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# Delirium after cardiac surgery. Incidence, phenotypes, predisposing and precipitating risk factors, and effects

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ABSTRACT

*Background:* In cardiac surgical patients little is known about different phenotypes of delirium and how the symptoms fluctuate over time.
*Objectives:* Evaluate risk factors, incidence, fluctuations, phenotypic characteristics and impact on patients' outcomes of delirium.
*Methods:* Prospective longitudinal study. In postoperative intensive care unit 199 patient were assessed three-times a day through an adapted versions of the Intensive Care Delirium Screening Checklist.
*Results:* Delirium and subsyndromal delirium incidence were 30.7% and 31.2%, respectively. Delirium manifested mostly in the hypoactive form and showed a fluctuating trend for several days.

Atrial fibrillation, benzodiazepine/opioids dosages, hearing impairment, extracorporeal circulation length, SAPS-II and mean arterial pressure were independent predictors for delirium. Delirium was a statistically significant predictor of chemical/physical restraint use and hospital length of stay.
*Conclusions:* Given the fluctuating and phenotypic characteristics, delirium screening should be a systematic/intentional activity. Multidisciplinary prevention strategies should be implemented to identify and treat the modifiable risk factors.



## Introduction

Delirium is a syndrome characterised by an acute change in mental status which can affect patients during an intensive care unit (ICU) stay.[1] According to the Diagnostic and Statistical Manual of Mental Disorders (DSM) V,[2] delirium is characterised by a disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention), awareness (reduced orientation to the environment) or cognition (e.g. disorientation, language, visuospatial ability, or perception). While such symptoms must not be attributable to a pre-existing or evolving dementia, the patient's clinical history, physical and cognitive assessment, or laboratory findings must point to a direct relationship of the disorder with the physiological consequences of a general medical condition.[2,3] After surgery, delirium symptoms typically have a rapid onset (hours to days), tend to fluctuate during the course of the day and usually resolve within 48 hours, although they can persist for longer.[4] Delirium can present with different cognitive and behavioural clinical characteristics; recognizing and understanding different phenotypes of delirium can improve clinical care.[5] For example, delirium can present with a combination of hyper- and hypoactive phenotypes, while some patients might show an acute change in cognition that does not meet full criteria for delirium (subsyndromal delirium).[5,6]

Although still poorly understood, the pathophysiological mechanism of delirium in postoperative cardiac surgery patients is considered to be multifactorial, resulting from a combination of pre-existing factors (e.g. older age, diabetes, atrial fibrillation, serum albumin) and precipitated by intra-operative and postoperative triggers (e.g. combined coronary artery bypass graft [CABG] and valvular surgery, low cardiac output, hypothermia, hypoxia, metabolic acidosis, poor pain control, use of extracorporeal circulation, duration

*Abbreviations:* AF, atrial fibrillation; APACHE, Acute Physiology and Chronic Health Evaluation; CABG, coronary artery bypass graft; CAM-ICU, Confusion Assessment Method for the ICU; DSM, Diagnostic and Statistical Manual of Mental Disorders; ECC, extracorporeal circulation; IABP, intra-aortic balloon pump; ICDSC, Intensive Care Delirium Screening Checklist; ICU, intensive care unit; LOS, length of stay; MAP, mean arterial pressure; MV, mechanical ventilation; OR, odds ratio; PICU, postoperative ICU; RASS, Richmond Agitation-Sedation Scale; SAPS, Simplified Acute Physiology Score; SD, standard deviation; SE, standard error.

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of surgery and mechanical ventilation [MV], effects of drugs such as benzodiazepines or inotropes).[7–12] Consequently, the risk factors associated with postoperative delirium can be classified according to whether they (1) predispose patients to or precipitate delirium or (2) are modifiable or non-modifiable.[1] In general, whereas predisposing factors relate to the patient's health history, precipitating factors relate to the patient's perioperative clinical conditions and the delivered or missed medical and nursing care.

In cardiac surgery patients the postoperative delirium reported incidences range between 3% and 70%.[9] This large variability depends on several factors such as the characteristics of patients (e.g. age, severity of illness) and the ability of the evaluators to recognise the delirium.[13,14] It is particularly difficult to identify delirium in critically ill patients because a standard clinical examination does not have adequate accuracy to detect this condition.[15] For this reason, all ICU patients need to be routinely monitored for delirium using a valid, reliable and easy to use standardised assessment tool[16,17] that accurately evaluates the primary components of delirium, i.e. consciousness, inattention, disorganised thinking and fluctuating course.[18]

The occurrence of delirium in cardiac surgical patients can affect the nursing workload[19,20] and negatively impact patient outcomes in terms of longer length of MV, longer length of stay (LOS) in ICU and hospital, higher hospital and late mortality, and long-term cognitive impairment.[1,21,22] For all these reasons, physicians and nurses have to give delirium the same attention they give to organ system failures in ICU patients;[23] developing a better understanding of the timing and fluctuation characteristics of delirium will help them to identify risk factors that can potentially be modified to reduce the impact of this syndrome on brain dysfunction and patient outcomes.[9] However, even though cardiac surgery patients are among the most extensively studied populations for postoperative delirium,[24] little is known about the characteristics of patients having one or more episodes of delirium[25] or the prevalence of subsyndromal delirium, and the relationship between such conditions and patient outcomes.

