Accelerated Cardiac Protocols in Emergency Laboratory Medicine: Four Case Studies

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This paper illustrates the diagnostic dilemmas in a small hospital emergency department when four patients present with similar symptoms of dyspnea, angina, and edema. These cases illustrate a new role for the clinical laboratory, as the new cardiac markers and protocols help overcome the ambiguity of symptoms, delays in diagnosis, and high costs of imaging tests that may be unavailable in many small hospitals.

Frequently, dyspnea and chest pain are associated with cardiac disorders such as congestive heart failure (CHF), unstable angina, and acute myocardial infarction (MI). However, these same presenting symptoms may also be seen in obstructive pulmonary disorders, pulmonary embolism, pneumonia, and non-pulmonary disorders as diverse as anemia and anxiety.

The recent addition of troponin and myoglobin to cardiac panels and the increasing use of accelerated cardiac protocols have improved speed and accuracy in the diagnosis of MI. While certain aspects of the interpretation of troponin data remain controversial, the use of accelerated testing protocols is gaining acceptance, following the recommendations of the National Academy of Clinical Biochemistry in 1999. With the introduction of rapid laboratory testing for B-type natriuretic peptide (BNP) in 2000, the diagnosis of CHF has also become faster, easier, and more reliable.

A companion paper in this issue reviews plaque development, acute coronary syndromes (ACS), and pathophysiology of CHF.[1] In addition, the biochemistry and physiology of BNP, and the clinical evidence supporting its use in the diagnosis, risk stratification, staging, and therapeutic monitoring of CHF patients are also reviewed.

Rapid BNP assays and high sensitivity C-reactive protein (hsCRP), along with other cardiac markers, such as troponin and myoglobin, enable the clinical laboratory to assume a more active role in the diagnosis of a wide range of cardiac conditions. Rapid advances in diagnosis of cardiac disease will force clinical laboratory science (CLS) training programs to expand discussion of such topics as CHF and stable/unstable angina that were previously minimized to reflect the minimal involvement of the clinical laboratory in their diagnoses.

The Focus section seeks to publish relevant and timely continuing education for clinical laboratory practitioners. Section editors, topics, and authors are selected in advance to cover current areas of interest in each discipline. Readers can obtain continuing education credit (CE) through P.A.C.E.® by completing the tearout form/examination questions included in each issue of CLS and mailing it with the appropriate fee to the address designated on the form. Suggestions for future Focus topics and authors, and manuscripts appropriate for CE credit are encouraged. Direct all inquiries to Vicki Freeman, Dept. of Clinical Laboratory Sciences, 301 University Boulevard, Galveston, TX 77555-1028; vfreemanutmb.edu, incoming Continuing Education Editor.

ABBREVIATIONS: ABG = arterial blood gas; ACS = acute coronary syndromes; BNP = B-type natriuretic peptide; CBC = complete blood count; CHD = coronary heart disease; CHF = congestive heart failure; CLS = clinical laboratory science; CMP = comprehensive metabolic profile; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; ED = emergency department; EMT = emergency medical technician; hsCRP = high sensitivity C-reative protein; MI = myocardial infarction; NPV = negative predictive value; RAAS = renin-angiotensin-aldosterone system; UA = urinalysis; WBC = white blood count;.

INDEX TERMS: acute coronary syndromes; BNP; cardiac protocols; coronary testing; myocardial infarction.

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Focus Continuing Education Credit: *see pages 188 to 190 for learning objectives, test questions, and application form.*

LEARNING OBJECTIVES

After reading the following articles, the reader will demonstrate his/her understanding of the material by achieving the following:

1. Describe the biochemistry of the BNP and the other natriuretic peptides.
2. Describe the major physiologic responses to the elevation of BNP levels.
3. Discuss the mechanism by which the binding of BNP to the target cell results in alteration of Na^+ and water reabsorption.
4. Describe the formation of arterial plaque and the development of coronary artery disease and acute coronary syndromes (ACS).
5. Describe the physiological conditions that develop into CHF and cause the release of BNP.
6. Describe and interpret the diagnostic accuracy, sensitivity, specificity, and negative predictive values reported for rapid BNP assays.
7. Describe the trend toward "accelerated cardiac protocols," including which markers are suggested, and the suggested time-course of sequential testing.
8. Evaluate patient data and derive appropriate diagnostic conclusions.
9. Discuss the use of BNP for prognosis and screening of patients for LV dysfunction.
10. Discuss the interpretations of slightly elevated levels of troponin and C - reactive protein (CRP) as they relate to ACS and risk analysis.

