

Delirium in the Cardiac Intensive Care Unit

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Delirium is an important diagnosis, both because it is challenging to manage and because it portends a poor prognosis in the hospital and beyond.¹ Delirium is particularly prevalent in the intensive care unit (ICU) setting, where it is associated with longer hospital stays,² prolonged mechanical ventilation,³ increased hospital costs,⁴ and increases in mortality.¹ In fact, studies have shown the incidence of delirium in mechanically ventilated patients to be as high as 85%.^{5,6} Furthermore, the negative ramifications of delirium extend beyond hospitalization, as afflicted patients are less likely to be discharged home and more likely to have long-term cognitive impairment.⁷ Consequently, prevention as well as prompt identification and treatment of delirium in the ICU is critical.

While ICU delirium has been the subject of intense research and numerous review articles, little attention has been placed on the unique aspects of delirium related to patients in the cardiac ICU (CICU). In this article, we review recent understanding of the etiology, epidemiology, prevention, and treatment of delirium in the CICU, concluding with suggested future directions.

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Definition and Subtypes

Delirium is a syndrome defined by the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-V), as an acute onset of a fluctuating disturbance in the following cognitive functions: attention; environmental awareness; and cognition and/or perception.⁸ Delirium may be most readily identified in patients with sleep/wake cycle disturbances, emotional lability, hallucinations or delusions; however, none of these are required for a diagnosis. There are three subtypes based on patients' motor activity: hypoactive, hyperactive, and mixed (Figure 1).⁹

Etiology of ICU Delirium: General and CICU Specific

The pathogenesis of ICU delirium is complex, with contributions from neurotransmitter alterations, physiological stressors, metabolic derangements, inflammation, electrolyte imbalances, and genetic factors. The development of delirium typically depends on a combination of predisposing, often nonmodifiable, risk factors, which are then subject to a "second hit" in the form of precipitating, often modifiable, factors (Figure 2).¹⁰ Both predisposing and precipitating factors are common in the CICU, as in other ICU settings. The vulnerability of the patient has significant influence on the development of delirium. In vulnerable patients, such as those with underlying dementia and multiple comorbidities, a mild insult, such as an uncomplicated urinary tract infection, may be enough to precipitate delirium. Conversely, in a young healthy patient, delirium may only occur after exposure to a series of insults, such as general anesthesia, sleep deprivation, multiple psychoactive medications, and an ICU stay.

The CICU has grown considerably more complex from its original inception as a unit treating sequelae of acute myocardial infarction and has several unique risk factors for delirium.^{11,12} For example, advanced heart failure patients are now commonplace in the CICU, as are temporary¹³ and permanent¹⁴ mechanical ventricular support devices. These devices may contribute to delirium given prolonged immobility and increased need for sedative medications. Other advances such as transcatheter aortic valve replacement (TAVR) have

