

BMJ Open Multimorbidity patterns of chronic conditions and geriatric syndromes in older patients from the MoPIM multicentre cohort study

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ABSTRACT

Objectives To estimate the frequency of chronic conditions and geriatric syndromes in older patients admitted to hospital because of an exacerbation of their chronic conditions, and to identify multimorbidity clusters in these patients.

Design Multicentre, prospective cohort study.

Setting Internal medicine or geriatric services of five general teaching hospitals in Spain.

Participants 740 patients aged 65 and older, hospitalised because of an exacerbation of their chronic conditions between September 2016 and December 2018.

Primary and secondary outcome measures Active chronic conditions and geriatric syndromes (including risk factors) of the patient, a score about clinical management of chronic conditions during admission, and destination at discharge were collected, among other variables. Multimorbidity patterns were identified using fuzzy c-means cluster analysis, taking into account the clinical management score. Prevalence, observed/expected ratio and exclusivity of each chronic condition and geriatric syndrome were calculated for each cluster, and the final solution was approved after clinical revision and discussion among the research team.

Results 740 patients were included (mean age 84.12 years, SD 7.01; 53.24% female). Almost all patients had two or more chronic conditions (98.65%; 95% CI 98.23% to 99.07%), the most frequent were hypertension (81.49%, 95% CI 78.53% to 84.12%) and heart failure (59.86%, 95% CI 56.29% to 63.34%). The most prevalent geriatric syndrome was polypharmacy (79.86%, 95% CI 76.82% to 82.60%). Four statistically and clinically significant multimorbidity clusters were identified: osteoarticular, psychogeriatric, cardiorespiratory and minor chronic disease. Patient-level variables such as sex, Barthel Index, number of chronic conditions or geriatric syndromes, chronic disease exacerbation 3 months prior to admission or destination at discharge differed between clusters.

Conclusions In older patients admitted to hospital because of the exacerbation of chronic health problems, it is possible to define multimorbidity clusters using soft clustering techniques. These clusters are clinically relevant and could be the basis to reorganise healthcare circuits or processes to tackle the increasing number of older, multimorbid patients.

Strengths and limitations of this study

- The multimorbidity analysis in this study has been developed considering a wide range of long-term conditions that may require healthcare in older people.
- To the best of our knowledge, this is the first published study of multimorbidity clusters in older patients to include chronic diseases weighted by a clinical management score and geriatric syndromes.
- Soft clustering is an innovative, methodologically robust technique that can lead to reliable results in the field of multimorbidity analysis.
- The list of chronic conditions and geriatric syndromes used in this study is comprehensive but not standardised, thus hindering comparability with other studies.

Trial registration number NCT02830425.

BACKGROUND

According to the most recent Eurostat baseline population projections, old-age dependency ratio (population 65 years and over divided by population 15–64 years) is about 32% in the European Union (EU) and it is expected to reach 52% in 2050, meaning that the EU's population will continue to grow older.¹ Together with the fact that chronic conditions (CC) are the main cause of disability and mortality in Europe, this implies that the coexistence of two or more chronic health conditions, which constitutes the classic definition of multimorbidity, is becoming increasingly common.²

Multimorbidity is therefore turning into an important challenge for the health system because of the expanding proportion of older people with multiple CC and treatments as well as the difficulties associated with their clinical management (CM).^{3 4} Most clinical

practice guidelines are focused on single diseases, with limited recommendations for multimorbid patients,⁵ and, in addition, randomised clinical trials often exclude older patients with multimorbidity.⁶ Despite the importance of multimorbidity in clinical practice, different criteria about which conditions should be considered and how to aggregate them are still under debate, which makes it difficult to compare different estimations around the world.^{7–9}

One of the novel, increasingly widespread definitions of multimorbidity considers the non-spurious association of certain CC by sharing pathophysiological mechanisms, giving rise to disease association patterns.¹⁰ In order to identify those patterns, different statistical methodologies have been explored. Among these techniques, soft clustering allows to focus on patients rather than diagnoses and is a useful method when there is a high overlap of diagnoses between patients, as it enables patients to belong to more than one multimorbidity pattern with a certain probability.¹¹

