Le comorbidità: la complessità del paziente geriatrico con demenza

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Geriatra ASP Catanzaro
Centro Demenze

T-Hotel 18 Maggio 2013

Progetto Obiettivi di piano: Formazione MMG
Il medico di medicina generale e le demenze: un approccio mirato
Outline

• Lo scenario epidemiologico

• Le comorbidità

• La gestione della demenza in comorbilità
We explored the role of age, gender, and socioeconomic status in the occurrence of chronic diseases and multimorbidity in 1099 elderly participants in the Kungsholmen Project. Cardiovascular and mental diseases were the most common chronic disorders. Of the participants, 55% had multimorbidity. Advanced age, female gender, and lower education were independently associated with a more than 50% increased risk for multimorbidity. Multimorbidity is the most common clinical picture of the elderly and may be increased by unhealthy behaviors linked to education. (Am J Public Health. 2008;98:1198–1200. doi:10.2105/AJPH.2007.121137)

If the pace of increase in life expectancy in developed countries over the past two centuries continues through the 21st century, most babies born since 2000 in France, Germany, Italy, the UK, the USA, Canada, Japan, and other countries with long life expectancies will celebrate their 100th birthdays.

- **Prevalence rates for dementia are estimated to double every 5 years after age 65.**
- **Rates of dementia in community studies increase from 30% for persons aged 85 through 89 years to 50% for persons aged 90 through 94 years to 74% for those 95 years or older.**
- **Given the burden of dementia on patients, families, and caregivers, the high rates in late life, and the clear demographic trends, it is imperative for research to find solutions that prevent, delay, slow, and treat Alzheimer disease and related dementias.**
Malattie più frequentemente associate alla demenza lieve-moderata:
malattie gastrointestinali, BPCO, diabete, ipertensione

Malattie più frequentemente associate alla demenza grave: polmoniti, malattie infettive in genere, stroke, malnutrizione, fratture di femore, piaghe da decubito
Undiagnosed diseases in patients with dementia – a potential target group for intervention.

Löppönen MK et al., Dement Geriatr Cog Disord, 2004

Percentuale dei soggetti con patologie non diagnosticate suddivisi in base alla severità della demenza
L’importanza della VMD

- CIRS
- ADL, IADL, Barthel Index
- MMSE
- GDS
  - MNA (perdita di peso di più del 10% del peso corporeo ideale in 6 mesi; livelli di albuminemia < 2.5 g/dl)

STRUMENTI DI VALUTAZIONE

• CIRS o indice cumulativo di comorbilità
• GIC o indice geriatrico di comorbilità

• Valutazione del “burden of illness” (carico che le malattie comportano, in termini di costi economici e/o emotivi per la famiglia e la società)
• Gravità funzionale (impatto della malattia sulla capacità individuale di svolgere un’attività adeguata alla propria età)
• Gravità fisiopatologica e morfologica (tests di laboratorio, referti anatomici)
To compare the medical comorbidity of older patients with and without dementia in primary care.

Cross-sectional study.

Three thousand thirteen patients aged 65 and older attending seven primary care centers in Indianapolis, Indiana.

An expert panel diagnosed dementia using International Classification of Diseases, 10th Revision, criteria. Comorbidity was assessed using ten physician-diagnosed chronic comorbid conditions and the Chronic Disease Score (CDS).

Patients with dementia attending primary care have on average 2.4 chronic conditions and receive 5.1 medications. Approximately 50% of dementia patients in this setting are exposed to at least one anticholinergic medication, and 20% are prescribed at least one psychotropic medication. After adjusting for patients' age, race, and sex, patients with and without dementia have a similar level of comorbidity (mean number of chronic medical conditions, 2.5 vs 2.3, P = .66; average CDS, 5.1 vs 6.2, P = .83).

