TRIPOM
An EBPOM Partner

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-
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Postoperative Cognitive Dysfunction

True or false

1. Post Operative Cognitive Decline:
- Is predictable in its onset
- Is a well recognised phenomenon
- Only affects those with established neurocognitive deficit
- Has a clear time frame of duration
- Affects up to 25% of those > 60 years for at least 1 week post-operatively

2. Proposed causes of of POCD include:
- Embolic
- Neuro-inflammatory
- Biochemical
- Anaesthetic toxicity
- Protein deposits

3. The following are recognised risk factors for POCD:
- High educational status
- Anaemia
- Age > 60
- Regional anaesthesia
- Depth of anaesthesia monitoring

4. Post Operative Delirium (POD) can be suggested by:
- Decreased activity
- New incontinence
- Quick changing emotions
- Altered sleep/wake cycle
- Rapid emergence from anaesthesia

5. It is recommended that:
- Anaesthetists avoid pre-medication
- Patients are assessed using the Montreal Mental State Examination (MMSE)
- All patients should be informed of the risk of POCD
- Midazolam should be given to patients with poor sleep
- Neurocognitive tests should be performed by a trained psychologist

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6. Management of POCD includes:

- Non-opioid pain control wherever possible
- Early orientation once back on the ward
- Post-operative risk assessment
- Post-operative cognitive assessment when POCD occurs
- Training of staff in recognition and management

Key points:

- Post operative cognitive decline is a well recognised phenomenon in cardiac surgery, and is becoming increasingly more important for an ageing population facing general surgery
- The consequences include earlier retirement, the use of more social services, and earlier mortality
- There is significant overlap in risk factors with dementia and delirium, and this reflects one of the challenges of nomenclature and diagnosis: that it is a non-homogenous process
- As yet, there is no consensus on the most appropriate diagnostic tool, and although the Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) are the most common so far, these are still open to bias and interpretation
- Consenting patients is a challenge, particularly in the face of incomplete research, data, and incidence.
- The pathophysiology is still unclear, although various hypotheses have suggested inflammatory, embolic, biochemical, and protein imbalances as possible factors.
- Anaesthetic management includes careful risk-assessment, avoidance of contributory drugs (sedatives, opioids, anticholinergics, increased depth of anaesthesia), and good post-operative care and re-orientation

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Introduction

Post-operative cognitive dysfunction (POCD) is defined as a new cognitive impairment arising after a surgical procedure. It is a recognised clinical phenomenon in patients

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undergoing major cardiac and non-cardiac surgery(1) and is commonly described as a short-term decline in cognitive function (especially in memory and executive functions), lasting a few days to a few weeks after major surgery(2) but may persist for several months(2) and has been implicated in long-term cognitive decline.

Bedford and colleagues first identified POCD in 1955 in a retrospective study published in the Lancet(3). He described it as "adverse cerebral effects of anaesthesia on old people". Fifty years later, the largest landmark study into non-cardiac POCD conducted by the ISPOCD study group demonstrated that amongst 1200 major non-cardiac surgical patients greater than 60 years old, POCD was present in 25.8% of patients at one week and 9.9% at 3 months post operatively (4). The impact of this is variable. It may be a decline of a few points on an MMSE, or it may be a global deterioration that prevents an individual living independently. Memory, cognitive processing and executive function are the key hallmarks, and a there is a temporal and pathophysiological distinction between delirium and dementia, although in practice these can often be difficult to separate and they may co-exist (5)

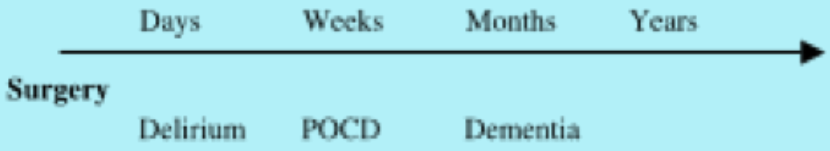

Fig. 1. Timeline in postoperative cognitive decline.

