External validation of the PROFUND index in polypathological patients from internal medicine and acute geriatrics departments in Aragón

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Jesús Díez-Manglano designed the study and performed data collection and analysys. José Luis Cabrerizo García, Ernesto García-Arilla Calvo, Araceli Jimeno Saínz, Eva Calvo Beguería, Rosa M. Martínez-Álvarez, Esperanza Bejarano Tello, Aránzazu Caudevilla Martínez performed data collection. The manuscript was drafted by J. Díez-Manglano. José Luis Cabrerizo García, Ernesto García-Arilla Calvo, Araceli Jimeno Saínz, Eva Calvo Beguería, Rosa M. Martínez-Álvarez, Esperanza Bejarano Tello and Aránzazu Caudevilla Martínez helped with its revision.

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LEARNING POINTS

- It is hard to establish a prognosis for polypathological patients.
- The one-year mortality in the study population was 38.5 %.
- The PROFUND index assess the probability of survival of polypathological patients after a year, taking into account demographic, clinical, analytical, psychometric-funcional-sociofamilial and healthcare aspects.
- The PROFUND index is a reliable tool for predicting mortality in internal medicine but not in geriatrics PP patients

ABSTRACT

Objective: To validate externally and prospectively the PROFUND index in order to predict survival of polypathological patients after a year.

Patients and methods: An observational, prospective and multicenter study was performed. Polypathological patients admitted to an internal medicine or geriatrics department and attended by investigators consecutively by the researchers between March 1st and June 30th 2011 were included. Data concerning age, sex, comorbidity, Barthel and Lawton-Brody indexes, Pfeiffer questionnaire, socio-familial Gijon scale, delirium, number of drugs and number of admissions during the previous year were gathered for each patient. The PROFUND index was calculated. The follow-up lasted one year. A Cox proportional regression model was used to analyze the association of the variables to mortality and C-statistic was calculated.

Results: 465 polypathological patients, 333 from internal medicine and 132 from geriatrics, were included. One-year mortality was associated with age [hazard ratio (HR) 1.52 95%CI 1.04-2.12; p=0.01], presence of neoplasia [HR 2.68 95%CI 1.71-4.18; p=0.0001] and dependence for basic activities of daily living [HR 2.34 95%CI 1.61-3.40; p=0.0009]. In predicting mortality, the PROFUND index showed good discrimination in patients from internal medicine (C-statistics 0.725 95%CI 0,670-0,781) and a poor one in those from geriatrics (0.546 95%CI 0,448-0,644).

Conclusions: The PROFUND index is a reliable tool for predicting mortality in internal medicine PP patients.

KEYWORDS

Polypathological patient; multimorbidity; mortality; geriatrics; internal medicine.

INTRODUCTION

The improvement of hygienic conditions among the population and the advances in medical care have resulted in an extension of life expectancy, so that it's becoming more and more frequent that patients have more than one chronic disease. In 2007, the Andalusian regional government coined the term polypathological patients (PP) to refer to those suffering two or more chronic, progressive diseases, linked between them and leading to a progressive disability, that result in frequent hospitalizations [1]. These are patients with a high mortality rate who consume a great deal of health resources. Their prevalence among the general population has been estimated in 1.38 % [2], and they would account for 30-38% of the admissions in Internal Medicine departments [3,4].

Medical care of PP must focus on improving their quality of life. The Marigliano-Cacciafesta polypathological scale includes 11 categories of disorders and has been used to identify frailty in patients [5,6]. In order to administer the most suitable treatment to each PP, a prognostic stratification is needed. Yet, it is hard to establish a prognosis for these patients. Indexes for assessing prognosis after hospitalization [7-9] have not been designed specifically for them. There is one prognosis index, recently developed in Spain and named PROFUND [10], that integrates demographic, clinical, analytical, functional, socio-familial and healthcare variables and has shown good discrimination and calibration.

The aim of our study was to apply the PROFUND index to PP in Aragon and externally and prospectively validate its usefulness in order to predict their survival after a year.

MATERIAL AND METHODS

The PLUPAR (Paciente PLUriPatológico en ARagón) study was an observational, prospective and multicentre study participated by 13 hospital centers throughout Aragon **(appendix)**. It was designed to be a prospective external validation study of the PROFUND index.

Exclusion and inclusion criteria

Each researcher included the polypathological inpatients from the internal medicine (IM) departments and acute geriatrics (G) units that were attended consecutively between March 1st and June 30th 2011. Polypathology was diagnosed according to the Andalusian government criteria (**table 1**). Absence of consent and death during hospitalization were considered exclusion criteria. For each patient, only the first admission was taken into account, excluding later readmissions.

Data

A comprehensive questionnaire with demographic and relevant clinical data was administered to patients upon admission. Data registered included age, sex, living at home or in a nursing residence, admission in internal medicine or geriatrics ward, diseases and diagnostic categories consistent with PP, comorbidity, ability to perform basic and instrumental activities of daily living prior to admission, cognitive function, socio-familial situation, number of drugs used in a chronic fashion, creatinine and hemoglobin values, number of hospital

admissions during the previous year, presence of delirium during the admission, need and availability of a caregiver and PROFUND index [10]. Comorbidity was measured with the Charlson index [11]. The Lawton-Brody index was used to measure ability to carry out instrumental activities of daily living, assessing 8 activities: using a telephone, shopping, food preparation, housekeeping, doing the laundry, using means of transportation, responsibility for own medications and ability to handle finances [12]. The scale scores range between 0 and 8, and a patient was considered to be dependent when the score was < 5 for men or < 8 for women. The Barthel index was used to measure ability to carry out basic daily living tasks in 10 areas: feeding, bathing, dressing, grooming, bladder control, bowels control, toilet use, transferring, moving on level surfaces, and walking up and down stairs [13]. It scores range between 0 and 100: the higher the score, the more independent the person. A patient was considered dependent if his or her score was below 60. Cognitive function was measured with the Pfeiffer questionnaire, consisting of 10 dichotomous questions, and it was considered there was cognitive impairment if more than three mistakes were made [14]. The socio-familial situation was measured with the Gijón scale, which includes 5 dimensions: familial situation, financial situation, housing, social relationships and support from the social network [15]. It scores range between 5 and 25: the higher the score, the worse the socio-familial situation. A risk of familial or social problem was considered to exist when the score was above 10.

