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Postoperative delirium: risk factors, diagnosis and perioperative care

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ABSTRACT

Postoperative delirium (PD) relates to increased morbidity –associated with prolonged hospital stay, institutionalization and persistent functional and cognitive decline- poor long term outcome and higher perioperative mortality. Aim of this literature review is to identify established risk factors for PD and to categorize them according timing of occurrence (pre, intra and post operative), and clinical impact (Odds ratio [OR], % increase in incidence of PD). Source of information: medical literature databases (medline and embase) were searched for published manuscripts on "postoperative delirium". Predictors and preoperative risk factors for PD were categorized into 4 groups: demographics; co morbidities; surgery and anesthesia-related (age, education, laboratory anomalies, smoking habits, benzodiazepines premedication, cardiac and thoracic surgery, etc). Intra operative risk factors for PD were categorized into 2 groups: surgery and anesthesia-related (anemia, duration and type of surgery, selected opioid, intraoperative hypotension, etc). Post operative risk factors and precipitating factors include various pathophysiological and environmental conditions (i.e. ICU admission, low cardiac output requiring inotropes infusion; new onset atrial fibrillation; persistent hypoxia or hypercarbia; use of narcotic analgesics, delayed ambulation, inadequate nutritional status; sensory deprivation, etc). In conclusion, the effective identification, prevention and treatment of pre, intra and postoperative risk factors are the cornerstones for the prevention of PD. A dedicated perioperative care path that encompasses a tailored selection of drugs used perioperatively, the appropriate anesthesia strategy, qualified nursing surveillance, systematic use of diagnostic tools and accurate staff communication reduces the incidence and clinical impact of PD. *(Minerva Anestesiol 2013;79:1-2)*

Key words: Delirium - Aged - Perioperative care - Education.

Postoperative delirium (PD) is a serious complication, sometime under recognized, that relates to an increase in length of hospital stay and poor outcomes.[1, 2] Occurrence of PD is characterized by fluctuating changes of cognitive capacity, altered perception with hallucination, acute decline in cognition and inappropriate behavior.[3, 4] It complicates the postoperative course

in up to 56% of the cases, with the highest incidence in elderly patients.[1, 6] Postoperative delirium (PD), postoperative cognitive dysfunction (POCD), persistent mild cognitive impairment (MCI) and dementia are different conditions that share common mechanisms. The PD is an acute impairment of cognitive and or spatial/temporal perception, that can be diagnosed at the bedside with dedicated diagnostic tools.[7] It has an acute onset and a fluctuating course, and therefore can be missed if not systematically tested.[7, 8] It is defined by three principal characteristics: altered consciousness; changes in cognitive abilities; recent and rapid onset.[9] The POCD affects global cognitive functions for several months/years after surgery and anesthesia, diagnosis requires detailed neuropsychological testing.[7] The MCI is an intermediate condition between normal ageing and dementia, can have multiple etiologies, diagnostic criteria are: 1) memory complaint; 2) normal general cognitive function; 3) memory impairment; 4) no functional impairment; and 5) no dementia.[10] Dementia is associated with multiple cognitive deficit that include memory impairment and at least one of the following cognitive disturbances: aphasia, apraxia, agnosia, altered executive functioning. In patients with dementia, cognitive disturbance is progressive and so severe that cause impairment in occupational and social life.[7, 9]

For the diagnosis of delirium the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), or International classification of disease and related health problems (ICD-10), are the gold standard and also apply in acutely ill and hospitalized patients, but their application is time consuming and require specific expertise.[4-7] Early diagnosis, prompt treatment of modifiable factors and adequate therapies promote recovery when PD occurs.[7] Occurrence of PD has relevant clinical implications since it relates to increased perioperative morbidity and mortality.[8, 9] In elderly patients after an episode of delirium the risk of institutionalization is increased by 10% and the risk of death within 2 years is increased by 27% as compared with control group.[8] In patients undergone CABG, occurrence of PD is associated with higher rate of postoperative stroke and mortality.[9] Hence the importance to identify related risk factors right from patients' arrival into the hospital. Risk factors for PD are categorized depending on timing of occurrence (pre-, intra- and postoperative) and structured according the following categories: demographics, comorbidities, surgery and anesthesia. When a pre operative risk factor is present, it should be detected before surgery and corrected to the largest extent. Furthermore, patients at higher risk for PD should have a dedicated postoperative path.

