

# Laboratory testing in the emergency department: an Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC) and Academy of Emergency Medicine and Care (AcEMC) consensus report

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## Abstract

The mainstay of patient-oriented laboratory testing in emergency settings entails selecting number and type of tests according to valid criteria of appropriateness.

Since the pattern of urgent tests requesting is variable across different institutions, we designed a joined survey between the Academy of Emergency Medicine and Care (AcEMC) and the Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC) for reaching tentative consensus about the most informative diagnostic tests in emergency settings. A survey, containing the most commonly performed urgent laboratory tests and the relative clinical indications, was disseminated to eight relevant members of AcEMC and eight relevant members of SIBioC. All contributors were asked to provide numerical scores for the different laboratory parameters, where 1 indicated *strongly recommended*, 2 *recommended in specific circumstances*, and 3 *strongly discouraged*. The mean results of the survey were presented as the mean of responders' values, and the parameters were finally classified as *strongly recommended* (mean value, 1.0-1.5), *somehow recommended* (mean value, 1.5-2.0), *discouraged* (mean value, 2.0-2.5) and *strongly discouraged* (mean value, 2.5-3.0). The results of the survey allowed defining a hierarchy of priority, wherein 24 tests were *strongly recommended*. The use of 5 common tests was instead *strongly discouraged*. For 16 additional parameters in the list, the consensus ranged between *somehow recommended* and *discouraged*. We hope that results presented in this joint AcEMC-SIBioC consensus document may help harmonizing panel of tests and requesting patterns in emergency setting, at least at a national level.

## Introduction

Despite it is now undeniable that laboratory tests are central to the clinical decision making in patients with both acute and chronic conditions, the appropriateness of test ordering remains crucial. Indeed, the large number of tests that become available in modern clinical laboratories thanks to automation may erode human and economic resources, especially when their prescription does not fulfill evidence-based criteria<sup>1</sup> or else inappropriate analyses may trigger additional, unjustified and even invasive investigations when eventually generating the so-called laboratory *incidentalomas* (*i.e.*, abnormalities detected by coincidence, without clinical symptoms or suspicion).<sup>2</sup> Notably, it was also shown that the median length of stay (LOS) in the emergency department (ED), even in a very developed setting, may increase by up to 10 minutes for every five additional tests ordered, and by up to 17 minutes for each 30-minute increase in turnaround time.<sup>3</sup>

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Reliable evidence attests that urgent testing represents a large part of laboratory activity, with median percentage of stat analyses approximating 33% of all tests performed in clinical laboratories.<sup>4</sup> Additional evidence suggests that the panels of tests made available to the emergency physicians are extremely heterogeneous and variegated worldwide, so highlighting a rather poorly standardized scenario.<sup>5,6</sup> A multicenter Spanish study involving 36 hospitals showed that the rate of request of stat tests ranged from 44 to 412 per 1000 ED patient admissions.<sup>7</sup> The same study showed that the Spanish hospitals would have saved up to 1,000,000 unnecessary tests if every single laboratory would have achieved the appropriate indicator.<sup>7</sup>

The mainstay of patient-oriented laboratory testing in the ED encompasses the selection of number and type of tests

according to solid criteria of appropriateness. Despite some reliable guidance about appropriate laboratory testing in the ED has been provided by the Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC-Laboratory Medicine; SIBioC),<sup>8</sup> both SIBioC and the Academy of Emergency Medicine and Care (AcEMC) have recognized the need to reach a tentative consensus about the panel of tests that could be considered more informative and hence appropriate in specific emergency conditions.

