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Città della Salute e della Scienza di Torino

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S.S. FORMAZIONE PERMANENTE E AGGIORNAMENTO

Evento Formativo Residenziale

GLI ACCESSI VENOSI:
COME MIGLIORARNE LA GESTIONE
COINVOLGENDO I SERVIZI
TERRITORIALI

DATE

Ediz.1: 17 OTTOBRE 2018

ORARIO

Dalle ore 9.30 alle ore 16.30

SEDE

Aula Dipartimento
Rete Oncologica, Torino

ECM REGIONE PIEMONTE

CODICE: 30061 - Crediti: 7

I trattamenti per via venosa nelle fasi avanzate: quali e quando?

Alessandro Valle
Torino

FONDAZIONE FARO

Trattamenti sintomatici

Gestione emergenze

Nutrizione parenterale

Idratazione parenterale

Sedazione palliativa

Terapia del dolore

Il “pentalogo” dell’OMS…

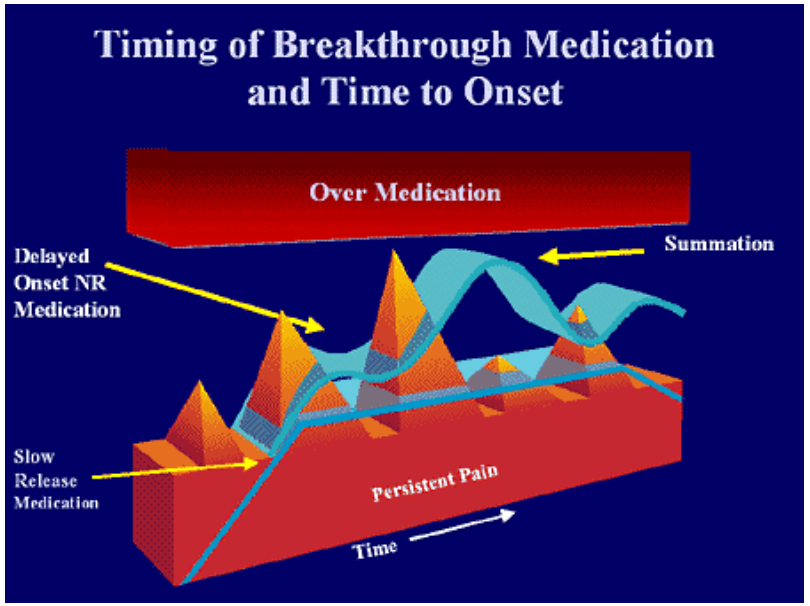
‘By mouth’
‘By the clock’
‘By the ladder’
‘For the individual’
‘Attention to detail’

World Health Organization. Cancer Pain Relief. 2nd ed. Geneva: WHO, 1996.

Breakthrough Cancer Pain (BTcP)

Nella maggior parte dei casi…

Comparsa del picco: 3-5 minuti
Intensità da moderata a severa
Durata: 30-60 minuti



Morfina solfato a rapido rilascio

Onset: 30 min
Picco: 60 min
Durata d'azione: 3-4 ore

Rapid Onset Opioids (ROOs)

oppure

Morfina endovenosa, se contesto confacente (soprattutto residenziale, accesso venoso disponibile)

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 29 (Supplement 4): iv149–iv174, 2018
doi:10.1093/annonc/mdy152

CLINICAL PRACTICE GUIDELINES

Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines†

M. Fallon[1], R. Giusti[2], F. Aielli[3], P. Hoskin[4], R. Rolke[5], M. Sharma[6] & C. I. Ripamonti[7], on behalf of the ESMO Guidelines Committee*

Treatment of moderate to severe pain

Strong opioids

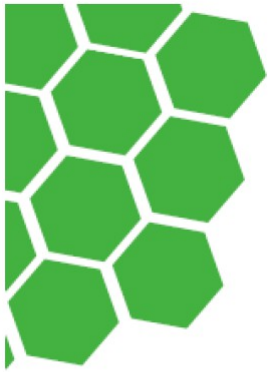
- The opioid of first choice for moderate to severe cancer pain is oral morphine [I, A]
- The average relative potency ratio of oral to i.v. morphine is between 1:2 and 1:3 [II, A]
- The average relative potency ratio of oral to s.c. morphine is between 1:2 and 1:3 [IV, C]
- Fentanyl and buprenorphine (via the t.d. or i.v. route) are the safest opioids in patients with chronic kidney disease stages 4 or 5 (estimated GFR < 30 mL/min) [II, B]
- A different opioid should be considered in the absence of adequate analgesia (despite opioid dose escalation) or in the presence of unacceptable opioid side effects [III, C]
- The s.c. route is simple and effective for the administration of morphine, diamorphine and hydromorphone and it should be the first-choice
- i.v. infusion should be considered when s.c. administration is contraindicated (peripheral oedema, coagulation disorders, poor peripheral circulation and need for high volumes and doses) [III, B]
- i.v. administration is an option for opioid titration when rapid pain control is needed [III, B]

