117,122,267,284], No incl. criterion, obsvd. POD+, 69.9 years, POD−, 67.4 years; [132], Incl. ≥60 years, obsvd. 74 years	A
• Sensory impairment	[270], SR; [276], 4; [277] SR; [278], 4; [279], NR		[276], No incl. criterion, obsvd. POD+, 67.4 years, POD−, 66.0 years; [278], Incl. ≥50 years, obsvd. 69.8 (range 53 to 84) years	A

Data presented as reference number, LoE. GoR, grade of recommendation (strong = A, conditional = B); Incl., inclusion criterion; IQR, interquartile range; LoE, level of evidence; NR, narrative review; obsvd., observed; POD, postoperative delirium; SR, systematic review.

elderly patients with acute hip surgery has been followed by a significant reduction in the incidence of POD.[242,326–332]

Paediatric patients

Delirium after anaesthesia in children is reported often. The majority of reported paediatric cases focus on emergence delirium (paedED) in the recovery room with a wide range of incidence from 2 to 80%.[50,181,333] PaedED is based on the theoretical framework of delirium defined by DSM.[40] PaedED was defined as a disturbance in a child's awareness of and attention to his or her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behaviour in the immediate postanaesthesia period.[181,334] The term 'emergence agitation' should not be used interchangeably with paedED because agitation is excessive motor activity, is more common than paedED in the postoperative period and is associated with discomfort, pain or anxiety.[335] The majority of children who develop paedED do so in the recovery room/PACU.[50,181,334,335] Research on paedED in peripheral wards is warranted.

For paediatric patients, risk factors for development of paedED should be considered, monitoring for paedED should be established and preventive and treatment measures should be taken to decrease the incidence of paedED. The evidence-based and consensus-based statements are listed in Table 11.

In addition to the Task Force's recommendations, there are several relevant topics of interest with regard to paedED. These topics need to be discussed and several of them warrant further studies.

Predisposing factors

Children with low adaptability to new situations seem more prone to develop paedED.[343] Other influences on emotional stress such as the temperament of the child or the anxiety of parents/guardians might have an influence on paedED.[352,383–385] The risk of recurrence of paedED after repetitive procedures is unclear. Research should be undertaken to identify preoperative (psychological, social and medical) risk factors for paedED to help the anaesthesiologist adapt preoperative preparation, whether psychological or pharmacological, to the child's needs.

Table 10 Evidence-based and consensus-based statements regarding prevention and treatment in elderly patients

Statement	LoE	Age group (inclusion criteria)		GoR
		All adults	≥65 years	
We suggest implementing nonpharmacological measures to reduce POD: orientation (clock, communication, etc.), visual/hearing aids, noise reduction and maintenance of a day/night rhythm avoidance of unnecessary indwelling catheters, early mobilisation and early nutrition[a]	[105], 5; [248], SR; [309], SR; [310], 4; [311], 4		[105,310,311]	B

Data presented as reference number, LoE. GoR, grade of recommendation (conditional = B); LoE, level of evidence; POD, postoperative delirium. [a] For example, implementation recommended in geriatric and/or fast-track surgical protocols.[105,159,208]

Premedication

Premedication with midazolam reduces paedED after sevoflurane anaesthesia.[361,362,364–366] However, different durations of procedures and different methods used to assess paedED make it difficult to provide a conclusion regarding the influence of midazolam on paedED.[363,367] Melatonin might be superior to midazolam to decrease the risk of paedED but it does not reduce anxiety.[386,387] Availability of melatonin differs widely among European countries. It is either an 'over the counter' drug or has to be prescribed.

