Cause e gestione del delirium

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Outline:

A) Delirium: definizione e criteri diagnostici

B) Patogenesi

C) Prevenzione

D) Diagnosi

E) Trattamento

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Delirium

Disturbo acuto, transitorio, globale, organico delle funzioni nervose superiori che comporta **perdita dell'attenzione** e **alterazione fluttuante dello stato di coscienza**

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(C) An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability or perception)
(D) The disturbances in criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma

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(D) The disturbances in criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma
(E) There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin, or is due to multiple aetiologies

Sottotipi clinici:

- ***Iperattivo (25%)***
- ***Ipoattivo (35%)***
- ***Misto (40%)***

JAMA | Review

Delirium in Older Persons
Advances in Diagnosis and Treatment

Esther S. Oh, MD, PhD; Tamara G. Fong, MD, PhD; Tammy T. Hshieh, MD, MPH; Sharon K. Inouye, MD, MPH

JAMA. 2017;318(12):1161-1174. doi:10.1001/jama.2017.12067

Table 1. Clinical Features of Diseases That Mimic Delirium

	Condition[a]			
Feature	Delirium	Dementia	Depression	Psychosis
Acute change in mental status	+	−	−	±
Inattention	+	±	±	±
Altered consciousness	+	−	−	−
Disorganized thinking	+	±	−	+
Altered psychomotor activity	+	±	+	+
Chronic duration	±	+	+	±