FOUR CASES IN THE EMERGENCY ROOM

The four cases described below illustrate a scenario in a small hospital emergency department (ED) prior to the recent advances in cardiac testing. The epilogue, which follows the discussion, represents a 'fast-forward' to a present-day ED, with the insertion of B-type natriuretic peptide (BNP), myoglobin, and high sensitivity C-reactive protein (hsCRP) into the cardiac panel, and the use of accelerated testing protocol with specimens drawn every two hours.

Table 1. Selected admission laboratory results for Michael

Analyte	Result	Flag	Reference range
pH	7.38		7.35-7.45
PCO_2	33.0	L	34.0-46.0 mm Hg
PO_2	132	H	80-97 mm Hg
HCO_3^-(calc)	19.9	L	22.0-26.0 mmol/L
% O_2 Sat (calc)	99		95-99%
Hct	37.5	L	42-50%
Hgb	11.9	L	14.0-18.0 g/dL
WBC	15.6	H	4.8-11.8 x 10^9/L
Troponin	0.3		AMI cutoff <0.40 ng/mL
Total CK	207		20 – 220 U/L
CK-MB	3.5		0.3 – 4.0 ng/mL

Michael

Michael, a 70-year-old man with a history of congestive heart failure (CHF), lay quietly on Bed # 4 in the small hospital ED. Quietly that is, except for the constant heaving of his chest, and rapid suction of his lungs demanding more oxygen from the mask covering his face.

The arterial blood gas (ABG), complete blood count (CBC), cardiac markers, and urinalysis (UA) results were now available, since Michael had arrived by ambulance one hour earlier (selected values are shown in Table 1). His ABG results showed full compensation for the respiratory alkalosis resulting from his dyspnea. Michael's CBC indicated an elevated white blood count (WBC) count and slight anemia, his UA results (not shown) were normal except for protein (1+) and Hgb (1+), and his admission cardiac markers were high-normal (Troponin 0.3 mg/mL, CK 207, and CK-MB 3.5%).

The nurse efficiently checked his monitor for changes in electrocardiogram (ECG) rhythms, pulse, and oxygen saturation while she adjusted the flow rate of his IV. She noted that his dyspnea had improved as the 50% oxygen therapy answered his lungs' demands. His chest pain had also decreased, thanks to medication. But Michael was left alone, wondering why this pain was worse than his previous CHF episodes as the nurse scurried from the room without hearing his questions.

Charles

In Bed #5, Charles, a 68-year-old man with no history of heart or pulmonary disease, looked down at his swollen feet and pondered his recent tendency to develop angina and shortness-of-breath during normal activities. His current episode had started the previous afternoon, when he was mowing the lawn.

His decision to trade the yard work for a couple of cans of beer had temporarily improved his symptoms, but they had reappeared early this morning. With no previous records to guide their test selections, the ED staff had ordered an ECG, chest X-ray, comprehensive metabolic profile (CMP), CBC, cardiac markers, and coagulation and lipid profiles (see Table 2 below for selected values).

Like his neighbor in Bed #4, Charles' CBC indicated a slight anemia; however he had only a slight increase in WBCs (11.9 x 10^9/L). His electrolytes, liver enzymes, and coagulation values were all normal. The lipid profile showed slightly elevated cholesterol, and a poor LDL/HDL ratio (see Table 2). Charles' renal function also appeared to be compromised, with elevations in both BUN and creatinine. The ED physician was relieved to see that the cardiac markers were normal and, despite an ambiguous ECG, an MI now seemed unlikely.

The doctor's explanation of Charles' condition was not particularly informative, and had a disconcerting effect on Charles. "We'll have to see the next set of cardiac markers to be sure, but considering the time of onset of your pain, the markers should have been positive by now if you had an MI. However, your heart is somewhat enlarged, and with the shortness of breath, we're concerned about the possibility of congestive heart failure. Tomorrow we'd like to transfer you to Memorial Hospital for an echocardiogram and other testing."

Charles hardly heard another word after the phrase "heart failure." He knew little about medicine, but had his own understanding about the inevitable outcome of heart failure.