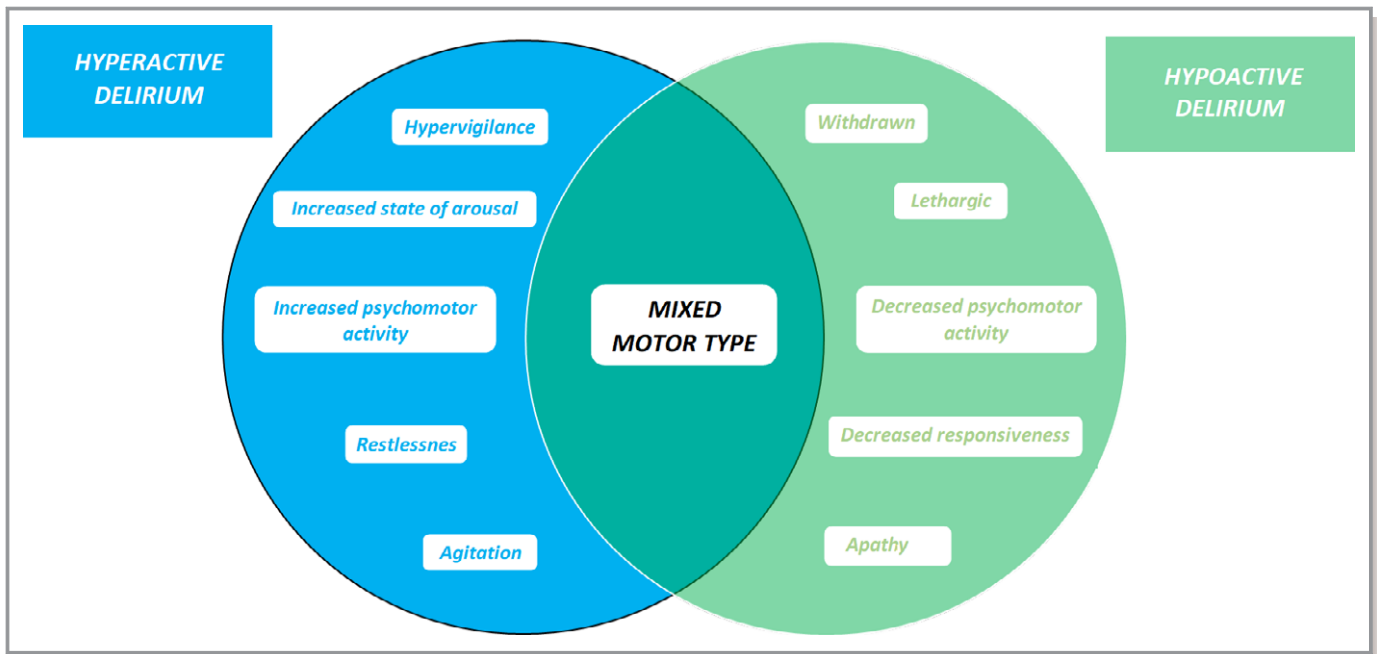


Figure 1. Subtypes of delirium and their characteristics.

enriched the CICU population with frail older patients.¹⁵ There is considerable use of targeted temperature management in CICU patients who have survived cardiac arrest, with high rates of delirium.¹⁶ In addition to the changing landscape of CICU technology and cardiology case-mix, there have also been concomitant increases in patient complexity.¹²

The following are considerations of particular relevance for the practicing CICU cardiologist:

1. Patients with heart failure may be especially predisposed to delirium with an incidence rate as high as 1 in 3 patients.¹⁷ B-type natriuretic peptide concentrations are often higher in patients with delirium, the link possibly

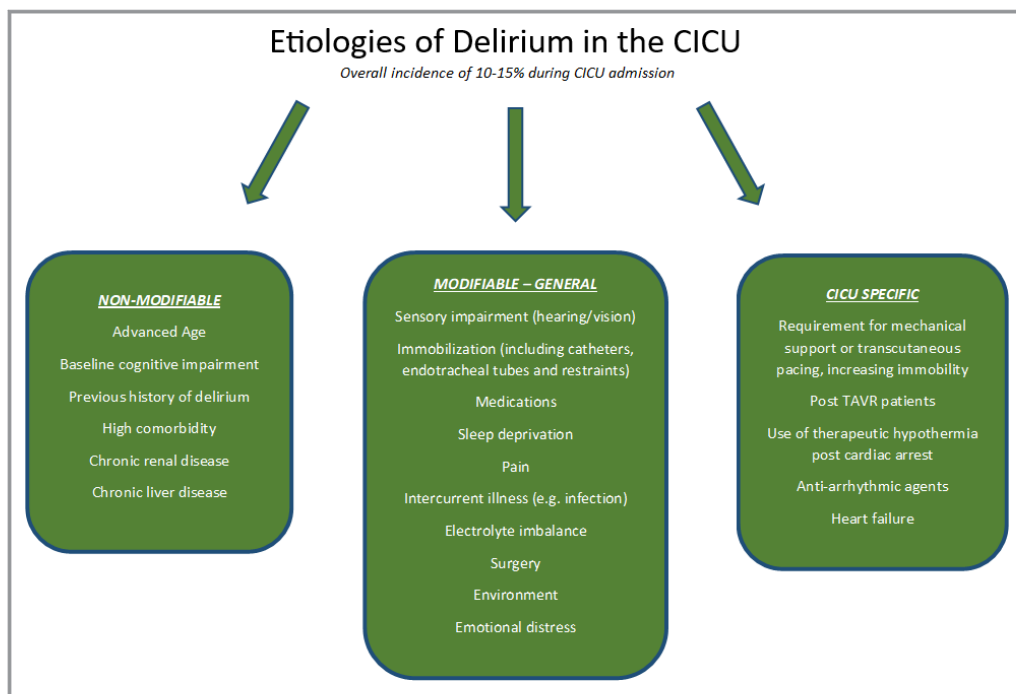


Figure 2. Risk factors and etiologies of delirium in the cardiac intensive care unit. TAVR indicates transcatheter aortic valve replacement, mechanical support refers to extracorporeal membrane oxygenation, impella, or other temporary cardiac support.

