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ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕ
ORIGINAL RESEARCH

Prognostic value of Charlson comorbidity index in patients admitted with acute myocardial infarction

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Abstract. *Relevance.* To investigate the prognostic value of the Charlson Comorbidity Index (CCI) and its components in assessing outcomes related to in-hospital and 18-month mortality and to determine additional prognostic value when incorporating them into the GRACE score among patients with acute myocardial infarction (MI). *Material and methods.* A prospective study enrolled 712 patients diagnosed with acute MI who underwent coronary angiography within 24 hours of hospitalization. *Results and Discussion.* Of the patients, 61 % were male, median age 65 (interquartile range [IQR] 56–74years). In-hospital and 18-month mortality rates were 5.1 % (n = 36) and 12.1 % (n = 86), respectively. Median GRACE, CCI scores were 117 (IQR: 98–141), and 4 (IQR: 3–6) respectively. Common comorbidities within the CCI components included previous MI (21.8 %), diabetes mellitus (21.1 %), chronic pulmonary disease (16.2 %), dementia (9.2 %), peptic ulcer disease (9.1 %), renal failure (8.6 %). Factors associated with in-hospital and 18-month mortality included chronic lung disease (odds ratio [OR] = 4.21 and 2.04, respectively) and renal failure (OR = 3.51 and 1.99, respectively) after adjusting for GRACE score. Dementia (OR 2.10; 95 % confidence interval [CI] 1.11–3.97) was a significant risk factor for 18-month mortality. CCI was associated with in-hospital and 18-month mortality (GRACE-adjusted OR 1.29, 95 % CI:1.07–1.57, p = 0.001 and 1.37, 95 % CI (1.20–1.57, p = 0.001, respectively). CCI demonstrated good predictive ability for in-hospital mortality (area under the ROC Curve [AUC]: 0.826) and modest performance for 18-month mortality (AUC: 0.797). Adding chronic lung disease, renal failure in the GRACE score

significantly improved the predictive efficacy for in-hospital mortality, with an AUC of 0.932 (95 % CI: 0.905–0.959, p = 0.001). Including CCI in the GRACE score enhanced the prediction efficiency for 18-month mortality (AUC 0.819, 95 % CI: 0.768–0.871, p = 0.001). *Conclusion.* The CCI demonstrated moderate prognostic value in assessing in-hospital mortality among patients with acute MI and good predictive ability for long-term mortality. The CCI and its components (chronic lung disease, renal failure) added prognostic significance in addition to the GRACE score for predicting both short-term and long-term adverse outcomes.
Keywords: Charlson Comorbidity Index, comorbidity, mortality, myocardial infarction, GRACE score

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Conflict of interest statement. The authors declare no conflict of interest.

Ethics approval. The study was approved by the Ethics committee of RUDN University, Moscow, Russia.

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Consent for publication. Voluntary written consent was obtained from the patients for the investigation and publication of relevant medical information according to WMA Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects, 2013.

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Introduction

A significant proportion of patients with myocardial infarction (MI) have concurrent comorbid conditions, which has been recognized as an important prognostic factor for MI prognosis [1,2]. The Charlson comorbidity index (CCI), which assesses comorbidity burden by assigning scores to 22 specific conditions, has validated in patients with acute coronary syndromes (ACS) [3, 4]. The Global Registry of Acute Coronary Events (GRACE) score is validated to predict risk of adverse outcomes among patients with ACS, yet its relationship with pre-existing comorbidities remains inadequately explored.

We sought to investigate the prognostic value CCI and its components in assessing outcomes related to in-hospital and 18-month mortality and determine additional prognostic value when incorporating them into the GRACE score among patients with acute MI, who underwent an invasive management strategy.

Materials and methods

In a single-center prospective observational cohort investigation carried out at the Vinogradov Municipal Clinical Hospital (Moscow, Russia), we included 712 acute MI patients undergoing coronary angiography (CAG) within 24 hours after symptom onset from January 2017 to December 2018. The diagnosis of MI was based on the Third universal definition of MI [5]. Exclusion criteria were all individuals who were with type 3, 4 and type 5 MI as well as those who developed MI during hospitalization.