Scheduling and titration

- Individual titration, e.g. normal-release morphine administered every 4 h plus rescue doses (up to hourly) for BTcP, is recommended in clinical practice [IV, C]
- Immediate and slow-release oral morphine formulations can be used to titrate the dose. Titration schemes for both types of formulation should be supplemented with immediate-release oral opioids, prescribed as required for BTcP [III, B]
- The regular dose of slow-release opioids can be adjusted to take into account the total amount of rescue morphine [IV, C]

Management of opioid side effects

- Laxatives must be routinely prescribed for both the prophylaxis and the management of OIC [I, A]
- The use of naloxone (in association with oxycodone) or methylnaltrexone to control OIC may be considered [II, B]
- Naloxegol has been shown to be highly effective in OIC [II, B], but, to date, there is no specific reported experience in the cancer population
- Metoclopramide and antidopaminergic drugs should be recommended for treatment of opioid-related nausea/vomiting [III, B]
- Psychostimulants (e.g. methylphenidate) to treat opioid-induced sedation are only advised when other methods to treat this have been tried (e.g. if it is not possible to rationalise all medication with a sedative side effect) [II, B]
- Mu receptor antagonists (e.g. naloxone) must be used promptly in the treatment of opioid-induced respiratory depression [I, B]



Linee guida

TERAPIA DEL DOLORE IN ONCOLOGIA

Edizione 2016

Qualità dell'evidenza SIGN	Raccomandazione clinica R12	Forza della raccomandazione clinica
A	La via sottocutanea è semplice ed efficace per la somministrazione di morfina e dovrebbe essere la prima scelta di via alternativa per pazienti che non possono ricevere oppioidi per via orale o transdermica; l'infusione endovenosa deve essere considerata quando l'infusione sottocutanea è controindicata (ad esempio, a causa di edema periferico, disturbi della coagulazione, deficit della circolazione periferica, esigenza di elevati volumi e dosi, ecc); la somministrazione endovenosa deve essere usata per la titolazione degli oppioidi, quando è richiesto un rapido controllo del dolore(1).	**Positiva forte**

clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v169–v173, 2015
doi:10.1093/annonc/mdv306

Treatment of dyspnoea in advanced cancer patients: ESMO Clinical Practice Guidelines†

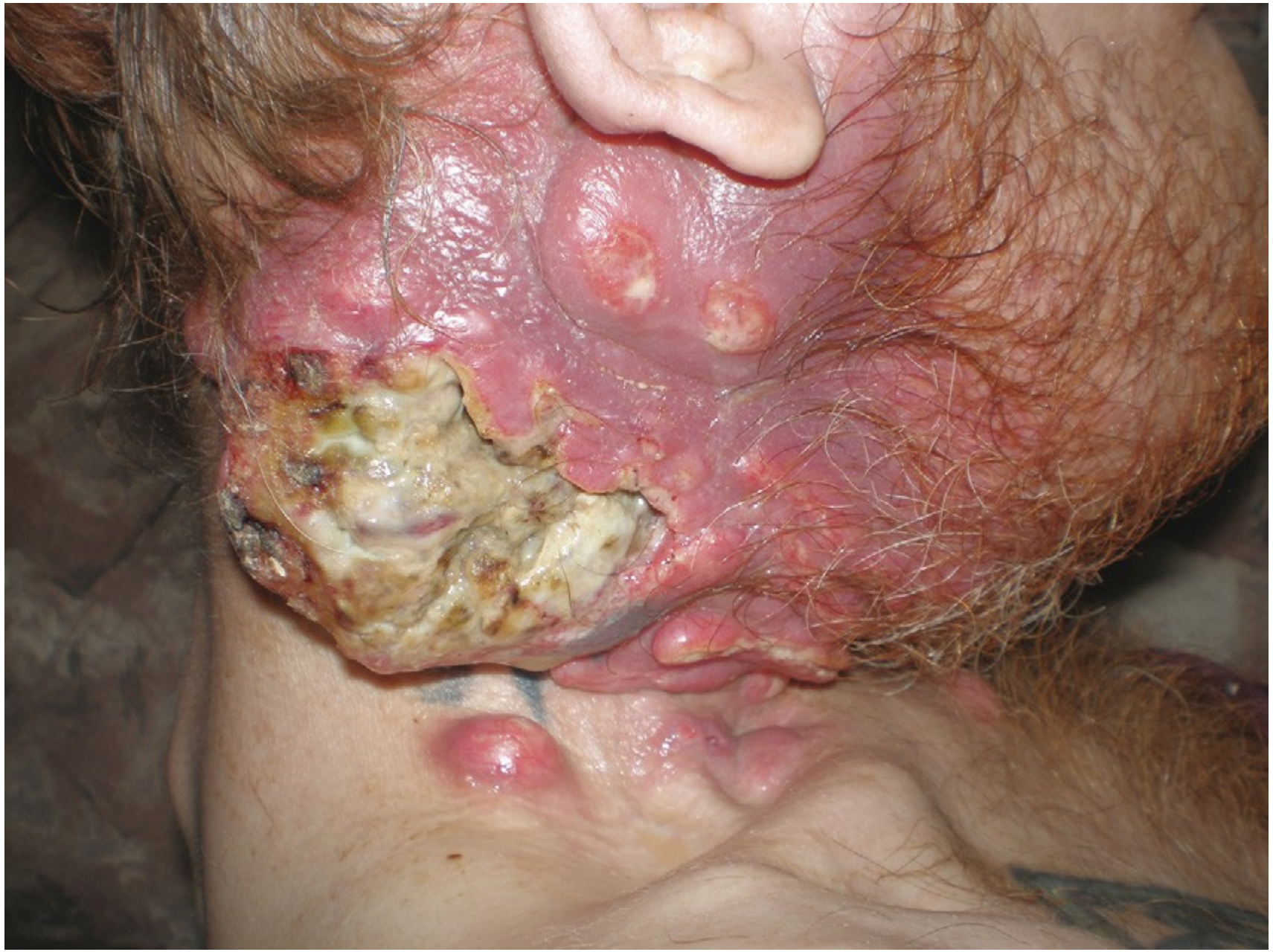
M. Kloke[1] & N. Cherny[2], on behalf of the ESMO Guidelines Committee*