- being cerebral hypoperfusion in the setting of a low cardiac output.¹⁷ Plasma clearance of deliriogenic medications is also reduced in heart failure, which can result in toxicity at standard doses.¹⁸
- Hardware-related immobility is a significant risk factor for CICU delirium. In addition to use of urinary catheters, vascular access devices, and endotracheal intubation, both temporary mechanical circulatory support and temporary cardiac pacing function as restraints in the CICU. A prospective study of 200 patients in the CICU reported that those with restraints or devices that precluded mobilization were more likely to develop delirium (odds ratio: 2.9, $P<0.01$).¹⁹
 - Patients undergoing TAVR are also at high-risk for delirium. The incidence of delirium appears to be higher in patients undergoing nontransfemoral TAVR compared with transfemoral (50% versus 10%; $P<0.001$).¹⁵ This association may reflect the presence of advanced vascular disease seen in the nontransfemoral cohort rather than a causal effect of access site.¹⁵ Ischemic brain injury is hypothesized as an additional risk factor for delirium in this cohort, triggered by cerebral embolization of aortic plaque or valve particles dislodged during prosthesis positioning and deployment.²⁰ Cerebral protection devices may reduce stroke in TAVR patients.²¹ A recent randomized trial of cerebral embolic protection in surgical aortic valve replacement patients suggested a reduction in delirium, a finding that warrants future study in the TAVR cohort.²²
 - The CICU also commonly admits patients after cardiac arrest. One recent study demonstrated that 100% of 107 noncomatose survivors of cardiac arrest who received targeted temperature management in the ICU had at least 1 day of delirium during their ICU stay, with a median delirium duration of 4 days (interquartile range, 2.0–7.5).¹⁶ However as there was no matched comparison group in this study, it is unclear whether the development of delirium was a consequence of targeted temperature management or if it was instigated by impaired cerebral

perfusion from the initial insult of the cardiac arrest, and this warrants further investigation.

- Several cardiovascular agents have been shown to be associated with delirium including: procainamide,²³ metoprolol,²⁴ lidocaine,²⁵ amiodarone,²⁶ and digoxin.²⁷ However, these reported associations are limited by the fact they are based on case reports. Lidocaine deserves a particular mention as it has been associated with a range of psychiatric reactions, it's often administered by cardiologists as a continuous intravenous infusion over many hours, and has drug levels that can be measured to assist with evaluation of toxicity.

Epidemiology

The reported burden of delirium in the CICU has varied greatly, likely reflecting the screening tool and methodology used for assessment (Table 1). In one cross-sectional study of 590 CICU patients, rate of delirium was 20% and had higher ICU mortality (27% versus 3%; $P<0.001$).²⁸ Whether delirium causes death or is a marker of people at high risk of death, or both, is not fully known. A recent prospective study of 726 European CICU patients reported that 15% of these patients were diagnosed with delirium during their hospital stay, a rate which was 50% in patients over the age of 85 years.²⁹ Another prospective study of 309 patients admitted to the CICU, found a 19% prevalence of delirium, with a 2-month incidence rate of 9% among those who were free of delirium at baseline.³⁰ Similarly, in the largest prospective study to date by Naksuk et al, the incidence rate of delirium among 11 079 patients was 8% while in the CICU.³¹

Screening

Despite the common occurrence of delirium in the CICU, cardiologists are often ill-prepared to diagnose, prevent and treat this condition. While this may not differ from physicians

Table 1. Cardiac ICU Specific Delirium Studies

Article	Study Enrollment Years	Study Design	Number of Patients	Prevalence/Incidence (Combined) of Delirium	In-Hospital Mortality	Limitations
Pauley et al ²⁸	2012 to 2014	Prospective observational study	590	NR/NR (20.3%)	33%	Single center, retrospective, observational
Falsini et al ²⁹	2014 to 2015	Prospective observational study	726	6.3%/8.9% (15.3%)	17.1%	Only two centers, observational
Lahariya et al ³⁰	2010	Prospective observational study	309	18.77%/9.27% (28.8%)	27%	Single center, observational
Naksuk et al ³¹	2004 to 2013	Prospective observational study	11 079	NR/8.3% (NR)	17.3%	Single center, observational

NR indicates not reported.

working in other ICU settings, further education of cardiologists is needed. For example, without routine use of assessment tools, delirium often goes undiagnosed; with ICU physicians recognizing as little as one-third of delirious critically ill patients.³² Several screening tests for delirium have been developed,³³ however, only 2 are recommended by the Society of Critical Care Medicine³⁴: the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Figure 3) and the Intensive Care Delirium Screening Checklist (ICDSC).

