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Predictive Validity of Measures of Comorbidity in Older Community Dwellers: The Insufficienza Cardiaca negli Anziani Residenti a Dicomano Study

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OBJECTIVES: To compare the ability of five measures of comorbidity to predict mortality and incident disability in basic activities of daily living (BADLs) in unselected older persons.

DESIGN: An assessment of the data obtained from the Insufficienza Cardiaca negli Anziani Residenti a Dicomano (ICARE Dicomano) Study, a longitudinal epidemiological survey on heart failure in older people.

SETTING: Dicomano, a small, rural town near Florence, Italy.

PARTICIPANTS: The entire population aged 65 and older living in Dicomano, Italy, was enrolled in the ICARE Dicomano Study.

MEASUREMENTS: At baseline (1995), comorbidity was quantified in 688 participants, based on clinical diagnoses, using disease count (DC), Charlson Comorbidity Index (CCI), Index of Co-Existent Diseases (ICED), and Geriatric Index of Comorbidity (GIC), or on drug use, using Chronic Disease Score (CDS). Incident ADL disability was assessed in 1999 and vital status in 2004.

RESULTS: Mortality increased with the severity of comorbidity, with hazard ratios around 2 when comparing the highest and the lowest quartiles of DC, CCI, and ICED in Cox regressions adjusted for age, sex, and physical and cognitive performance. Prediction of mortality with GIC and CDS was only borderline significant. All measures predicted incident ADL disability; the strongest risk gradient (hazard ratio = 8.2 between the highest and lowest quartiles) was observed with ICED. Physical and, to a minor extent, cognitive performance added significantly to predicting mortality and incident BADL disability.

CONCLUSION: All the measures of comorbidity predict death and BADL disability in older community dwellers.

DC, CCI, and ICED performed better than GIC and CDS. Physical performance measures are strong, independent contributors to the prediction of these outcomes. *J Am Geriatr Soc* 54:210–216, 2006.

Key words: comorbidity; epidemiology; disability; mortality

At an advanced age, chronic diseases eventually coexist in a substantial proportion of individuals. Therefore, the burden of coexisting chronic conditions, called comorbidity,¹ progressively increases in the aging populations of industrialized countries. From the standpoint of the practicing physician, comorbidity is important, because it strongly influences the diagnostic process, the therapeutic approach, the effect of treatment, and ultimately the patient's outcome.² In particular, comorbidity increases the risk of functional decline and mortality in older persons with a variety of clinical conditions. In terms of public health, comorbidity has a major role in escalating health-care costs.³

As summarized in a recent review,² several measures have been proposed to quantify comorbidity, some of which have been validated in older persons.⁴ The simplest approach is merely to sum up the number of coexisting diseases into a disease count (DC), as done by several authors, although with substantial adaptations with regard to the diagnostic source considered.^{5–9} Other measures weigh the importance of each disease with respect to a given outcome, and a summary score is then calculated from the individual weights. With the Charlson Comorbidity Index (CCI), weights reflect the ability of each condition to predict mortality, as originally documented in cancer patients.¹⁰ In the Index of Disease Severity (IDS), a score, ranging from 0 to 4 with increasing severity, is assigned to each disease.¹¹ The individual scores can then be added to obtain the Index of Co-Existent Diseases (ICED)¹¹ or, as proposed by other authors,¹² used to assign patients to classes of progressively

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Table 1. Chronic Conditions with Their Diagnostic Clues and Frequency Distribution of Individual Disease Severity (IDS) Scores in 688 Older Community-Dwellers of Dicomano, Italy, Ranked by Increasing Prevalence of IDS0 (Absence of Disease)