Mary

Mary's entrance into the ED was a dramatic contrast to the quiet anxiety of the other patients. She arrived by ambulance with an entourage of emergency medical technicians (EMTs) and ED staff rushing her into Room #1, while her vitals were recited rapidly. Her pale face was etched with anxiety and pain (she later rated it a 7 on the 10-point scale), but she was mainly concerned about catching her next breath without experiencing the intense pain that she knew would accompany a deep breath. Her ECG pattern was not definitive, so the ED physician ordered the standard cardiac testing profiles. The low hemoglobin and hematocrit values (included along with other selected laboratory results shown in Table 3) helped explain Mary's pale complexion, but the rest of her chemistry and hematology data offered no clear explanation of her condition.

As the oxygen mask reduced her need to gasp for breath, Mary relaxed a bit and reflected on her last, turbulent hour. Luckily, several people had witnessed her collapse, and she had received immediate attention. Mary didn't want to think about what might have happened if she had been alone. The short time between her collapse and the admission blood draws meant that the traditional cardiac markers would not yet be elevated. This, along with the inconclusive ECG had caused the physician to delay thrombolytic intervention until the next set of laboratory results could confirm her condition.

Edward

Across the hallway in Bed #2, 38-year-old Edward also gasped for breath and wondered why the pain in his chest was so intense. As a rotund, long-time smoker with worsening emphysema, Edward was accustomed to dyspnea, but he was alarmed by the intensity of this new pain. Edward also had edema, and complained of increasing lethargy. He noted that his chronic, dry cough had produced discolored sputum in recent days. Edward's chemistry test results were already available, since he had arrived four hours earlier. His coagulation values, chemistry profile, and cardiac markers were all normal (data not shown), as was his CBC, except for elevated WBCs (17.3 x 10^9/L). A sputum gram stain, showed purple diplococci with apparent capsular 'halos'. "Clearly, you have developed a strep-

Table 2. Selected admission laboratory results for Charles

Analyte	Result	Flag	Reference Range
Hct	38.1	L	42-50%
Hgb	12.9	L	14.0-18.0 g/dL
BUN	23.0	H	5-17 mg/dL
Creatinine	2.7	H	0.7-1.7 mg/dL
Cholesterol	210	H	120-200 mg/dL
LDL chol	135	Mod risk	95-130 mg/dL
HDL chol	22	L	30-75 mg/dL
Troponin	0.01		AMI cutoff <0.40 ng/mL
Total CK	45	Mod risk	20 – 220 U/L
CK-MB	Cancelled		0.3 – 4.0 ng/mL

tococcal pneumonia," the doctor stated confidently, without waiting for culture results. "We're concerned about one of your cardiac markers, but we'll watch that closely, and we'll need a few more tests to determine whether or not heart failure is contributing to your chest pain and causing the edema."

In the end, all four patients were left with several hours of discomfort and anxiety while the doctors tried to diagnose their conditions as MI, CHF, other cardiac diseases, or one of several possible pulmonary diseases.

RECENT DEVELOPMENTS IN CARDIAC MEDICINE

ACS and accelerated cardiac testing

Acute coronary syndromes (ACS) represent a wide spectrum of conditions ranging from the partial occlusions associated with mild exertional angina to the thrombosis and total occlusion of a coronary artery, which defines MI.[1,2] Plaque development is the central process in the development of ACS, and contributes directly to more than three million hospital admissions, 500,000 cardiac deaths, and over $10 billion in healthcare costs per year.[3]

Patients presenting with chest pains and dyspnea create a major diagnostic challenge for ED physicians. Physicians must quickly and accurately distinguish between MI patients in need of immediate thrombolytic intervention, and angina patients for whom thrombolytic therapy may be detrimental or even life threatening. Given the relatively short time span (20 to 30 minutes) between a thrombolytic event of an MI and the beginning of myocardial necrosis, it is obviously essential that the distinction be made rapidly. Similarly, thrombolytic therapy has a relatively short 'window' of maximum benefit once a clot has occurred. Essential laboratory data must be rapidly available so that diagnostic decisions can be made quickly. The recent emphasis on accelerated cardiac testing protocols has enabled some cardiac units to strive for diagnosis and initiation of treatment of all cardiac patients within 90 minutes of arrival at the ED.[4,5]

