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RESEARCH ARTICLE

Characterization of Patients with Chronic Diseases and Complex Care Needs: A New High-Risk Emergent Population

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ABSTRACT

Background: To analyze the prevalence and main epidemiological, clinical and outcome features of in-Patients with Complex Chronic conditions (PCC) in internal medicine areas, using a pragmatic working definition.

Methods: Prospective study in 17 centers from Spain, with 97 in-hospital, monthly prevalence cuts. A PCC was considered when criteria of polypathological patient (two or more major chronic diseases) were met, or when a patient suffered one major chronic disease plus one or more of nine predefined complexity criteria like socio-familial risk, alcoholism or malnutrition among others (PCC without polypathology). A complete set of baseline features as well as 12-months survival were collected. Then, we compared clinical, outcome variables, and PROFUND index accuracy between polypathological patients and PCC without polypathology.

Results: The global prevalence of PCC was 61% (40% of them were polypathological patients, and 21% PCC withouth polypathology) out of the 2178 evaluated patients. Their median age was 82 (59.5% men), suffered 2.3 ± 1.1 major diseases (heart diseases (70.5%), neurologic (41.5%), renal (36%), and lung diseases (26%)), 5.5 ± 2.5 other chronic conditions, met 2.5 ± 1.5 complexity criteria, and presented functional decline (Barthel index 55 (25-90)). Compared to polypathological patients, the subgroup of PCC without polypathology were younger, with a different pattern of major diseases and comorbidities, a better functional status, and lower 12-months mortality rates ((36.2% *vs* 46.8%; p = .003; OR 0.7(0.48-0.86). The PROFUND index obtained adequate calibration and discrimination power (AUC-ROC 0.67 (0.63-0.69)) in predicting 12-month mortality of PCC.

Conclusion: Patients with complex chronic conditions are highly prevalent in internal medicine areas; their clinical pattern has changed in parallel to socio-epidemiological modifications, but their death-risk is still adequately predicted by PROFUND index.

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Introduction

In the last years the terminology in the chronic diseases' arena has evolved and enriched. Many authors have made efforts in building a taxonomy by different methods like diseases clustering, big data mining or experts' panels [1-6]. Many

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factors, like ageing of most societies, important changes in socioeconomic conditions and family environments, together with the progress of health care delivery, have introduced additional complexity elements, transforming the classic daguerreotype of chronic conditions, into a digital photo with many more shades and areas of uncertainty [1,3,5,6]. Recently the new term 'patient with chronic diseases and complex health-care needs' or simply 'Patients with Complex Chronic conditions' (PCC) has been incorporated when referring to patients with one or more major chronic disease(s) and any of the above-mentioned condition(s), which makes their care more complex [7-10]. Nevertheless, there is no available formal and homogeneous definition of PCC, and their main clinical characteristics have not yet been outlined.

Since their first description and characterization, polypathological patients have been one of the paradigmatic populations within the wide range groups encompassed by the term 'multimorbidity' [11-13]. A patient is considered polypathological when suffering from chronic diseases included into two or more of eight predefined categories; these categories were established by a panel of experts using criteria of end-effect on function of key organs (independent of the primary disease), frequent chronic conditions with high mortality/potential of becoming unstable, or frequent comorbidities when mental/functional impairment thresholds were definitively reached (Table 1). Therefore, this concept is more transversal because it is globally centered on the patient, and not on any "protagonist" disease, nor any professional healthcare worker who attends him/her [11-13]. Their main features

Table 1: Pragmatic working definition of patient with complex chronic conditions, used in the identification and recruitment of candidates in a prospective cohort of 17 Spanish hospitals.