| Condition | Diagnostic Clues | IDS 0 | IDS 1 | IDS 2 | IDS 3 | IDS 4 |
|-----------------------------|---|-------|-------|-------|-------|-------|
| | | % | | | | |
| High blood pressure | Q, PE | 15.6 | 12.6 | 5.7 | 65.7 | 0.4 |
| Musculoskeletal disorder | Q, PE | 39.4 | 37.4 | 10.9 | 10.3 | 2.0 |
| Peripheral vascular disease | Q, PE, ABI | 54.4 | 23.4 | 16.3 | 4.5 | 1.5 |
| Organic heart disease | Q, PE, chest x-ray, ECG, two-dimensional Doppler echocardiography | 60.8 | 20.5 | 9.6 | 7.4 | 1.7 |
| Gastrointestinal disease | Q | 67.0 | 20.3 | 2.2 | 10.0 | 0.4 |
| Respiratory tract disease | Q, PE, bell spirometry | 69.6 | 4.9 | 15.6 | 9.3 | 0.6 |
| Hepatobiliary disease | Q, L | 77.6 | 19.3 | 1.3 | 1.3 | 0.4 |
| Cerebrovascular disease | Q, PE | 82.8 | 4.5 | 9.0 | 3.6 | 0.0 |
| Cardiac arrhythmia | Q, PE, ECG | 83.3 | 4.2 | 3.2 | 8.1 | 1.2 |
| Diabetes mellitus | Q, L | 85.8 | 2.0 | 3.5 | 7.7 | 1.0 |
| Cancer | Q, PE | 90.3 | 5.2 | 2.0 | 1.7 | 0.7 |
| Anemia | Q, L | 90.3 | 8.4 | 1.2 | 0.1 | 0.0 |
| Renal disease | Q, L | 94.5 | 2.8 | 2.5 | 0.3 | 0.0 |
| Parkinsonism | Q, PE | 96.9 | 0.1 | 1.9 | 0.9 | 0.1 |

Note: Because of rounding, the sum of percentages may not equal 100.

Q = questionnaire(s); PE = physical examination; ABI = ankle-brachial index; ECG = electrocardiogram; L = laboratory testing.

more-severe comorbidity in the Geriatric Index of Comorbidity (GIC). Finally, a completely different approach has been proposed when pharmacy or administrative databases are available and clinical information is lacking; prescription of specific drugs, or combinations of drugs, can be taken as a proxy for the diagnosis. A score is assigned accordingly, and a summary score, the Chronic Disease Score (CDS), is then calculated by summation.¹³

Unfortunately, all these methods have limitations. In particular, none has been developed and validated in non-institutionalized older persons. Therefore, their validity in predicting relevant outcomes, such as mortality and onset of disability, is uncertain in community-dwelling older persons. The current study was conducted to compare the predictive validity, in terms of vital and functional status, of DC, CCI, ICED, GIC, and CDS in an unselected older population.

MATERIALS AND METHODS

Study Population and Protocol

Data were obtained from the Insufficienza Cardiaca negli Anziani Residenti a Dicomano (ICARE Dicomano) Study, a longitudinal epidemiological survey of heart failure in older people that was conducted in Dicomano, a small, rural town near Florence, Italy. The methods of the study have been previously published.¹⁴ Briefly, in 1995, the ICARE Dicomano Study, which is consistent with the principles of the Declaration of Helsinki on clinical research involving human subjects, enrolled the entire unselected, community-dwelling elderly (≥ 65) population recorded in the city registry office. The only exclusion criterion was living in a nursing home.

The original cohort was reexamined in 1999 to detect the occurrence of disability, and the city registry office was consulted again in 2004 to define vital status.

Data Collection

After informed consent, expert study physicians collected multidimensional, geriatric assessment data, including complete clinical examination, physical performance tests, 12-lead electrocardiogram, echocardiography, carotid ultrasound, and bell spirometry, at baseline.

Assessment of Comorbidity

As detailed elsewhere,¹⁴ diagnostic algorithms, based on questionnaires, physical examination, laboratory tests, and data collected using instruments, were used to identify 14 chronic diseases (Table 1), which were used to compute the first four measures of comorbidity previously mentioned. DC was calculated as the number of coexisting diseases. The CCI was calculated as originally proposed, by summing the weight assigned to each disease.¹⁰ Weights, derived from the relative risk of death in a cohort of cancer patients, are fixed for each diagnosis and range from 1 (for conditions, such as myocardial infarction or mild liver disease, with a relative risk ≥ 1.2 and < 1.5) to 6 (assigned to metastatic cancer, with a relative risk ≥ 6).¹⁰ To determine the IDS, disease severity was graded following rules previously proposed;¹¹ a score of 0 was assigned when the disease was absent, 1 when it was asymptomatic, 2 when symptoms were mild and controlled by treatment, 3 when symptoms were severe, and 4 when the disease was life-threatening or had the highest possible level of severity. ICED was calculated as the sum of the individual IDSs.¹¹ Finally, participants were assigned to the four GIC classes as follows: Class I when they had no disease with an IDS greater than 1, Class II when they had one or more conditions with an IDS of 2, Class III when they had only one condition with an IDS of 3, and Class IV when they had at least two conditions with an IDS of 3 or at least one condition with an IDS of 4.¹²