Defining POCD

Despite clinical recognition, POCD is not yet formally recognised in the International Classification of Diseases and is not listed as a diagnosis in the Diagnostic and Statistical Manual. The elusive nature of its diagnosis and management suggests that POCD is arguably under-reported and patients may be under-informed of the risk.

One of the main difficulties has been in finding a unifying definition. Broadly, POCD refers to deterioration in cognition alongside a temporal link to surgery. Research-based descriptions(6) have defined it as a "deterioration in performance in a battery of neuropsychological tests that would be expected in <3.5% of controls." In a consensus

statement by Murkin and colleagues(7), POCD after cardiac surgery was described as "a spectrum of postoperative central nervous system (CNS) dysfunction both acute and persistent ... including brain death, stroke, subtle neurologic signs and neuropsychological impairment." In more practical, clinically useful terms this equates to a catastrophic loss of cognitive ability representing a decline in a variety of neuropsychological domains including memory, executive functioning, and speed of processing.

Impact

Whilst for the vast majority, POCD seems to be a transient phenomenon, studies have demonstrated that it is still associated with impaired function, premature retirement, and increased welfare dependency8. For some patients, the impairment may even become permanent and its occurrence is a strong predictive risk factor for dementia in later life8,9. Whether this is causative, or whether there is an association due to poor physical health and reduced physiological reserve is unclear. What *has* been shown is that age is the biggest risk factor in developing POCD8. The patient group being studied often have significant co-morbidities, and the mere nature of being admitted to hospital have an increased risk of cognitive decompensation and delirium(10,11). POCD has been associated with increased duration of hospital stay, less productive working status leading to premature withdrawal from the labour market and an overall reduced quality of life (12). This can significantly impact on both health resource utilisation and patients' health-related quality of life and rehabilitation.

Diagnosis

Diagnosing POCD is dependent upon pre- and post-operative psychometric testing assessing cognitive performance, and this poses a significant practical challenge. Initial variability in choice of testing led to the consensus guideline, highlighting 4 core tools (Rey auditory verbal learning test, Trail-making A, Trail-making B, Grooved pegboard (7). However, there was no theoretically derived model on which to base appropriate test choice when considering the outcome of surgical experience. In addition, the consensus guidelines had no explanation of how the tests within the battery met the consensus definition of POCD so raised doubt as to whether they were in fact assessing the presence and effect of POCD.

More recent systematic reviews of POCD after cardiac 7 and non-cardiac12 surgery reveal that the two most commonly assessed cognitive domains assessed were 1) learning and memory and 2) attention and concentration. Test selection is guided by

choosing those that have been validated for detecting changes in those domains expected to be negatively affected by the surgical experience. Investigators agree that baseline tests, practice bias and testing through more than one neuropsychological method should be considered in any scoring system(12).

More commonly, composite measures have been widely used in the literature. Rasmussen et al(13) support composite scoring systems justifying them as being necessary to support the diagnosis of general decline rather than looking at specific changes in cognitive function. The Mini Mental State Examination (MMSE) has been widely used; Newman et al(12) in their systematic review concluded that MMSE was used in up to 21% of reviewed studies and has been the assessment of choice. More recently, The Montreal Cognitive Assessment (MoCA) has gained favour amongst clinicians responsible for managing POCD patients in the short and longer term. In an observational cohort study by Partridge et al(14) assessing cognitive impairment in older vascular surgical patients, the MoCA was used as a bedside assessment tool. The 30 point assessment takes 10 minutes to complete and has high retest reliability (correlation coefficient 0.92; $p<0.001$) and internal consistency (Cronbach 〈 0.83) with a mixed study cohort of patients with mild to more severe cognitive impairment (15) mportantly, this could be used in the elective and emergency setting where a full battery of tests is not appropriate, and it has been shown to be superior to the MMSE in terms of sensitivity and specificity(16)
[1]