### Table 3. Comorbidity Profile of Older Adults with and without Dementia Attending Primary Care Clinics

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Dementia</th>
<th>Dementia</th>
<th>P-value</th>
<th>Adjusted P-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic comorbid conditions, mean ± SD*</td>
<td>2.3 ± 1.4</td>
<td>2.4 ± 1.4</td>
<td>.37†</td>
<td>.66</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>73.5</td>
<td>82.2</td>
<td>.04‡</td>
<td>.06</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>34.9</td>
<td>39.3</td>
<td>.36§</td>
<td>.19</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>20.5</td>
<td>20.6</td>
<td>1.00†</td>
<td>.97</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>9.4</td>
<td>10.3</td>
<td>.74‡</td>
<td>.89</td>
</tr>
<tr>
<td>Heart failure, %</td>
<td>14.6</td>
<td>14.0</td>
<td>1.00‡</td>
<td>.47</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease, %</td>
<td>16.7</td>
<td>12.2</td>
<td>.24‡</td>
<td>.33</td>
</tr>
<tr>
<td>Cancer, %</td>
<td>12.0</td>
<td>8.4</td>
<td>.36‡</td>
<td>.17</td>
</tr>
<tr>
<td>Osteoarthritis, %</td>
<td>36.5</td>
<td>41.1</td>
<td>.36‡</td>
<td>.65</td>
</tr>
<tr>
<td>Liver failure, %</td>
<td>0.8</td>
<td>0.0</td>
<td>1.00‡</td>
<td>.98</td>
</tr>
<tr>
<td>Renal failure, %</td>
<td>8.3</td>
<td>11.2</td>
<td>.28‡</td>
<td>.77</td>
</tr>
</tbody>
</table>

**Medication-based comorbidity**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Dementia</th>
<th>Dementia</th>
<th>P-value</th>
<th>Adjusted P-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic disease score, mean ± SD</td>
<td>6.2 ± 4.7</td>
<td>5.8 ± 4.0</td>
<td>.39†</td>
<td>.83</td>
</tr>
<tr>
<td>Number of medications, mean ± SD</td>
<td>6.1 ± 5.0</td>
<td>5.1 ± 3.8</td>
<td>.05†</td>
<td>.24</td>
</tr>
<tr>
<td>Receiving definite ACh, %</td>
<td>25.7</td>
<td>21.5</td>
<td>.37‡</td>
<td>.68</td>
</tr>
<tr>
<td>Receiving possible ACh, %</td>
<td>46.5</td>
<td>40.2</td>
<td>.24‡</td>
<td>.27</td>
</tr>
<tr>
<td>Receiving any ACh, %</td>
<td>55.4</td>
<td>49.5</td>
<td>.24‡</td>
<td>.37</td>
</tr>
<tr>
<td>Receiving anxiolytics, %</td>
<td>7.2</td>
<td>6.5</td>
<td>1.00‡</td>
<td>.82</td>
</tr>
<tr>
<td>Receiving antidepressants, %</td>
<td>19.7</td>
<td>11.2</td>
<td>.03‡</td>
<td>.17</td>
</tr>
<tr>
<td>Receiving antipsychotics, %</td>
<td>2.3</td>
<td>3.7</td>
<td>.31‡</td>
<td>.26</td>
</tr>
<tr>
<td>Receiving any psychotropic, %</td>
<td>24.9</td>
<td>19.6</td>
<td>.25‡</td>
<td>.73</td>
</tr>
</tbody>
</table>

### Table 2. Demographic Characteristics of the Study Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Dementia</th>
<th>Dementia</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± standard</td>
<td>71.1 ± 5.6</td>
<td>75.6 ± 6.2</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>deviation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female, %</td>
<td>70.6</td>
<td>62.6</td>
<td>.09†</td>
</tr>
<tr>
<td>African American, %</td>
<td>59.7</td>
<td>69.2</td>
<td>.06†</td>
</tr>
</tbody>
</table>

**Conclusion:** Multiple medical comorbid conditions are common in older adults with and without dementia in primary care. Despite their cholinergic deficit, a substantial proportion of patients with dementia are exposed to anticholinergic medications. Models of care that incorporate this medical complexity are needed to improve the treatment of dementia in primary care. J Am Geriatr Soc 54:104–109, 2006.
Comorbidity and the rate of cognitive decline in patients with Alzheimer dementia.