To calculate CDS, the methodology for data collection proposed previously¹³ was slightly modified, because drug history was recorded directly from the participants, and drug information was processed using the ATC coding system,¹⁵ a hierarchical classification that groups pharmacological agents on the basis of their main anatomic (A) site of action and therapeutic (T) and chemical (C) characteristics. ATC classes, corresponding to drug classes proposed previously to diagnose and grade diseases, were then assigned a score, following the usual algorithm to calculate the CDS.¹³ For example, heart disease was diagnosed in participants taking antithrombotic agents (ATC code B01), cardiac agents/angiotensin-converting enzyme inhibitors (ATC codes C01 and C09), or loop diuretics (ATC code C03C); scores of 3, 4, and 5 were assigned if drugs from one, two, or three classes were taken, respectively.

Functional Assessment

To assess baseline functional status, a modified version of Guralnik's lower extremity physical performance battery¹⁶ was used. This tool, well established in comprehensive geriatric assessment, includes three tests for balance, short distance walk, and lower extremity strength. The performance in each test is evaluated by assigning a score ranging from 0 (worst performance) to 4 (best performance) based on the quartile distribution of the test results in a reference older population. A summary performance score (SPS, range 0–12) is then calculated as the sum of individual test scores.

In survivors who were not disabled at baseline, incident disability was evaluated in 1999 as onset of need for help in at least one of the following basic activities of daily living (BADLs): walking in the house, washing and dressing self, toileting, transferring from bed to chair, and eating.¹⁷ This definition, which excludes lower levels of impairment such as "difficulty in performing," is a standard way to assess disability that has clear implications in terms of provision of adequate care and therefore is clinically relevant.

Other Covariates

Cognitive impairment and depressive symptoms, which are frequent nonsomatic comorbidities of late life, were evaluated using the Mini-Mental State Examination (MMSE)¹⁸ and the Geriatric Depression Scale (GDS).¹⁹ Given the strong prognostic value of cognitive²⁰ and affective disorders in older persons,²¹ the results of these tests were entered separately in the analyses and not included into the measures of comorbidity.

Marital status (contrasting participants with a living spouse to those unmarried or widowed) and years of education were also recorded and included in the analyses.

Analytical Procedures

Statistical analysis was performed using SPSS for Windows 12.0 (SPSS, Inc., Chicago, IL) and Stata 8.0 (Stata Corp., College Station, TX). To facilitate comparison with the four classes of GIC, the continuous scores of DC, CCI, ICED, and CDS were categorized into quartiles; the term "levels" will be used to refer to classes (as in GIC) or quartiles (as in DC, CCI, ICED, and CDS) of comorbidity. Continuous variables were reported as mean \pm standard error of the

mean. Relative frequencies were compared using the chi-square test.

Cox proportional hazards regression models were fitted to the follow-up data to evaluate differences in total mortality across levels of comorbidity. Hazard ratios (HRs), with 95% confidence intervals (CIs), were used to estimate the relative risk of death by contrasting Level 2, 3, and 4 of each measure with Level 1, taken as the reference category. The assumption of proportionality was checked with visual inspection of survival curves. Potential confounding factors included in all Cox models were age and sex in the first step and years of education, marital status, MMSE, GDS, and SPS scores in the second step, with backward deletion of redundant variables.