A patient was deemed to be in need of a caregiver when the Barthel index was below 60 or the score in the Pfeiffer questionnaire higher than three mistakes.

The PROFUND index [10] was designed to assess the probability of survival of PP after a year. It included PP at hospital discharge, in outpatient clinics and at home hospitalization. It took into account demographic, clinical, analytical, psychometric-funcional-sociofamilial and healthcare dimensions. It included the following variables: age ≥ 85 years (3 points), active neoplasia (6 points), dementia defined as 5 or more errors in Pfeiffer questionnaire (3 points), III-IV functional class on the New York Heart Association or dyspnea 3-4 on the modified Medical Research Council scale (3 points), delirium during the previous admission (3 points), hemoglobin < 10 g/dL (3 points), Barthel index score < 60 (4 points), absence of caregiver or caregiver other than spouse (2 points) and 4 or more admissions during the 12 previous months (3 points). It scored from 0 to 30 points, establishing 4 levels of death risk: low (0-2 points), intermediate (3-6 points), high (7-10 points) and very high (11-30 points). In this study the PROFUND index was calculated at discharge.

A follow-up of the patients was carried out for a year in order to know their survival and number of hospitalizations, be it through outpatient consultations, through medical records or via telephone calls to the patients, their relatives or caregivers. The patients were followed up in a blinded fashion,

i.e. the investigators did not know the patient PROFUND index value when the outcome was assessed.

A direct comparison between PROFUND and PLUPAR population was performed. Comparisons were performed for IM and G cohorts in our study. To perform these analyses, M. Bernabeu-Wittel, main author of PROFUND project, transfered us the PROFUND database.

The study was approved by the Ethics Committee for Clinical Research of Aragon. All patients (or their caregivers, in case of cognitive impairment) signed an informed, written consent form.

Statistical analysis

Quantitative variables are expressed as mean (standard deviation). Comparisons between groups were made with Student's t-test.

Qualitative variables are expressed as absolute number and percentage. Comparisons between them were made with the Chi-square test applying Yates correction, and with the Fisher exact test when necessary.

To study the variables associated with mortality, a Cox regression model was used. All variables considered in the PROFUND index were included in the univariate model, then a multivariate model was performed using those with a statistical significance $p<0.1$ in the univariate model.

The discriminatory properties of the model were tested by estimating the Kaplan–Meier survival curves for quartiles of risk score reported in PROFUND project. To validate the PROFUND index, the calibration of the index was determined by comparing in the PLUPAR cohort the predicted mortality by PROFUND strata. The predicted mortality was calculated using the percentages found in the original whole PROFUND cohort. Finally the discrimination power of the index was compared in the whole PROFUND cohort with PLUPAR study cohorts by calculating the AUC of their ROC curves.

In every case, the level of statistical significance was established for a value of $p<0.05$.

The analysis of data was carried out with the G-Stat statistics program (www.e-biometria.com).

RESULTS

Figure 1 displays the patient inclusion flowchart. 1870 hospital admissions were attended to during the period of study. In the end, after excluding non-PP, readmissions, deceased patients and those who didn't give their informed consent, 465 patients were included, 333 of them from IM departments and 132 from acute G units. 210 were men and 255 were women. Their average age was 80.9 (8.9) years. **Tables 2 and 3** show the characteristics of the patients compared to those of the cohort of the PROFUND study. In ours, patients were older, more frequently female and living in nursing homes. They more frequently presented diseases of the nervous system, specially dementia and hemiplegia, and locomotor system diseases (all p<0.0001), and less frequently heart and respiratory diseases (both p<0.0001). Moreover, they presented more delirium and more cognitive impairment, and they were more frequently dependant for basic and instrumental activities of daily living (all p<0.0005). Also, they more frequently needed and had a caregiver (p<0.0001) (**table 4**).

Survival

During the one-year follow-up, 179 (38.5%) patients died. Deceased patients were older, more dependent for daily living activities and more frequently were in need of a caregiver, lived in nursing homes and suffered neoplasias in an advanced stage (**table 5**). They also had higher scores in the PROFUND index [10.7 (4.1) vs. 7.8 (4.8) points; p=0.0004]. The factors associated with death during the follow-up are shown in **table 6**. Old age (1.52 IC 95% 1.04-2.12; p=0.01), dependence for basic activities of daily living (2.34,

IC95% 1.61-3.40; p=0.0009) and solid neoplasias in an advanced stage (2.68 IC95% 1.71-4.18; p=0.0001) were independently associated with mortality.

Validation of the PROFUND index

After stratifying the patients according to the risk levels of the PROFUND index, 33 of them (7.1%) showed a low risk of death during the first year, 129 (27.7%) an intermediate risk, 125 (26.9%) a high risk, and 178 (38.3%) a very high risk. The higher the risk was, the lower their survival proved to be (**figure 2)**.

A comparison between the mortality observed among the cohort of the PLUPAR study with the predicted mortality for the cohort of the PROFUND study showed differences only in those patients with very high risk, who presented less mortality in our study (54% vs 64%; p=0.03) (**figure 3**). These differences were mainly observed in PP from acute Geriatrics units.

Figure 4 displays the receiver operating characteristics (ROC) curves of the PROFUND index applied to the PROFUND cohort and to the cohorts from PLUPAR-IM and PLUPAR-G in our study. The area under the curve (AUC) was 0.686 95%CI 0.638-0.734. The curves showed a good discrimination of the index in the patients of the PLUPAR-IM cohort (AUC 0.725 95%CI 0,670-0,781) and a poor one in those of the PLUPAR-G cohort (AUC 0.546 95%CI 0,448-0,644).

