Protocols and guidelines

Cardiac markers in the emergency department

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Life needs answers

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A global challenge: acute cardiovascular diseases

The WHO estimates that 23.4 million people will die of CVD in 2030.[1]

Cardiovascular diseases (CVD) are a leading global cause of death. According to World Health Organization (WHO) estimates, 17.5 million people died of CVD in 2005. This is 30% of all deaths worldwide.[1] Coronary heart disease accounts for a large share of these deaths in industrialized countries.[2] Extrapolated figures suggest emerging countries will have caught up with these death rates from heart disease by 2030.[3] In India and China, the most populous countries of the world, death from coronary heart disease is expected to double between 1990 and 2020.[4]

Hence the number of patients admitted to emergency departments (ED) with acute symptoms suggestive of CVD will increase, and demands on doctors, healthcare professionals, hospitals and both public and private health services will continue to rise. For this reason, adjustments will have to be made in the structures, clinical settings and efficiency of medical care. One of the challenges for hospitals will be to provide evidence-based disease management to patients. For diseases such as acute coronary syndrome (ACS), acute heart failure (AHF) and pulmonary embolism (PE), medical societies have developed national and international guidelines to provide supporting recommendations and protocols for evidence-based diagnosis and therapy.

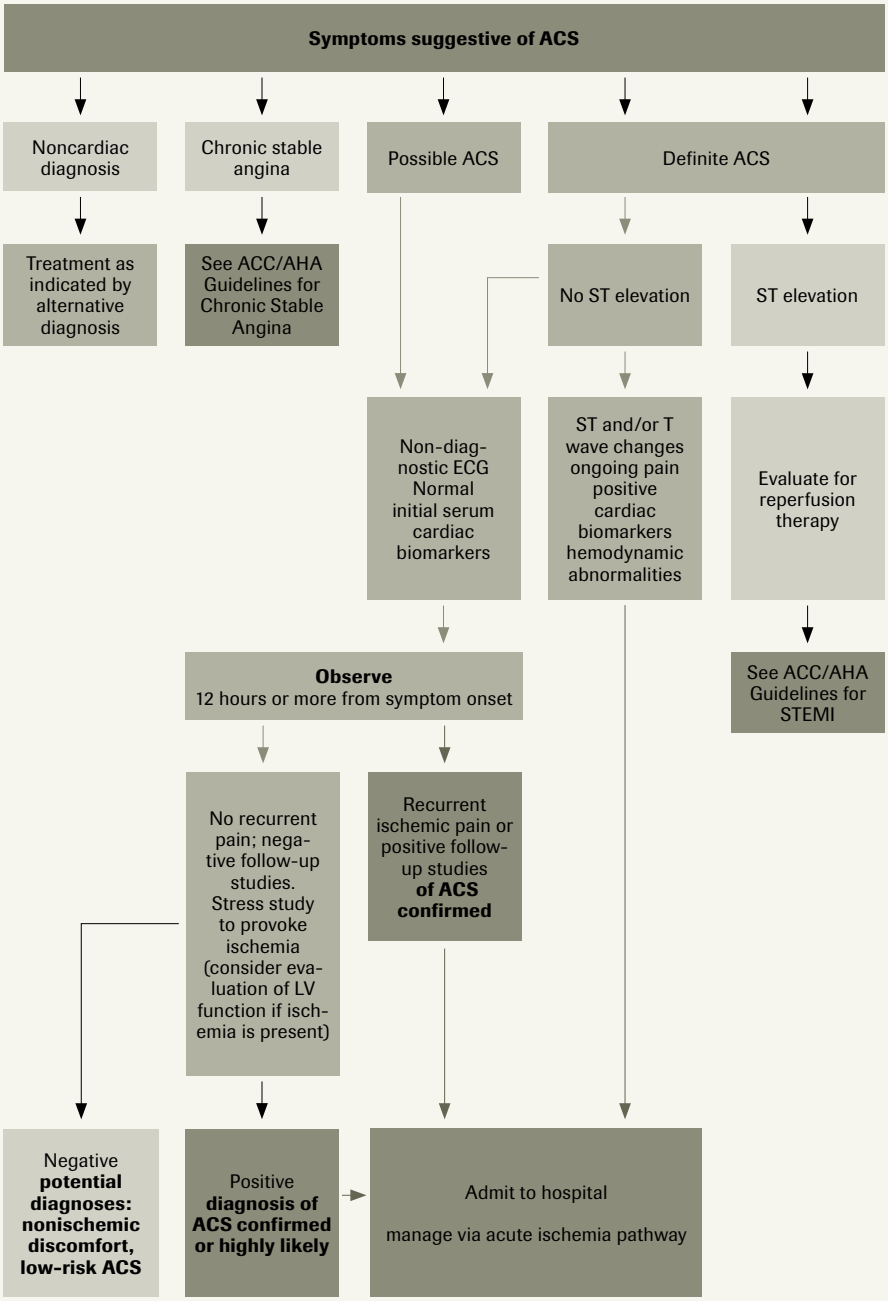
Guidance on acute coronary syndrome (ACS)

"Patients with a suspected heart attack have a right to expect prompt diagnosis, pain relief, resuscitation and, if indicated, reperfusion treatment."[5]