Logistic regression models were used to evaluate the ability of each measure of comorbidity, expressed in four levels of increasing severity, to predict incident ADL disability. In these models, odds ratios and 95% confidence intervals were calculated to contrast Level 2, 3, and 4 with Level 1, taken as the reference category. For each measure, an initial model included only age and sex as covariates. Marital status; years of education; and SPS, MMSE, and GDS scores were entered subsequently and backward deleted, if redundant, to obtain a final parsimonious model. The Hosmer-Lemeshow method was used to evaluate the fit of the predictive equation. The area under the receiver operating characteristic (ROC) curve was calculated from the logistic models.

A two-tailed *P*-value $< .05$ was considered statistically significant.

RESULTS

Of 864 subjects eligible as of April 25, 1995, 697 underwent clinical examination. Reasons for nonparticipation were death before data collection in three cases and refusal in 164. After excluding nine other cases with incomplete data, the final study sample included 688 participants (80% of the eligible cohort), of whom 286 (42%) were men. Mean age was 74 ± 0.3 (range 65–96); 422 (61%) participants were aged 65 to 74, 202 (29%) 75 to 84, and 64 (9%) 85 and older. The 176 who were not included had similar mean age (74 ± 0.5 ; $P = .92$) to the 688 participants included in the study and a proportion of men only slightly higher (49%; $P = .38$).

Distribution of Measures of Comorbidity

Table 1 shows the frequency distribution of the 14 diseases used to calculate DC, CCI, ICED, and GIC, graded according to their IDS. The three most prevalent conditions were high blood pressure, musculoskeletal disorders, and peripheral vascular diseases. As expected, given the population-based sample, most diseases were graded as asymptomatic or mild (IDS 1 and 2), with the exception of high blood pressure, whose IDS Level 3 encompassed the majority of the sample (Table 1). The ATC codes used to assign the drug-derived comorbidity score, the algorithm used to calculate CDS, and the corresponding frequency distribution are available on request from the authors. Drugs for the treatment of heart diseases and cardiovascular risk factors (diabetes mellitus and high blood pressure)

Table 2. Quartile Cutoff Points and Frequency Distribution of Five Measures of Comorbidity

| Level | Disease Count | | Charlson Comorbidity Index | | Index of Coexistent Diseases | | GIC* | Chronic Disease Score | |
|-------|---------------|----------|----------------------------|----------|------------------------------|----------|----------|-----------------------|----------|
| | Cutoff | n (%) | Cutoff | n (%) | Cutoff | n (%) | n (%) | Cutoff | n (%) |
| 1 | 0–2 | 153 (22) | 0 | 219 (32) | 0–4 | 152 (22) | 47 (7) | 0 | 306 (45) |
| 2 | 3 | 150 (22) | 1 | 204 (30) | 5–7 | 223 (32) | 77 (11) | 1 | 35 (5) |
| 3 | 4–5 | 265 (39) | 2 | 139 (20) | 8–10 | 166 (24) | 290 (42) | 2–3 | 168 (24) |
| 4 | 6–10 | 120 (17) | 3–10 | 126 (18) | 11–23 | 147 (31) | 274 (40) | 4–12 | 179 (26) |

* Cutoffs do not apply to Geriatric Index of Comorbidity (GIC), because with this measure no continuous score is calculated and participants are assigned directly to four classes.

prevailed strongly, compared with other classes of therapeutic agents.

Table 2 shows the cutoff scores and the frequency distribution of all the measures of comorbidity. Of the four measures expressed using a continuous score and categorized into quartiles, only CDS had a markedly uneven distribution, with most participants assigned a score of 0 and belonging to the first quartile, and a few receiving a score of 1 and belonging to the second quartile. Assignment to GIC classes, which depends on a priori rules, resulted in more than 80% participants in the two classes of more-severe comorbidity. With all the measures considered, except DC in men, more-severe comorbidity were more prevalent in participants aged 75 and older than in those younger than 75 in both sexes (data not shown).

Mortality

Two hundred forty participants (35%) died during follow-up. Cumulative mortality was higher in men (116/286, 41%) than in women (124/402, 31%; *P* = .008), in participants aged 75 and older (170/266, 64%) than in those younger than 75 (70/422, 17%; *P* < .001), and in those without (127/281, 45%) than in those with a living spouse (113/407, 28%; *P* < .001). Participants who died were less educated (3.7 ± 0.2 vs 4.4 ± 0.1 years; *P* = .001) and had poorer cognitive (MMSE score: 21.9 ± 0.5 vs 26.3 ± 0.2; *P* < .001) and functional status (SPS: 7.0 ± 0.2 vs 9.5 ± 0.1; *P* < .001) and more depressive symptoms (10.0 ± 0.5 vs 8.3 ± 0.3; *P* = .003) than survivors.

