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CLINICAL ARTICLE - VASCULAR

The value of the Charlson Co-morbidity Index in aneurysmal subarachnoid haemorrhage

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Abstract
Background Several studies have included different co-morbid conditions in prediction models for stroke patients. For subarachnoid haemorrhage (SAH), it is not known whether the Charlson Co-morbidity Index (CCI) is associated with outcome. We evaluated if this index was associated with outcome in patients with ruptured intracerebral aneurysms.
Methods The data of all consecutive aneurysmal SAH (aSAH) patients treated at the Radboudumc, Nijmegen, The Netherlands and entered in the database were retrospectively analysed. Clinical condition at admission was recorded using the WFNS (World Federation of Neurological Surgeons Grading System) grade was collected, as were the age and treatment modality. The burden of co-morbidity was retrospectively registered using the CCI. Outcome was dichotomised on the modified Rankin Scale (mRS; 0–2, favourable outcome; 3–6, unfavourable outcome). A binary logistic regression analysis was performed.
Results Between 6th May 2008 and 31st July 2013, 457 patients were admitted because of non-traumatic SAH (aSAH). Seventy-seven (16.8 %) patients had no aneurysm. Of the 380 patients with aSAH, information on co-morbid conditions was available for 371 patients. Thirty-six of those 371 had no treatment because of: bad clinical condition in 34 (9.2 %), a non-treatable dissecting aneurysm in 1 (0.3 %) and the explicit wishes of another. Co-morbidity was present in 113 (31.5 %) patients. Binary logistic regression analysis revealed no added value of using the CCI in predicting the outcome (p=0.91).
Conclusions This study reports that the CCI is not associated with the outcome classified on the mRS at 6 months in patients after aSAH. The CCI has no added value in case-mix correction.

Keywords SAH · Outcome · Charlson · Morbidity · Mortality

Introduction

The Charlson Co-morbidity Index (CCI) is an index used to weight co-morbid conditions in predicting mortality [3]. Depending on the strength of the relationship with mortality, between 1 and 6 points are assigned to a set of co-morbidities [8]. The CCI has been evaluated for use in cases of intracerebral haemorrhage and ischaemic stroke, but not for aneurysmal subarachnoid haemorrhage (aSAH) [1, 8]. Co-morbid conditions can, however, influence the outcome in SAH [4–6, 9, 11, 13, 15, 19]. Aneurysmal SAH is a distinct group of stroke patients, in which perhaps other co-variables should be taken in to account when assessing the weight of the CCI. A recent review of prediction models in aSAH revealed the most commonly identified and valuable patient factors that are associated with outcome; namely, age and initial condition at presentation [10]. Treatment modality (endovascular coiling or clipping) is also known to influence outcomes

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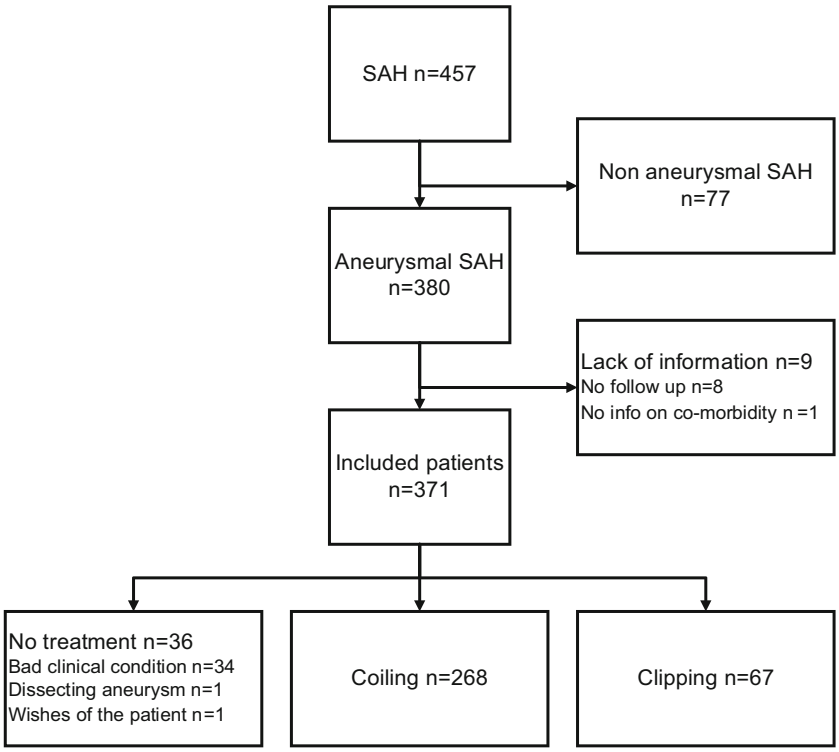

Fig. 1 Flowchart for the progression of 457 patients admitted because of non-traumatic subarachnoid haemorrhage (SAH)

[12, 14]. The purpose of this study was to evaluate whether the CCI is associated with a 6-month functional outcome in aSAH.

