SYLLABUS

TC30: Palliative Care

Tuesday, November 15, 2011 14:30-18:00 Hall K

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH World Congress of Neurology

WFN

SMN SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Tuesday, 15 November, 2011

14:30-18:00

PALLIATIVE CARE

Chairperson: **Marianne de Visser**, *The Netherlands*

PALLIATIVE CARE IN NEUROLOGY - AN OVERVIEW
Gian Domenico Borasio,*Germany*

PALLIATIVE CARE IN SEVERE TRAUMATIC BRAIN INJURY: WHEN, WHY, HOW?
Pieter E. Vos, *The Netherlands*

ALS, A PARADIGMATIC DISEASE FOR PALLIATIVE CARE
Marianne de Visser, *The Netherlands*

16:00-16:30 *Coffee Break*

Teaching Course
Session Title: TC30: Palliative Care To take place on:
Tuesday, November 15, 2011 from 14:30-18:00

Gian Domenico Borasio - Palliative Care in Neurology
Pieter Vos – Palliative care in severe traumatic brain Injury: When, why, how?
Marianne de Visser – Palliative care in amyotrophic lateral sclerosis

Palliative Care is an approach which improves quality of life of patients and their families facing life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual (WHO 2002).
In this teaching course an introduction to palliative care in neurological disorders will be given. Subsequently palliative care in two specific disease categories (ALS and severe traumatic brain injury) will be discussed.

Course objectives
The course will explore the core concepts related to palliative care, including symptom management, communication skills, and evidence based practice, psychosocial issues and the role of the family caregiver.

XX World Congress of Neurology
Marrakesh, Morocco
TC30: Palliative Care

UMC St Radboud

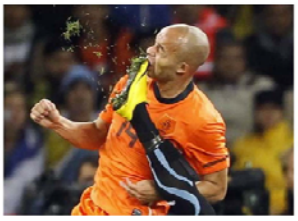
Palliative care in severe traumatic brain injury When, why, how?

P. E. Vos

Radboud University Nijmegen Medical Centre
Department of Neurology
Nijmegen
The Netherlands

Outline

- Introduction Traumatic Brain Injury
- When: Problem to determine end stage of recovery in TBI
- Why: From care - palliative care - end of life decisions
- How: Procedures in the acute and chronic phase



UMC St Radboud

"The circumstances leading to head injury and the physiological effects are short and sharp; but the consequences of such injuries may blight the lives of affected individuals for a very long time"

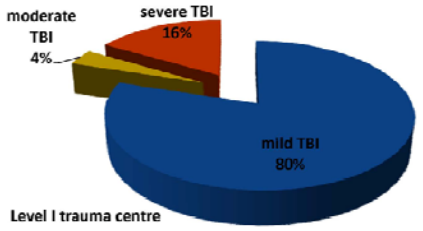
Alastair Compston

Brain (2007) 130,2479-2481

TBI: among the most frequent neurological disorders

Mild TBI: 100-300/ 100.000 (Cassidy, 2004)

TBI: 235-556/ 100.000 (Rutland-Brown, 2006; Tagliaferri, 2006)



Jacobs et al.; *J Neutrau*; 2010, 27:655-68

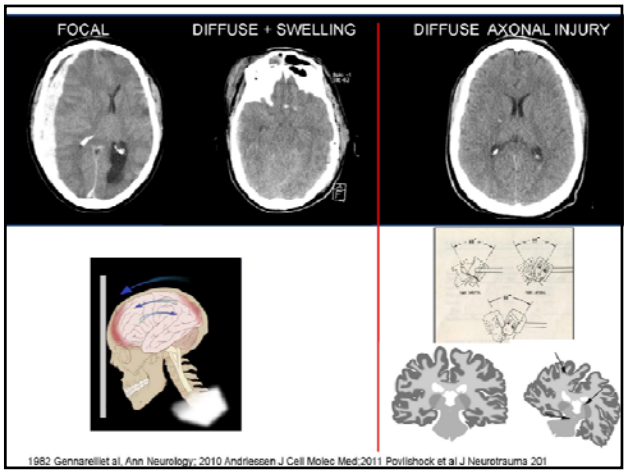
TBI: definitions

Mild TBI → **GCS: 13-15**
- LOC ≤ 30 minutes
- PTA ≤ 24 hours
- alteration of mental state
- retrograde amnesia

Moderate TBI → **GCS: 9-12**

Severe TBI → **GCS ≤ 8**

MTBI committee of the American Congress of Rehabilitation Medicine, 1993, *J Head Trauma Rehabil*



1982 Gennarelliet al, Ann Neurology; 2010 Andriessen J Cell Molec Med;2011 Povlishock et al J Neurotrauma 201

Intensive Care

- Monitoring
- Intubation/ sedation
- ICP measurement- treatment
  - sedation + analgetics
  - csf drainage
  - osmotherapy mannitol, hyertonic saline
  - hyperventilation
  - craniectomie
- Maintaining normothermia

Traumatic Brain Injury
"Disease" rather than "Event"

phases

- ❑ Coma arousal-consciousness — weeks
- ❑ Vegetative State- consciousness
- ❑ Minimally Conscious State- consciousness basic attention — months
- ❑ Post traumatic amnesia (disorientation, memory disorders and behavioral disturbances)
- ❑ Recovery from functions (motor, cognitive and behavioral) memory self awareness — years
- ❑ Chronic disability-acceptation and compensation — decades

Levin, J Nerv Ment Dis, 1979 Rao,Psychosomatics, 2000, Masel J Neurotrauma 2010

End of life decisions in TBI

- Acute phase
- Chronic phase

When: Therapy decisions in the care of critically ill

- Acute phase during Intensive care "futility of care"
- Chronic phase Vegetative State end point of recovery

Witholding and withdrawing therapy at the ICU

- 22.4% of americans die using ICU services
- Most ICU deaths occur after a decision to withhold life-sustaining interventions

