Postoperative delirium – treatment and prevention

Thomas Duning[a], *Katharina Ilting-Reuke*[a], *Mara Beckhuis*[a], *and Daniel Oswald*[b]

Purpose of review
Postoperative delirium (POD) is one of the most severe complications after surgery. The consequences are dramatic: longer hospitalization, a doubling of mortality and almost all cases develop permanent, yet subtle, cognitive deficits specific to everyday life. Actually, no global guideline with standardized concepts of management exists. Advances in prevention, diagnosis and treatment can improve recognition and risk stratification of delirium and its consequences.

Recent findings
Management of POD is a multiprofessional approach and consists of different parts: First, the detection of high-risk patients with a validated tool, preventive nonpharmacological concepts and an intraoperative anesthetic management plan that is individualized to the older patient (e.g. avoiding large swings in blood pressure, vigilance in maintaining normothermia, ensuring adequate analgesia and monitoring of anesthetic depth). In addition to preventive standards, treatment and diagnostic concepts must also be available, both pharmaceutical and nonpharmacological.

Summary
Not every POD can be prevented. It is important to detect patients with high risk for POD and have standardized concepts of management. The most important predisposing risk factors are a higher age, preexisting cognitive deficits, multimorbidity and an associated prodelirious polypharmacy. In view of demographic change, the implementation of multidisciplinary approaches to pharmacological and nonpharmacological POD management is highly recommended.

Keywords
nonpharmacological, pharmacological, postoperative delirium, prevention, treatment

INTRODUCTION

Postoperative delirium (POD) is a common and severe but potentially preventable condition in older individuals. Often known as geriatric syndrome, POD can also occur in younger patients. Even today, the medical and economic consequences of delirium are often underestimated. Especially in older patients, POD is associated with cognitive impairments relevant to everyday life [1▪]. The mortality of a POD is similar to that of a myocardial infarction [2▪]. In addition, the rate of rehospitalization is increased, and POD leads to economic disadvantage to the hospital [3▪▪]. Due to this medical and also economic impact, concepts for prevention and treatment of POD are urgently needed and are currently under discussion.

The most predisposing risk factors for delirium are higher age (≥65 years), cognitive impairment, comorbidities and the associated polypharmacy [4▪]. The cause of POD is not an underlying psychiatric disease, but always has a somatic genesis. It requires an acute noxious event or complication in intensive care stay such as infection, prolonged general anesthesia, prolonged intensive care, exsiccosis or electrolyte disorder to promote delirium [5▪].

PATHOPHYSIOLOGY

POD is multicausal. Several risk factors are known to increase the incidence. Here, it takes an acute noxious agent or complication during pre, peri or postoperative management such as infection, exsiccosis, prolonged analgosedation, intensive care stay or electrolyte imbalance to induce a delirium [5▪].

[a]Department of Neurology, University Hospital of Münster, Münster and [b]Department of Anesthesiology, Intensive Care Medicine, and Pain Therapy, Clinic Centre Westfalen, Dortmund, Germany

Correspondence to Thomas Duning, MD, Department of Neurology, University Hospital of Münster, Albert-Schweitzer-Campus 1, 48149 Münster, Germany. Tel: +49251 83 48195; e-mail: Thomas.Duning@ukmuenster.de

Curr Opin Anesthesiol 2021, 34:27–32
DOI:10.1097/ACO.0000000000000939

KEY POINTS

- There are many risk factors for postoperative delirium. The leading ones are advanced age (>65 years of age) and preexisting cognitive deficits. Cognitive screening of older patients is therefore recommended.
- There is no recommended pharmaceutical delirium prevention, but effective nonpharmaceutical preventive concepts already exist.
- Not every delirium can be prevented. In addition to delirium prevention, standardized therapeutical concepts (nonpharmaceutical and medications) are necessary.
- Postoperative delirium in the elderly:

  Avoidance of benzodiazepines

  Haloperidol less effective, better Risperidone

  Agitation: prefer Melperone or Pipamperone

  For alcohol withdrawal: benzodiazepines/Haloperidol or Clomethiazole

  With additional Parkinson's disease: Quetiapine or Clozapine

In contrast to dementia, delirium is based on an acute neurotransmitter imbalance that is not yet fully clarified. Different physiological trigger factors lead to the same symptoms. The common end of all the published hypotheses is an increased dopamine activity accompanied by an additional cholinergic deficit [6]. Inflammation processes such as oxidative stress during surgery, infection or pain all activate neuronal microglia cells [7,8]. The activation of microglia cells is also triggered by reduced cholinergic inhibition. Thus, patients with reduced cholinergic synthesis caused by Alzheimer's disease or use of anticholinergic medication carry a high risk to develop a delirium [8].