The term acute coronary syndrome (ACS) is used to describe the spectrum of clinical conditions ranging from unstable angina (UA) to myocardial infarction (MI), which is differentiated into non-ST-segment-elevation myocardial infarction (NSTEMI) and ST-segment-elevation myocardial infarction (STEMI).[6]

ED clinicians face the challenge of differentiating ACS from noncardiac disease. At the same time, early access to revascularization is crucial to prognosis in ACS. The guidelines of the American Heart Association (AHA), the American College of Cardiology (ACC) and the European Society of Cardiology (ESC) agree that the mainstays of rapid ACS diagnosis are history taking, 12-lead ECG, and cardiac biomarker testing.[7] A first ECG should be traced within 10 minutes when ACS is suspected.[8] A seemingly "normal" ECG does not exclude ACS. If the ECG shows no ST-segment-elevation, cardiac biomarker testing may show whether the patient has NSTEMI or UA (Figure 3).[8]

Figure 1: *Algorithm for evaluation and management of patients with suspected acute coronary syndrome (ACS)*[7]



ACC/AHA = American College of Cardiology/American Heart Association, ACS = acute coronary syndrome, STEMI = ST-segment-elevation myocardial infarction, ECG = electrocardiogram, LV = left ventricular

Biomarkers guiding ACS assessment

Several biomarkers have been investigated in recent years for use in diagnosing ACS, including cardiac troponin T and I, myoglobin, creatine kinase-MB (CK-MB) and the N-terminal prohormone fragment of the brain type natriuretic peptide (NT-proBNP).[8]

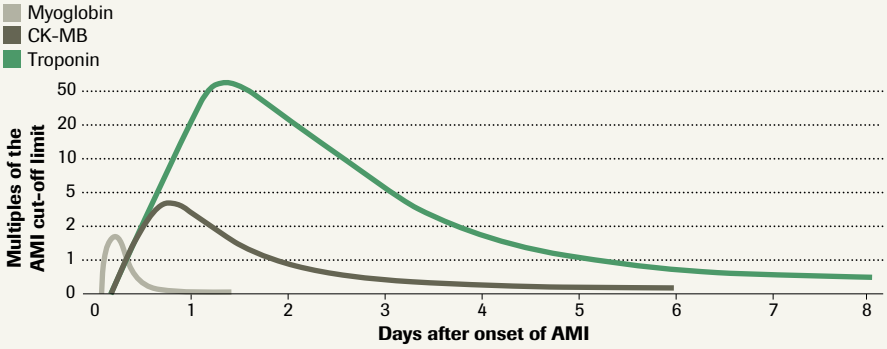
The recommendations of the American Association for Clinical Chemistry´s (AACC) guidelines reflect the guiding role of biomarkers in diagnosing ACS. These recommendations are as follows:

- Biomarkers of myocardial necrosis should be measured in all patients who present with symptoms consistent with ACS.
- Blood should be obtained for testing at hospital presentation followed by serial sampling with timing of sampling based on the clinical circumstances.
- A rapid "rule-in" protocol with frequent early sampling of markers of myocardial necrosis may be appropriate if tied to therapeutic strategies.[9]

Troponin – preferred biomarker for myocardial necrosis

American (AHA/ACC) and European (ESC) guidelines agree that the preferred marker for myocardial necrosis is cardiac troponin (I or T).[10] The subunits T and I are heart-specific proteins, generally not detected in the blood of a healthy person.[7] Troponin has nearly 100% myocardial tissue specificity as well as high clinical sensitivity. Elevated troponin levels reflect even microscopic zones of myocardial necrosis.[10] Troponin can be detected in blood as early as two to four hours after the onset of symptoms, but elevation can be delayed for up to eight to twelve hours. This timing of elevation is similar to that of CK-MB but persists longer, for up to five to 14 days (Figure 2).[7]

Figure 2: *Timing of release of various biomarkers after acute ischemic myocardial infarction*[7]



Data are plotted on a relative scale, where 1.0 is set at the AMI cut-off concentration.
AMI = acute myocardial infarction

The prominent role of troponin in diagnosing ACS is reflected in the recent definition of acute myocardial infarction (MI). The AHA defines MI as evidence of myocardial necrosis given by detecting the rise and/or fall of cardiac biomarkers (preferably troponin) above the decision limit together with a clinical setting consistent with myocardial ischemia, including symptoms of ischemia, ECG changes (new ST-T changes), new left bundle branch block (LBBB, pathological Q waves) or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.[10]

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On-the-spot decision support for acute patients

Parameters	Reaction time
Myoglobin, D-dimer	8 min
Troponin T, NT-proBNP, CK-MB	12 min