Besides CC, other clinically relevant situations such as geriatric syndromes (GS) may also be considered in the definition of these patterns, since they might have a great impact on the health-related quality of life and CM of old patients.¹² In fact, the purpose of multimorbidity characterisation (ie, predicting outcomes or use of health services, improving quality of care, organising healthcare services, etc), will have an influence on its definition. In order to have an accurate picture of the morbidity of each patient, a global consideration of all conditions that may require healthcare attention is necessary, even if they are not the reason for hospitalisation. Along these lines, some countries have explicitly recommended to acknowledge all long-term conditions for optimising care of adult patients by reducing, for example, possible inappropriate treatments, multiple healthcare appointments or poor health-related quality of life.^{13–15}

During the past decade, there has been an increasing amount of publications that consider multimorbidity,¹⁶ but few have focused on multimorbidity patterns in older patients and even fewer take into account GS.¹⁷ For this reason, we launched a multicentre study in 2016 with multiple aims related to multimorbidity, appropriateness of chronic treatments and adverse drug reactions in older patients.¹⁸ The objectives of the present analyses were to estimate the frequency of CC and GS in older patients admitted to hospital because of an exacerbation of their CC, and to identify possible multimorbidity patterns in these patients.

METHODS

Design and setting

A multicentre, prospective cohort study including older patients hospitalised at the internal medicine or geriatric services at five general teaching hospitals in three different regions of Spain between September 2016 and

December 2018 was designed. The detailed protocol was previously published.¹⁸

For the purposes of the study, older patients (≥ 65 years old) admitted as a result of the exacerbation of their chronic pathology were included. Patients referred to home hospitalisation, admitted because of an acute process not related to any chronic disease or with a fatal outcome expected at the time of admission were not included.

No written informed consent was deemed necessary for this study.

Data acquisition and variables

The following sociodemographic and clinical data was retrieved by the clinical team responsible for the patient: patient's code, date of birth, sex, functional status just before entering the hospital (Barthel Index),¹⁹ household (alone, with relatives or other people, in a nursing home), existence of any contact with healthcare services (primary care, emergencies, hospital admission, outpatient care, home care) in the 3 months prior to hospitalisation due to exacerbation of any chronic disease, and destination at discharge from the present episode of hospitalisation (home, transfer to another hospital, transfer to a nursing home, exitus).

Active CC of the patient at arrival to hospital, including some risk factors, were collected (see online supplemental table 1). For this purpose, the physicians of the project defined, on a consensual basis, a limited list of 64 CC, coming from the 114 groups defined by Salisbury *et al*.²⁰ and including the 19 categories of the Charlson Index.²¹ Following the same criteria as Salisbury *et al*, a condition was considered to be chronic when it lasted for at least 6 months, including past conditions that require ongoing disease or risk management, important conditions with a significant risk of recurrence, or past conditions that have continuing implications for patient management.²⁰ Drug-related conditions of this list refer to poor management of medication related to a chronic disease that has clinical implications in that hospitalisation (such as any drug intolerance or an excess drug poisoning).

Additionally, for each of the CC, it was also recorded if they had required CM (both at admission and during hospitalisation) by assigning a (subjective) correlative score (CM=1, 2, 3...) to each one, according to their clinical importance during the attention process. Thus, CC that did not have any significance during hospitalisation, although recorded, had a score equal to zero. This correlative score was later used to compute a ratio to reflect the weight of each CC in each patient in the index hospitalisation.

Specific GS and risk factors (acute confusional syndrome/delirium, chronic pain, cognitive/intellectual impairment, constipation, depression or anxiety, dysphagia, frailty, immobility, incontinence (urinary/faecal), instability/falls, malnutrition, polypharmacy, pressure ulcers, sensorial deficit, sleep disorders/insomnia) were also recorded. Two of the departments

systematically apply a recently developed scale for frailty,²² while the others consider clinical judgement (although based on the same variables).

In order to address potential sources of bias, a pilot study was conducted with the first 10 admissions per centre to validate the data collection process and identify problems that could arise. After that, proper changes were made in the protocol and questionnaire. All available information sources were consulted in order to register CC and GS, and the defined list was not closed. Nonetheless, the registration of CC and GS was based on clinical criteria.