To ease and expedite the diagnosis of PD various diagnostic tools have been proposed. The use of clinical evaluation, when not supported by objective criteria, can lead to an underestimate of the actual incidence of PD, while subjective estimate is associated with substantial over diagnosis. Hence the importance to adopt, in the postoperative period, a systematic approach that relies on dedicated diagnostic tool and fixed time schedule.

To adequately treat PD, reversible factors - including pain, anemia, etc. — should be removed and an appropriate therapy should be established. Optimal treatment should encompass pharmacological and non-pharmacological therapeutic measures with physiological day light exposure, allowance of relatives visits in the hospital and assisted return to home activities the sooner. Aim of this article is to review current evidence on risk factors for PD in adults, to present diagnostic tools currently available to detect PD and to discuss optimal perioperative care of patients at risk for and affected by PD.

Risk factors

Risk factors for PD can be categorized according to the timing of occurrence as preoperative, intraoperative and postoperative. Within each of these categories it is possible to discriminate the following categories: demographics, comorbidities, surgery and anesthesia. The assessment of preoperative risk factors related to PD is of great importance and allows to select patients at increased risk in whom a dedicated perioperative path is indicated.[5, 9] Because of the clinical relevance of PD, various prediction models have been proposed for general practice and for

surgery-based procedure-specific subgroups of patients.[10, 15] A structured screening interview, that include some of the most relevant variables to detect preoperative risk factors for PD is reported in Table I.[12-62]

Pre operative risk factors.—The risk for PD is dependent on several predictors (Table I). Patient's age is a major demography-related preoperative risk factor: age >70 years is associated with an odds ratio of 3.3 for PD and age>80 is as-

Table I.—*Predictors for postoperative delirium.*

Predictors for delirium	Odds Ratio or % increase in incidence of PD		Reference
Demography-related			
– Age >70	3.3 (1.9-5.9)		16, 12
– Sex (Male)	1.12 (0.73- 1.74)		16, 28
– Educational level (High school graduation or lower *vs.* college or higher)	33 %		16, 6
– Alcohol & drugs abuse	3.3 (1.4-8.3)		12
– Malnutrition (Low serum albumin and dehydration)			7, 30, 39
Comorbidities-related			
– Cognitive status (Dementia, attention deficits, psychiatric disorders)	4.2 (2.4-7.3)		12
– Physical impairment (Inability to perform activities of daily living)	2.5	(Neurological and psychiatric, metabolic, laboratory abnormalities, genitourinary, cardiovascular and respiratory)	12
– Abnormal preoperative sodium, potassium, glucose level, albumin	3.4 (1.3-8.7)		7, 12, 30, 32
– Anemia (Hb<10)	0.2		7, 33
– Smoking status (Preoperative smoking,COPD)	18 %		7, 39 7, 34, 39
– Hypertension	8 %		34, 39
– DM	9 %		32, 34, 39
– Peripheral vascular disease	7 %		34
– Heart failure			34
– Cerebral vascular accident or TIA	8 %		34
– CAF	3.8		34
– Genetic profile (polymorphism Apo E)	3.64 %		17
– Obstructive sleep apnea	4.3 %		19
Surgery-related			
– Aortic aneurysm surgery	8.3 (3.6-19.4)		12
– Cardiac surgery	3.5 (1.6-7.4)		12
– EURO-score			26
– Thoracic surgery	1.25		12
– Abdominal surgery	1.83		28
– Hip replacement surgery	16-62 %		62
– Cataract extraction	1.7 %		
Anesthesia-related			
– Premedication with benzodiazepines	1.8		6, 9, 34
– ASA classification (III-IV vs I-II)	7 %		16
– Transfusions >800 mL	2.5		33
– Fluid fasting time >6 h	10.5		28
– Medication (Use of Anticholinergic drugs)	1.3		4, 7, 64