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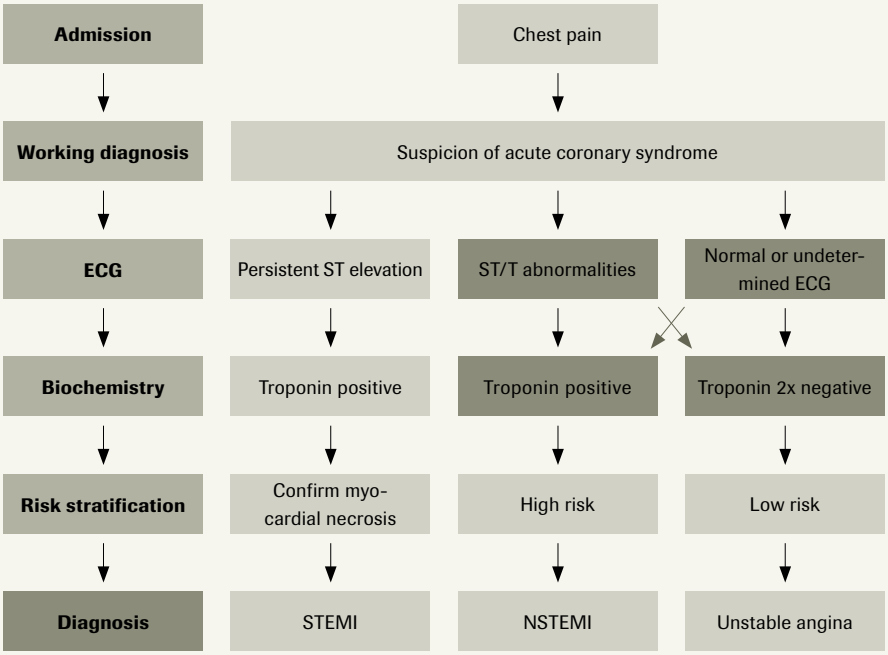
Given the marker's elevation profile (Figure 2), a single negative troponin test on arrival of the patient in the emergency department (ED), particularly within 6 hours of chest pain onset, is not sufficient to exclude MI.[11] Thus, guidelines all emphasize the need for serial troponin measurements after ED admission to detect a characteristic rise (or fall) of troponin.[8,10] Serial testing can safely distinguish patients with NSTEMI with elevated levels of troponin T or I from patients with UA (non elevated level of troponin).[8] The intervals between troponin measurements recommended in guidelines vary between 3 and 9 hours after ED admission.[8,9,10,11]

"The preferred biomarker for myocardial necrosis is cardiac troponin (I or T)."[10]

Figure 3: *Differentiating acute coronary syndromes (ACS)*[8]



STEMI = ST-segment-elevation myocardial infarction, NSTEMI = non-ST-segment-elevation MI
ECG = electrocardiogram

Although cardiac troponin accurately identifies myocardial necrosis, it does not inform as to the causes of necrosis, which can be multiple. Therefore, in making the diagnosis of NSTEMI, cardiac troponin should be used in conjunction with other criteria[7] and should be interpreted in the context of other clinical findings[8]. An elevated value of cardiac troponin in the absence of clinical evidence of ischemia should prompt a search for other etiologies of myocardial necrosis (Table 1).[10]

Table 1: *Elevations of troponin in the absence of overt ischemic heart disease*[10]

• Cardiac contusion, or other trauma including surgery, ablation, pacing, etc.
• Congestive heart failure (acute and chronic)
• Aortic dissection
• Aortic valve disease
• Hypertrophic cardiomyopathy
• Tachy- or bradyarrhythmias, or heart block
• Apical ballooning syndrome
• Rhabdomyolysis with cardiac injury
• Pulmonary embolism, severe pulmonary hypertension
• Renal failure
• Acute neurological disease, including stroke or subarachnoid hemorrhage
• Infiltrative diseases (e.g. amyloidosis, hemochromatosis, sarcoidosis, scleroderma)
• Inflammatory diseases (e.g. myocarditis, myocardial extension of endo-/pericarditis)
• Drug toxicity or toxins
• Critically ill patients, especially with respiratory failure or sepsis
• Burns (especially if affecting more than 30% of body surface area)
• Extreme exertion

Troponin elevation permits the identification of high-risk patients who will benefit from aggressive therapies such as low molecular weight heparin administration and platelet glycoprotein IIb/IIIa inhibitors or, in conjunction with overall risk assessment, a routine invasive strategy.[7] Troponins are the best biomarkers to predict short-term outcome (30 days) with respect to myocardial infarction and death. The prognostic value of troponin measurements has also been confirmed for the long term (one year and beyond). The increased risk associated with elevated troponin levels is independent of, and additive to, other risk factors such as ECG changes at rest or upon continuous monitoring, or markers of inflammatory activity.[8]

Myoglobin – an early marker of cardiac injury

Myoglobin is a low-molecular-weight heme protein found in both cardiac and skeletal muscle. It is not cardiac-specific, but is released rapidly (as early as two hours) after the onset of myocardial necrosis (Figure 2). Because it is not specific, myoglobin is not recommended for routine diagnosis and risk stratification.[8] It may be useful to assist in rapidly "ruling out" rather than "ruling in" NSTEMI, which should be confirmed by troponin measurements.[12]

Of particular emergency department interest is the recommendation concerning patients who present within six hours of the onset of symptoms consistent with ACS. Assessment of an early marker of cardiac injury (e.g. myoglobin) in conjunction with a later marker (e.g. troponin) may be considered.[7] Two myoglobin assays – each in conjunction with troponin – should be conducted 90 minutes apart.[6]

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CK-MB – marker of reinfarction

