Comorbidity indices

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Received on September 2, 2014; accepted in revised form on September 10, 2014.

Clin Exp Rheumatol 2014; 32 (Suppl. 85): S131-S134.

Key words: comorbidity, indices

Competing interests: none declared.

ABSTRACT

Comorbidities are conditions that coexist with a disease of interest, and may lead to a delayed diagnosis, be confounders in analysis of clinical status and course, and increase morbidity and mortality. Therefore, it appears desirable to summarise efficiently one or multiple comorbidities into a single score in an efficient manner, using comorbidity indices and self-administered co-morbidity questionnaires. The two most commonly used comorbidity indices are the Charlson Comorbidity Index (CCI) and the Elixhauser et al. comorbidity measure (ECM). The CCI was constructed based on the mortality rates of 607 patients admitted to the general internal medicine service over 1 month; sixteen diseases were included in this index, with different weights, and were selected and weighted based on the strength of their association with mortality. Elixhauser et al. used administrative data to identify the 30 comorbidities that had a major impact on short-term outcomes in acutely hospitalised patients. Although ECM appeared to have better performance in all aspects of validity, difficulty in terms of feasibility in collecting 30 comorbidities may encourage investigators to use the CCI. Self-administered questionnaires could be a valid and reliable alternative approach to assess comorbidities, and a tool to be included in prospective studies.

Introduction

A comorbidity is a condition that coexists with the disease of interest. Comorbidities may lead to a delayed diagnosis, may be confounders in analysis and more importantly, may increase mortality: indeed, comorbidity has been found to be a more significant predictor of premature death than shared epitope, rheumatoid factor or erosions (1). Therefore it seems important to be able to collect them in an efficient manner.

Comorbidities can be collected in 2 ways: either collecting each comorbidity separately (*e.g.* diabetes, heart failure, etc.) or summarising comorbidity information into a single score that provides a single parameter for measuring multiple comorbidities (*e.g.* comorbidity indices and self-administered co-morbidity questionnaires).

The advantage of comorbidity indices and questionnaires is that by reducing all coexistent illnesses and the severity of those into a single numeric score, comparison of comorbidity between patients is possible

In this present manuscript we will review the most used comorbidity indices and self–administered comorbidity questionnaires

Comorbidity indices

We will present in the present manuscript the two most commonly used comorbidity indices: the Charlson Comorbidity Index (2) and the Elixhauser *et al.* (3) comorbidity measure. Other comorbidity indices have been proposed (4, 5) but they are far less used.

Charlson comorbidity index

The Charlson comorbidity index (CCI) was published in 1987, and based on the mortality rates of 607 patients admitted to the general internal medicine service for a period of 1 month. The objective was to develop a method that could be prospectively applicable for classifying comorbidities that might alter the risk of mortality for use in longitudinal studies. Sixteen diseases were included in this index, with different weights, and were selected and weighted based on the strength of their association with mortality (Table I).

- *Content validity* refers to the completeness and relevance of the content of the items to measuring what they claim to measure (6). Regarding the items and the weights included in the CCI, they were statistically derived by the relative risk estimates of the proportional regres-

Table I. Charlson Comorbidity Index.

Disease	Points
Myocardial Infarction	1
Congestive Heart Failure	1
Peripheral Vascular disease	1
Cerebrovascular disease	1
Dementia	1
COPD	1
Connective Tissue disease	1
Peptic Ulcer disease	1
Diabetes Mellitus	1 point if uncomplicated
	2 points if end-organ damage
Moderate to severe CKD	2
Hemiplegia	2
Leukaemia	2
Malignant Lymphoma	2
Solid Tumour	2 points
	6 points if metastatic
Liver disease	1 point if mild
	3 points if moderate to severe
AIDS	6 points

Adapted from: Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*.1987; 40: 373-83.
Calculation: Add all items of the Comorbidity score: The total score is the Charlson Comorbidity Index.
COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease.

sion model to predict mortality using clinical data; furthermore, items are explicit and mutually exclusive. However some comorbidities collected in other indices, such as alcoholism (5), were not included in this index. Furthermore, it is worth noting that fibromyalgia, one of the most relevant comorbidities in rheumatology, and especially important when assessing disease activity, is not included in any comorbidity indices or self-reported comorbidity questionnaires.