DM: diabetes mellitus; TIA: transitory ischemic attack; CAF: chronic atrial fibrillation.

sociated with an odd ratio of 5.2 for PD.[12] Type of surgery is also strong predictor of PD and for some surgical procedures - including orthopedic, abdominal aortic aneurysm and cardiac thoracic surgery - it links to an increased risk.[16] The EUROscore is a clinical risk factors index, based on 18 variables, that predicts perioperative survival in cardiac surgery patients and is also useful to estimate the risk for PD.[25, 26]

Genetic profile, including the polymorphism for APO lipoprotein E that is also related to chronic neurodegenerative disorders and dementia, is among comorbidities-related risk factors for PD. The importance of genetic profile for PD is not yet completely quantified and several isoforms and genetically determined diseases are currently under evaluation.[17-20]

Among comorbidity-related risk factors that have a major role in predicting PD some deserve to be described in detail. Chronic obstructive pulmonary disease (COPD) is an important risk factor for PD, the pathophysiological underlying mechanism is possibly based on chronic hypoxia that facilitates mitochondrial dysfunction and promotes brain dysfunction and cognitive decline. Patients with COPD have worst performance than controls in a number of neuropsycological tests when cortical and subcortical functions are assessed, including: executive functions, attention, non verbal logical reasoning and problem solving ability.[20, 21]

Obstructive sleep apnea (OSA) is also associated with an increased risk for PD, in these patients the causative mechanisms are possibly related to: "respiratory encephalopathy" and the imbalance between brain oxygen requirement and oxygen supply; intermittent hypoxia that induces oxidative stress and changes in the protein profile in the hippocampus and prefrontal cortex; prevalence of nocturnal occurrence might also be related to blood gas analysis abnormalities that specifically occur during the night time; neurotransmitter abnormalities related to sleep disorder and chronic sleep deprivation.[19, 22]

Whatever the pathogenic mechanisms implicated in OSA-related PD, it is of interest that in these patients the use of continuous positive pressure ventilation (CPAP) during the night time is an effective approach for treatment.[22]

Psychiatric and neurodegenerative disorders are associated with an increased risk for PD (7.4 times greater risk of developing higher psychological distress when admitted to ICU), especially in patients with dementia and depressive symptoms it is important to make a differential diagnosis that can be established considering some characteristic features of PD: fluctuating course, short time of onset and offset, impact on global cognitive function and impairment in social functioning.[9, 20, 23] An increased risk for PD is also reported in patients with an history of alcohol or illicit drugs abuse (2.4 folds).[24]

There are various factors associated with an increased risk for PD that are suitable of preoperative correction, these include: fluid fasting time, electrolytes, low serum albumin, malnutrition, anaemia, glycemia abnormalities, preoperative premedication with benzodiazepines (Table I).[17, 21, 27]

Preoperative fluids fasting time (>6 hours *vs.* 2-6 hours) is independently associated with an increased incidence of postoperative delirium.[28] Electrolytes abnormalities and especially hyponatremia that is a frequent complication of renal disease (including Colton blood group mutation of renal aquaporin P1), chronic diuretic therapy, and often detected in elderly patients should be corrected preoperatively right from patient's admission.[29]

Serum albumin concentration (SAC) is related with the cognitive performance and can be considered as a predictor and a precipitating factor for PD.

Serum albumin elicit a drugs and hormones binding activity along with an antioxidant and oxygen radical trapping, that prevents toxic cognitive impairment. Furthermore, low levels of albumin in the brain and cerebrospinal fluid are associated with increased formation of amyloid beta-peptide fibrils and the risk for chronic neurodegenerative disorders including Alzheimer's disease.[30]

Quantifying nutritional intake can be really important in elderly undergoing surgery: the Preoperative nutritional status is a predictor of the risk for PD. The use of Malnutrition Universal Screening Tool (MUST) is a five-step screening tool, that provides an effective approach to

quantitatively assess adequacy of nutrition. This tool can be used by all care workers to derive a malnutrition risk score of either low, medium or high. It consists of three components: BMI, history of unexplained weight loss, and acute illness effect [31]