In bivariate analysis, mortality rates increased from Level 1 through Level 4 of all the measures of comorbidity

(Table 3). In Cox regression models, the risk of death was always higher in men than in women and increased with advancing age. The prognostic value of all the measures of comorbidity was confirmed in separate regression models, adjusted initially only for demographics and eventually also for education, marital status, physical performance (SPS), cognition (MMSE), and depressive symptoms (GDS) at baseline (Table 4). DC and ICED showed a similar level of statistical significance for trend and a fairly homogeneous risk gradient from Level 1 through Level 4. The CCI obtained the highest significance for trend, although pairwise comparisons showed a significantly greater risk of death only when Level 4 was contrasted with Level 1. With these three measures, the risk of death was approximately double when participants in Level 4 were compared with those in Level 1. GIC and CDS were only borderline significant predictors of death in models fully adjusted for covariates.

SPS always added significantly to predicting mortality, independent of the specific measure of comorbidity considered; the risk of death increased 7% to 9% per each 1-point decrease in SPS. MMSE was also associated with the risk of death, except when comorbidity was expressed using the CCI. The prognostic value of these sets of variables was confirmed when analyses were restricted to participants who were not disabled at baseline (data not shown). Education, marital status, and GDS were always backward deleted and did not appear in final parsimonious models.

Incident Disability

Of the 633 participants who were independent in ADLs at baseline, 134 could not be reexamined in 1999 (83 had

Table 3. Mortality Rates Across Levels of Increasing Comorbidity

| Level | Disease Count | | | Charlson Comorbidity Index | | | Index of Coexistent Disease | | | Geriatric Index of Comorbidity | | | Chronic Disease Score | | |
|-------|---------------|-------|-----------------|----------------------------|-------|-----------------|-----------------------------|-------|-----------------|--------------------------------|-------|-----------------|-----------------------|-------|-----------------|
| | N | P-Y | Rate (/100 P-Y) | N | P-Y | Rate (/100 P-Y) | N | P-Y | Rate (/100 P-Y) | N | P-Y | Rate (/100 P-Y) | N | P-Y | Rate (/100 P-Y) |
| 1 | 32 | 1,261 | 2.5 | 49 | 1,777 | 2.8 | 26 | 1,284 | 2.0 | 9 | 406 | 2.2 | 83 | 2,428 | 3.4 |
| 2 | 39 | 1,189 | 3.3 | 57 | 1,621 | 3.5 | 68 | 1,735 | 3.9 | 18 | 622 | 2.9 | 12 | 277 | 4.3 |
| 3 | 96 | 1,937 | 5.0 | 51 | 1,005 | 5.1 | 60 | 1,218 | 4.9 | 83 | 2,285 | 3.6 | 59 | 1,225 | 4.8 |
| 4 | 73 | 747 | 9.8 | 83 | 731 | 11.4 | 86 | 897 | 9.6 | 130 | 1,822 | 7.1 | 86 | 1,205 | 7.1 |

N = number of deaths; P-Y = person-years.

Table 4. Final Parsimonious Cox Proportional Hazard Models Predicting Death, Obtained Using Backward Deletion of Redundant Variables