Premedication with or intraoperative use of α_2-agonists (dexmedetomidine[372–374] or clonidine[50]) decreases the incidence of paedED.[50,359,375–378] In a recent double-blind RCT, preoperative intranasal dexmedetomidine was more effective than clonidine in decreasing the incidence and severity of emergence agitation and also

Table 11 Evidence-based and consensus-based statements regarding paediatric patients

Statements		LoE	GoR
Risk factors	We recommend considering pre-school age as a risk factor for paediatric emergence delirium (paedED)	[336], 4; [337], 1b; [338], 1b; [339], 2b; [340], SR; [341], 1b; [342], 1b; [343], 2b	A
	We suggest not considering sex as a risk factor for paedED	[344], 1b; [345], 2b; [346], 1b; [347], 2b; [348], 2b	B
	We suggest considering ENT surgery as a risk factor for paedED	[336], 4; [343], 2b	B
	We recommend evaluating pain as a risk factor for paedED	[333], SR & MA	A
		[348], 1b; [349], 2b; [350], 2b	
Monitoring	We suggest assessing anxiety by a validated score	[337], 2b; [342], 1b; [343], 2b; [344], 2b; [351], 2b; [352], 1b; [353], 2b; [354], 1b	B
	We recommend treating pain according to a validated age-adapted scale	[181], 1b; [355], 2b; [356], 2b	A
	We recommend assessing paedED using an age-adapted validated tool	[340], SR; [357], 2b; [358], 2b	A
	We recommend assessing pain at the same time as paedED	[181], 1b; [355], 2b	A
Prevention and treatment	We suggest implementing the ADVANCE[a] strategy of cognitive preparation for surgery, this is considered superior to premedication with midazolam for the reduction of paedED incidence	[352], 1b; [359], MA; [360], 2b	B
	We suggest using midazolam to reduce preoperative anxiety in children	[339], 2b; [361], 1b; [362], 1b; [363], 1b; [364], 1b; [365], 1b; [366], NR; [367], 1b	B
	We suggest implementing nonpharmacological strategies included in the treatment of paedED to calm the patient and limit harm	[352], 1b; [359], MA; [360], 2b	B
	We suggest balancing the use of short acting volatile anaesthetics (Sevoflurane/Desflurane > Isoflurane) against their risk for paedED.	[345], 1b; [349], 2b; [368], 1b; [369], MA; [370], 1b; [371], 1b	B
	We suggest using α_2-agonists (clonidine and dexmedetomidine) intravenously, intranasally or epidurally to reduce the risk of paedED	[382], 1b; [373], MA; [374], MA; [375], 1b; [376], 1b; [377], 1b; [378], SR & MA	B
		[379], 1b	
	We suggest using propofol as a bolus on emergence to decrease paedED	[380], 1b	B
	We suggest using preventive analgesia, e.g. caudal, fascia iliaca block, to reduce paedED	[354], 1b; [381], 2b; [382], 1b	B

Data presented as reference number, LoE. GoR, grade of recommendation (strong = A; conditional = B); LoE, level of evidence; MA, meta-analysis; NR, narrative review; paedED, paediatric anaesthesia emergence delirium; SR, systematic review. [a] The ADVANCE strategy describes a family-centred preparation programme for children. The acronym stands for Anxiety-reduction, Distraction, Video-modelling and education, Adding parents, No excessive reassurance, Coaching and Exposure/shaping.[352]

decreased fentanyl consumption after surgery.[379] More recently, in small series, premedication with gabapentin,[388] premedication with ketamine,[389] intraoperative dexamethasone[390] or magnesium[391] were also found to decrease paedED.

Neuromonitoring

Continuous EEG monitoring might help to distinguish between patients who will or will not develop paedED. Increased frontal lobe cortical functional connectivity observed in paedED, immediately after the termination of sevoflurane anaesthesia, might have important implications for the development of methods to predict paedED.[392]

Anaesthesia

For short-term procedures, propofol is considered to be well tolerated in children. The best model to provide total intravenous anaesthesia in small children seems to be the model designed by Short for adults.[393] One should always bear in mind the small risk of developing a propofol infusion syndrome (PRIS), the pathophysiology of which is complex and may involve mitochondria.[394] The risk of PRIS seems to be reduced if propofol can be titrated to $4\,mg\,kg^{-1}\,h^{-1}$ and is used for a short duration (<48 h)[395] and if IV glucose is provided ($6\,mg\,kg^{-1}\,min^{-1}$) to avoid lipid catabolism.[396]