## Materials and Methods

The Board of the two Societies preliminarily identified eight members each to whom a questionnaire containing a comprehensive list of the most commonly performed urgent laboratory tests and the relative clinical indications was administered. Briefly, the survey was disseminated by sending personal emails to eight relevant members of AcEMC and eight relevant members of SIBioC, providing a short deadline for collecting responses. All contributors were asked to indicate a numerical value for each of the different laboratory parameters included in the questionnaire, in which 1 indicated *strongly recommended*, 2 indicated *recommended in exceptional circumstances* and 3 indicated *strongly discouraged*. The results of the survey were then pooled and analyzed by calculation of the mean and standard deviation (SD) of all replies. Differences between AcEMC and SIBioC replies were analyzed with Student's T test (Analyse-it, Analyse-it Software Ltd, Leeds, UK). The scored parameters were finally classified as follows: mean value between 1.0-1.5: strongly recommended; mean value between 1.5-2.0: somehow recommended; mean value between 2.0-2.5, discouraged; mean value between 2.5-3.0, strongly discouraged.

## Results

The results of the survey are shown in Table 1, including the mean values ( $\pm$ SD) and the statistical significance between SIBioC and AcEMC responders. Twenty-four parameters received such a high priority score, so that they could be defined as *highly recommended*. For two of these [*i.e.*, total creatine kinase (CK) in trauma patients and D-dimer for diagnosing venous thromboembolism], the difference of values assigned by the member of the two societies reached statistical significance, but only for total CK the priority was finally different

between SIBioC and AcEMC (highly recommended for SIBioC and recommended for AcEMC, respectively). The consensus could be listed as satisfactory (*i.e.*, P value comprised between 0.05-0.50) or optimal (*i.e.*, P>0.50) for the remaining 22 *highly recommended* tests (Table 1). For the other parameters mentioned in the survey, the final consensus ranged between *somehow recommended* and *discouraged*, whereas high consensus was found for *strongly discouraging* the use of CK isoenzyme MB and myoglobin for diagnosing acute myocardial infarction, cystatin C for diagnosing renal disease, presepsin in patients with suspected infections and hemoglobin A<sub>1c</sub> for evaluating glycemic status. The range of recommendations for the other parameters was comprised between *somehow recommended* (10 tests) and *discouraged* (6 tests) (Table 1). Among those, a disagreement between AcEMC and SIBioC was found for fibrinogen (P<0.001; strongly recommended for SIBioC and discouraged for AcEMC), CK-MB (P=0.02; strongly discouraged for SIBioC and discouraged for AcEMC), natriuretic peptides (P<0.01; somehow recommended for SIBioC and discouraged for AcEMC), urea (P=0.02; recommended for SIBioC and highly recommended for AcEMC), myoglobin in trauma (P=0.02; highly recommended for SIBioC and discouraged for AcEMC) and total calcium (P=0.01; highly recommended for SIBioC and recommended for AcEMC).

## Discussion

Previous evidence emphasized that the pattern of urgent tests requesting in emergency setting is highly variable,<sup>7</sup> thus underpinning the need to reach a more widespread consensus for harmonizing requesting attitudes. The main drivers for prescribing urgent laboratory tests in emergency settings entails obtaining data that may actually imply a substantial change in the diagnostic reasoning and/or managed care, combined with a low turnaround time (TAT), so that a timely intervention can be effectively established.<sup>9</sup> Rather understandably, inappropriateness of test ordering may have a dramatic impact on both laboratory organization and patients care. In the former case, excessive diagnostic testing may produce a negative impact on laboratory efficiency, by increasing the TAT, but also unnecessarily enhancing laboratory expenditures. More importantly, patient outcome may also be affected, since performing a large volume of inappropriate tests may encumber the possibility to rapidly analyze

the samples of patients really needing urgent data or else may potentially produce some laboratory *incidentalomas*, *i.e.*, values outside the conventional reference interval but with little clinical significance, which may then trigger unjustified, expensive and even invasive investigations.<sup>10</sup>

The term appropriateness in laboratory medicine conventionally implies the optimization of human and economic resources, contextually offering the most useful data for improving outcomes and maintaining a high level of safety.<sup>11</sup> Implicitly comprised within this concept is the fact that *inappropriateness* may also be referred to underutilization of diagnostic tests, which may potentially lead to underdiagnosis or delayed diagnosis when essential laboratory analyses are overlooked.<sup>12</sup>