Moreover, demented patients have a higher number of admissions to hospital, with consequently, an increased risk of death during hospitalization.
Co-Morbidity and Dementia

- Poor control of or acute exacerbation of conditions such as congestive heart failure, coronary artery disease, or chronic obstructive pulmonary disease may adversely affect the cognitive function of patients with dementia.

- Thus, attention to and aggressive treatment of co-morbidity is an important part of the care plan.

- As the dementia progresses, treatment goals vary, depending on patient-family values, quality of life, and symptoms and burden of proposed interventions.

- In the late stages of dementia, a more purely palliative or hospice care plan may call for treatment of other medical conditions only if they are producing symptoms.
Co-Morbidity and Dementia

• Abrupt changes in clinical status for patients with dementia usually signal an intercurrent illness, which is often treatable (e.g., urinary tract infection, pneumonia, malnutrition, constipation). Appropriate steps should be taken to identify and treat the underlying problem.

• Pain, dyspnea, agitation, depression, and other symptoms should be treated. Sometimes this can best be accomplished by treating the underlying condition (e.g., treating congestive heart failure or chronic obstructive pulmonary disease to relieve dyspnea). At other times, symptomatic measures may be more appropriate (e.g., morphine for dyspnea).
**CAUSE DI MORTE DI PZ CON AD PROBABILE, CLASSIFICATI SECONDO IL LIVELLO DI COMPROMISSIONE COGNITIVA (Kukull et al., 1994, mod.)**

<table>
<thead>
<tr>
<th></th>
<th>Lievemente compromessi</th>
<th>Moderat. compromessi</th>
<th>Gravemente compromessi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasie</td>
<td>3 (27.3%)</td>
<td>2 (12.5%)</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>Demenza/AD</td>
<td>5 (45.4%)</td>
<td>4 (25.0%)</td>
<td>22 (81.5%)</td>
</tr>
<tr>
<td>Ischemia cardiaca</td>
<td>2 (18.2%)</td>
<td>1 (6.3%)</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>Altra malattia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cardiovascolare</td>
<td>7 (63.6%)</td>
<td>8 (50.0%)</td>
<td>9 (33.3%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (36.4%)</td>
<td>3 (18.7%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Polmonite</td>
<td>2 (18.2%)</td>
<td>3 (18.7%)</td>
<td>11 (40.7%)</td>
</tr>
<tr>
<td>Altre malattie infettive</td>
<td>2 (18.2%)</td>
<td>7 (43.7%)</td>
<td>7 (25.9%)</td>
</tr>
<tr>
<td>Cause esterne</td>
<td>1 (9.1%)</td>
<td>1 (6.3%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
Comorbid Alzheimer’s Disease and OSAS: Does CPAP Slow Cognitive Decline?


Kathy C. Richards, PhD, RN, FAASM

- Treatment of obstructive sleep apnea syndrome (OSAS) with continuous positive airway pressure (CPAP) may delay cognitive decline in older adults with Alzheimer’s disease and related dementias (AD).

- In this study, the investigators contacted all participants who had completed a 6-week randomized controlled trial (RCT) of the use of CPAP in persons with mild to moderate dementia and OSAS after approximately 1 year had elapsed.

- The authors reported that sustained CPAP use in patients with AD resulted in moderate to large effect sizes on cognitive measures, depressive symptoms, daytime sleepiness, and patient and caregiver subjective sleep quality.
Impact of geriatric comorbidity and polypharmacy on cholinesterase inhibitors prescribing in dementia

Falk Hoffmann¹, Hendrik van den Bussche², Birgitt Wiese³, Gerhard Schön⁴, Daniela Koller¹, Marion Eisele², Gerd Glaeske¹, Martin Scherer² and Hanna Kaduszkiewicz²

We suggest that a lack of contacts to specialists and geriatric morbidity patterns reduce the chance for patients with incident dementia of being prescribed a ChEI. It seems that not age as such but the occurrence of care dependency and geriatric comorbidities influences prescriptions.
Key points

• 12% of patients who are admitted to medical ward from the emergency department suffer from severe dementia, so it is possible to envisage a double rate if we include patients with dementia in mild to moderate impairment.