Both dys-glycemia (that include hyper and hypo blood glucose levels) and anaemia, because of the effects on brain metabolism and oxygen transport, are important risk factors that should be aggressively treated in the preoperative period.[32, 33]

Beside the various anesthesia-related risk factors that deserve to be headed before surgery, it is important to underline that to avoid premedication with benzodiazepines is associated with a reduced risk for PD.[34]

Intra operative risk factors. Some intraoperative complications associated with an increased risk to develop PD, including severe bleeding and acute anaemia (Table II), are surgery-related risk factors, others are anesthesia-related.[35] Intraoperative mean arterial pressure (MAP) and partial pressure of carbon dioxide ($PaCO_2$) are among the physiologic variables more tightly related to occurrence of PD.[34] Especially in elderly patients it is extremely relevant to prevent intraoperative hypotension and hypocapnia, because it induce a significant reduction of cerebral blood flow and are strongly related to an increased incidence of PD. Several drugs, including atropine, ketamine, the use of propofol as compared with sevoflurane are associated with an higher incidence of PD.[36-38]

Post operative risk factors.—In the post operative setting several clinical conditions, including severe pain, administration of benzodiazepine and anticholinergic drugs, sensory deprivation, delayed ambulation, inadequate nutritional status should be aggressively prevented (Table III).[25, 39, 40] Of interest, several postoperative complications, such as: low cardiac output requiring inotropes infusion, new onset atrial fibrillation, persistent hypoxia or hypercarbia and ICU admission- are associated with an increased risk for PD (Table III).[39]

Precipitating factors.—In the postoperative period several factors, such as: sleep deprivation, bladder and central venous catheterization, etc., can precipitate PD. Especially in high risk patients, whenever possible, these elements should be avoided (Table III).[25, 35, 40, 41]

The effective identification, prevention and treatment of pre, intra and post operative risk factors for PD is associated with a reduced in-

Table II.—*Intraoperative risk factors for postoperative delirium.*

Surgery-related	Odds ratio Or % increase in incidence of PD	Reference
– Blood loss >1000 mL		16, 33
– Duration of surgery	1	28
Anaesthesia-related		
– Fasting fluid	10.6	28
– Hypothermia	11.4 %	34
– Hypotension	3 %	34
– Hypoxia, hypercarbia, hypocarbia	17 %	34
– Use of Propofol (TIVA vs volatile anaestethetic)	1.37	38
– Ketamine, Benzodiazepine		36, 37, 38
– BIS-value >80 (*vs.* BIS-value =50)	40 % vs 19 %	38
– Anticholinergic medication (Atropine or meperidine)	1.3	9, 36, 37, 38
– Long acting opioids (fentanyl vs remifentanil)	2.27	9, 64, 28,66
– Insertion of Pulmonary Artery Catheter	3.1 %	34

TIVA: total intravenous anesthesia; BIS: Bispectral Index

Table III.—*Postoperative risk factors for delirium.*

	Odds ratio Or % increase in incidence of PD	Reference
– Need of inotrope		34
– New onset of CAF	0.7 %	34
– Hypotension requiring vasopressors	3.8 %	34
– Low cardiac output	2.4 %	34
– Persistent hypoxia or hypercarbia 17.2 %	1.8 %	34
– Pain management	2.59	8
– Midazolam administration (each additional mg)	7 %	34
– Delayed ambulation	2.5	61
– Sensory deprivation (visual and hearing impairment)	1.8	57, 58, 61
– Adequate nutritional intake		31
– Length of stay in the hospital	14 %	16
– Admission to the ICU: mechanical ventilation		41
– Intercurrent precipitating medical illness (infections, metabolic derangements, fever, hypothermia, sepsis, use of physical constrains, urinary catheter, prolonged sleep deprivation)	3.8	40, 41, 54, 55, 60, 61

CAF: chronic atrial fibrillation.

cidence of this serious complication and a more appropriate patient's care. Nursing surveillance and accurate staff communication can play a critical role in this process.[42]