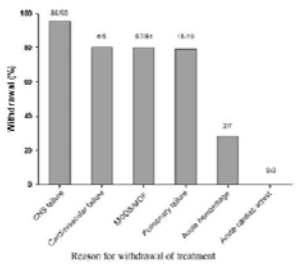
Kuschner et al, Implementation of ICU Palliative Care Guidelines and procedures. Chest 2009;135: 26-32
Angus et al, Use of intensive care at the end of life in the United States:An epidemiologic studyCrit Care Med 2004; 32:638 –643

neurocritical care society Neurocrit Care
DOI 10.1007/s12028-011-9567-y

ETHICAL MATTERS

Withdrawal of Life-Sustaining Treatment in a Mixed Intensive Care Unit: Most Common in Patients with Catastropic Brain Injury

Martijn A. Verkade · Jelle L. Epker · Mariska D. Nieuwenhoff · Jan Rakker · Erwin J. O. Kompanje



WHO Definition of Palliative Care

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

How: Therapy decisions in the care of critically ill

- 1. withholding or withdrawing of some or all ICU therapy
- 2. withdrawing certain or total intensive care treatment
- 3. to anticipate and treat, for the patient, relatives or care givers, symptoms caused by withholding or withdrawal of treatment

Limiting, withholding, withdrawal therapy

- Clinicians are psychologically more comfortable withholding treatments than withdrawing them

Cf Truog, et al Crit Care Med 2008; 36:953–963

Limiting therapy

- Yes/no act when arterial oxygen saturation drops (i.e SaO2 < 90%
- Yes/no act when apnea
- Yes/no act when difficulites with breathing
- Yes/no treat respiratory insufficiency
- Yes/no renal replacement therapy
- Yes/no (repeat) surgical operation

Cf Truog, et al Crit Care Med 2006; 36:953–963

Withdrawal of therapy

1. Paralytic agents should never be introduced at the time of withdrawal of life support.
2. When patients have been receiving paralytic agents, neuromuscular function should ideally be restored before withdrawal of life support.

Cf Truog, et al Crit Care Med 2006; 36:953–963

Withdrawal of therapy

1. Withdrawal of mechanical ventilation.
2. Adequate sedation and analgesia
3. Prevent post extubation stridor and death rattle

Dutch national ICU guideline on palliative care 2009; Committee on National Guideline for Palliative Sedation, Royal Dutch Medical Association. Guideline for palliative sedation. Available from Utrecht:KNMG, 2009.

Symptom Management in End-of-Life Care

1. Dyspnea and Respiratory Distress
2. Delirium and agitated delirium
3. Pain

Truog, et al Crit Care Med 2008; 36:953–963

Drug treatment as a component of end of life care

OPIOIDS

	Equivalent Dose, IV[a]	Onset to Peak Effect, mins	Duration of Effect, hrs	Typical Adult Dose, IV	Typical Pediatric Dose, IV	Typical Infusion Rate
Morphine	10 mg	20–30	3–4	2–10 mg	0.1 mg/kg	0.05–0.5 mg·kg^{-1}·hr^{-1}
Fentanyl	100 µg	2–5	0.5–2	0.5–2 µg/kg	1–5 µg/kg	0.5–10 µg·kg^{-1}·hr^{-1}
Hydromorphone	1.5–2 mg	20–30	3–4	0.5–2 mg	—	—

SEDATIVES

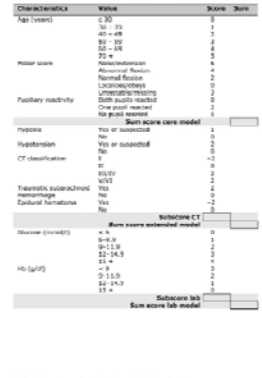
	Onset to Peak Effect, mins	Duration of Effect, hrs	Typical Initial Adult Dose, IV	Typical Initial Pediatric Dose, IV	Typical Initial Infusion Dose, Adult	Typical Initial Infusion Dose, Pediatric
Sedatives						
Lorazepam	20–25	2–4	1–3 mg	0.05 mg/kg	0.5–4 mg/hr	0.05–0.1 mg·kg^{-1}·hr^{-1}
Midazolam	5–10	1.5–2	0.02–0.1 mg/kg	0.1 mg/kg	1–5 mg/hr	0.05–0.1 mg·kg^{-1}·hr^{-1}
Propofol	1–2	0.1–0.4	1 mg/kg	1 mg/kg	10–50 µg·kg^{-1}·min^{-1}	10–50 µg·kg^{-1}·min^{-1}
Neuroleptics						
Haloperidol	25–30	2–4	0.5–20 mg	—	3–5 mg/hr	—

Truog, et al Crit Care Med 2008; 36:953–963

When: Prognostic models in TBI

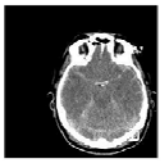
- Acute phase Intensive care "futility of care"
- Chronic phase Vegetative State

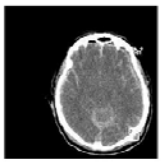
Acute Phase Prediction Models



Steyerberg EW, et al. (2008) PLoS Med 5(8): e165. doi:10.1371/journal.pmed.0050165

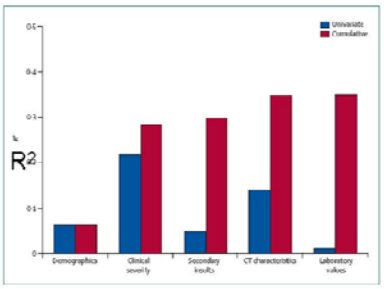
Perel et al.; *BMJ* 2008; online





Male 79,
GCS=3 without sedation, severe hypotension-reanimation
PR-/-

Acute Phase Prediction Models



- **Demographic and clinical factors account for 35% of the variation in outcome**

Lingsma, Lancet Neurology 2010

When recovery from TBI stagnates? The vegetative state

WHO Definition of Palliative Care

Palliative care:
•provides relief from pain and other distressing symptoms;
•affirms life and regards dying as a normal process;
•intends neither to hasten or postpone death;
•integrates the psychological and spiritual aspects of patient care;
•offers a support system to help patients live as actively as possible until death;
•offers a support system to help the family cope during the patients illness and in their own bereavement;
•uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
•will enhance quality of life, and may also positively influence the course of illness;
•is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