Sampling and analysis

A consecutive sample of 740 patients meeting the inclusion criteria were included, proportionally distributed to the annual volume of hospitalisations of the medicine and/or geriatric services of each centre. The estimated sample of 800 patients (see protocol¹⁸) could not be reached due to organisational reasons in one of the participating centres.

For the purposes of the analyses, some CC were grouped according to clinical criteria: Hemiplegia was included in cerebrovascular disease; metastatic solid tumour, leukaemia, lymphoma and any malignancy were grouped into 'neoplasia'; hepatitis B and C were included in mild liver disease, and both congestive and non-congestive heart failure were grouped into 'heart failure'. Other diseases were finally excluded of the analyses considering that they have no impact on acute healthcare (cataract, dermatitis, diverticular disease of the colon, glaucoma, haemorrhoids, other vascular diseases and prostatic benign hypertrophy). In the end, 51 CC and 15 GS were analysed.

The updated Charlson Comorbidity Index,²³ age adjusted, was computed and categorised according to tertiles distribution.

Descriptive statistics were performed to assess patient clinical and sociodemographic characteristics and to obtain overall prevalence estimates of CC and GS, stratified by sex. Multimorbidity was first defined as the presence of two or more CC. Cumulative number of CC and GS per patient were computed, respectively.

Multimorbidity patterns

CC or GS with a prevalence <2% were excluded to avoid statistical noise and therefore spurious findings in the cluster solutions, leaving a list of 40 CC and 15 GS. In order to take into account if a CC had required CM, a ratio variable (R) was computed as follows:

If CC=0 & CM=0 → R=0

If CC=1 & CM=m → R=1/m; max (m)=max value (CM)=8;

If CC=1 & CM=0 → R=0.1

Multimorbidity patterns were identified using the fuzzy c-means cluster analysis algorithm, which belongs to the family of *soft* clustering algorithms. The algorithm estimates *c* cluster centres (similar to *k*-means) but with fuzziness so that individuals may belong to more than one

pattern. Through this technique, we obtained clusters of individuals and a membership matrix, which indicates the degree of participation of each subject in each cluster.

As a first step, and similarly to Violán *et al*,²⁴ the PCAmix algorithm for categorical and continuous data (GS and R variables, respectively) was implemented to reduce and transform the dataset to all continuous data.²⁵ To decide the number of retained dimensions, the Karlis-Saporta-Spinaki rule was used.²⁶ Then, a soft clustering algorithm was applied to fuzzily distribute the population into a set of clusters, corresponding to the different multimorbidity patterns. We computed three validation indices to obtain the optimal number of clusters (K) and the optimal value of the fuzziness parameter (m): the partition coefficient whose optimal choice for coefficient is at the maximum and the Xie-Beni and the partition entropy validation indices, whose optimal indices are at the minimum.²⁷ Considering the stochastic nature of the clusters, and the requirement of stable multimorbidity clusters, 100 independent clustering repetitions were applied to obtain the stable final solution.

To describe each identified cluster of individuals, the prevalence of CC and GS in each one was calculated. Observed/expected (O/E) ratios were calculated by dividing the prevalence of a given disease within a cluster by its prevalence in the overall population. The exclusivity of CC and GS, defined as the fraction of patients with the disease in the cluster over the total number of patients with the disease, was also calculated. A CC or a GS was considered to be relevant in a given cluster of individuals when its O/E ratio was >1 and its exclusivity was >25%.^{28–30} The statistical significant final solution ranged from 4 to 8 clusters. After clinical revision and discussion among the research team, four different clusters were considered to be consistent with the clinical observations as well as the objective of the clustering. There is currently no consensus in the literature on the criteria used to select the number of clusters or the O/E ratio cut-off point due to, in part, the novelty of the analysis.

Finally, sociodemographic and clinical variables were described for all patients assigned to each cluster. Analyses were performed using R V.3.6.0 and SPSS V.22.

Patient and public involvement

Since this was an observational study with variables and outcomes related to the healthcare process, this research was developed without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results.