• It is necessary that the staff of the DEA is prepared (and not just on the field) to the assessment and planning of the elderly patient with dementia: **how to recognize cognitive, sensory deficits**, to identify the patient’s functional status and social resources at home are fundamental factors that drive both the diagnostic orientation and treatment choices (hospital care versus at home care).

• The low level of experience, and the lack of specific training in geriatric medicine for acute care and in relation to the elderly and their families, are factors contributing to increased stress for staff.
Management of Demented Patients in Emergency Department
Lavinia Valerian

Table 1: The diseases that most often drive the elderly to apply for an urgent evaluation.

<table>
<thead>
<tr>
<th>Medical emergency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular diseases (angina, heart failure, arrhythmias, syncope)</td>
</tr>
<tr>
<td>Respiratory (acute exacerbation of chronic bronchitis, bronchial asthma, pneumonia)</td>
</tr>
<tr>
<td>Cancer (cancer of the lung, breast, large bowel)</td>
</tr>
<tr>
<td>Neurological diseases (acute cerebrovascular disease, altered state of consciousness)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chirurgical emergency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma and fractures</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical emergency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration, urinary tract infections, intestinal sub-ileus, delirium, behavioral disturbances and subsequent guidance of therapeutic prescription</td>
</tr>
<tr>
<td>Acute respiratory failure from respiratory infection, acute myocardial infarction, sepsis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical problems related to an incorrect home management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oversedation from psychopharmacological treatment, side effects from medications (iatrogenic hypotension, hypoglycemia jatrogena)</td>
</tr>
</tbody>
</table>

Table 2: Principal pathologies associated with patients with dementia.

<table>
<thead>
<tr>
<th>For mild to moderate dementia:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumours, diabetes, gastrointestinal disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>For severe dementia:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia and other infectious diseases, stroke, malnutrition, hip fractures, bed sores</td>
</tr>
</tbody>
</table>

SAGE-Hindawi Access to Research
International Journal of Alzheimer’s Disease
Volume 2011, Article ID 840312, 5 pages
doi:10.4061/2011/840312
<table>
<thead>
<tr>
<th>Clinical assessment of patients with dementia.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anamnesis:</strong> medical history collected or at least confirmed by the principal caregiver or a person who knows the history</td>
</tr>
<tr>
<td>Risk of underestimation of the symptom in older cognitively compromised</td>
</tr>
<tr>
<td><strong>Objective examination:</strong> patient visit in order to capture significant clinical signs</td>
</tr>
<tr>
<td>Useful indicator of an underlying organic disease not reported or underestimated by the patient and the family</td>
</tr>
<tr>
<td><strong>Pharmacological anamnesis:</strong> drug history of the patient</td>
</tr>
<tr>
<td>Many drugs may cause side effects, especially when administered by not clinical prepared persons</td>
</tr>
<tr>
<td><strong>Vital signs:</strong> for better understanding of the patient’s general condition</td>
</tr>
<tr>
<td>Determination of blood pressure, heart rate, oxygen saturation (blood gas, or), body temperature, and glycemia</td>
</tr>
</tbody>
</table>
**OBJECTIVES:** To quantify the association between cholinesterase inhibitors (ChE-I s) and a new diagnosis of bradycardia and to evaluate the clinical significance of bradycardia.

Because bradycardia in an older population is associated with syncope, cardiovascular outcomes, and other arrhythmias,\(^{19,20}\) it is important to identify high-risk patients. Most blinded trials of ChE-I s have been 6 months in duration, although a few have been shorter, and one was 1 year long.\(^1\) The current large study offers considerably longer follow-up in a real-world setting, with a median length of follow-up of longer than 2 years. It suggests that there is a greater risk of bradycardia in patients treated with ChE-I s, particularly those taking 15 or 20 mg/day of donepezil. Patients who appeared to be at the greatest risk of a decrease in heart rate were those with dementia diagnosed as nonspecific or Alzheimer’s disease; those taking beta-blockers; those who had fallen since diagnosis; and those with a history of MI, heart failure, or hypertension. Therefore, higher rates of heart rate monitoring and surveillance may be warranted in patients with dementia taking a ChE-I, particularly those identified as high risk.