Frequence of the vegetative state after TBI cohort studies

	Int. Databank	TCDB	GB4	EBIC	ATBIS	AUSTRIA	POCON
Study specifications							
Cohort size	2978	746	988	583	363	492	339
Period	1968-1983	Jan 1984-Sep 1987	1986-1988	Feb-Apr 1995	Apr-Sep 2000	Oct 1999-Mar 2004	June 2008-2009
Centers	5 (UK, NLD, USA)	6 (USA)	4 (GB)	67 (Europe)	16 (AUS, NZL)	5 (AUT)	5 (NLD)
Age	Any	Any	Any	≥16 yrs	≥16 yrs	Any	≥16 yrs
Admission	None	<48 hrs	<72 hrs	<24 hrs	None	None	<72 hrs
GCS	Coma (E=1, V≤2, M≤5) >6 hrs	≤8 post-resuscitation or after deterioration	Coma (E=1, V≤2, M≤5) or EML	≤8 At NSU admission	≤8 At ED	≤8 post-resuscitation or within 48 hrs	≤8 at ED admission
Demographics and injury characteristics							
Age, mean (sd)	36 (21)	30 (NR)	34 (21)	41 (20)	39 (19)	49 (21)	46 (20)
Gender, male	79%	77%	75%	73%	74%	72%	70%
Injury mechanism							
Traffic	56%	75%	57%	52%	60%	44%	51%
Fall	NR	NR	NR	NR	24%	40%	37%
Fall with Alc.	19%	16%	16%	11%	NR	NR	12%
Alcohol intoxication	20%	NR	39%	NR	NR	30%	27%
Major extracr. injury	35%	NR	39%	41%	NR	NR	48%
TCDB CT classification							
%CT assessed	42%	97%	93%	95%	87%	84%	94%
Diffuse I/II	26%	32%	25%	37%	55%	NR	50%
Diffuse III/IV	19%	22%	12%	12%	12%	NR	19%
EML	37%	37%	36%	28%	10%	NR	26%
NEML	18%	5%	27%	20%	20%	NR	16%
SAH	NR	39%	NR	47%	37%	36%	46%
Management							
Direct admission	NR	61%	12%	45%	56%	NR	85%
ICP monitoring	35%	NR	31%	43%	45%	64%	38%
Intracranial operation	47%	37%	39%	37%	42%	67%	23%
Outcome (6 month GOS)							
% Follow up	60%	100%*	60%	83%	93%	88%***	85.40%****
1: Dead	49%	36%	39%	40%	32%	44%	46%
2: VS	7%	5%	1%	4%	1%	7%	0.7%
3: SD	13%	16%	17%	16%	22%	9%	13%
4: MD	15%	16%	16%	19%	27%	12%	18%
5: GR	20%	27%	24%**	21%	16%	27%	20%
REF's	(Jennett et al., 1977; Murray, 1986; Murray et al., 1999a)*	(Foulkes et al., 1991; Marshall et al., 1983; Marshall et al., 1991b)	(Murray et al., 1999a; Murray et al., 1999b)*	(Murray et al., 1999a)	(Myburgh et al., 2008)	(Leitgeb et al., 2007; Rosso et al., 2007; Rusnak et al., 2007)	This paper

Andriessen et al J Neurotrauma 2011;28(10):2019-2031

Sedation for the imminently dying

Survey results from the AAN Ethics Section

The Vegetative State= A clinical syndrome with a differential diagnosis

- Minimally Conscious State
- Locked-in- Syndrome
- Coma
- Brain Death
- Akinetic mutism
- Dementia (PVS working group 1994)

Comparison of clinical features associated with coma, vegetative state, minimally conscious state, and locked-in syndrome

Condition	Consciousness	Sleep/ wake	Motor function	Auditory function	Visual function	Communication	Emotion
Coma	None	Absent	Reflex and postural responses only	None	None	None	None
Vegetative state	None	Present	Postures or withdraws to noxious stimuli	Startle	Startle	None	None
			Occasional nonpurposeful movement	Brief orienting to sound	Brief visual fixation		Reflexive crying or smiling
Minimally conscious state	Partial	Present	Localizes noxious stimuli	Localizes sound location	Sustained visual fixation	Contingent vocalization	Contingent smiling or crying
			Reaches for objects	Inconsistent command following	Sustained visual pursuit	Inconsistent but intelligible verbalization or gesture	
			Holds or touches objects in a manner that accommodates size and shape				
			Automatic movements (e.g., scratching)				
Locked-in syndrome	Full	Present	Quadriplegic	Preserved	Preserved	Aphonic/Anarthric	Preserved
						Vertical eye movement and blinking usually intact	

Giacino et al, Neurology 2002;58:349-353

How to make the diagnosis?

- Preconditional to the diagnosis
- Compatible with the diagnosis
- Compatible-atypical
- Incompatible – red flags

MSTF VS NEJM 1994, Working Party of Royal Physicians Clin Med 2003

Preconditional checklist

- Cause should be established
- Possibility of a treatable structural lesion
- Possibility of a continuing metabolic disturbance
- Possibility of sedatives/antipsychotics/anti-epileptics-myorelaxants(baclofen)- centrally acting drugs
- Recommendation: Need for imaging to establish the diagnosis to rule out hydrocephalus or other potential treatable causes (recommendation level C)
- Check laboratory/ medication before each assessment (recommendation level C)

How to make the diagnosis?

- Compatible with the diagnosis

The Vegetative State: Still a Clinical Diagnosis
Qualitive Assesment
Clinical (Behavioral) Criteria

(1) no evidence of awareness of self or environment and an inability to interact with others

(2) no evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to
- Visual
- Auditory
- Tactile
- Noxious stimuli

(3) no evidence of language comprehension or expression;

(4) Intermittent wakefulness manifested by the presence of sleep-wake cycles;

(5) Sufficiently preserved hypothalamic and brain-stem autonomic functions to permit survival with medical and nursing care;

(6) bowel and bladder incontinence; and

(7) variably preserved cranial-nerve reflexes (pupillary, oculocephalic, corneal, vestibulo-ocular, and gag) and spinal reflexes.

34

MSTF VS NEJM 1994, Working Party of Royal Physicians Clin Med 2003, Von Wild Eur J Trauma Emerg Med 2007

How to make the diagnosis?