Methods

Retrospectively, the data of all consecutive aSAH patients treated in the Radboudumc, Nijmegen, The Netherlands from May 6th 2008 to July 31st 2013 were analysed. Clinical condition at admission as recorded by the WFNS (World Federation of Neurological Surgeons Grading System) scale was used in analysis, as were treatment modality and age [7, 21]. The primary outcome was recorded using the modified Rankin Scale (mRS) after 6 months, because of protocolised combined imaging and clinical follow-up after the same period. The co-morbidities were extracted from the electronic patient files. The total CCI score for each patient was computed and four categories of co-morbidity were defined as previously used by others: 0 (none), 1 (moderate), 2 (severe) and 3 or higher (very severe) [1, 20]. The study was approved by the institutional review board. The results are reported according to the STROBE statement guidelines [22].

Statistical analysis

A binary logistic regression analysis was performed using the mRS score as a dichotomised variable (0–2, favourable outcome; 3–6, unfavourable outcome). SPSS (version 20; SPSS, Chicago, IL, USA) was used for the statistical analysis and the significance was considered to be $p<0.05$.

Results

Between 6th May 2008 and 31st July 2013, 457 patients were admitted because of a non-traumatic SAH (aSAH). Seventy-seven (16.8 %) patients had no aneurysm. Of the 380 patients with aSAH, eight (2.1 %) did not have a follow-up because

Table 1 Patient characteristics

Variable	*n* (%)
Sex	
Male	115 (31.0)
Female	256 (69.0)
Age, mean [SD]	55.4 [13.2]
WFNS	
I	133 (35.8)
II	82 (22.1)
III	15 (4.0)
IV	80 (21.6)
V	61 (16.4)
Treatment modality	
Clip	67 (18.1)
Coil	268 (72.2)
Not treated	36 (9.7)

n number of patients, *SD* standard deviation, *WFNS* World Federation of Neurological Surgeons Grading System for SAH

Table 2 Charlson Co-morbidity Index (CCI) categories in aneurysmal subarachnoid haemorrhage

Condition	CCI weight	Total frequency, *n* (%)
Myocardial infarct	1	11 (3.0)
Congestive heart failure	1	0 (0.0)
Peripheral vascular disease	1	15 (4.0)
Cerebrovascular disease	1	28 (7.5)
Dementia	1	0 (0.0)
Chronic pulmonary disease	1	30 (8.1)
Connective tissue disease	1	12 (3.2)
Ulcer disease	1	0 (0.0)
Mild liver disease	1	2 (0.5)
Diabetes	1	18 (4.9)
Diabetes with end-organ damage	2	0 (0.0)
Hemiplegia	2	2 (0.5)
Moderate or severe renal disease	2	6 (1.6)
Any tumour	2	21 (5.7)
Leukaemia	2	2 (0.5)
Lymphoma	2	0 (0.0)
Moderate or severe liver disease	3	0 (0.0)
Metastatic solid tumour	6	1 (0.3)
AIDS/HIV	6	0 (0.0)

*AIDS*acquired immune deficiency syndrome, *HIV* human immunodeficiency virus

they returned to their home country. One (0.3 %) patient had no information on his co-morbid condition, meaning that analysis was possible for 371 patients. Thirty-six of those 371 had no treatment (Fig. 1). Treatment was preferentially endovascular in patients with aneurysms equally suitable for clipping or coiling. The last follow-up was 1st February 2014. The characteristics of the patients are set out in Table 1, while the frequency of each co-morbidity is provided in Table 2. The distribution of the CCI sum-scores is given in Fig. 2, and is categorised according to severity within each outcome group in Table 3. Co-morbidity was present in 113 (31.5 %) patients. There were no differences in CCI frequency distribution within the two outcome (mRS) categories (Pearson chi-squared test $p=0.084$). A binary logistic regression analysis revealed no beneficial use of the CCI in predicting outcome (odds ratio, 1.020; $p=0.91$) (Table 4). In this model, strong predictors of outcome were initial grade (WFNS), age and treatment modality (area under the receiver operating characteristic curve, 0.86; SE, 0.02). In a sub-analysis using no versus any co-morbidity, no added value was found ($p=0.95$). An ordinal regression analysis using non-dichotomised mRS outcomes did not change the previous findings.