A promising approach for enhancing appropriateness of urgent testing encompasses obtaining widespread consensus between emergency physicians and laboratory professionals about a list of informative tests according to specific emergency conditions. This consideration has prompted the AcEMC and SIBioC to merge their efforts and try identifying a potential list of urgent tests that can be recommended in ED patients with the most frequently diagnosed pathologies. Our survey, disseminated to eight relevant members of either society, has ultimately allowed to identify a group of 24 high priority tests, which were defined as *strongly recommended*, as well as assigning low priority to other five common tests, instead defined as *strongly discouraged* (Table 1). 16 additional tests were either ranked as *somehow recommended* or *discouraged*, so leaving some wiggle room for their implementation or elimination from the list of tests made available to the ED. This particularly refers to the 10 parameters scored as *somehow recommended* by the surveyed AcEMC-SIBioC representatives.

Along with the tests for which a general consensus was reached by the responders of the survey, other tests have necessarily to be added to the offered panel, since they allow the diagnosis and/or monitoring of certain emergency conditions. This refers, for instance, to the cerebrospinal fluid (CSF) analysis for diagnosing infections and other acute disorders of the central nervous system (*i.e.*, subarachnoid haemorrhage, acute neuroimmunological disorders, intracranial hypertension), serum  $\beta$ -HCG in the case of suspected pregnancy, specific drug testing (*e.g.*, anticonvulsants, direct oral coagulation inhibitors, *etc.*), drug of abuse screening (including ethanol) and carboxyhemoglobin measurement for suspect poisoning or intoxication. Supplementary tests to the

**Table 1. Summary of scores for laboratory testing proposed for use in the emergency department. Overall, Italian Society of Clinical Biochemistry and Laboratory Medicine and Academy of Emergency Medicine and Care mean values are reported.**