Population	Definition
Patient with complex chronic conditions [19] ↓↓↓↓	A patient with complex chronic conditions is a patient with any of the following criteria: 1 - A polypathological patient: patient with chronic diseases included into two or more of the eight defining categories 2 - A complex chronic patient without polypathology: patient with only one defining category of polypathological patient plus one or more complexity criteria
1. Polypathological patient: 2 or more defining categories [12,18] **OR** ↓↓↓↓	Polypathological Patient Defining Categories 1.1. Category A: A.1 Chronic heart failure with past/present stage II dyspnea of NYHA[a] A.2 Coronary heart disease 1.2. Category B: B.1 Vasculitides and/or systemic autoimmune diseases B.2 Chronic renal disease (glomerular filtration rate < 60 ml/min or albumin creatinine index > 30 mg/g) 1.3. CATEGORY C: Chronic lung disease with past/present stage 2 dyspnea of mMRC[b], or FEV1 < 65%, or basal Sat. O2 ≤ 90% 1.4. Category D: D.1 Chronic inflammatory bowel disease D.2 Chronic liver disease with evidence of liver failure[c] or portal hypertension[d] 1.5. Category E: E.1 Stroke E.2 Neurological disease with permanent motor deficit, leading to severe impairment of basic activities of daily living (BI < 60) E.3 Neurological disease with permanent moderate-severe cognitive impairment[e] 1.6. Category F: F.1 Symptomatic peripheral artery disease F.2 Diabetes mellitus with proliferate retinopathy or symptomatic neuropathy 1.7. Category G: G.1 Chronic anemia (Hemoglobin < 10 g/dl during ≥ 3 months) due to digestive-tract losses or acquired hemopathy not tributary of treatment with curative intention G.2 Solid-organ or hematological active neoplasia not tributary of treatment with curative intention 1.8. Category H: H.1. Chronic osteoarticular disease, leading to severe impairment (limitation of the patient's ability to transfer alone safely from bed to chair or wheelchair) H.2. Having suffered an osteoporotic hip fracture.
2. Complex chronic patient without polypathology: One defining category of polypathological patient plus one or more complexity criteria [18]	Complexity Criteria 2.1. Severe mental disorder (schizophrenia, manic-depressive psychosis, major depression). 2.2. Extreme polypharmacy (10 or more chronically prescribed drugs). 2.3. Socio-familial risk (score on the Gijón score ≥ 10 points). 2.4. Stage ≥II skin pressure injuries. 2.5. Current delirium or episodes of delirium in previous hospital admissions. 2.6. Malnutrition (BMI<18.5). 2.7. Chronic prescription of nasogastric/nasoenteric tube feeding (3 or more months). 2.8. Two or more hospital admissions in the previous 12 months. 2.9. Alcoholism.

NYHA: New York Heart Association; mMRC: modified Medical Research Council; FEV1: Forced Expiratory Volume in one second; BI; Barthel Index; BMI: Body Mass Index; a: Slight limitation of physical activity. Regular physical activity causes dyspnoea, angina, tiredness or palpitations; b: Inability to keep pace with another person of the same age, walking on level ground, due to shortness of breath or having to stop to rest when walking on level ground at own pace; c: INR > 1.7, albumin < 3.5 g/dl, bilirubin > 2 mg/dl; d: Defined by the presence of clinical, laboratory, ultrasound or endoscopic data; e: Pfeiffer with 5 or more errors or Lobo cognitive mini-exam with less than 23 points.

are homogeneous and very similar: they share an advanced age, severe major diseases as well as multiple additional co-morbidities, polypharmacy, frailty, clinical vulnerability, and high mortality risk [14-17]. So, strictly they can also be considered fully as PCC. Nevertheless, the increase in life expectancy in recent years may have led to changes in the profile of these patients, resulting in a more predominant role of ageing processes and their associated syndromes in the clinical picture of currently attended polypathological patients.

Attending these issues, a pragmatic working definition of PCC has been proposed to standardize this population [18]. This definition is detailed in table 1, and includes all patients with polypathology, as well as those patients with only one major disease of the polypathology definition categories with one or more of nine additional complexity criteria, like socio-familial risk, alcoholism, polypharmacy, or malnutrition among others. Nevertheless, despite this homogenizing effort, until now, the prevalence of PCC, the global weight of PCC without polypathology with respect to polypathological patients, and their mortality risk are unknown.

Similarly, the accuracy of prognostic instruments adapted to patients with chronic diseases has not been assessed in this new group of PCC. The two most used indices are the Charlson index, which was developed more than 30 years ago and is still widely used; and the PROFUND index, which was developed more recently in the specific population of polypathological patients [15,19].

For all these reasons we have conducted this study, with the aim of explore the prevalence and main epidemiological, clinical, and prognostic features of PCC, and to assess the accuracy of PROFUND and Charlson indices in predicting their 12-month death risk (both are the most used tools in predicting survival of patients with multimorbidity and polypathology). We hypothesized, that PCC are highly prevalent in Internal Medicine areas, and that PROFUND index maintains its accuracy in stratifying their death-risk.

Patients and Methods

This was an observational prospective, multi-institutional study carried out by researchers from the Polypathological Patient and Advanced Age Study Group of the Spanish Society of Internal Medicine (a complete list of participant researchers and centers is detailed in Acknowledgment section). The study inclusion period ranged from March to October 2019.