Common side effects of using a continuous infusion of propofol for 60 min in small children are reversible increases in plasma lipid, triglyceride and pancreatic enzymes concentrations.[397] Propofol infusions appear to be well tolerated when limiting doses to $4\,mg\,kg^{-1}\,h^{-1}$ −1 for less than 24 h.[398]

Postoperative pain

Acute perioperative pain in infants and children is still often undertreated.[399,400] Three of the most commonly performed surgical procedures in children (tonsillectomy, appendicectomy and orchidopexy) are more painful than usually expected. Up to 44% of children still suffer from severe pain until day 3, and up to 30% until day 7 after surgery.[401] Several analgesic techniques, such as regional anaesthesia (caudal block[354,381] and fascia iliaca compartment block[349,402]) or pharmacological interventions (fentanyl[350,382] or nalbuphine[351,403,404]) are available and seem to reduce the incidence of paedED.

Implementation

Strategies to reduce the risk of paedED require a protocol to facilitate implementation. Figure 3 presents a condensed version of the statements. This figure can be used to integrate evidence-based recommendations into local standards to fulfil the requirements of the best practice care of the hospital.

Conclusion

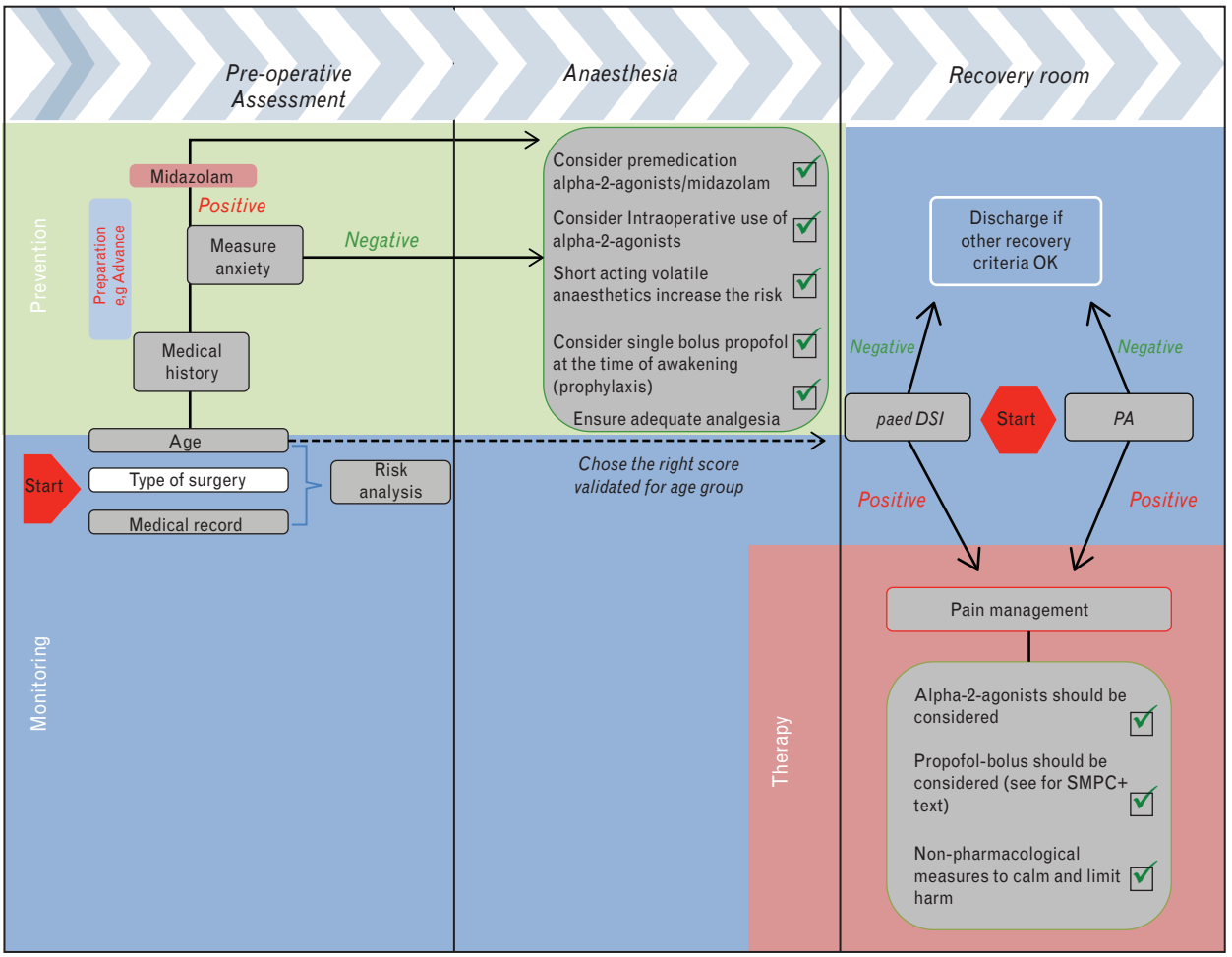
POD is a frequent complication and requires preventive measures as well as immediate and adequate treatment. Although numerous studies have documented the clinical and economic consequences of POD, systematic interventions aimed to reduce its incidence and duration are rarely implemented. Currently, care is not sufficiently focussed on the patient's safety with the aim of reducing long-term harms such as cognitive dysfunction and post-traumatic stress disorder, which can impair quality of life. Despite the huge costs of POD and its preventability, it receives little attention in terms of resource allocation from hospital administrators and healthcare institutional governance representatives. To date, no nation-based strategies have been applied in Europe to minimise POD or monitor its incidence. However, process control has become a key issue for success in many healthcare organisations.