CK-MB, a longtime standard marker for the diagnosis of myocardial infarction (MI), is less sensitive and specific than cardiac troponins; however, it remains useful for the diagnosis of early infarct extension (reinfarction) and periprocedural MI because its short half-life better permits the detection of secondary increases in marker levels. The AHA MI definition states that if troponin assays are not available, there is consensus around creatine kinase-MB (CK-MB) as the best alternative marker.[10] When troponin and CK-MB are combined, patients with positive results for both markers are at highest short-term risk, those with troponin elevation alone are at intermediate risk, and those with isolated CK-MB are at lowest risk, equivalent to those with normal marker levels.[7]

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An accurate NT-proBNP test for rapid assessment of heart failure

Natriuretic peptides – markers with prognostic value

Neurohumoral activation of the heart can be monitored by measurements of systemic levels of natriuretic peptides secreted by the heart. Natriuretic peptides, such as brain type natriuretic peptide (BNP) or its N-terminal prohormone fragment (NT-proBNP), are highly sensitive and fairly specific markers for the detection of left ventricular dysfunction.[8] There are robust retrospective data in non-ST-segment-elevation ACS showing that patients with elevated natriuretic peptide levels have a mortality rate three- to five-fold higher than patients with lower levels. Values taken a few days after onset of symptoms seem to have superior predictive value when compared with measurements on admission.[8] Natriuretic peptides have been shown to provide incremental prognostic value in patient cohorts with STEMI and UA/NSTEMI and are now included in guidelines' recommendations.[8] Among patients with suspected ACS and normal troponin values, NT-proBNP was shown by a recent study to help discriminate individuals at higher risk of subsequent death.[13] A decision limit of 500 pg/ml was suggested. Furthermore NT-proBNP is a significant predictor of cardiovascular death or heart failure both in patients who did and did not undergo coronary revascularization.[14]

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- Novel markers such as S100 (brain injury) and Cystatin C (acute kidney failure)

Looking ahead: long-term prognosis with other parameters

Beside markers of myocardial injury (troponin, myoglobin, CK-MB) and of neurohumoral activation (natriuretic peptides) markers of renal function like creatinine clearance (CrCl), glomerular filtration rate (GFR) and Cystatin C as well as markers of inflammatory activity are useful predictors for long-term mortality in ACS patients.[8] Elevated levels of high-sensitive C-reactive protein (hsCRP), an inflammatory marker, are for instance predictive of long-term mortality (>6 months) even among patients with troponin negative non-ST-segment-elevation ACS.[8]

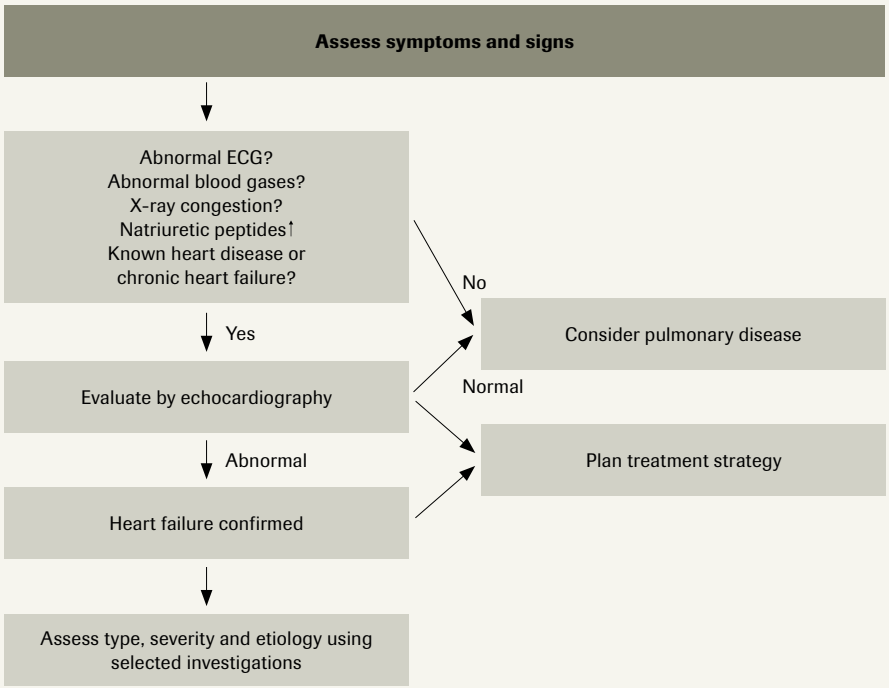
Guidance on acute heart failure (AHF)

Acute heart failure (AHF) syndrome is defined as the "gradual or rapid deterioration in heart failure signs and symptoms resulting in a need for urgent therapy".[12] Dyspnea, edema and fatigue are typical symptoms, probably accompanied by many others. AHF can present itself as acute de novo or acute decompensation of chronic heart failure. The syndrome is complex and encompasses multiple diagnoses and etiologies.[15] In the elderly population, the etiology of AHF is coronary heart disease in 60 to 70% of patients. In younger subjects, AHF is frequently caused by dilated cardiomyopathy, arrhythmia, congenital or valvular heart disease, or myocarditis.[15] The large heterogeneity of disease among AHF patients has contributed to a variability in reported definitions and terminology.[12]

"It is recommended that all AHF patients should have therapy started as early as possible, in the pre-hospital setting and in the emergency department."[16]