Reference population

All in-hospital patients treated in the Internal Medicine and Geriatric areas from the 17 Spanish hospitals (6 tertiary teaching centers and 5 secondary, and 6 basic general hospitals) participating in the study (all participant centers are listed on the CRONICOM Researchers list).

Inclusion criteria

Patients ≥ 18 years old, who met criteria detailed in Table 1, were considered candidates to be included.

Development of the study, data collection and follow-up

During the inclusion period, a coordinated monthly prevalence assessment was performed in order to identify the prevalence of PCC in the evaluated areas. Those who met inclusion criteria were offered to be recruited in the study. After receiving informed consent, a complete set of demographical, socio-familial, clinical, functional, biological, and prognostic data were collected from all included patients.

Demographic and socio-familial data included age, gender, residence, employment data, the need for a caregiver, and the main caregiver´s profile. Clinical data included the different diseases, and all possible comorbidities, stage of different diseases (NYHA class and mMRC dyspnea score [20,21], and Child-Pugh stage [22]), assessment of Charlson´s and PROFUND comorbidity indices [15,19], different symptoms and signs, and assessment of basal ability in performing Activities of Daily-Living (ADL) by means of Barthel´s Index (BI) [23], respectively. Laboratory data included basal plasma Creatinine (Cr (mg(dL)), Albumin (ALB (g/dL), Hemoglobin (HB (g/dL)), Lymphocytes (n°/µL), and Cholesterol (mg/dL).

All patients were followed-up during a 12-month period. In this visit, the number of admissions during follow-up as well as survival were recorded. Survival time was assessed and, in the case of death, the cause, and the number of days to death were gathered. Therefore, we looked at mortality as both a dichotomous and a time-dependent outcome. For the dichotomous outcome, subjects were categorized depending on whether or not they survived 12 months from their initial interview date. For the continuous outcome, survival time was defined as the number of days between the inclusion date, and the date of death [15-17].

Definitions

Obesity was defined as BMI > 30 and cachexia as < 16.5 [24]; hypoalbuminemia was defined as albumin levels <3.5 g/dL (severe when <1.8 g/dL, moderate when 1.8-2.69 g/dL, and slight when 2.7-3.5 g/dL); dependence in functional status for ADL was defined by a BI < 60 points; the need for a caregiver was defined when the patient was functionally dependent (BI < 60) and/or cognitively impaired (Pfeiffer Questionnaire ≥ 3 errors) [25].

Statistical analysis

The dichotomous variables were described as whole integers and percentages, and the continuous variables as mean and standard deviation (or median and interquartile

range in those with no criteria of normal distribution). The distribution of all variables was analyzed with the Kolmorogov-Smirnov test. Missing data were managed by re-interviewing patients and exploring exhaustively their medical records; and for those which could not be recovered, an imputation process by means of educated guessing, common-point and average imputation was performed.

Possible differences in survival, and number of hospital admissions during follow-up were firstly investigated performing the Chi-square test (with the Yates correction and, when necessary, the Fisher exact test); the Student's *t* for normally distributed quantitative variables; Mann-Whitney U test in the case of quantitative variables that were not normally distributed; Pearson's R; and Spearman's Rho. We included the factors which showed statistical differences in unadjusted analysis, in a multivariable Cox proportional hazards model for time to death, in order to obtain those independently associated to survival. The strength of associations was quantified by calculating Hazard Ratio (HR) using 95% confidence intervals [15-17].

To assess PROFUND and Charlson indices prognostic accuracy, we determined their calibration comparing the predicted mortality (divided into probability risk-quartiles) pointed by the indices with the observed mortality by means of calculating the Hosmer-Lemeshow (H-L) goodness-of-fit test, and by constructing calibration curves; we also considered their calibration attending mortality as a continuous variable (survival time), performing Kaplan-Meier curves (and log-rank test). Then, we evaluated the discrimination of both indices by applying the indices scores, thereby determining risk scores for each participant, and calculating the Area under the Curve of the Receiver Operating Characteristic (AUC-ROC) [15-17].

Statistic analysis was performed using the SPSS 22.0 software. A $p < .05$ was considered significant.

Ethical aspects

All patients or their legal representatives accepted the use of their anonymous clinical data for clinical research purposes, by signing a written informed consent. The study was approved by the by the Andalusian Central Ethics Committee (internal code 1444-N-17), and by local ethics committees of all participating centers. In this prospective project the collection, process and analysis of all data was anonymously carried out, and only for the purposes of the project. All data were protected in accordance with the World Medical Association Declaration of Helsinki, and the European Union directive 2016/679 of the European Parliament and the European Council, of April 27, 2016, regarding the protection of persons and their personal data. All authors declared no conflict of interest with respect to this work.