Patient data included clinical characteristics, cardiovascular risk factors, comorbidities, physical

examination findings, blood test results, and imaging data (including electrocardiography, echocardiography, and CAG. Cardiac Troponin I levels were measured using the Access 2 Immunoassay System (Beckman Coulter, USA), with 99th percentile upper reference limit being 0.02 ng/L. Inpatient and 18-month all-cause mortality rates were recorded. GRACE 2.0 [6] and CCI scores [3, 7] were calculated for all patients. All patients provided written informed consent. The study was approved by the local Ethics Committee of the Institute of Medicine, Peoples' Friendship University of Russia named after Patrice Lumumba. Voluntary written consent was obtained from the patients for the investigation and publication of relevant medical information according to WMA Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects, 2013.

Statistical analysis utilized IBM SPSS Statistics 25.0 (SPSS Inc., Chicago, IL, USA). Continuous variables adhering to a normal distribution were presented as means ± SD, while skewed variables were expressed as median (Me) and interquartile range (IQR). Categorical variables were reported with frequencies and percentages. Logistic regression examined the association between CCI score and its components and mortality. Odds ratios [OR] for continuously distributed variables represented a one-unit increase unless stated otherwise. Receiver operating characteristic (ROC) curve analysis was performed to assess the performance of CCI and its components when adding to GRACE score in predicting in-hospital and 18-month mortality, generating the area under the curve (AUC) and 95 % confidence interval (CI) [8]. Significance was used when $p < 0.05$ for all analysis.

Results and discussion

The median age was 65 (IQR: 56–74) years, 61 % were male, 47.8 % presented with ST elevation. Arterial hypertension was more prevalent (89 %), followed by history of coronary artery disease (CAD) — 46.1 %. Among CCI components, previous MI was the most frequent comorbidity (21.8 % of population) followed by diabetes mellitus (21.1 %), chronic lung disease (16.2 %), dementia (9.3 %), peptic ulcer disease (9.1 %) and renal failure (8.6 %). Median GRACE, CCI scores were 117 (IQR: 98–141), and 4 (IQR: 3–6) respectively. The clinical and laboratory results of the patients were shown in Table 1.

Table 1

The baseline characteristics of the 712 myocardial infarction patients

Variables	Population
n	712
Age, years, Me (IQR)	65 (56; 74)
Females, n (%)	278 (39)
ST-elevation, n (%)	340 (47.8)
Arterial hypertension, n (%)	634 (89)
Coronary artery disease, n (%)	328 (46.1)
Charlson comorbidity index components:	
Previous myocardial infarction, n (%)	155 (21.8)
Mild to moderate diabetes mellitus, n (%)	150 (21.1)
Chronic lung disease, n (%)	115 (16.2)
Dementia, n (%)	66 (9.3)
Peptic ulcer disease, n (%)	65 (9.1)
Renal failure, n (%)	61 (8.6)
Previous admission for heart failure, n (%)	57 (8.0)
Cerebrovascular disease, n (%)	51 (7.2)
Malignant tumors, n (%)	27 (3.8)
Peripheral artery disease, n (%)	26 (3.7)

End of the table 1

Variables	Population
Mild liver disease, n (%)	4 (0.6)
Acquired immunodeficiency syndrome, n (%)	1 (0.1)
Rheumatic disease, n (%)	0 (0)
Hemiplegia or paraplegia, n (%)	0 (0)
Charlson comorbidity index, points, Me (IQR)	4 (3; 6)
Anemia, n (%)	189 (26.5)
Clinical findings:	
Chest pain, n (%)	658 (92.4)
Dyspnea, n (%)	124 (17.4)
Killip class II–IV, n (%)	160 (22.5)
Systolic blood pressure, mmHg, Me (IQR)	140 (120; 159)
Diastolic blood pressure, mmHg, Me (IQR)	80 (76; 89)
Troponin I, ng/mL, Me (IQR)	0.39 (0.09; 2.85)
Hemoglobin, g/L, Me (IQR)	136 (123; 147)
Creatinine, μmol/L, Me (IQR)	94 (80; 107)
Left ventricular ejection fraction, %, Me (IQR)	45 (40; 54)
No lesions/Coronary stenosis = 50 %, n (%)	73 (10.3)
Three-vessel coronary artery disease, n (%)	390 (54.8)
Percutaneous coronary intervention, n (%)	566 (79.5)
GRACE score, points, Me (IQR)	117 (98; 141)