![Flowchart Diagram](image)
Dual Use of Bladder Anticholinergics and Cholinesterase Inhibitors: Long-Term Functional and Cognitive Outcomes

Kaycee M. Sink, MD, MAS,* Joseph Thomas, III, PhD, Huiping Xu, PhD, Bruce Craig, PhD, Steven Kritchevsky, PhD, and Laura P. Sands, PhD

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Journal compilation © 2008, The American Geriatrics Society

The goals of this study were, therefore, to examine changes in function in activities of daily living (ADLs) and cognition over time in NH residents taking ChIs while receiving concomitant therapy with a bladder anticholinergic (dual use) and in those taking ChIs without a bladder anticholinergic. It was hypothesized that the bladder anticholinergics oxybutynin and tolterodine would decrease the efficacy of ChIs with respect to cognitive and functional outcomes. Loss of functioning in persons with dementia is

Even though dual use of anticholinergics and ChIs is common, prior studies have not documented the long-term detrimental effects of dual therapy on patients’ functioning. This study revealed that, for NH residents with higher levels of functioning, the rate of functional decline was 50% faster when bladder anticholinergics were used in combination with ChIs than when ChIs were used without anticholinergics. To the authors’ knowledge, this is the first
Comorbidità dei pz con demenza severa visitati negli ultimi 15 mesi

- Ipertensione Arteriosa: 26.7%
- Cardiopatia: 15.4%
- S.Immobilizzazione: 16.9%
- Pregresso ictus cerebrale: 9.8%
- Diabete Mellito, LoD: 7.1%
- BPCO, depressione: 5.6%
- Neoplasie, fratture anca, conv...: 4.2%
- IRC, MRGE, vasculopatie peri...: 2.8%

Somatic comorbidities and Alzheimer’s disease treatment

Alessandra Clodomiro · Pietro Gareri · Gianfranco Puccio · Francesca Frangipane · Roberto Lacava · Alberto Castagna · Valeria Graziella Laura Manfredi · Rosanna Colao · Amalia Cecilia Bruni

Table 1 Some examples on interactions among ChEIs, memantine and other drugs via CYP450

<table>
<thead>
<tr>
<th>Cytochrome</th>
<th>Substrates</th>
<th>Inhibitors</th>
<th>Inducitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP3A4</td>
<td>Antipsychotics: haloperidol, clozapine, risperidone, ziprasidone, sertrindole, quetiapine, aripiprazole&lt;br&gt;Antidepressants: tricyclics, venlafaxine, citalopram, mirtazapine&lt;br&gt;Benzodiazepines: diazepam, bromazepam&lt;br&gt;Nonbenzodiazepine anxiolytics: buspirone&lt;br&gt;Anticonvulsants: carbamazepine, felbamate, tiagabine&lt;br&gt;Calcium antagonists: nifedipine, diltiazem, verapamil&lt;br&gt;Other drugs: macrolides (erythromycin, clarithromycin), terfenadine, astemizole, tamoxifen, cyclosporine, amidarone, quinidine</td>
<td>Antifungal drugs (ketoconazole, fluconazole, itraconazole)&lt;br&gt;Erythromycin&lt;br&gt;Fluvoxamine&lt;br&gt;Nefazodone&lt;br&gt;Grapefruit juice (at least 250 ml)</td>
<td>Barbiturates&lt;br&gt;Phenytoin&lt;br&gt;Rifampicin&lt;br&gt;Carbamazepine&lt;br&gt;Hypericum&lt;br&gt;Topiramate&lt;sup&gt;b&lt;/sup&gt;&lt;br&gt;Oxcarbazepine&lt;sup&gt;b&lt;/sup&gt;&lt;br&gt;Felbamate&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>CYP2D6</td>
<td>Antipsychotics: haloperidol, thioridazine, perphenazine, fluphenazine, zuclopenthixol, risperidone, clozapine, olanzapine, aripiprazole&lt;br&gt;Antidepressants: tricyclics, fluvoxamine, fluoxetine, paroxetine, citalopram, mianserine, venlafaxine, mirtazapine&lt;br&gt;Opiates: codeine, tramadole, dextrometorphan&lt;br&gt;β-Blockers: metoprolol, propranolol, pindolol, timolol&lt;br&gt;Antiarrythmics: propafenon, flecainide, encainide&lt;br&gt;Other drugs: debrisoquine, spartein, phenformin&lt;br&gt;AChEIs: donepezil, galantamine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Fluoxetine&lt;br&gt;Paroxetine&lt;br&gt;Quinidine&lt;br&gt;Propaphenon&lt;br&gt;Thioridazine&lt;br&gt;Perphenazine</td>
<td>No known agent</td>
</tr>
</tbody>
</table>