Discussion

The CCI for co-morbid conditions is not associated with the outcome at 6 months in aSAH in these data. The value of the CCI for acute ischaemic stroke and non-traumatic (non-aneurysmal) intracerebral haemorrhage (ICH) is often reported [1, 8, 20]. Stroke patients are generally much older, with a mean age of over 70 years, compared with aSAH patients in general and this cohort in particular (mean age, 55.4) [20, 25] (Table 1). Increased age is associated with the increased prevalence of co-morbidities, and strokes share risk factors with many chronic diseases (e.g. myocardial infarction,

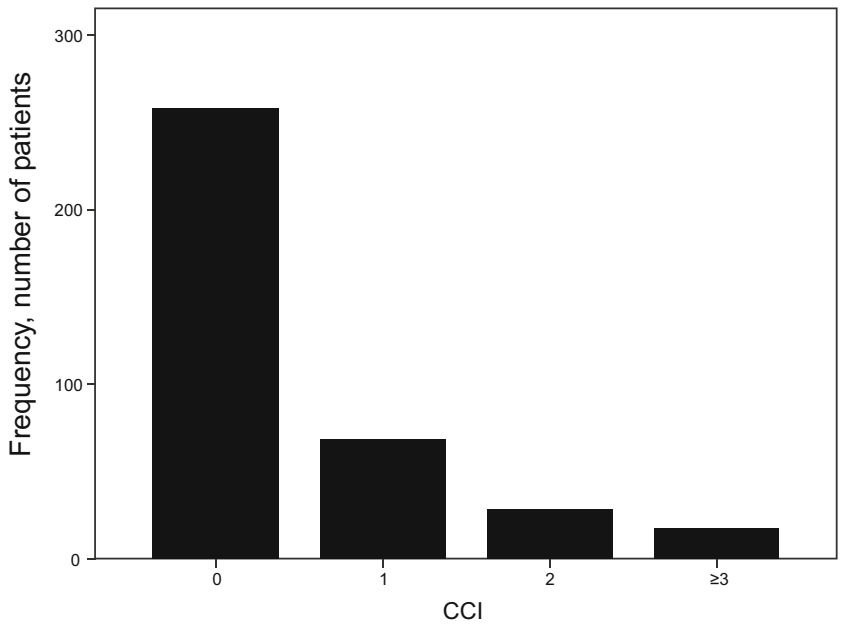

Fig. 2 Distribution of the Charlson Co-morbidity Index (CCI) sum-scores

Table 3 Cross-tabulation Charlson Co-morbidity Index (CCI) categories by dichotomised modified Rankin Scale (mRS)

CCI	mRS		Total
	0–2	3–6	
0	167 (72.6 %)	91 (64.5 %)	258 (69.5 %)
1	39 (17.0 %)	29 (20.6 %)	68 (18.3 %)
2	18 (7.8 %)	10 (7.1 %)	28 (7.5 %)
≥3	6 (2.6 %)	11 (7.8 %)	17 (4.6 %)
total	230 (100 %)	141 (100 %)	371 (100 %)

Percentages are given within mRS group

diabetes) [20]. Several limitations of this study have to be noted. First, the chart review was conducted retrospectively. However, studies including co-morbidity frequently rely on administrative hospital (coding) data that are retrospectively gathered [4, 6]. Secondly, the analysis was carried out on 371 patients. If the investigated group of patients were larger, it is possible that there would have been a small significant result. Thirdly, the CCI was developed to predict 1-year mortality, but in our series we evaluated outcome at 6 months because of protocolised imaging and clinical follow-up. Recent studies have revealed that a minority of patients improve between 6 and 12 months [23].

