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Original Study

Cardiac and Inflammatory Biomarkers and In-hospital Mortality in Older Medical Patients

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A B S T R A C T

Objectives: Increasing evidence has mounted in recent years on the potential prognostic role of biomarkers out of cardiac-specific medical settings. We aimed to test whether cardiac and inflammatory biomarkers are independently associated with in-hospital mortality in older unselected medical inpatients undergoing standardized multidimensional evaluation.

Design: Observational study conducted in a metropolitan university-teaching hospital. A standardized, multidimensional analysis was carried out on all patients by using medical and hospital discharge documentation and interview results integrated with information collected from family members or caregivers.

Participants and setting: Patients older than 65 years consecutively admitted to the acute geriatric ward and to 2 acute medical wards of the hospital.

Results: Male sex; low systolic blood pressure; APACHE score; functional impairment in activities of daily living (ADLs), instrumental ADLs, and Short Physical Performance Battery (SPPB); cognitive impairment; malnutrition; low albumin values; and elevated values of inflammatory and cardiac biomarkers were significantly associated with in-hospital mortality at univariate analysis. After multivariate analysis, male sex, low systolic blood pressure values at entry, severe cognitive impairment, and low functional performance measured by the SPPB resulted to be independently associated with in-hospital mortality.

Conclusions: The main finding of the present study is that these biomarkers, although associated with in-hospital mortality, do not have independent predictive significance when a comprehensive and multidimensional evaluation is conducted. The main clinical implication is that our findings should discourage the indiscriminate recourse to measurement of cardiac and inflammatory biomarkers, at least in older medical inpatients, thereby reducing a patient's hospital cost and potentially minimizing further unnecessary diagnostic procedures.

Many years have passed since cardiac and inflammatory biomarkers have been recognized as important tools for diagnosis and prognosis of well-defined disease-groups in medical settings. Cardiac troponins (cTns) and natriuretic peptides (NPs) are the cornerstone for diagnosis of acute cardiac ischemic syndromes and decompensated heart failure, respectively.[1–3] C-reactive protein (CRP) has been shown to be of clinical utility for diagnosis and prognosis of several inflammatory and infective diseases.[4] Moreover, cTns, NPs, and CRP have been demonstrated to be of prognostic value in most acute and subacute cardiac diseases.[5,6]

However, increasing evidence has mounted in recent years on the potential prognostic role of these biomarkers outside of these specific medical settings.[7,8] High levels of cTns have been reported to be associated with increased mortality among older critical patients admitted to intensive medical units,[9] as well as in patients with end-stage renal disease, acute stroke, and pulmonary embolism.[10–12] High levels of CRP have been described to be associated with an increased risk of dying in patients hospitalized with several acute medical problems.[13,14] Therefore, there seems to be a potential prognostic role for these biomarkers in several medical acute conditions, and it is becoming common clinical practice, despite the absence of definitive evidence, to include these biomarkers in the routine chemistry at hospital admission in most acutely hospitalized patients.

The authors declare no conflicts of interest.

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Evidence about the prognostic significance of these biomarkers in elderly patients is sparse and conflicting. Elevated levels of CRP have been found to be associated with functional impairment,[15] with reduced adjusted overall survival among community-dwelling older individuals,[16,17] and with increased mortality among older critical patients admitted to intensive medical units[13]; moreover, increased levels of CRP are commonly associated with presence and severity of frailty syndrome, which is a recognized predictor of unfavorable outcomes, such as mortality and institutionalization.[18,19]

Actually, evaluation of prognosis in older hospitalized medical patients is a complex procedure, including not only the acute physiological impairment, but also several preexisting conditions, such as loss of functional independence or poor physical performance.[20,21] Although short standardized tools for this comprehensive evaluation of older inpatients have been proposed in recent years,[20,22] it remains a time-expensive procedure, not easily affordable in the overcrowded setting of acute and intensive medical units.

Therefore, there seems to be a solid background to hypothesize that inflammatory and cardiac biomarkers might have predictive value for unfavorable outcome in elderly hospitalized patients. If cardiac and inflammatory biomarkers proved to carry an independent prognostic value, above clinical multidimensional evaluation, it would be of clinical relevance and might substantially simplify the prognostic evaluation in older medical patients.

To our knowledge, no study has addressed the potential utility of cardiac and inflammatory biomarkers for in-hospital prognosis in older medical unselected patients. We hypothesized that in older patients these biomarkers might act as surrogates of frailty and acute cardiac and physiological impairment, and hence might be a reliable substitute for conventional comprehensive evaluation. Therefore, in the present study we aimed to test whether cardiac and inflammatory biomarkers are independently associated with in-hospital mortality in older unselected medical inpatients undergoing standardized multidimensional evaluation.

Methods

This observational study was conducted in a metropolitan university teaching hospital, in northern Italy, according to the Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects. It was conducted on patients older than 65 years consecutively admitted to the Acute Geriatric Ward and to 2 Acute Medical Wards of the hospital between July 1, 2011 and January 30, 2012.

All patients signed an informed consent the first hospitalization day.