DISCUSSION

The results of our study showed that, in Aragon, PP were elderly afflicted mostly with heart and neurological diseases and with major functional and cognitive impairment that made them dependant, requiring help from caregivers. Their mortality within the year was high, and the PROFUND index was found to be a valid predictor of mortality for PP in IM departments, but not for those in G.

Comparing our cohort with the cohort of the PROFUND study, the PP of Aragon showed a slightly different profile. They were older, more frequently suffered from neurological and osteoarticular diseases and not so much from heart and respiratory ones. Also, they presented greater functional and cognitive impairment. These differences may be explained by the structure of the Aragonese population, with an average age 1.9 years older than the Spanish one [16]. It is well known that the older the age, the higher the frequency of degenerative nervous and locomotor systems diseases.

Mortality within the year was 38.5 %, a figure similar to the 37% observed in the PROFUND study [10]. These data confirm the prognostic severity of PP in Spain, regardless of their geographic origin. It would be interesting to carry out similar studies in other European countries and different regions of the world in order to confirm these death rates.

The factors associated with mortality were age, neoplasias and dependence for basic activities of daily living, all of them included in the PROFUND index [10]. Other variables from that index, such as cognitive impairment, delirium, hemoglobin < 10 g/dL and the number of hospitalizations during the previous year were not independently associated with higher mortality. Nevertheless, when PROFUND was applied, the validity of the index proved satisfactory. Only patients in the highest risk stage showed a significantly lower mortality. This fact is hard to explain, but it is most likely due to the older age of the Aragonese population. The PP in our study were in average two years older than those in the PROFUND cohort. We believe that it might have been the cause of the higher prevalence of patients in the highest risk stage in our study, since age ≥ 85 scores more in the PROFUND index. It is possible that in Aragon this increase in age does not have as much prognostic influence as in other Spanish regions. Attention should be paid also to the important difference in clinical settings between the PROFUND and PLUPAR study. In PLUPAR study all patients were inpatients whereas in PROFUND project only 37% were inpatients and 27% and 34% of patients were recruited in outpatient clinics and home hospitalization respectively. We think that the exclusive recruitment of inpatients at discharge in our study might be associated with a higher but not not with a lesser or similar mortality. It is well known that mortality is higher in patients with a recent hospitalization than in patients from outpatient clinics. Another factor is the place where patients live. In our study, a significantly higher percentage of the PP lived in nursing homes, a fact that might have determined the difference in mortality. However, the calibration of

the PROFUND index may be considered good. In their systematic review of prognostic indexes for older patients, Yourman et al [17] consider a 10% difference between predicted and observed mortality as the threshold that marks the difference between good and poor calibration. In our study, only the patients in the very high risk stage showed a significantly different mortality, and it was a 10% difference. This usefulness of the PROFUND index in different cohorts reinforces its value in establishing a prognosis for PP, who are usually excluded from clinical trials.

Another interesting finding was the difference observed between patients from IM and G departments. Such differences have previously been described: a greater prevalence of heart, digestive and oncohaematological diseases in patients from IM and of neurological and locomotor system diseases in patients from G [4]. The predictive ability of the PROFUND index differed too, showing a better validity in patients from IM. In fact, discrimination in this group of patients was practically identical (C-statistic 0.77 and 0.7 in the derivation and validation cohorts of the PROFUND project and 0.725 in the PLUPAR-IM cohort). The applicability of this index might be limited to PP from IM services, and its generalizability might be restricted to patients attended to in those services. It would be interesting to carry out a study with a greater number of patients from acute G units in order to recalibrate the index and test its validity in that context. This would allow identifying new variables to be introduced or variables to be excluded and recalibrating the weight of each one in the index.

Many prognostic indexes have been described for specific diseases, taken separately. Examples include the BODE index, for patients with chronic obstructive pulmonary disease [18] or the Seattle Heart Failure Model, for patients with heart failure [19]. There are also different indexes assessing prognosis for hospitalized elderly patients [17]. But as far as we know, the PROFUND index is the only one specifically developed for PP [10]. One of its peculiarities is that it includes not only age and clinical variables, but also functional variables such as dependence for daily living activities, social variables as the need for a caregiver and other variables related with the use of hospital resources. Such multidimensionality reinforces the validity of its predictions. The Multidimensional Prognostic Index was developed by Pilotto et al in hospitalized older patients to predict one-year mortality [20]. The discrimination was good, 0.751 (95%CI 0.71-0.80), and it has been applied to patients with dementia, transient ischemic attack and upper gastrointestinal bleeding and liver cirrhosis [21-23]. Further studies to evaluate the potential usefulness of this prognostic tool in PP could be interesting. However this index includes six scales, the Katz Index, the Lawton-Brody Index, the Pfeiffer Questionnaire, the Cumulative Illness Rating Scale, the Mini Nutritional Assessment and the Exton-Smith Scale, and requires about 45-60 minutes. The PROFUND index was specifically developed in PP and it requires only ten minutes. That is its added value.

We present a prospective external validation of the PROFUND index which is something not so usual in the literature. Indeed, usually the external validation of a prediction model is made retrospectively using as validation

cohort a cohort of patients participating in another study designed and conducted with different objectives and only later used for the validation purpose. This is strength of our study. However, our study has some limitations. In the first place, patients deceased during hospitalization were excluded. The same was done in the PROFUND project, and we decided to reproduce the conditions of that study in designing ours. We think that it was not a selection bias, but rather a criterion to appropriately define the cohort of application of PROFUND index. Secondly, the number of G units patients included was significantly lower than the number of internal medicine patients, thus reflecting the reality of the health system in Aragon, where the number of beds is much lower in acute G units than in IM departments.

In conclusion, given the progressive ageing of the population and the advances in healthcare, the prevalence of polypathology is a growing phenomenon that poses a challenge to health systems. Knowing the probability of survival of these patients is essential for health care providing, case management and clinical governance, and it may help to assign to each PP the health resource best adjusted to his or her needs and life expectancy. Using the PROFUND index might help make such decisions.