Timing of the test also plays an important part of diagnosing POCD as it can be can be broadly divided into acute, intermediate and late/long-term. Acute POCD describes cognitive decline occurring within one week after surgery, intermediate POCD for changes within 3 months, and long-term POCD for changes 1-2 years following surgery. In a recent review of POCD by Tsai et al (17) the authors emphasise performing neuro-cognitive testing and delirium assessment simultaneously within the first several days after surgery will improve understanding of the relationship between POCD and delirium, particularly as most cases of delirium occur in the early postoperative period. As delirium is associated with deficits in attention (as is POCD), the Confusion Assessment Method (CAM) score is a validated scoring system with high sensitivity and specificity for detecting POD (Post Operative Delirium)(18).

Distinguishing Delirium:

Three clinical conditions are worthy of discussion and need to be distinguished from each other, and they are delirium, dementia, and postoperative cognitive dysfunction (POCD). Delirium is an acute confusional state featuring disturbances in attention and

decreased awareness of the environment(6) patients may display inappropriate communication or behaviours and this may be accompanied by hallucination, disorientation, or temporary memory dysfunction. Importantly, the patient may express *hyper*-active but also *hypo*-active (or *mixed*) behaviours, and it should be remembered that a reduction in interaction may indicate acute delirium.

Post Operative Delirium is a reversible change in mental status occurring shortly after surgery and is associated with delayed recovery and increased mortality(19). POCD in contrast is new cognitive impairment arising after a surgical procedure. It is a more persistent condition identified by neuropsychological testing which demonstrate a decline in cognitive function without an alteration in mental status or awareness(20). A typical patient with POCD is oriented but exhibits a significant decline from his or her own baseline level in one or more neuropsychological domains. After surgery, changes in cognitive status may present in the form of a frank delirium or POCD, or both.

Table 3. Symptoms Associated with Delirium

1. Change in level of arousal: drowsiness or decreased arousal*or increased arousal with hypervigilance
2. Delayed awakening from anesthesia*
3. Abrupt change in cognitive function (worsening confusion over hours or days), including problems with attention, difficulty concentrating, new memory problems, new disorientation
4. Difficulty tracking conversations and following instructions
5. Thinking and speech that is more disorganized, difficult to follow, slow,* or rapid
6. Quick-changing emotions, easy irritability, tearfulness, uncharacteristic refusals to engage with postoperative care
7. Expression of new paranoid thoughts or delusions (ie, fixed false beliefs)
8. New perceptual disturbances (eg, illusions, hallucinations)
9. Motor changes such as slowed or decreased movements,* purposeless fidgeting or restlessness, new difficulties in maintaining posture such as sitting or standing*
10. Sleep/wake cycle changes such as sleeping during the day* and/or awake and active at night
11. Decreased appetite*
12. New incontinence of urine or stool*
13. Fluctuating symptoms and/or level of arousal over the course of minutes to hours

*Hypoactive symptoms.

Pathophysiology

Although the exact mechanism of POCD is unknown, different mechanisms have been proposed, and among them embolic, neuro-inflammatory, and biochemical theories tend to predominate. Other mechanisms include an exacerbation of existing impairment, damage due to anaesthetic drugs, and protein damage (such as S-100 beta protein)(21). However, it is agreed that it is undoubtedly multifactorial, with a number of non-modifiable and modifiable factors reported to have a contributory effect.

The ISPOCD study(4) found that at 3 months POCD was found in 7% of patients aged 60-69 and in 14% of patients over 69. In this study age was the single strongest predictor, with pre-existing cognitive impairment, multiple co-morbidities, and lower education level all contributing to *non-modifiable* risk. Intra-operative, post-operative, and surgical related complications again contributed further *modifiable* risk, but despite this, it remains inconclusive how surgery and anesthesia type actually affects POCD.

