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Geriatric Index of Comorbidity: validation and comparison with other measures of comorbidity

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Abstract

Background: the debate about measures of chronic comorbidity in the elderly is mainly due to the lack of consensus on pathogenetic models.
Objective: the aim of the present study was to compare the concurrent validity of a number of measures of chronic comorbidity assuming different pathogenic models, *versus* disability in elderly patients.
Setting: the Geriatric Evaluation and Rehabilitation Unit for subacute and disabled patients.
Participants: 493 new and consecutive elderly patients (mean age 79 years, 71% females) admitted to the Geriatric Evaluation and Rehabilitation Unit.
Measurements: we evaluated age, gender, cognitive status, depressive symptoms, functional status, somatic health, and nutritional status on admission. Functional status was assessed by the self- or proxy reported Katz's BADL scale and by the performance-based Reuben's Physical Performance Test. Somatic health was assessed as presence and severity of diseases according to standardized criteria. Comorbidity was measured as number of diseases, sum of disease severity, and with a composite score (Geriatric Index of Comorbidity) which takes into account both number of diseases and occurrence of very severe diseases. Mortality was assessed after 12 months.
Results: specific diseases and their severity were found to be associated with disability measures. All measures of comorbidity were significantly correlated with disability, but only the Geriatric Index of Comorbidity was independently associated after adjustment for severity of individual diseases. In addition, increasing severity of comorbidity as defined by Geriatric Index of Comorbidity was associated with greater disability while this was not true for the other comorbidity measures (F statistics for the regression model including the Geriatric Index of Comorbidity=19.9). The Geriatric Index of Comorbidity, but not the other comorbidity measures, predicted mortality (relative risk of death 2.3, 95% confidence interval 1.7–3.1).
Conclusion: the Geriatric Index of Comorbidity, a measure of comorbidity assuming that both number of diseases and occurrence of very severe diseases are determinants of health, has the greatest concurrent validity with disability and is the best predictor of mortality.

Keywords: *comorbidity, functional status, Activity of Daily Living, performance test*

Introduction

The role of chronic somatic conditions in determining disability is intuitively important but the causal pathway leading to disability is still unclear.

It is widely recognized that comorbidity, the co-presence of multiple pathological conditions in the same patient, has a negative effect on health status as well on physical and cognitive function that goes beyond the bare sum of the effect of the single diseases.

To establish the risk of disability, to estimate prognosis, and to establish therapeutic alternatives in older patients affected by a specific disease, information on comorbidity is essential. Ideally, only a full understanding of how different diseases with different severity affect the same or different anatomical/functional entities, how they share risk factors and consequences, and how they affect response to or side effects of treatments may provide a clue on how comorbidity should be taken into account. This knowledge is an essential research goal, but, given the number of possible combinations of multiple diseases which may affect the same older patient, it is unlikely to be available soon. Meanwhile, even a simpler synthetic estimate of comorbidity may be very useful both in clinical practice and in medical research.

The two main practical problems relate to the effect of the presence or the severity of a given disease on disability, and how they interact to give disability [1]. These issues are of paramount relevance in the elderly patient, who is often disabled due to the effect of a number of diseases, with wide variability in their severity.

It is well recognized that greater severity of a given disease (for example osteoarthritis, stroke, heart failure, etc) causes greater disability [2–7]. Recently, particular attention has been devoted to the issue of measuring disease severity, leading to the development of some new and useful instruments [8–15]. One such instrument is the physiological dimension of Greenfield's Individual Disease Severity (IDS) index [10], which has the appealing property of not including disability as an indicator of disease severity, but has never been tested in the elderly.

Different approaches have been used to sort out the second problem, i.e. the interaction of diseases to give disability, which is more complicated. The most basic measure of comorbidity is a sum of conditions present. Another approach incorporates disease severity measures into comorbidity indices and defines severity of comorbidity as the sum of all disease severities [14] or on the basis of severity of the most severe comorbid diseases [10]. It is unclear which approach is superior in describing comorbidity in the elderly.

