Cocaine Positivity in ST-Elevation Myocardial Infarction: A True or False Association

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ABSTRACT

Introduction: Every year, more than 500,000 US Emergency Department visits are associated with cocaine use. People who use cocaine tend to have a lower incidence of true ST-elevation myocardial infarction (STEMI).

Objective: To identify the factors associated with true STEMI in patients with cocaine-positive (CPos) findings.

Methods: We retrospectively analyzed 1144 consecutive patients with STEMI between 2008 and 2013. True STEMI was defined as having a culprit lesion on coronary angiogram. Multivariate and univariate analyses were used to identify risk factors and create a predictive model.

Results: A total of 64 patients with suspected STEMI were CPos (mean age 53.1 ± 11.2 years; male = 80%). True STEMI was diagnosed in 34 patients. Patients with CPos true STEMI were more likely to be uninsured than those with false STEMI (61.8% vs 34.5%, p = 0.03) and have higher peak troponin levels (21.1 ng/mL vs 2.12 ng/mL, p = < 0.01) with no difference in mean age between the 2 groups (p = 0.24). In multivariate analyses, independent predictors of true STEMI in patients with CPos findings included age older than 65 years (odds ratio [OR] = 19.3, 95% confidence iterval [CI] = 1.2-318.3), lack of health insurance (OR = 4.9, 95% CI = 1.2-19.6), and troponin level higher than 0.05 (OR = 24.0, 95% CI = 2.6-216.8) (all p < 0.05). A multivariate risk score created with a C-statistic of 82% (95% CI = 71-93) significantly improved the identification of patients with true STEMI.

Conclusion: Among those with suspected STEMI, patients with CPos findings had a higher incidence of false STEMI. Older age, lack of health insurance, and troponin levels outside of defined limits were associated with true STEMI in this group.

INTRODUCTION

Among the 250,000 patients who arrive at US Emergency Departments each year with ST-elevation myocardial infarction (STEMI), a subpopulation will test positive for cocaine use.[1] The diagnosis of true STEMI in the setting of cocaine positivity can be a challenge because more than 500,000 US Emergency Department visits each year are related to symptoms and complications associated with cocaine use and, in particular, cardiovascular symptoms,[2] which usually necessitate an electrocardiogram (ECG). A new ECG ST-segment elevation finding in a patient with cardiovascular symptoms, especially chest pain and worsening shortness of breath, usually triggers cardiac catheterization laboratory activation in adherence with current guidelines.[3] However, false activation of the cardiac catheterization laboratory when treating the general population may be as high as 36%.[4] A US prospective observational study revealed a false STEMI rate of 11%,[5] and this value may be higher in the cocaine-use setting considering the prevalence of a true myocardial infarction is 0.7% to 6.0% for chest pain presentations.[2] False findings may occur because various mechanisms can cause chest pain symptoms and cardiovascular complications.[6] A better understanding of the predictors of true STEMI in the cocaine-positive (CPos) population would enable better-informed decisions between patients and physicians, leading to optimal care and avoiding complications associated with unnecessary and invasive coronary angiography. The aims of this study were to identify the frequency and factors associated with true STEMI in patients with CPos findings who present with suspected STEMI and to create a predictive model to help classify those who may be more likely to experience a true positive STEMI.

METHODS

We performed a retrospective analysis of 1144 consecutive patients with STEMI as diagnosed in our Emergency Department or an outside referring facility on presentation to the Methodist University Hospital between January 2008 and December 2013. Methodist University Hospital, a large tertiary hospital in downtown Memphis, TN, is the largest primary percutaneous coronary intervention site in the region and receives transfers from numerous outlying facilities. Institutional review board approval was obtained with an informed consent requirement waived. Coronary angiogram results in the cardiac catheterization laboratory were retrieved and analyzed. A positive urine drug screen result determined CPos. True STEMI was defined as having a culprit lesion as detected on coronary angiogram, whereas a false STEMI was defined as an absence of partial or total thrombotic coronary occlusion and/or reduced thrombolysis in myocardial infarction grade flow. Information on patient demographics, risk factors, history, initial vital signs, laboratory data, presenting ECG findings, symptom onset time, procedure times, cardiac catheterization findings, and outcomes were collected. Data were deidentified, extracted by medical residents and research assistants, and verified

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by cardiology fellows and staff cardiologists. Statistical analysis was performed with SPSS version 24 (IBM Corporation, Armonk, NY). A univariate comparison of baseline characteristics was performed using the χ^2 test. Descriptive measures used were percentages for categorical variables and means ± standard deviation for continuous variables. The incidence of false-positive STEMI was calculated as the percentage of all patients diagnosed with STEMI at presentation without a culprit lesion on coronary angiography. We conducted a comparative analysis between patients without (false-positive) and with a culprit lesion as previously described by Nfor et al,[5] and identified risk factors associated with a true STEMI in patients with CPos findings using the stepwise multivariate logistic regression and created a predictive model using logistic regression coefficients.