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Patogenesi

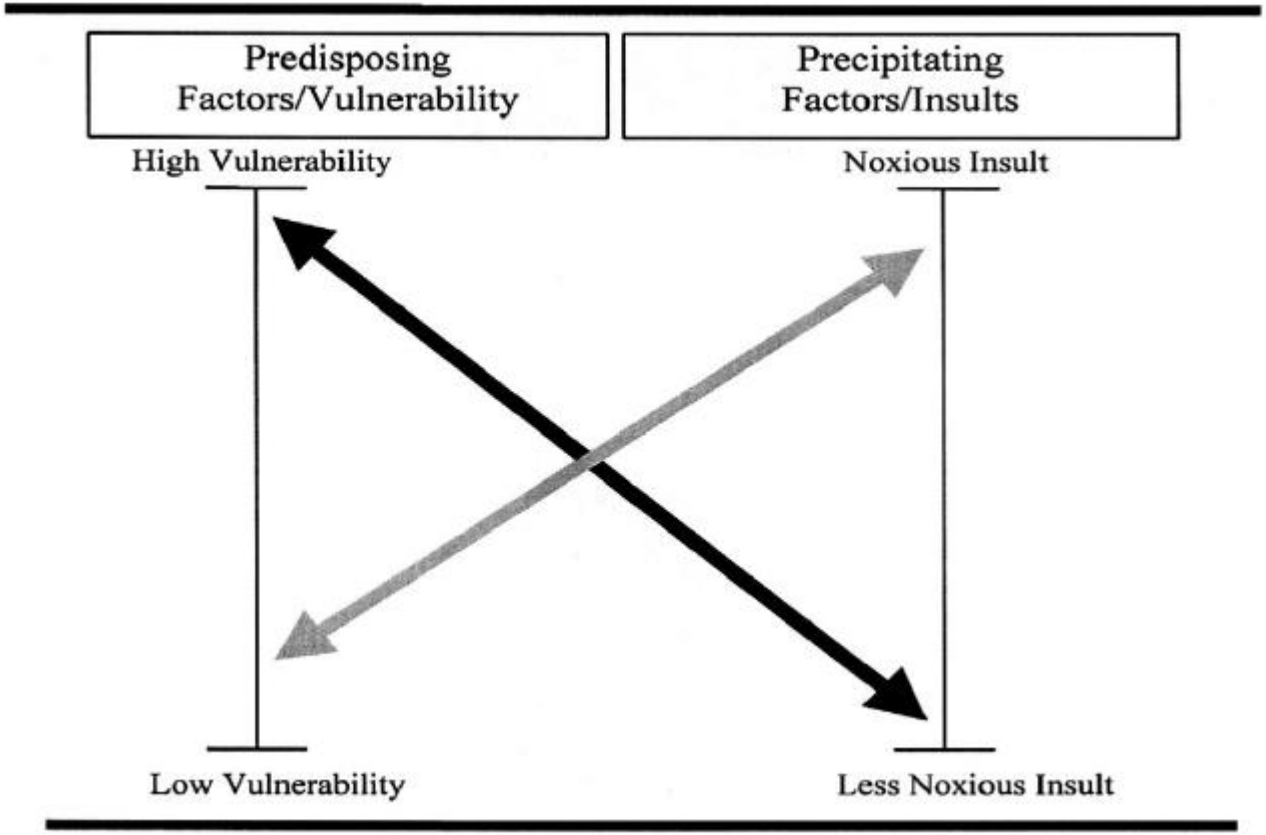
Delirium in elderly people

Sharon K. Inouye, M.D., MPH[1,2], **Rudi G. J. Westendorp, M.D., PhD**[3,4], and **Jane S. Saczynski, Ph.D.**[5]

Lancet. 2014 March 8; 383(9920): 911–922. doi:10.1016/S0140-6736(13)60688-1.

Delirium can be thought of as "acute brain failure," a multifactorial syndrome analogous to acute heart failure and may provide a novel approach to elucidate brain functioning and pathophysiology. With its acute onset in response to noxious insults, such as major surgery or sepsis, delirium may help to shed light on cognitive reserve; that is, the brain's resilience to withstand external factors.[10] In this context, delirium may serve as a marker of the vulnerable brain with diminished reserve capacity. Recent evidence further suggests that the trajectory of "normal" cognitive aging may not be a smooth linear decline, but rather a series of punctuated declines and recoveries in the face of delirium and major medical insults.[11, 12] Finally, in addition to serving as a marker of the vulnerable brain, accumulating evidence (see "Current Controversies" section below) suggests that delirium itself may lead to permanent cognitive decline and dementia in some patients.

Patogenesi (1/3)