A meta-analysis of 5 ICU delirium screening tools found that the CAM-ICU and ICDSC screening tests were the most sensitive and specific tools for identifying delirium.³⁵ In another systematic review and meta-analysis of nine studies evaluating CAM-ICU (including 969 patients) and four evaluating the ICDSC (including 361 patients), the pooled sensitivity of CAM-ICU was 80% (95% confidence interval (CI): 77–83%), with a specificity of 96% (95% CI: 95–97%) and an AUC of 0.97. The pooled sensitivity of ICDSC was 74% (95% CI: 65–82%), with a specificity of 82% (95% CI: 77–86%) and an AUC of 0.89.³⁶ While not developed specifically for ICU, the 3D-CAM is also a useful tool with a median assessment time of just 3 minutes.³⁷ Implementation of screening tools has been shown to be feasible on daily rounds and requires minimal training of nurses to implement. Therefore every attempt should be made to incorporate it as a daily report on rounds.³⁸

Prevention

Central to the management of delirium is effective prevention (Figure 4), as treatment options are more limited. Nonpharmacological methods of prevention focus on minimizing the disorienting aspects of hospital care and are proven to reduce delirium in the non-ICU setting.³⁹ Several studies have demonstrated that implementing a multicomponent structured approach to reorientation including: the use of clocks and calendars; daily reminders to the patient on date, time, place, and reason for hospitalization; sleep preservation by avoiding late night medication administration; early mobilization from bed; early urinary catheter removal; and use of home hearing aids and glasses may reduce the incidence and duration of delirium compared with usual care.^{40,41} Unfortunately, to our knowledge, no data have reported on how often such reorientation strategies are performed in the CICU setting.

Balas et al, implemented the combination of awakening and breathing coordination, delirium monitoring/management and early exercise/mobility (ABCDE) bundle in intubated ICU patients. In this pre-post comparison, a 50% decrease in the odds of delirium was reported (OR 0.55, $P=0.03$).⁴² Note that

“awakening and breathing coordination” refers to frequent use of spontaneous awakening trials and spontaneous breathing trials. In addition, several trials have demonstrated that physical and occupational therapy decrease delirium in the ICU. One group demonstrated that when early rehabilitation interventions were performed during daily interruption of sedation the median duration of delirium was 2.0 days compared with 4.0 days without rehabilitation ($P=0.02$).⁴³ Similar results were reported in a study randomizing mechanically ventilated surgical ICU patients to early mobilization versus standard therapy.⁴⁴

Occupational therapy may also play an important role. A randomized control study showed that occupational therapy in nonintubated ICU patients reduced delirium incidence (3% versus 20%, $P<0.001$).⁴⁵ Finally, a quality improvement study implementing early physical and occupational interventions along with reduced benzodiazepine use for mechanically ventilated patients in the medical ICU resulted in a reduced incidence of delirium (21% versus 53%, $P=0.003$) and a reduction in hospital length of stay by 3.1 days (95% CI; 0.3–5.9 days), compared with historical rates before the interventions were implemented.⁴⁶ As described above, early mobilization is an important tool in preventing delirium, however, this can prove challenging in certain CICU patients, particularly patients with mechanical support devices and temporary pacemakers. However, just as medical ICUs have worked successfully to mobilize intubated patients, CICU’s should work to increase mobility, for example by opting for mobile friendly devices such as subclavian intra-aortic balloon pumps and active fixation temporary pacemakers when feasible.

The ICU is known to contribute to poor sleep; such sleeplessness increases the risk of delirium.⁴⁷ By enacting a series of nonpharmacologic interventions (closing doors, decreased alarm volumes, ear plugs, eye masks, and timed “lights off”) to improve sleep in the ICU, Patel et al were able to reduce the incidence of delirium compared with the nonintervention arm (33% versus 14%, $P<0.001$).⁴⁸ Similarly, in a quality improvement initiative, Kamder et al found that implementing a 3-stage strategy to improve sleep decreased the incidence of delirium/coma (OR: 0.46; 95% CI, 0.23–0.89; $P=0.02$).⁴⁹ In this study, stage 1 focused on reducing sleep disruptions by minimizing overhead pages, turning off patient televisions, dimming hallway lights, and grouping care activities.⁴⁹ Stage 2 used nonpharmacological sleep aids such as earplugs, eye masks and soothing music for nondelirious patients. For patients unable to sleep despite the stages 1 and 2 interventions, pharmacological agents were initiated (stage 3).⁴⁹ Benzodiazepines, opiates, and diphenhydramine were avoided. While these studies all derived from noncardiac ICU settings, many of these steps are applicable to patients in the CICU and, thus, every