Abbreviation: GRACE: Global Registry of Acute Coronary Events; IQR: interquartile range; Me: median

During hospitalization, 36 (5.1 %) patients died. The 18-month mortality rate was 12.1 % (n = 86). In logistic regression analysis, after adjusting GRACE score, chronic lung disease (OR 4.21 for in-hospital and 2.04 for long-term mortality, respectively) and renal failure (OR 3.51 for in-hospital and 1.99 for long-term mortality, respectively) remained as significant factors associating with adverse outcomes throughout all time frames. Dementia (OR 2.10; 95 % CI 1.11–3.97, p = 0.022) was a significant risk factor for mortality at 18 months. A one-unit increase in the CCI was associated with a 1.65-fold increase in OR of both in-hospital and 18-month mortality. When adjusting CCI with GRACE score, the association was attenuated but remained statistically significant with OR of 1.29 (95 % CI: 1.07–1.57, p = 0.001) for in-hospital and OR of 1.37 (95 % CI: 1.20–1.57, p = 0.001) for 18-month mortality (Table 2).

Table 2

Logistic regression analysis of the association between different components of the Charlson comorbidity index (CCI) and the risk of in-hospital and 18-month mortality in patients with acute myocardial infarction, adjusted for GRACE Score

Variables	In-hospital mortality	p-value	Long-term mortality	p-value
	OR (95 % CI)		OR (95 % CI)	
Peripheral artery disease	–	–	2.46 (0.91–6.61)	0.075
Cerebrovascular disease	1.13 (0.37–3.48)	0.825	1.96 (0.98–3.95)	0.058
Previous MI	1.27 (0.55–2.92)	0.574	1.66 (0.98–2.84)	0.061
Chronic lung disease	4.21 (1.66–10.66)	0.002	2.04 (1.09–3.79)	0.025
Peptic ulcer disease	1.90 (0.39–9.34)	0.430	1.05 (0.45–2.46)	0.905
Previous heart failure	1.51 (0.45–5.08)	0.509	1.41 (0.68–2.93)	0.357
Dementia	1.92 (0.82–4.51)	0.132	2.10 (1.11–3.97)	0.022
Diabetes	1.36 (0.82–2.25)	0.235	1.19 (0.84–1.69)	0.328
Malignancy	1.43 (0.92–2.22)	0.116	1.39 (0.99–1.95)	0.055
Renal failure	3.51 (1.42–8.69)	0.006	1.99 (1.01–3.93)	0.046
CCI, points	1.29 (1.07–1.57)	< 0.001	1.37 (1.20–1.57)	< 0.001

Abbreviation: CCI: Charlson comorbidity index; CI: confidence interval; OR: odds ratio

ROC curve analysis revealed that CCI alone predicted in-hospital mortality well (AUC 0.826, 95 % CI 0.759–0.894, p = 0.001) and modestly predicted 18-month mortality (AUC 0.797, 95 % CI 0.746–0.849, p = 0.001) (Table 3). The GRACE score demonstrated excellent predictive capability for predicting in-hospital death and modest capability for 18-month outcome.

Inclusion of chronic lung disease, renal failure in the GRACE score improved in-hospital mortality prediction ability with AUC of 0.921, whereas inclusion of CCI in the GRACE score improved 18-month mortality prediction ability with AUC of 0.819.

Table 3

Performance of prognostic risk scores for myocardial infarction

All-cause mortality				
Parameters	In-hospital		18-months	
	AUC	95 % CI	AUC	95 % CI
CCI	0.826	0.759–0.894	0.797	0.746–0.849
GRACE	0.912	0.877–0.947	0.794	0.740–0.848
GRACEc	0.932 *	0.905–0.959	0.805 **	0.751–0.859
GRACE + CCI	0.921	0.886–0.956	0.819	0.768–0.871

Note: * GRACEc included GRACE score, chronic lung disease, renal failure, was used for in-hospital mortality prediction.