- Incompatible – red flags

Diagnostic Criteria The Minimal Conscious State

- Following simple commands.
- Gestural or verbal yes/no responses (regardless of accuracy).
- Intelligible verbalization.
- Purposeful behavior, including movements or affective behaviors that occur in contingent relation to relevant environmental stimuli and are not due to reflexive activity. Some examples of qualifying purposeful behavior include:
  - appropriate smiling or crying in response to the linguistic or visual content of emotional but not to neutral topics or stimuli
  - vocalizations or gestures that occur in direct response to the linguistic content of questions
  - reaching for objects that demonstrates a clear relationship between object location and direction of reach
  - touching or holding objects in a manner that accommodates the size and shape of the object
  - pursuit eye movement or sustained fixation that occurs in direct response to moving or salient stimuli

36 Giacino et al, Neurology; 58:349-353, 2002

Inaccurate diagnosis may result from

- Confusion in terminology
- Lack of extended observation of patients
- Lack of skill or training
- Lack of eye blink to threat

Inaccurate Diagnosis

	Author	Start	N	Inaccurate	Confounders	Outcome
1993	Childs	➢ 1 month	18/47	37%	visual pursuit & fixation	Severely disabled
1996	Andrews	➢ 6 months	17/40	43%	Blind or severely visually impaired	
2009	Schnakers	< 2 weeks >22 months	18/44	41%	MCS-failure to detect visual pursuit & fixation	

Childs, Neurology, 1993; Andrews, BMJ,1996; Schnakers, BMC Neurology ,2009

Absence or presence of a blink reflex to visual threat is compatible with the Diagnosis Vegetative State

Recovery(REC) for patients in vegetative state (VS) with and without blink to visual threat after 1 year in trauma (TBI) or 3 months non-trauma (NTBI)

VS with blink to visual threat (n=46)			VS without blink to visual threat (n=45)		
REC	VS	DIED	REC	VS	DIED
14 (5 NTBI)	22 (14NTBI)	10 (7NTBI)	9 (2NTBI)	28 (17NTBI)	8 (5NTBI)

Vanhaudenhuyse, Neurology, 2008

Quantitative assessment

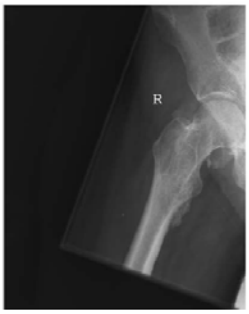
- Bedside methods lack sensitivity and specificity to refute or demonstrate the diagnosis of VS when based on consensus rather than on standardized neurobehavioral assessment

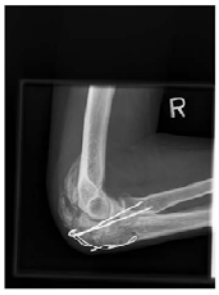
40

Complications in vegetative state patients

- Pneumonia
- Decubitus
- Spasticity
- Contractures (elbow, ankle)
- Pain?
- Heterotopic Ossifications
- Seizures
- Autonomic dysregulation

Heterotopic ossifications





Hendricks, Van Ginneken, Heeren, Geurts, Vos Clinical Rehabilitation 2007
Van Kampen, Martina, Hoedemakers, Vos, Hendricks Brain Injury 2010

The Vegative State Treatment

Systemic
- Infection prevention
- Ulcer prevention
- Ventilatory-tracheotomy
- Spasticity
- Swallowing-Feeding
- Heterotopic Ossifications

Non-Pharmacological
- Early Rehabilitation
- Sensory stimulation
- Music Therapy
- Dorsal Column Stimulation
- Deep Brain Stimulation
- Hyperbaric Oxygen

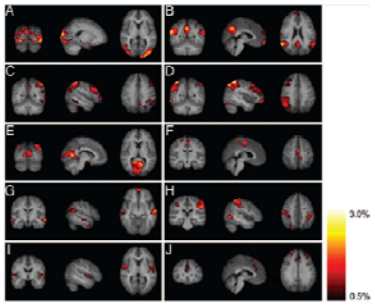
Pharmacological
- Dopamine agonists(Amantadine ,bromocryptine,pergolide)
- Baclofen
- Levodopa
- Zolpidem
- Amphetamine

Von Wild J Trauma Emerg Med , 2007

When has recovery reached an endpoint? Prognosis of the vegetative state

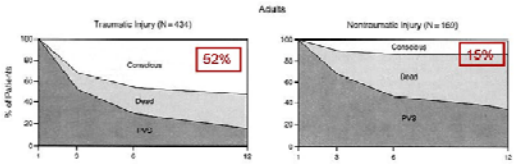
Functional brain networks related to consciousness

A: visual
B. Default Mode Network
C: Memory
D: memory
E: visual
F: motor &sensory
I: auditory cortex
J: execut.control & WM



Damoiseaux et al., 2006 (PNAS); Hillary et al Int J Psychophysiol 2011

Prognosis of the vegetative state



Permanent > 1jr

Permanent > 3 mnd

1 month patients in VS 50% regained consciousness after a year

3 month patients in VS 1/3 regained consciousness after a year

The Multi-Society Task Force on PVS Medical aspects of the Persistent Vegetative State-First of Two Parts *N Engl J Med* 1994; 330: 1499-1508.

46

End of life decision making in European Countries

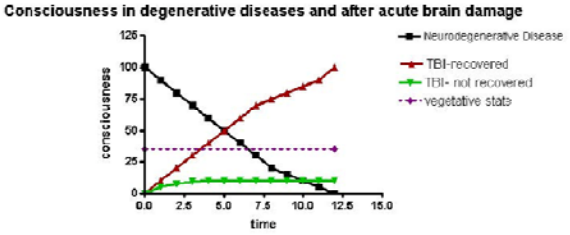
Alleviation of pain and symptoms with possible life-shortening effect: Belgium 22%, Denmark 26%, Italy 19%, Netherlands 20%, Sweden 21%, Switzerland 22%

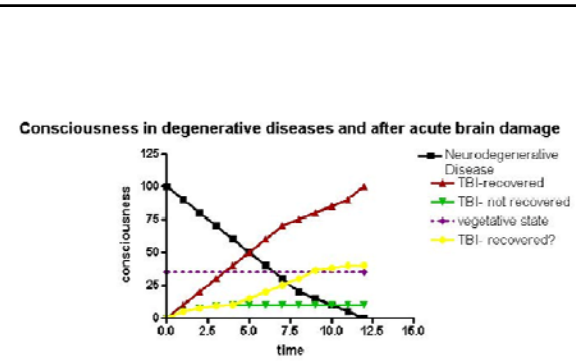
End of life decisions any ranged from 23% in Italy to 51% (Switzerland)

Vander Heide, The Lancet, 2003

Acute brain disorders like TBI: Are they different from neurodegenerative disease?