The aims of this study were: i) to assess the validity of Greenfield's IDS as a measure of severity of individual diseases as a correlation of disability and predictor of mortality in the elderly comorbid patient, and ii) to compare three different approaches to measure comorbidity, i.e. the sum of chronic diseases, the sum of all disease severities, and a new index of comorbidity derived from Greenfield's scoring system (Geriatric Index of Comorbidity, GIC) which take into account both numbers and severity of diseases.

Methods

We obtained data for this study from the evaluation of 576 elderly patients consecutively admitted for the first time to the Geriatric Evaluation and Rehabilitation Unit (GERU) (P. Richiedei Hospital, Gussago, Brescia, Northern Italy) over a period of 14 months.

Patients coming from the community were referred by their general practitioner and patients coming from acute hospital wards by the ward physicians. Patients were admitted to the GERU after a preliminary staff physician's assessment performed in the outpatient service. Admittance was warranted if diagnostic, therapeutic, and rehabilitative interventions were judged to be of potential benefit to the patient. Patients in immediate and obvious need of nursing home placement were excluded [16]. A multidimensional evaluation with a standard protocol, performed in the first three days after admission, assessed demographics, cognitive, affective, and functional status, somatic health, and nutritional status. Discharge followed when the maximum achievable functional level as judged by the medical staff was reached.

Patients with single diseases that directly and severely affected disability were excluded, e.g. patients with recent stroke without comorbidity ($n=21$), recent hip fracture ($n=35$), and metastatic or highly malignant cancer ($n=29$). Two patients were affected by a combination of two of the three conditions. Included in this study were 493 patients.

The Mini Mental State Examination (MMSE) [17] evaluated cognitive status. Depressive symptoms were assessed with the Geriatric Depression Scale (GDS) [18].

Basic Activities of Daily Living (BADL) [19] scale, and the seven-item version of the Physical Performance Test (PPT) [20] were used to assess functional disability. PPT included multiple domains of physical function by means of observed performance on timed tasks that simulate activities of daily living with different degrees of difficulty (writing a sentence, eating, lifting a book from a table to the interviewer's shoulder level, wearing and taking off a jacket, picking up a coin from the floor, turning around 360 degrees, walking 15 metres). Total scores ranged from 0 (worst) to 28 (best).

Somatic health was evaluated as single diseases and their combination.

Single diseases

Presence/absence of individual diagnoses of chronic conditions

These were taken from the 15 conditions that were identified by Greenfield *et al.* [10] as the most frequent in hospitalized elderly patients and were: heart diseases of ischaemic or organic pathogenesis, primary arrhythmias, other heart diseases (cardiomyopathies, myocarditides, and cor pulmonale due to chronic pulmonary embolism, primary pulmonary hypertension or chronic obstructive lung disease), hypertension, stroke, peripheral vascular

diseases, diabetes mellitus, anemia, gastro-intestinal diseases, hepatobiliary diseases, renal diseases, respiratory diseases, parkinsonism and non-vascular neurologic disases, musculoskeletal disorders, malignancies. For each category, a list of diseases is provided pertaining to the category. For example, hepatobiliary diseases are: toxic/drug induced hepatitis, viral hepatitis, cirrhosis, cholelithiasis, cholecystitis, and cholangitis.

Severity of the 15 conditions, as evaluated by the physiological dimension of Greenfield's IDS

This requires a trained physician—not necessarily a geriatrician—who has full access to the clinical data (history, physical examination, laboratory data, and current drug therapy) of a given patient and can be done on charts and medical records. Theoretically, it can easily be taken both in outpatients and in nursing home patients, although validity data in these settings are to our knowledge not available.

The IDS grades each condition on a 0–4 scale on the basis of the following general framework: 0=absence of disease, 1=asymptomatic disease, 2=symptomatic disease requiring medication but under satisfactory control, 3=symptomatic disease uncontrolled by therapy, and 4=life-threatening disease or greatest severity of the disease. A detailed description of what operationally defines severity for each condition is provided by the original developers of the instrument. For example, for "hepatobiliary diseases", 0 is absence of disease; 1 is hisory ($\geqslant$1 year ago) of hepatitis B; asymptomatic cholelithiasis or previous surgery for cholelithiasis; 2 is biliary obstruction, common duct obstruction; recent ($<$1 year) history of hepatitis B or C; uncomplicated toxic/drug induced hepatitis; symptomatic cholelithiasis, mild cirrhosis (Child A); 3 is chronic persistent or active hepatitis, Child B cirrhosis; 4 is Child C cirrhosis [21]. For "other heart diseases", 0, 1, 2, 3, and 4 correspond to NYHA severity classes.

