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# Frailty Level in Alzheimer's Disease Patients Predicts the Caregiver Burden Level

**Grazia D Onofrio*, Daniele Sancarlo, Cesar Garcia Fernandez, Filomena Addante, Davide Seripa and Antonio Greco**

Department of Medical Sciences, San Giovanni Rotondo, Italy

***Corresponding author:** Grazia D Onofrio, Geriatric Unit & Gerontology-Geriatrics Research Laboratory, IRCCS Casa Sollievo della Sofferenza, Viale Cappuccini 1, 71013 San Giovanni Rotondo, Foggia, Italy. Tel: +39 0882-410271; Fax: +39 0882-410271; Email: g.donofrio@operapadrepio.it

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## ABSTRACT

**Background:** It is known that caring in Alzheimer's disease **(AD)** patients amplifies caregiver burden significantly. The aim of this study was to evaluate the efficacy of the Comprehensive Geriatric Assessment **(CGA)**, from which a frailty index Multidimentional Prognostic Index **(MPI)** is possible to calculate, for evaluating the frailty risk in AD and the caregiver burden level. The MPI is expressed as three grades of mortality risk: MPI-1 low risk (MPI value ≤ 0.33), MPI-2 moderate risk (MPI value between 0.34 and 0.66) and MPI-3 severe risk (MPI value > 0.66).

**Methods:** A total of 253 consecutive AD outpatients were included in this study: of these, 122 were in MPI-1, 107 in MPI-2 and 24 in MPI-3. All outpatients underwent a CGA, Mini-Mental State Examination **(MMSE)**, Clinical Dementia Rating **(CDR)**, and Neuropsychiatric Inventory **(NPI)**. To all caregivers were administered the Caregiver Burden Inventory **(CBI)**, a 24-item multidimensional questionnaire in which 5 subscales explore 5 dimensions of caregiver burden: (1) CBI-Objective, (2) CBI-Developmental, (3) CBI-Physical, (4) CBI-Social and (5) CBI-Emotional.

**Results**: Patients with MPI-3 showed a significantly higher cognitive impairment in MMSE ($p<0.0001$), and a higher score in NPI ($p<0.0001$) than MPI-1 and MPI-2 patients. Caregivers of patients with MPI-3 devoted significantly more length of time care (in months, $p<0.0001$) and time of daily care (in hours, $p<0.0001$) and showed a significantly higher burden level in CBI-Objective ($p<0.0001$), CBI-Developmental ($p<0.0001$), CBI-Physical ($p<0.0001$), CBI-Social ($p<0.0001$), CBI-Emotional ($p<0.0001$), and CBI-total score ($p<0.0001$) than caregivers of patients with MPI-1 and MPI-2.

**Keywords:** Frailty; Comprehensive Geriatric Assessment **(CGA)**; Multidimensional Prognostic Index **(MPI)**; Caregiver burden; Alzheimer's disease

## INTRODUCTION

Worldwide, 47.5 million people have dementia, and there are over 7.7 million new diagnosed cases every year [1], with significant social and economic implications in terms of direct medical costs, direct social costs and the costs of informal care of US$ 604 billion in 2010 [1].

Alzheimer's disease **(AD)** is the 60–70% of cases of dementia [1] and represents one of the major causes of disability, dependency, burden and stress of caregivers increasing institutionalization among older people worldwide [2].

AD leads to severe social consequences decreasing quality of life and well-being, increasing family burdens, health care demand and longer term utilization of care facilities, and generating very significant impacts on consequently costs [3].

A recent study had suggested that caring in AD patients may amplify caregiver burden significantly [4]. Who have a major role in the care and home support of patients with AD are the informal caregivers [5], who often referred as the "hidden patient" [2], are known to have a higher risk of depressive, anxiety, sleep disorders, reduced quality of life, a higher risk of cardiovascular morbidity and mortality [6-12].

The prognostic evaluation of frailty in AD patients plays a key role in the decision analyses of care processes including the organization of social health care system, the support to families and caregivers [13]. For this reason, a Comprehensive Geriatric Assessment **(CGA)** is a widely used tool in geriatric practice to assess the frailty in older patients. The collected data got through the CGA administration can be integrated in a single score called Multidimensional Prognostic Index **(MPI)** [14]. The MPI is a recent frailty index developed and validated in older hospitalized patients with dementia and with various acute and chronic diseases [15-20].

The aim of this study was to evaluate the efficacy of the CGA and MPI in order to evaluate the frailty risk in AD and the caregiver burden level, and estimate their relationship.