As cognitive impairment predominates in the older population, it follows that a rise in cardiovascular disease in the older population leaves the, vulnerable to to the risk of developing POCD or POD. Risk factors for peripheral vascular or aortic disease (hypertension, hyperlipidaemia, and smoking) predisposes patients to vascular cognitive impairment and have been shown to be independently associate with POD and POCD.

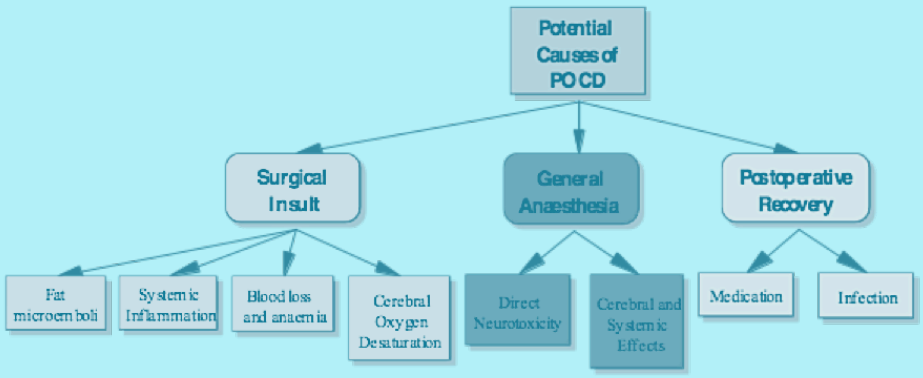

Figure [16]

In the UK, Partridge et al (14) undertook a prospective observational cohort study in older vascular surgical patients undergoing elective or emergency vascular procedures (aortic or lower limb arterial interventions). They demonstrated a significant burden of undiagnosed cognitive impairment in patients over 60 years of age (67.5% with a MOCA score < 24/30) advocating preoperative assessment of cognitive dysfunction in a high risk population.

Figure [5]

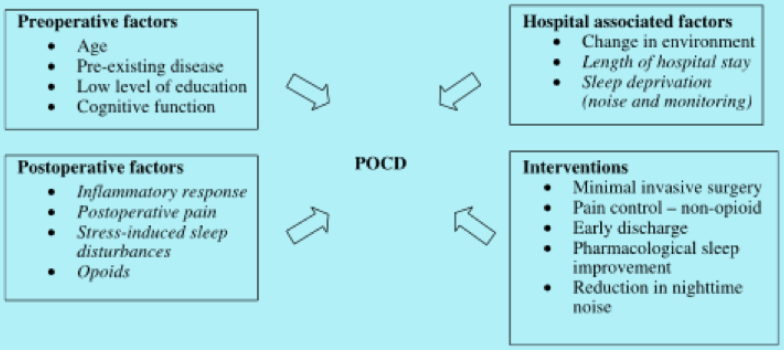

Fig. 2. Pathogenic mechanisms for POCD and possible interventions. Italics, not yet evaluated.

Risk Assessments

An integral part of the American Geriatric Society 2015 guidelines has been risk assessment of the potential POD/POCD patient(22). Pre-operative risk assessments of physiological frailty and co-morbidities help to inform physicians and surgeons of the risks involved of conducting extensive surgical procedures on an elderly co-morbid patient. In the high risk patient this may prompt more invasive intra-operative monitoring, such as arterial lines, the use of cerebral oxygenation monitoring, and depth of anaesthesia monitoring. Post-operative neuropsychological testing should then be conducted by a trained, multidisciplinary team.