PHARMACOLOGICAL PREVENTION

A reasonable number of pharmacological agents were introduced and intensively investigated to prevent POD. This incorporates various pharmacological approaches such as, among others, antipsychotics and acetylcholinesterase inhibitors. As neuroinflammation and neuronal injury increase the incidence of delirium, steroids and statins have also been examined. In summary, all these approaches failed to hold their promise. There is no evidence to advocate the use of these substances in the pharmacological prevention of delirium [9]. Maybe one exception is Dexmedetomidine that might be recommended as the only preventive agent, in particular in older patients. However, a very recent large-scale multicentre trial in elderly cardiac surgery patients showed no significant benefits in preventing POD [10▪▪]. Conclusively, the authors do not recommend the use of Dexmedetomidine as a prevention of delirium in elderly patients.

It is deemed that one of the most important aspects in pharmacological prevention is pharmaceutical counselling, in particular the evaluation of the home-medication. Before surgery, a clinical pharmacist has to evaluate the home-medication and has to stop or exchange drugs with, for example high anticholinergic burden, such as promethazine, tricyclic antidepressants or urological spasmolytics, as well as benzodiazepines as a sleep-inducing medication or long-term neuroleptic therapy without underlying psychiatric disease [11▪▪]. Pharmaceutical counselling comprises the verification of indications, aims to find adequate alternatives when appropriate and triggers a patient tailored, adequate dosing of medication (Table 1).

Table 1. Inappropriate medication and recommended alternatives

Potentially inadequate medication	Appropriated alternative medication
Benzodiazepines for insomnia	Mirtazapine 7.5–15 mg
Nonbenzodiazepines (Zopiclone, zolpidem)	Mirtazapine 7.5–15 mg Melperone 25 mg
Tricyclic antidepressants	Mirtazapine 7.5–15 mg Pregabaline
SSRI	Pregabaline
Antipsychotics for sedation (e.g. Promethazine)	Mirtazapine 20–40 mg Melperone 25 mg Pipamperone 20 mg
Typical/ atypical antipychotics without any indication or off-label use for dementia	Stop medication, no alternatives
Tramadol	Hydromorphone
Piritramide	Hydromorphone
Oxycodone	Hydromorphone
Morphine (except palliative care)	Hydromorphone
Fentanyl (except palliative care)	Hydromorphone
Buprenorphin (except palliative care)	Hydromorphone
Fluorchinolone	Cephalosporines, Fosfomycin or Pivmecillinam for uncomplicated cystitis in females

SSRI, selective serotonin reuptake inhibitors.

NONPHARMACOLOGICAL PREVENTION STRATEGIES

Unfortunately, the evidence for nonpharmacological strategies to reduce POD is also low [12▪]. It is necessary to identify patients at high risk for delirium to implement preventive interventions. As there are several and multifactorial risk factors for a POD, multicomponent interventions are required [12▪,13▪]. Table 2 summarizes the nonpharmaceutical interventions with the strongest evidence. A combination of these interventions decrease the incidence rate of POD by 44% [12▪,14]. In addition, there is less evidence that single-component interventions such as staff education and reorientation may help to prevent POD. Other interventions such as bright light therapy, using earplugs and music therapy, have not been proven to be significant [12▪]. The Hospital Elder Life Program (HELP) is a worldwide implemented, multidisciplinary and multifactorial evidence-based model for elderly persons in hospitals, which includes the prevention and therapeutic management of a delirium. The program effectively reduces the incidence of delirium by 53% [15▪▪], especially by using many of the mentioned nonpharmaceutical interventions.