Table 1. Polypathological patient criteria

CATEGORY A

A.1. Heart failure which in a situation of clinical stability has been in class II of the NYHA[a] scale (symptoms with ordinary physical activity)

A.2. Ischemic heart disease (angina or infarction)

CATEGORY B

B.1. Vasculitis and systemic autoimmune diseases

B.2. Chronic renal disease defined by elevated levels of creatinine (>1.4 mg/dl in men, >1.3 mg/dl in women) or proteinuria[b], sustained for 3 months

CATEGORY C

C.1. Chronic lung disease which in a situation of clinical stability has scored grade 2 on the MRC[c]dyspnea scale), or FEV1<65%, ó SatO2 ≤ 90%

CATEGORY D

D.1. Chronic inflammatory bowel disease

D.2. Chronic liver disease with evidence of hepatocellular insufficiency[d] or portal hypertension[e]

CATEGORY E

E.1. Stroke.

E.2. Neurological disease with permanent motor deficit causing impairment for basic activities of daily living (Barthel index under 60)

E.3. Neurological disease with permanent cognitive impairment, at least moderate (5 or more errors on Pfeiffer)

CATEGORY F:

F.1. Symptomatic peripheral artery disease

F.2. Diabetes mellitus with proliferative retinopathy or symptomatic neuropathy

CATEGORY G:

G.1. Chronic anemia due to digestive loss or acquired hemopathy non-subsidiary of healing treatment presenting Hb< 10 g/dl in two determinations more than three months apart

G.2. Solid or active hematologic neoplasia non-subsidiary of healing treatment

CATEGORY H:

H.1. Chronic osteoarticular disease leading by itself to an impairment for basic activities of daily living (Barthel index under 60)

A patient is considered to be PP if he or she meets at least one criterion from two different categories.

[a1] Mild impairment of physical activity. Ordinary physical activity causes dyspnea, angina, fatigue or palpitations.

[b] Albumin/creatinine ratio > 300 mg/g, microalbuminuria> 3mg/dl in urine sample or albumin>300 mg/day in 24-h urine or >200 µg/min

[c] Short of breath when hurrying or walking up a slight hill.

[d] INR >1.7, albumin <3.5 g/dl, bilirrubin >2 mg/dl.

[e] Defined by presence of clinical, analytical, echographic or endoscopic data.

Table 2. Baseline characteristics of the patients. Comparisons between PROFUND cohort and PLUPAR cohorts.

	PROFUND Cohort		PLUPAR Cohort								
	n=1525		Internal Medicine n=333		p	Geriatrics n= 132		p	Total n=465		p
Age*	78.7	(9.4)	79.3	(9.0)	0.29	84.6	(7.1)	0.0002	80.9	(8.9)	0.0005
Female	685	(45.4)	168	(50.3)	0.11	86	(65)	<0.0001	255	(54.8)	0.0006
Living											
In nursing res.	90	(5.9)	62	(18.8)	<0.0001	45	(34.1)	<0.0001	108	(23,5)	<0.0001
At home	1426	(94.1)	267	(81.2)		87	(65.9)		352	(76,5)	
Category A	1183	(78.0)	209	(62.6)	<0.0001	66	(50.0)	<0.0001	273	(58.7)	<0.0001
A1	883	(58.2)	154	(46.1)	<0.0001	46	(34.8)	<0.0001	198	(42.6)	<0.0001
A2	620	(40.9)	89	(26.6)	<0.0001	30	(22.7)	<0.0001	120	(25.8)	<0.0001
Category B	486	(32.1)	114	(34.1)	0.46	35	(26.5)	0.18	147	(31.6)	0.83
B1	34	(2.2)	3	(0.9)	0.11	1	(0.8)	0.26	4	(0.9)	0.06
B2	465	(30.7)	112	(33.5)	0.31	34	(25.8)	0.23	144	(31.0)	0.93
Category C	696	(45.9)	123	(36.8)	0.002	39	(29.5)	0.0003	160	(34.4)	<0.0001
Category D	109	(7.2)	28	(8.4)	0.45	4	(3.0)	0.07	32	(6.9)	0.84
D1	14	(0.9)	1	(0.3)	0.25	3	(2.3)	0.13	4	(0.9)	0.91
D2	95	(6.3)	27	(8.1)	0.42	1	(0.8)	0.01	29	(6.2)	0.99
Category E	572	(37.7)	135	(40.4)	0.59	86	(65.1)	<0.0001	220	(47.3)	0.0002
E1	386	(25.5)	66	(19.8)	0.03	34	(25.8)	0.94	98	(21.0)	0.05
E2	139	(9.2)	29	(8.7)	0.78	26	(19.7)	0.0001	56	(12.0)	0.08
E3	229	(15.1)	68	(20.4)	0.02	55	(41.7)	<0.0001	124	(26.7)	<0.0001
Category F	389	(25.7)	83	(24.8)	0.75	26	(19.7)	0.13	108	(23.2)	0.31
F1	205	(13.5)	42	(12.6)	0.64	10	(7.6)	0.05	50	(10.9)	0.12

F2	257	(17.0)	46	(13.8)	0.15	19	(14.4)	0.47	66	(14.2)	0.17
Category G G1 G2	391 261 161	(25.8) (17.2) (10.6)	102 59 45	(30.5) (17.7) (13.5)	0.08 0.85 0.03	25 17 8	(18.9) (12.9) (6.1)	0.08 0.19 0.10	127 76 53	(27.3) (16.3) (11.4)	0.53 0.63 0.17
Category H	259	(17.1)	67	(20.1)	0.20	50	(37.9)	<0.0001	118	(25.4)	<0.0001
Number of categories*	2.7	(0.8)	2.6	(0.8)	0.02	2.5	(0.7)	0.01	2.5	(0.7)	0.001
Number of drugs*	8.0	(3.3)	8.4	3.4	0.04	8.0	(3.5)	0.89	8.2	(3.4)	0.09
Delirium	186	(12.3)	50	(15.3)	0.14	41	(31.3)	<0.0001	93	(20.3)	<0.0001
Admissions in 12 previous months *	1.9	(1.6)	2.1	1.4	0.04	1.8	(1.1)	0.72	2.0	(1.3)	0.15
Charlson index*	4.0	(2.1)	4.0	(2.1)	0.97	3.5	(2.1)	0.01	3,8	(2,1)	0.17
The results are presented as n (%) or *mean (standard deviation)											