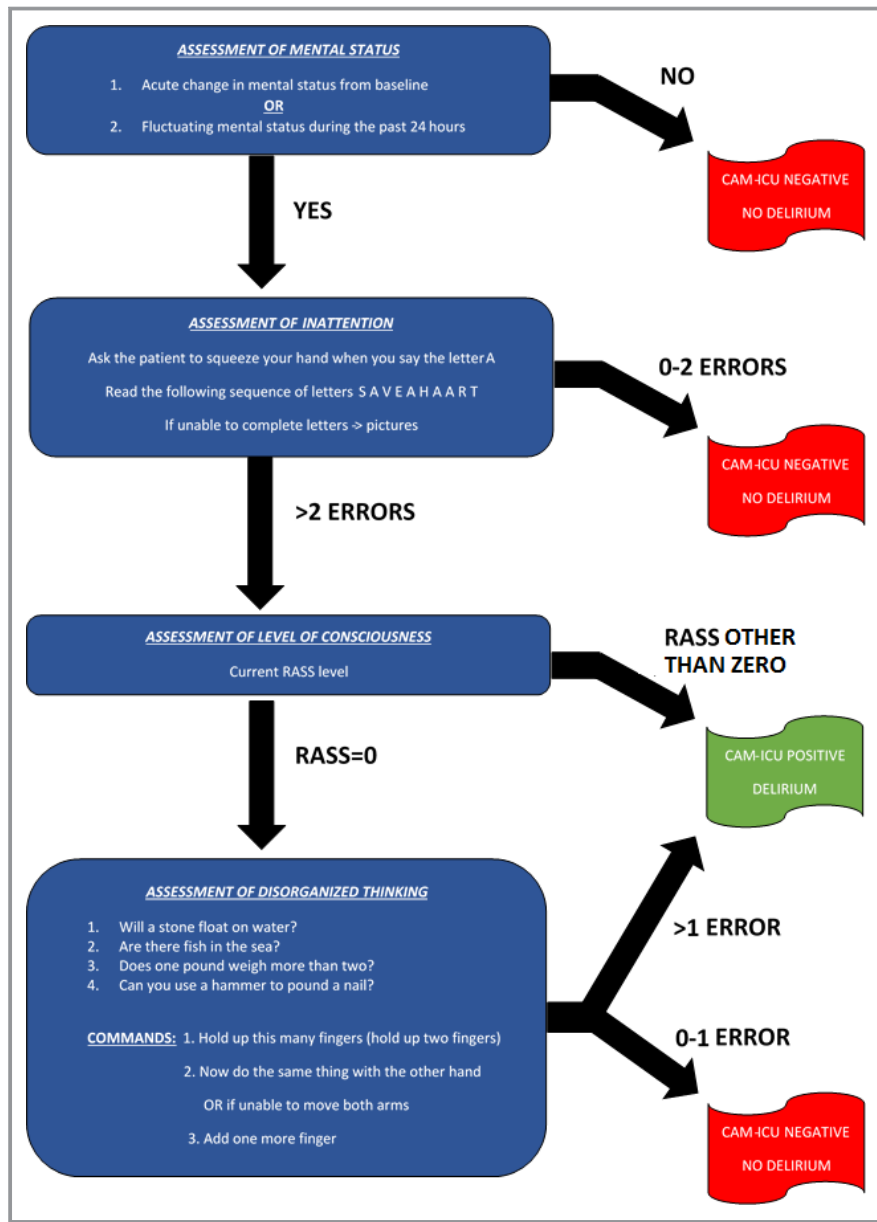


Figure 3. Confusion assessment method for the intensive care unit tool. This tool should be used daily for each patient. Steps for completion; (1) Assess for mental status—if patient has had a change in mental status from baseline or fluctuating mental status in the past 24 hours proceed to second step; (2) Assess for inattention—have the patient squeeze your hand when you say the letter “A” then read 10 letters in a row, 3 seconds apart. A suggested series is SAVEAHAART. Errors are counted when the patient fails to squeeze on the letter “A” or squeezes for letters other than “A”. If greater than 2 errors then proceed to third step; (3) Assess level of consciousness—if RASS is anything other than zero then the patient is CAM-ICU positive. RASS of zero equates to being alert and calm. If RASS is zero then proceed to final step; (4) Assess for disorganized thinking—ask the following set of yes/no questions, (a) Will a stone float on water?, (b) Are there fish in the sea? (c) Does one pound weigh more than 2 pounds?, and (d) Can you use a hammer to pound a nail? Then proceed with the following commands: Say to patient: “Hold up this many fingers” (Hold 2 fingers in front of the patient) and “Now do the same thing with the other hand” (Do not repeat number of fingers) *if patient is unable to move both arms, for 2nd part of command ask patient to add one more finger. An error is counted if patient is unable to complete the entire command if >1 error then the patient is CAM-ICU positive. Reprinted from Ely et al¹ with permission. Copyright © 2002, E. Wesley Ely and Vanderbilt University, all rights reserved. CAM-ICU indicates Confusion Assessment Method for the Intensive Care Unit; and RASS, the Richmond Agitation and Sedation Scale.

