Short Communication

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Chest pain management: use of troponins in internal medicine wards

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Abstract

Objectives: To probe the reference biomarkers used to manage chest pain (CP) by Italian internists.
Methods: Two hundred and fifty-seven doctors registered as members of the Federation of Associations of Hospital Doctors on Internal Medicine of the Campania Region (FADOI-Campania) were surveyed by means of Google Forms platform. Each participant was asked to report his/her sex, age, and location and hospital size (beds in hospital) in which he/she worked. Furthermore, they were asked to indicate the reference biomarker he/she usually employed in the management of patients with CP, choosing from four possible answers. In line with national and international guidelines, cardiac troponins are the gold standard biomarkers.
Results: Eighty-two internists (30 females) completed the survey. Interestingly, only 30.5% of participants indicated the cardiac troponins as reference biomarker. Moreover, internists working in medium-sized hospitals appeared to prefer the simultaneous measurement of cardiac troponins and Creatine Kinase MB Isoenzyme.
Conclusions: Given the economic impact of performing inappropriate examinations and the frequency of the CP symptom and associated diseases, rethinking pathways in a multidisciplinary and shared fashion can promote optimization and appropriateness, and therefore stop wastefulness.

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Chest pain (CP) is one of the most frequent causes of access to the emergency room [1]. A clear and meticulous definition of CP was provided by Ottani and coworkers, i.e., "a pain occurring, anteriorly, between the base of the nose and the umbilicus and, posteriorly, between the occiput and the 12th vertebra, which has no traumatic or other clearly identifiable underlying cause" [2].

In the presence of CP, the clinician's attention is mainly focused on acute myocardial infarction (AMI) and unstable angina (i.e., Acute Coronary Syndrome, ACS). However, it should not be forgotten that other factors could be included in the etiopathogenesis of CP, namely, herpes zoster, dissection, stenosis of the aortic valve, esophageal motility disorders, or gastroesophageal reflux [3]. On the other hand, CP can be the onset manifestation of various respiratory diseases: pneumonia, spontaneous pneumothorax, pleuritis and pleural effusions, pulmonary embolism, or lung cancer [4].

ACS still remains the most frequent diagnosis in patients with CP, with serious medical-legal consequences for clinicians unable to recognize it; among them, internists and emergency-medicine doctors are the most vulnerable professionals. Misdiagnosis could be due to the lack of experience, the young age of the patient, or atypical presentation [5]. Furthermore, in a high proportion of cases, the electrocardiogram may not be sufficiently diagnostic [6].

When electrocardiographic alterations are not evident, having reliable biomarkers can be of considerable diagnostic help. These markers could be the cardiac troponins (cTn), type I (cTn-I) or type T (cTn-T), i.e., regulatory proteins involved in controlling the interaction between actin and myosin. Levels of cTn increase between the 2nd and 4th hour from the onset of symptoms [7]. The well-documented clinical value of cTn, compared to other markers such as creatine kinase (CK) and its MB isoenzyme (CK-MB), has led to their adoption as gold standard cardiac biomarkers [8]. In 2016, the European Society of Cardiology (ESC) guidelines recommended the use of high-sensitivity

cardiac troponins (hs-cTn) [9]. In this manner, it is possible to detect troponin concentrations that are 5–100 times lower than those detected by conventional tests [10]. With the "new" troponins, the negative predictive power of a single test is up to 95%, becoming 100% with two tests [11].

In line with these preliminary considerations, our study aimed at assessing the correct use of biomarkers for the management of CP in Italian internal medicine wards.

Convenience sampling was used. After obtaining authorization from the presidency of the Federation of Associations of Hospital Doctors on Internal Medicine (FADOI) of the Campania Region, we accessed the FADOI-Campania member list database, and a total of 257 internists were surveyed. For each participant, the answer to the key question, i.e., "Which do you consider as the biomarker/s of reference in case of chest pain?", was stratified based on his/her sex, age, and location and hospital size in which he/she operated. Descriptive statistics are summarized in Table 1 (methods are reported underneath Table 1 in more detail). Also, a two-way chi-squared test (χ^2) was used to explore possible relationships between the qualitative independent (sociodemographic) variables and the reference laboratory tests (see Table 2). A p-value ≤0.05 was considered statistically significant. Statistical analyses were performed with IBM SPSS Statistics version 26.