# MATERIALS AND METHODS

## Subjects

This study was conducted on the basis of the guidelines for Good Clinical Practice, the Strengthening the Reporting of Observational Studies in Epidemiology **(STROBE)** and was approved by the local ethics committee. Written informed consent for research was obtained from each patient or from.

Patients consecutively evaluated, from February 2013 to November 2016, at the Alzheimer's Evaluation Unit of the Geriatrics Unit of the IRCCS "Casa Sollievo della Sofferenza" (Italy) were screened for eligibility.

Inclusion criteria were: 1) age ≥ 65 years; 2) ability to provide an informed consent or availability of a relatives or a legal guardian in the case of severe demented patients. 3) Diagnosis of AD in according National Institute on Aging-Alzheimer's Association **(NIAAA)** criteria [21]; 4) a complete cognitive and neuropsychiatric assessment; 5) a complete CGA.

Exclusion criteria were: presence of serious comorbidity, tumors and other diseases that could be causally related to cognitive impairment (ascertained blood infections, vitamin $B_{12}$ deficiency, anaemia, disorders of the thyroid, kidneys or liver), history of alcohol or drug abuse, head trauma, and other causes that can cause memory impairment. No specific inclusion/exclusion criteria for caregivers were used.

## Cognitive Evaluation and Diagnosis of Dementia

In all patients, cognitive status was screened by means of the Mini-Mental State Examination **(MMSE)** [22] and the Clinical Dementia Rating scale **(CDR)** [23,24]. The MMSE was used to assess the orientation, memory, attention and calculation, language, ability to follow commands, reading comprehension, ability to write a sentence and ability to copy a drawing. The CDR was a scale designed to grade subjects from normal function through various stages of dementia. It is composed of several domains assessing cognition and function and rated according to the degree of cognitive loss as follows: 0 (no dementia), 0.5 (uncertain or deferred diagnosis), 1 (mild dementia), 2 (moderate dementia), 3 (severe dementia).

Dementia was diagnosed following the Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition **(DMS-5)** [25]. Diagnoses of possible/probable AD were made according to the NIAAA criteria [21].

## Neuropsychiatric Evaluation

Neuropsychiatric assessment was performed using the Neuropsychiatric Inventory **(NPI)** that is based on a structured interview with a caregiver and/or patient's relative [26]. The following 12 neuropsychiatric domains were evaluated: delusions, hallucinations, agitation/aggression, depression mood, anxiety, euphoria, apathy, disinhibition, irritability/lability, aberrant motor

activity, sleep disturbances, and eating disorders. For each domain, a screening question is asked to determine if the behavioural change is present or absent. If the answer is positive the domain is explored at greater depth with the sub-questions. If the sub-questions confirm the screening question, frequency is rated from 1 to 4 and severity is scored from 1 to 3. The product (severity x frequency) is calculated for each behavioural change present during the previous month or since the last evaluation. Patients with NPS were identified on the basis of the following parameters: presence of any delusions or hallucinations on the NPI (i.e., a score of ≥ 1 on either subscale), and/or disphoria score > 6, anxiety score > 6, disinhibition score > 4, irritability/lability score > 2, and/or score on the apathy, agitation/aggression, euphoria, aberrant motor behaviour, sleep disturbance, and eating disorder subscale > 1.

## Comprehensive Geriatric Assessment (CGA) and Multidimentional Prognostic Index (MPI)

A CGA was carried out evaluating the following domains: functional status with activities of daily living **(ADL)** index [27], and by instrumental activities of daily living **(IADL)** scale [28]; cognitive status with the Short Portable Mental Status Questionnaire **(SPMSQ)** [29]; comorbidity with the Cumulative Illness Rating Scale **(CIRS)** [30]; nutritional status with the Mini Nutritional Assessment **(MNA)** [31]; the risk to develop pressure sores with the Exton-Smith Scale **(ESS)** [32]; the number of drugs used by patients and the co-habitational status. From these data the MPI was calculated, which was expressed as three grades of frailty risk: MPI-1 low risk (MPI value ≤ 0.33), MPI-2 moderate risk (MPI value between 0.34 and 0.66) and MPI-3 severe risk (MPI value > 0.66).

## Care-Giving Assessment

The following parameters were collected by a systematic interview about the caregivers: gender, relationship with the patient, length of time care (in months) and time of day care (in hours). To all caregivers were administered the Caregiver Burden Inventory **(CBI)** [33,34].