[1]*Department of Palliative Medicine and Institute for Palliative Care, Kliniken Essen-Mitte, Academic Teaching Hospital University Essen-Duisburg, Essen, Germany;*
[2]*Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem, Israel*

"Opioids are the only pharmacological agents with sufficient evidence in the palliation of dyspnoea"

Analogo discorso vale per il trattamento della dispnea di base e della «breakthrough dyspnoea»

Gestione delle emergenze



Nutrizione parenterale

Clinical Nutrition xxx (2016) 1–12

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

e-SPEN guideline

ESPEN guideline on ethical aspects of artificial nutrition and hydration

Christiane Druml [a, *], Peter E. Ballmer [b], Wilfred Druml [c], Frank Oehmichen [d], Alan Shenkin [e], Pierre Singer [f], Peter Soeters [g], Arved Weimann [h], Stephan C. Bischoff [i]

[a] UNESCO Chair on Bioethics at the Medical University of Vienna, Collections and History of Medicine – Josephinum, Medical University of Vienna, Währingerstrasse 25, A-1090 Vienna, Austria
[b] Department of Medicine, Kantonsspital Winterthur, Brauerstrasse 15, Postfach 834, 8401 Winterthur, Switzerland
[c] Division of Nephrology and Dialysis, Department of Internal Medicine III, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria
[d] Department of Early Rehabilitation, Klinik Bavaria Kreischa, An der Wolfsschlucht 1-2, 01731 Kreischa, Germany
[e] Department of Clinical Chemistry, University of Liverpool, Duncan Building, Daulby Street, Liverpool L69 3GA, UK
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[g] Department of Surgery, Academic Hospital Maastricht, Peter Debeyelaan 25, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
[h] Department of General Surgery and Surgical Intensive Care, St Georg Hospital, Delitzscher Straße 141, 04129 Leipzig, Germany
[i] Department of Nutritional Medicine, University of Hohenheim, Fruwirthstr. 12, 70599 Stuttgart, Germany

Statement 2:

The ethical principles "autonomy, beneficence, non-maleficence and justice" are internationally recognized. They are interrelated and have to be applied in the act of medical decision making. [Strong Consensus]

Statement 3:

Autonomy does not mean that a patient has the right to obtain every treatment him or her wishes or requests, if this particular treatment would not be medically indicated. [Strong Consensus]

FNOMCeO

Art. 13
Prescrizione a fini di prevenzione, diagnosi, cura e riabilitazione
(…)
La prescrizione deve fondarsi sulle evidenze scientifiche disponibili, sull'uso ottimale delle risorse e sul rispetto dei principi di efficacia clinica, di sicurezza e di appropriatezza.
(…)
Il medico tiene conto delle linee guida diagnostico-terapeutiche accreditate da fonti autorevoli e indipendenti quali raccomandazioni e ne valuta l'applicabilità al caso specifico. L'adozione di protocolli diagnostico-terapeutici o di percorsi clinico-assistenziali impegna la diretta responsabilità del medico nella verifica della tollerabilità e dell'efficacia sui soggetti coinvolti.
(…)
Il medico non acconsente alla richiesta di una prescrizione da parte dell'assistito al solo scopo di compiacerlo.

Statement 5:

If the risks and burdens of a given therapy for a specific patient outweigh the potential benefits, then the physician has the obligation of not providing (withholding) the therapy. [Strong Consensus]

Statement 11:

Every individual is entitled to obtain the best care available. Resources have to be distributed fairly without any discrimination. On the other hand treatments which are futile and do only prolong the suffering or the dying phase, have to be avoided. In regard to limited resources there has to be proper use of ethically appropriate and transparent criteria. [Strong Consensus]

Statement 33:

A medical treatment, which does not provide any benefit or has become disproportionate can be withdrawn or withheld. Limitation of treatment may imply progressively withdrawing it or reducing the dose administered to limit side effects. [Strong Consensus]

Statement 19:

Artificial nutrition has become a part of palliative care, e.g. in neurological and in cancer patients, with the potential to increase survival and quality of life in selected patients. Long term home enteral and parenteral nutrition programs should be considered (for details see disease-related guidelines). [Strong Consensus]

Statement 7:

Artificial nutrition is used in accordance with a realistic goal of individual treatment, and the wishes of the patient himself/herself, and based on assessment of the situation by the doctor and other health-care professionals. [Strong Consensus]

Statement 10:

The continued medical justification for artificial nutrition must be reviewed at regular intervals, determined in accordance with the patient's condition. [Strong Consensus]

Statement 20:

There are no clear criteria to ascertain the beginning of the dying phase. Therefore, a nutritional intervention in this phase of life should be followed in an individualized manner. [Consensus]

Statement 32:

In the absence of an indication and lack of achieving a treatment goal or in the absence of consent, nutritional therapy should be discontinued. This may lead to individual emotional and/or ethical conflicts among family members or team members (doctors, nursing staff and members of other therapeutic professions). [Consensus]

Clinical Nutrition xxx (2016) 1–38

Contents lists available at ScienceDirect

Clinical Nutrition

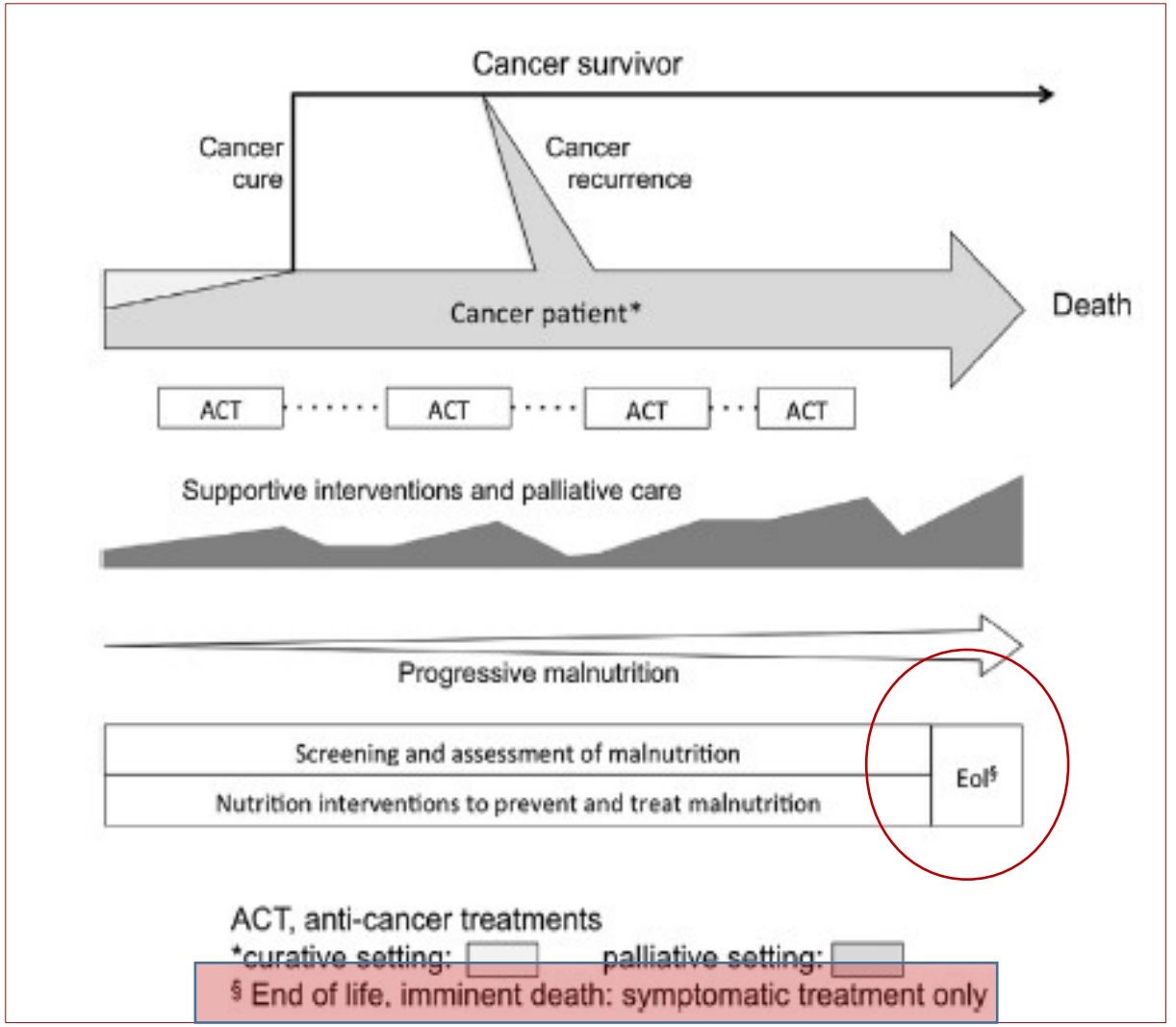
journal homepage: http://www.elsevier.com/locate/clnu