Diagnostic tools for PD

In several cases PD can be diagnosed on the basis of subjective clinical impression when related symptoms and signs occur, namely: agitation, reduced cognition and memory, loss of attention, hallucinations.[43] Subjective diagnosis of PD is frequently associated with overrating hyperactive cases, when compared to objective assessment, and underrating hypoactive cases, where up to 66% of the cases remain undiagnosed.[44, 45] Hence the importance of standard diagnostic criteria and reliable diagnostic and grading tools. Two standard definitions are available in the literature -Diagnostic and Statistical Manual of Mental Disease (DSM-IV) and the World Health Organization ICD10 classification of mental and behavioral disorders - but these are infrequently used because the need for a dedicated training.[46] In clinical practice several diagnostic and grading tools are used to detect and to evaluate delirium. Five of these scales are suitable for diagnosis of postoperative and ICU delirium (Table IV).[42, 47] The confusion assessment method was originally presented in 1990 and subsequently modified for ICU (CAM-ICU) is a rapid assessment tool - time necessary for administration is <5 min - based on DSM III delirium definition, that encompasses the evaluation of 4 delirium features: acute onset, inattention, altered level of consciousness, disorganized thinking.[46, 47] The intensive care delirium screening checklist (ICDSC) is based on the DSM IV delirium definition and take into account 8 features, that include: altered level of consciousness, inattention, disorientation, hallucination-delusion-psychosis, psychomotor agitation and retardation, inappropriate speech or mood, sleep-wake cycle disturbance, symptoms fluctuation.[48] The cognitive test for delirium (CTD), is based on DSM III delirium definition and evaluates 5 cognitive domains: orientation, attention, memory, comprehension and vigilance.[48, 49] Each domain is evaluated with 0-6 scores, leading to 0 to 30 total score (having 30=normal). The nursing delirium screening scale (Nu-DESC) is based on DSM IV delirium criteria and encompasses the evaluation of 5 items: disorientation, inappropriate behavior and communication, hallucination, psychomotor retardation.[50] For Nu-DESC based diagnosis each symptom is rated from 0 (no symptom) to 1 (mild) or 2 (pronounced), diagnosis is established when symptoms score is ≥2. The delirium rating scale (DRS) is based on 13 items for sever-

Table IV.—*Diagnostic and grading tools for postoperative delirium screening and grading.*[42-50]

Diagnostic Tools	Sensitivity (%)	Specificity (%)	Features/diagnosis/time
CAM-ICU	86	93	Features: acute onset and fluctuating course; Inattention; Altered level of consciousness; Disorganized thinking. Diagnosis: presence of items 1&2 + either 3 or 4. Time: <5 min.
ICDS	99	64	Features: altered level of consciousness; hallucination-delusion-psychosis; psychomotor agitation and retardation; inappropriate speech or mood; sleep-wake cycle disturbance; symptoms fluctuation. Score: 0-1. Range 0-8. Diagnosis: Cut off ≥4. Time: not available.
CTD	94.7	98.8	Features: orientation; attention; memory; comprehension; vigilance. Score: 0=impaired to 6=normal. Range 0-30. Diagnosis: Cut off ≤11. Time: 10-15 min.
Nu-DESC	83	81	Features: disorientation; Inappropriate behavior; Inappropriate communication; Illusions/Hallucinations; Psychomotor retardation. Score: 0=none, 1=mild, 2=pronounced. Diagnosis: cut off ≥2. Time: 1 min.
DRS	92	93	Features for severity: sleep-wake cycle disturbance; Perceptual disturbances and hallucination; delusions; lability of affect; language; thought process; motor agitation; motor retardation; orientation; Attention; short term memory; long term memory; visuospatial ability. Features for diagnosis: onset of symptoms; fluctuation; physical disorder. Score: 0=not present to 3=severe. Range: 0-46. Diagnosis: cut off ≥15. Time: not available.