The CBI is a 24-item multidimensional questionnaire in which 5 subscales explore 5 different dimensions of caregiver burden: 1) CBI-Objective: the burden on the caregiver due to shortage of time (items 1–5); 2) CBI-Developmental: the caregiver's sense of being left behind, unable to enjoy the same expectations and opportunities as his or her peers (items 6–10); 3) CBI-Physical: feelings of fatigue and chronic health problems (items 11–14); 4) CBI-Social, which results from a perceived conflict of roles (items 15–19); 5) CBI-Emotional, which originates from awareness of negative feelings towards the patient that can be induced by the patient's bizarre and unpredictable behavior (items 20–24).

Scores for each item are evaluated using a 5-point Likert scale ranging from 0 (not at all disruptive) to 4 (very disruptive) for a total ranging from 0 to 20 for each subscale, with the exception of the CBI-Physical which is composed 4-item: is then applied a correction factor 1.25.

The range of the total score ranges from 0 to 96: a score >36 indicate a risk of "burning out" whereas scores near or slightly above 24 indicate a need to seek some form of respite care. The time to administer is approximately 10-15 minutes.

### Statistical Analyses

For dichotomous variables, hypotheses regarding differences between the groups were tested using the Fisher's exact test. This analysis was made using the 2-Way Contingency Table Analysis. For continuous variables, normal distribution was verified by the Shapiro-Wilk normality test and the one-sample Kolgomorov-Smirnov test. For normally-distributed variables, hypotheses regarding differences among the groups were compared by means of the Welch two sample t-test or by means of the analysis of variance **(ANOVA)** under general linear model. For non-normally-distributed variables, hypotheses regarding differences among the groups were compared by means of the Wilcoxon rank sum test with continuity correction or by means of the Kruskal-Wallis rank sum test. Finally, AD cases as independent predictor of caregiver burden was assessed using univariate multinomial logistic regression analysis **(ANCOVA)** including into the model gender, length of time care (in months) and time of day care (in hours). Risks will be reported as odds ratios **(OR)** along with their 95% confidence interval **(CI)**.

All the statistical analyses were made with the R Ver. 2.8.1 statistical software package (The R Project for Statistical Computing; available at URL http://www.r-project.org/). Tests in which the p value was smaller than the Type I error rate $\alpha = 0.05$ were declared significant.

## RESULTS

### Clinical and Functional Characteristics of Patients

During the enrolment period, 285 AD patients were screened for the inclusion in the study. Of these, 7 patients were excluded because they were younger than 65 years, 11 patients had an incomplete examination and 14 patients had severe comorbidity associated with cognitive impairment. Thus, the final population included 253 AD patients, 99 men (39.1%) and 154 women (69.1%) with a mean age of 78.44 ± 5.15 years (range: 65 - 90 years). Of these patients, 122 were in MPI-1, 107 in MPI-2 and 24 in MPI-3.

Demographic and clinical characteristics of AD patients according to the MPI grades are summarized in **Table 1**.

**Table 1**: Demographic and clinical characteristics of Alzheimer's disease **(AD)** according to the Multidimensional Prognostic Index **(MPI)** grades.

| | All | MPI-1 | MPI-2 | MPI-3 | p |
|---|---|---|---|---|---|
| | (n = 253) | (n = 122) | (n = 107) | (n = 24) | |
| **Gender** | | | | | |
| Males/Females | 99/154 | 53/69 | 37/70 | 9/15 | 0.385 |
| Males (%) | 39.10 | 43.40 | 34.60 | 37.50 | |
| **Age** (years) | | | | | |
| Mean ± SD | 78.44 ± 5.15 | 77.06 ± 5.36 | 78.92 ± 4.63 | 83.30 ± 2.09 | **< 0.0001** |
| Range | 65 - 90 | 65 - 87 | 70 - 90 | 80 - 87 | |
| **Educational level** (years) | | | | | |
| Mean ± SD | 6.62 ± 5.11 | 7.50 ± 5.07 | 5.70 ± 4.95 | 6.17 ± 5.59 | **0.026** |
| Range | 0 - 18 | 2 - 18 | 0 - 18 | 1 - 13 | |
| **MMSE** | | | | | |
| Mean ± SD | 18.48 ± 3.83 | 20.18 ± 2.41 | 16.93 ± 4.23 | 16.89 ± 4.25 | **< 0.0001** |
| Range | 11 - 23 | 15 - 23 | 11 - 23 | 11 - 23 | |
| **CDR** | | | | | |
| Mean ± SD | 1.32 ± 0.51 | 1.10 ± 0.40 | 1.50 ± 0.51 | 1.52 ± 0.53 | **< 0.0001** |
| Range | 1 - 2 | 1 - 2 | 1 - 2 | 1 - 2 | |
| **NPI** | | | | | |
| Mean ± SD | 18.76 ± 16.35 | 16.80 ± 5.95 | 20.30 ± 16.10 | 37.00 ± 24.38 | **< 0.0001** |
| Range | 0 - 67 | 0 - 38 | 0 - 62 | 2 - 67 | |
| **NPI-Distress** | | | | | |
| Mean ± SD | 10.05 ± 7.67 | 7.62 ± 5.43 | 10.86 ± 7.13 | 18.75 ± 11.92 | **< 0.0001** |
| Range | 0 – 31 | 0 – 18 | 0 – 28 | 0 – 31 | |