| Models and Variables | Hazard Ratio (95% Confidence Interval) | P-value |
|--------------------------------|--|---------|
| Model 1 | | |
| Disease count | | .01* |
| Level 1 | 1 | |
| Level 2 | 1.4 (0.9–2.4) | .16 |
| Level 3 | 1.6 (1.0–2.5) | .048 |
| Level 4 | 2.2 (1.4–3.6) | .001 |
| Age | 1.12 (1.11–1.15) | <.001 |
| Sex (female vs male) | 0.5 (0.4–0.7) | <.001 |
| SPS | 0.92 (0.88–0.97) | .002 |
| MMSE | 0.97 (0.94–0.997) | .03 |
| Model 2 | | |
| Charlson Comorbidity Index | | <.001* |
| Level 1 | 1 | |
| Level 2 | 1.0 (0.7–1.5) | .99 |
| Level 3 | 1.2 (0.8–1.9) | .43 |
| Level 4 | 2.3 (1.5–3.4) | <.001 |
| Age | 1.12 (1.10–1.16) | <.001 |
| Sex (female vs male) | 0.5 (0.4–0.7) | <.001 |
| SPS | 0.91 (0.87–0.96) | <.001 |
| Model 3 | | |
| Index of Coexistent Diseases | | .01* |
| Level 1 | 1 | |
| Level 2 | 1.5 (0.9–2.4) | .10 |
| Level 3 | 1.8 (1.1–3.1) | .02 |
| Level 4 | 2.2 (1.3–3.6) | .002 |
| Age | 1.12 (1.11–1.15) | <.001 |
| Sex (female vs male) | 0.5 (0.4–0.6) | <.001 |
| SPS | 0.93 (0.88–0.99) | .008 |
| MMSE | 0.98 (0.94–0.996) | .03 |
| Model 4 | | |
| Geriatric Index of Comorbidity | | .048* |
| Level 1 | 1 | |
| Level 2 | 1.0 (0.4–2.4) | .96 |
| Level 3 | 1.0 (0.5–2.1) | .92 |
| Level 4 | 1.6 (0.8–3.2) | .200 |
| Age | 1.13 (1.11–1.15) | <.001 |
| Sex (female vs male) | 0.5 (0.3–0.6) | <.001 |
| SPS | 0.93 (0.88–0.99) | .005 |
| MMSE | 0.97 (0.94–0.99) | .02 |
| Model 5 | | |
| Chronic Disease Score | | .04* |
| Level 1 | 1 | |
| Level 2 | 1.2 (0.6–2.3) | .61 |
| Level 3 | 1.2 (0.8–1.7) | .40 |
| Level 4 | 1.7 (1.2–2.3) | .005 |
| Age | 1.13 (1.11–1.15) | <.001 |
| Sex (female vs male) | 0.5 (0.4–0.7) | <.001 |
| SPS | 0.93 (0.88–0.99) | .008 |
| MMSE | 0.96 (0.93–0.99) | .01 |

Note: Other variables initially included and backward deleted were years of education, marital status, GDS, and (limited to Charlson Comorbidity Index), Mini-Mental State Examination (MMSE).

* P-value for trend referring to the comorbidity measure.

SPS = Summary Performance Score.

died, 36 refused to be interviewed, and 15 could not be traced). Of the remaining 499, 48 (9.6%) were disabled at 1999 follow-up. Incidence of disability was similar in men (17/197, 9%) and women (31/302, 10%; $P = .55$) and in those without (23/194, 12%) and with a living spouse (25/305, 8%; $P = .18$), whereas it was higher in participants aged 75 and older (30/141, 21%) than in those younger than 75 (18/358, 5%; $P < .001$). Participants who became disabled were less educated (3.5 ± 0.4 vs 4.3 ± 0.1 years; $P = .05$) and had lower MMSE scores (22.7 ± 1.0 vs 26.4 ± 0.1 ; $P < .001$) and worse SPS (7.5 ± 0.4 vs 9.6 ± 0.1 ; $P < .001$) and GDS scores (11.7 ± 1.3 vs 8.1 ± 0.3 ; $P = .001$) than those who remained independent.

All measures of comorbidity predicted incident disability in bivariate comparisons (data not shown). These findings were confirmed using multivariate logistic regression models adjusted for age, sex, education, marital status, SPS, MMSE, and GDS at baseline (Table 5). ICED showed the smallest P-value for trend and a homogeneous risk gradient from Level 1 through Level 4 in pairwise contrasts; participants with Level 4 ICED were eight times as likely as those with minimal comorbidity to become disabled.

Of the other covariates, advancing age and SPS were significant predictors of disability in all logistic regression models, whereas marital status was significantly associated with this outcome only in the models based on DC and ICED. Each 1-point decrease in SPS was associated with a 30% higher risk of incident disability.