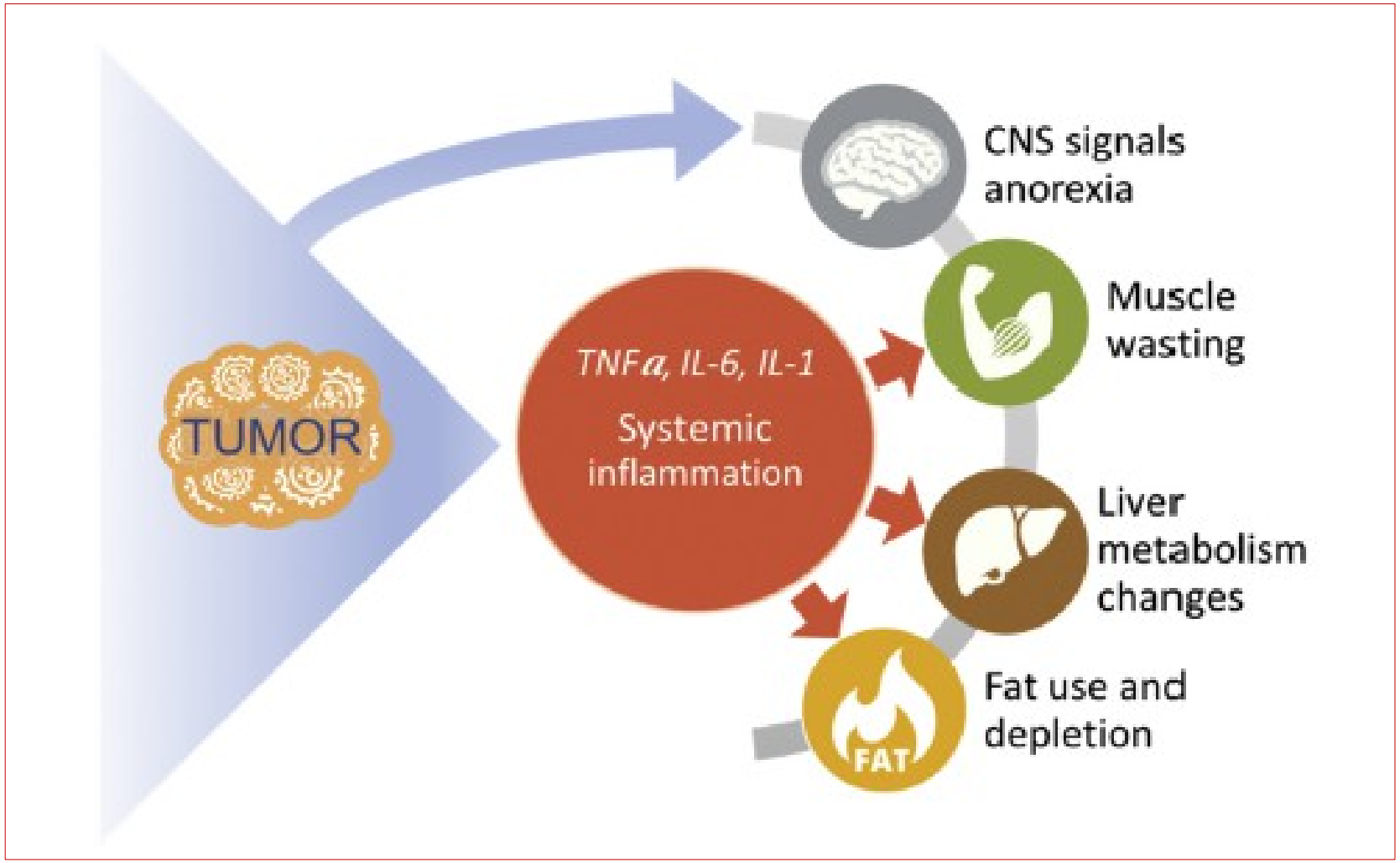
ESPEN Guideline

ESPEN guidelines on nutrition in cancer patients*

Jann Arends [a], Patrick Bachmann [b], Vickie Baracos [c], Nicole Barthelemy [d], Hartmut Bertz [a], Federico Bozzetti [e], Ken Fearon [f, l], Elisabeth Hütterer [g], Elizabeth Isenring [h], Stein Kaasa [i], Zeljko Krznaric [j], Barry Laird [k], Maria Larsson [l], Alessandro Laviano [m], Stefan Mühlebach [n], Maurizio Muscaritoli [m], Line Oldervoll [i, o], Paula Ravasco [p], Tora Solheim [q, r], Florian Strasser [s], Marian de van der Schueren [t, u], Jean-Charles Preiser [v, *]

Nearing the end of life treatment needs to focus on symptomatic support including alleviating hunger and thirst while all additional nutritional support may do more harm than good.