CHD, risk assessment, and inflammation

A primary focus in prevention of CHD for many years has been the identification of risk factors, such as family history, smoking, obesity, and total cholesterol. Overweight patients who were smokers, and had high cholesterol were counseled to alter their lifestyle to improve those risk factors that were modifiable. Recently, researchers have identified molecular level analytes that are associated with increased risk of developing CHD, such as hsCRP, homocysteine, LDL/HDL ratios, and apolipoproteins such as Apo a-1.[6] In addition, research into the plaque formation process has shown similarities with normal inflammatory processes as described in the companion review paper in this issue. For example, elevated baseline levels of the inflammatory response protein, hsCRP, have been shown to have a strong association with increased cardiac risk.[7-9]

Table 3. Selected admission laboratory results for Mary

Analyte	Result	Flag	Reference Range
Hct	32.1	L	42-50%
Hgb	9.9	L	14.0-18.0 g/dL
BUN	18	H	5-17 mg/dL
Creatinine	0.7		0.7-1.7 mg/dL
Troponin	0.01		AMI cutoff <0.40 ng/mL
Total CK	58		20 – 220 U/L
CK-MB	0.4		0.3 – 4.0 ng/mL

Background of CHF

CHF is characterized by an inability of the heart to supply sufficient circulation to the body (ischemia). Nearly five million Americans are afflicted, and it is particularly prevalent in the elderly, causing 20% of their hospital admissions.[10,11] CHF represents a major national health crisis, with 400,000 new diagnoses, 2.5 million hospitalizations per year, and nearly 50% five-year mortality.

Conditions that lead to CHF (listed in Table 1 of the companion review article)[1] can include increased vascular resistance, damaged or malfunction of cardiac tissue, and many other conditions that force the heart to compensate until it fails to maintain adequate circulation and oxygenation.[10-12]

Early stages of CHF are often asymptomatic because the heart initially compensates for the decreased circulation with an increased heart rate and hypertrophy (to increase strength of contraction). However, as circulation continues to decrease (ischemia) the kidney responds by activation of the RAAS described in the companion review article.[1] If hypoxia develops, the kidney also responds with the secretion of erythropoietin. These responses may be beneficial in cases of trauma and blood loss to protect against dehydration, hypoxia, and circulatory shock by

maintaining blood pressure and volume.[10-12] However, to the CHF patient these increases may represent harmful increases in workload for the already failing heart.

The release of BNP represents another compensation by an overloaded heart. The net effect of natriuretic peptides and BNP is the release of both sodium and water in urine, which leads to decreases in blood pressure and blood volume.[13,14] Thus, BNP counteracts the RAAS, which caused vasoconstriction, increased sodium reabsorption, and increased blood pressure.

Traditionally, the diagnosis of CHF has been based on medical history, symptoms, physical examination, ECG, chest x-ray, and non-laboratory diagnostic tests to rule out all other causes of dyspnea. Follow-up testing involved echocardiography and exercise stress tests to assess the heart's size, shape, and function. The clinical relevance of BNP relates to its critical role in the biochemical and physiological response to the pressure and volume overload conditions characteristic of CHF. The rapid and easy BNP assays now available make BNP determinations especially useful in the ED setting.

Rapid BNP improves speed of CHF diagnosis

Since their introduction in 2000, rapid BNP assays (turnaround times as low as 15 minutes) have been shown to provide valuable information for the diagnosis of CHF, which previously took several hours or even days to diagnose. One study of 250 patients reported mean BNP levels of 1076 for CHF patients, compared with a mean of 86 in chronic obstructive pulmonary disease (COPD) patients without CHF.[15] Another study reported patients presenting with dyspnea had a mean BNP levels of 758 pg/mL in those diagnosed with CHF, compared to 61 pg/mL in patients with non-CHF pulmonary diseases.[16] Numerous other studies (reviewed in reference 1) have reported similarly elevated levels of BNP in patients with CHF.

With a BNP level of 80 pg/mL established as the cutoff, the rapid assay had a sensitivity of 98% and specificity of 92% for the diagnosis of CHF.[15,17] Perhaps more important was the 98% negative predictive value (NPV), which allows physicians to confidently rule out CHF as the cause of dyspnea in patients with BNP levels below the cutoff.