RESULTS

A total of 740 patients aged 65 years or older were included, with a mean age of 84.12 years (SD 7.01), a 53.24% of females and a mean Barthel Index of 65.07 (median 75). Sociodemographic and clinical variables are summarised in table 1. Almost all patients had two

Table 1 Sociodemographic and clinical variables of the studied cohort

Sociodemographic and clinical variables		N	%	95% CI
Age	<70	33	4.46	3.19 to 6.20
	70–74	48	6.49	4.93 to 8.50
	75–79	82	11.08	9.02 to 13.55
	80–84	181	24.46	21.50 to 27.68
	85–89	232	31.35	28.11 to 34.78
	90–94	134	18.11	15.50 to 21.05
	≥95	30	4.05	2.85 to 5.73
Sex	Female	394	53.24	49.64 to 56.81
	Male	346	46.76	43.19 to 50.36
Barthel Index	<20	90	12.16	10.00 to 14.71
	20–35	76	10.27	8.28 to 12.67
	40–55	124	16.76	14.24 to 19.62
	60–95	294	39.73	36.27 to 43.30
	100	156	21.08	18.30 to 24.17
Age adjusted, updated Charlson Comorbidity Index	2–5	148	20.00	17.28 to 23.03
	6–8	411	55.54	51.94 to 59.08
	9–14	181	24.46	21.50 to 27.68
Household	With relatives/other people	523	70.68	67.30 to 73.84
	Nursing home	95	12.84	10.62 to 15.44
	Alone	122	16.49	13.99 to 19.33
Chronic disease exacerbation 3 months prior to admission	No	225	30.41	27.20 to 33.81
	Yes (total)	515	69.59	66.19 to 72.80
	Primary care	342	46.22	42.65 to 49.82
	Emergencies	263	35.54	32.17 to 39.06
	Hospital admission	193	26.08	23.05 to 29.36
	Outpatient care	8	1.08	0.55 to 2.12
	Home care	14	1.89	1.13 to 3.15
Conditions requiring clinical management	1	302	40.81	37.36 to 44.39
	2	216	29.19	26.03 to 32.57
	3	106	14.32	11.98 to 17.03
	4	72	9.73	7.80 to 12.08
	5	28	3.78	2.63 to 5.41
	6	13	1.76	1.03 to 2.98
	7	2	0.27	0.07 to 0.98
	8	1	0.14	0.007 to 0.76
Destination at discharge	Home	468	63.24	59.71 to 66.64
	Nursing home	105	14.19	11.86 to 16.89
	Another hospital	101	13.65	11.36 to 16.31
	Exitus	66	8.92	7.07 to 11.19
Multimorbidity	No	10	1.35	1.35 to 1.36
	Yes	730	98.65	98.23 to 99.07

or more CC (98.65%; 95% CI 98.23% to 99.07%), with a median of 8 CC and 6 GS per patient. Nearly 70% had consulted a healthcare service in the 3 months prior to hospitalisation due to chronic disease exacerbation.

Figure 1 shows the distribution of the number of CC by age groups. The most frequent CC were hypertension (81.49%, 95% CI 78.53% to 84.12%) and heart failure (59.86%, 95% CI 56.29% to 63.34%) (see online

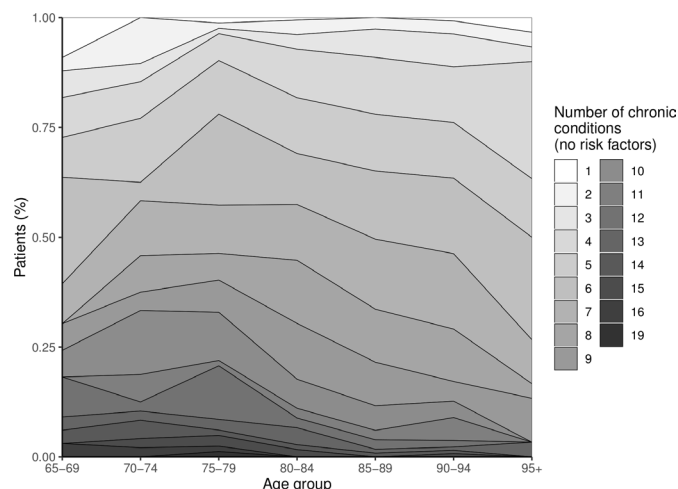


Figure 1 Distribution of the number of chronic conditions (excluding the following risk factors: hypertension, dyslipidaemia, obesity, osteoporosis and drug-related conditions) in relation to age groups.

supplemental table 2). Heart failure was also the main cause of hospitalisation (30.7% of patients had CM score=1), followed by chronic obstructive pulmonary disease (COPD) (20.7%) (online supplemental table 3).