The emergency department (ED) plays a critical role in the management of AHF since approximately 80% of patients hospitalized for the condition (in the United States) are admitted through the ED.[12] The ACC/AHA and ESC guidelines direct the management of AHF patients, but specific consensus on early in-hospital management (first 6 to 12 hours after presentation) has not been published, primarily because few early management trials have been conducted.[15] The Heart Failure Society of America and the ESC guidelines provide some recommendations for AHF, but many of them are categorized as level of evidence C (expert opinion or small studies), recognizing the paucity of available clinical trial data supporting the recommendations. Randomized, controlled trials are needed to fully explore these hypotheses.[15]

Figure 4: *The ESC algorithm on acute heart failure diagnosis*[17]



ESC = European Society of Cardiology, ↑ = elevated natriuretic peptide level

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- Full Co-Oximetry module
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- Measured oxygen saturation

All required parameters measured in <2 min

Diagnosing acute heart failure (AHF): biomarkers and blood gases

The diagnosis of AHF in the ED is a bedside diagnosis based on clinical signs and symptoms rather than any stand-alone test results.[9] The patient should be classified according to criteria for systolic and/or diastolic dysfunction and by characteristics of forward or backward left or right heart failure.[18]

Arterial blood gas analysis (assessment of oxygenation (pO_2), respiratory function (pCO_2), acid-base balance (pH)) should be performed in all patients with severe respiratory distress.[17] Diagnostic work-up should, furthermore, include twelve-lead electrocardiogram, chest x-ray, Doppler echocardiography, clinical chemistry and specific biomarkers (e.g. BNP, NT-proBNP or troponins).

Biomarker testing has three important goals:
- To identify possible underlying (and potentially reversible causes) of heart failure
- To confirm the presence or absence of the heart failure syndrome and
- To estimate the severity of heart failure and risk of disease progression[9]

Troponin I or T should be sampled in suspected heart failure when the clinical picture suggests ACS. An elevated troponin is a strong prognostic marker in heart failure, especially in the presence of elevated natriuretic peptides.[17]

Natriuretic peptides – markers for elevated filling pressures

"In clinical practice today, the place of BNP and NT-proBNP is as, rule out, tests to exclude significant cardiac disease. … the cost effectiveness of the test suggests that a normal result should obviate the need for further cardiological tests such as in the first instance, echocardiography as well as more expensive investigations."[19]

Brain natriuretic peptide (BNP) and its co-secreted N-terminal fragment (NT-proBNP) are produced and released by cardiac myocytes in response to increased end-diastolic pressure and volume, as occurs in the setting of heart failure. Plasma concentrations of natriuretic peptides are useful biomarkers in the diagnosis of acute heart failure and in the management of patients with established chronic heart failure. Evidence exists supporting their use for diagnosing and staging heart failure, as well as making hospitalization/discharge decisions and identifying patients at risk for clinical events.[18] A single measurement is associated with reductions in treatment costs and time to discharge among patients presenting to the ED with severe acute dyspnea.[9] The analysis of natriuretic peptide levels in association with echocardiographic filling patterns can improve diagnostic accuracy, e.g. a normal level along with completely normal diastolic filling parameters make heart failure unlikely.

Despite these advances, a diagnosis of acute heart failure (AHF) will remain dependent also on a clinical assessment (Figure 4).[17,20] Several other diagnoses go along with an elevation of natriuretic peptides levels in the absence of AHF (Table 2).

Table 2: *Other diagnoses with elevated natriuretic peptide levels apart from AHF*[21]

• Acute coronary syndrome
• Cardiac structural abnormalities without acute heart failure (such as heart muscle or valve disease) arrhythmia
• Pulmonary hypertension
• Pulmonary embolism
• Sleep apnea
• Numerous other, including critical illness/sepsis syndrome, stroke, or toxic-metabolic insults (such as cancer chemotherapy)

Also, natriuretic peptide levels are reduced following long-term treatment with angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, and spironolactone.[9] These drugs are administered in patients with chronic heart failure. Age and body mass index may also influence natriuretic peptide measurements. More research is necessary to better understand the direction and magnitude of these effects to provide further specific guidance in the interpretation of results.[12]

Recommendations on NT-proBNP cut-off values

The latest ESC guidelines state that natriuretic peptides tested in the acute phase have a reasonable negative predictive value to exclude heart failure: A normal natriuretic peptide concentration in an untreated patient makes heart failure unlikely as the cause of symptoms.[17] According to the American College of Emergency Physicians (ACEP), the addition of a single BNP or NT-proBNP measurement can improve the diagnostic accuracy compared to standard clinical judgment alone in the diagnosis of acute heart failure among patients presenting to the ED with acute dyspnea (level B).[12] The Society of Chest Pain Centers (SCPC) has recently incorporated NT-proBNP as a suggested diagnostic and prognostic tool.[16] However, there are different recommendations for BNP or NT-proBNP cut-off values in the diagnosis of AHF issued by scientific societies.