**Abbreviations: AAO:** Age at Onset; **MMSE:** Mini-Mental State Examination; **CDR:** Clinical Dementia Rating; **GDS-15**: Geriatric Dementia Rating; **NPI:** Neuropsychiatric Inventory.

The three groups of patients did not differ in gender distribution (p = 0.385). Patients with MPI-1 were younger (MPI-1: 77.06 vs. MPI-2: 78.92 vs. MPI-3: 83.30, p < 0.0001) and had a significantly higher instruction level (MPI-1: 7.50 vs. MPI-2: 5.70 vs. MPI-3: 6.17, p = 0.026) than MPI-2 and MPI-3 patients.

As shown in **Table 1**, patients with MPI-3 showed a significantly higher cognitive impairment in MMSE (MPI-1: 20.18 vs. MPI-2: 16.93 vs. MPI-3: 16.89, p<0.0001), more severity stage of dementia in CDR (MPI-1: 1.10 vs. MPI-2: 1.50 vs. MPI-3: 1.52, p<0.0001), an higher score in NPI (MPI-1: 16.80 vs. MPI-2: 20.30 vs. MPI-3: 37.00, p<0.0001) and in NPI-Distress (MPI-1: 7.62 vs. MPI-2: 10.86 vs. MPI-3: 18.75, p<0.0001) than MPI-1 and MPI-2 patients.

In **Table 2,** the CGA domains in AD patients according to the MPI grades were shown. Patients with MPI-3 showed significantly an higher impairment in ADL (MPI-1: 5.43 vs. MPI-2: 4.10 vs.

MPI-3: 1.50, p<0.0001), IADL (MPI-1: 5.45 vs. MPI-2: 0.84 vs. MPI-3: 0.37, p<0.0001), SPMSQ (MPI-1: 1.16 vs. MPI-2: 5.53 vs. MPI-3: 8.17, p<0.0001), CIRS (MPI-1: 1.41 vs. MPI-2: 3.12 vs. MPI-3: 4.58, p<0.0001), MNA (MPI-1: 24.47 vs. MPI-2: 19.52 vs. MPI-3: 12.38, p<0.0001), ESS (MPI-1: 18.56 vs. MPI-2: 16.38 vs. MPI-3: 11.00, p<0.0001), and an higher number of drugs used (MPI-1: 1.28 vs. MPI-2: 3.07 vs. MPI-3: 4.04, p<0.0001), than MPI-1 and MPI-2 patients.

**Table 2:** Comprehensive geriatric assessment **(CGA)** domains in Alzheimer's disease **(AD)** patients according to the Multidimensional Prognostic Index **(MPI)** grades.