Pre-operative Screening For Risk Factors

(This is not an exclusive list, but the general principle is that any factors that increase the frailty score, will increase the risk of POCD)

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Patient:	**Age >65yrs (the most significant risk factor)**
	Education level
	Existing cognitive impairment
	Severe co-morbidities
	Anaemia
	Poor nutrition
	Presence of infection
	Alcohol use
Anaesthetic:	**Depth of Anaesthesia**
	Hypoxia/hypercarbia
	Electrolyte abnormalities
	Mode of analgesia
Surgical:	**Length of surgery**
	Second operation
	Intraoperative haemorrhage

Interventions

Interventions capable of reducing the occurrence of POD/POCD are important from a public health perspective and the emphasis is on prevention. With the knowledge of potential risk factors, recent clinical practice guidelines have included number of evidence-based recommendations on how the perioperative management of surgical patients can help prevent POCD in the elderly surgical patient (22,23).

These recommendations include:
Intraoperative Management

- Avoidance of psychoactive medications (sedatives, anti-cholinergics, steroids)
- Avoid hypoxia/hypotension

- Minimise length of anaesthesia/surgery
- Minimise use of opioids
- Use of depth of anaesthesia monitoring (BIS/EEG) is suggested, but an evidence base is still lacking
- Some evidence to suggest regional anaesthesia reduces POCD rates initially, but the rate of persistent POCD at 3 month is the same(13)

Post-operative Management

- Active reorientation in recovery, and early treatment of pain/nausea
- Haloperidol for management of POD
- Post-op cognitive assessment to compare to pre-operative function
- Cognitive rehabilitation

Delirium

- Training in recognition of delirium, and its subsequent management
- Well documented pre-operative cognitive function in at-risk patients

Conclusions

In summary, POCD is a recognised yet diagnostically elusive phenomenon. There is clear evidence that it occurs, yet the precise diagnostic criteria may depend on complex neuro-cognitive testing, and is still open to debate. The aetiology is still to be clarified, and most likely it has a multifactorial pathophysiology encompassing embolic, inflammatory, and biochemical aspects. There is also symptomatic overlap with dementia and post-operative delirium, further complicating the diagnosis.

The effect of this is to complicate discussion and management of the condition, and there are further issues in adequately consenting patients about a condition in which we are unaware of the precise incidence, diagnosis, and appropriate management.

What can be surmised from the existing research however, is that the phenomenon is real and that its significance will increase with an ageing, and increasingly frail population. Increased use of social resources and earlier retirement have been demonstrated, and the occurrence of POCD has been shown to be a strong predictor of dementia in later life.

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The management starts with identifying high-risk patients, assessing their cognitive function using an appropriate scoring system, and adequately consenting the patients as to surgical risk. Intraoperative management consists of good anaesthesia - avoidance of hypoxia, hypotension, pain, acidosis, electrolyte imbalance, and monitoring adequate depth of anaesthesia. Following this, post-operative prevention/treatment of delirium and assessment of function are important in determining any cognitive decline. Whether this can be treated is difficult to predict and the main aim of identifying risk is to prevent the occurrence. Just as anaesthesia on the developing brain is not undertaken lightly, anaesthesia on the 'cognitively at-risk' should also not be taken lightly. It should be considered it in all at-risk patients, and steps should be taken to counsel for it and prevent it wherever possible.

Answers:

1 FTFFT
2 TTTTT
3 FTTTF
4 TTTTF
5 TFFFF
6 TFFFT

References

1 1.Rundshagen I. Postoperative Cognitive Dysfunction. *Deutsches Ärzteblatt International*. 2014;111(8):119-125. doi:10.3238/arztebl.2014.0119.
2 Tsai TL, Sands LP, Leung JM. An Update on Postoperative Cognitive Dysfunction. *Advances in anesthesia*. 2010;28(1):269-284. doi:10.1016/j.aan.2010.09.003.
3 Bedford PD. Adverse cerebral effects of anaesthesia on old people. Lancet 1955; 269
4 Moller JT, Cluitmans P, Rasmussen LS, Houx P et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998 Mar 21;351(9106):857-61
5 Krenk L , Rasmussen, LS and Kehlet H. (2010), New insights into the pathophysiology of postoperative cognitive dysfunction. Acta Anaesthesiologica Scandinavica, 54: 951–956.