TUMOR
TNFα, IL-6, IL-1
Systemic inflammation
CNS signals anorexia
Muscle wasting
Liver metabolism changes
Fat use and depletion
FAT

Ricapitolando, la nutrizione parenterale può essere:

- **Utile: il paziente, seppur in fase avanzata, è ancora in discrete condizioni generali ed ha un'aspettativa di vita di almeno 1-3 mesi (Palliative Prognostic Score, Palliative Prognostic Index)**

Palliative Prognostic Score

Dyspnea	No Yes	0 1
Anorexia	No Yes	0 1.5
Karnofsky Performance Status	> 30 10 – 20	0 2.5
Clinical Prediction of Survival (weeks)	> 12 11 – 12 7 – 10 5 – 6 3 – 4 1 – 2	0 2 2.5 4.5 6 8.5
Total WBC (x10 9/ L)	< 8.5 8.6 – 11 >11	0 0.5 1.5
Lymphocyte Percentage	20 – 40 % 12 – 19.9 % < 12 %	0 1 2.5
RISK GROUP	**30 DAY SURVIVAL**	**TOTAL SCORE**
A	**> 70 %**	**0 – 5.5**
B	**30 – 70 %**	**5.6 – 11**
C	**< 30 %**	**11.1 – 17.5**

Pirovano 1999, Glare 2004

Palliative Prognostic Index

Variable		Partial Score Value
PPS		
	10-20	4
	30-50	2.5
	60+	0
Oral Intake		
	Severely Reduced	2.5
	Moderately Reduced	1.0
	Normal	0
Edema		
	Present	1.0
	Absent	0
Dyspnea at Rest		
	Present	3.5
	Absent	0
Delirium		
	Present	4.0
	Absent	0

Total Score	6-week survival	
	PPV	NPV
>4	0.83	0.71

Morita 2001

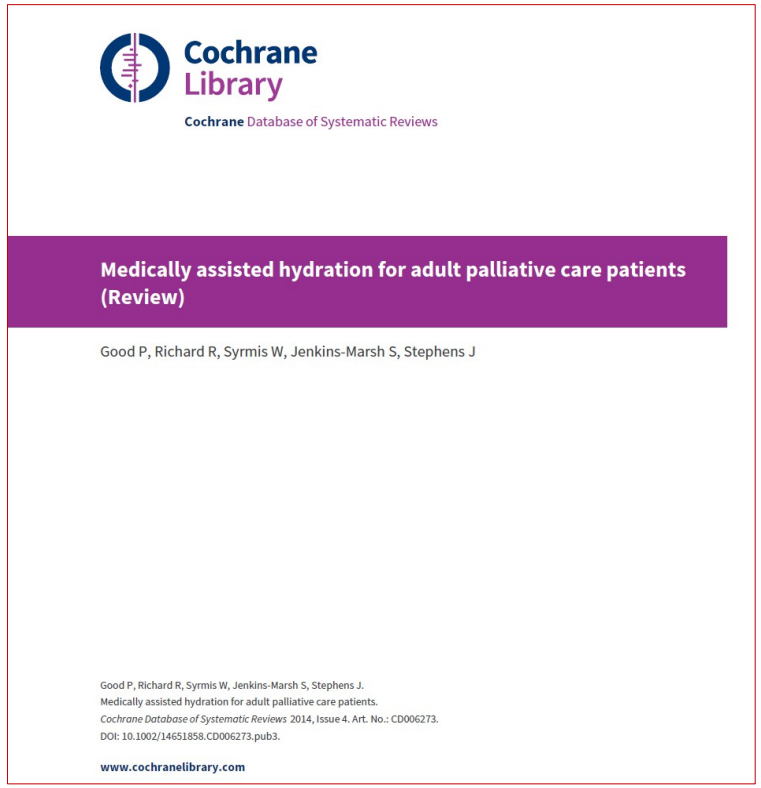
Ricapitolando, la nutrizione parenterale può essere:

- **Utile: il paziente, seppur in fase avanzata, è ancora in discrete condizioni generali ed ha un'aspettativa di vita di almeno 1-3 mesi (Palliative Prognostic Score, Palliative Prognostic Index)**

- **Futile: le alterazioni metaboliche indotte dalla malattia non consentono più l'utilizzo dei nutrienti somministrati**

- **Controindicata: la debilitazione dell'ammalato è tale che l'impegno metabolico e soprattutto emodinamico indotto dall'alimentazione artificiale può determinare uno scompenso cardiaco acuto**

Idratazione parenterale



Authors' conclusions

Since the last version of this review, we found one new study. The studies published do not show a significant benefit in the use of medically assisted hydration in palliative care patients; however, there are insufficient good-quality studies to inform definitive recommendations for practice with regard to the use of medically assisted hydration in palliative care patients.

Invited Review

Artificial Hydration at the End of Life

Alexandria J. Bear, MD[1]; Elizabeth A. Bukowy, DO[2]; and Jayshil J. Patel, MD[3]

Nutrition in Clinical Practice
Volume 32 Number 5
October 2017 628–632

DOI: 10.1177/0884533617724741
journals.sagepub.com/home/ncp

Table 1. Randomized Controlled Trials Evaluating the Impact of Artificial Hydration at the End of Life.

Author	Year	Interventions	Primary Outcome	Results
Bruera et al[21]	2013	Parenteral hydration (1000 mL normal saline) vs placebo (100 mL normal saline) daily	Change in dehydration symptoms score[a]	No significant difference in symptoms score
Cerchietti et al[19]	2000	Subcutaneous hydration (1000 mL 5% dextrose at 42 mL/h) vs placebo	Change in thirst, chronic nausea, and delirium	No significant difference in change in thirst or delirium; significant change in relief of chronic nausea at 48 hours
Bruera et al[20]	2005	Parenteral hydration (1000 mL) vs placebo (100 mL) over 4 hours for 2 days	Change in hallucinations, myoclonus, fatigue, and sedation	Significant difference in composite outcome of target symptoms and myoclonus in study group; no significant difference in hallucinations, fatigue

[a]Score includes symptoms of fatigue, myoclonus, sedation, and hallucinations.