- Vegetative state may characterize the end stage of progressive dementing conditions in children and adults
- Vegetative state after acute brain insults may characterize the end stage of recovery. But when does recovery end.





Witholding and withdrawing therapy in vegetative state patients

- Accuracy of diagnosis (MCS,Locked in syndrome)!
- Treatment limitations
- Withdrawal of treatment not very different from neurodegenerative disease

Palliative care in amyotrophic lateral sclerosis

Marianne de Visser
Academic Medical Centre
Amsterdam, The Netherlands

Learning objectives

After this lecture the learner will be able

- to appreciate the prognostic factors in MND
- to become acquainted with the standards of care in MND
- to appreciate the importance of end-of-life issues

Prognosis of

- Rapidly progressive disease
- Life expectancy determined by respiratory function. Aspiration pneumonia usually causes death
- Median survival from onset to death in ALS is 20-36 months (5-10% of ALS patients survive > 10 years)

Prognostic factors in ALS: A critical review

Chiò et al. Amyotrophic Lateral Sclerosis 2008, 1-14

- Age is a strong prognostic factor:
  - patients with onset < 40 years of age of whom 80% are men have longer survival, often >10 years;
  - median survival among patients presenting >80 years of age (males = females) is < 2 years
- Time delay from onset to diagnosis seem to have prognostic relevance
- Gender has no effect on ALS outcome

Prognostic factors in ALS: A critical review

Chiò et al. Amyotrophic Lateral Sclerosis 2009, 310

- Bulbar and respiratory onset are negative prognostic factors
- Psychological distress (perceived stress, depression, hopelessness, anger expression, and purpose in life) had a 2.24-fold (95% CI 1.084.64) increased risk of dying as compared to patients with psychological well-being
- Nutritional status: (BMI value ≤18.5) is an independent prognostic factor for death

Place and cause of death amongst French patients with ALS

Gil et al. Eur J Neurol 2008;15:1245.

- Prospective study: 302 consecutive patients who died between April 2006 - March 2007 whilst under the care of one of 16 ALS centres in 15 French regions.
- Standardized questionnaires completed by ALS specialists and GPs who certified the deaths and by interviewing the patients' relatives and relevant hospital staff.

Results

Reported circumstances by place of death in 302 ALS patients

Circumstances of death	Total, *N* (%)	Place of death: Medical facility (189), *n* (%)	Place of death: Outside a medical facility (113), *n* (%)	*P**
During the night (11 pm – 6 am)	60 (20.0)	44 (23.0)	16 (14.0)	**0.049**
During the day (6 am – 11 pm)	242 (80.0)	145 (77.0)	97 (86.0)	
Particular circumstances	23 (7.6)	16 (8.5)	7 (6.2)	0.471
At mealtime	6 (2.0)	2 (1.1)	4 (3.5)	0.201
During physical activity	6 (2.0)	3 (1.6)	3 (2.7)	0.203
Post-surgery	5 (1.7)	5 (2.6)	0 (0.0)	0.125
Following gastrostomy placement	3 (1.0)	3 (1.6)	0 (0.0)	0.295
Post-trauma	3 (1.7)	3 (1.6)	0 (0.0)	0.295

*Chi-square or Fisher exact tests.
Bold values indicated a level of significance with $P < 0.05$.

Results cont'd

Reported causes according to place of death in 302 ALS pts

Causes of death	Total, *N* (%)	Place of death: Medical facility (189), *n* (%)	Place of death: Outside a medical facility (113), *n* (%)	*P**
Terminal respiratory insufficiency	176 (58.0)	122 (65.0)	54 (48.0)	**0.004**
Pneumonia (infectious or aspiration)	42 (14.0)	32 (17.0)	10 (9.0)	**0.049**
Asphyxia/foreign body	9 (3.0)	4 (2.1)	5 (4.4)	0.302
Pulmonary embolism	6 (2.0)	6 (3.2)	0 (0.0)	0.087
Dysrhythmias	6 (2.0)	2 (1.1)	4 (3.5)	0.201
Head trauma	5 (1.7)	4 (2.1)	1 (0.9)	0.654
Suicide	4 (1.3)	0 (0.0)	4 (3.5)	**0.019**
Septic shock	3 (1.0)	3 (1.6)	0 (0.0)	0.295
Cachexia	3 (1.0)	0 (0.0)	3 (2.7)	0.052
Myocardial infarction	2 (0.7)	2 (1.1)	0 (0.0)	0.530
Acute pulmonary oedema	2 (0.7)	1 (0.5)	1 (0.9)	0.985
Sudden death	2 (0.7)	1 (0.5)	1 (0.9)	0.985
Acute renal insufficiency	1 (0.3)	1 (0.5)	0 (0.0)	0.843
Haematemesis	1 (0.3)	0 (0.0)	1 (0.9)	0.860
Bronchospasm	1 (0.3)	0 (0.0)	1 (0.9)	0.860
Undetermined	39 (13.0)	11 (6.0)	28 (25.0)	**<0.001**

Causes of death in a post-mortem series of ALS patients

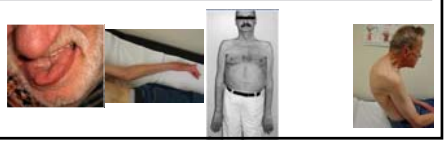
Gorcia et al. Amyotrophic Lateral Sclerosis 2008;9:59–62

- Clinical and pathological records of 100 ALS patients followed up in the ALS clinic of Pitié-Salpêtrière between 1983-2005.
- 65 autopsies performed < 2000 (2 < 1990, 63 from 1991-1999) and 35 performed >2000.
- At autopsy, bronchopneumonia and pneumonia main causes of death.
- Heart failure (10%) 2x more frequent in bulbar than in spinal ALS.
- Pulmonary embolism (6%) only found in spinal onset patients, related to lower limbs disability.
- Concordance between clinical and pathological conclusions insufficient (20%) to consider clinical assessment as reliable marker of causes of death.