One must however realize that many of the studies on preventive interventions are of poor quality and rather heterogenous in design. Moreover, healthcare systems and structures in different countries are difficult to compare. It is reasonable to recommend that nonpharmaceutical interventions should be tailored to the existing hospital structure and healthcare system.

INTRAOPERATIVE MANAGEMENT

Various interventions have been investigated in different populations and various types of surgery are subjects of ongoing trials [16]. Due to the multifactorial genesis of delirium, the results are largely conflicting and clear recommendations are thus impossible; however, as in prophylaxis, reasonable measures as part of prevention bundles might be valuable bricks in the basement of solid defense walls against delirium [17▪].

One brick is avoiding known triggers of delirium. Maintaining normothermia and homeostasis as well as avoiding long periods of sedation and blood-pressure fluctuations prevent delirious symptoms. Especially, preoperative medication with anticholinergic effects (including Diphenhydramine) and (long acting) benzodiazepines should be avoided. Well tolerated and effective pharmacological approaches for premedication do not exist, especially in older patients. Only Melatonine appears to be well tolerated, with a small, but certain benefit with regards to preoperative sleep stress [18▪]. The best choice for drugs during anaesthesia is unclear as well. To whether or not perform total intravenous anaesthesia or to use volatile anesthetics, including Xenon, appears to be irrelevant with regard to safety and postoperative delirious symptoms [19▪].

The highly selective α2-adrenergic receptor agonist Dexmedetomidine administered as prophylaxis during and post anaesthesia lately emerged as an upcoming star to lighten the dark field of delirium. Safety and a reduction of delirium were suggested in many trials in various settings at the prize of side effects such as relevant bradycardia. Summarizing

Table 2. Nonpharmaceutical intervention and treatment of postoperative delirium

Intervention	Examples
Staff education [12▪]	Assessment tools Theoretical foundations Sensitization
Early mobilization [12▪,13▪]	Minimization of immobilizing equipment Collaboration with physical therapists, occupational therapists
Pain control [12▪]	Constant use of adequate pain assessments
Reorientation [13▪,14]	Use of hearing and visual aids Orientation guides (clock, calendar) Orientating communication Approach of family members, friends Avoiding room changes
Sleep-wake cycle preservation [12▪,14]	Environmental cues for normal sleep-wake cycles Minimize sound and light in the night Use of ear-plugs
Optimization of hydration and nutrition [12▪]	Fluid repletion Collaboration with dietician

the results, these effects still appear to hold true, although the trials are largely heterogeneous and mostly of low quality [20]. Confusingly, a very recent high-quality large prospective multicenter trial (DECADE) showed no positive effect with respect to delirium in older cardiac surgery patients, but a significantly increased number of critical events and was therefore stopped after the last interim analysis [10▪▪].

Another brick in the defense wall against delirium is adequate pain therapy. But how to achieve 'adequate' remains unclear. Neither regional anesthesia techniques nor sophisticated regimes based on systemic drugs proved superiority in large meta-analysis; however, regional techniques are well tolerated and frequently provide favourable pain relief [21▪]. A third brick might be to avoid inadequate depth of sedation during anaesthesia. Indeed, there is moderate-quality evidence that anaesthesia guided by processed EEG monitoring to indicate brain state could reduce the risk of POD, especially in patients aged older than 60 years [22]. However, a very recent large prospective trial (ENGAGES) in elderly patients could not undermine this notion [23]. The maintenance of adequate cerebral oxygen supply is another brick in the wall, although difficult to quantify during anesthesia. Several sophisticated methods have been suggested, their benefit surmounting a meticulous control of arterial blood-pressure to individual normal values remains to be elucidated [24▪].

Conclusively, a solid basement for well tolerated anaesthesia in patients at risk for delirium is an individually patient and hospital-tailored bundle comprising procedures and technical support with special respect to avoiding the mentioned delirium triggers, assuring an adequate depth of sedation and sufficient pain therapy.