CAM-ICU: Confusion Assessment Method Intensive Care Unit; ICDS: intensive care delirium screening checklist; CTD: Cognitive Test for Delirium; Nu-DESC: Nursing Delirium Scale; DRS: Delirium Rating Scale.

ity and 3 items for diagnosis: sleep-wake cycle disturbance; perceptual disturbances and hallucination; delusions; lability of affects; language; thought process; motor agitation; motor retardation; orientation; attention; short term memory; long term memory; visuospatial ability; onset of symptoms; fluctuating symptoms, physical disorder.[49] Each item is scored with from 0 (absent) to 3 (severe), thus leading to a score range of 0-46, diagnosis is established with a cut off ≥15. Because some of the important features of delirium, including variability of symptoms, are not included in this scale it is more suitable for PD grading than for diagnosis.[51]

Early and accurate diagnosis of PD is the prerequisite to institute adequate treatment and to minimize related complications. The systematic screening for PD, by dedicated diagnostic tool and a predetermined time schedule, allows prompt detection and to establish appropriate therapeutic measures. In adults patients the CAM-ICU scale is the most commonly used because leads to a quick and accurate diagnosis having high sensitivity and specificity and good inter-rater reliability. In our experience, the Nu-Desc is an accurate and useful tool to detect the occurrence of PD. The Nu-Desc 5-points scale questionnaire can be easily integrated into routine care and clinical practice and takes into account the underlying medical condition and unusual psychomotor retardation. A score of 2 or more correctly identifies the presence of PD. In order to detect PD, we suggest administering the Nu-Desc test every 6-8 hours and up to 72 hours in the post anesthesia period.[37]

Perioperative care of patients at risk for and affected by PD

Clinical management of PD is based on 4 steps: identification and treatment of underlying causes, use of supportive non-pharmacological

measures, pharmacological treatment of symptoms, clinical case review and follow-up.[45, 52]

Several non-pharmacological measures are effective in preventing and treating PD in the perioperative period: early mobilization and nutrition; verbal communication (with clear and repeated contacts by nursing staff and family and friends visits) and appropriate environmental stimuli (including eyeglasses and hearing aids and the provision of calendar and clocks to maintain time orientation); to minimize sleep deprivation and bowel and bladder dysfunction; and to reduce the use of invasive catheterization (central venous and bladder).[53-55]Maintaining a safe, familiar environment for the patient, with familiar objects, such as family photos or favorite possessions -that should be placed within reach for reassurance- will provide comfort. Having a clock and calendar within sight will help the patient stay in the present. Reorientation to time, place, and person when and if appropriate is often helpful. Soft, soothing music may promote a healing environment. Gentle reorientation and reassurances that you will keep them safe may help. Glasses and hearing aids must be in working order and properly placed to maximize communication. Family members should be allowed to stay with the patient, especially if the surroundings are unfamiliar, such as in a hospital. Physical restraints should never be used because they are a precipitating risk factor for delirium and can escalate the behaviors rather than alleviate them.[56] To minimize sleep deprivation is also extremely important and the use of earplugs does contribute to improve sleep quality and to reduce the incidence of PD.[57] The use of bright light therapy in the immediate postoperative period is effective in reducing the risk of PD. In a prospective study in patients treated for esophageal cancer exposed to the bright light straight after extubation, with intensity of the light of 5000lx immediately with a distance from the light source of 100 cm, the study group had a better delirium score and were ready to be discharged from the ICU 2 days earlier than control group.[58] Educational intervention may be also effective way in detecting risk factors and preventing delirium. In a prospective study a multicomponent strategy that included preoperative medical assessment, education, reorientation, and support, reduced risk of PD by 13 %.[59] Staff training is a critical step in the prevention and treatment of PD. An educational program that included a package for staff on one ward consisting of a 1 hour formal presentation and group discussion, written management guidelines and follow-up sessions designed for doctors and nurses was effective in reducing the prevalence of PD in a case control study.[60] Early diagnosis with the identification of delirium prodromal symptoms may help in treating PD and in minimizing its consequences through early intervention and timely identification and treatment of underlying causes. Therefore, staff needs to be vigilant to the development of such early symptoms.[61]