Annals of Oncology 0 (Supplement 0): iv1–iv23, 2018
doi:10.1093/annonc/mdy147

CLINICAL PRACTICE GUIDELINES

Delirium in adult cancer patients: ESMO Clinical Practice Guidelines†

S. H. Bush[1,2,3,4], P. G. Lawlor[1,2,3,4], K. Ryan[5,6,7], C. Centeno[8,9,10], M. Lucchesi[11], S. Kanji[2,12], N. Siddiqi[13,14], A. Morandi[15], D. H. J. Davis[16], M. Laurent[17,18], N. Schofield[19], E. Barallat[20] & C. I. Ripamonti[21], on behalf of the ESMO Guidelines Committee*

Table 5. Summary of recommendations

Clinical assessment, diagnosis and screening

- The diagnosis of delirium should be made by a trained and competent healthcare professional using a clinical assessment based on DSM or ICD criteria [II, C]
- The evidence is insufficient to recommend the routine use of screening tools in making a diagnosis of delirium in cancer patients [III, C]
- If any changes in cognitive or emotional behaviour or psychomotor activity suggestive of delirium are present, a trained healthcare professional with expertise in evaluating delirium should carry out a clinical assessment to confirm the diagnosis of delirium [III, C]
- The evidence is insufficient to recommend for or against the routine use of tools to assess delirium severity in daily practice [III, C]

Management of potentially reversible causes of the delirium episode

- For cancer patients whose assessments indicate delirium, identify the predisposing and precipitating factors through a comprehensive initial assessment [III, A]
- Opioid rotation (or switching) may be appropriate if signs of OIN are present [V, B]

- There is limited research evidence for the role of clinically assisted hydration in the symptomatic management of delirium [V, C]

- Bisphosphonates (such as i.v. pamidronate and zoledronic acid) may control hypercalcaemia and reverse delirium in a substantial number of cases [I, A]
- The discontinuation of implicated medications, fluid restriction and adequate oral salt intake is recommended for the management of confirmed SIADH [V, C]
- Magnesium replacement is recommended for the management of hypomagnesaemia [V, C]
- Medication or therapy withdrawal is recommended in patients with delirium related to anticancer treatments such as chemotherapy and immunotherapies [V, C]

Non-pharmacological interventions for delirium prevention and treatment in adults with cancer

- Clinically assisted hydration is not more effective than placebo in preventing delirium [II, C]

- Given the absence of studies evaluating pharmacological prevention of delirium in cancer patients, no evidence-based recommendations are proposed [V, C]
- Based on available evidence, deprescribing would appear to be worthwhile in older patients for many reasons, although there is insufficient data to support this recommendation for all cancer patients from the specific perspective of delirium prevention [V, B]
- Opioid rotation (or switching) to fentanyl or methadone is an efficacious strategy in the context of opioid-associated delirium [V, B]
- Administration of either haloperidol or risperidone has no demonstrable benefit in the symptomatic management of mild-to-moderate delirium and is not recommended in this context [I, D]
- Administration of olanzapine may offer benefit in the symptomatic management of delirium [III, C]
- Administration of quetiapine may offer benefit in the symptomatic management of delirium [V, C]
- Administration of aripiprazole may offer benefit in the symptomatic management of delirium [IV, C]
- Methylphenidate may improve cognition in hypoactive delirium in which neither delusions nor perceptual disturbance are present and for which no cause has been identified [V, C]
- Benzodiazepines are effective at providing sedation and potentially anxiolysis in the acute management of severe symptomatic distress associated with delirium [II, C]

Experiential impact of delirium, support and education

- While not all patients with cancer will develop delirium, we recommend that relatives have access to information about delirium pre-emptively and at repeated intervals, especially if the patient's condition is declining due to disease progression. This information should also be disseminated to the wider family who are likely to visit [V, A]
- If delirium develops, written information should be supplemented with educational and psychological support for families by suitably trained staff [V, A]
- Interprofessional delirium education interventions should be a core component of an interprofessional unit- or hospital-wide strategy to improve the recognition, assessment and management of delirium by the whole healthcare team [II, A]

DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Diseases; i.v., intravenous; OIN, opioid-induced neurotoxicity; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