Table 3. Comorbidities included in the Charlson index. Comparisons between PROFUND cohort and PLUPAR cohorts.											
	PROFUND Cohort n=1525		PLUPAR Cohort								
			Internal Medicine (n=328)		p	Geriatrics (n=132)		p	Total (n=460)		p
Myocardial infarct	473	(31.0)	82	(25.0)	0.03	20	(15.3)	0.0002	102	(22.3)	0.0003
Chronic heart failure	875	(57.4)	174	(52.7)	0.11	52	(39.7)	<0.0001	226	(49.0)	0.001
Peripheral artery disease	239	(15.7)	55	(16.7)	0.59	15	(11.4)	0.20	70	(15.0)	0.73
Cerebrovascular disease	387	(25.4)	92	(27.9)	0.34	48	(36.6)	0.005	140	(29.9)	0.049
Dementia	275	(18.3)	97	(29.4)	<0.0001	67	(51.5)	<0.0001	164	(36.2)	<0.0001
Chronic pulmonary disease	646	(42.4)	117	(35.4)	0.02	37	(28.5)	0.002	154	(33.5)	0.0007
Connective tissue disease	42	(2.7)	7	(2.1)	0.51	2	(1.5)	0.40	9	(2.0)	0.35
Peptic ulcer	105	(6.9)	7	(2.1)	0.0009	10	(7.6)	0.75	17	(3.7)	0.01
Mild chronic liver disease	69	(4.5)	12	(3.6)	0.08	5	(3.8)	0.72	17	(3.7)	0.14
Diabetes	518	(34.0)	114	(34.6)	0.84	35	(26.7)	0.0008	149	(32.0)	0.14
Hemiplegia	87	(5.7)	21	(6.4)	0.58	21	(16.0)	<0.0001	42	(9.1)	0.009

Mild-severe chronic kidney insufficiency	385	(25.2)	94	(28.6)	0.21	24	(18.3)	<0.08	118	(25.4)	0.92
Diabetes with target organ damage	285	(18.7)	55	(16.7)	0.39	10	(7.6)	0.001	65	(13.9)	0.02
Any tumor	146	(9.6)	30	(9.1)	0.80	14	(10.7)	0.68	44	(9.6)	1.00
Leukemia	11	(0.7)	3	(0.9)	0.72	1	(0.8)	0.96	4	(0.9)	0.75
Lymphoma	7	(0.5)	1	(0.3)	0.69	0	(0.0)	0.44	1	(0.2)	0.47
Mild-severe chronic liver disease	63	(4.1)	20	(6.1)	0.13	1	(0.8)	0.05	21	(4.6)	0.68
Metastatic solid tumor	63	(4.1)	13	(3.9)	0.86	3	(2.3)	0.30	16	(3.5)	0.53
AIDS	3	(0.2)	1	(0.3)	0.71	0	(0.0)	0.61	1	(0.2)	0.93
The results are presented as n (%)											

Tabe 4. Functional, cognitive and sociofamilial situation. Comparisons between PROFUND cohort and PLUPAR cohorts.											
	PROFUND cohort (n=1512)		PLUPAR cohort (n=465)								
			MI (n=333)		p	G (n=132)		p	Total (n=465)		p
Barthel index	69.5	(31.3)	61.1	(34.4)	0.0001	38.0	(32.6)	<0.0001	54.8	(35.4)	<0.0001
Lawton-Brody index	3.3⌂	(2.9)	3.1	(2.9)	0.17	1.0	(1.6)	<0.0001	2.5	(2.8)	0.0001
Pfeiffer's questionnaire	2.9‡	(3.2)	3.8	(3.3)	0.0005	5.4	(3.7)	0.0009	4.2†	(3.5)	0.0001
Gijón scale	10.5¶	(3.3)	10.5	(3.2)	0.99	10.6	(3.4)	0.70	10.5∆	(3.2)	0.79
Dependency for basic activities of daily living*	475	(31.4)	140	(41.7)	0.0003	92	(69.7)	<0.0001	230	(49.4)	<0.0001
Dependency for instrumental activities of daily living *	1137⌂	(76.8)	255	(75.9)	0.97	117	(97.5)	<0.0001	383	(82.0)	0.02
Cognitive impairment*	499‡	(33.2)	154	(46.5)	<0.0001	70	(60.9)	<0.0001	223†	(50.1)	<0.0001
Risk of social problem *∆	668	(45.6)	150	(46.3)	0.81	53	(48.2)	0.59	203∆	(46.9)	0.63
Needs caregiver*	789	(52.7)	181	(54.0)	0.67	115	(87.8)	<0.0001	294	(63.2)	<0.0001
Has caregiver*	1106	(74.2)	229	(85.4)	<0.0001	122	(100.0)	<0.0001	350	(87.3)	<0.0001
The results are presented as mean (standard deviation) or *n (%). ⌂Data from 1482 cases. †Data from 445 cases. ‡Data from 1501 cases. ∆Data from 433 cases. ¶Data from 1466 cases.											