6 Fines DP, Severn AM; Anaesthesia and cognitive disturbance in the elderly. *Contin Educ Anaesth Crit Care Pain* 2006; 6 (1): 37-40. doi: 10.1093/bjaceaccp/mki066
7 Murkin J, Newman S, Stump D, Blumenthal J. Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. Annals of Thoracic Surgery 1995 May;59(5):1289-95
8 Steinmetz J, Christensen KB, Lund T, Lohse N, Rasmussen LS. Long-term consequences of postoperative cognitive dysfunction. Anesthesiology. 2009;110:548–55
9 Bekker AY, Weeks EJ (2003) Cognitive function after anaesthesia in the elderly. Best Pract Res Clin Anaesthesiol 17: 259-272
10 Selnes OA, Royall RM, Grega MA, Borowicz LM Jr, Quaskey S, et al (2001) Cognitive changes 5 years after coronary artery bypass grafting: is there evidence of late decline? Arch Neurol 58: 598-604
11 Canet J, Raeder J, Rasmussen LS, Enlund M, Kuipers HM, et al. (2003) Cognitive dysfunction after minor surgery in the elderly. Acta Anaesthesiol Scand 47: 1204-1210
12 Newman S, Stygall J, Hirani S, Shaefi S, Maze M. Postoperative cognitive dysfunction after noncardiac surgery. Anesthesiology. 2007;106:572–590
13 Rasmussen LS, Johnson T, Kuipers HM, et al. Does anaesthesia cause post- operative cognitive dysfunction? A randomised study of regional versus general anaesthesia in 438 elderly patients. Acta Anaesthesiol Scand 2003; 47: 260–6
14 Partridge JS, Dhesi JK, Cross JD, Lo JW et al. The prevalence and impact of undiagnosed cognitive impairment in older vascular surgical patients. J Vasc Surg. 2014 Oct;60(4):1002-11.e3. doi: 10.1016/j.jvs.2014.04.041. Epub 2014 Jul 11
15 Pendlebury ST, Cuthbertson FC, Welch SJ, et al. Underestimation of cognitive impairment by Mini-Mental State Ex- amination versus the Montreal Cognitive Assessment in patients with transient ischemic attack and stroke: a population-based study. Stroke 2010;41:1290-3
16 Gauge N. Long Term Post-Operative Cognitive Dysfunction; A 12 month longitudinal cohort study of elderly non- cardiac patients. British Geriatric Amulree Prize Essay 2011. https://www.scribd.com/document/267660120/2011-Gauge-Amulree
17 Tsai TL, Sands LP, Leung JM. An Update on Postoperative Cognitive Dysfunction. *Advances in anesthesia*. 2010;28(1):269-284. doi:10.1016/j.aan.2010.09.003
18 Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method (CAM): A Systematic Review of Current Usage. *Journal of the American Geriatrics Society*. 2008;56(5):823-830. doi:10.1111/j.1532-5415.2008.01674.x.
19 Rundshagen I. Postoperative Cognitive Dysfunction. *Deutsches Ärzteblatt International*. 2014;111(8):119-125. doi:10.3238/arztebl.2014.0119

20 Hanning CD. Postoperative cognitive dysfunction. Br J Anaesth. 2005;95:82–7
21 C. Aldecoa, G. Bettelli, F. Bilotta et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol 2017; 34:192–214
22 American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. J Am Geriatr Soc. 2015 Jan;63(1):142-50. doi: 10.1111/jgs.13281. Epub 2014 Dec 12.
23 M.P. Vizcaychipi, Post-Operative Cognitive Dysfunction: Pre-Operative Risk Assessment and Peri-Operative Risk Minimization: A Pragmatic Review of the Literature (2016). Journal of Intensive and Critical Care. Vol 2, No 2: 13