The IDS was taken by one of the authors (RR) on the third day after admission by examining medical charts. Inter-rater and test-retest reliability have been addressed on 50 consecutive patients by two independent raters (RR and PB) for each of the 15 conditions. Intraclass correlation coefficients, ranged from 0.83–1.00 and from 0.96–1.00, respectively.

Comorbidity

Number of diseases

Defined as the total number of chronic conditions irrespective of severity. The theoretical range (0–15) was stratified into four levels: 0–2, 3 and 4, 5 and 6, and 7 or more. This stratification will be used throughout the analysis.

Disease burden

Defined as the sum of the severities of the 15 conditions. The theoretical range (0–60) was stratified into four levels: 0–4, 5–8, 9–11, and 12 or more. This stratification will be used throughout the analysis.

Geriatric Index of Comorbidity (GIC)

This classified patients into 4 classes of increasing somatic comorbidity. The GIC was defined based on information coming from two domains: i) number of diseases, and ii) severity of diseases as measured by Greenfield's IDS. Class I includes patients with one or more conditions with IDS=1 or lower. Class II includes patients with one or more conditions with IDS=2. Class III includes patients with one condition with IDS=3, other conditions having IDS=2 or lower. Class IV includes patients with two or more conditions with IDS=3 or one or more conditions with IDS=4. Inter-rater and test-retest reliability were re-assessed for the GIC on the same patients used to assess the reliability of the severity of the 15 conditions. Concordance between raters was present in 89% and within the same rater in 97% of cases.

The total number of prescribed drugs was also recorded.

Nutritional status was evaluated by the Prognostic Nutritional Index (PNI) [22] with the original formula: 150−16.6×serum albumin (g/dl)−0.78×triceps skin fold thickness (mm)−0.2×serum transferrin (mg/dl) −5.8×delayed hypersensitivity on PPD tine test (non-reactive=0, induration smaller than 5 mm=1, induration of 5 mm or larger=2).

Mortality was considered in-hospital and after discharge. The latter was assessed 12 months after admission, by telephone interview with patients or family members. The state of all patients was known.

We performed statistical analysis with SPSS statistical package release 5.0 [23]. We assessed crude associations of functional variables (BADL lost functions and PPT score) with independent variables of interest (diseases and measures of comorbidity) with Spearman's rank correlation [24]. The significance of the better association of the GIC with functional variables was assessed by comparing the fit of linear regression models through analysis of deviance [25]. We assessed adjusted associations with multiple linear regression models. The predictive value of diseases and measures of comorbidity was assessed against mortality, where Kaplan–Meyer curves [26] were used as exploratory tools and Cox regression analysis [26] to correct for potential confounders.

Results

Table 1 shows the clinical and functional characteristics of the population.

Patients were all white, mainly women, very old, with average mild cognitive impairment and mild depressive symptoms. Disability was moderate to severe, as shown by BADL lost functions and PPT (PPT score in the community-dwelling elderly of the same age being around 18 points) [20, 27]. Patients had a high level of somatic comorbidity, having about 5 diseases and taking about 5 different drugs. One fifth of patients had low or high comorbidity (GIC Classes I and IV), while the majority had intermediate (GIC Classes II and III). The poor somatic health status was confirmed by PNI score indicating a significant level of malnutrition.

Table 2 shows disability across levels of increasing severity of somatic health problems/conditions as assessed by number of diseases, disease burden, and GIC. Data show that overall functional abilities worsen with increasing degree of comorbidity. Furthermore, comorbidity measured with GIC was more strongly associated with disability as assessed by both BADL and PPT. Evidence for this is that mean values of BADL and PPT disability showed greater differences between the poorest and best comorbidity levels when these were measured by GIC rather than by disease burden or number of diseases.