Table 5. Characteristics of surviving and deceased patients during the follow-up year.					
	Living (n=286)		Deceased (n=179)		p
Age (years)	79.5	9.1	83.2	8.0	0.0001
Sex (female)	157	55	98	55	0.97
Living* At home In nursing residence	 227 55	 80 19	 125 53	 70 30	 0.01
Category A A1 A2	164 114 76	57 40 27	110 84 44	61 47 25	0.38 0.13 0.63
Category B B1 B2	87 2 85	30 1 30	60 2 59	33 1 33	0.48 0.63 0.46
Category C	97	34	63	35	0.78
Category D D1 D2	23 3 21	8 1 7	9 1 8	5 1 4	0.21 0.57 0.22
Category E E1 E2 E3	137 65 34 75	48 21 12 26	84 33 22 49	47 18 12 27	0.84 0.27 0.90 0.78
Category F F1 F2	65 33 38	23 11 13	43 17 28	24 9 16	0.75 0.49 0.48
Categoría G G1 G2	74 50 26	26 17 9	53 26 28	30 14 16	0.38 0.40 0.03
Category H	69	24	50	28	0.36
Number of categories	2.5	0.7	2.6	0.8	0.09
Charlson index	3.7	2.0	3.9	2.3	0.28
Lawton-Brody index	2.9	2.8	1.6	2.3	0.0002
Dependency IADL	224	78	159	89	0.004
Barthel index	62	33	42	35	0.0005
Dependency BADL	109	38	121	68	<0.0001
Pfeiffer's questionnaire	3.8	3.3	4.9	3.6	0.0009
Cognitive impairment (>3)	125	45	98	58	0.008
Gijón scale†	10.3	3.1	10.8	3.4	0.16
Social risk†	146	55	103	62	0.15
Needed caregiver§	154	54	140	79	<0.0001
Had caregiver‡	196	83	153	93	0.003
Lack of caregiver other than spouse¶	164	72	132	81	0.046
Number of drugs#	8.5	3.7	8.0	3.0	0.16
Delirium#	50	18	43	25	0.08
Dyspnea 3-4	83	29	62	35	0.20

Admissions 12 months	1.9	1.3	2.1	1.3	0.22
PROFUND index	7.8	4.8	10.7	4.1	0.0004
Hemoglobin<10 g/dL	58	21	41	24	0.44
eGFR < 60 mL/min	142	50	86	49	0.84
BADL:basic activities of daily living; eGFR:estimated glomerular filtration rate; IADL: instrumental activities of daily living; *Data from 460 patients. # Data from 457 patients. † Data from 431 patients. § Data from 463 patients. ‡ Data from 399 patients. ¶ Data from 341 patients.					

Table 6. Association of items of PROFUND index with mortality (Cox regression)						
	Global PLUPAR cohort		PLUPAR-IM cohort		PLUPAR-G cohort	
Variable	HR (95%CI)	p	HR (95%CI)	p	HR (95%CI)	p
Age ≥ 85	1.62 (1.17-2.25)	0.004	1.84 (1.21-2.79)	0.004	1.78 (0.94-3.38)	0.078
Category G2 (neoplasia)	2.80 (1.81-4.32)	0.0003	3.01 (1.85-4.89)	0.0009	3.47 /1.07-11.27)	0.038
Dementia	0.72 (0.51-1.02)	0.067	0.83 (0.52-1.32)	0.436	0.55 (0.32-0.96)	0.035
Delirium	1.12 (0.77-1.61)	0.553	1.25 (0.76-2.03)	0.376	1.04 (0.57-1.90)	0.895
Class III-IV NYHA or dyspnea 3-4 mMRC scale	1.32 (0.96-1.82)	0.087	1.64 (1.11-2.44)	0.014	0.72 (0.38-1.39)	0.330
Hb < 10 g/dL	1.08 (0.76-1.54)	0.678	0.88 (0.55-1.40)	0.595	1.55 (0.84-2.84)	0.158
Dependency BADL	2.91 (2.03-4.17)	0.0007	2.72 (1.77-4.18)	0.0004	2.86 (1.28-6.42)	0.018
Lack of caregiver or other than spouse	1.20 (0.83-1.74)	0.329	1.63 (1.04-2.58)	0.035	0.64 (0.32-1.30)	0.218
≥ 4 admissions 12 previous months	1.45 (0.92-2.28)	0.108	1.31 (0.76-2.27)	0.325	3.36 (1.27-8.87)	0.014
BADL: basic activities of daily living; CI: confidence interval; HR: hazard ratio; mMRC: modified Medical Research Council; NYHA: New York Heart Association						

Appendix

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Figure legends

Figure 1. Flowchart of patients included in the study. G: geriatrics. IM: internal medicine. PP: polypathological patient

Figure 2. Kaplan-Meier survival curves

Figure 3. One-year observed and predicted mortality. A: Total PLUPAR cohort. B: Internal medicine cohort. C: Acute geriatrics units cohort.