Survival in ALS and other phenotypes

Table 2 Demographic and clinical characteristics of the London patients

	Bulbar onset	Classical limb onset	Flail arm	Flail leg	PMA
Total n(%) from 1,189 cases	318 (26.9)	609 (51.3)	135 (11.4)	75 (6.3)	51 (4.3)
Survival, mo					
Mean (95% CI)	33.5 (29-37.8)	45.2 (42-48.5)	76.8 (66.6-87)	75.9 (67.4-84)	56.8 (43-70)
Median (95% CI)	27 (25.4-28.6)	34 (31.9-36)	61 (51.7-70.3)	69 (62.5-75.5)	40 (30.5-50)
Five-year survival rate, %	9.3	20	52.6	43.9	32.1
Ten-year survival rate, %	2.1	6.3	15.8	5.3	11.5



Natural history and clinical features of the flail arm and flail leg ALS variants

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ABSTRACT

Objective: We sought to define the significance of brachial amyotrophic diplegia (flail arm syndrome [FA]) and the pseudopolyneuritic variant (flail leg syndrome [FL]) of amyotrophic lateral sclerosis (ALS; motor neuron disease).

Methods: We analyzed survival in clinic cohorts in London, UK (1,188 cases), and Melbourne, Australia (432 cases). Survival from disease onset was analyzed using the Kaplan-Meier method and Cox proportional hazards model.

Results: In the London cohort, the FA syndrome represented 11% and the FL syndrome 6% of the sample. Median survival was 35 months for limb onset and 27 months for bulbar onset ALS, whereas this was 61 months for FA syndrome ($p < 0.001$) and 69 months for FL syndrome ($p < 0.001$). Five-year survival in this cohort was 8.8% for bulbar onset, 20% for limb onset, 52% for FA syndrome, and 44% for FL syndrome. The ratio of men to women was 4:1 in the FA group compared to 2:1 in other limb onset cases. Excluding lower motor neuron FA and FL cases, progressive muscular atrophy comprised 4% of the sample and had a prognosis similar to typical limb onset ALS. In the Melbourne cohort, median survival for limb onset ALS was 31 months, bulbar onset 27 months, FA syndrome 66 months ($p = 0.001$), and FL syndrome 71 months ($p = 0.001$).

Conclusions: The flail arm (FA) and flail leg (FL) syndromes had significantly better survival than typical amyotrophic lateral sclerosis (ALS) or progressive muscular atrophy cases that were not classified as FA or FL. Our findings underline the clinical and prognostic importance of the FA and FL variants of ALS. *Neurology*® 2009;72:1087-1094

Disease Course and Prognostic Factors of Progressive Muscular Atrophy

Arch Neurol. 2007;64:522-528

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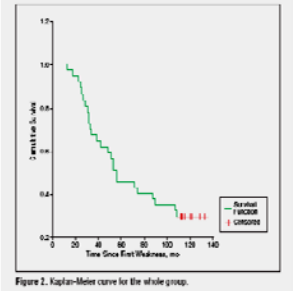


Figure 2. Kaplan-Meier curve for the whole group.

Cohort of 37 PMA patients. Five years after the end of the study, median 7 years after inclusion, 11 patients were alive.
1-, 3-, 5-, and 9-year survival rates were 100%, 67%, 45%, and 30%, respectively, with a median survival duration of 56 months.

Survival in PLS

Table 1. Clinical findings from published series of patients with primary lateral sclerosis.

Reference no.	Number of patients	F	Mean age of onset (years)[a]	Mean duration (years)[a]	Site of onset			Bladder symptoms (%)[a]	Abnormal EMG (%)
					LE (%)	Bulbar (%)	Other/mixed (%)		
57	4	2	59 (54-64)	7.2 (5.5–9.5)	100	0	0	100	0
27	5	3	47 (25–69)	13 (5–28)	20	60	20	0	0
74	6	1	47 (30–75)	9.7 (2–18)	100	0	0	0	0
53	8	4	50.4 (35–66)	14.5 (4–34)	63	12	25	50	25
41	20	5	53.4 (26–64)	8.5 (4–14)	55	35	10	70	95
40	10	1	44.5 (23–57)	12.7 (6–35)	80	10	10	30	40
76	25	15	45.4 (37–53.6)	9.7 (3–59)	80	0	20	48	67
29	167	6	51 (40–71)	8.3 (1.3–30)	81	13	6	Nil	0
58	26	11	53.7 (32–76)	7.9 (3–16)	76	8	16	20	40

Singer et al. Muscle Nerve **35:** 291–302, 2007

PLS may be heterogeneous

Clinically pure PLS is characterised by slow progression, high function, normal breathing, and no weight loss, and includes no evidence of LMN dysfunction on examination or EMG 4 years after symptom onset.

PLS may convert to classical ALS/upper motor neuron dominant ALS

Palliative care

'ALS may be viewed as a paradigmatic disease for palliative care'

Borasio 2001

Standards of care

Survey conducted among members of European ALS Study Group
(Borasio DG. Amyotroph Lateral Scler 2001;2:159-64)

- Great efforts were made by the centres to offer the best possible palliative care to ALS patients
- Many areas in which there was consensus on the type of care offered
- Also differences between centres concerning symptomatic drug treatment, availability of services, ventilation and terminal care

Conclusion: Evidence-based standards for management are required

Evidence-based guidelines

Good practice in the management of amyotrophic lateral sclerosis: Clinical guidelines. An evidence-based review with good practice points. EALSC Working Group

Amyotrophic Lateral Sclerosis 2007;8:195

PETER MUNCH ANDERSEN[1], GIAN DOMENICO BORASIO[2], REINHARD DENGLER[3], ORLA HARDIMAN[4], KATJA KOLLEWE[3], PETER NIGEL LEIGH[5], PIERRE-FRANCOIS PRADAT[6], VINCENZO SILANI[7] & BARBARA TOMIK[8]

Special Article

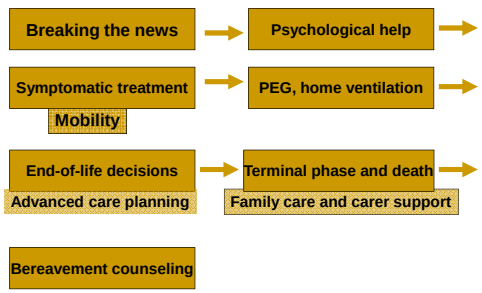
AMERICAN ACADEMY OF NEUROLOGY.

Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review)

Report of the Quality Standards Subcommittee of the American Academy of Neurology

Neurology® 2009;73:1227-1233

Palliative care in ALS



A 63-year-old female with bulbar ALS

In April 2002 she is diagnosed with bulbar-onset ALS.
She has dysarthria and pseudobulbar affect.
Normal strength in the limbs, but fasciculations are ubiquitous.
She is in denial of this serious disease and initially refuses follow-up.
She is a divorcee with 3 adult children.
Her GP is informed about the diagnosis and the implications by telephone.

Communication and goal setting

Communication with patients and families should be open, including the setting of goals and therapy options, and should be structured following models, such as SPIKES (Level B)

➔*Breaking bad news skills and end-of-life communication skills*

Why is follow-up in a *dedicated* ALS-team important?

- Palliative care should be considered early in the disease trajectory
- Rapidly progressive disease which requires accurate monitoring of swallowing and respiratory function.
- Continued support should be provided by a single point of access.

NB Ng, L., F. Khan, and S. Mathers, Multidisciplinary care for adults with amyotrophic lateral sclerosis or motor neuron disease. Cochrane Database Syst Rev, 2009(4): p. CD007425

Traynor et al. J Neurol Neurosurg Psychiatry 2003;74:1258-1261

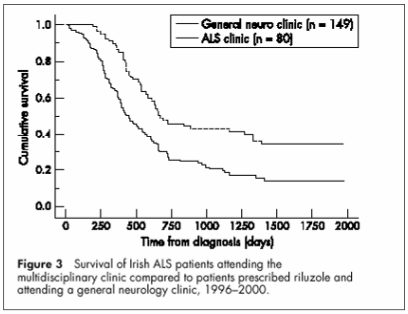


Figure 3 Survival of Irish ALS patients attending the multidisciplinary clinic compared to patients prescribed riluzole and attending a general neurology clinic, 1996–2000.

ALS patients who are treated by a multidisciplinary team live 7.5 months longer as compared to usual care.

Follow-up

The patient was prescribed Riluzole.

Class I evidence: Oral administration of 100 mg riluzole daily prolonged survival (3 months after 18 months treatment).
Miller RG, et al. Riluzole for amyotrophic lateral sclerosis.
Cochrane Database Syst Rev. 2002

Monitoring of swallowing

- Dysphagia leads to malnutrition, dehydration and aspiration pneumonia. Malnutrition (present in 16-50% of ALS patients) is considered an independent prognostic factor for worsened survival (Desport et al. 2000).
- PEG improves nutrition, but there is no convincing evidence that PEG prevents aspiration or improves quality of life or survival (Miller et al. 1999; Heffernan et al. 2004).
- We initiated a RCT: Does a timely placed PEG (i.e. at a moment where supplementary feeding is beneficial but not urgent) in ALS patients with dysphagia lead to longer survival, better nutritional status, functional status and quality of life than a later placed PEG?
- Power calculation: 60 patients in each arm

Results (2004-2008)

Table 1: results per group

		Early PEG n = 6	PEG: wait and see n = 6	unwilling to participate n = 20
Survival (months)	T = 15	5 (83%)	5 (83%)	16 (80%)
No. of patients receiving PEG		6 (100%)	4 (67%)	14 (70%)
Vital capacity (%)	T = 0	101,8 ± 18,9	88,5 ± 17,2	88,6 ± 21,6
	T = 15	60,6 ± 17,5	44,8 ± 9,1	NA
Vital capacity (%) Latest value before PEG		101,8 ± 18,9	84,0 ± 25,0	
Body mass index (kg/m2)	T = 0	25,5 ± 3,2	24,1 ± 1,7	25,3 ± 4,6
	T = 15	23,9 ± 4,5	22,9 ± 1,4	NA
ALSFRS-R	T = 0	34,8 ± 8,3	37,0 ± 5,2	NA
	T = 15	18,0 ± 5,1	23,8 ± 9,9	
VAS score QoL (mm.)	T = 0	66,2 ± 17,7	71,5 ± 19,8	NA
	T = 15	48,2 ± 21,5	44,6 ± 16,9	
Delta VAS pre and post PEG (VAS pre - VAS post, mm.)		9 ± 19 (n = 6)	4 ± 18 (n =4)	NA
mean time to PEG (days)		16 ± 8 (n=6)	172 ± 122 (n=4)	170 ± 97

Results cont'd

Table 2: Reasons to refuse participation

	unwilling to participate n = 20
"I want to keep control over timing"	2
"I am not ready for a PEG"	9
"I just got the diagnosis, I have too many appointments with (para) medics, I don't have time"	2
" I don't want anything anymore"	1
" I want the PEG *now*"	1
" I want to leave things as they are"	1
" I don't want a PEG yet, it will restrain my ability to do sports"	1
" A PEG is a very serious operation, my family physician doesn't think it is necessary right now"	1
" I first want to go to Africa with my family"	1
unknown	1

Causes of death amongst French patients with ALS (Gil et al. Eur J Neurol 2008;15:1245). 37% of French patients had received PEG. At time of death, the nutritional status of these patients did not differ from that of non-gastrostomised patients.

Follow-up in our patient

The patient has lost weight (4 kg in 3 months), the meals take considerably longer and she does not eat steaks anymore.
Her VC is 1.74 litre (60% of expected normal value).

Initially, she refuses a PEG, but when VC drops further (50%) and the meals take more than 1 hour she changes her mind.