<sup>a</sup> Neither the AChEI rivastigmine nor the NMDA receptor antagonist memantine present hepatic metabolism. Protein binding is 96 % for donepezil, 40 % for rivastigmine, 18 % for galantamine and 145 % for memantine

<sup>b</sup> Weak enzymatic inductor
Figure 1. Behavioural disorders in cognitive impairment

Gareri et al, JCP 2013, in press
The risk of developing depression when suffering from neurological diseases

GMS German Medical Science 2013, Vol. 11, ISSN 1612-3174

C. Thielscher¹ ²
S. Thielscher³
K. Kostev²

- Parkinson's
  - Men: 27.6% [26.3-29.0]
  - Women: 38.7% [37.2-40.1]

- Multiple Sclerosis
  - Men: 28.5% [26.2-30.8]
  - Women: 37.2% [35.6-38.8]

- Alzheimer's/Dementia
  - Men: 27.8% [26.5-29.1]
  - Women: 33.4% [32.4-34.4]

- Epilepsy
  - Men: 18.1% [17.3-18.9]
  - Women: 26.9% [25.9-27.9]

- All patients in the database
  - Men: 6.6% [6.6-6.6]
  - Women: 9.7% [9.7-9.7]
SINDROMI EXTRAPIRAMIDALI

SEGNI MOTORI DI TIPO EXTRAPIRAMIDALE MOLTO DIFFUSI NELLA DEMENZA

QUESTI MALATI PRESENTANO

* DETERIORAMENTO CLINICO PIU’ VELOCE

* SONO PIU’ ISTITUZIONALIZZATI

* SOPRAVVIVONO DI MENO

(Stem et al., 1994)
Segni extrapiramidali

Nella demenza compaiono dopo il disturbo cognitivo

Nel Parkinson seguito da demenza sono presenti fin dall’inizio
Delirium

• Demenza tra i principali fattori di rischio negli anziani

• Riguarda dal 22% all’89% degli anziani dementi ospedalizzati

• Aggrava quadro cognitivo e funzionale

• Bisogna riconoscerlo e trattarlo precocemente

Fick et al.,2002
ANTICHOLINERGIC DRUG-INDUCED DELIRIUM IN AN ELDERLY ALZHEIMER'S DEMENTIA PATIENT

P. GARERI\textsuperscript{a,b}, P. DE FAZIO\textsuperscript{c}, A. COTRONEO\textsuperscript{d}, R. LACAVA\textsuperscript{b}, L. GALLELLI\textsuperscript{a}, S. DE FAZIO\textsuperscript{a}, and G. DE SARRO\textsuperscript{a,*}
Valproate-induced delirium in a demented patient.
P. Gareri, R. Lacava, A. Cotroneo, N.M. Marigliano, A. Castagna, D.S. Costantino, G. Ruotolo, G. De Sarro
Figure 1. β-Amyloid (Aβ) can affect neuronal activity at multiple levels of complexity. High levels of Aβ depress excitatory synaptic transmission and impair synaptic plasticity at the level of specific synapses (A) but elicit epileptiform activity and seizures at the network level (B). Whether there is a causal relationship between these Aβ effects is unknown. F indicates frontal; fEPSP, field excitatory postsynaptic potentials; H, hippocampal; hAPPJ20, human amyloid precursor protein transgenic mice; L, left; NTG, nontransgenic mice; O, posterior-parietal; P, parietal; R, right; T, temporal; and TBS, θ-burst stimulation. Adapted from Neuron^4 and Nature.^22