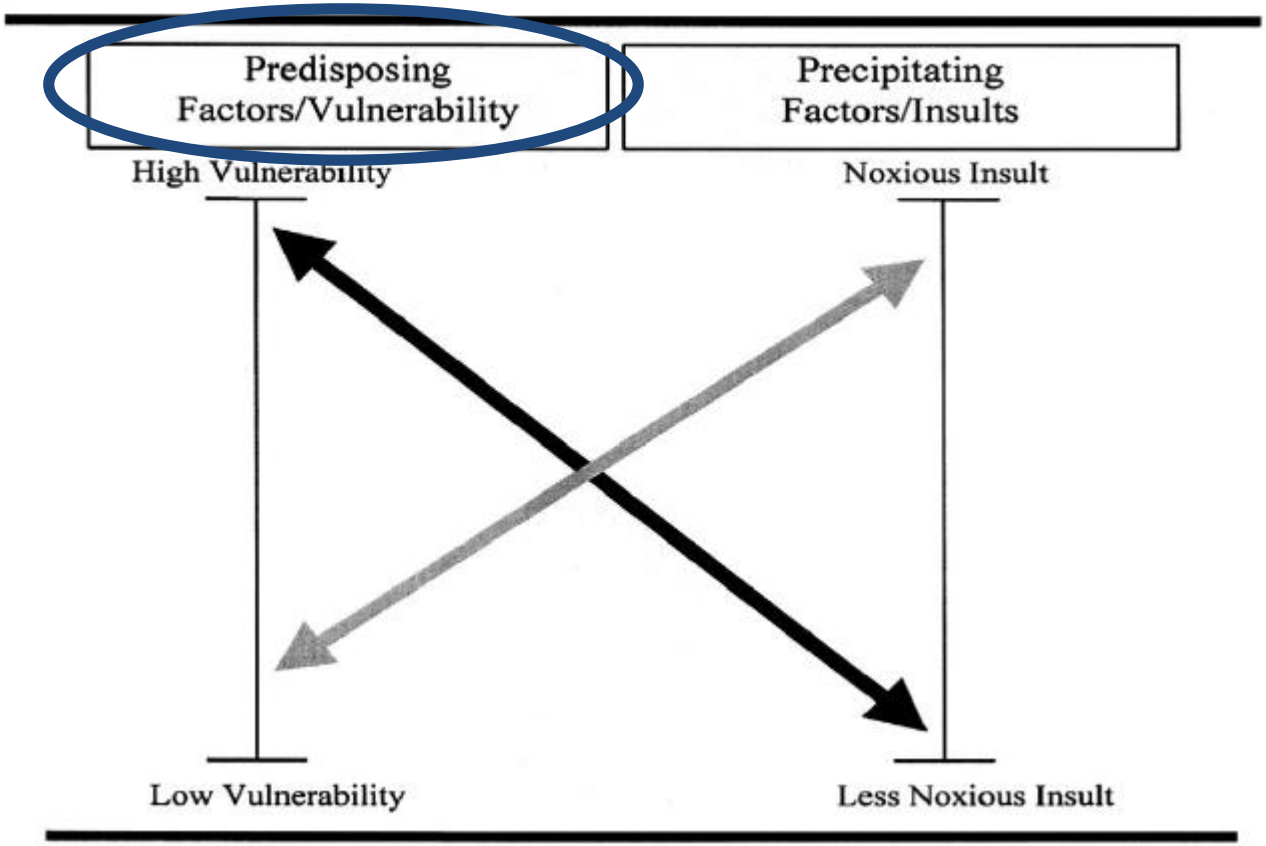
deficit colinergico

e/o

ipertono dopaminergico

Inouye et al., 2014

Patogenesi (2/3)