The area under the ROC curve for DC, CCI, ICED, GIC, and CDS was 0.803, 0.802, 0.829, 0.780, and 0.827, respectively, in logistic regressions adjusted only for demographics and 0.850, 0.828, 0.874, 0.844, and 0.860, respectively, for fully adjusted models.

All logistic regression models showed a good fit when analyzed using the Hosmer-Lemeshow method.

DISCUSSION

All the measures of comorbidity tested in this study, four based on clinical diagnoses and one on drug use, significantly predicted death and incident ADL disability in older community dwellers. Their predictive validity was confirmed after adjusting for indicators of physical performance, cognition, and mood, which are important determinants of health status in old age. Yet these measures were not equivalent. Overall, DC, CCI, and ICED performed better than GIC and CDS, as indicated by lower P-values and homogeneous risk gradients, from Level 1 through Level 4, for both outcomes. Moreover, GIC was distributed somewhat paradoxically, with the majority of participants belonging to the two classes of most-severe comorbidity, a finding inconsistent with the population-based nature of the study sample.

In previous studies, several measures have been proposed and validated to quantify the burden of comorbidity, but in general, the validation process has been limited to a single instrument, tested in disease-specific samples, whereas only a few studies have compared the predictive validity of different measures in the same target population of unselected individuals. As in the present study, another study³ examined the ability of five measures of comorbidity, including DC, CCI, and CDS, to predict mortality and costs

Table 5. Final Parsimonious Logistic Regression Models Predicting Incident Disability, Obtained Using Backward Deletion of Redundant Variables

| Model and Variable | Odds Ratio (95% Confidence Interval) | P value |
|--------------------------------|---|---------|
| Model 1 | | |
| Disease count | | .01 |
| Level 1 | 1 | |
| Level 2 | 0.9 (0.2–3.8) | .93 |
| Level 3 | 1.9 (0.6–5.7) | .28 |
| Level 4 | 4.7 (1.5–15.1) | .009 |
| Age | 1.14 (1.06–1.21) | <.001 |
| Sex (female vs male) | 0.8 (0.3–1.8) | .51 |
| SPS | 0.7 (0.5–0.8) | <.001 |
| Marital status | 2.8 (1.1–7.2) | .03 |
| Model 2 | | |
| Charlson Comorbidity Index | | .005 |
| Level 1 | 1 | |
| Level 2 | 0.8 (0.3–2.3) | .67 |
| Level 3 | 1.3 (0.4–3.9) | .65 |
| Level 4 | 3.8 (1.5–10.1) | .006 |
| Age | 1.12 (1.05–1.19) | <.001 |
| Sex (female vs male) | 0.7 (0.3–1.5) | .32 |
| SPS | 0.7 (0.6–0.9) | .04 |
| Model 3 | | |
| Index of Coexistent Diseases | | <.001 |
| Level 1 | 1 | |
| Level 2 | 1.2 (0.3–5.1) | .81 |
| Level 3 | 3.6 (0.9–13.9) | .07 |
| Level 4 | 8.2 (2.2–30.4) | .002 |
| Age | 1.15 (1.07–1.23) | <.001 |
| Sex (female vs male) | 0.8 (0.3–1.8) | .53 |
| SPS | 0.7 (0.6–0.8) | <.001 |
| Marital status | 2.8 (1.1–7.4) | .04 |
| Model 4 | | |
| Geriatric Index of Comorbidity | | .009 |
| Level 1 | 1 | |
| Level 2 | 0.3 (0.04–2.6) | .29 |
| Level 3 | 0.5 (0.1–2.5) | .38 |
| Level 4 | 1.7 (0.4–8.2) | .497 |
| Age | 1.13 (1.06–1.20) | <.001 |
| Sex (female vs male) | 0.5 (0.2–1.0) | .06 |
| SPS | 0.7 (0.6–0.8) | <.001 |
| Model 5 | | |
| CDS | | .003 |
| Level 1 | 1 | |
| Level 2* | — | — |
| Level 3 | 0.7 (0.2–2.2) | .55 |
| Level 4 | 3.6 (1.6–8.2) | .002 |
| Age | 1.14 (1.07–1.21) | <.001 |
| Sex (female vs male) | 0.6 (0.3–1.4) | .27 |
| SPS | 0.7 (0.6–0.9) | <.001 |

Note: Other variables initially included and backward deleted were years of education, marital status, Mini-Mental State Examination score, and Geriatric Depression Scale score.