Figure 4. ROC curves

Figure 1

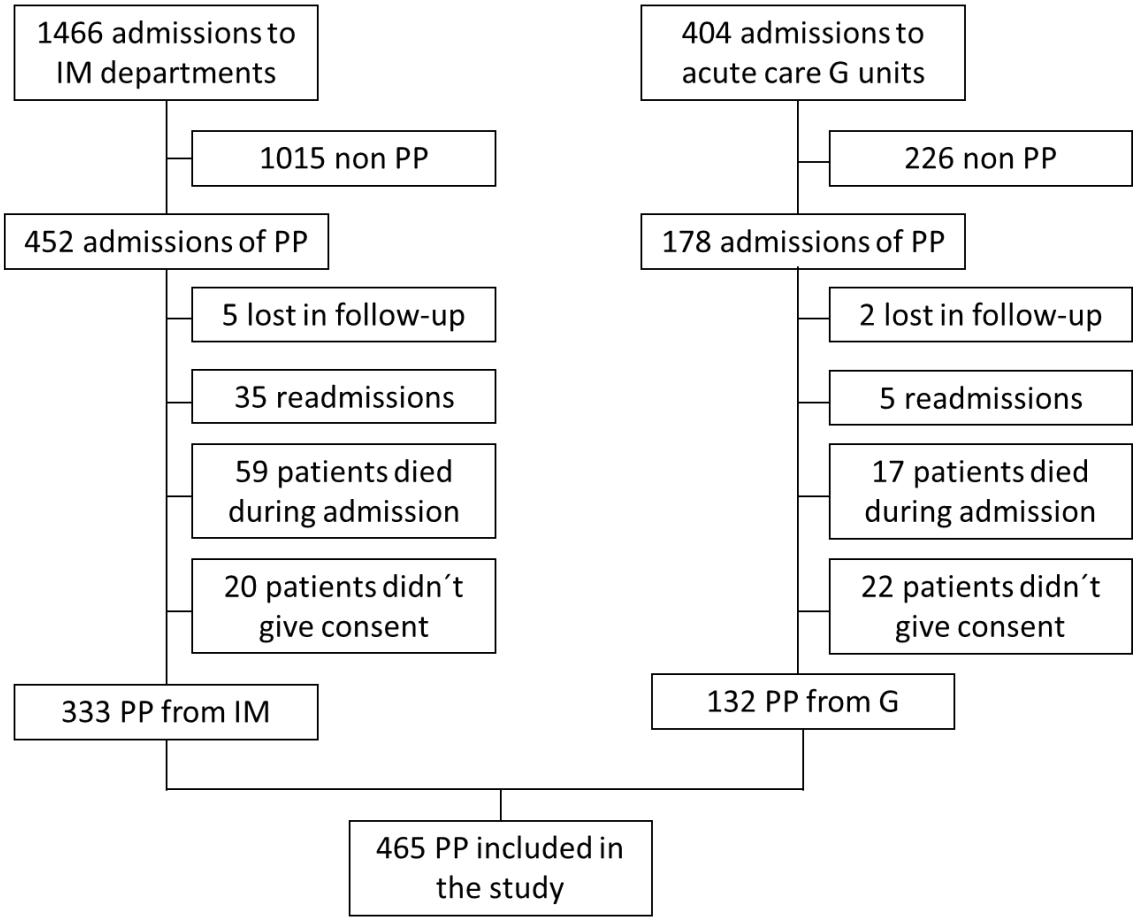
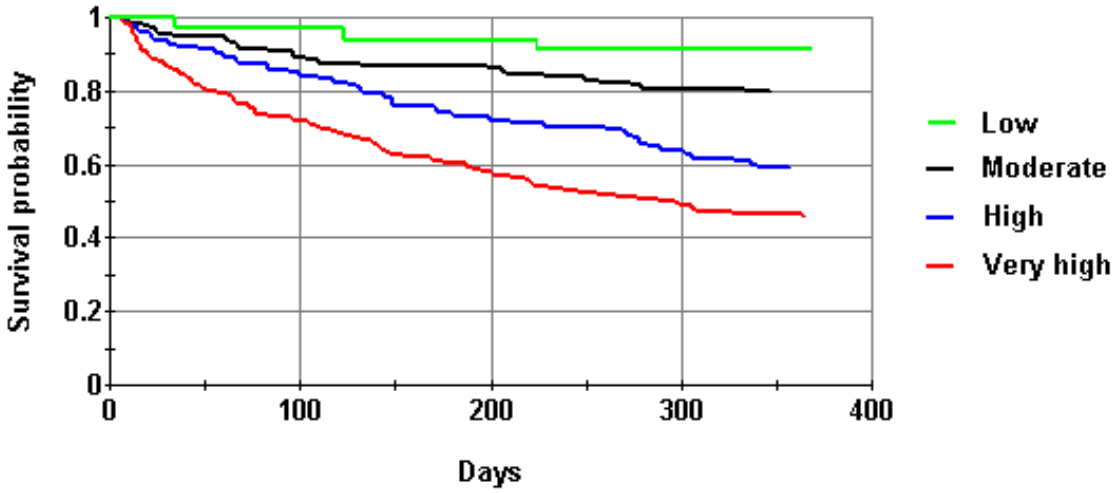

1466 admissions to IM departments
1015 non PP
452 admissions of PP
5 lost in follow-up
35 readmissions
59 patients died during admission
20 patients didn´t give consent
333 PP from IM
404 admissions to acute care G units
226 non PP
178 admissions of PP
2 lost in follow-up
5 readmissions
17 patients died during admission
22 patients didn´t give consent
132 PP from G
465 PP included in the study

Figure 2


Survival probability
1
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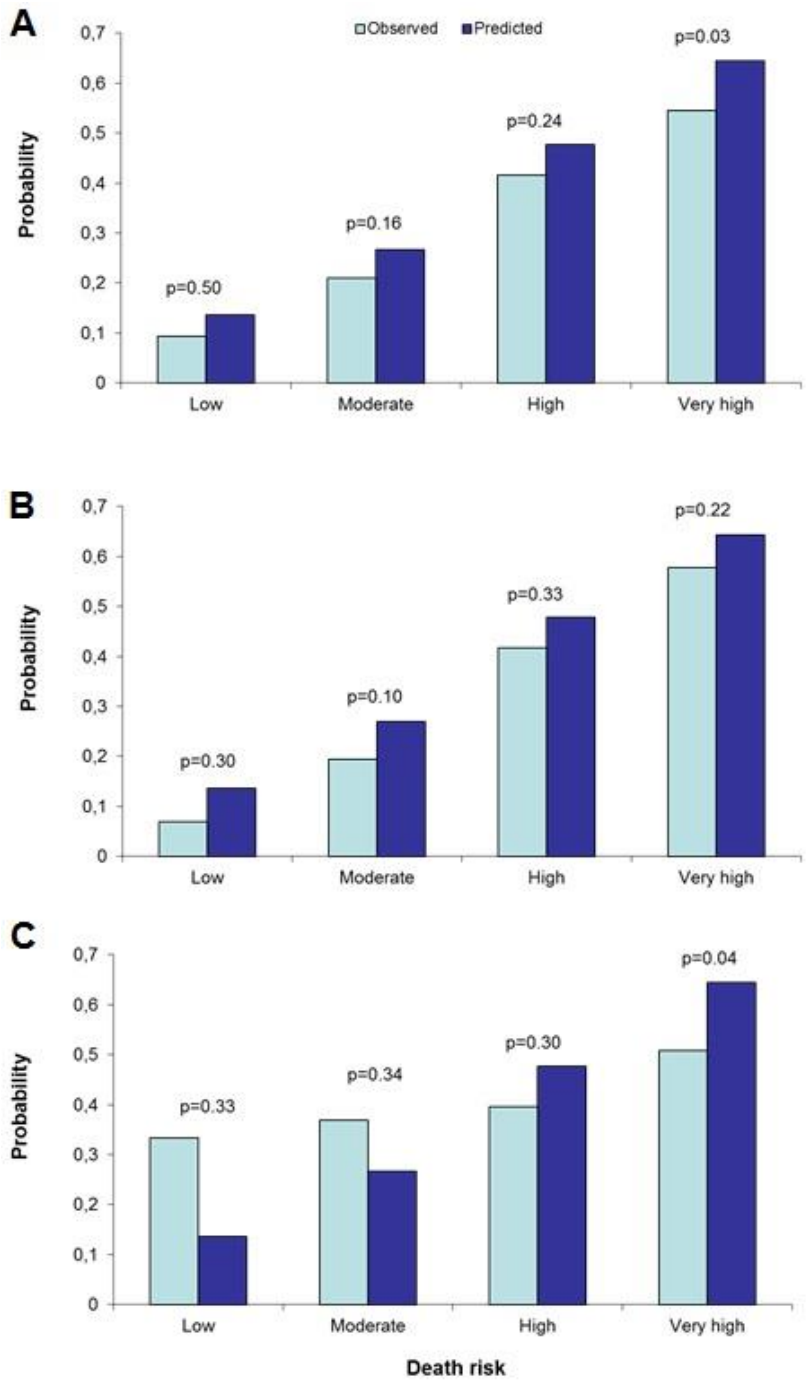
0.6
0.4
0.2
0
0
100
200
300
400
Days
Low
Moderate
High
Very high