Inouye et al., 2014

Fattori predisponenti

Demografici

- Età avanzata
- Sesso maschile

Comorbilità

- Numero di malattie
- Gravità delle comorbilità
- Malattie terminali
- Demenza

Farmaci e sostanze

- Polifarmacoterapia
- Uso di neurolettici
- Storia di abuso

Stato funzionale

- Sindrome da immobilizzazione
- Ipomobilità

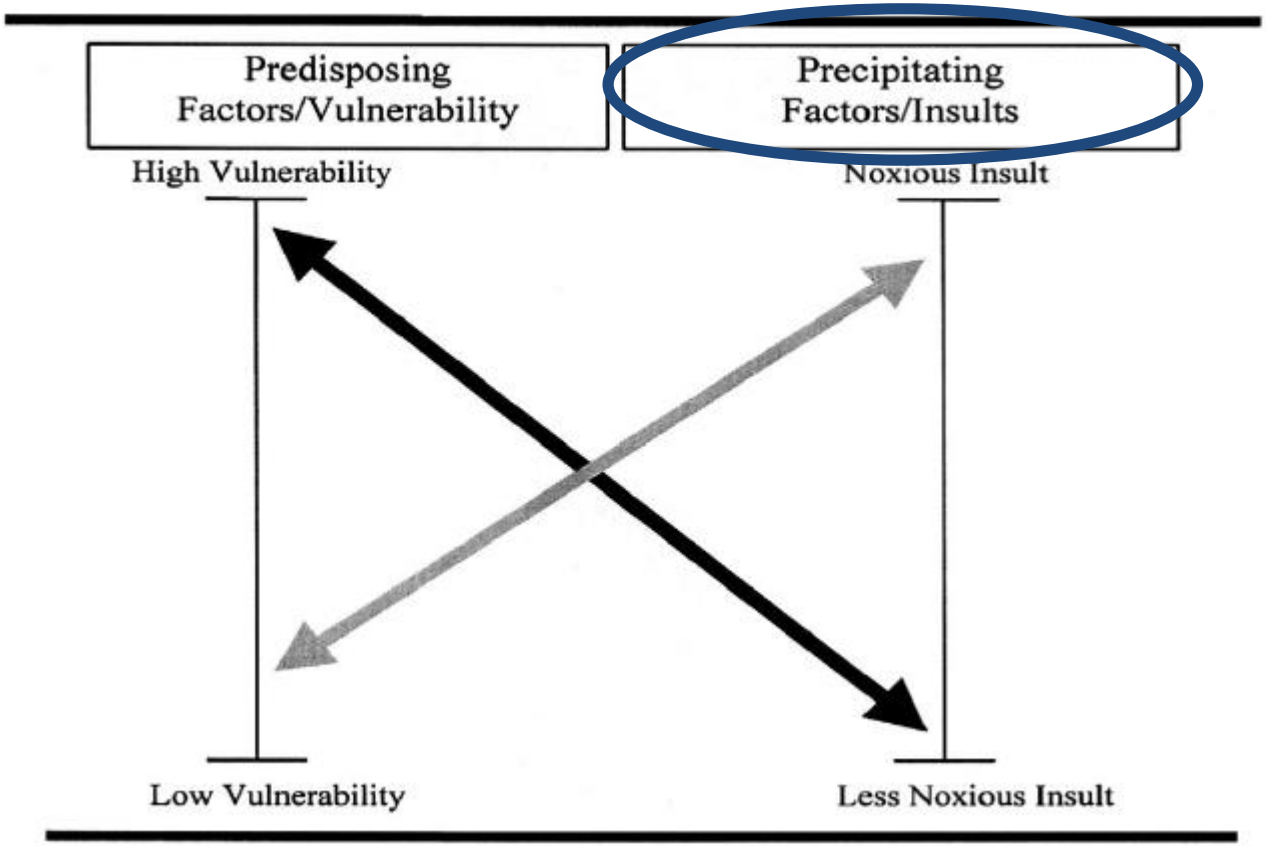
Deficit sensoriali

- Uditivi
- Visivi

Malnutrizione e disidratazione

Disordini psichiatrici

Patogenesi (3/3)



Inouye et al., 2014

Fattori precipitanti

Sistemici

- Infezioni
- Inadeguato controllo del dolore
- Trauma
- Ipo-ipertermia
- Disidratazione

Metabolici

- Deficit di tiamina
- Insufficienza epatica o renale
- Disturbi elettrolitici
- Disfunzione tiroidea

Farmaci e sostanze

- Cambiamenti terapeutici
- Intossicazione o sospensione

Sistema Nervoso Centrale

- Eventi cerebrovascolari
- Emorragie
- Ematoma subdurale/epidurale
- Meningiti/encefaliti
- Epilessia/stato epilettico

Cardio-polmonari

- Infarto del miocardio
- Scompenso acuto cardiogeno
- Insufficienza respiratoria
- Shock

Iatrogene

- Procedure invasive e chirurgiche
- Contenzione fisica
- Posizionamento CV

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"Primary prevention with **multicomponent nonpharmacologic** approaches has been consistently demonstrated to be the most effective strategy for delirium prevention among hospitalized, non-ICU medical and surgical patients"

Table 4. Multicomponent Nonpharmacologic Approaches to Delirium Prevention

Approach	Description
Orientation and therapeutic activities	Provide lighting, signs, calendars, clocks Reorient the patient to time, place, person, your role Introduce cognitively stimulating activities (eg, reminiscing) Facilitate regular visits from family, friends
Fluid repletion	Encourage patients to drink; consider parenteral fluids if necessary Seek advice regarding fluid balance in patients with comorbidities (heart failure, renal disease)
Early mobilization	Encourage early postoperative mobilization, regular ambulation Keep walking aids (canes, walkers) nearby at all times Encourage all patients to engage in active, range-of-motion exercises
Feeding assistance	Follow general nutrition guidelines and seek advice from dietician as needed Ensure proper fit of dentures
Vision and hearing	Resolve reversible cause of the impairment Ensure working hearing and visual aids are available and used by patients who need them
Sleep enhancement	Avoid medical or nursing procedures during sleep if possible Schedule medications to avoid disturbing sleep Reduce noise at night
Infection prevention	Look for and treat infections Avoid unnecessary catheterization Implement infection-control procedures
Pain management	Assess for pain, especially in patients with communication difficulties Begin and monitor pain management in patients with known or suspected pain
Hypoxia protocol	Assess for hypoxia and oxygen saturation
Psychoactive medication protocol	Review medication list for both types and number of medications

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Cochrane Library

Cochrane Database of Systematic Reviews

Interventions for preventing delirium in hospitalised non-ICU patients (Review)

Siddiqi N, Harrison JK, Clegg A, Teale EA, Young J, Taylor J, Simpkins SA

No clear benefit of antipsychotics

Minimal evidence to support the use of medications to prevent delirium, including cholinesterase inhibitors, melatonin, and melatonin receptor agonist (ramelteon)

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Annals of Internal Medicine. 1990;113:941-948.