The following steps of the analysis aimed to evaluate whether the association of comorbidity with BADL and PPT held also after controlling for those diseases that can *per se* cause disability. In other words, we tried to answer the following question: given that it can be expected that single conditions (for example, stroke, parkinsonism, etc.) and their severity are correlates of disability, are comorbidity measures independently associated with disability? In this analysis, diseases were evaluated both as presence/absence and severity. Five regression models (models 1–5) were built with BADL as dependent variable and five identical models with PPT disability as dependent and the different disease measures as independent variables and age, gender, cognition, and depression as covariates. The results of models 3–5 are reported in Table 3. In models 1 (data not shown), presence/absence of "other heart diseases", stroke, parkinsonism, and anaemia was independently associated with greater BADL and PPT disability. In models 2 (data not shown) disease severity proved a better correlate of disability than presence/absence of

Table 1. Characteristics of 493 elderly patients consecutively admitted to a Geriatric Evaluation and Rehabilitation Unit

	n	%	Mean	(SD)	Range
Women	349	70.8			
Age (years)			78.9	(7.4)	60–97
Education (years)			5.2	(2.6)	0–19
Mini Mental State Examination			21.8	(6.3)	0–30
Geriatric Depression Scale			13.2	(6.4)	1–29
Drugs (*n*)			4.7	(1.9)	0–11
Prognostic Nutritional Index			35.6	(16.5)	4–89
Basic Activities of Daily Living (Lost functions)			2.6	(1.9)	0–6
0	75	15.2			
1	128	26.0			
2	63	12.8			
>2	227	46.0			
Physical Performance Test			11.8	(6.6)	0–27
>21	30	6.1			
15–21	150	30.4			
8–14	175	35.5			
0–7	138	28.0			
Number of diseases			5.0	(1.7)	0–10
0–2	28	5.7			
3–4	156	31.6			
5–6	214	43.4			
7 or more	95	19.3			
Disease burden[a]			8.5	(3.1)	0–19
0–4	37	7.5			
5–8	216	43.8			
9–11	169	34.3			
12 or more	71	14.4			
Geriatric Index of Comorbidity[b]					
Class I	16	3.2			
Class II	195	39.6			
Class III	206	41.8			
Class IV	76	15.4			

[a]Sum of the severities (0–4) on IDS of 15 chronic diseases.
[b]Class I: one or more conditions with IDS = 1 or lower; Class II: one or more conditions with IDS = 2; Class III: one condition with IDS = 3, other conditions having IDS = 2 or lower; Class IV: two or more conditions with IDS = 3 or one or more conditions with IDS = 4.

Table 2. Value of functional status variables (BADL lost functions and PPT score) across the four levels of comorbidity detected by number of diseases, disease burden, and classes of the Geriatric Index of Comorbidity in 493 elderly hospitalized patients

	BADL lost functions		PPT score	
	Mean	(SD)	Mean	(SD)
Number of diseases				
0–2	1.7	(1.8)	15.7	(5.9)
3–4	2.5	(2.1)	12.2	(6.7)
5–6	2.7	(2.0)	11.5	(6.8)
7–9	3.0	(1.9)	10.6	(5.7)
	R = 0.12, $p = 0.007$		R = −0.15, $p = 0.001$	
Disease burden				
0–4	1.4	(1.4)	16.3	(5.5)
5–8	2.4	(2.0)	12.6	(6.6)
9–11	2.9	(1.9)	10.8	(6.4)
12–19	3.4	(1.9)	9.2	(5.7)
	R = 0.23, $P < 0.0005$		R = −0.26, $P < 0.0005$	
GIC classes				
Class I	1.1	(1.1)	18.2	(4.4)
Class II	2.1	(1.8)	13.6	(5.9)
Class III	2.9	(2.1)	10.7	(6.5)
Class IV	3.6	(1.9)	8.8	(6.7)
	R = 0.30, $P < 0.0005$		R = −0.32, $P < 0.0005$	

R denotes Sperman rank correlation.