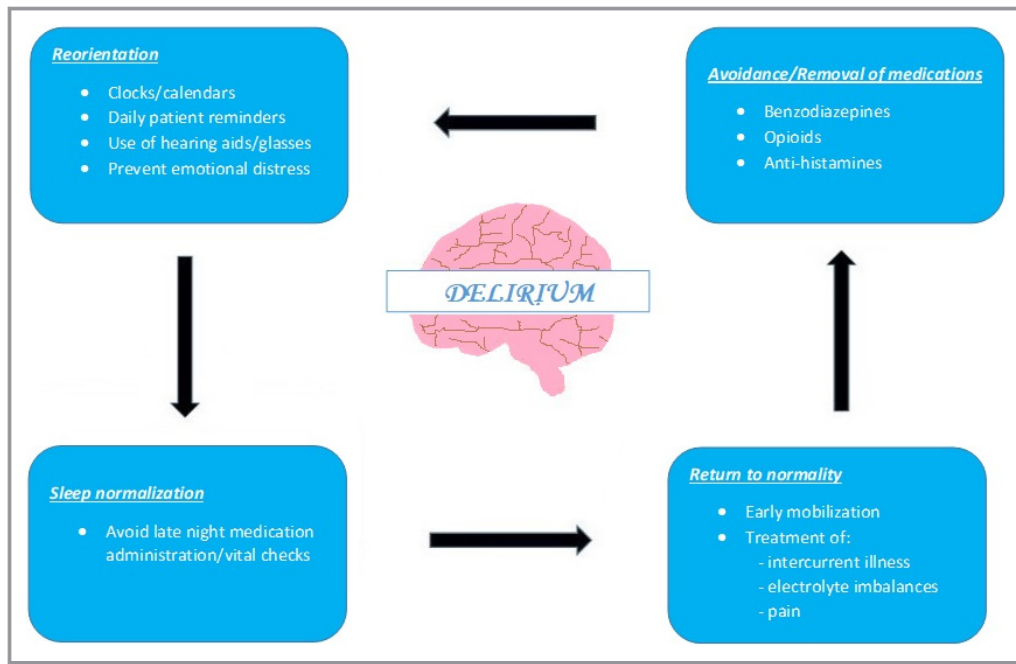


Figure 4. Preventative strategies for delirium.

attempt at reorientation and nonpharmacologic prevention should be made.

In terms of pharmacologic interventions, antipsychotics are frequently used for the prevention of delirium, however, there is no high-quality evidence to support their use. A recent meta-analysis examined pharmacologic prevention and treatment of delirium in ICU patients.⁵⁰ Among 5 studies that examined antipsychotics compared with placebo, only 1 showed a reduction in the incidence of delirium. Based on the lack of evidence, the 2013 Society of Critical Care Medicine guidelines on pain, agitation and delirium provide no recommendation for using antipsychotics for delirium prevention in adult ICU patients.³⁴ It is also worth mentioning that antipsychotics are known to cause several cardiovascular side effects, most notably QT prolongation.⁵¹

Sedatives are an important modifiable risk factor for delirium. Clegg and Young showed that delirium was associated with benzodiazepines (OR 3.0, 95% CI 1.3–6.8) in hospital patients and long-term care residents.⁵² Thus, there has been interest in finding alternative sedatives to reduce the incidence of delirium. One widely used alternative to benzodiazepines is propofol, which has quick onset/offset and may be useful for sedation interruption protocols as mentioned above. Several studies have shown that propofol compared with midazolam reduces length of mechanical ventilation.^{53–55} However, high quality evidence evaluating delirium outcomes is still evolving. Sleep deprivation has been shown to be a risk factor for the development of ICU delirium, and critically ill patients have been shown to have low levels of melatonin.⁵⁶ There have been several trials examining the use of melatonin

in ICU patients with delirium and some have shown promise but overall these studies are limited by small sample sizes and varied methodologies, and larger randomized trials are needed.⁵⁷

Opiate use should be minimized at every opportunity but not at the expense of uncontrolled pain. The acronym eCASH has been developed which stands for early Comfort using Analgesia, minimal Sedatives and maximal Humane care. The concept is designed to achieve early pain control and maintain comfort with minimal use of sedation in order to promote natural sleep and early mobilization, all of which may reduce the likelihood of developing delirium.⁵⁸