Clarifying Confusion: The Confusion Assessment Method

A New Method for Detection of Delirium

Sharon K. Inouye, MD, MPH; Christopher H. van Dyck, MD; Cathy A. Alessi, MD; Sharyl Balkin, MD; Alan P. Siegal, MD; and Ralph I. Horwitz, MD

I Insorgenza acuta della confusione mentale e andamento fluttuante
La domanda è posta di solito a un familiare: "c'è stato un cambiamento acuto nello stato mentale del paziente rispetto alla sua situazione di base?". "Il comportamento anomalo varia durante la giornata, per esempio va e viene o si modifica d'intensità?".
0 = no 1 = sì

II Perdita dell'attenzione
Il paziente presenta difficoltà nel concentrare la sua attenzione, per esempio è facilmente distraibile, non riesce a mantenere il filo del discorso, ecc.
0 = no 1 = sì

III Disorganizzazione del pensiero
Il pensiero del paziente è disorganizzato e incoerente, passa da un argomento all'altro senza filo logico, in modo imprevedibile?
0 = no 1 = sì

IV Alterato livello di coscienza
0 = vigile 1 = iperallerta, letargia, stupor, coma

Per fare diagnosi di *delirium* occorre che la risposta sia sì a: I + II + III o I + II + IV.

Sensitivity: 94%-100%

Specificity: 90%-95%

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Screening Instruments (Last 6 Years)

Table 2. Characteristics of Delirium Screening Tools (Last 6 Years)[a]

Screening Tool	Setting	No. (% Male)	Age, Mean (SD), y	Assessment Time	Scoring	Sensitivity (Cognitively Impaired), %[b]	Specificity (Cognitively Impaired), %[b]	Interrater Reliability (95% CI)	Description (No. of Question Items)
3D-CAM[28]	Hospital	201 (38)	84 (5.4)	3 min (median)	Possible delirium if (1) acute onset or fluctuation AND (2) inattention AND EITHER (3) disorganized thinking OR (4) altered level of consciousness	95 (96)	94 (86)	95%	Screening tool derived from the CAM (10 PQI, 10 ORI)[c]
CAM-S[29,d]	Hospital	1219 (41)	77-80[e]	Long form, 10-15 min; Short form, NR	Maximum score: 19 (long form), 7 (short form)	NA[f]	NA	Long form, ICC = 0.88; Short form, ICC = 0.92	Delirium assessment tool derived from the CAM (long form: 4 PQI, 2 CQI, 4 ORI; short form: 1 PQI, 1 CQI, 2 ORI)
4AT[30,g]	Hospital	234 (36)	84 (5.9)	<2 min	Maximum score = 12; possible delirium when score ≥4	90 (94)	84 (91)	NR	Screening tool for delirium and cognitive impairment (5 PQI, 2 ORI)
DelApp[31]	Hospital	156	85 (delirium group 87 (dementia group) 75 (control group)	<5 min	Maximum score = 10; median, 6 (IQR, 4-7) in delirium group, 10 (IQR, 10-10) in control group	98	93	NR	Software for objective measurement of attention (9 ORI, 1 PQI)[h]
FAM-CAM[32]	Home[i]	52 (33)[j]	82 (8)	NR	Possible delirium if (1) acute onset or fluctuation AND (2) inattention AND EITHER (3) disorganized thinking OR (4) altered level of consciousness	(88)	(98)	κ = 0.85 (0.65-1.0)	Screening tool for caregivers (11 CQI)
I-AGeD[33]	Hospital	88 (27)[k]	86.4 (8.5)	NR	Maximum score = 10; possible delirium when score ≥4	77.4[l]	63.2	NR	Caregiver-based questionnaire (10 CQI)
Inter-RAI[34,m]	Hospital	239 (49)	82 (6.4)	NR	Possible delirium if (1) acute change in mental status and (2) mental function varies over the course of the day	82 (90)	91 (69)	κ = 0.65-0.76	Screening tool for acute care (4 ORI)
MOTYB + signs of confusion[35]	Hospital	265 (51.1)	69 (27)	NR	Possible delirium if the patient failed MOTYB or was confused (subjectively or objectively)	93.8 (87.5)	84.7 (71.4)	NR	Screening tool for acute care (2 PQI, 6 ORI)
RADAR[36]	Hospital, long-term care	193 (40)	80.8 (7.8)	7 s (average)	Maximum score = 3; possible delirium when score ≥1	73 (71.4)	67 (42.9)	κ = 0.34-0.79	Tool for nursing staff (3 ORI)
SQeeC[37]	Hospital	100 (40)	87	30 s to 3 min	Possible delirium if unable to answer first question or provides wrong answer to second question	83 (83)	81 (59)	NR	Tool for evaluating level of consciousness (2 PQI)
Sour Seven[38]	Hospital	80 (36)	81.3 (8.9)	1-2 min (nurses); 2-5 min (caregivers)	Maximum score = 18; possible delirium when score ≥4	89.5	90	64.3%-92.8%[n]	Tool for informal caregivers and untrained nurses (7 ORI)