NONPHARMACOLOGICAL TREATMENT OF POSTOPERATIVE DELIRIUM

The first step to deal with POD is the identification of delirium. Standardized and routine screening of patients with an elevated risk of delirium after surgery is essential. A valid and the most established screening tool for delirium identification is the CAM-ICU (Confusion Assessment Method for the Intensive Care Unit) with a sensitivity of 0.79 and a specificity of 0.97 [14]. Other assessment tools to detect a delirium (e.g. Memorial Delirium Assessment Scale, Delirium Rating Scale-Revised-98) could be useful, but are described as less valid and more time consuming in clinical routine [13▪]. To manage POD in the daily routine, the staff needs to be qualified and sensitized. Specific staff education is the mainstay for effective delirium management [13▪]. It is also useful to have elder-life specialists in different professions, as considered, for example, by the HELP model [25▪].

In summary, the focus of nonpharmaceutical POD management is to avoid or to minimize trigger factors of delirium [13▪]. Programs are always complex and require a multidisciplinary team approache [15▪▪]. Thus, nonpharmacological interventions for POD are akin to preventive interventions shown in Table 2.

PHARMACOLOGICAL TREATMENT OF POSTOPERATIVE DELIRIUM

The pharmacological treatment of delirium symptoms in older patients is important and necessary. It should be always a temporary medication regimen consisting of an antipsychotic and a sedative medication, if necessary. Thus, regularly monitoring of symptoms is important, and we recommended the CAM [26▪].

(1) Atypical antipsychotics are used to treat the positive symptoms such as optical hallucinations and delusions. Atypical antipsychotics have a limited effect on sedation (only in high doses), and should not used as sedative medication. Risperidone is recommended for a temporary treatment of hallucinations and aggression in older patients, especially with existing cognitive deficits [27▪,28▪▪]. Haloperidol is not or barely effective in older patients [29▪▪]. It is possible to use Haloperidol up to 2 mg per day (maximum daily dose) in patients less than 70 years of age with psychotic symptoms and without any neurodegenerative and cardiac diseases. Haloperidol is an unselective dopamine agonist and regularly leads to arrhythmia and extrapyramidal symptoms. An intravenous injection is not effective for treating delirium because a constant drug level cannot be reached, which is important for the antipsychotic effect [29▪▪].
(2) Treatment of psychomotor agitation, which originates from hallucinations and delusions and often lead to endangerment oneself and others, should be treated with sedative antipsychotics. Melperone and Pipamperone have no anticholinergic side effects and are mostly used and recommended. Benzodiazepines should not be use in the elderly due to paradoxical effects (up to 30%), increased risk of falls and fractures, risk of dependency, deterioration of cognitive deficits.

The combination of two antipsychotics increases the risk of QTc-prolongation. Before

Table 3. Overview of recommended medication for delirium treatment

Substance	Dosing frequency	Special instructions
Typical und atypical antipsychotics		
Risperidone	0.5 - 0 - 0.5 - 0 mg po max. 1 - 0 - 1 - 0 mg po	Reduction by GFR <15 ml/min
Haloperidol	1 - 0 - 1 - 0 mg po	Patients >70 years no intravenous application
Quetiapine	25 - 0 - 25 - 50 mg po max. 150 mg/day	Low antipsychotic effect. Recommended use for Parkinson's-syndrome
Clozapine	0 - 0 - 25 - 0 mg po	Agranulocytosis as a main side effect
Sedative antipsychotics		
Melperone	0 - 0 - 25 - 50 mg or 25 - 0 - 50 - 0 mg	Dosage depends on psychomotor agitation Half-life of 7.5 h
Pipamperone	0 - 0 - 40 - 0 mg or 20 - 0 - 40 - 0 mg	Dosage depends on psychomotor agitation Half-life of 20 h
Short acting types of benzodiazepines for an acute situation		
Lorazepam	2 mg i.v.	Single dosing, until patient amenable to oral medication

Dosing refers to interval of four times a day.
GFR, glomerular filtration rate; i.v., intravenous; po, per os.

starting treatment, an ECG should be conducted [30▪]. Pharmacological treatment period should not exceed 7 days. The treatment of delirium differs from patients with alcohol withdrawal and from patients with Parkinson's syndrome. Alcohol withdrawal delirium should be treated according to the current guidelines, prefering Thiamin substitution and long-term benzodiazepines, because of their effective GABAergic potency [31,32]. The only antipsychotics that are recommended in delirious patients with Parkinson's syndrome are Clozapine and Quetiapine, because they have only a minor effect on dopamine D2 receptors (see Table 3 for an overview).