Jorge J. Palop, PhD; Lennart Mucke, MD Arch Neurol. 2009;66(4):435-440
Conseguenze della perdita di peso nell’ AD

• Compromissione del sistema immunitario = aumento del rischio di infezioni

• Perdita di massa muscolare = atrofia muscolare, declino funzionale, cadute e fratture

• Atrofia cutanea = rischio di ulcerhe

• Aumentato rischio di istituzionalizzazione
Il trattamento delle infezioni nel paziente affetto da demenza

• Le infezioni (polmonite e infezioni delle vie urinarie in particolare) rappresentano una complicanza frequente soprattutto nelle fasi avanzate della demenza.

• Si caratterizzano per una maggiore mortalità rispetto ai soggetti cognitivamente integri.

• La **prognosi** dei pazienti con demenza avanzata e comorbidità acuta è **sfavorevole**, anche quando il paziente viene ricoverato in ambiente ospedaliero e ciò sottolinea l’esigenza di una terapia che tenga conto anche della qualità della vita del paziente.
Survival in End-Stage Dementia Following Acute Illness

Figure. Kaplan-Meier Survival Curves for Patients With Hip Fracture and Pneumonia

Morrison RS, Siu LA
JAMA. 2000;284:47-52
Sintomi più comunemente riportati dalle persone affette da demenza nell’ultimo anno di vita

- confusione 83%
- incontinenza urinaria 72%
- dolore 64%
- umore triste 61%
- stipsi 59%
- perdita di appetito 57%

Fig. 1 A three-step hierarchy of drugs for pain relief (based on World Health Organization, 2006).

Box 1 Review of evidence of tube feeding in patients with advanced dementia (Finucane et al, 1999)

- **Aspiration pneumonia.** No published studies to suggest tube feeding reduces risk
- **Prevention of malnutrition.** Delivering extra nutrients may not provide benefit to those in a catabolic state; additional nutrients might be beneficial in other instances, but effects might be outweighed by the adverse effects of tube feeding
- **Improving survival.** No published studies to suggest tube feeding prolongs survival in people with dementia and dysphagia
- **Prevention of pressure ulcers.** No published studies found to suggest tube feeding improves outcome for pressure sores
- **Risks of other infections.** No evidence that tube feeding reduces the risks of infection; in fact nasogastric feeding may increase the chances of sinus and middle-ear infection and PEG tubes the risk of diarrhoea, cellulitis and abscess
- **Functional status.** No published studies to support claims that tube feeding might improve functional abilities
- **Comfort.** No published studies to support claims that tube feeding might improve comfort
Fattori di rischio per problemi farmaco-correlati

- Età avanzata
- Demenza
- Farmaci a più elevato rischio
- Basso BMI
- Politerapia
- Numerosi prescrittori
- Condizioni croniche multiple
- Pazienti recentemente ospedalizzati
- Insufficienza renale cronica

Gareri & De Sarro, 2011
FARMACI POTENZIALMENTE IN GRADO DI CAUSARE ALTERAZIONI DELLE FUNZIONI COGNITIVE

Psicofarmaci

Barbiturici
Neurolettici (soprattutto i classici)
Benzodiazepine
Oppiacei
Antidepressivi triciclici

La gestione della politerapia

Corticosteroidi
Anticolinergici
Anti-ipertensivi
Digitalici
Farmaci somministrati in combinazione (vedi interazioni possibili a livello dei citocromi)
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD) or Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PWD in RACFs</strong> (n = 226)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>85.9 ± 7.7</td>
</tr>
<tr>
<td>NPI burden-of-care subscore</td>
<td>169 (74.8)</td>
</tr>
<tr>
<td>MMSE</td>
<td>15.9 (5.9)</td>
</tr>
<tr>
<td>PIM(s) by Modified Beers criteria</td>
<td>19.8 (2.3)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>6.9 (3.7)</td>
</tr>
<tr>
<td>Gender (Female sex)</td>
<td>44 (19.5)</td>
</tr>
<tr>
<td>MMSE</td>
<td>2 (0.9)</td>
</tr>
</tbody>
</table>

Values are means ± SD or numbers with percentages in parentheses.
Daily Medication Use in Nursing Home Residents with Advanced Dementia