Table 3. Association of severity of single diseases and comorbidity measures with disability in 493 GERU elderly patients

	Model 3			Model 4			Model 5		
	B	(95% CI)	*p*	B	(95% CI)	*p*	B	(95% CI)	*p*
BADL lost function									
Severity of diseases									
Heart dis. (non isch/org)	–	–	–	–	–	–	–	–	–
Peripheral vascular dis.	0.25	(0.06 to 0.41)	0.008	0.16	(−0.01 to 0.34)	0.069	0.15	(−0.01 to 0.31)	0.074
Renal diseases	0.27	(0.07 to 0.47)	0.009	0.19	(−0.01 to 0.39)	0.058	0.16	(−0.30 to 0.35)	0.099
Parkinsonism	0.27	(0.05 to 0.50)	0.016	0.24	(0.02 to 0.47)	0.032	0.24	(−0.02 to 0.45)	0.035
Musculoskeletal diseases	–	–	–	–	–	–	–	–	–
Anemia	0.36	(0.12 to 0.59)	0.002	0.29	(0.05 to 0.53)	0.018	0.26	(0.03 to 0.49)	0.025
Stroke	0.52	(0.36 to 0.68)	<0.001	0.47	(0.31 to 0.63)	<0.001	0.45	(0.29 to 0.60)	<0.001
Comorbidity									
Number of diseases	–	(−0.37 to 0.07)	0.192	–	–	–	–	–	–
Disease burden	–	–	–	0.11	(−0.11 to 0.33)	0.336	–	–	–
GIC classes	–	–	–	–	–	–	0.39	(0.18 to 0.61)	<0.001
Model R^2		0.30			0.30			0.32	
F statistics		$7.4_{(1,491)}$; $p=0.007$			$24.5_{(1,490)}$; $P<0.00005$			$19.4_{(1,489)}$; $p=0.00005$	
PPT score									
Severity of diseases									
Heart dis. (non isch/org)	–	(−2.30 to −0.19)	0.02	−1.14	(−2.21 to −0.07)	0.038	−1.07	(−2.10 to −0.03)	0.044
Peripheral vascular dis.	−0.92	(−1.46 to −0.37)	0.001	−0.74	(−1.29 to −0.18)	0.009	−0.65	(−1.17 to −0.14)	0.013
Renal diseases	−0.80	(−1.43 to −0.18)	0.011	−0.59	(−1.22 to 0.02)	0.059	−0.45	(−1.03 to 0.14)	0.135
Parkinsonism	−1.24	(−1.93 to −0.54)	<0.001	−1.14	(−1.83 to −0.44)	0.001	−1.09	(−1.77 to −0.42)	0.002
Musculoskeletal diseases	–	(−1.55 to −0.58)	<0.001	–	(−1.43 to −0.45)	<0.001	−0.89	(−1.36 to −0.42)	<0.001
Anemia	–	(−1.76 to −0.2)	0.006	−0.84	(−1.58 to −0.09)	0.027	−0.70	(−1.41 to −0.02)	0.049
Stroke	−1.18	(−2.33 to −0.31)	<0.001	−1.67	(−2.18 to −1.53)	<0.001	−1.56	(−2.04 to −0.27)	<0.001
Comorbidity									
Number of diseases	0.47	(−0.23 to 1.17)	0.193	–	–	–	–	–	–
Disease burden	–	–	–	–	(−0.96 to 0.51)	0.546	–	–	–
GIC classes	–	–	–	–	–	–	−1.32	(−1.98 to −0.67)	<0.001
Model R^2		0.37			0.37			0.39	
F statistics		$11.1_{(1,491)}$; $p=0.0009$			$26.1_{(1,490)}$; $P<0.00005$			$19.9_{(1,489)}$; $p=0.00005$	

Values were computed in multiple linear regression models adjusted for age, gender, cognition, and depression. All models include severity of diseases. Model 3 includes also Number of diseases, model 4 Disease burden, and model 5 GIC classes.

Number of diseases, Disease burden, and GIC classes are entered as four-level continuous variables.