CONCLUSION

The prevention and treatment of POD is an interdisciplinary task. There is no evidence for an effective pharmacological prevention, so avoiding trigger factors seems essential. Nonpharmaceutical prevention programmes already exist, but they need to be adapted to the healthcare system. A pharmaceutical consultation is important, because prodelirogenic polypharmacy is an important trigger factor.

There is no evidence that one anesthetic technique is 'safer', with respect to limiting POD, than any other technique. It is an individual patient and hospital-tailored bundle with special attention focused on avoiding delirium triggers, assuring an adequate depth of sedation and sufficient pain therapy.

The nonpharmaceutical treatment is similar to prevention. It is essential to establish a delirium screening. The evidence for pharmacotherapy is poor, but benzodiazepines and permanent neuroleptic therapy should be avoided.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. Malik AT, Quatman CE, Phieffer LS, *et al.* Incidence, risk factors and clinical
▪ impact of postoperative delirium following open reduction and internal fixation (ORIF) for hip fractures: an analysis of 7859 patients from the ACS-NSQIP hip fracture procedure targeted database. Eur J Orthop Surg Traumatol 2019; 29:435–446.

Several risk factors are associated with the occurrence of POD in patients undergoing ORIF for hip fracture.

2. Hapca S, Guthrie B, Cvoro V, *et al.* Mortality in people with dementia, delirium,
▪ and unspecified cognitive impairment in the general hospital: prospective cohort study of 6,724 patients with 2 years follow-up. Clin Epidemiol 2018; 10:1743–1753.

Having delirium alone is associated with higher early mortality during the 6 months after admission, whereas dementia (alone or with delirium superimposed) had no early increase in mortality but did have higher mortality after 3 months and unspecified cognitive impairment only after 6 months.

3. Bulic D, Bennett M, Georgousopoulou EN, *et al.* Cognitive and psychosocial ■■ outcomes of mechanically ventilated intensive care patients with and without delirium. Ann Intensive Care 2020; 10:104.

Delirium in ICU was independently associated with short-term but not long-term cognitive function, and with long-term posttraumatic stress disorder symptoms.

4. Bergjan M, Zilezinski M, Schwalbach T, *et al.* Validation of two nurse-based ■ screening tools for delirium in elderly patients in general medical wards. BMC Nurs 2020; 19:72.

The Nursing Delirium Screening Scale (Nu-DESC) proved to be an efficient delirium screening tool that can be integrated into routine patient care.

5. Chung H-Y, Wickel J, Brunkhorst FM, Geis C. Sepsis-associated encephalo- ■ pathy: from delirium to dementia? J Clin Med 2020; 9:703.

The acute phase of sepsis is often accompanied by sepsis-associated encephalopathy, which is highly associated with increased mortality. In the chronic phase, more than 50% of surviving patients suffer from severe and long-term cognitive deficits compromising their daily quality of life and placing an immense burden on primary caregivers.

6. Braune S, Gurlit S. Management of delirium in the intensive care unit. Dtsch Med Wochenschr 2019; 144:1611–1618.
7. Rengel KF, Pandharipande PP, Hughes CG. Postoperative delirium. Presse Med 2018; 47:e53–e64.
8. Westhoff D, Engelen-Lee JY, Hoogland ICM, *et al.* Systemic infection and microglia activation: a prospective postmortem study in sepsis patients. Immun Ageing 2019; 16:18.
9. Barbateskovic M, Krauss SR, Collet MO, *et al.* Pharmacological interventions for prevention and management of delirium in intensive care patients: a systematic overview of reviews and meta-analyses. BMJ Open 2019; 9:e024562.
10. Turan A, Duncan A, Leung S, *et al.* Dexmedetomidine for reduction of atrial ■■ fibrillation and delirium after cardiac surgery (DECADE): a randomised placebo-controlled trial. Lancet 2020; 396:177–185.