Figure 3


A
Observed
Predicted
Probability
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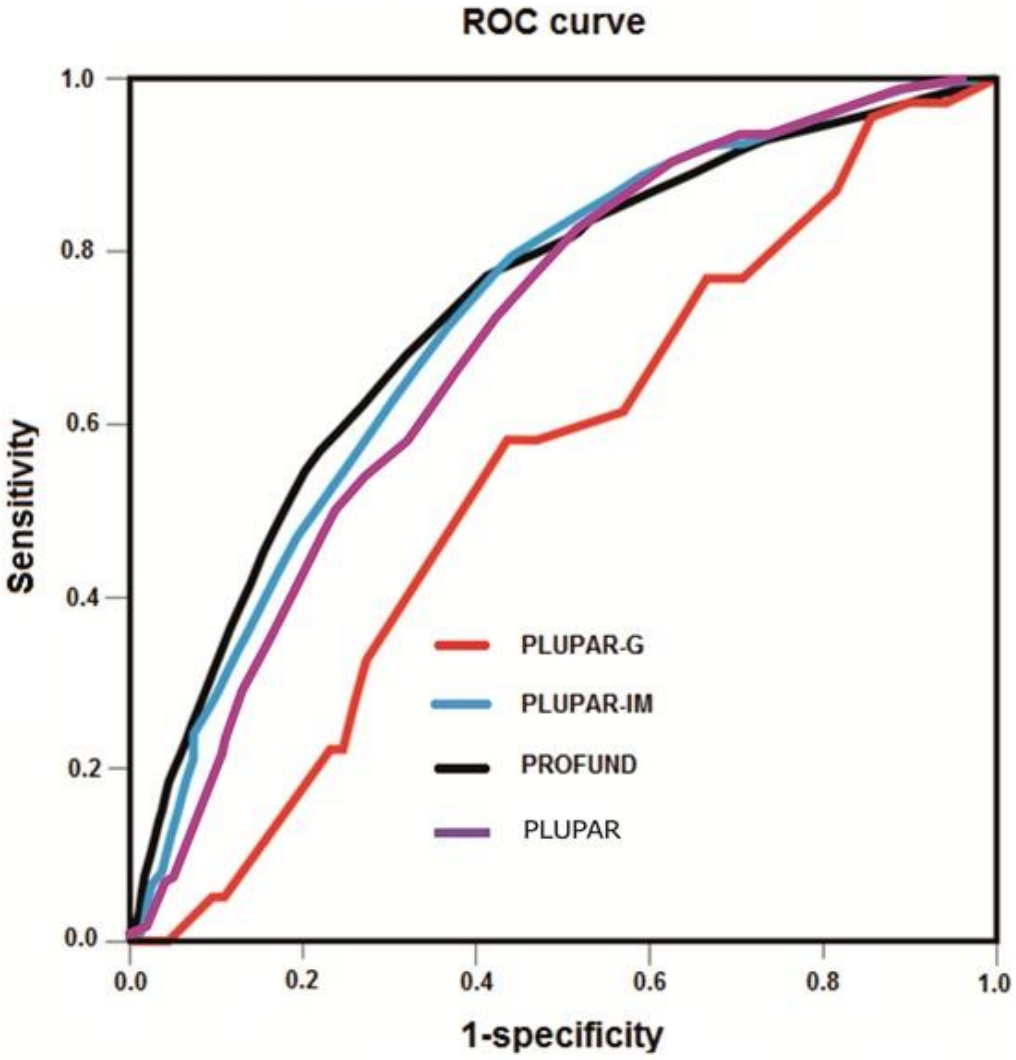
0,6
0,5
0,4
0,3
0,2
0,1
0
p=0.50
p=0.16
p=0.24
p=0.03
Low
Moderate
High
Very high
B
Probability
p=0.30
p=0.10
p=0.33
p=0.22
Low
Moderate
High
Very high
C
Probability
p=0.33
p=0.34
p=0.30
p=0.04
Low
Moderate
High
Very high
Death risk

Figure 4


ROC curve
Sensitivity
1-specificity
0.0
0.2
0.4
0.6
0.8
1.0
PLUPAR-G
PLUPAR-IM
PROFUND
PLUPAR