This prospective study demonstrates that daily medications for chronic conditions are commonly and persistently prescribed to NH residents with advanced dementia. Although some medications of questionable benefit were discontinued toward the end of life (e.g., antidementia drugs), reductions often occurred only when death was imminent, and some drugs with unclear benefits (e.g., lipid-lowering agents) or potential harmful side effects (e.g., antipsychotics) did not decline. In addition, although the stated primary goal of care was comfort for 90% of residents, up to 40% were prescribed drugs deemed inappropriate in end-stage dementia when palliation is the goal of care. These findings raise concerns not only about the burden of medication use in advanced dementia, but also about how decisions regarding drug treatment are made for these residents.
Diabetes-related complications, glycemic control, and falls in older adults

Schwartz et al, Diabetes Care 2008


Currie et al, The Lancet 2010
Fig. 2. Il percorso assistenziale e la dimissione

Antenna ospedaliera

Reparto ospedaliero
Reparto ospedaliero
Reparto ospedaliero

Unità di valutazione interaziendale

Incontro team ospedaliero con quello extraospedaliero e con il MMG dell’utente

Strutture residenziali
Assistenza domiciliare sanitaria
Strutture riabilitative

Hospice

Gareri et al., Giorn Gerontol, 2012
Targeting Amyloid: Points of Intervention

- Increase clearance
- Block Aβ Production
- Decrease Aβ aggregation
- Lower production of toxic Ab fragments
Benefici di una diagnosi precoce

**Terapeutici**
- iniziare precocemente il trattamento
- partecipare a clinical trials con farmaci disease-modifying

**Caregiving**
- Aiutare la famiglia a comprendere ed accettare
- Consentire al paziente ed alla famiglia di adottare uno stile di vita corretto

**Legali**
- Progetti finanziari e legali fino a quando è conservata la capacità di critica e giudizio
- Adottare provvedimenti appropriati per prevenire danni alla persona (guida, maneggiare armi)

**Di cura**
- Ottenere in modo più tempestivo accessi al servizio sanitario ed all’interno della comunità
The projected effect of risk factor reduction on Alzheimer’s disease prevalence

A 10–25% reduction in all seven risk factors could potentially prevent 1.1–3.0 million AD cases worldwide.
Figure 11:
Impact of Slowed Progression by Stage of Disease, Americans Age 65 and Older with Alzheimer’s Disease, 2050

2050 Current Trajectory
- Mild: 23%
- Moderate: 29%
- Severe: 48%
Total 13.5 Million

2050 Slowed Progression
- Mild: 59%
- Moderate: 33%
- Severe: 8%
Total 15 Million
Take home messages

- Il numero di pazienti anziani dementi raddoppia ogni 5 anni nei soggetti con più di 65 anni d’età, toccando punte del 74% negli ultranovantacinquenni.
- La gestione del paziente sul territorio è complessa in particolare per la presenza dei BPSD, della comorbidità e della politerapia.
- Esistono complicazioni che possono cambiare repentinamente il quadro clinico e che pertanto andrebbero prevenute (fratture, polmoniti, malnutrizione).
- Esiste nella nostra ASP un protocollo di dimissione protetta con l’A.O. Pugliese-Ciaccio volto a facilitare l’individuazione di un adeguato setting assistenziale nei pazienti anziani in genere, inclusi coloro affetti da demenza di vario grado.
- Il segreto per un’assistenza facilitata è legato allo sviluppo di future prospettive che consentano una precoce diagnosi di demenza, presupposto indispensabile per i nuovi potenziali targets farmacologici, così da poter rallentare l’evoluzione e ridurre il peso assistenziale complessivo.
A SINE QUÀ NON.

Patient: "Do you mean to say my complaint is a dangerous one?"

Doctor: "A very dangerous one, my dear friend. Still, people have been known to recover from it; so you must not give up all hope. But recollect one thing: your only chance is to keep in a cheerful frame of mind, and avoid anything like depression of spirits."
Il più grande ostacolo alla scoperta non è l'ignoranza ma l'illusione della conoscenza.

Daniel J. Boorstin