Table 3: *The ACEP guidelines on assessing heart failure*[12]

NT-proBNP <300 pg/dL	Acute heart failure syndrome unlikely
NT-proBNP >1,000 pg/dL	Acute heart failure syndrome likely

NT-proBNP conversion: 300 pg/mL = 35 pmol/L

When NT-proBNP levels are elevated, the consensus workshop during the 3rd Cardiovascular Clinical Trialists Forum 2006 recommends age-related assessments of patients (Table 4).[15] The impact of introducing the age stratification of NT-proBNP is that it "reduces false-negative findings in younger patients, reduces false-positive findings in older patients, and improves the over all positive predictive value of the marker without a change in the overall sensitivity or specificity."[21] Conversely, a lack of age stratification would lead to missing younger patients as well as false positives in the older age group, which would have a negative impact on patient prognosis and hospital resources.

Table 4: *Assessment of NT-proBNP in patients with dyspnea*[15]

<300 pg/mL	Any age	Decreases the likelihood of an acute heart failure diagnosis
>450 pg/mL	In patients <50 years of age	Likely indicator of acute heart failure
>900 pg/mL	In patients 50–75 years of age	Likely indicator of acute heart failure
>1,800 pg/mL	If age is >75 years	Likely indicator of acute heart failure

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An accurate NT-proBNP test for rapid assessment of heart failure

"The most fundamental step in making the diagnosis of pulmonary embolism is first to consider it."[22]

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Roche CARDIAC D-Dimer

Highly sensitive D-dimer assay to rule out PE/DVT

Guidance on pulmonary embolism (PE)

Acute pulmonary embolism may occur rapidly and unpredictably and may be difficult to diagnose. The presentation ranges from a dramatic acute shock event to clinical silence. PE most commonly originates from deep vein thrombosis (DVT) of the legs. DVT and PE are two clinical presentations of venous thromboembolism (VTE). Symptoms and signs of VTE may reduce diagnostic delays. Leg pain, warmth, or swelling may serve as a clue. Patients with acute PE often have dyspnea or chest pain, either sudden in onset or evolving over a period of days and weeks. Pleuritic chest pain and hemoptysis occur more frequently in patients with pulmonary infarctions. Tachypnea and tachycardia are common but also nonspecific. Overall, while signs and symptoms of both DVT and PE may be highly suggestive, they are neither sensitive nor specific. Thus, when either condition is suspected, further testing must be considered.[23]

Delay in diagnosis of PE contributes to death and disability. Therefore, it is important in cases of suspected pulmonary embolism to initiate the right diagnostic measures immediately and systematically to facilitate early treatment. Guidelines agree on the steps that should be taken. Suspected PE demands prompt diagnostic testing. The basic tools for diagnosing PE are vital signs, chest x-rays, an ECG and blood gas analysis. Though the significance of each parameter on its own is limited[24], collectively they convey a good overall idea of the situation. In parallel, a careful assessment based on history, physical examination and known risk factors using one of several validated clinical prediction scores should be conducted. The tool used for this task may be less important than the principle that the individual clinical probability of actually having pulmonary embolism should be determined for each suspected PE patient.[23]

A definitive diagnosis requires imaging techniques, but clinical assessment, together with D-dimer testing, may sometimes circumvent the need for imaging and rule-out PE.[23]

Figure 5: *Diagnostic approach to suspected pulmonary embolism*[23]

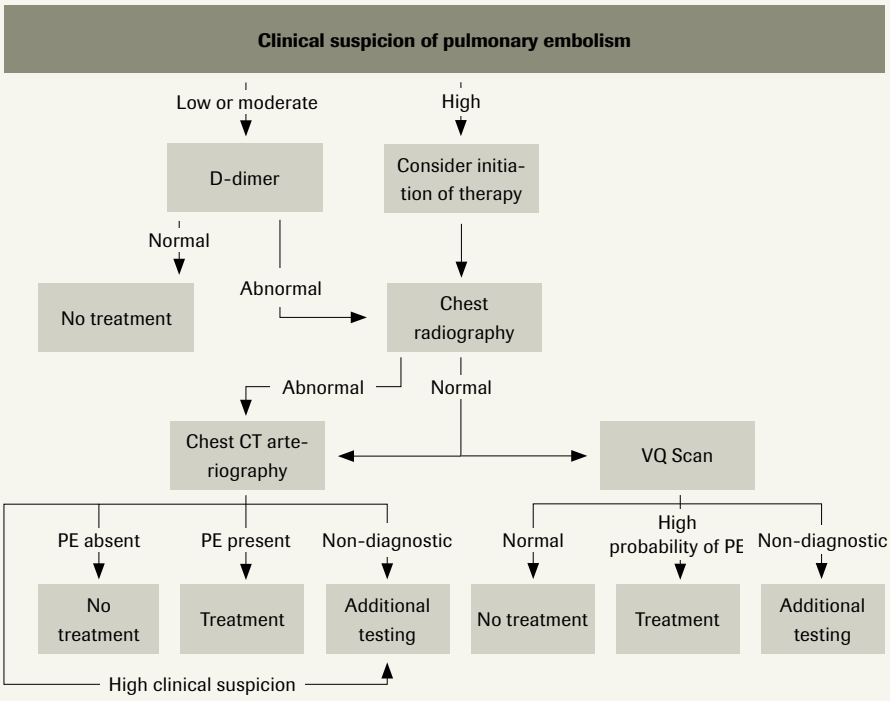

Figure modified from Tapson VF et al.
CT = computed tomography; VQ = ventilation-perfusion scan; PE = pulmonary embolism