There were some differences in CC between sexes, with females having more frequently heart failure, degenerative arthropathy, obesity, hip fracture, thyroid disease, asthma, osteoporosis, vertigo and non-schizophrenic mental disorders. Males, in turn, had more frequently COPD, gout, neoplasia, peripheral arteriopathy and ulcerative disease.

The most prevalent GS was polypharmacy (79.86%, 95% CI 76.82% to 82.60%), followed by frailty (61.76%, 95% CI 58.20% to 65.19%). Females had a significantly higher number of GS compared with males (Wilcoxon rank sum test, $p < 0.001$), as well as a higher prevalence of depression/anxiety, chronic pain, constipation, frailty, urinary/faecal incontinence and immobility.

Four statistically and clinically significant multimorbidity clusters or patterns were identified in our study population. For all clusters, CC and GS with an observed/expected ratio > 1 and exclusivity $> 25\%$ are represented in figure 2 (see also online supplemental table 4) for all CC and GS). Sociodemographic and clinical characteristics of patients in each cluster are described in table 2.

The first cluster, named osteoarticular, included 132 patients (17.8%) having osteoporosis, fractures, inflammatory osteoarticular disease, chronic pain and degenerative arthropathy. Moreover, vertigo, sleep apnoea, asthma, depression/anxiety and sleep disorders were also over-represented. This cluster included patients with the highest number of both CC and GS. About three-quarters were female, and most of them (82%) accessed healthcare services 3 months prior to this admission.

Cluster 2, called psychogeriatric, had 152 patients (20.7%) and included mostly GS: pressure ulcers, immobility, malnutrition, cognitive impairment, dementia,

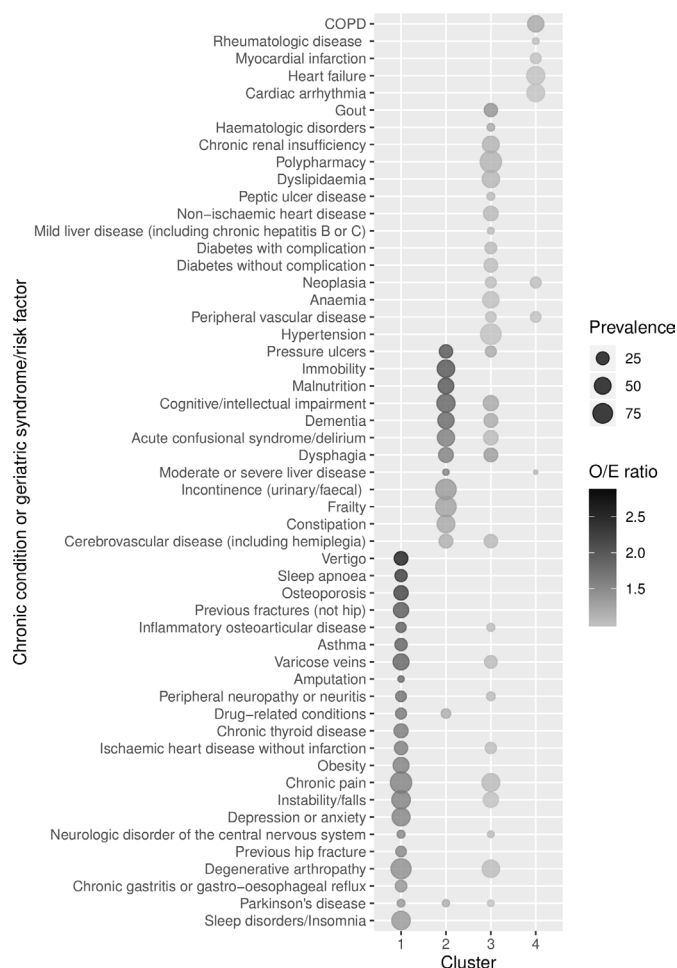


Figure 2 Observed/expected (O/E) ratio and prevalence of chronic conditions and geriatric syndromes/risk factors per multimorbidity cluster. Conditions with exclusivity $> 25\%$ and O/E ratios > 1 in each cluster are represented. Conditions are ordered by O/E ratio and from cluster 1 to 4. COPD, chronic obstructive pulmonary disease.

