

Delirium and other cognitive disorders in cancer patients

癌症病患的譫妄和認知錯亂

三總精神部
曾念生

譫妄

- Delirium is highly **distressing/suffering** experience for **patients, spouses/ caregivers and nurses**
- Delirium is especially distressing when delirium is more severe and is characterized by the presence of **delusions and hallucinations**
- **Hypoactive delirium** is as distressing as **heperactive delirium**

譫妄盛行率

Prevalence of delirium

- 年齡是重要因素

TABLE 28.1. PREVALENCE OF DELIRIUM

Age	Patients	Delirium (%)	Reference
>55	2,000	15 (prev)	186
>60	99	53 (prev)	3
>60	184	22 (prev)	187
>65	588	24 (prev)	7
>65	282	21	188
>65	325	11 (prev) 31 (inc)	29
>70	235	16 (prev)	189
>70	229	16 (prev) 7 (inc)	190
>70	331	14	191
82 (mean)	315	42	192

prev, prevalence; inc, incidence.

臨終病患譫妄盛行率

Prevalence of delirium in terminally ill

- 85% terminally ill cancer patients
- 39% of patients in PCU（安寧緩和照顧單位） in last week of life
- 42% upon admission to PCU, 45% more during course, 88% terminal phase
- 20% on admission to PCU, 33% incidence

癌症病人譫妄盛行率

Prevalence of delirium in patient with cancer

- Ranges from 15-30% in hospitalized cancer patients
- Highly prevalent in the last weeks of life (40%-85%)
- Associated with increased morbidity/ distress in patients, family and staff
- Interferes with **symptom assessment and control**

前置因子

Predisposing factors

TABLE 28.2. PREDISPOSING FACTORS IN DELIRIUM

General	Older age Male sex Alcoholism Severity of physical illness
CNS	Presence and severity of dementia and degenerative disease Cerebrovascular disease and stroke Primary brain tumor Head trauma Metastatic spread to central nervous system
Cardiopulmonary	Myocardial infarction Anemia Arrhythmia Respiratory failure
Metabolic	Dehydration Hepatic and renal impairment Nutritional deficiencies Metabolic abnormalities Hypoalbuminemia

Systemic	Neoplasm Infection Hematologic abnormalities Paraneoplastic syndrome
Other	Functional dependence and immobility Visual impairment Hip fracture

促發因子

Precipitating factors

TABLE 28.3. PRECIPITATING FACTORS IN DELIRIUM

General	Severe, acute illness Intensive care unit admission High number of hospital procedures
Central nervous system	Stroke Seizures Bleeding Narcotics
Cardiopulmonary	Myocardial infarction Cardiac surgery Shock Hypoxia
Metabolic	Hyponatremia, hypercalcemia, and other electrolyte imbalances Dehydration Acid-base disturbances Endocrinopathies
Systemic	Urinary tract infection and other infections
Other	Pain Physical restraint Orthopedic surgery Noncardiac surgery

譫妄間接原因

- Treatment side effects from chemotherapeutic agents, steroid, biological response modifiers
- Radiation
- Opioids
- Anticholinergics
- Antiemetics
- Infection
- Hematologic abnormalities

譫妄直接原因

- Primary brain tumor
- Metastatic spread
- Indirect
- Hypoxia
- Metabolic encephalopathy due to organ failure
- Electrolyte imbalance
- Withdrawal states

Medications that may cause delirium

MEDICATIONS WITH HIGH ANTICHOLINERGIC ACTIVITY

Cimetidine

Prednisone

Theophylline

Tricyclic antidepressants

Digoxin

Nifedipine

Antipsychotics (e.g., chlorpromazine)

Trihexyphenidyl (Cogentin)

Biperiden (Akineton)

Furosemide

Ranitidine

Isosorbide dinitrate

Warfarin

Dipyridamole

Codeine

Dyazide (triamterene with thiazide)

Captopril

Medications that may cause delirium

OTHER MEDICATIONS ASSOCIATED WITH DELIRIUM

Benzodiazepines

Narcotics

Antiparkinsonian agents (e.g., levodopa)

Nonsteroidal anti-inflammatory drugs

Laxatives

Antibiotics

OVER-THE-COUNTER MEDICATIONS

Diphenhydramine (e.g., Benylin)

Triprolidine (e.g., Actifed)

Chlorpheniramine (e.g., Piriton)

Promethazine (e.g., Phenergan)

Antidiarrheal agents (containing belladonna)

Irritable bowel syndrome treatments with hyoscine
(e.g., Buscopan)