Parameters	Overall	SIBioC	AcEMC	P	Recommendation
<b>Anemia</b>					
Hemoglobin	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
Hematocrit	1.19 (0.53)	1.00 (0.00)	1.38 (0.70)	0.09	Strongly recommended
RBC count	1.06 (0.24)	1.13 (0.33)	1.00 (0.00)	0.17	Strongly recommended
MCV	1.13 (0.33)	1.25 (0.43)	1.00 (0.00)	0.07	Strongly recommended
RDW	2.00 (0.87)	2.25 (0.83)	1.75 (0.83)	0.14	Discouraged
<b>Bleeding</b>					
PT	1.06 (0.24)	1.00 (0.00)	1.13 (0.33)	0.17	Strongly recommended
APTT	1.06 (0.24)	1.00 (0.00)	1.13 (0.33)	0.17	Strongly recommended
Fibrinogen	1.56 (0.50)	1.13 (0.33)	2.00 (0.00)	<0.001	Somehow recommended
Platelet count	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
<b>Venous thromboembolism</b>					
D-dimer	1.25 (0.01)	1.00 (0.00)	1.50 (0.50)	0.01	Strongly recommended
<b>Acute pancreatitis</b>					
mylase (total)	2.50 (0.87)	2.75 (0.66)	2.25 (0.97)	0.14	Discouraged
Amylase (pancreatic)	2.00 (0.71)	1.88 (0.78)	2.13 (0.60)	0.26	Discouraged
Lipase	1.25 (0.43)	1.25 (0.43)	1.25 (0.43)	0.50	Strongly recommended
<b>Liver disease</b>					
ALT	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
AST	1.81 (0.81)	2.13 (0.78)	1.50 (0.71)	0.07	Somehow recommended
GGT	2.06 (0.56)	2.25 (0.66)	1.88 (0.33)	0.10	Discouraged
Bilirubin (total)	1.25 (0.56)	1.13 (0.33)	1.38 (0.70)	0.20	Strongly recommended
Bilirubin (conjugated)	1.94 (0.56)	1.88 (0.33)	2.00 (0.71)	0.34	Somehow recommended
<b>Acute myocardial infarction</b>					
cTnI or cTnT	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
CK-MB	2.69 (0.58)	3.00 (0.00)	2.38 (0.70)	0.02	Strongly discouraged
Myoglobin	2.94 (0.24)	2.88 (0.33)	3.00 (0.00)	0.17	Strongly discouraged
Natriuretic peptides	2.25 (0.56)	1.88 (0.33)	2.63 (0.48)	<0.01	Discouraged
<b>Renal disease</b>					
Creatinine	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
eGFR	1.63 (0.78)	1.50 (0.71)	1.75 (0.33)	0.28	Somehow recommended
Urea	1.50 (0.50)	1.75 (0.43)	1.25 (0.43)	0.02	Somehow recommended
Cystatin C	2.69 (0.46)	2.63 (0.48)	2.75 (0.43)	0.31	Strongly discouraged
Neutrophil gelatinase-associated lipocalin	2.25 (0.66)	2.13 (0.78)	2.38 (0.48)	0.24	Discouraged
<b>Muscle trauma</b>					
CK, total	1.38 (0.60)	1.00 (0.00)	1.75 (0.66)	<0.01	Strongly recommended
Myoglobin	1.81 (0.81)	1.38 (0.70)	2.25 (0.66)	0.02	Somehow recommended
Creatinine	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
LDH	2.50 (0.61)	2.38 (0.70)	2.63 (0.48)	0.22	Strongly discouraged
<b>Infection</b>					
WBC	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
C-reactive protein	1.13 (0.33)	1.00 (0.00)	1.25 (0.43)	0.07	Strongly recommended
Procalcitonin	1.81 (0.53)	1.63 (0.70)	2.00 (0.00)	0.09	Somehow recommended
Presepsin	2.88 (0.33)	2.88 (0.33)	2.88 (0.33)	0.50	Strongly discouraged
Lactate	1.19 (0.39)	1.13 (0.33)	1.25 (0.43)	0.28	Strongly recommended
<b>Ion imbalance</b>					
Calcium (total)	1.50 (0.61)	1.13 (0.33)	1.88 (0.60)	0.01	Somehow recommended
Calcium (ionized)	1.25 (0.43)	1.13 (0.33)	1.38 (0.48)	0.14	Strongly recommended
Magnesium	1.94 (0.66)	2.13 (0.78)	1.75 (0.43)	0.14	Somehow recommended
Sodium	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
Chloride	1.06 (0.24)	1.00 (0.00)	1.13 (0.33)	0.17	Strongly recommended
Potassium	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
Blood gas analysis	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
<b>Diabetes</b>					
Glucose	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)	1.00	Strongly recommended
Hemoglobin A1c	2.69 (0.46)	2.88 (0.33)	2.50 (0.50)	0.06	Strongly discouraged
Osmolality	1.50 (0.61)	1.50 (0.71)	1.50 (0.50)	0.50	Somehow recommended

SIBioC, Italian Society of Clinical Biochemistry and Laboratory Medicine; AcEMC, Academy of Emergency Medicine and Care; RBC, red blood cell; MCV, mean corpuscular volume; RDW, RBC distribution width; PT, prothrombin time; APTT, activated partial thromboplastin time; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; cTnI or cTnT, cardiac troponin I or T; CK-MB, creatine kinase MB; e-GFR, estimated glomerular filtration rate; CK, creatine kinase; LDH, lactate dehydrogenase; WBC, white blood cell count. Difference between SIBioC and AcEMC. Values within brackets express the standard deviation.

basic list that were indicated by one or more responders included ammonia, coagulation protein C, antithrombin, thyroid-stimulating hormone (TSH), surface antigen of the hepatitis B virus (HBsAg) hepatitis B core antibody (HBcAb), malaria testing, reticulocyte count, blood culture, indirect Coombs test, estimate of cardiac troponin slope, serum albumin and white blood cell (WBC) differential.

## Conclusions

Despite a few emergencies can hardly affect efficiency of laboratory services, multiple emergencies, accompanied by many tests to be performed, may disrupt the ability to timely provide test results, so influencing patient management and extending the LOS in short stay units. We hope that this joint AcEMC-SIBioC consensus report will help harmonizing the panel of tests and the requesting patterns in emergency settings, at least at the national level.

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