Contrasting reports have appeared for co-morbid conditions in aSAH [1, 4–6, 8, 13, 18, 19, 24]. Using administrative databases, O'Kelly et al. [16] found a significant increase in the hazards of death and re-admission for SAH per unit increase on the Deyo adaptation of the CCI (HR, 1.14 [1.08–1.21]; $p<0.001$) in a retrospective cohort of 3,120 patients. Other reports evaluated several individual co-morbid conditions in relation to outcome for aSAH with predominantly negative or contrasting results (see ESM 1, which illustrates the value of co-morbidity in aneurysmal SAH reported in the literature). Meanwhile, Langham et al. [11] found a significant contribution of any co-morbid condition to outcome, which was defined as death or severe disability at 6 months, in a cohort of 2,397 patients (univariate, 1.87 [1.56–2.25], $p<0.001$; multivariate, 1.46 (1.20–1.78), $p=0.0003$). In the Langham report, the CCI itself was not used, and other co-morbid conditions like hypertension (not part of the CCI) were included. Finally, in their retrospective study of the treatment of ruptured and unruptured aneurysms, Cowan et al. [4] found that co-morbid conditions (not specifically in the form of CCI) were significant predictors of death (OR, 1.08 [1.04–1.12], $p<0.001$, for each condition increase).

Table 4 Odds ratios for variables in outcome analysis using binary logistic regression analysis. Higher odds ratio is related to worse outcome in dichotomised mRS

Variable	Odds ratio	Level of sign (p value)
Age	1.052	0.00
WFNS	2.067	0.00
CCI	1.020	0.91
Treatment (coil)	1.000	0.00
Treatment (clip)	2.205	0.02
Treatment (none)	47.544	0.00

Treatment reference group is coiling

WFNS World Federation of Neurological Surgeons grading system for SAH, *CCI* Charlson Co-morbidity Index sum score

For a comparison of outcome in the treatment of aSAH, case-mix correction is essential. A major clinical variable is initial grade as evaluated by the WFNS scale. The odds ratio associated with WFNS is reported to be between 2.14 and 13.51 depending on the grade [17, 18]. De Toledo found a relative risk for poor outcome (Expβ) dependent on the WFNS scale of 3.43–78.1. An often reported co-morbid condition associated with bad outcome is hypertension, but this is not included in the CCI [5, 13, 18, 19].

Due to the evolving interest in healthcare outcomes overall, the registration burden is growing enormously. To increase data entry by healthcare providers, focusing on items of significant interest is of utmost importance. This study will contribute to the selection of items that are relevant for outcome measurement of SAH; strong predictors of outcome were initial grade, age and treatment modality. Regarding treatment modality, we had a relatively high ratio of endovascular treated patients. According to a European internet survey, high-volume centres have a significantly higher proportion of coiled ruptured aneurysms in comparison with low-volume centres [2]. Within these high volume centres, we are at the high end of the spectrum of proportion coiled aneurysms. We showed that the CCI as a whole set of co-morbidity parameters is not associated with clinical outcome.

Conclusions

This study reports that the CCI is not associated with the outcome classified on the mRS at 6 months in patients after aSAH. The CCI has no added value in case-mix correction.

Conflicts of interest None.

References

1. Bar B, Hemphill JC 3rd (2011) Charlson comorbidity index adjustment in intracerebral hemorrhage. Stroke 42:2944–2946
2. Bradac O, Hide S, Mendelow DA, Benes V (2012) Aneurysm treatment in Europe 2010: an internet survey. Acta Neurochir (Wein) 154:971–978

3. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 40:373–383
4. Cowan JA Jr, Ziewacz J, Dimick JB, Upchurch GR Jr, Thompson BG (2007) Use of endovascular coil embolization and surgical clip occlusion for cerebral artery aneurysms. J Neurosurg 107:530–535
5. Cross DT 3rd, Tirschwell DL, Clark MA, Tuden D, Derdeyn CP, Moran CJ, Dacey RG Jr (2003) Mortality rates after subarachnoid hemorrhage: variations according to hospital case volume in 18 states. J Neurosurg 99:810–817
6. Crowley RW, Yeoh HK, Stukenborg GJ, Ionescu AA, Kassell NF, Dumont AS (2009) Influence of weekend versus weekday hospital admission on mortality following subarachnoid hemorrhage. Clinical article. J Neurosurg 111:60–66
7. Fisher CM, Kistler JP, Davis JM (1980) Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 6:1–9
8. Goldstein LB, Samsa GP, Matchar DB, Horner RD (2004) Charlson Index comorbidity adjustment for ischemic stroke outcome studies. Stroke 35:1941–1945
9. Hoh BL, Chi YY, Lawson MF, Mocco J, Barker FG 2nd (2010) Length of stay and total hospital charges of clipping versus coiling for ruptured and unruptured adult cerebral aneurysms in the Nationwide Inpatient Sample database 2002 to 2006. Stroke 41:337–342
10. Jaja BN, Cusimano MD, Etminan N, Hanggi D, Hasan D, Ilodigwe D, Lantigua H, Le Roux P, Lo B, Louffat-Olivares A, Mayer S, Molyneux A, Quinn A, Schweizer TA, Schenk T, Spears J, Todd M, Torner J, Vergouwen MD, Wong GK, Singh J, Macdonald RL (2013) Clinical prediction models for aneurysmal subarachnoid hemorrhage: a systematic review. Neurocrit Care 18:143–153
11. Langham J, Reeves BC, Lindsay KW, van der Meulen JH, Kirkpatrick PJ, Gholkar AR, Molyneux AJ, Shaw DM, Copley L, Browne JP, Steering Group for National Study of Subarachnoid H (2009) Variation in outcome after subarachnoid hemorrhage: a study of neurosurgical units in UK and Ireland. Stroke 40:111–118
12. McDougall CG, Spetzler RF, Zabramski JM, Partovi S, Hills NK, Nakaji P, Albuquerque FC (2012) The barrow ruptured aneurysm trial. J Neurosurg 116:135–144
13. Mocco J, Ransom ER, Komotar RJ, Schmidt JM, Sciacca RR, Mayer SA, Connolly ES Jr (2006) Preoperative prediction of long-term outcome in poor-grade aneurysmal subarachnoid hemorrhage. Neurosurgery 59:529–538, discussion 529–538
14. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R, International Subarachnoid Aneurysm Trial Collaborative G (2002) International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet 360:1267–1274
15. Nuno M, Patil CG, Lyden P, Drazin D (2012) The effect of transfer and hospital volume in subarachnoid hemorrhage patients. Neurocrit Care 17:312–323
16. O'Kelly CJ, Kulkarni AV, Austin PC, Wallace MC, Urbach D (2010) The impact of therapeutic modality on outcomes following repair of ruptured intracranial aneurysms: an administrative data analysis. Clinical article. J Neurosurg 113:795–801
17. Risselada R, Lingsma HF, Bauer-Mehren A, Friedrich CM, Molyneux AJ, Kerr RS, Yarnold J, Sneade M, Steyerberg EW, Sturkenboom MC (2010) Prediction of 60 day case-fatality after aneurysmal subarachnoid haemorrhage: results from the International Subarachnoid Aneurysm Trial (ISAT). Eur J Epidemiol 25:261–266
18. Rosen DS, Macdonald RL (2004) Grading of subarachnoid hemorrhage: modification of the world World Federation of Neurosurgical Societies scale on the basis of data for a large series of patients. Neurosurgery 54:566–575, discussion 575–566
19. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL (2007) Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke 38:2315–2321
20. Schmidt M, Jacobsen JB, Johnsen SP, Botker HE, Sorensen HT (2014) Eighteen-year trends in stroke mortality and the prognostic influence of comorbidity. Neurology 82:340–350
21. van Heuven AW, Dorhout Mees SM, Algra A, Rinkel GJ (2008) Validation of a prognostic subarachnoid hemorrhage grading scale derived directly from the Glasgow Coma Scale. Stroke 39:1347–1348
22. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 370:1453–1457
23. Wilson DA, Nakaji P, Albuquerque FC, McDougall CG, Zabramski JM, Spetzler RF (2013) Time course of recovery following poor-grade SAH: the incidence of delayed improvement and implications for SAH outcome study design. J Neurosurg 119:606–612
24. Zacharia BE, Ducruet AF, Hickman ZL, Grobelny BT, Fernandez L, Schmidt JM, Narula R, Ko LN, Cohen ME, Mayer SA, Connolly ES Jr (2009) Renal dysfunction as an independent predictor of outcome after aneurysmal subarachnoid hemorrhage: a single-center cohort study. Stroke 40:2375–2381
25. Ziemba-Davis M, Bohnstedt BN, Payner TD, Leipzig TJ, Palmer E, Cohen-Gadol AA (2014) Incidence, epidemiology, and treatment of aneurysmal subarachnoid hemorrhage in 12 Midwest communities. J Stroke Cerebrovas Dis 23:1073–1082