Dexmedetomidine infusion, initiated at anaesthetic induction and continued for 24 h, did not decrease postoperative atrial arrhythmias or delirium in patients recovering from cardiac surgery. Dexmedetomidine should not be infused to reduce atrial fibrillation or delirium in patients having cardiac surgery.

11. Vondeling AM, Knol W, Egberts TCG, Slooter AJC. Anticholinergic drug ■■ exposure at intensive care unit admission affects the occurrence of delirium. A prospective cohort study. Eur J Intern Med 2020; 78:121–126.

Anticholinergic drug exposure at ICU admission increases the risk of delirium in critically ill patients. This effect was most pronounced in patients older than 65 years without severe sepsis and/or septic shock, and declining over time.

12. Salvi F, Young J, Lucarelli M, *et al.* Nonpharmacological approaches in the ■ prevention of delirium. Eur Geriatr Med 2020; 11:71–81.

The majority of studies that investigated nonpharmacological prevention of delirium were designed as explanatory studies aimed at demonstrating the efficacy of the intervention. In the future, pragmatic studies should be conducted, in which the aim is to investigate effectiveness in usual clinical practice.

13. Oh S-T, Park JY. Postoperative delirium. Korean J Anesthesiol 2019; ■ 72:4–12.

POD is a common complication and exerts an enormous burden on patients, their families, hospitals and public resources. Its management should be maintained throughout all stages of surgery with regards to the following three aspects: prevention, assessment and treatment.

14. Zoremba N, Coburn M. Acute confusional states in hospital. Dtsch Arztebl Int 2019; 116:101–106.
15. Hshieh TT, Yang T, Gartaganis SL, *et al.* Hospital elder life program: ■■ systematic review and meta-analysis of effectiveness. Am J Geriatr Psychiatry 2018; 26:1015–1033.

The Hospital Elder Life Program is effective in reducing incidence of delirium and rate of falls, with a trend towards decreasing length of stay and preventing institutionalization

16. Hughes CG, Boncyk CS, Culley DJ, *et al.* American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on postoperative delirium prevention. Anesth Analg 2020; 130:1572–1590.
17. Chuan A, Zhao L, Tillekeratne N, *et al.* The effect of a multidisciplinary care ■ bundle on the incidence of delirium after hip fracture surgery: a quality improvement study. Anaesthesia 2020; 75:63–71.

A perioperative, multimodal, multidisciplinary care bundle approach for patients having surgical repair of a hip fracture can result in a clinically significant reduction in the incidence POD.

18. Khare A, Thada B, Jain N, *et al.* Comparison of effects of oral melatonin ■ with oral alprazolam used as a premedicant in adult patients undergoing various surgical procedures under general anesthesia: a prospective randomized placebo-controlled study. Anesth Essays Res 2018; 12:657–662.

Oral melatonin (6 mg) when used as a premedicant is an effective alternative to alprazolam regarding providing better anxiolysis, lesser sedation along with maintenance of cognitive and psychomotor function.

19. Miller D, Lewis SR, Pritchard MW, *et al.* Intravenous versus inhalational ■ maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing noncardiac surgery. Cochrane Database Syst Rev 2018; 8:CD012317.

It remains uncertain whether maintenance with propofol-based TIVA or with inhalational agents affect incidences of POD, mortality or length of hospital stay because certainty of the evidence was very low.

20. Shen Q-H, Li H-F, Zhou X-Y, Yuan X-Z. Dexmedetomidine in the prevention of postoperative delirium in elderly patients following noncardiac surgery: a systematic review and meta-analysis. Clin Exp Pharmacol Physiol 2020; 47:1333–1341.
21. Patel V, Champaneria R, Dretzke J, Yeung J. Effect of regional versus general ■ anaesthesia on postoperative delirium in elderly patients undergoing surgery for hip fracture: a systematic review. BMJ Open ; 8:e020757.

Although there is no evidence to suggest that anaesthesia types influence POD, the evidence base is lacking. There is a need to ascertain the impact of type of anaesthesia on outcomes with an adequately powered, methodologically rigorous study.