| | All | MPI-1 | MPI-2 | MPI-3 | p |
|---|---|---|---|---|---|
| | (n = 253) | (n = 122) | (n = 107) | (n = 24) | |
| **ADL** | | | | | |
| Mean ± SD | 4.50 ± 1.53 | 5.43 ± 0.86 | 4.10 ± 1.19 | 1.50 ± 0.51 | **< 0.0001** |
| Range | 1 - 6 | 3 - 6 | 2 - 6 | 1 - 2 | |
| **IADL** | | | | | |
| Mean ± SD | 3.02 ± 2.96 | 5.45 ± 2.40 | 0.84 ± 0.99 | 0.37 ± 0.49 | **< 0.0001** |
| Range | 0 - 8 | 0 - 8 | 0 - 5 | 0 - 1 | |
| **SPMSQ** | | | | | |
| Mean ± SD | 3.68 ± 2.91 | 1.16 ± 0.62 | 5.53 ± 1.92 | 8.17 ± 1.74 | **< 0.0001** |
| Range | 0 - 10 | 0 - 3 | 0 - 10 | 4 - 10 | |
| **CIRS-CI** | | | | | |
| Mean ± SD | 2.43 ± 1.44 | 1.41 ± 0.80 | 3.12 ± 0.98 | 4.58 ± 1.53 | **< 0.0001** |
| Range | 0 - 7 | 0 - 4 | 1 - 6 | 3 - 7 | |
| **MNA** | | | | | |
| Mean ± SD | 21.70 ± 5.01 | 24.47 ± 3.15 | 19.52 ± 3.84 | 12.38 ± 4.62 | **< 0.0001** |
| Range | 10 - 29 | 18 - 29 | 13 - 26 | 10 - 20 | |
| **EES** | | | | | |
| Mean ± SD | 17.11 ± 2.93 | 18.56 ± 1.58 | 16.38 ± 2.62 | 11.00 ± 2.45 | **< 0.0001** |
| Range | 9 - 20 | 14 - 20 | 10 - 19 | 9 - 15 | |
| **N of medications** | | | | | |
| Mean ± SD | 2.30 ± 1.41 | 1.28 ± 0.74 | 3.07 ± 1.02 | 4.04 ± 1.57 | **< 0.0001** |
| Range | 0 – 6 | 0 – 3 | 1 – 6 | 2 – 6 | |
| **Social support network:** | | | | | |
| Living with family | | | | | |
| N (%) | 230 (90.9) | 116 (95.1) | 96 (89.7) | 18 (75.0) | **< 0.0001** |
| Institutionalized | | | | | |
| N (%) | 4 (1.6) | 0 (0) | 0 (0) | 4 (16.7) | |
| Living alone | | | | | |
| N (%) | 19 (7.5) | 6 (4.9) | 11 (10.3) | 2 (8.3) | |

**Abbreviations: ADL:** Activities of Daily Living; **IADL:** Instrumental Activities of Daily Living; **SPMSQ:** Short Portable Mental Status Questionnaire; **CIRS-CI:** Cumulative Illness Rating Scale Comorbidity Index; **MNA:** Mini Nutritional Assessment; **ESS:** Exton-Smith Scale.

## Caregiver's Burden Level

The general characteristics of AD caregivers are summarized in **Table 3**. Caregivers of patients with MPI-3 devoted significantly more length of time care (MPI-1: 11.56 vs. MPI-2: 20.16 vs. MPI-3: 23.00, p<0.0001) and time of daily care (MPI-1: 7.96 vs. MPI-2: 8.04 vs. MPI-3: 9.50, p<0.0001) than caregivers of patients with MPI-1 and MPI-2. In all groups of caregivers, it showed a higher presence of spouses and sons in patient care (p < 0.0001) than others relative and carers.

**Table 3:** Characteristics of Alzheimer's disease **(AD)** caregivers according to the Multidimensional Prognostic Index **(MPI)** grades.

| | MPI-1 | MPI-2 | MPI-2 | p |
|---|---|---|---|---|
| **Sex** (M/F) | 48/74 | 54/53 | 12/12 | 0.211 |
| Male | 39.3% | 50.5% | 50.0% | |
| **Length of time care** (months)* range | 11.56 ± 5.13<br>6 - 24 | 20.16 ± 7.72<br>6 - 40 | 23.00 ± 9.19<br>8 - 30 | **<0.0001** |
| **Time of day care** (hours)* range | 7.96 ± 0.57<br>7 – 10 | 8.04 ± 0.49<br>7 – 10 | 9.50 ± 0.88<br>8 – 10 | **<0.0001** |
| **Relationship with patient** | | | | |
| ***Spouses*** N(%) | 78 (63.9) | 42 (39.3) | 6 (25.0) | **<0.0001** |
| ***Sons*** N(%) | 20 (16.4) | 53 (49.5) | 18 (75.0) | |
| ***Other relatives*** N(%) | 18 (14.8) | 12 (11.2) | 0 (0) | |
| ***Private carers*** N(%) | 6 (4.9) | 0 (0) | 0 (0) | |
| *Values are presented as mean ± standard deviation. | | | | |