* No participant in Chronic Disease Score (CDS) Level 2 became disabled at follow-up.

SPS = Summary Performance Score.

related to health care in a large cohort of primary care patients aged 60 and older. Diagnosis-based measures were slightly better at predicting mortality, whereas drug-based measures were more accurate in predicting use of healthcare services. Nonetheless, the performance of these measures was remarkably similar overall, the areas under the ROC curves, adjusted for age, race, and sex, ranged between 0.648 and 0.685 for the outcome of hospital admission and between 0.662 and 0.767 for mortality. Taken together, these results and those of the previous study³ indicate that, despite substantial differences in data input and scoring, measures of comorbidity are all significant predictors of important health outcomes in older persons, possibly beyond the intended purpose of each instrument. This finding suggests that even a simple measure, such as a list of diagnoses obtained from hospital databases, can reasonably account for the burden of comorbidity, at least when groups of patients—not single diseased individuals—are compared. Thus, of the three measures performing better in the present study, DC probably represents the best compromise between accuracy and ease of use, because it performs fairly well and is simple and extensively applicable in different settings.

The present study adds to ongoing work to validate measures of comorbidity in community-dwelling elderly populations. A major concern in this area is to compare the benefits and the costs of using thorough clinical data with those of pure administrative data.²⁰ Unlike other studies,^{3,20} other clinical covariates were available in the present investigation. This, together with the selection of the study sample from the general population, represents a major strength of the current study. Guralnik's short battery for lower extremity motor performance provided a major contribution to the prediction of both death and disability, and poorer cognitive status was associated with a greater risk of death. These findings underline the prognostic role of comorbidity, which persisted even after a complex adjustment procedure. They also suggest that the ultimate outcome of older persons cannot be predicted solely on the basis of their somatic diagnoses. As is well known and was recently confirmed,²¹ survival without physical dependence (i.e., active life expectancy) at an old age requires maintenance of good physical and cognitive performance. Low SPS was demonstrated to predict nursing home admission or death²² and incident disability in a 4-year follow-up of nondisabled older individuals.¹⁶ Similarly, poor cognitive scoring is a risk factor for disability²³ and death.^{24,25} The findings of this study robustly demonstrate that the prognostic value of functional and mental status in late life is independent of the severity of comorbidity, regardless of the specific measure used to quantify it.

According to previous investigations of large cohorts of older persons, depressive symptoms are independent predictors of physical decline²⁶ and death.^{27,28} On the contrary, in the present study sample, the associations between depressive symptoms and death or incident disability, observed in bivariate analyses, were not confirmed in multivariate models. The discrepancy between these and previous findings might stem from differences in the instruments used to quantify depressive symptoms or might be due to the fact that, in those studies, adjustment for coexisting diseases was based not on a single measure of

comorbidity but rather on a series of dichotomous variables, coding for the presence or the absence of individual somatic diagnoses.^{26–28}

Study limitations should be acknowledged. The findings described were obtained in a small sample of seniors, free-living in a rural community. Hence, they might be poorly generalized to oldest populations at large and to old patients in hospitals or in other care settings. Furthermore, no information was available on healthcare-related costs, another important area of interest in comparing measures of comorbidity. Finally, because this study was conducted as a secondary analysis from an existing database, reliability of the measures of comorbidity could not be assessed; this limitation was likely of some importance only for CDS, whose methodology of data collection was changed from the original, and for ICED, whose scoring system has some degree of subjectivity. Nevertheless, having discounted these limitations, the study may have important implications, because it suggests that almost any measure can be used to capture and, when necessary, adjust for the burden of comorbidity. At the same time, it indicates that all these measures are incomplete predictors of death and disability in older persons, which are both strongly and independently affected by physical performance measures. Based on these findings, these measures of physical and cognitive performance should be included whenever possible in predictive models for death and incident disability, because adjustment procedures that ignore them may not be completely able to prognosticate disability-free survival of older persons accurately.

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