- *Construct validity* refers to testing hypotheses about how a scale should perform under various conditions, *e.g*. with different groups of patients, or before and after treatment. Construct validity is not commonly tested using comorbidity indices but for example, Kiefe *et al*. (8) hypothesised that chronic disease was a barrier to cancer screening and found that the proportion of women presenting for routine screening tests declined with increasing CCI scores, suggesting a good construct validity of the CCI.
- *Criterion validity* refers to the correlation of a scale with some other measure of the disorder under study, ideally, a *gold standard* that has been used and accepted in the field (9). However, no gold standard exists for measuring comorbidity, so what is usually done is to use another comorbidity measures for comparison. CCI presented moderate to good correlation with other comorbidity indices (10-12), and with various outcome criterion such as disability, mortality and length of stay (9, 13).
- *Reliability* refers to the overall consistency of a measure, and has been also defined as the extent to which repeated measurements of a stable phenomenon by different people, at different times and places get similar results (14). This is usually reported by the intra-class correlation coefficient (ICC) in case of several raters, and ICCs for CCI have been reported to be moderate to very good (15, 16).

Elixhauser's Comorbidity Measure (ECM)

Elixhauser *et al*. used administrative data to identify the 30 (the 17 from CCI + 13 new ones) comorbidities that had a major impact on short-term outcomes in acute hospital patients (Table II). Elixhauser et al. treated conditions separately or as a count.

Table II. Comorbidities included in the Elixhauser's Comorbidity Measure.

Comorbidity
Congestive heart failure
Valvular disease
Pulmonary circulation disorders
Peripheral vascular disorders
Hypertension
Paralysis
Other neurological disorders
COPD
Diabetes uncomplicated
Diabetes complicated
Hypothyroidism
Renal Failure
Liver disease
Peptic ulcer excluding bleeding
AIDS
Lymphoma
Metastatic cancer
Solid tumour without metastasis
Rheumatoid arthritis/collagen vascular diseases
Coagulopathy
Obesity
Weight loss
Fluid and electrolyte disorders
Blood loss anaemia
Deficiency anaemia
Alcohol abuse
Drug abuse
Psychosis
Depression

Adapted from: Elixhauser A, Steiner C, Harris DR, Coffey RM: Comorbidity measures for use with administrative data. *Med Care* 1998; 36: 8-27.
Calculation: 1 point per comorbidity; add all items. The total score is the Elixhauser's Comorbidity Measure.
COPD: Chronic Obstructive Pulmonary Disease; AIDS: Acquired Immuno-Deficiency Syndrome.

- *Content validity:* the ECM comprises a larger number of items compared to the CCI: in addition of the empirical-generated items (that were also included in the CCI), 17 additional judgemental items were added, based on a systematic literature review. On the other hand, no weight is attributed to each comorbidity, implicitly assuming that all conditions are equally important in their relationship to outcomes, which is unlikely to be true.
- *Construct validity:* no studies have evaluated the construct validity of this specific comorbidity index.
- *Criterion validity:* ECM has been compared to other comorbidity indices; when compared to CCI, in most of the studies ECM tended to outperform CCI (17-20), while in oth-

ers performances were similar (21). When compared to other illness indicators, such as previous years expenditures (22), ECM also tended to perform better.

- *Reliability:* No data was available on the reliability ECM, but inter-rater reliability may appear less relevant since it uses administrative data. It might be noted that diagnosis from administrative data may be less accurate than those from physicians, although diagnoses from physicians are not perfectly accurate, possibly particularly in rheumatic diseases.

Self-administered comorbidity questionnaires

The CCI has also been adapted into a self-administered questionnaire (23), but specific comorbidity self-administered questionnaires for assessing comorbidities have been developed; these tools might be a useful alternative to medical records or administrative data when these are not available.