Eighty-two internists (30 females and 52 males) participated in the survey (32% of the totals). The sample mainly included physicians working in Naples (54.9%), in medium-sized hospitals (52.4%), and aged 50–59 years (40.2%). Surprisingly, only 30.5% of participants selected the option "cTn or hs-cTn" as the most appropriate. Furthermore, 26.8% of participants preferred the simultaneous measurement of cTn and CK-MB, while 32.9% used to require the additional measurement of myoglobin. Finally, 9.8% of participants answered "cTn, total CK, CK-MB, myoglobin, and LDH". No significant association between the laboratory tests and sex, age, and location was shown (Table 2). Conversely, we found a significant association between laboratory test and hospital size ($\chi^2(6) = 17.053$, p=0.009, φ=0.46). The analysis of the adjusted-standardized residuals (z_r) was used as post-hoc analysis. On the one hand, the number of physicians working in medium-sized hospitals and requiring measurement of cTn/hs-cTn for CP management was significantly smaller than expected (z_r=−2.5); on the other hand, the number of physicians working in medium-sized hospitals and requiring measurement of cTn and CK-MB was larger than expected (z_r=3.2). In other words, these findings appear to suggest that internists of medium-sized hospitals preferred the measurement of cTn and CK-MB to cTn/hs-cTn.

Table 1: Descriptive statistics (n=82).

Socio-demographic variables	Participants
Sex, F/M	30/52
Age	
<40 years of age, frequency (%)	19 (23.2)
40–49 years of age, frequency (%)	14 (17.1)
50–59 years of age, frequency (%)	33 (40.2)
≥60 years of age, frequency (%)	16 (19.5)
Location	
Avellino, frequency (%)	6 (7.3)
Benevento, frequency (%)	6 (7.3)
Caserta, frequency (%)	8 (9.8)
Napoli, frequency (%)	45 (54.9)
Salerno, frequency (%)	17 (20.7)
Hospital size (beds)	
≤150, frequency (%)	19 (23.2)
151–500, frequency (%)	43 (52.4)
501–1,000, frequency (%)	20 (24.4)
Laboratory tests	
cTn or hs-cTn, frequency (%)	25 (30.5)
cTn and CK-MB, frequency (%)	22 (26.8)
cTn, total CK, CK-MB, and myoglobin; frequency (%)	27 (32.9)
cTn, total CK, CK-MB, myoglobin, and LDH; frequency (%)	8 (9.8)

cTn, cardiac troponin; CK, creatine kinase; CK-MB, creatine kinase MB isoenzyme; LDH, lactate dehydrogenase. The Google Forms platform was used to construct the survey. The latter is available, in the Italian language, at the following link: https://forms.gle/b6WGJdC9LXqpAwMn8. Each participant was asked to provide some basic information, namely, his/her sex, age, and location and hospital size in which he/she operated. The latter was obtained from the number of beds in hospital. In order to standardize the alternative answers and avoid any missing (or approximative) values, age and hospital size were operationalized as ordinal variables, with age including four levels (i.e., <40, 40–49, 50–59, ≥60 years of age) and hospital size including three levels (i.e., small: ≤150, medium: 151–500, large: 501–1,000). Thus, participant was required to indicate the reference biomarker he/she usually used for the management of patients with CP, choosing from four possible alternatives, namely, cTn or hs-cTn (correct); cTn and CK-MB; cTn, total CK, CK-MB, and myoglobin; cTn, total CK, CK-MB, myoglobin, and LDH (distractors). The incorrect answers were constructed based on the Ottani and colleagues' review on the evidence-based utility and efficacy of various CP diagnostic tools. Particularly, the authors underlined the unnecessary usage of myoglobin with respect to the cardiac troponins. Also, they strongly discouraged the evaluation of other obsolete biomarkers, such as CK-MB, total CK, and lactate dehydrogenase. The order of the alternatives was randomized within subjects. Compilation takes not even a minute. After filling in the questionnaire, participants gave their informed consent to the treatment of data by clicking on "yes". Participants were informed that data processing would be exclusively intended for the research activity, in compliance with anonymity and current privacy legislation. Conversely, participants clicking on "no" denied the consent, and their data were deleted. Data were acquired, encoded, and analyzed within one month following the survey submission. A total of 257 internists of the Campania Region were surveyed, 82 of whom gave their informed consent and completed the questionnaire in full (32%).