G. Bellelli et al.

Age and Ageing 2014; **43:** 496–502
doi: 10.1093/ageing/afu021
Published electronically 2 March 2014

© The Author 2014. Published by Oxford University Press on behalf of the British Geriatrics Society.
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Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people

ALERTNESS

AMT4

ATTENTION

ACUTE CHANGE OR FLUCTUATING COURSE

PUNTEGGIO 4AT: **0-12**

≥4: possibile delirium +/- deficit cognitivo
1-3: possibile deficit cognitivo
0: delirium o deficit cognitivo severo improbabile

[1] VIGILANZA

Valuta lo stato di vigilanza del paziente (dal sopore, caratterizzato ad esempio da difficoltà a risvegliarsi o addormenti durante l'esecuzione del test, all'agitazione /iperattività). Osservare il paziente. Se dorme, provare a risvegliarlo, richiamandolo, o con un leggero tocco sulla spalla. Chiedere al paziente di ripetere il proprio nome e l'indirizzo della propria abitazione.

Normale (completamente vigile, non agitato durante tutta la valutazione)	**0**
Moderata sonnolenza per <10 secondi dopo il risveglio, poi normale	**0**
Chiaramente anomala (iperattivo, agitato o marcatamente soporoso)	**4**

[2] AMT4

Età, data di nascita, luogo (nome dell'ospedale e dell'edificio), anno corrente.

Nessun errore	**0**
1 errore	**1**
≥2 errori/ intestabile	**2**

[3] ATTENZIONE

Chiedere al paziente: "per favore, mi dica i mesi dell'anno in ordine contrario, partendo da dicembre"
Per aiutare la comprensione della domanda, è consentito inizialmente questo suggerimento: "qual è il mese prima di dicembre?"

Mesi dell'anno a ritroso	è in grado di ripetere senza errori ≥7 mesi	**0**
	Inizia ma riporta < 7 mesi/ rifiuta di iniziare	**1**
	test non effettuabile (paziente indisposto, assonnato o disattento)	**2**

[4] CAMBIAMENTO ACUTO O DECORSO FLUTTUANTE

Dimostrazione di un evidente cambiamento o di un decorso fluttuante relativamente all'attenzione, alla comprensione o altre funzioni cognitive -comportamentali (ad esempio ossessioni e/o allucinazioni) con esordio nelle ultime 2 settimane e ancora presenti nelle ultime 24 ore

No	**0**
Si	**4**

The 4AT had a sensitivity of 89.7% and specificity 84.1% for delirium

Aging Clin Exp Res
DOI 10.1007/s40520-016-0621-7

ORIGINAL ARTICLE

Delirium assessment in hospitalized elderly patients: Italian translation and validation of the nursing delirium screening scale

Valentina Spedale[1] · Stefania Di Mauro[2] · Giulia Del Giorno[3] · Monica Barilaro[1] · Candida E. Villa[1] · Jean D. Gaudreau[4] · Davide Ausili[2]

Table 7 Nursing delirium screening scale (Nu-DESC)

Caratteristiche e descrizioni	Valutazione dei sintomi (0–2)		
Rilevazione	24–8.00	8.00–16.00	16.00–24
Sintomi			
I. Disorientamento			
Manifestazione verbale o comportamentale di disorientamento nel tempo o nello spazio.			
Percezione distorta di persone nell'ambiente.			
II. Comportamento Inappropriato			
Comportamento inappropriato nell'ambiente e/o nei confronti di persone; ad esempio trazione di tubi e medicazioni,tentativo di scendere dal letto quando controindicato e simili.			
III. Comunicazione Inappropriata			
Comunicazione inappropriata nell'ambiente e/o nei confronti delle persone;ad esempio incoerenza,incapacità di comunicare,linguaggio privo di significato o incompresibile.			
IV. Illusioni/Allucinazioni			
Vedere o sentire cose che non ci sono;distorsione visiva degli oggetti.			
V. Ritardo Psicomotorio			
Ritardo nella reazione,poche o assenti azioni/parole spontanee;ad esempio quando il paziente è stimolato la reazione è rallentata e/o il paziente è incapace di risvegliarsi.			
Totale			