An effective non-pharmacological approach to reduce PD in elderly patients that undergoes surgery, is to involve a pro active geriatric consultation in the perioperative evaluation (preoperative or within 24 hours after surgery). In a prospective study in orthopedic surgery patients, geriatric evaluation with a structured interview that included 10 items (adequate CNS oxygen delivery, correction of fluid and electrolyte balance, treatment of severe pain, elimination of unnecessary medication, regulation of bowel and bladder function, adequate nutritional intake, early mobilization and rehabilitation, early detenction of postoperative complication, appropriate environmental stimuli, treatment of agitated delirium) effectively reduced the incidence of PD by over one-third.[62]

Etiology of PD is generally multifactorial and often involve abnormalities of physiologic variables. Acute anemia, electrolytes and volume disturbances and hypothermia are among the physiological variables that deserve tight monitoring and treatment.[63]

Pharmacological treatments to prevent and to treat PD encompass adequate oxygen supply and pain control.[8, 21] The symptomatic pharmacological treatment of PD is based on antipsychotic drug and haloperidol (1-10 mg/d, using a fixed dosing regimen - rather than "as required" - from the time of diagnosis) is the is the preferred agent.[16, 45] In those patients that develop PD it is important to schedule long term follow-up to

optimize long term prognosis.[47] To use antipsychotics drugs to treat PD, effectively decreases severity and duration of symptoms by 50%. Intravenous haloperidol is frequently used in ICU because of it induces limited sedation and limited anticholinergic effects but its use is associated with an increased risk of Q-T prolongation and extrapyramidal symptoms. The use of risperidone has the potential advantage of being not associated to anticholinergic activity and extrapyramidal effects although in elderly patients with dementia its use is potentially associated with increased mortality. Current guidelines of the Society of Critical Care Medicine recommend haloperidol as line treatment for delirium.[6, 9, 62]

While the use of benzodiazepine in the perioperative period is strongly discouraged because is associated with an higher incidence of PD (OR 3.0, with a dose dependant relationship, having each mg of midazolam is associated with up to a 7-8% incidence excess).[34, 36] Benzodiazepine have a therapeutic role when PD is associated with withdrawal syndrome form alcohol and chronic sedative use.[62, 63]

Profilactic citicoline use - a precursor for cell membrane components - has positive effect on memory and behavior in short-medium term in old people and can mitigate ischemic cell damage and has been successfully used to prevent and treat PD.[64] Several case reports demonstrate that prophilaxic use of donezepil -an acetylcholinesterase inhibitor, approved for the treatment of patients with Alzheimer disease- reduces the incidence of PD.[65]

Perioperative care for patients at risk for and affected by PD encompass non-pharmacological and pharmacological treatments. These measures, including the evaluation of timing of early postoperative cognitive recovery after anesthesia, when systematically included in the clinical practice effectively reduce the incidence, severity and complications related to PD.[66, 67]. In those patients that develop PD a dedicated follow-up monitoring is important to detect residual cognitive and behavioral disturbances. Given the multifactorial aetiology of PD, it is important to use dedicated strategies in the different clinical setting; overall in last 2 decades the clinical research in the field of PD has progressively reduced the room for pharmacologic therapies, while the management of risk factors along with the early detection and the use of supportive non-pharmacological measures are gaining the role of first tier therapies.[53, 60, 68]

Conclusions

Occurrence of PD is a serious perioperative complication that affects morbidity and mortality rates. To recognize individual risk factors is a prerequisite for optimal clinical management and should be accomplished right from patients admission, it allows to minimize modifiable risk factors and to address those patients at "high risk" to a dedicated path. Clinical willingness and the use of an appropriate diagnostic scale with a predefined time schedule, is associated with accurate and early diagnosis. Should PD develops appropriate care, by pharmacologic and non-pharmacologic therapeutic measures, is effective in reducing symptoms duration and short term and long term PD-related complications.

Key messages

— Occurrence of PD relates to an increased postoperative morbidity, mortality, length of hospital stay and poor long term outcome.

— Preoperative identification of risk factors for PD effectively contributes to select patients that need a dedicated perioperative care path.

— Tailored use of anesthetics, nursing surveillance and accurate staff communication contributes to reduce the incidence and clinical impact of PD.

— Systematic use of dedicated diagnostic tools, allows a prompt diagnosis should PD develops.

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