RESULTS

Patients with CPos findings were much younger (age 53.1 vs 59.2 years) and were more likely to be African American, have false STEMI, be uninsured, and have a history that included tobacco and alcohol use; however, these patients on average had fewer coronary artery disease risk factors than patients with negative cocaine findings (Table 1). There was no significant difference in average admission and peak troponin levels. Among patients who had true STEMI (Table 2), those with CPos findings were younger (age 54.6 vs 58.9 years, p = 0.05), more likely to be African American and uninsured and have histories including tobacco and alcohol use. They also were less likely to have multivessel disease on coronary angiography. Table 3 illustrates the differences in patient groups with true vs false STEMI who were CPos (64 patients with CPos findings were identified). One patient who was transferred from an outside facility had symptoms suggesting neurologic problems and did not undergo cardiac catheterization. Among 63 patients with CPos findings who underwent cardiac catheterization, 34 had confirmed (true) STEMI. When compared with CPos patients with false STEMI, those with true STEMI were much more likely to be uninsured, had relatively higher peak troponin levels, and had a lower left ventricle ejection fraction (43.1 vs 54.8, p < 0.01). They also required interventions to address coronary lesions in addition to medical management.

Using a stepwise multivariate analysis to eliminate interactions between confounding variables, significant independent predictors of true STEMI in cocaine positivity included age older than 65 years (odds ratio [OR] = 19.3, 95% confidence interval [CI] = 1.2-318.3), self-pay (uninsured) status (OR = 4.9, 95% = CI 1.2-19.6), and troponin level higher than 0.05 (OR = 24.0, 95% CI = 2.6-216.8; Table 4). A multivariate risk score was created using a formula for a population with relatively few events as seen in Pavlou et al[6] and the area under the curve as shown in Figure 1 with a C-statistic of 82% (95% CI = 71-93).

Table 1. Study group baseline characteristics

Variable	Positive for cocaine use (n = 64)[a]	Negative for cocaine use (n = 1069)[a]	p value χ^2
Age (SD)	53.1 (11.2)	59.2 (12.9)	< 0.01
Sex (men)	51 (79.7)	712 (66.6)	0.03
Length of stay in days (SD)	3.64 (3.9)	4.65 (5.96)	0.18
Death in hospital	1 (1.6)	78 (7.3)	0.12
Race			< 0.01
African American	59 (92.2)	585 (55.0)	
White	5 (7.8)	460 (43.3)	
Married	18 (28.1)	426 (39.5)	0.08
Self-pay (uninsured)	31 (48.4)	221 (20.7)	< 0.01
Diabetes mellitus	12 (19.0)	330 (31.2)	0.04
Hypertension	40 (63.5)	727 (68.6)	0.4
Hyperlipidemia	16 (25.4)	385 (36.4)	0.08
Prior myocardial infarction	12 (19.0)	280 (26.4)	0.19
Family history of CAD	17 (27.0)	424 (41.1)	0.03
CHF	3 (4.8)	100 (9.4)	0.27
CKD	2 (3.2)	61 (5.8)	0.39
ESRD	1 (1.6)	35 (3.3)	0.72
Smoking	55 (87.3)	574 (54.6)	< 0.01
Alcohol use	32 (50.8)	248 (23.6)	< 0.01
Chest pain	59 (92.2)	898 (83.1)	0.06
Hypotension	5 (8.1)	73 (7.1)	0.77
True STEMI	34 (54.0)	721 (70.2)	0.01
IABP	5 (8.2)	121 (11.7)	0.54
Vascular complications	1 (1.6)	24 (2.4)	0.71
Transvenous pacer	1 (1.6)	52 (5.1)	0.36
Ejection fraction by angiography	48.6 (12.7)	46.3 (13.0)	0.24
LVEDP	22.1 (7.6)	23.0 (12.5)	0.56
Admission troponin level	1.84 (5.7)	4.75 (13.8)	0.11
Peak troponin level	12.51 (24.9)	14.36 (25.08)	0.59

[a] Responses are no. (%) unless otherwise indicated.

CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; ESRD = end-stage renal disease; IABP = intra-aortic balloon pump; LVEDP = left ventricular end-diastolic pressure; SD = standard deviation; STEMI = ST-elevation myocardial infarction.

DISCUSSION

Cardiac catheterization is an invasive procedure associated with known complications.[7] Risk for adverse events remains even as procedure-related complications decline because of better devices, methods, and operator skill. The goal is to maintain a healthy balance between avoiding unnecessary invasive procedures and providing appropriate procedures for patients with true STEMI. Other causes of ST-elevation as determined

Table 2. Demographic differences associated with cocaine positivity in patients with true ST-elevation myocardial infarction