Occurrence, course, outcome of delirium in advanced cancer patients

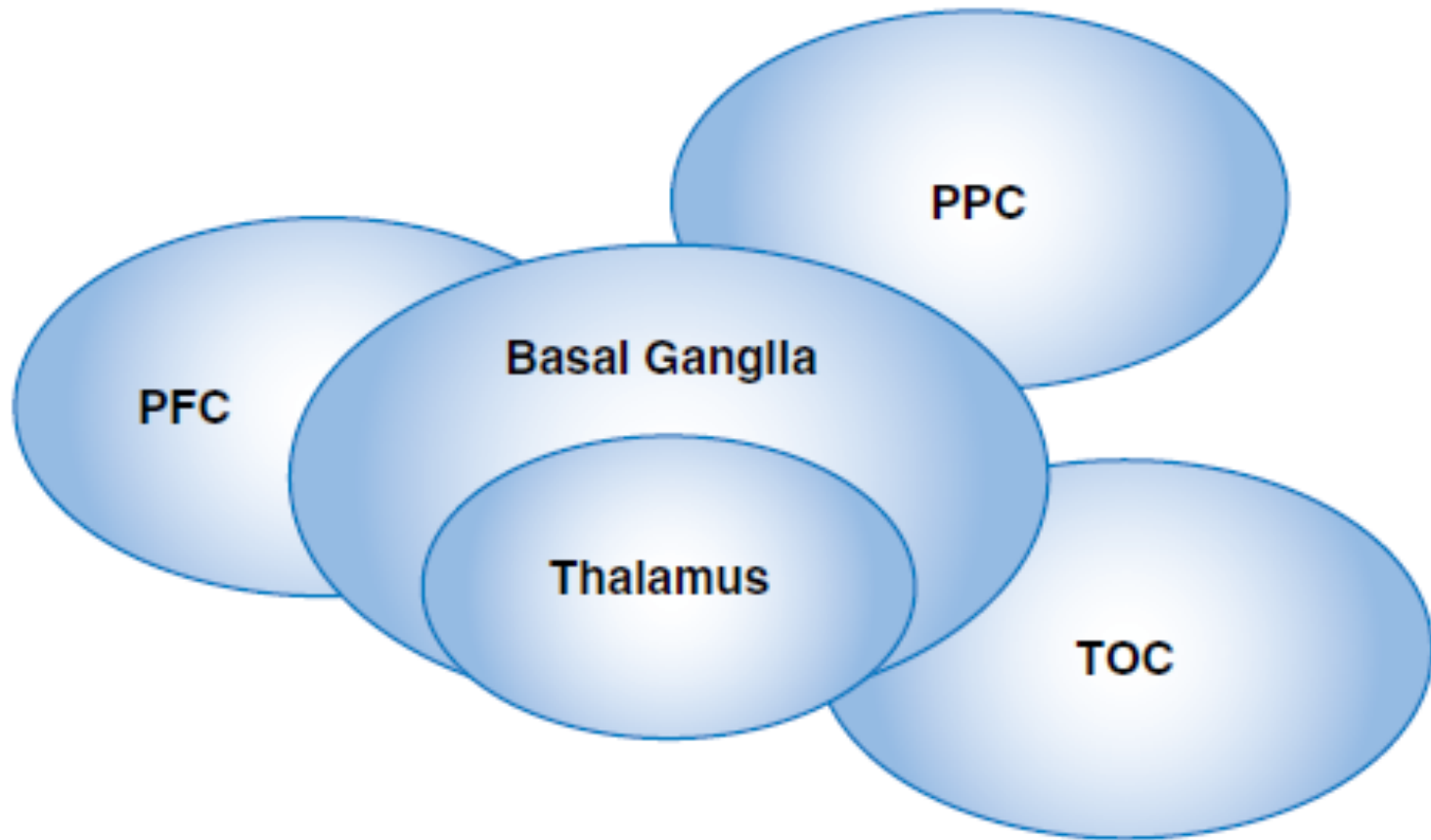
- Terminal delirium occurred in 88% of deaths
- An average of 3 etiologic factors for delirium
- Delirium is reversible in 50% of terminally ill
- Psychoactive medications (i.e. opioids) and dehydration were associated with reversibility of delirium
- Hypoxic encephalopathy and metabolic factors were associated with irreversibility
- Patients with delirium had poorer survival rates than controls ($p < 0.001$)

Neuroanatomic correlates of delirium symptoms

TABLE 28.5. NEUROANATOMIC CORRELATES OF DELIRIUM SYMPTOMS

Symptoms	Neuroanatomic Site
Alertness/arousal	Ascending reticular activating system (ARAS) Thalamus
Orientation	Right prefrontal cortex
Attention	Right prefrontal cortex Right posterior parietal cortex Thalamus
Memory	Hippocampus Thalamus
Delusions	Frontal and/or temporolimbic circuits
Hallucinations	Temporo-occipital circuits
Sleep-wake cycle	ARAS Thalamus

Common pathway delirium



■ **Figure 28.1** Final common pathway in delirium (PFC, prefrontal cortex; PPC, posterior parietal cortex; TOC, temporo-occipital cortex). Brain regions that are highly susceptible in the development of delirium and may be involved as a final common pathway in delirium.