Caregiver's burden level in AD caregivers according to the MPI grades is summarized in **Table 4**. Caregivers of patients with MPI-3 showed a significantly higher burden level in CBI-total score (MPI-1: 56.99 vs. MPI-2: 69.74 vs. MPI-3: 81.50, p<0.0001), and in all CBI-5 subscales than caregivers of patients with MPI-1 and MPI-2: CBI-Objective (MPI-1: 10.05 vs. MPI-2: 13.16 vs. MPI-3: 17.12, p<0.0001), CBI-Developmental (MPI-1: 10.90 vs. MPI-2: 13.81 vs. MPI-3: 16.13, p<0.0001), CBI-Physical (MPI-1: 13.48 vs. MPI-2: 15.22 vs. MPI-3: 18.00, p<0.0001), CBI-Social (MPI-1: 11.25 vs. MPI-2: 14.27 vs. MPI-3: 15.13, p<0.0001), and CBI-Emotional (MPI-1: 11.30 vs. MPI-2: 13.28 vs. MPI-3: 15.13, p<0.0001).

**Table 4:** Caregiver's burden level in Alzheimer's disease **(AD)** caregivers by CBI-5 subscales according to the Multidimensional Prognostic Index **(MPI)** grades.

| | MPI-1 | MPI-2 | MPI-3 | p |
|---|---|---|---|---|
| **CBI Total** (score)* | 56.99 ± 10.13 | 69.74 ± 5.42 | 81.50 ± 5.63 | **< 0.0001** |
| Range | 33 - 74 | 54 - 79 | 68 - 86 | |
| **CBI- Objective** (score)* | 10.05 ± 2.39 | 13.16 ± 1.90 | 17.12 ± 2.01 | **< 0.0001** |
| Range | 4 - 15 | 10 - 16 | 14 - 19 | |
| **CBI-Developmental** (score)* | 10.90 ± 2.49 | 13.81 ± 1.07 | 16.13 ± 0.95 | **< 0.0001** |
| Range | 4 - 14 | 11 - 15 | 15 - 17 | |
| **CBI-Physical** (score)* | 13.48 ± 1.99 | 15.22 ± 1.20 | 18.00 ± 1.75 | **< 0.0001** |
| Range | 9 - 17 | 12 - 17 | 14 – 19 | |
| **CBI-Social** (score)* | 11.25 ± 2.73 | 14.27 ± 1.12 | 15.13 ± 1.65 | **< 0.0001** |
| Range | 4 – 15 | 11 – 16 | 11 – 16 | |
| **CBI-Emotional** (score)* | 11.30 ± 1.96 | 13.28 ± 1.28 | 15.13 ± 0.61 | **< 0.0001** |
| Range | 8 – 16 | 10 – 16 | 14 – 16 | |

*Values are presented as mean ± standard deviation.

## DISCUSSION

In this study, using a relatively large sample of AD patients and their caregivers, we investigated whether the frailty level is related to caregivers' reported burden. Initially, we showed that AD patients with MPI-3 had worse MMSE, CDR, NPI, NPI-Distress and CGA domains than patients with MPI-1 and MPI-2. However caregivers of patients with MPI-3 gift more length of time care (in months) and time of day care (in hours) than caregivers of patients with MPI-1 and MPI-2. In all caregiver groups showed a higher presence of spouses and sons than other relatives and carers.

The caregivers of patients with MPI-3 showed a significantly higher burden level in CBI-total score and in all CBI-5 subscales (CBI-Objective, CBI-Physical, CBI-Social, and CBI-Emotional), than caregivers of patients with MPI-1 and MPI-2.

Thus, this study suggests that increased frailty risk in AD patients amplify caregiver burden significantly. As such, effective patient management (i.e., cognitive rehabilitation, teaching skills and strategies, or tempering caregiver reactions) should ease perceived burden.

Unfortunately, reviews of the therapy literature have not been able to identify any one consistently effective method for reducing distress or improving well-being in caregivers of patients with AD Recommendations for developing sophisticated caregiver education programs have included components that address: acknowledging the disease, making the cognitive shift into a care giving role, developing emotional tolerance, becoming assertive and proactive, establishing realistic goals, gauging the patient's capacities, designing opportunities for satisfying work and leisure, and becoming a sleuth [35].

Results from the present study serve to emphasize selected elements of the global recommendations, as well as the interventions that target caregivers' ability to psychologically and practically handle patients with AD.

Limitations of the present study should also absence of age at onset of the patient cognitive impairment.

Interestingly, the present findings do show that being caregiver of AD patients with MPI-3 places one at high risk for coping difficulties. Perhaps these variables are contributing to depression and burden in some mediating way.

At the least, appropriate targeted interventions should be put in place for the patient's family in advance of escalating patient impairment and frailty.

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## CONCLUSION

CGA should be a useful measure for predict the caregiver burden in patients with AD.

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