An alternative to the traditional sedatives of benzodiazepines and propofol is dexmedetomidine, which is an α^2 -agonist and has been the subject of intense delirium research because it has analgesic properties and results in a sedate but arousable state with little effect on respiratory drive.⁵⁹ These properties may decrease delirium, both by avoiding deliriogenic opiates and sedatives but also by more direct neuroprotective mechanisms.⁶⁰ This has led to several clinical studies involving dexmedetomidine in the ICU. The SEDCOM (Safety and Efficacy of Dexmedetomidine Compared with Midazolam) trial was a multicenter trial, randomizing 375 intubated ICU patients to dexmedetomidine or midazolam and showed that patients in the dexmedetomidine group had less time on the ventilator and less delirium (54% versus 76.6%, $P<0.001$). Of note, several common cardiac conditions were exclusion criteria for this trial including: unstable angina or acute myocardial infarction, ejection fraction less than 30%, heart rate less than 50/min, second

or third-degree heart block, and a systolic blood pressure less than 90 mm Hg despite continuous infusions of 2 vasopressors, which could limit the generalizability of this trial to CCU patients.⁶¹

In a randomized placebo-controlled trial, Su et al demonstrated that patients over 65 years who received prophylactic dexmedetomidine (administered from ICU admission to postoperative day 1) significantly decreased the incidence of ICU delirium during the first 7 days after surgery (9% versus 23%, $P < 0.0001$).⁶²

Three studies, of special relevance to the CICU, involved post-cardiac surgery patients in the ICU. The DEXCOM (Dexmedetomidine Compared to Morphine) study randomized such patients to dexmedetomidine or morphine and showed that dexmedetomidine reduced the duration but not incidence of delirium.⁶³ Djaiani et al randomized patients to dexmedetomidine versus propofol and found that dexmedetomidine reduced the incidence of delirium (17.5% versus 31.5%, OR 0.46; $P = 0.028$) and reduced duration (2 days versus 3 days, $P = 0.04$).⁶⁴ However, a randomized placebo controlled trial undertaken by Li et al failed to demonstrate any reduction in the incidence of delirium when dexmedetomidine was administered during anaesthesia and during the early postoperative period (4.9% in the dexmedetomidine group versus 7.7% in the control group, $P = 0.345$).⁶⁵ However, the incidence of delirium was low in this trial and thus the trial may have been underpowered.

In the PRODEX (Propofol Compared to Dexmedetomidine) and MIDEX (Midazolam Compared to Dexmedetomidine) trials⁶⁶ patients who were already sedated were randomized to continue their current regimen (midazolam or propofol) or switch to dexmedetomidine, demonstrating that the combined endpoints of anxiety, agitation, and delirium were lower in the dexmedetomidine group. Important cardiac exclusion criteria included: heart rate less than 50/min, second or third-degree heart block, mean arterial blood pressure less than 55 mm Hg despite appropriate vasopressor use, and use of α agonists or antagonist within 24 hours of randomization.

An important caveat to the above trial results relates to a Cochrane meta-analysis reporting that there is insufficient high-quality evidence that dexmedetomidine lowers the risk of delirium.⁶⁷ These investigators found that only a small proportion of dexmedetomidine studies investigated its effect on delirium, reflecting a potentially lower quality of evidence influenced by risk of bias, imprecision, and significant publication bias. However, further trials favoring dexmedetomidine were published since this meta-analysis⁶² and a recent meta-analysis comparing dexmedetomidine to propofol in post-cardiac surgery patients that included 8 randomized trials demonstrated that dexmedetomidine was associated with a lower risk of delirium (risk ratio, 0.4; 95% CI, 0.24–0.64; $P = 0.0002$) as well as shorter length of intubation, but more bradycardia.⁶⁸

Dexmedetomidine has a similar mechanism of action as clonidine, and, as such, leads to a reduced sympathetic outflow and augmented vagal activity and can lead to reduced levels of catecholamines, bradycardia, reduced cardiac output, and hypotension.⁶⁹ These hemodynamic consequences should be anticipated by treating cardiologists and influence patient selection.

Finally, there is conflicting data on the impact of statin use on incidence of delirium in the ICU. Several retrospective and prospective cohort studies have found that statin use in ICU patients is associated with a reduced risk of delirium^{70,71}; however, 2 recent randomized control trials showed no benefit to statins in preventing ICU delirium.^{72,73}

Treatment

Initial management of delirium should involve treating any identifiable precipitating factors. Further management goals are aimed at reducing its severity and duration. Unfortunately, there are few data to guide the treatment of CICU patients with delirium once it has occurred. Nonpharmacological strategies to reorientate the patient should be employed; including the use of home hearing aids and glasses. There are conflicting and limited data to suggest that antipsychotics reduce the duration of delirium (Table 2). For example, 1 small trial randomizing 36 ICU patients with delirium to quetiapine or placebo demonstrated that patients who received quetiapine had a shorter duration of delirium (1 day versus 4.5 days, $P = 0.001$).⁷⁴ However, another study that randomized 103 patients to either haloperidol, ziprasidone, or placebo showed no difference in duration of delirium.⁷⁵ Based on the above evidence, the Society for Critical Care Medicine guideline on delirium provides no recommendation for the use of haloperidol in the treatment of ICU delirium, while stating that atypical antipsychotics may reduce the duration of delirium; noting that these should not be used in patients at significant risk for torsades de pointes.