Diagnosis of delirium

Signs and symptoms of delirium

- Confusion
- Disorientation
- Impaired memory
- Poor attention/concentration
- Disorganized speech
- Hallucination
- Delusions/paranoia
- Restlessness
- Sleep disturbance
- Anxiety
- Emotional lability
- Somnolence/withdrawn
- Agitation/combatative
- Fluctuating course

TABLE 28.6. DSM-IV CRITERIA FOR DELIRIUM

Delirium due to a general medical condition:

- A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention
- B. Change in cognition (e.g., memory deficit, disorientation, language disturbance, or perceptual disturbance) that is not better accounted for by a pre-existing, established, or evolving dementia
- C. The disturbance develops over a short period of time (usually hours to days) and tends to *fluctuate* during the course of the day
- D. There is *evidence* from the history, physical examination, or laboratory findings of a *general medical condition* judged to be *etiologically related* to the disturbance

From American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: APA; 1994, adapted with permission.

Subtypes of delirium

- Based on the type of arousal disturbance
- Hyperactive 激動興奮型
- Hypoactive 活力降低型
- Mixed 混合型

Distress in hyperactive vs hypoactive delirium

- There were no significant differences in the report of distress for patients, spouses, caregivers, or nurses based on subtype of delirium
- Hypoactive delirium was equally as distressing as hyperactive delirium for patients and nurses.

Assessment methods

TABLE 28.7. ASSESSMENT METHODS FOR DELIRIUM

Diagnostic classification systems

DSM-IV

ICD-9, ICD-10

Diagnostic interviews/instruments

Delirium Symptom Interview

Confusion Assessment Method

Delirium rating scales

Delirium Rating Scale

Delirium Rating Scale—Revised 98

Confusion Rating Scale

Saskatoon Delirium Checklist

Memorial Delirium Assessment Scale

Abbreviated Cognitive Test for Delirium

Cognitive impairment screening instruments

Mini-Mental State Exam

Short Portable Mental Status Questionnaire

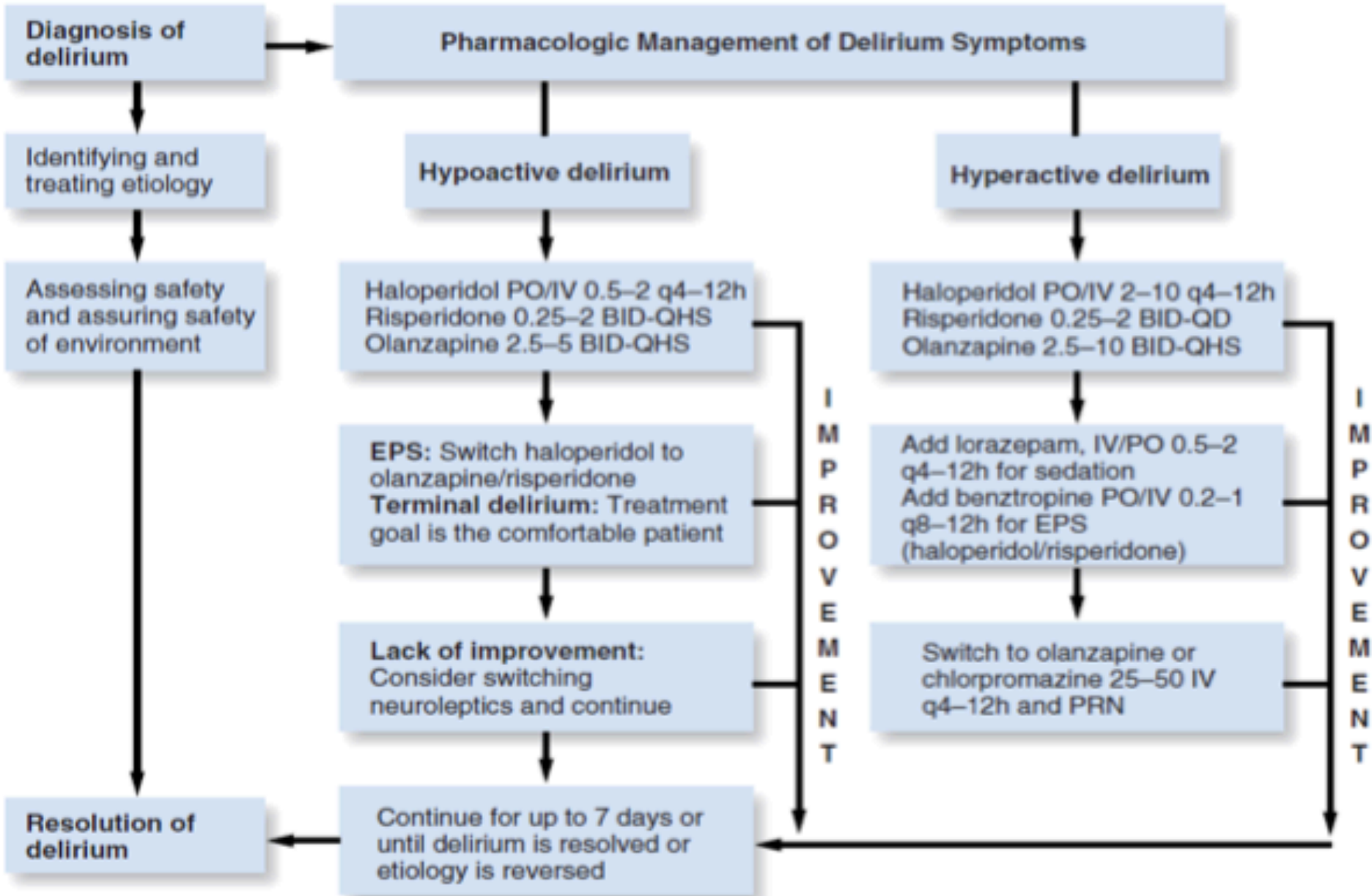
Cognitive Capacity Screening Examination