Results

A total of 2178 patients were evaluated in the 97 coordinated monthly prevalence cuts performed during the study period; 1331 (61%) of them fulfilled criteria for PCC (P25-P75 of cuts = 42.5%-86%); with polypathology prevalence being 40% (P25-P75 of cuts = 25%-60%) and PCC without polypathology prevalence 21% (P25-P75 = 9%-33%). The prevalence of PCC was higher in tertiary teaching hospitals (77%; $p < .0001$) and county hospitals (69%; $p = .06$) than in regional hospitals (44%), and this trend was also observed in polypathological patients (52%, 38%, 32%, respectively) and PCC without polypathology (25%, 31%, 12%, respectively). There were no significant differences in the prevalence of PCC among the coldest months (72%), compared to temperate (64%) and warm months (65%).

Among the 1331 identified PCC, 1121 agreed to be recruited in the study, and 1070 of them (96.2%) completed the follow-up period (802 polypathological patients (75%) and the remaining 268 (25%) PCC without polypathology). The study flowchart is detailed in supplementary appendix **figure S1**. Most patients lived in their family home (89.5%) and the remaining 110 (10.5%) in long term care facilities. Their main global and differential clinical features are detailed in table 2. Patients with complex chronic conditions are characterized by advanced age, notable major diseases, several additional criteria of clinical complexity as well as multiple comorbidities; additionally they present frequent functional impairment, significant vulnerability and high death-risk in prognostic scores. Evident differences were observed between the two populations of PCC; so that polypatholgical patients were older, with a greater number of additional comorbidities (mainly cardiovascular and endocrinological), a poorer basal functional status, and greater clinical vulnerability and 12-months death risk with respect to PCC without polypathology.

Overall mortality was 44% (472 patients), this being related to chronic diseases in 402 (85.2% of deaths); only 6 patients in the cohort died of confirmed new coronavirus disease 2019 (COVID-19). Mortality was significantly lower among PCC without polypathology (36.2% *vs* 46.8%; $p = .003$; OR 0.7 (0.48-0.86). Factors independently associated with overall mortality were chronic neurological diseases (HR 1.3(1.01-1.6)), malnutrition (HR 1.6 (1.15-2.2)), albumin levels (HR 0.7 (0.5-0-8)), as well as the Charlson (HR 1.09 (1.05-1.3) for each point) and PROFUND (HR 1.04 (1.01-1.06) for each point) indices. During the 12-month follow up, the mean number of admissions and days of hospital stay was 1.15 ± 1.4 and 14 ± 26, respectively, with no differences between polypathological patients and PCC without polypathology. The only factor that correlated to a higher number of admissions and days of hospital stay was the number of additional comorbidities (R = 0.13 and R = 0.132, respectively; $p < .0001$).

Table 2: Main global and differential clinical features of Patients with Complex Chronic conditions (PCC) of a multicenter cohort from 17 Spanish hospitals.