incontinence and frailty. Patients in this group had a mean Barthel index lower than 50 and a high number of GS. Furthermore, nearly 20% of them were living in a nursing home and in-hospital mortality was about 13%.

Cluster 3, named minor chronic disease, had 179 (24.2%) patients, and represents a group of patients with a variety of conditions, such as hypertension, dyslipidaemia, anaemia, gout, chronic renal insufficiency, polypharmacy, non-ischaemic heart disease, and diverse GS. O/E ratios were close to 1 in most cases.

Finally, cluster 4, called cardiorespiratory, included 276 (37.3%) patients. The over-represented diagnoses were COPD, heart failure and cardiac arrhythmia, although the O/E ratios were very low. In this cluster, with the lowest number of CC and GS, and a Barthel index greater than 75, nearly 40% had no healthcare consultation for a chronic disease exacerbation in the previous 3 months. This group had the lowest in-hospital mortality (5%).

Table 2 Sociodemographic and clinical variables of the multimorbidity clusters

	Osteoarticular	Psychogeriatric	Minor chronic disease	Cardiorespiratory
Number of patients included, n (%)	132 (17.8)	153 (20.7)	179 (24.2)	276 (37.3)
Age at admission (year, mean $\pm$ SD)	84.03 $\pm$ 6.48	84.51 $\pm$ 7.25	83.94 $\pm$ 7.19	84.06 $\pm$ 7.03
Sex, n (%)				
Male	34 (25.7)	66 (42.8)	99 (55.5)	147 (53.4)
Female	98 (74.3)	87 (57.2)	80 (44.5)	129 (46.6)
Barthel Index (mean $\pm$ SD)	63.06 $\pm$ 24.78	47.62 $\pm$ 34.94	64.96 $\pm$ 33.56	75.76 $\pm$ 27.52
Total no chronic conditions (mean $\pm$ SD)	11.5 $\pm$ 3.64	7.68 $\pm$ 3.19	8.86 $\pm$ 3.08	7.59 $\pm$ 2.61
Total no geriatric syndromes/risk factors (mean $\pm$ SD)	7.76 $\pm$ 2.07	8.16 $\pm$ 2.82	6.4 $\pm$ 3.32	4.42 $\pm$ 2
Charlson Comorbidity Index, n (%)				
2–5	26 (19.9)	24 (15.6)	37 (20.4)	61 (22.2)
6–8	73 (55.1)	89 (58.5)	96 (53.8)	153 (55.3)
9–14	33 (25.0)	40 (25.9)	46 (25.7)	62 (22.6)
Household, n (%)				
With relatives/other people	91 (68.7)	103 (67.2)	133 (74.5)	196 (71.1)
Nursing home	16 (11.8)	28 (18.4)	23 (12.8)	28 (10.3)
Alone	26 (19.5)	22 (14.3)	23 (12.7)	52 (18.7)
Chronic disease exacerbation 3 months prior to the index admission, n (%)				
No	24 (18.3)	46 (30.1)	48 (27.0)	106 (38.5)
Yes (total)	108 (81.7)	107 (69.9)	130 (73.0)	170 (61.5)
Primary care	83 (62.7)	66 (43.3)	92 (51.6)	101 (36.5)
Emergencies	71 (53.6)	40 (26.2)	69 (38.5)	83 (30.2)
Hospital admission	49 (37.1)	46 (30.1)	47 (26.1)	51 (18.6)
Outpatient care	1 (0.7)	0 (0.3)	3 (1.4)	4 (1.4)
Home care	2 (1.5)	2 (1.1)	3 (1.8)	7 (2.6)
Destination at discharge, n (%)				
Home	86 (65.3)	83 (54.0)	111 (62.0)	188 (68.1)
Nursing home	15 (11.1)	33 (21.3)	26 (14.5)	32 (11.5)
Another hospital	15 (11.3)	17 (11.3)	26 (14.7)	42 (15.3)
Exitus	16 (12.3)	20 (13.3)	16 (8.8)	14 (4.9)