22. Chan MTV, Hedrick TL, Egan TD, *et al.* American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on the role of neuromonitoring in perioperative outcomes: electroencephalography. Anesth Analg 2020; 130:1278–1291.
23. Jones F, Kruger C. Utilization and referral patterns in the acute illness department of a multispecialty clinic. IMJ Ill Med J 1975; 148:640–644.
24. Yu Q, Qi J, Wang Y. Intraoperative hypotension and neurological outcomes. ■ Curr Opin Anaesthesiol 2020; 33:646–650.

Despite the lack of a known threshold value, intraoperative hypotension is a modifiable risk factor targeted to improve neurological outcomes. Ideal blood pressure management is recommended in order to maintain target blood pressure based on the monitoring of regional cerebral oxygen saturation or cerebral pressure autoregulation.

25. Wang Y-Y, Yue J-R, Xie D-M, *et al.* Effect of the tailored, family-involved ■ hospital elder life program on postoperative delirium and function in older adults: a randomized clinical trial. JAMA Intern Med 2019; e194446.

The Tailored, Family-Involved Hospital Elder Life Program, with family involvement at its core, is effective in reducing POD for older patients, maintaining or improving their physical and cognitive functions, and shortening the length of hospital stay.

26. Lee S, Gottlieb M, Mulhausen P, *et al.* Recognition, prevention, and treatment ■ of delirium in emergency department: an evidence-based narrative review. Am J Emerg Med 2020; 38:349–357.

Older emergency department patients are at a high risk for current or subsequent development of delirium, and a focused screening, prevention and intervention for those who are at risk for delirium and its associated complications are the important next steps.

27. Yunusa I, El Helou ML. The use of risperidone in behavioral and psychological ■ symptoms of dementia: a review of pharmacology, clinical evidence, regulatory approvals, and off-label use. Front Pharmacol 2020; 11:596.

Given the current evidence on the clinical effectiveness and safety of risperidone in the management of behavioural and psychological symptoms of dementia, its use should be restricted to patients with severe symptoms (aggression, agitation or psychosis) who fail to respond adequately to nonpharmacological treatments. In this case, a low dose (0.25–2 mg daily) and short treatment duration (6–12 weeks) must be favoured. Moreover, risperidone must be avoided in patients with a history of cerebrovascular adverse events or with risk factors for stroke.

28. Pluta MP, Dziech M, Czempik PF, *et al.* Antipsychotic drugs in prevention of ■■ postoperative delirium: what is known in 2020? Int J Environ Res Public Health 2020; 17:6069.

Currently, on the basis of the available data, no recommendations can be made for the routine prophylaxis of POD with antipsychotic drugs. However, some studies have shown the benefit of the prophylactic use of neuroleptics with a minimal risk of serious side effects, opening the way for further research to answer the question which patients can benefit from the pharmacological prevention of delirium and how to use these agents effectively based on high-quality evidence. The potential role of dexmedetomidine in POD prevention cannot be neglected.

29. Girard TD, Exline MC, Carson SS, *et al.* Haloperidol and ziprasidone for ■■ treatment of delirium in critical illness. N Engl J Med 2018; 379:2506–2516.

The use of haloperidol or ziprasidone, as compared with placebo, in patients with acute respiratory failure or shock and hypoactive or hyperactive delirium in the ICU did not significantly alter the duration of delirium.

30. Morris NP. Antipsychotics for delirium: the consent conundrum. Lancet ■ Psychiatry 2020; 7:e5.

Routine antipsychotic prescribing for delirium is not only ineffective but also potentially harmful to patients. These medications bring risks of side effects, including extrapyramidal symptoms, QTc prolongation and medication interactions.

31. Attilia F, Perciballi R, Rotondo C, *et al.* Alcohol withdrawal syndrome: diagnostic and therapeutic methods. Riv Psichiatr 2018; 53:118–122.
32. Airagnes G, Ducoutumany G, Laffy-Beaufils B, *et al.* Alcohol withdrawal syndrome management: is there anything new? Rev Med Interne 2019; 40:373–379.