F statistics denotes the improving of the fit of each model compared to the previous one. For example, the F statistics of $19.4_{(1,489)}$ and $P<0.00005$ implies that model 5 has significantly greater fit than model 4, and that of $24.5_{(1,490)}$; $P<0.00005$ implies that model 4 has significantly greater fit than model 3.

diseases since when both presence/absence and severities of diseases were tested in a stepwise fashion, only the latter entered the models. Moreover, in addition to those of model 1, additional diseases (peripheral vascular, renal, and musculoskeletal), were independently correlated with disability. Models 3, 4 and 5 (Table 3) tested the measures of comorbidity (number of diseases, disease burden, and GIC classes, respectively) as correlates of disability. GIC, but not number of diseases or disease burden, was independently associated with both BADL and PPT disability. Age, MMSE, and GDS were also significantly associated with BADL and PPT disability in all models. It should be noted that in Table 3, despite the expected multicollinearity between severity of diseases and GIC, most diseases remained statistically associated with disability even when the GIC was entered in the model. The inclusion of number of diseases and burden of disease did not increase fit of the model, while the inclusion of GIC did. Moreover, a direct comparison between models 4 and 5 showed that the latter had a better fit for both BADL ($F_{(1,483)}=13.8$; $p=0.0002$) and PPT disability ($F_{(1,481)}=16.6$; $p=0.0001$).

Table 4 shows the proportion of concordance among measures of comorbidity. The classification of comorbidity by GIC was in agreement with that of number of diseases in about 35% (upper table, white cells on the diagonal; Spearman correlation coefficient 0.17, $P<0.0005$) and with that of disease burden in about 51% of patients (lower table, white cells; correlation 0.56, $P<0.0005$). The association in a relevant proportion of patients, GIC and the other measures were not in agreement. In particular, those patients below the diagonal (light grey cells) are classified by GIC as having lower comorbidity, and those above the diagonal (dark grey cells) as having greater comorbidity. When patients were classified by GIC and number of diseases (upper table), the severity of disability increased with increasing comorbidity as defined by GIC (groups A through C; ANOVA for BADL lost functions $p=0.01$ and for PPT

Table 4. Classification of number of diseases and disease burden across Geriatric Index of Comorbidity classes

	Geriatric Index of Comorbidity			
	Class I *n* (%)	Class II *n* (%)	Class III *n* (%)	Class IV *n* (%)
Number of diseases				
0–2	6 (1.2)	11 (2.2)	10 (2.0)	1 (0.2)
3–4	6 (1.2)	59 (12.0)	74 (15.0)	17 (3.4)
5–6	3 (0.6)	94 (19.1)	84 (17.0)	33 (6.7)
7–9	1 (0.2)	31 (6.3)	38 (7.7)	25 (5.1)
Disease burden				
0–4	12 (2.4)	22 (4.5)	3 (0.6)	0
5–8	4 (0.8)	114 (23.1)	93 (18.9)	5 (1.0)
9–11	0	52 (10.5)	85 (17.2)	32 (6.5)
12–19	0	7 (1.4)	35 (5.1)	39 (7.9)

Cells of different color define different groups of patients: Group A □; Group B □; Group C ▒.
Group B includes patients for whom GIC classification of comorbidity agrees with that of the other measures. Group C includes patients classified by GIC as more severe and by the other measures as less severe than patients in Group B. The opposite applies to patients in Group A.
Spearman rank correlation is 0.14 ($P=0.002$) between the GIC and number of diseases and 0.53 ($P<0.0005$) and between the GIC and disease burden.

score $p=0.007$). When patients were classified by GIC and disease burden (lower table), the trend was less obvious. Point estimates of BADL and PPT disability were in the same direction as before, but failed to reach significance.

Twelve months after admission, 117of the 493 patients had died. Figure 1 shows crude mortality according to GIC classes. A Cox regression model was built including age, gender, cognition, depression, and the disease severities listed in Table 3 as fixed covariates. Measures of comorbidity were tested for independent association in a stepwise fashion. Of the three measures of comorbidity, only GIC proved significant (relative risk 2.3, 95% confidence interval 1.7–3.1), while the others failed to reach the criterion for entering the model (RR of number of diseases: 0.8, 95% CI 0.8–1.1; RR of disease burden: 1.0, 95% CI 0.9–1.2). For the GIC, the risk of death at 6 months was basically similar (RR 2.2, 95% CI 1.7–2.9). The inclusion of BADL and PPT disability in the Cox model changed only marginally the relative risk estimates both for 6- and 12-month mortality (RR 2.1, 95% CI 1.6–2.7 and RR 2.1, 95% CI 1.6–2.9, respectively).