Dexmedetomidine has also been studied for treating ICU patients with established delirium. The DahLIA (Dexmedetomidine to Lessen ICU Agitation) study randomized 74 patients deemed too delirious to extubate to dexmedetomidine versus placebo and found that delirium resolved more rapidly with dexmedetomidine (23.3 hours versus 40.0 hours; 95% CI, 3.0–28.0 hours; $P = 0.01$).⁷⁶ Two important caveats of this study are that the incidence of alcohol withdrawal was not reported and that analgesia control and opioid use were suboptimal. The Society of Critical Care Medicine guideline on delirium suggests the use of dexmedetomidine may be considered for the treatment of ICU delirium unrelated to alcohol or benzodiazepine withdrawal for which benzodiazepines would be the treatment of choice.³⁴

Table 2. Pharmacological Agents Investigated for the Treatment of Delirium in the ICU, With Special Consideration to CICU Patients

Medication	Recommended Dosage	Side Effects	Contraindications	Costs	FDA Approved for Delirium	Evidence	Reference
Quetiapine	100 to 200 mg orally per d in 2 divided doses	QTC prolongation, less extrapyramidal effects than haloperidol	Prolonged QTC	Cheap	No	Quetiapine shortened the duration of delirium compared with placebo (1 d vs 4.5 d, $P=0.001$)	74
Dexmedetomidine	0.2 to 0.7 $\mu\text{g}/\text{kg}$ per h maintenance dose	Bradycardia, hypotension	Bradycardia, high degree AV block, caution in hypotension	Expensive	No (but approved as an alternative sedative)	Dexmedetomidine shortened the duration of delirium compared with placebo in intubated patients (23.3 h vs 40.0 h, $P=0.01$)	76
Haloperidol	Oral: 0.5 to 5 mg every 6 to 8 h IV (haloperidol lactate only): 0.5 to 10 mg q15 to 30 min until response achieved, then give 25% of last bolus dose Q6H	QTC prolongation, large potential for extrapyramidal effects	Prolonged QTC, Parkinson's disease	Cheap	No	Mixed data and is not currently recommended by guidelines for the treatment of delirium	75
Ziprasidone	10 mg Q2H or 20 mg Q4H IM (max 40 mg/daily) for acute agitation	QTC prolongation, less extrapyramidal effects than haloperidol	Prolonged QTC, heart failure, recent myocardial infarction	Cheap	No	Ziprasidone has not been shown to reduce delirium free days compared with placebo (median 15.0 d vs 12.5 d) ($P=0.66$)	75

CICU indicates cardiac intensive care unit; FDA, US Food and Drug Administration; IM, intramuscular; ICU, intensive care unit; IV, intravenous; and QTC, corrected QT.

Future Directions and Conclusion

As the landscape of the CICU continues to evolve and the patient population becomes increasingly more complex, sick, and aged,^{77,78} the burden of delirium will only increase. One notable aspect of this review article is that none of the studies cited regarding the prevention and treatment of delirium enrolled CICU patients exclusively, which highlights the significant need for more delirium studies specific to the CICU given the generalizability of delirium studies from other ICU settings may not overlap perfectly with cardiac patients. Tools to screen for delirium should be familiar to cardiologists practicing in the CICU and should be incorporated into the nursing assessment of at-risk patients. Despite the difficulties of conducting randomized control trials in the critical care setting, high quality studies examining the efficacy and safety of sedation agents, antipsychotics, and other novel therapies for the prevention and treatment of delirium in patients in the

CICU are urgently needed. Specifically, studies examining the efficacy and cardiovascular safety of dexmedetomidine and antipsychotics in CCU patients with complex cardiovascular disease are needed. More research is also needed on medications and hardware unique to the CICU (such as antiarrhythmic drugs and temporary mechanical support devices); investigating their impact on delirium and specific treatment options in this patient population. Furthermore, just as other medical ICUs have developed and championed algorithms and pathways for daily ventilator weans, interruptions in sedation and early mobilization, the CICU needs to develop similar strategies for its unique patients (including those requiring mechanical support and with other hardware-related causes of immobility). Specific examples of such strategies would include active fixation temporary pacemakers that can facilitate ambulation, as well as brachial intra-aortic balloon pump placement for patients requiring more prolonged ventricular support. Finally, many of the current

mainstays of treatment for delirium have important cardiac side effects and their use should be further studied and tailored to the complex cardiac patients in the CICU.

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