Using 3 as a cut-off value, Nu-DESC showed 100 % sensibility and 76 % specificity

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Perform clinical evaluation
- History (including alcohol and drug use)
- Physical examination
- Vital signs
- Search for occult infections, metabolic abnormalities

Review medications
- Minimize Beers criteria medications[e]
- Use less harmful alternatives
- Administer lowest effective doses

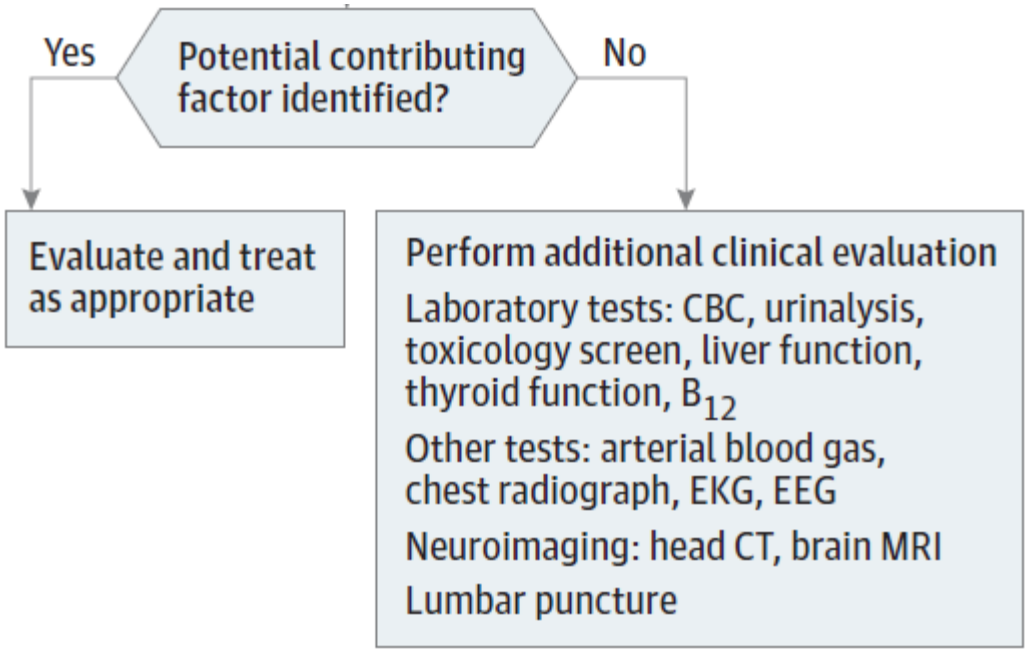

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Table 6. Selected Delirium Treatment (Typical and Atypical Antipsychotics) Studies, Last 6 Years[a]