Table 2: Relationships between socio-demographic variables and laboratory tests as quantified by chi-squared test.

Socio-demographic variables	Laboratory tests, observed frequencies (expected)				χ^2 Test, p-value
	cTn or hs-cTn	cTn and CK-MB	cTn, total CK, CK-MB, and myoglobin	cTn, total CK, CK-MB, myoglobin, and LDH	
Sex					
Male	15 (15.9)	15 (14)	16 (17.1)	6 (5.1)	χ^2 (3)=1.005, p=0.80
Female	10 (9.1)	7 (8)	11 (9.9)	2 (2.9)	
Age					
<40 years of age	4 (5.8)	6 (5.1)	8 (6.3)	1 (1.9)	χ^2 (9)=8.108, p=0.52
40–49 years of age	4 (4.3)	4 (3.8)	4 (4.6)	2 (1.4)	
50–59 years of age	12 (10.1)	9 (8.9)	7 (10.9)	5 (3.2)	
≥60 years of age	5 (4.9)	3 (4.3)	8 (5.3)	0 (1.6)	
Location					
Avellino	1 (1.8)	1 (1.6)	4 (2)	0 (0.6)	χ^2 (12)=11.425, p=0.49
Benevento	1 (1.8)	2 (1.6)	2 (2)	1 (0.6)	
Caserta	5 (2.4)	2 (2.1)	1 (2.6)	0 (0.8)	
Napoli	15 (13.7)	13 (12.1)	12 (14.8)	5 (4.4)	
Salerno	3 (5.2)	4 (4.6)	8 (5.6)	2 (1.7)	
Hospital size					
≤150 beds in hospital	8 (5.8)	3 (5.1)	4 (6.3)	4 (1.9)	χ^2 (6)=17.053, p=0.009
151–500 beds in hospital	8 (13.1)	18 (11.5)	15 (14.2)	2 (4.2)	
501–1,000 beds in hospital	9 (6.1)	1 (5.4)	8 (6.6)	2 (2)	

cTn, cardiac troponin; CK, creatine kinase; CK-MB, creatine kinase MB isoenzyme; LDH, lactate dehydrogenase.

These results are quite interesting since (1) only a small percentage of the sampled internists followed the national and international guidelines [8, 9] and (2) the simultaneous measurement of troponins and creatine kinase does not provide substantial advantages in diagnostic terms, also against increased costs [2]. Further studies involving larger samples are needed to disentangle these controversial findings.

As for the first issue, a constant effort within the Departments of Medicine is required to maintain a high level of adherence to diagnostic prescriptions based on the available scientific evidence. This objective can be achieved, for instance, promoting further the evidence-based practice and the culture of ongoing learning.

As for the second issue, note that large-sized hospitals are those able to guarantee all the specialist expertise. Due to the wide range of services offered, these hospitals are burdened by a high number of accesses to the emergency room and accustomed to developing strict, and periodically updated, internal protocols in order to deal with the most important welfare problems in the population. Conversely, small-sized hospitals, due to the equally smaller number of beds and size of the care proposal, require a more widespread search for diagnostic and therapeutic appropriateness, with the aim of directing the instrumental tests to real positives or at least to patients with a high probability of pre-test diagnosis.

However, the medium-sized hospitals are the most representative in the Campania Region. The large number of accesses to the emergency room often makes it necessary to hospitalize patients in wards other than internal medicine's ones. This pattern can affect both the overall quality of care and diagnostic/therapeutic appropriateness, with the adoption of prescriptive panels deviating from the recommendations of experts and consensus documents. Certainly, these hypotheses alone are not sufficient to give a clear answer to our survey's results but may represent a useful point where to start from for future investigations.

In the diagnostic process of CP, the dosage of cTn is the gold standard for several years. Data that emerged from this study suggest that the tests required by internists are not always appropriate than the available scientific evidence, especially in medium-sized hospitals. Therefore, given the economic impact of carrying out inappropriate examinations and the frequency of the CP symptom, it is necessary to rethink pathways in a multidisciplinary and shared manner, in order to optimize the appropriateness and stop wastefulness.

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