Clinical Features Mean (SD)/Median [Q1-Q3]/N° (%)	Global (*n* = 1070)	Polypathological Patients (*n* = 802)	PCC Without Polypathology (*n* = 268)
Age and male gender	82 (74-87); 546 (51%)	83 (75-87); 418 (52%)	80 (72-86)*; 128 (48%)
Number of categories (major diseases)	2.3 (1.1.)	2.7 (0.9)	1 (0)
Most frequent major diseases			
Chronic heart failure	495 (46%)	433 (54%)	62 (23%)*
Chronic neurologic disease	444 (41.5%)	344 (43%)	100 (37%)
Chronic kidney disease	382 (36%)	361 (45%)	21 (7.8%)*
Chronic lung failure	289 (27%)	259 (32%)	30 (11%)*
Coronary heart disease	262 (24.5%)	225 (28%)	37 (14%)*
Severe osteoarthritis	180 (17%)	157 (20%)	23 (9%)*
Chronic anemia - hematologic disease	150 (14%)	140 (17.5%)	10 (3.7%)*
Active Neoplasm	107 (10%)	92 (11.5%)	15 (5.6%)*
Number of complexity criteria	2.5 (1.5)	2.3 (1.6)	3.1 (1.1)
Most frequent complexity criteria			
Extreme polypharmacy (> 10 drugs)	363 (34%)	259 (32%)	104 (39%)
≥ 2 hospital admissions in last year	338 (31.6%)	226 (28%)	112 (42%)
Delirium	213 (20%)	138 (17%)	75 (28%)
Social-familial frailty	187 (17.5%)	113 (14%)	74 (27.6%)
Severe mental illness	65 (6.1%)	31 (4%)	34 (12.7%)
N° of additional comorbidities per patient	5.5 (2.5)	5.9 (2.4)	4.3 (2.2)*
Cardiovascular	2.1 (1.3)	2.3 (2)	1.7 (1.3)*
Endocrine	0.9 (0.8)	0.9 (0.8)	0.8 (0.8)#
Respiratory	0.7 (0.9)	0.8 (1)	0.4 (0.7)*
Most frequent additional comorbidities			
Hypertension	813 (76%)	636 (79%)	177 (66%)*
Dyslipidemia	528 (49%)	419 (52%)	109 (41%)*
Diabetes mellitus	467 (43.6%)	370 (46%)	97 (36%)*
Atrial fibrillation	417 (39%)	337 (42%)	80 (30%)*
Osteoporosis	178 (16.5%)	158 (19%)	31 (11%)*
Obesitas	170 (16%)	134 (17%)	36 (13%)
Benign prostate hyperplasia	149 (14%)	120 (15%)	29 (11%)
Depression	135 (13%)	92 (11.5%)	43 (16%)
Anxiety disorders	126 (12%)	85 (10.6%)	41 (15%)
Hypothyroidism	89 (8.3%)	65 (8.1%)	24 (9%)
Other vulnerability and severity tracers			
Caregiver need	694 (65%)	551 (66%)	173 (61%)
NYHA grade of dyspnea ≥ 3	239 (22%)	213 (27%)	26 (9.7%)*
mMRC grade of dyspnea ≥ 3	151 (14%)	133 (16.5%)	18 (6.7%)*
Main biological parameters			
Hemoglobin (g/dL)	11.2 (3.2)	11.1 (3.4)	11.6 (2)*
Lymphocytes (n°/µL)	1804 (3089)	1770 (2976)	1853 (3167)
Creatinine (mg/dL)	1.38 (1)	1.5 (1)	1.1 (0.9)*
Cholesterol (mg/dL)	119 (69)	116 (69)	124 (68)
Albumin (g/dL)	3.1 (0.6)	3.1 (0.6)	3 (0.6)
Functional and stratification parameters			
Basal Barthel´s Index	55 (25-90)	55 (25-85)	65 (20-95)
PROFUND index	9 (5-12)	9 (5-12)	8 (3-10)*
Charlson index	6 (5-8)	7 (5-8)	4 (3-6)*

SD: Standard Deviation; Q1-Q3: Quartile1-Quartile3; N°: Number; %: Percentage; PCC: Patient with Complex Chronic conditions; NYHA: New York Heart Association; mMRC: modified Medical Research Council; *$p < .01$; #$p < .05$

The calibration of PROFUND and Charlson indices are detailed in figures 1a,b (calibration curves), and in supplementary appendix **table S1** (H-L test). Using H-L test both of them showed good calibration. In the calibration curves, however, the highest calibration comparing predicted and observed mortality curves was obtained by PROFUND index, whereas Charlson index low- and low-intermediate risk strata showed a suboptimal calibration. Cumulative survival during follow-up according to risk groups of PROFUND and Charlson indices are detailed in figures 2a,b, in which significant differences in outcome trajectories according to risk strata, were obtained with both indices (log rank test $p < .0001$); nevertheless only 4 and 39 patients formed part of in the low- and low-intermediate risk strata of Charlson index, whereas 816 (more than 75% of the cohort) were in the highest risk group.

The discrimination power of PROFUND and Charlson indices is detailed in figure 3. The most discriminative tool was PROFUND Index (AUC-ROC = 0.67(0.63-0.69); $p < .001$); whereas Charlson index showed less discriminative power (AUC-ROC = 0.61(0.58-0.64); $p = <.001$), similarly, no discrimination power differences were detected when specific assessment of polypathological patients and PCC without polypathology was performed.