A standardized, multidimensional analysis was carried out on all of the patients using medical and hospital discharge documentation, and interview results integrated with information collected from family members or caregivers in the case of patients with cognitive impairment or incapable of collaboration. The data were collected by 2 resident doctors under the supervision of 2 senior specialists in geriatrics, by means of standardized protocols. Demographic (age, gender, and marital status) and clinical information (main and secondary discharge diagnosis according to the International Classification of Diseases, Ninth Revision, Clinical Modification) were collected. Standardized scales were used for the evaluation of functional autonomy, cognitive status, number and severity of diseases, nutritional status, and acute physiopathological impairment. Functional status was classified according to the activities of daily living (ADL) and instrumental activities of daily living (IADL) scales in reference to the patient's condition before admission. Cognitive status was evaluated using the Short Portable Mental Status Questionnaire (SPMSQ). Nutritional status was evaluated using the Mini Nutritional Assessment short form (MNA) through direct interview of the patient or carer for patients incapable of collaboration. Comorbidity was evaluated using the Cumulative Illness Rating Scale (CIRS), including a severity index and a comorbidity index. Severity of acute critical illness was evaluated using the Acute Physiology and Chronic Health Point Evaluation (APACHE II) score. The lower body function has been evaluated using the Short Physical Performance Battery (SPPB), which includes 3 objective tests: a timed walk, repeated chair stands, and standing balance.

The first day of hospitalization, common vital signs were collected for every patient (blood pressure, heart rate, respiratory rate, oxygen saturation, body temperature). Venous blood samples for CRP, N-terminal prohormone of brain natriuretic peptide (NTproBNP), and high-sensitivity cardiac troponin T (hs-cTnT) were obtained with routine blood chemistry at hospital admission. CRP was measured using immunoturbidimetric assay on Cobas Roche automated clinical chemistry analyzers as described by producer: human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies; the aggregates are determined turbidimetrically. NTproBNP levels were measured using Cobas Roche, located in the laboratory of San Giovanni Battista Hospital, proBNP assay that contains 2 monoclonal antibodies that recognize epitopes located in the N-terminal part of pro-BNP. The hs-cTnT was measured using the ultrasensible technique Cobas Roche Troponin T hs assay, which uses 2 monoclonal antibodies specifically directed against human cardiac troponin T, as described by producer.

Exclusion criteria included incomplete data collection, patients not admitted from the emergency department, terminal illness, and death within 48 hours from admission.

Table 1
Baseline Sample Characteristics

Variable	
Age, y, mean ± SD	82.0 ± 7.7
Male sex, n (%)	571 (35.2)
Systolic blood pressure, mm Hg, mean ± SD	127.7 ± 21.2
Diastolic blood pressure, mm Hg, mean ± SD	73.7 ± 10.6
Heart rate, beats per minute, mean ± SD	83.4 ± 16.9
ADL (number of lost functions), median (25°–75°)	3 (1–6)
Dependent in daily basal activities (ADL ≥2), n (%)	881 (54.3)
Dependent in instrumental daily activities (IADL ≤9), n (%)	1321 (81.5)
SPPB (score), median (25°–75°)	1 (0–5)
Poor lower extremity performance (SPPB7), n (%)	1220 (75.3)
Cognitive impairment (SPMSQ ≥3), n (%)	941 (58)
Malnutrition (MNA ≤7), n (%)	1049 (64.8)
APACHE II score, mean ± SD	9.3 ± 3.9
CIRS: severity index (score), median (25°–75°)	1.61 (1.38–1.85)
CIRS: comorbidity index (score), median (25°–75°)	3 (2–4)
Main diagnosis: cardiologic diseases, n (%)	319 (19.7)
Main diagnosis: vascular diseases, n (%)	99 (6.2)
Main diagnosis: respiratory diseases, n (%)	370 (22.8)
Main diagnosis: gastrointestinal diseases, n (%)	213 (13.1)
Main diagnosis: renal diseases, n (%)	50 (3.1)
Main diagnosis: genital-urinary diseases, n (%)	31 (1.9)
Main diagnosis: muscle-skeletal-skin diseases, n (%)	129 (8.0)
Main diagnosis: nervous system diseases (exclusion of dementia), n (%)	161 (9.9)
Main diagnosis: endocrine-metabolic diseases, n (%)	129 (7.9)
Main diagnosis: psycho-comportamental diseases (inclusion of dementia), n (%)	120 (7.4)
Creatinine, mg/dL, median (25°–75°)	1.08 (0.82–1.53)
Hemoglobin, g/dL, median (25°–75°)	11.6 (10.2–13)
Albumin, mg/dL, mean ± SD	3.3 ± 0.6
CRP, mg/L, median (25°–75°)	23.1 (4.8–81.4)
NTproBNP, pg/mL, median (25°–75°)	1140 (565.5–3243.2)
hs-cTnT, pg/mL, median (25°–75°)	0.030 (0.015–0.059)

ADL, activities of daily living; APACHHE II, Acute Physiology and Chronic Health Point Evaluation; CIRS, Cumulative Illness Rating Scale; CRP, C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; IADL, instrumental ADL; MNA, Mini Nutritional Assessment; NTproBNP, N-terminal prohormone of brain natriuretic peptide; SPMSQ, Short Portable Mental Status Questionnaire; SPPB, Short Physical Performance Battery.