D-dimer – a marker for endovascular thrombus

Studies on the Roche CARDIAC D-Dimer PoC test prove the high clinical correlation with other D-dimer assays.[27]

D-dimer is released as a result of fibrinolysis, and serves as a circulating marker for the presence of endovascular thrombi. Thus a negative D-dimer test can help exclude the diagnosis of pulmonary embolism (PE), following a pretest probability assessment using one of the various scoring algorithms (e.g. Wells, Wicki, GENEVA scores).[25]

Recommendations of the ESC 2008 Guidelines[26]

- D-dimer test is not useful for confirming PE.
- D-dimer should not be measured in patients with a high clinical probability of PE.
- A negative D-dimer result in a highly sensitive assay safely excludes PE in patients with a low or moderate clinical probability, while a moderately sensitive assay excludes PE only in patients with a low clinical probability.

The 2008 ESC guidelines state that "D-dimer measurement combined with clinical probability assessment is the logical first step" in patients admitted to the ED.[26]

On the other hand, raised levels of D-dimer do not infer the presence of venous thromboembolism (VTE) because such results are commonly found in hospitalized and/or post-surgery patients[28], obstetrics, peripheral vascular disease, cancer, and many inflammatory diseases, as well as increasing age.[29] Heparin use may affect the interpretation of D-dimer assays, too. Several studies have shown a fall in D-dimer levels following anticoagulation with heparin. These changes in D-dimer levels would have altered the interpretation of the assay performed as a screening test for excluding the diagnosis of VTE.[28]

Markers for risk stratification in pulmonary embolism (PE): brain natriuretic peptides and troponin

PE presents in up to 50% of cases without shock but signs of right ventricular (RV) dysfunction and/or injury.[26] Thus biomarkers are seen as useful tools in risk stratification of PE patients: "There is growing evidence that in acute PE levels of natriuretic peptides reflect the severity of RV dysfunction and hemodynamic compromise."[26] Low levels of natriuretic peptides can be reliably used for identification of patients with a good prognosis for short-term mortality or a complicated clinical outcome (NPV 94 – 100%).[26] Positive troponin test results are related to an intermediate risk of short-term mortality in acute PE. In the subgroup of hemodynamically stable patients, elevated troponin levels are associated with increased mortality. In patients with high levels of both cardiac troponin T and NT-proBNP 40-day mortality exceeded 30%, while low levels of both biomarkers indicated a good short-term prognosis.[26,30]

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A precise PoC troponin T assay

Roche CARDIAC proBNP
An accurate NT-proBNP test for rapid assessment of heart failure

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cobas h 232 system

On-the-spot decision support for acute patients

Parameters	Reaction time
Myoglobin, D-dimer	8 min
Troponin T, NT-proBNP, CK-MB	12 min

Recommendations for point of care (PoC) testing of cardiac markers

Cardiac markers can be measured in the central laboratory or with PoC instruments in the emergency department (ED) (Figure 6).

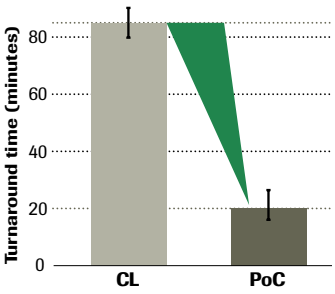
The National Academy of Clinical Biochemistry (USA) guidelines recommend:[31]

- "The laboratory should perform cardiac marker testing with a turnaround time (TAT) of 60 minutes, optimally 30 minutes, or less. The TAT is defined as the time from blood collection to the reporting of results."
- "Institutions that cannot consistently deliver cardiac marker TATs of one hour or less should implement PoC testing devices."

Studies in the ED showed that PoC tests can accelerate decision-making by providing results for cardiac markers and other time-critical parameters (e.g. electrolytes and blood gases) within 15 to 20 minutes after presentation.[11] These tests can be performed by various members of the healthcare team after adequate training. In the presence of a remaining suspicion of unstable coronary artery disease, negative tests should be repeated at a later time point and verified by a central laboratory.[8]