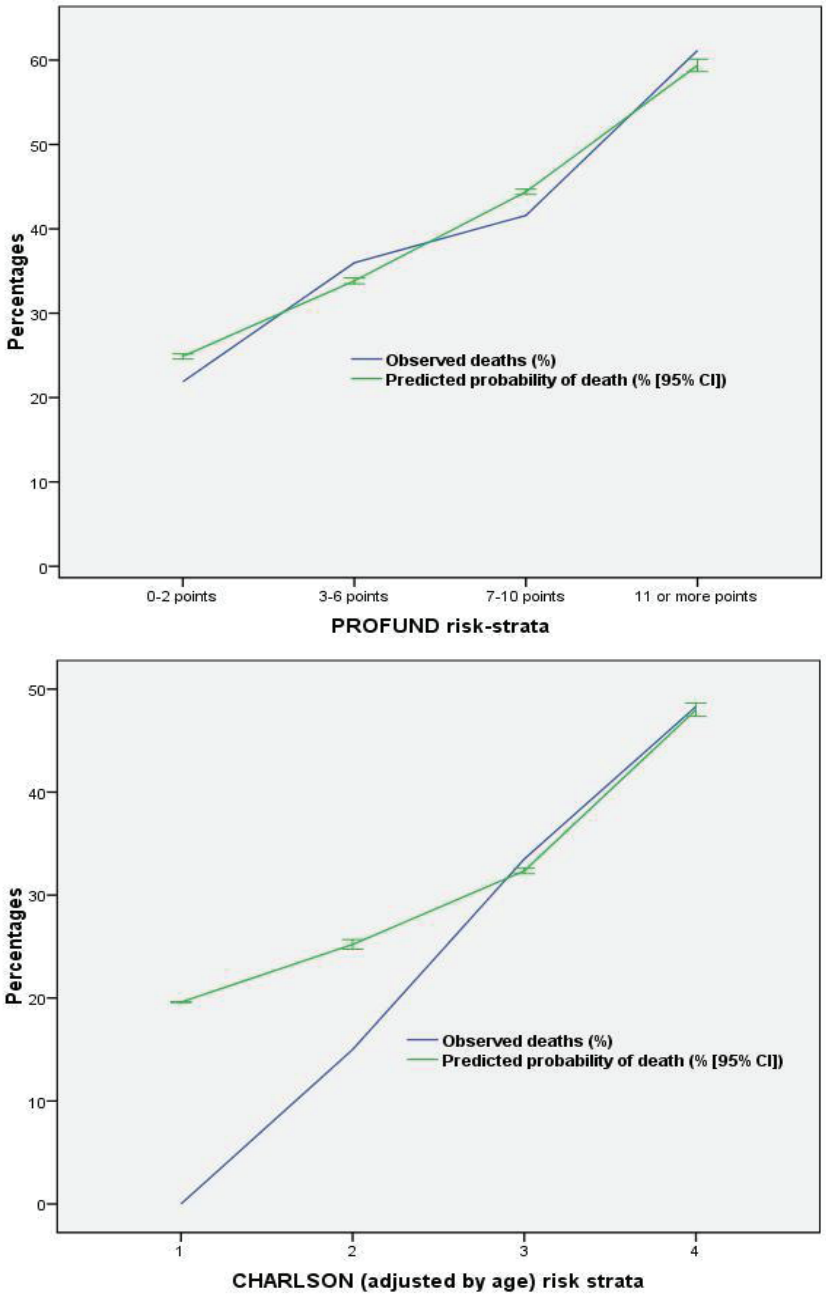

Figure 1 Calibration curves of predicted mortality risk and observed mortality in a multicenter cohort of patients with complex chronic conditions.
1a). According to PROFUND index risk-strata.
1b). According to Charlson index risk-strata.

Discussion

In the present study PCC made up the majority of patients attended in internal medicine departments of 17 Spanish hospitals. Polypathological patients make up two thirds of them, with PCC without polypathology making up the remaining third. With these results we are witnessing the progressive increase in the prevalence and weight of PCC in hospital, medical areas, and specifically in Internal Medicine. This epidemiological evolution should make us think about the importance of incorporating and strengthening the necessary competencies in the management of these populations [26-28]. Hospital doctors must be prepared for an optimal approach to preventing and treating geriatric syndromes, polypharmacy, family and social aspects, and prognostic stratification that will allow them to offer the best care while avoiding deviations towards futility or nihilism [26-30]. Most of today's doctors are trained in a 'hi-tech' culture of care, but we probably need to recover our atavistic roots and offer 'hi-touch' medicine as well. On the other hand, the current institutional culture of hospitals must also adapt to this new reality by offering more friendly