DISCUSSION

This study aimed to identify multimorbidity patterns in patients aged 65 and above admitted to hospital because of an exacerbation of CC. The soft clustering technique used, together with clinical criteria, was able to identify four different multimorbidity patterns, named osteo-articular, psychogeriatric, cardiorespiratory and minor chronic disease, in a patient-centred approach taking into account the importance of each disease in hospital management. Remarkably, high chronic multimorbidity was found in all patients, regardless of the cluster. To the best of our knowledge, this is the only study published to date that has analysed multimorbidity patterns taking into account both CC (with their weight during CM) and GS in this type of patients. Hence, these identified patterns allow us to take a further step towards understanding the patients' current or future healthcare needs.

Two very important aspects of multimorbidity patterns analysis are the purpose for designing such patterns and the target population, which clearly condition the obtained results or conclusions. For instance, our aim in defining multimorbidity patterns in this cohort was to identify profiles of patients with similar clinical needs during the index hospitalisation and even a similar short-term prognosis at that time. For this reason, the importance of their pathologies in the course of hospitalisation was also taken into account. Hence, the ones that tend to have a minimal impact on CM, such as risk factors like hypertension or dyslipidaemia did not have a leading role in the patterns.

All clusters contain coherent groups of conditions that are mostly pathophysiologically related. From the clinical point of view, these clusters resemble patient profiles that are intuitively perceived. Moreover, some descriptive variables such as sex, Barthel Index, mean number of CC or GS, chronic pathology exacerbations in previous months, or hospital mortality, are distributed in such a way that they may reinforce the distinction of these groups.

Coexistence of CC and GS was observed in all clusters except for the cardiorespiratory, reinforcing the need to consider other clinically relevant situations rather than only CC. In particular, the exclusivity and prevalence of GS such as immobility, malnutrition, cognitive impairment or dementia were considerable in the psychogeriatric cluster.

Interestingly, highly prevalent CC, such as heart failure and COPD, which also frequently involve CM, only showed remarkable exclusivity and O/E ratio in the cardiorespiratory pattern and were not over-represented elsewhere. This highlights the fact that even though some CC may not be over-represented in a cluster, they can have a high prevalence and therefore need to be properly addressed too.

With respect to the osteoarticular cluster, it displayed a pattern of female predominance, with many CC and GS, high healthcare needs in recent months due to their

chronic pathology, and high in-hospital mortality. Thus, this profile would identify a group of patients with a high probability of decompensation and death.

Finally, the so-called minor chronic diseases cluster was not very well defined. It included some risk factors (hypertension, dyslipidaemia, polypharmacy) as well as some CC and GS. Thus, it would be possible that it does not represent a real cluster but either the set of cases that did not belong anywhere else.

Comparison with other studies

Given the type of patients under study and the methodological approach to identify multimorbidity patterns, there are few publications to directly compare our results to. Clerencia-Sierra *et al*¹⁷ analysed multimorbidity patterns in hospitalised older patients. Their methodological and analytical approach was slightly different, and they did not take into account the weight of the diseases during the hospitalisation process; however, they found a similar percentage of multimorbidity (99.7%) and four patterns that partially coincide with those of our study: cardiovascular, induced-dependency, falls and osteoarticular.

Furthermore, several authors have published data on patterns identified from primary care electronic records in different age groups, with lists of non-comparable chronic problems and using different techniques (cluster analysis, exploratory factor analysis or latent class analysis).^{17 29-34} These results would not be directly comparable with our study, but all of them highlight the ability to identify association patterns of chronic diseases.