BNP improves the accuracy of CHF diagnosis

In one study, two cardiologists (using additional data not available to the ED physicians) identified 30 of 250 patients who were misdiagnosed by ED physicians using traditional criteria. The use of BNP levels alone would have correctly identified 29 of these 30 misdiagnosed patients.[15] Similarly, a multinational study showed a higher diagnostic accuracy (82.1%) with BNP levels alone than clinical judgment of ED physicians who were blinded to BNP levels (74.0%). Combining clinical judgment to BNP levels only increased the diagnostic accuracy 82.5%.[17]

CHF and the clinical utility of BNP

CHF is the leading cause of hospitalization of patients over 65 years of age, with an estimated 900,000 hospitalizations a year, costing roughly $30 billion. The use of the BNP assay for CHF has the strong potential to reduce diagnostic time, reduce misdiagnosis, identify those patients most likely to experience recurrence, and monitor treatments.[10,11] In addition to the rapid diagnosis of CHF patients with very high BNP levels, the implications of normal low levels are equally valuable. The reported NPVs of greater than 98%, indicate that CHF can essentially be eliminated from the differential diagnosis when a patient's BNP level is low.

Delayed diagnosis and even misdiagnosis of patients presenting with dyspnea has been shown to be a significant and costly problem when BNP was not available and initial diagnosis was based on traditional clinical judgment. A multinational study showed that elevated BNP levels had a higher diagnostic accuracy than traditional clinical judgment by ED physicians.[17]

In general, the prognosis for CHF patients has not been encouraging, with 50% re-admission within six months after discharge, and nearly 50% five-year mortality.[10,11] Numerous studies have indicated that BNP levels could help identify patients with the poorest prognosis.[18-24] One study found that patients with high BNP levels (above 480 pg/mL) had a 51% risk of a further cardiac event (readmission or death) within six months, compared to only 2.5% reoccurrence in CHF patients with lower BNP levels.[20] Once identified, these patients could receive a more aggressive treatment and therapy could be carefully monitored using BNP levels to avoid readmissions and possibly decrease mortality rates.

ACCELERATED PROTOCOLS FOR RULE-OUT OF AMIs

Researchers have suggested the use of myoglobin, troponin, hsCRP, and BNP in accelerated protocols for exclusion of AMI as a diagnosis within 90 minutes, and diagnosis and risk stratification for most cardiac patients within the first few hours.[4,5,25-27] One group suggests that cardiac markers be repeated at 30-minute intervals for the first 90 minutes and McCord pro-

posed a protocol for exclusion of MIs within 90 minutes.[5,26] These protocols use myoglobin, a rapidly appearing, but relatively non-specific marker to obtain a rapid diagnosis or exclude MI.[25-27] Because of its non-specific nature, myoglobin's diagnostic value is limited, primarily suggesting a quick rule-out of MI in patients with normal levels.[27]

The Laboratory Practice Guidelines of the National Academy of Clinical Biochemists recommended in 1999 that markers should include troponin, to be tested at least every two to four hours. The emphasis of early decision-making within emergency medicine and cardiology is based on the benefits for patients who receive thrombolytics quickly, and the expenses saved by avoiding unnecessary admissions for observation of patients whose possible MI might be quickly ruled-out.[4,27]

Similarly, a low BNP value for a patient might avoid costly follow-up tests or hospital admission for many non-CHF patients.[11,14,18,28-30] The benefits of improved diagnostic accuracy and a NPV of 98% described earlier could prevent the enormous financial cost of misdiagnosis and, more important, avoid unnecessary suffering.[28] Thus, recent advances in cardiac diagnosis and treatments are likely to reduce hospitalization of patients, reduce hospital costs, improve the quality of patients' lives, and reduce mortality.

FAST FORWARD TO PRESENT

So what ever happened to Michael, Charles, Edward, and Mary?
In the traditional setting, the ED physician treating our four 'chest pain' patients could not reach a diagnosis, based on the data available earlier. In fact, the diagnosis for all four patients may take several hours or days, while expensive imaging or catheterization procedures are performed and interpreted. In addition 'ruleout of MI' will require sequential sets of cardiac markers to be performed at traditional six to eight hour intervals.

Was Michael having an MI or was his chest pain and dyspnea simply due to an extreme episode of his previously diagnosed CHF? Was Charles' problem related to a developing CHF, or was his dyspnea caused by development of a lung disease or infection? Was Edward's pain due to the pneumonia or was he also having an MI or possibly developing CHF? And finally, was Mary's pain and difficulty breathing due to an MI, CHF, acute respiratory disease, a pulmonary embolism, or extreme anxiety?

Answers to each of the patient conditions can be derived by analysis of the additional data in Tables 4 through 6. Additional admission results, including BNP and myoglobin levels for all four patients are shown in Table 4. Unlike the other cardiac markers, elevations in BNP and myoglobin frequently precede the patient's arrival in the ED, thus avoiding the agonizing hours of waiting for the more data. This hospital has changed its emergency procedures to adopt an accelerated protocol for cardiac cases, based upon repeat testing at two-hour intervals (data seen in Tables 5 and 6).