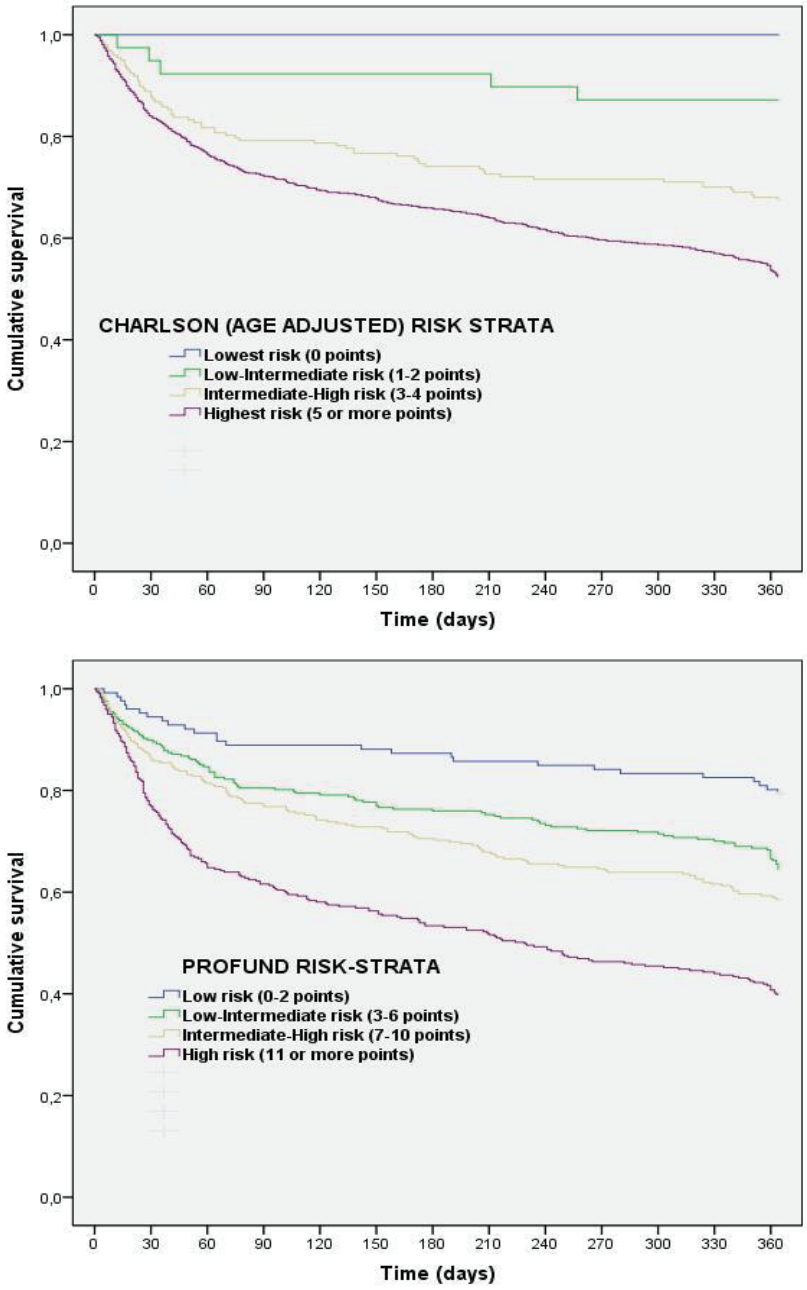

Figure 2 Kaplan-Meier curves comparing survival of patients with complex chronic conditions in a prospective cohort of 17 Spanish centers residents.
2a). According to PROFUND index risk-strata.
2b). According to Charlson index risk-strata.

care to these emerging populations, such as active policies to promote and maintain autonomy, assuring an optimal night's rest, a correct nutrition by adapting textures and avoiding prolonged fasting, or rationalizing and improving the timetables for administering medicines or extracting blood samples [31-33].

We have observed a significant change in the clinical profile of polypathological patients compared to previous cohorts. The data obtained in the present study point to an increase in their age, the prominence of chronic neurological diseases, and a higher vulnerability and 12-month mortality. This tendency could be the result of the improvement in socioeconomic conditions, and the generalized preventive measures implemented in last 20-30 years, which may have delayed the onset of the most common chronic diseases (cardiovascular, pulmonary, neurological...) [34-36]. Thus, it is probable, that the impact of chronic diseases is now being intertwined with the impact of ageing processes such as frailty, sarcopenia, and other geriatric conditions in most polypathological patients.