** GRACEc included GRACE score, chronic lung disease, renal failure, and dementia.

Abbreviation: AUC: area under the ROC curve: CCI: Charlson comorbidity index; CI: confidence interval; GRACE: The Global Registry of Acute Coronary Events score.

Our study to revealed that the most common comorbid conditions were prior MI and diabetes mellitus, whereas chronic lung disease and dementia were the most frequent non-cardiovascular conditions. Patients with acute MI often have multiple coexisting conditions, including common cardiovascular risk factors like diabetes mellitus and arterial hypertension, as well as manifestations of CAD such as prior MI or heart failure. For instance, in one study, diabetes mellitus, arterial hypertension, and heart failure were the most prevalent comorbidities among ACS patients, with 68 % of participants having at least three comorbidities [9].

Prevalence chronic lung disease and renal failure in our study, at 16.2 % and 8.6 % respectively, were consistent with prior research findings [4,10–14]. Moreover, chronic lung disease and renal failure also posed an increased risk of death during hospitalization and follow-up after acute MI, that consistent with previous studies [11–14]. Recognizing the prognostic significance of these non-cardiovascular comorbidities is essential for enhancing risk assessment and improving patient outcomes in the context of acute MI.

The prognostic value of comorbidity have been demonstrated in the previous studies [4,15–18]. For instance, In a prospective multicenter observational study involving 29,620 acute MI patients, 46.8 % had comorbidities [4], after adjusting for age and gender, strong predictors of in-hospital mortality were heart failure (adjusted OR 1.88; 95 % CI 1.57–2.25), metastatic tumors (OR 2.25; 95 % CI 1.60–3.19), renal diseases (OR 1.84; 95 % CI 1.60–2.11), and diabetes mellitus (OR 1.35; 95 % CI 1.19–1.54). Further adjustment revealed that the CCI was an independent predictor of in-hospital mortality: CCI = 1 had an OR of 1.36 (95 % CI 1.16–1.60; p = 0.001), CCI = 2 was 1.65 (95 % CI 1.38–1.97; p = 0.001), and CCI ≥ 3 showed an OR of 2.20 (95 % CI 1.86–2.57; p = 0.001). When combining all comorbidities in the CCI, age, and sex in ROC curve analysis, the AUC was 0.761 (95 % CI 0.748–0.773) for in-hospital mortality prediction. In a separate investigation involving 1,035 acute MI cases, Núñez et al. included 1,035 consecutive patients diagnosed with acute MI, demonstrating that a higher

CCI score independently predicted mortality or acute MI within 30 days and one year [18].

While the CCI demonstrates satisfactory predictive capabilities for mortality [4, 19], data on its potential additional prognostic value in comparison to the GRACE score remains limited [20, 21]. The GRACE score is routinely utilized to forecast in-hospital and 6-month mortality among ACS patients but does not incorporate comorbidity information. In a study by Erickson et al. [21] involving 1,202 ACS patients, have suggested that the performance of GRACE score improves when co-morbidity scores such as CCI are added to the risk scores. The GRACE score exhibited the highest AUC for predicting inpatient mortality (0.73, compared to 0.68 for CCI). When CCI was combined with the GRACE score, the AUC reached 0.81 for predicting death during the 6-month follow-up period, that consistent with our results. In contrast, in the MADDEC study (Mass Data in Detection and Prevention of Serious Adverse Events in Cardiovascular Disease), included 1576 consecutive patients undergoing invasive evaluation and treated for ACS were found that the CCI was not superior to the GRACE score at the 2-year follow-up and made no additional contribution [20]. However, the age disparity between the participants in that study and ours, coupled with the exclusion of patients not receiving invasive treatment in our study due to their poor overall prognosis, likely attributed to a high comorbidity burden, may explain this difference. Comorbidity indices assume greater importance for these patients, given that comorbidity burden tends to increase with age, rendering elderly patients more susceptible and fragile.