Blessed Orientation Memory Concentration Test

Memorial delirium assessment scale (MDAS)

- Reduced level of consciousness (awareness)
- Disorientation
- Short-term memory impairment
- Impaired digit span
- Reduced ability to maintain and shift attention
- Disorganized thinking
- Perceptual disturbance
- Delusions
- Decreased or increased psychomotor
- Sleep-wake cycle disturbance (disorder of arousal)

Overview of delirium management



Non-pharmacological interventions for delirium in the advanced cancer patient

- Provide safe and supportive environment for patient, staff, and family 安適環境
- Reassure family of the medical nature of delirium 家屬安撫
- Their family member is not having a nervous breakdown 腦衰竭 而非精神崩潰
- Depending on stage of disease, either reassure family of transient nature of delirium or describe as a hallmark of approaching death 事實適時解釋

- Provide proper sensory environment for patient
- Quiet, well-lit room
- Visible clock, calendar
- Familiar people, objects
- Communicate with patient and family
- Goals of care and desirable outcomes, i.e., sedation vs. awake but agitated
- Regarding hallucinations and their management or meaning

Pharmacological management of delirium

TABLE 28.9. MEDICATIONS FOR MANAGING DELIRIUM IN PATIENTS WITH ADVANCED DISEASE

Generic Name	Approximate Daily Dosage Range ^a	Route
NEUROLEPTICS		
Haloperidol	0.5–5 mg every 2–12 h	PO, IV, SC, IM
Thioridazine	10–75 mg every 4–8 h	PO
Chlorpromazine	12.5–50 mg every 4–12 h	PO, IV, IM
Methotrimeprazine	12.5–50 mg every 4–8 h	IV, SC, PO
Molindone	10–50 mg every 8–12 h	PO
Droperidol	0.625–2.5 mg every 4–8 h	IV, IM
ATYPICAL NEUROLEPTICS		
Olanzapine	2.5–20 mg every 12–24 h	PO
Risperidone	0.5–3 mg every 12–24 h	PO
Quetiapine	12.5–200 mg every 12–24 h	PO
Ziprasidone	10–80 mg every 12–24 h	PO, IM ^a
BENZODIAZEPINES		
Lorazepam	0.5–2.0 mg every 1–4 h	PO, IV, IM
Midazolam	30–100 mg every 24 h	IV, SC
ANESTHETICS		
Propofol	10–70 mg every hour Up to 200–400 mg/h	IV

PO, orally; IV, intravenously; SC, subcutaneously; IM, intramuscularly.

^aMaximum intramuscular daily dose is 40 mg.

Assessment of etiologies of delirium in advanced cancer patients

- Unclear or never discovered in over 50% of patients
- Three or more etiologies usually present
- Irreversible 30-40% of the time, especially in the terminal ill
- Etiology found in 40%-50% of cases
- 30-70% improve with treatment of etiology

Assessment of etiologies of delirium in the advanced cancer patients

- Diagnostic work-up must be consistent with the goals of cancer
- Minimally invasive in the terminally ill
- Treatments are effective and/or minimally burdensome or distressing

conclusion

- Delirium is a common neuropsychiatric complication in terminal cancer
- Medical staff must be familiar with the proper assessment, diagnosis, and management of delirium
- Appropriate management of delirium is important to minimize morbidity and improve quality of care