The self-administered comorbidity questionnaire (SCQ) was first published by Sangha *et al*. (24), and asks the patients to indicate whether they suffer at the moment from 12 additional medical conditions (Table III) selected by an expert panel based on the comorbidities collected on the CCI; the score of the SCQ ranges from 0 to 45 points.

Construct validity was measured by the correlation between SCQ and CCI, and was moderate (0.55). Test-retest *reliability* was very good (ICC 0.94 [95%CI 0.72–0.99]).

Criterion validity was measured by correlation of SCQ to SF-36 and was fair to moderate (from r=0.03 to 0.39 depending on the SF-36 subscale, with better correlations observed for physical-related subscales), and with the number of prescriptions in a year (r=0.37).

Stolwijk *et al*. (25) have recently published a validation study for SCQ in patients with ankylosing spondylitis (AS), where *criterion validity* was assessed by the agreement between the SCQ answers and comorbidities identified in medical records, and was moderate to perfect for most conditions (κ 0.47–1.00), except for ulcer disease, depression and OA. Other validation studies using this questionnaire in other pathologies are currently on going.

Table III. Self-Administered Comorbidities Questionnaire.

Instructions: The following is a list of common health problems. Please indicate (circle correct answer) if you currently have the problem in the first column. *If you do not have the problem*, skip to the next problem. *If you do have the problem*, please indicate in the second column if you receive medications or some other type of treatment for the problem. Also, indicate in that case in the third column if the problem limits any of your activities. Finally, indicate also medical conditions that are not listed under "other medical problems" at the end of the list.

	Do you have the problem?		Do you receive treatment for it?		Does it limit your activities?	
Problem	No	Yes	No	Yes	No	Yes
Heart disease	N	Y	N	Y	N	Y
High blood pressure	N	Y	N	Y	N	Y
Lung disease	N	Y	N	Y	N	Y
Diabetes	N	Y	N	Y	N	Y
Ulcer or Stomach disease	N	Y	N	Y	N	Y
Kidney disease	N	Y	N	Y	N	Y
Liver disease	N	Y	N	Y	N	Y
Anaemia or other blood disease	N	Y	N	Y	N	Y
Cancer	N	Y	N	Y	N	Y
Depression	N	Y	N	Y	N	Y
Pain and swelling in joints other than the back	N	Y	N	Y	N	Y
Osteoporosis	N	Y	N	Y	N	Y
Fractures	N	Y	N	Y	N	Y
Other medical problems:(please write in):						
1.	N	Y	N	Y	N	Y
2.	N	Y	N	Y	N	Y
3.	N	Y	N	Y	N	Y

Adapted from: Frenkel WJ, Jongerius EJ, Mandjes-van Uitert MJ, van Munster BC, de Rooij SE: Validation of the Charlson Comorbidity Index in acutely hospitalized elderly adults: a prospective cohort study. *J Am Geriatr Soc* 2014; 62: 342-6.

Calculation: An individual can receive a maximum of 3 points for each medical condition: 1 point for the presence of the problem, another point if he/she receives treatment for it, and an additional point if the problem causes a limitation in functioning. Because there are 12 defined medical problems and 3 optional conditions, the maximum score totals 45 points if the openended items are used and 36 points if only the close-ended items are used.

Conclusion

Comorbidities are major confounders in longitudinal non-randomised studies, and the most efficient way to adjust for such confounders seems to be the collection of all comorbidities in one index (either by record/administrative databases review or by a self-administered questionnaire).

Regarding the indices, in this present review we have presented the properties of the CCI and the ECM. Although ECM seemed to perform better in all aspects of validity, the difficulty in terms of feasibility in collecting 30 comorbidities (vs. 17 in the CCI) may encourage investigators to use the CCI. In the absence of medical records, self-administered questionnaires would be a valid and reliable alternative, and a tool to be included in prospective studies.

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