Our study has limitations. Firstly, being an observational study, it is subject to inherent constraints such as nonrandomization and the presence of unmeasured confounding factors, which cannot be entirely eliminated. Nevertheless, well-designed observational studies can yield valid results without systematically inflating outcomes compared to randomized controlled trials. Secondly, the CCI employed in our study is over 30 years old, and the clinical definitions of specific conditions, such as renal failure, have undergone significant evolution since its inception. This evolution may render it impractical to accurately assess the impact of these conditions on comorbidity burden and prognosis using the traditional CCI format.

Conclusion

The CCI exhibited moderate prognostic efficacy in evaluating in-hospital mortality outcomes in patients with acute MI and demonstrated good predictive performance for long-term mortality. Furthermore, the inclusion of the CCI and its specific components, namely chronic lung disease and renal failure, contributed additional prognostic significance beyond the GRACE score, enhancing the ability to predict both short-term and long-term adverse outcomes.

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Прогностическая значимость индекса коморбидности Чарльсона у пациентов, госпитализированных с острым инфарктом миокарда

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Аннотация. *Актуальность*. Изучить прогностическую значимость индекса коморбидности Чарльсона (ИКЧ) и его компонентов в оценке исходов внутрибольничной и 18-месячной смертности и определить дополнительную прогностическую ценность при включении их в шкале GRACE у больных острым инфарктом миокарда (ИМ). *Ма-*

териал и методы. В проспективном исследовании включали 712 пациентов с диагнозом острым ИМ, подвергшихся коронарографии в течение 24 часов после госпитализации. *Результаты и обсуждение.* Среди пациентов 61 % были мужчины, медиана возраста составила 65 лет (интерквартильный размах [ИКР] 56–74 года). Частота внутрибольничной и 18-месячной смертности составила 5,1 % (n = 36) и 12,1 % (n = 86), соответственно. Медианы баллов по шкалам GRACE и ИКЧ составили 117 (ИКР: 98–141 балл) и 4 (ИКР: 3–6 баллов) соответственно. Среди ИКЧ компонентов, распространенными сопутствующими заболеваниями были предыдущий ИМ (21,8 %), сахарный диабет (21,1 %), хроническое заболевание легких (16,2 %), деменция (9,2 %), язвенная болезнь желудка и двенадцатиперстной кишки (9,1 %), почечная недостаточность (8,6 %). Факторы ассоциированы с внутрибольничной и 18-месячной смертностью были хроническое заболевание легких (отношение шансов [ОШ] = 4,21 и 2,04, соответственно) и почечная недостаточность (ОШ = 3,51 и 1, 99, соответственно) после коррекции шкалы GRACE. Деменция (ОШ 2,10; 95 % доверительный интервал [ДИ] 1,11–3,97) была значимым фактором риска для летальности в течение 18 месяцев. CCI ассоциировался с внутрибольничной и 18-месячной летальностью (GRACE скорректированный ОШ 1,29, 95 % ДИ: 1,07–1,57, p = 0,001 и 1,37, 95 % ДИ: 1,20–1,57, p = 0,001, соответственно). CCI продемонстрировал хорошую предсказательную способность для внутрибольничной смертности (площадь под ROC-кривой [AUC]: 0,826) и умеренную эффективность для смертности через 18 месяцев (AUC: 0,797). Добавление хронического заболевания легких и почечной недостаточности в шкале GRACE значительно улучшило эффективность предсказания внутрибольничной летальности, с AUC 0,932 (95 % ДИ: 0,905–0,959, p = 0,001). Для предсказания летальности через 18 месяцев включение CCI в шкалу GRACE повысило эффективность предсказания (AUC 0,819, 95 % ДИ: 0,768–0,871, p = 0,001). *Выводы.* ИКЧ имел умеренное прогностическое значение в оценке исходов внутрибольничной смертности у больных с острым ИМ и хорошее для прогнозирования долгосрочной смертности. ИКЧ и его компонентов (хронические заболевания легких, почечная недостаточность) добавили прогностическую значимость в дополнение к шкале GRACE в прогнозировании внутрибольничных и долгосрочных неблагоприятных исходов.

Ключевые слова: индекс коморбидности Чарльсона, сопутствующие заболевания, смертность, инфаркт миокарда, шкала GRACE

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