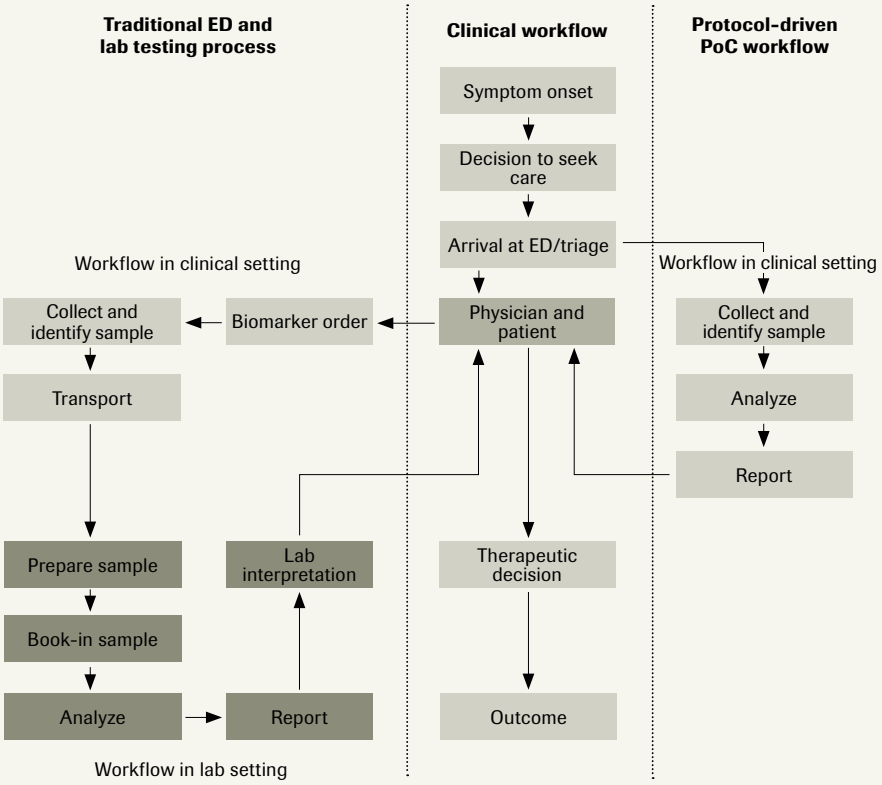
Rapid testing and reporting of cardiac marker concentrations may produce other benefits for cardiac patients. Identification of high-risk patients by rapid troponin testing has been suggested to improve outcome in those patients eligible for advanced therapies.[31]

Figure 6: *Reduction of turnaround time by PoC testing*[32]



Data for central laboratory (CL, n = 3,447) and PoC (point of care, n = 4,609) taken from 5 hospitals, blood samples from 4 emergency departments and 1 coronary care unit.
± = range (minutes)

Figure 7: *Overview of workflows using laboratory or point of care (PoC) tests*



The clinical workflow of patient management (central column) using laboratory testing (left) covers many steps in the ED and lab. Lighter boxes represent workflow the lab does not control. Darker boxes represent workflow in the lab. Each step can affect turnaround time (TAT). Clinical focus is on the time from physician order to therapeutic decision (vein to brain time). Evidence-based protocols in combination with on-site point of care (PoC) testing (right) can reduce TAT significantly by eliminating the number of steps and opportunities for delay.

Conclusions

Patients presenting with suspected cardiovascular disease in the emergency department need a rapid diagnosis and the earliest treatment decision possible. Initial diagnosis results should be considered in patient management. By speeding up evaluation time through the use of point of care (PoC) testing and guideline-recommended protocols, emergency physicians can more easily rule out or verify life-threatening conditions. PoC testing of cardiac markers adds valuable benefits to clinical assessment not only for the initial diagnosis but also in critical situations when additional risk stratification is required. A multimarker approach tailored to patient condition and history may significantly add to the ability to correctly identify patients who are at high risk. Future research and evaluation will strengthen and broaden the clinical utilization spectrum of PoC testing of cardiac markers in emergency cardiac care.

"The ability to have results available rapidly was valued by clinicians and nursing staff … as there was a direct relationship between the results produced, patient diagnosis and final patient disposition."[33]

Table 5: *Guideline recommendations on key markers used in rapid emergency care of cardiovascular diseases*

Marker	Recommendations
Troponin Troponins are the preferred markers for diagnosis and risk stratification of ACS patients.[34,35]	"The preferred biomarker for myocardial necrosis is cardiac troponin (I or T), which has nearly absolute myocardial tissue specificity as well as high clinical sensitivity, thereby reflecting even microscopic zones of myocardial necrosis."[34,35] The prominent role of troponin in diagnosing ACS is reflected in the recent definition of acute myocardial infarction (AMI): ACC, AHA and ESC define MI as evidence of myocardial necrosis given by detecting the rise and/or fall of cardiac biomarkers (preferably troponin) above the decision limit together with a clinical setting consistent with myocardial ischemia.[10]
NT-proBNP A negative NT-proBNP result safely and rapidly rules out heart failure.	ACC/AHA 2005 guidelines state that measurement of NT-proBNP can be useful in the evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of heart failure is uncertain.[20] According to the 2008 ESC guidelines NT-proBNP is useful for diagnosing and staging heart failure, as well as making hospitalization/discharge decisions and identifying patients at risk for clinical events.[17]
D-dimer D-dimer testing is used for rapid rule-out of suspected pulmonary embolism.	The ACEP recommends: "use D-dimer testing to exclude the diagnosis of pulmonary embolism in combination with pretest probability assessment."[25] The 2008 ESC guidelines state that "D-dimer measurement combined with clinical probability assessment is the logical first step" in patients admitted to the ED.[26]

ACC = American College of Cardiology, AHA = American Heart Association,
ESC = European Society of Cardiology, ACEP = American College of Emergency Physicians

cobas® contribution

Dedication to PoC testing

- Blood gas pH, pO_2, pCO_2
- Glucose, lactate
- Renal urea, creatinine
- Coagulation PT/INR
- Co-Oximetry sO_2, O_2Hb, HHb, COHb, MetHb
- Liver markers bilirubin, ALT, AST, GGT
- Electrolytes Na^+, Ca^{2+}, K^+, Cl^-
- Hematology tHb
- Cardiac markers troponin T, CK-MB, myoglobin, D-dimer, NT-proBNP

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