Sources by Category	Study Design	Setting (Study Duration)	Sample Size (Intervention/ Control)	Intervention	Control	Outcome	Results, Intervention vs Control, No.(%)	Overall Quality Score[b]
Atalan et al,[93] 2013	RCT	Cardiac surgery (2010-2012)	53 (27/26)	Morphine sulfate, intramuscular (5 mg, up to 20 mg/d)	Haloperidol, intramuscular (5 mg, up to 20 mg/d)	Delirium duration in those with hyperactive delirium	31.56 h vs 33.9 h $P = .61$	4
Boettger et al,[94] 2015	Open-label, matched	Hospital, oncology (2000-2006)	84 (21 haloperidol/21 risperidone, 21 aripiprazole, 21 olanzapine)	Haloperidol (5.5 mg)	Risperidone (1.3 mg) Aripiprazole (18.3 mg) Olanzapine (7.1 mg) (mean doses 4-7 d)	Delirium resolution and adverse-effect profiles (typical vs atypical)	16/21 (76.2) vs 18/21 (85.7) [risperidone], 16/21 (76.2) [aripiprazole], and 13/21 (61.9) [olanzapine] $P = .42$[c]	3
Kishi et al,[95] 2012	Case series	Hospital, cancer[d]	29 (intervention)	Risperidone, oral (0.5-1 mg to start, then titrated)	No control group	Delirium severity (responder, 25% reduction in the DRS-R-98 from baseline to day 7)	No significant differences in the number of treatment responders vs nonresponders, 14/29 (48) vs 15/29 (51)	2
Maneeton et al,[96] 2013	RCT	Hospital, medical (2009-2011)	52 (24/28)	Quetiapine, oral (25-100 mg/d for 1-7 d)	Haloperidol, oral (0.5-2 mg/d for 1-7 d	Delirium severity by DRS-R-98 (higher score = more severe)	22.9 (6.9) vs 21.7 (6.7) $P = .59$	5
Schrøder Pedersen et al,[97] 2014	Prospective cohort	Cardiac surgery (2012)	240 (123/117)	Standardized treatment with haloperidol, oral (2.5-5 mg 3 times daily ×1.5 d, then taper)	No standardized treatment protocol	Delirium duration	3 (range, 1-5) d vs 1 (range, 1-4) d $P = .23$	3
Yoon et al,[98] 2013	Prospective observa-tional	Hospital, medical surgical[d]	80 (23 haloperidol/21 risperidone, 18 olanzapine, 18 quetiapine)	Haloperidol, oral (0.5-10 mg/d)	Risperidone, oral (0.25-4 mg/d) Olanzapine, oral (1-20 mg/d) Quetiapine, oral (25-200 mg/d)	Delirium severity ≥50% reduction from baseline by DRS-K	15/23 (65.2) vs 14/21 (66.6) [risperidone], 12/18 (66.6) [olanzapine], and 13/18 (72.2) [quetiapine] $P = .97$	2
Agar et al,[99] 2017	RCT	Inpatient hospice, hospital palliative care (2008-2014)	249 (81 haloperidol, 82 risperidone/86 placebo)	Haloperidol, risperidone, oral (0.25 mg every 12 h, up to 2 mg/d)[e]	Placebo	Delirium symptom scores on day 3 (higher score = more severe)	Haloperidol vs placebo: 0.24 U higher in haloperidol group, $P = .009$ Risperidone vs placebo: 0.48 U higher in risperidone group, $P = .02$	6

“Most studies do not show benefit of antipsychotics in decreasing the duration or severity of delirium”

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Table 3. American Geriatrics Society Clinical Practice Guidelines for the Prevention and Treatment of Postoperative Delirium[a]

Recommendation	Description
Strong: Benefits Clearly Outweigh Risks or Vice Versa	
Medications to avoid	Any medications associated with precipitating delirium (eg, high-dose opioids, benzodiazepines, antihistamines, dihydropyridines) Cholinesterase inhibitors should not be newly prescribed to prevent or treat postoperative delirium Benzodiazepines should not be used as first-line treatment of delirium-associated agitation Benzodiazepines and antipsychotics should be avoided for treatment of hypoactive delirium

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Advances in Diagnosis and Treatment

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Table 3. American Geriatrics Society Clinical Practice Guidelines for the Prevention and Treatment of Postoperative Delirium[a]

Recommendation	Description
Weak: Evidence in Favor of These Interventions, But Level of Evidence or Potential Risks Limit Strength of Recommendation	
Antipsychotics	The use of antipsychotics (haloperidol, risperidone, olanzapine, quetiapine, or ziprasidone) at the lowest effective dose for shortest possible duration may be considered to treat delirious patients who are severely agitated, distressed, or threatening substantial harm to self, others, or both

Trattamento

- Non esiste il farmaco ideale

- Iniziare con basse dosi di uno dei farmaci elencati e mantenere una dose efficace per almeno 2 giorni prima di modificare
  - Quetiapina, orale (25 mg una/due volte al giorno)
  - Olanzapina, orale (2,5-5 mg due volte al giorno)
  - Risperidone, orale (0,5-1 mg due volte al giorno)
  - Aloperidolo, per via orale o im (non superare i 3-5 mg in 24 ore)

- Quando la risposta terapeutica è stabile da 36 ore, il farmaco va sospeso

Sospetto di astinenza da alcol o BDZ

- Lorazepam, orale o im o ev (1-2 mg)
- Diazepam, orale o im o ev (5-10 mg)

Take home message

Conoscere cause e fattori di rischio significa:

1- identificare i pazienti ad alto rischio

2- *stato confusionale intramoenia: misura di scadente qualità dell'assistenza*
→ costi sanitari

INDISPENSABILI IL COINVOLGIMENTO E LA FORMAZIONE DEL PERSONALE PARAMEDICO

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