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Clinical Research

Usefulness of Clinical Data and Biomarkers for the Identification of Frailty After Acute Coronary Syndromes

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ABSTRACT

Background: Frailty predicts mortality after acute coronary syndrome (ACS). The standard frailty scales, such as the Fried score, consist of a variety of questionnaires and physical tests. Our aim was to investigate easily available clinical data and blood markers to predict frailty at discharge, in elderly patients after ACS.

Methods: A total of 342 patients older than 65 years, survivors after ACS, were included. A high number of clinical variables were collected. In addition, blood markers potentially linked to frailty and related to the processes of inflammation, coagulation, hormonal dysregulation, nutrition, renal dysfunction, and heart dysfunction were determined. Frailty was evaluated using the Fried score at discharge. The main

RÉSUMÉ

Renseignements généraux : La présence de fragilité après un syndrome coronarien aigu (SCA) est un prédicteur de mortalité. Les échelles d'évaluation normalisées de la fragilité, telles que l'échelle de Fried, sont composées d'un éventail de questionnaires et de tests physiques. L'objectif de l'étude était d'évaluer les données cliniques facilement accessibles ainsi que les marqueurs sanguins, afin de prédire le risque de fragilité chez les patients âgés qui ont subi un SCA à leur sortie de l'hôpital.

Méthodologie : Un total de 342 patients âgés de plus de 65 ans ayant survécu à un SCA ont été admis à l'étude. Un grand nombre de variables cliniques ont été recueillies. De plus, les marqueurs sanguins

Frailty is a state of functional decline affecting elderly patients that increases their vulnerability to adverse events beyond age.[1] Its role in cardiovascular disease is increasingly acquiring importance.[2,3] Indeed, frailty has demonstrated to worsen the prognosis in a wide variety of cardiovascular syndromes and interventions.[4-10] The underlying mechanisms involved in frailty status are not well defined. Conceivably, deficits in multiple organs can occur, particularly in the brain, endocrine system, immune system, and skeletal muscle.[11] As a surrogate of these dysfunctions, a biochemical profile has been suggested for the frail patient consisting of the elevation of inflammatory markers, hypercoagulability, and hormonal as well as nutritional alterations.[12]

Some tools are used to classify and categorize frailty including questionnaires and physical tests.[13] It is unclear, however, how practical it is to implement all these assessments outside of the geriatric clinic. Currently, elderly patients admitted with acute coronary syndromes receive early invasive management and tend to be quickly discharged.[14,15] Furthermore, cardiologists are not familiar with the standard frailty tools.

In a previous study, we analyzed the prognostic value of several geriatric conditions, such as frailty, physical disability, instrumental disability, cognitive impairment, and comorbidity, in elderly patients hospitalized with an acute coronary syndrome (ACS).[16] Frailty was the strongest predictive geriatric condition for postdischarge mortality. In the present study, we investigated easily available clinical data and blood markers for the identification of frailty at the time of hospital discharge among survivors after an ACS. The Fried score, one

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outcome was frailty defined by a Fried score ≥ 3 points. Secondary endpoints were mortality and myocardial infarction at 30-month median follow-up.

Results: A total of 116 patients were frail. Seven clinical variables or biomarkers predicted frailty: age ≥ 75 years, female, prior ischemic heart disease, admission heart failure, haemoglobin ≤ 12.5 g/dL, vitamin D ≤ 9 ng/mL, and cystatin-C ≥ 1.2 mg/L. This model based on clinical data and biomarkers showed an excellent discrimination accuracy for frailty (C-statistic = 0.818). During the follow-up, 105 patients died and 137 died or suffered myocardial infarction. The clinical data and biomarker model (C-statistics = 0.730 and 0.691) performed better than the Fried score (C-statistics = 0.676 and 0.650) for death and death or myocardial infarction, respectively.

Conclusions: Easy available clinical data and biomarkers can identify frail patients at discharge after ACS and predict outcomes better than the standard Fried's frailty scale.

possiblement associés à la présence de fragilité et aux processus de l'inflammation, de la coagulation, du déséquilibre hormonal, de la nutrition et de la dysfonction rénale et cardiaque ont été déterminés. Le degré de fragilité a été évalué au moyen de l'échelle de Fried à la sortie de l'hôpital. Le critère d'évaluation principal était le degré de fragilité, défini par un score ≥ 3 points à l'échelle de Fried. Les critères d'évaluation secondaires étaient les taux de mortalité et d'infarctus du myocarde notés lors du suivi médian de 30 mois.