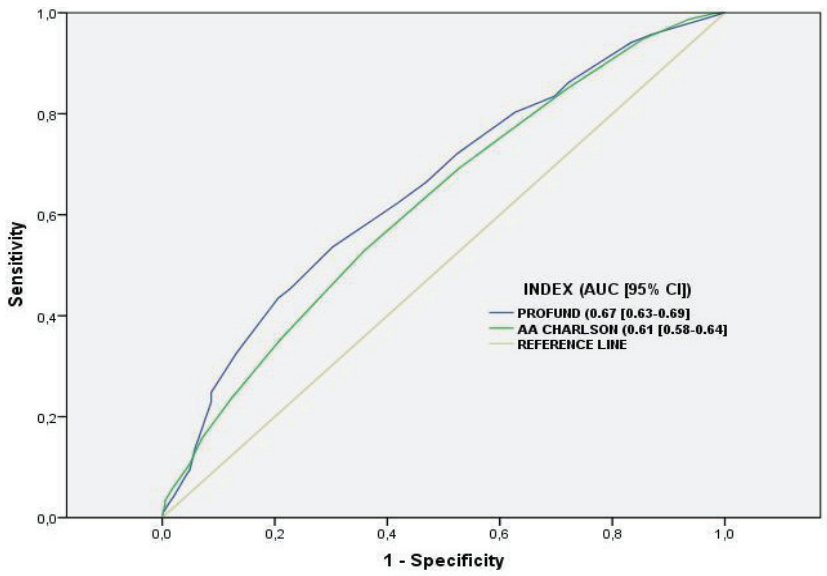

Figure 3 Discrimination power of PROFUND and Charlson indices by comparison of their Area under Receiver Operator Curve (AUC) in multicenter cohort of patients with complex chronic conditions from Spain.

Another remarkable finding was the high prevalence of PCC without polypathology, which accounted nearly a third of all PCC. This population was younger than polypathological patients, and was composed more predominantly with women with chronic neurological conditions. The significant number of these patients detected in the present study highlights the importance of monitoring sociological, epidemiological and clinical changes in the onset and behaviour of chronic diseases. The identification of similar and emergent populations, as the case of PCC without polypathology, which can benefit from an integrated care model, is a key element of this approach. The complexity pattern of these patients, as detailed in the definition criteria, is a mixture of socio-familial determinants, biological consequences of diseases, and clinical care issues; and, in our opinion, reflect and include the most frequent scenarios in daily clinical practice.

Finally, the PROFUND index demonstrated an adequate prognostic accuracy, higher than the Charlson index, when applied to PCC. Establishing an accurate prognostication is essential in the clinical care of vulnerable and frail populations. PROFUND index was originally developed to predict one-year mortality in hospital-based patients with multimorbidity, but its generalizability was subsequently demonstrated in other populations of patients with chronic conditions (in primary care polypathological patients, in other geographical areas, in patients with heart diseases, and in shorter as well as longer periods of follow-up) [37-41]. Recently a systematic review of prognostic tools in multimorbid populations found its quality as satisfactory [42]. With the results obtained in the present work this index may also be suitable and useful in PCC populations.

This study has some limitations that should be remarked. First, the consecutive monthly assessment, for patients recruitment could have introduced some biases, since patients attended between assessment dates were lost; in this sense the broad inclusion period, including all year seasons and the large number of participating centers makes difficult this bias to occur. And second, the intrusion of COVID-19 pandemic in the last months of follow-up could have increased mortality in the cohort; nevertheless, this was not the fact, since only 6 patients died due to this new disease.

In conclusion our work show, that patients with complex chronic conditions were highly prevalent in Internal Medicine areas, corresponding two third of them to polypathological patients, and the remaining third to patients with complex chronic conditions without polypathology. The PROFUND index maintains its accuracy in evaluating death-risk of this emergent vulnerable population. Monitoring pattern changes in populations with multimorbidity is useful and allows the detection of emergent groups for potential health interventions.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the Andalusian Central Ethics Committee (internal code 1444-N-17), and by local ethics committees of all participating centers (Hospital de la Vega Baja Ethics Committee; Hospital Royo Villanova Ethics Committee; Corporación Sanitaria Parc Taulí Ethics Committee; Hospital Universitario de Elche Ethics Committee; Hospital General Universitario de Valencia Ethics Committee; Hospital Clínico Universitario de Salamanca Ethics Committee; Hospital Santa Caterina

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All patients or their legal representatives accepted the use of their anonymous clinical data for clinical research purposes, by signing a written informed consent. In this prospective project the collection, process and analysis of all data was anonymously carried out, and only for the purposes of the project. All data were protected in accordance with the World Medical Association Declaration of Helsinki, and the European Union directive 2016/679 of the European Parliament and the European Council, of April 27, 2016, regarding the protection of persons and their personal data

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Competing interests

Authors declare no conflicts of interest.

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Author contributions

All authors have contributed substantially to the work as follows:

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