The risk of PEG placement increased when the FVC declined below 50% of predicted (Class III). Practice parameter, Neurology, 2009

Follow-up in our patient

- She develops weakness of her limbs and is nearly anarthric. Communication takes place via a light writer.
- She moves into her daughter's house.
- The occupational therapist provides all sorts of aids in the house.
- Once, at a follow-up visit, she mentions that she is opting for euthanasia.

➔ *Early advance care planning is recommended, especially when impaired communication and cognitive deterioration is possible*

N Engl J Med 2002;346:1638.

EUTHANASIA AND PHYSICIAN-ASSISTED SUICIDE AMONG PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS IN THE NETHERLANDS

JAN H. VELDINK, M.D., JOHN H.J. WOKKE, M.D., PH.D., GERRIT VAN DER WAL, M.D., PH.D., J.M.B. VIANNEY DE JONG, M.D., PH.D., AND LEONARD H. VAN DEN BERG, M.D., PH.D.

This retrospective study showed that 20% of the ALS patients in The Netherlands dies due to euthanasia or physician assisted suicide (fear of suffocation and dependency). In the French study (Gil et al. 2008): 4/302 (1.3%).

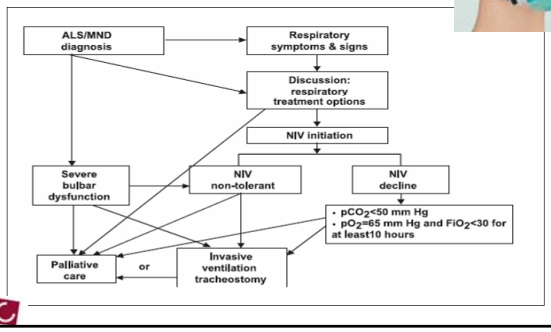
Follow-up of our patient

The patient explains that she is afraid to choke and that talking about euthanasia with her GP would be a relief.

The neurologist discusses the consequences of respiratory insufficiency and checks whether there is nocturnal hypoventilation.

➔ *Continued and repeated discussion is essential due to changes in function – physical and cognitive - and preferences*

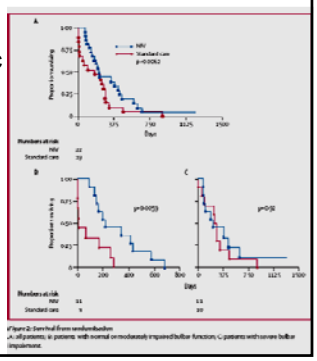
Monitoring and management respiratory dysfunction in AL



Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial

Bourke et al. Lancet Neurol 2006; 5: 140

NIV (if pts are symptomatic or VC<50%) extends life expectancy (205 days), with maintenance or even improvement of QoL without increasing the burden of the carers.



Palliative treatment of dyspnea

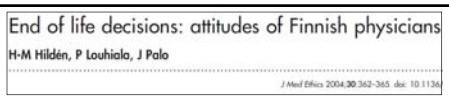
- For symptomatic treatment of dyspnoea use of opioids alone or in combination with benzodiazepines if anxiety is present. Titrating the dosages against the clinical symptoms will almost never result in a life-threatening respiratory depression.
- For treating terminal restlessness and confusion due to hypercapnia, neuroleptics may be used.
- Use oxygen only if symptomatic hypoxia is present.

➔*Recognition of deterioration over the last weeks and months is relevant for the appropriate management.*

Follow up of our patient

She receives information about NIV. However she opts out and the neurologist discusses end-of-life issues, in particular DNR.

➔*Encourage open discussion about the dying process and explain that most patients will die peacefully, with appropriate care*
➔*Encourage open discussion for the wish for hastened death and assess regularly*


End of life decisions: attitudes of Finnish physicians
H-M Hildén, P Louhiala, J Palo
J Med Ethics 2004;30:362-365. doi: 10.1136/

Study on Finnish physicians' experiences of decisions concerning living wills and do not resuscitate orders and also their views on the role of patients and family members in these decisions.

Design: Questionnaire sent to 800 physicians: GPs (n = 400); internists (n = 207); neurologists (n = 100), and oncologists (n = 93)

Results

- Response rate: 56%.
- Positive attitude toward (92%), and respect for (86%) living wills, 72% thought it could be helpful.

Table 1 The most important advantages of the living will according to the respondents and the numbers of responses for each statement

Response	N
Promotes patient autonomy	363
Acts as an ice breaker in discussing end of life treatment	275
Makes decision making easier	261
Decreases stress	116
Total responses	432

Results

- 13% had completed a living will of their own.
- DNR orders were interpreted in two ways: resuscitation forbidden (70%) or only palliative (symptom oriented) care required (30%).
- 72% discussed DNR decisions always or often with patients able to communicate, and 76% discussed DNR orders with the family members of patients unable to communicate.
- Most respondents were able to approach a dying patient without difficulty.
- They also felt that education in general was needed.

Follow up of our patient

Since she is wheelchair-bound she decides – after consultation of her children – that she does not want any life-extending intervention.
She receives low dosages of opioids and oxygen when the dyspnoea worsens.
After a few days (September 2003) she dies in peace at home, surrounded by her children.

➔*Diagnosis of the beginning of the dying phase is relevant for the appropriate management, including the use of appropriate medication and intervention and care of families and carers.*

BMJ 2009;338:b2391 **RESEARCH**

Exploring preferences for place of death with terminally ill patients: qualitative study of experiences of general practitioners and community nurses in England

Daniel Munday, associate clinical professor in palliative medicine, Mila Petrova, research fellow, Jeremy Dale, professor of primary care

- Numerous studies suggested that home death is the most common choice patients express, but that this preference becomes less pronounced as death approaches
- Recent UK programmes for end of life care have encouraged primary care professionals to seek out patient preferences for place of death. The Gold Standards Framework aims to enable GPs and community nurses to optimise practice in palliative and end of life care and were interviewed.

Results of qualitative study of experiences of GPs and community nurses in England

- Most interviewees (17 GPs, 19 nurses) reported that they did not find discussing preferred place of death an easy area of practice.
- Further research is needed to enable development of appropriate training and support for primary care professionals and to obtain better understanding of the importance of place of death to patients and their carers.