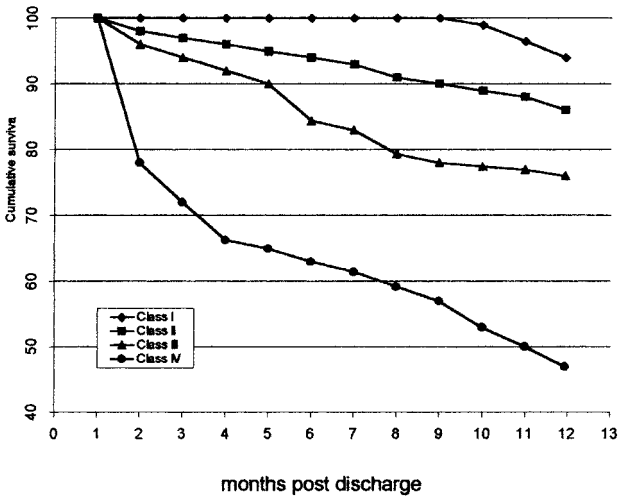

Figure 1. Survival in Geriatric Index of Comorbidity (GIC) classes in older patients consecutively admitted to a GERU. • $P<0.0001$ for different survival GIC classes on log-rank test

	Class I *n* (%)	Class II *n* (%)	Class III *n* (%)	Class IV *n* (%)
Patients	16	195	206	76
Deaths	1 (6)	27 (14)	49 (24)	40 (53)

Discussion

The definition and clinical relevance of somatic comorbidity in elderly patients is debated. Our data show that comorbidity is independently associated with disability in elderly patients of a rehabilitative geriatric hospital ward. The association held when comorbidity was evaluated by the GIC measure taking into account both number and severity of diseases. Of all measures of comorbidity, the GIC was the best predictor of mortality.

Disability caused by some diseases and injuries (for example major stroke without comorbidity and hip fracture) is disease-specific. Although the causal

pathway leading from these diseases to disability is still relatively unclear [28–32], it is easier to conceptualize. For example, disability following stroke might be related to location and size of the cerebral lesion. On the contrary, the typical geriatric patient is that in whom the causal relation between single diseases and disability is much less obvious [2, 28]. Evidence suggests that the causal relationship between single conditions and disability is not sufficient adequately to explain the latter in a given patient. For example, osteoarthritis alone is sufficient to cause a certain amount of disability, as well as heart disease alone can cause another load of disability. The co-occurrence of osteoarthritis and heart disease gives a load of disability that is not necessarily the mere sum of the single disabilities. The operational definition and clinical relevance of comorbidity are much debated. Guralnik [1] concluded that a variety of assessment techniques have been used for measurement of comorbidity and have demonstrated the association of an increased level of comorbidity with a variety of adverse health outcomes. In this study we have compared measures of comorbidity represented by the sum of conditions present and the sum of disease severities with a measure (GIC) incorporating both number and severity of diseases and found that the latter is more appropriate to elderly patients of a rehabilitative geriatric hospital ward. While these findings provide only a partial understanding of the causal intricacies linking co-occurring diseases with disability, they certainly add meaningful practical information. The association of GIC comorbidity with disability was present when the latter was measured with both self-reported and performance-based scales.

The strength of the association of GIC comorbidity with disability scales was greater for the performance-based (PPT) than for the self reported (BADL) scale. The strength of the association with PPT may be partially explained by the comparative complexity of PPT, which requires integration of musculoskeletal and cognitive functions [33]. On the other hand, this is an objective and timed test of performance that might reduce the confounding effect of psychosocial and environmental variables. For this reason, it might be more influenced by somatic health. The lower association of self-reported BADL with GIC is probably due to environmental factors or to disease-independent individual abilities that can compensate or adjust for functional limitations.

It has been suggested that information on the severity of acute and chronic diseases is needed to understand the relationship between diseases and disability [34–37]. This hypothesis is intuitive, has face validity and is in agreement with the experience of any clinician. Indeed, studies on specific diseases (e.g. arthritis, heart diseases and others) have directly demonstrated the existence of a relationship between markers of severity of disease and disability in activities of daily living.