Therefore, the aim of this study is to evaluate the incidence of delirium and subsyndromal delirium in a postoperative cardiac surgery population and to describe the time of onset, the duration and the phenotypic characteristics of the condition. Furthermore, this study explores the demographic, clinical and treatment-related predictive factors for delirium occurrence and analyses the impact of delirium on the length of ICU and hospital stays.

## Materials and methods

### *Study design, setting and population*

This prospective observational longitudinal study was carried out in the 10-bed postoperative ICU (PICU) of the Cardiac Surgery Unit of the Trieste University Hospital in Italy. All adult patients (aged > 17 years) undergoing open-chest cardiac surgery and extracorporeal circulation (ECC), admitted to the PICU, and who were able to understand and speak the Italian language were considered eligible for the study, irrespective of whether or not they were mechanically ventilated. Based on their past medical history, patients were excluded if they had pre-existing dementia or neuropsychiatric disorders, such as mood disorders (e.g. bipolar disorder), neurotic disorders (e.g. obsessive compulsive disorder) or psychosis (e.g. schizophrenia). Moreover, patients were excluded if they showed a level of consciousness precluding delirium assessment for the entire observation period (as explained below in Procedure section).

A minimum required sample size of 187 patients was calculated a priori for a multiple regression model including 30 predictors to detect a medium anticipated effect size ($f^2$) of 0.15 with a probability of a type I error of 0.05 and a desired statistical power level of 0.8.[26]

### *Delirium screening tool*

The Confusion Assessment Method for the ICU (CAM-ICU)[27] and the Intensive Care Delirium Screening Checklist (ICDSC)[28] have been validated for non-comatose critically ill patients with variable degrees of alertness[29] and showed the strongest level of evidence to support their use in clinical practice.[21] Both tools have beneficial features that would justify their use at different times or even jointly.[15] The ICDSC was adopted as the delirium screening tool in the present study since, compared to the CAM-ICU, (1) is more accurate in cardio-surgical ICU patients, (2) evaluates more symptoms of delirium and (3) can identify subsyndromal delirium.[21,30,31]

Nevertheless, the ICDSC presents some potential weaknesses, since it relies solely on observational methods to detect *inattention*, *disorientation*, *hallucinations/delusion*, *sleep disturbance*, and *inappropriate speech or mood*; these features might be particularly difficult to detect and come with the risk of subjective interpretation.[17] Conversely, CAM-ICU describes in detail how to evaluate each feature by using specifically defined, validated and much more objective measures requiring interaction with the patient (e.g. by asking the patient to perform tasks like recognising images, answering 'yes' or 'no' to simple logic questions, or executing simple commands), providing a reproducible measure.[6] For example, the field of *disorganised thinking*, which evaluates whether the patient's thinking is disorganised or incoherent (e.g. rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject),[32] is objectively assessed by the CAM-ICU, but it is not evaluated in any depth by the ICDSC because the creators considered a more detailed evaluation of cognitive functions too time-consuming.[28]

Based on above considerations, similar to previous studies,[33] the ICDSC was adapted to ensure that each item contained detailed instructions, key questions or psychometric methods to which the nurses had to refer (available as Supplementary item). In detail:

- items 1 and 2 were replaced respectively with features 3 (*altered level of consciousness*) and 2 (*inattention*) of the CAM-ICU
- item 3 was integrated by listing standard examples, as suggested by the ICDSC
- items 4, 5, 7 and 8 were assessed based on the changes proposed by Gesin et al.[33]
- item 6 aims to assess *inappropriate speech or mood*. Inappropriate speech (e.g. rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject) is a symptom that the patient's thinking is disorganised or incoherent[32]; this aspect is not further clearly evaluated by the ICDSC. Moreover, inappropriate speech assessment is precluded in intubated patients.[17] Consequently, for patients who were able to talk, the indications of the Aberrant Behavior Checklist to identify patients presenting with inappropriate speech were used,[34] while for intubated patients the assessment was performed by adopting the method suggested by the CAM-ICU in feature 4 (*disorganised thinking*).

### *Procedure*

Before starting the study, a group of four research nurses was trained to detect delirium using the adapted ICDSC tool as described in previous section. At the end of the training, 10 patients were independently evaluated by such nurses and assessment