Michael did have an MI, probably related to the extra stress of CHF on his overworked heart. On admission his traditional cardiac markers were not yet positive for AMI (see Table 1). However, one can see from Table 4 that the initial ambiguity of his condition would have been clarified if the doctor had been aware of his admission myoglobin and BNP levels. The two-hour data confirmed that Michael was having an MI (see Table 5). Only then, was a thrombolytic initiated to dissolve Michael's clot. It was fortunate that the ED's cardiac protocol determined his diagnosis after only a two-hour delay, rather than the six to eight hour delay of their previous cardiac protocol. The data also suggests that Michael's MI had occurred several hours earlier, since his myoglobin level decreased between the two- and four-hour draws, while other markers continue to elevate. Unfortunately, the combination of damage from his MI, delayed treatment, and elevated BNP levels gave Michael a poor prognosis. His New York Heart Association (NYHA) classification had previously been II, which translates to some limitation of physical activity. The current MI further reduced his cardiac function, and Michael was reclassified to category III following this incident.
Charles was also diagnosed with CHF, which was later con-

Table 4. Admission BNP and myoglobin results for all four patients

Marker	Michael	Charles	Mary	Edward
Myoglobin (20-90 ng/mL)	1235	43	107	87
BNP (0 – 100 pg/mL)	>1300	1070	36	59
hsCRP (<1µg/mL)	35.2	1.3	3.8	105

firmed by echocardiography to be left ventricle (LV) dysfunction. Had his doctor been aware that his admission myoglobin was normal and BNP level was markedly elevated (Table 4), his preliminary diagnosis of CHF might have occurred within minutes after Charles' arrival. Without this information, the rule-out of MI took several hours (see Tables 5 and 6), and his final CHF diagnosis was only confirmed two days later, after his transfer to a larger hospital for echocardiography. His follow-up BNP levels declined significantly over the next few days with medication, indicating a much better prognosis than Michael.

Mary was also having an MI, as suggested by her slightly elevated myoglobin on admission (Table 4), and confirmed by her two- and four-hour cardiac markers (Tables 5 and 6). Mary's case illustrates one of the benefits the accelerated protocols. Her initial results, including the slightly elevated myoglobin, were hardly conclusive for an MI. When accelerated diagnostic protocols are used, the non-specificity of myoglobin leads to low confidence in positive values. Myoglobin elevations can be correlated chronologically with the chest pain when a 'delta myoglobin' value is used.[26] This method simply looks for increased myoglobin levels for sequential tests. When compared to her admission level of 107 ng/mL, Mary's two-hour level of 278 ng/mL (Table 5) represents a large increase, or delta myoglobin. Thus, despite the ambiguous results of her other two-hour markers, the large increase in myoglobin would suggest an MI before the other markers became elevated. Mary's low BNP level on admission would have essentially ruled out any likelihood of a preexisting CHF.

Edward's pneumonia was confirmed by culture, and was eventually resolved with antibiotics. His initial total CK value (185 U/L) had concerned the physician; however, subsequent decreases (Tables 5 and 6) erased the concern. Given Edward's large size, these CK values were probably normal. Both Edward and his doctor were relieved to find no evidence of CHF, as evidenced by both the admission BNP value in Table 4, and follow-up data in Tables 5 and 6. In the end, Edward was released following a stern lecture about his lifestyle and the long-term consequences of smoking.

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Table 5. Two-hour cardiac marker results for all four patients

Marker	Michael	Charles	Mary	Edward
Troponin (AMI <0.40 ng/mL)	4.3	0.014	0.4	0.012
Total CK (20 – 220 U/L)	1367	46	126	174
CK-MB (0.3 – 4.0 ng/mL)	11.8	Cancelled	3.6	Cancelled
Myoglobin (20-90 ng/mL)	1452	53	278	81

Table 6. Four-hour cardiac marker results for all four patients

Marker	Michael	Charles	Mary	Edward
Troponin (AMI < 0.40 ng/mL)	28.5	0.010	2.3	0.012
Total CK (20 – 220 U/L)	2166	55	426	171
CK-MB (0.3 – 4.0 ng/mL)	21.8	Cancelled	5.8	Cancelled
Myoglobin (20-90 ng/mL)	1128	56	572	84

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