Given the enormous burden exerted by POD on patients, their families, healthcare organisations and public resources, anaesthesiologists operating in Europe should engage to make efforts in designing integrated actions aimed to reduce the incidence and duration of POD. These efforts will become effective when conceived through a team-based multi-component approach. Single items reported may not gain sufficient power alone to ensure effective results. A collaborative path with all the suggested measures to improve the 'quality chain' is highly warranted. The main steps include

(1) preoperative evaluation of POD risk and identification of patients at risk
(2) communication about this risk to patients, their family and care team members
(3) best possible preoperative conditions to be achieved
(4) perioperative avoidance of use of anticholinergic agents and benzodiazepines except when needed. Benzodiazepines can be considered in cases of alcohol withdrawal
(5) attempts to reduce surgical stress, together with organ-protective intraoperative management, including neuromonitoring to avoid excessively deep anaesthesia
    (a) effective multimodal opioid-sparing analgesia
    (b) implementation of enhanced recovery programmes
(6) cognitive monitoring to be aimed at recognition of preoperative cognitive decline and to detect POD as early as possible, including in the recovery room
(7) effective treatment of POD by protocols
(8) follow-up of POD patients all along their hospital stay
(9) patient information on adequate medical support, to ensure continuity of care after discharge.

Patient organisations, politicians and decision-makers for resource allocation and quality assurance, as well as

Fig. 3



1) paedDSI paediatric delirium screening tool, validated for certain age group
2) PA pain assessments tool
3) ADVANCE strategy for cognitive preparation for surgery

Algorithm for pre-operative, intra-operative and post-operative management of postoperative delirium in children. The algorithm shows the different time stages of surgery (left to right) and, in a different axis, preventive (top), diagnostic (middle) and therapeutically (lower) actions that should be taken. The red 'start button' helps the user to start at the first step in the different time stages.

healthcare institutional representatives, should consider reduction of POD as a main goal of their activity for the benefit of the community.

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