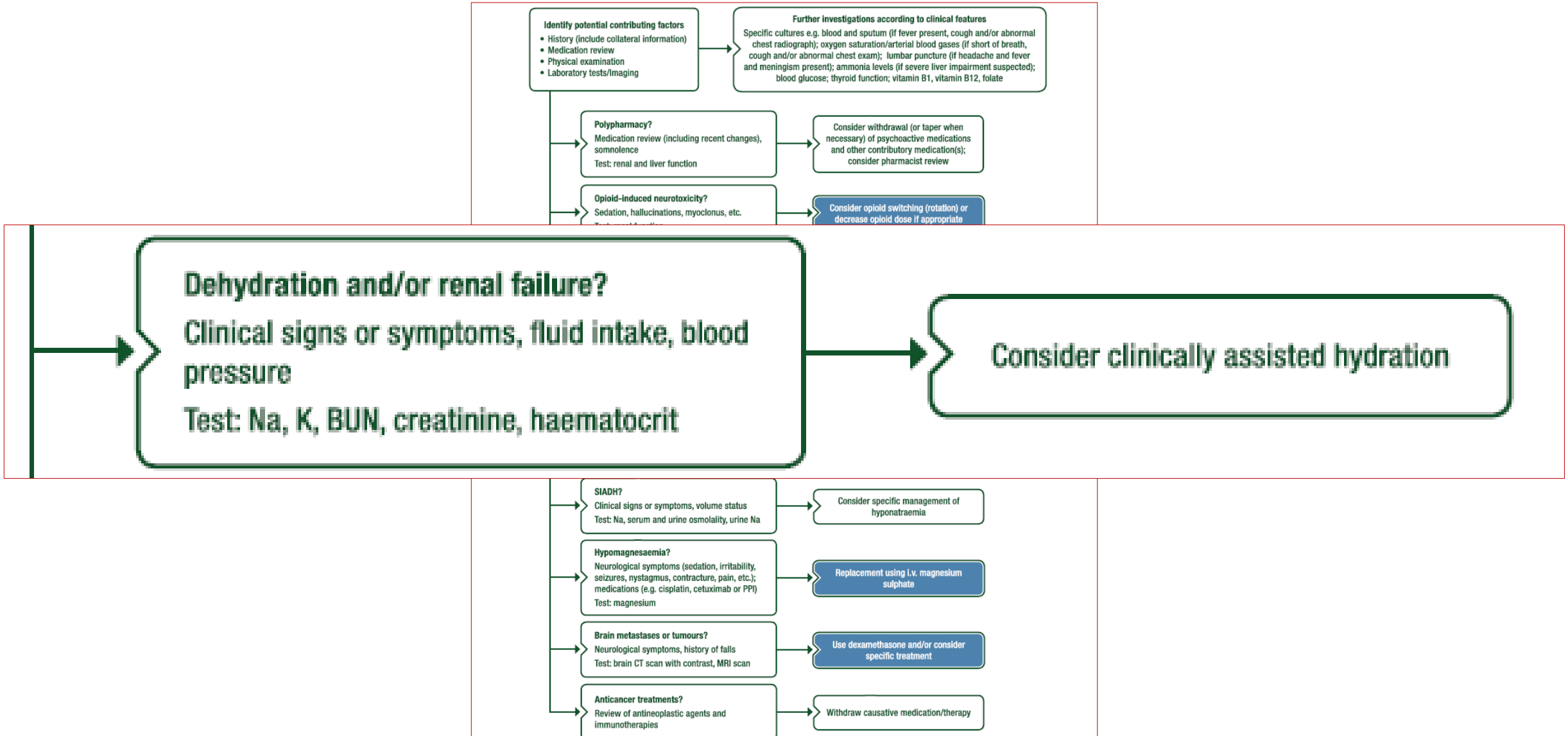


Figure 2. Evaluation* of the adult cancer patient for underlying causes of delirium.
*This should be guided by the patient's goals of care.
BUN, blood urea nitrogen; CT, computed tomography; EoL, end of life; i.v., intravenous; K, potassium; MRI, magnetic resonance imaging; Na, sodium; PCR, polymerase chain reaction; PPI, proton pump inhibitor; SIADH, syndrome of inappropriate antidiuretic hormone secretion; WBC, white blood cell.

L’idratazione parenterale può essere:

- **(Forse) Utile: favorisce l’eliminazione dei metaboliti tossici prodotti dall’organismo e dei metaboliti dei farmaci; può prevenire i sintomi della disidratazione (ottundimento del sensorio, nausea, ecc.)**
- **Futile: non arreca beneficio ma neppure effetti collaterali**
- **Controindicata: la debilitazione dell’ammalato è tale che l’impegno emodinamico indotto dall’(iper)idratazione artificiale può determinare uno scompenso cardiaco acuto**

Sedazione palliativa

“Pratica volta ad alleviare sintomi refrattari riducendo lo stato di coscienza in misura adeguata e proporzionata alle necessità, effettuata quando la morte è attesa entro un lasso di tempo compreso tra poche ore e pochi giorni”

Sedazione profonda temporanea

(ad es. crisi asfittica, momenti di particolare sofferenza esistenziale)

Sedazione palliativa profonda continua

Elementi indispensabili…

- **Consenso informato (paziente «competent»)**
- **Sintomo refrattario (non difficile…)**
- **Imminenza della morte (prognosi di qualche giorno)**

Sedazione palliativa profonda continua

- La via sottocutanea è utilizzabile in assenza di alternative, però l'ipotensione arteriosa in queste fasi rende incerto l'assorbimento dei farmaci
- Alcuni farmaci sono somministrabili per via sottocutanea (midazolam, aloperidolo), altri no (fenotiazine)
- La via endovenosa garantisce il completo assorbimento dei farmaci somministrati

In buona sostanza…

…appropriatezza e flessibilità

Grazie per l'attenzione