In this study, few chronic conditions were individually associated with disability. This might be due to the fact that some conditions need to have a relatively high degree of severity in order to cause disability. Therefore, collapsing lower and higher degrees of severity into a single class (as in the analysis considering presence/absence of conditions) dilutes the effect of severity. This is supported by the observation that more diseases were significantly associated with disability when all levels of severity were taken into account. The independent association of GIC with disability that we found after controlling for severity of single conditions, indicates that GIC can capture a significant part of the excess disability due to the co-occurrence of diseases. It should be underlined that these results leave open the question of the pathogenic links between diseases and disability. However, the data suggest that the understanding of comorbidity should take into account both number of diseases and occurrence of very severe diseases.

Some points of this study deserve discussion. First, concerning the criteria used to define the severity of the condition: while we recognize that symptoms and the intensity of treatment may be related to disability, we also believe that symptoms and intensity of treatment are conceptually very different from the disability itself. This difference is clearly stated in the definitions provided by the WHO international classification for Diseases, Disabilities and Handicaps [38], and even more clearly by the modification of this theoretical model recently proposed by the Institute of Medicine [39]. First of all, symptoms can be usually linked to a specific condition while sorting out in an older patient the specific cause of disability may be very difficult. Second, the relationship between symptoms and disability is not linear. For example, under a certain threshold pain is not disabling. Third, a number of other personal (e.g. depression) and environmental factors (e.g. social network) modulate the relationship between symptoms and their functional consequences. Fourth, many studies have demonstrated a correlation between the severity of symptoms and the extension of anatomical damage. For example, the extension of the necrotic area after a myocardial infarction predicts the magnitude of the reduction in the cardiac output and, in turn, the severity of dyspnea and the need for a more intensive treatment in heart failure. Thus symptoms may be used to grade the severity of a disease in creating a comorbidity index.

The comorbidity that can accompany severe conditions could not be captured by GIC; in fact the hierarchical construction of the GIC does not allow one to discriminate degrees of comorbidity of conditions whose severity is below that of the most severe conditions. For example, a patient with IDS=3 heart disease is classified as GIC class III as well as a patient with IDS=3 heart disease plus IDS=2 arthritis, IDS=2 stroke, etc. In theory, the relevance of the conditions of lower severity might be addressed by developing scales

with higher resolution. However, elderly patients of the first kind, at least in a hospital setting, are exceptions rather than the rule.

The GIC had much better concurrent validity with disability when compared to disease number, but this did not hold for the comparison with disease burden. However, we have shown (Table 3) that the GIC but not number of diseases and disease burden were associated with disability.

In comorbidity studies, one of the central issues is the definition of how many conditions are to be considered [1, 5]. Solutions such as open lists should be avoided for their poor consistency across researchers and settings. In this study we have addressed comorbidity on the basis of a closed standard list of the somatic chronic conditions that most frequently affect elderly patients; this makes our results comparable with others' clinical assessments. It should however be noted that its feasibility in other clinical settings still needs to be assessed with field testing with larger patient groups.

The spectrum of disability has been extensively explored in recent years with the development of a number of sensitive and useful assessment tools. However, since disability is more the consequence than the cause of poor health, greater efforts should be devoted to probe its determinants and risk factors, among which somatic comorbidity has a key role. Furthermore, the effect of chronic comorbidity on the progression of disability or sensitivity to interventions will need to be addressed. Indeed, we have previously found that a measure of physical comorbidity related to the one of the present study was a powerful predictor of failure to recover mobility following rehabilitation in disabled patients [31]. Future work will need to address the clinical utility of comorbidity indices by evaluating their prognostic capacity to predict improvement following intervention. This work will hopefully lead to a better understanding of the pathogenic pathway leading from disease to disability.

Key points

- Elderly patients are often disabled because they have several diseases, with wide variability in their severity.
- The co-existence of multiple pathological conditions in the same patient has a negative effect on health status and disability that goes beyond the sum of the effect of the individual diseases.
- In the detection of the relationship between disease and disability, the two main practical problems are related to the effect of the presence or the severity of a given disease on disability, and to how the presence and/or the severity of diseases interact to give disability.
- The GIC, a measure assuming that both number of diseases and occurrence of very severe diseases are determinants of health, has (among other comorbidity measures evaluated) the strongest association with disability and, predicts mortality.
- Future studies should address the clinical utility of comorbidity indices by evaluating their prognostic capacity to predict improvement following intervention.

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