Strengths and limitations

The strengths of this study are the prospective design, ensuring data quality by thorough record keeping, the ascertainment of all CC and GS of the patient, as well as the use of a novel clustering technique. Soft clustering is a methodologically robust technique less susceptible to outliers in the data, choice of distance measure and the inclusion of inappropriate or irrelevant variables.²⁴ Besides, our approach focuses beyond organ diseases by incorporating GS, and using a comprehensive list retrieved by the clinical team. Additionally, we have taken into account the relative importance of the different CC in the CM of the patient during hospitalisation, thus providing a better picture of the possible complexity and needs during hospitalisation.

Furthermore, our work is not only limited to the identification of possible patterns. We have validated them, in some way, by analysing some of the patients' variables such as sex, number of CC, previous contacts with the health system, hospital mortality or need for a nursing home.

Nonetheless, our study presents some limitations that need to be considered. First, the identification of chronic pathologies does not exclusively follow a validated list of codes but either an adaptation of different ones, a fact that could hinder comparability with other studies on

multimorbidity. Second, as this study is not longitudinal, the chronology in which CC or GS appear cannot be analysed. It is possible for a patient to evolve from one pattern to another throughout life, as some authors have already pointed out,³⁵ and therefore, the results only show the present situation. However, given the purpose of the defined patterns, this would not in itself be a limitation.

From a clinical point of view, the lack of usage of standard scales or diagnostic criteria for determining all CC or GS could question the validity of this information. However, the study gathered the data as it was routinely registered in the different departments. Frailty should derive from a comprehensive assessment of the patient in a standardised way that still lacks of systematic implementation in the healthcare routine.³⁶ Nevertheless, our multimorbidity study wanted to go a little further, also considering GS (frailty included), an unusual fact in the bibliography on clusters of multimorbidity in older patients in spite of its importance for decision making in the clinical practice.

The clinical conditions severity or other possible aggravating factors have neither been gathered. Nevertheless, the registration of a variable that takes into account the relevance of each CC during the care process acts, in some way, as a proxy of the importance of each disease in the index hospitalisation when dealing with patients admitted because of decompensation. Considering the purpose of defining the patterns in the whole study, and not knowing useful precedents in the consulted bibliography, the assignment made by the medical professional who attended the patient was an easy, simple measure, and shared by all professionals at the time of writing the clinical course.

Clinical implications

These patterns are not a picture of the community but of older patients in geriatric or internal medicine departments, which are generally in more need of health services and more complex CM. However, not all of these patients have the same requirements. In fact, one in five patients (the psychogeriatric cluster) caused a great burden to both the patient and their relatives while the patients in the most frequent cluster (cardiorespiratory), with lower dependency and less GS, seemed to have better immediate outcome. Therefore, it is possible that the therapeutic objectives should be different in these patients. More importantly, the ability to distinguish patients more objectively than with the mere clinical impression may allow the design of better processes, services or alternatives to conventional hospitalisation. Indeed, the identification of multimorbidity patterns in subsets of the population in order to detect underlying factors, understand their burden on patients and develop preventive strategies is considered a research priority. Finally, the development of clinical practice guidelines according to these patterns needs to be considered, although it may be difficult given the magnitude of the diseases comprised in each pattern.^{4 14} In addition, some patterns may include

patients with an increased risk of potentially inappropriate prescription or adverse drug reactions. These aspects will be the object of future analyses.

CONCLUSIONS

In conclusion, in older patients admitted to hospital because of the exacerbation of chronic health problems, it is possible to define multimorbidity clusters or patterns using appropriate statistical techniques. These patterns seem clinically coherent and could be the basis to reorganise circuits, processes or healthcare models to tackle the increasing number of older, multimorbid patients.

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Contributors MB conceived and supervised the study, discussed the results, wrote the first version of the manuscript and is responsible for the overall content as guarantor. SH, RJ, MA, RE and GJN participated in patient inclusion, data collection and discussion of the results and revised the manuscript. AR-L executed the analysis and interpretation of multimorbidity clusters. CV collaborated in the execution of the analyses and in the interpretation of the multimorbidity patterns. ML participated in the statistical and graphical analysis of the results, in the discussion of the results and the revision of several manuscript versions. PR-P collaborated in the questionnaires' design, patient inclusion, data collection and discussion of results and revised the manuscript. All authors read and approved the final manuscript.

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