Résultats : Un total de 116 patients ont démontré des signes de fragilité. Sept variables cliniques et biomarqueurs ont permis de mettre en évidence la présence de fragilité : âge ≥ 75 ans, sexe féminin, antécédents de cardiopathie ischémique, insuffisance cardiaque nécessitant une hospitalisation, taux d'hémoglobine ≤ 12,5 g/dl, taux de vitamine D ≤ 9 ng/ml et taux de cystatine C ≥ 1,2 mg/l. Ce modèle, basé sur les données cliniques et les biomarqueurs, a démontré une excellente exactitude discriminatoire quant à la fragilité (statistique C [surface sous la courbe de la fonction d'efficacité de l'observateur] = 0,818). Au cours du suivi, 105 patients sont décédés et 137 ont subi un infarctus du myocarde ou en sont décédés. Le modèle basé sur les données cliniques et les biomarqueurs (statistique C = 0,730 et 0,691) a généré de meilleurs résultats que l'échelle de Fried (statistique C = 0,676 et 0,650) quant au taux de mortalité et au taux d'infarctus du myocarde ou de décès y étant associé, respectivement.

Conclusions : Les données cliniques facilement accessibles et les biomarqueurs permettent de cibler les patients fragiles ayant subi un SCA à la sortie de l'hôpital et de prédire des résultats plus justes que l'échelle d'évaluation normalisée de la fragilité de Fried.

of the best-known frailty instruments, was used as a gold standard reference for the definition of frailty.[13]

Methods

Study design

This is a prospective, single centre cohort study including 342 consecutive patients (from October 1, 2010, to February 1, 2012), more than 65 years old, hospitalized for an ACS, who survived the hospitalization period and in whom frailty status was assessed at discharge. Therefore, this study focused on post-ACS frailty because the patient status before the ACS was unknown and, consequently, we cannot rule out that the frail status had been acquired with hospitalization. The setting was the Cardiology Department of the University Clinic Hospital, Valencia, Spain. Precise details of the study design are available in a previous study.[16] In brief, all patients presented at the hospital with the chief complaint of acute chest pain leading to the diagnosis of ACS. Both ST-segment elevation and non−ST-segment elevation ACSs were included. Troponin elevation was observed in 92% of the patients (Elecsys hs-cTnT assay, Roche Diagnostics, Basel, Switzerland; myocardial infarction diagnosis cutoff ≥ 14 ng/mL). In the remaining patients with normal troponin, the diagnosis of unstable angina was established by a positive noninvasive stress test (either exercise test or cardiac magnetic resonance with dipyridamole) or by the evidence of significant stenosis in the coronary angiogram. Exclusion criteria were a prior diagnosis of heart disease other than ischemic heart disease, and the indication of coronary surgery during hospitalization because the assessment of frailty was timed at discharge, so the own consequences of the surgical procedure would confound this assessment. The study was reviewed and approved by the Ethics Committee of the Hospital Clínico Universitario of Valencia. All patients provided consent to enter the study.

Frailty assessment

Frailty was measured using the Fried scale.[13] This scale requires the evaluation of 5 items: weight loss (self-reported unintentional weight loss), physical activity (Minnesota Leisure Time Activity questionnaire), walk time (defined as the time taken to walk 4.57 m), grip strength (using a hand-held isometric dynamometer), and exhaustion (self-reported based on 2 questions from the Center for Epidemiological Studies−Depression scale). The method for quantifying the scale is described in Supplemental Table S1.

Data collection

A large amount of data was collected on the following domains: clinical (age, gender, smoking, hypertension, hypercholesterolemia, diabetes, prior documented ischemic heart disease if prior documented myocardial infarction or coronary revascularization, prior admission by heart failure, prior stroke, and prior peripheral artery disease), hemodynamic (admission systolic and diastolic blood pressure, heart rate, and heart failure [Killip grade ≥ 2]), electrocardiogram (ST-segment elevation, ST-segment depression, T-wave inversion, and atrial fibrillation at admission), routine blood tests (admission haemoglobin, white cell count, and