Variable	Positive for cocaine (n = 34)[a]	Negative for cocaine use (n = 719)[a]	p value χ^2
Age (SD)	54.6 (11.5)	58.9 (12.2)	0.05
Sex (men)	28 (82.4)	494 (68.5)	0.09
Length of stay in days (SD)	4.7 (4.0)	4.8 (5.7)	0.99
Death in hospital	1 (2.9)	35 (4.9)	1
Race			< 0.01
African American	30 (88.2)	370 (51.6)	
White	4 (11.8)	337 (47.0)	
Married	9 (26.5)	282 (39.5)	0.15
Self- pay (uninsured)	21 (61.8)	160 (22.2)	< 0.01
Diabetes mellitus	6 (17.6)	226 (31.4)	0.09
Hypertension	22 (64.7)	478 (66.5)	0.83
Hyperlipidemia	10 (29.4)	268 (37.3)	0.35
Prior myocardial infarction	6 (17.6)	199 (27.7)	0.2
Family history of CAD	12 (35.3)	312 (44.3)	0.3
CHF	2 (5.9)	40 (5.6)	0.71
CKD	0	33 (4.6)	0.39
ESRD	0	13 (1.8)	1
Smoking	31 (91.2)	407 (57.2)	< 0.01
Alcohol use	17 (50.0)	166 (23.3)	< 0.01
Chest pain	32 (94.1)	636 (88.2)	0.29
Hypotension	3 (9.1)	49 (6.8)	0.62
Transferred	11 932.4)	306 (42.4)	0.24
IABP	3 (9.1)	101 (14.0)	0.72
Intubation	4 (12.1)	57 (8.0)	0.394
CABG	3 (9.1)	70 (9.8)	0.89
Medical management	1 (3.0)	34 (4.8)	0.64
Troponin level at admission (SD)	2.70 (7.2)	5.65 (15.3)	0.29
Troponin level at peak (SD)	21.2 (30.9)	18.43 (27.6)	0.59
HGb (SD)	13.5 (2.2)	13.6 (2.0)	0.91
RDW (SD)	14.9 (2.7)	14.4 (2.4)	0.19
Creatinine level (SD)	1.23 (0.4)	1.24 (1.1)	0.95
LV ejection fraction by ECHO, % (SD)	42.9 (13.6)	45.2 (11.9)	0.4
LV ejection fraction by angiography, % (SD)	43.1 (11.8)	45.4 (11.9)	0.33
LVEDP (SD)	23.2 (7.6)	24.3 (12.7)	0.64
Multivessel disease	16 (47.1)	494 (68.8)	0.01
LBBB	0 (0.0)	24 (3.3)	0.28
ECG pattern			
Anterior	18 (52.9)	249 (34.5)	0.03
Inferior	11 (32.4)	294 (40.8)	0.33
Lateral	1 (2.9)	42 (5.8)	0.48
Culprit lesion			
LAD	18 (52.9)	313 (43.4)	0.27
RCA	13 (38.2)	271 (37.6)	0.94
LCX	2 (5.9)	89 (12.3)	0.26

[a] Responses are no. (%) unless otherwise indicated.

CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; ECG = electrocardiogram; ECHO = echocardiography; ESRD = end-stage renal disease; HGb = hemoglobin; IABP = intra-aortic balloon pump; LAD = left anterior descending; LBBB = left bundle branch block; LCX = left circumflex; LV = left ventricle; LVEDP = left ventricular endiastolic pressure; RCA = right coronary artery; RDW = red blood cell distribution width; SD = standard deviation.

on ECG are not associated with myocardial infarction, such as disease processes that necessitate therapy attributable to benign causes such as a normal variant (especially in men) and early repolarization.[8] These factors are present when cardiovascular symptoms arise from potential cocaine use. Patients who test positive for cocaine use usually are men and typically are younger than those with negative cocaine use findings. The benign conditions causing ECG ST-elevation cannot be easily identified if previous ECG results are not available for comparison; this scenario can lead to an unnecessary invasive procedure, especially when patients are admitted to the hospital.[9] Cocaine-associated myocardial infarction usually occurs within 24 hours of cocaine use,[10] so use of a urine test to confirm cocaine positivity might implicate many people for whom cocaine use is not the direct cause of myocardial infarction. Because the benefits of cardiac catheterization usually outweigh the risks, most patients opt to undergo the procedure; however, for the subgroup that is inclined to refuse any invasive procedure, use of a predictive model showing an increased possibility for having true STEMI may serve to encourage them to undergo coronary angiography with possible intervention.

Our study shows that an uninsured patient with positive cocaine and troponin findings who is older than age 65 years is more likely to have a true STEMI. Each factor individually increases the probability of true STEMI, and a combination of these factors further increases the likelihood. We believe that uninsured patients might be sicker at baseline because of poor primary care follow-up, or they may present only when they have symptoms that cannot be managed without a visit to a medical facility. Patients older than age 65 years and those with positive troponin results are more likely to experience an acute coronary event. The prevalence of true STEMI in this population was 70.2% and 54% in the CPos subgroup. Published data from other centers revealed a higher true STEMI rate.[11,12] This finding might be explained because our facility is a large regional center to which patients are referred for cardiac catheterization,

which leads to an increased likelihood of intervention even while ruling out other factors. Our institutional policy that ensures we intervene within the recommended door-to-balloon time and risk-benefit analysis of complications vs death resulting from nonintervention also influence these findings.

A limitation of this study is that use of a urine drug screen as a yardstick for CPos does not account for the possibility that cocaine use may have occurred up to 5 days before presentation, which limits our interpretation of this factor as the main cardiovascular complication trigger and false STEMI in our population. CPos was 5.6%; this prevalence may be unique, which would limit generalization. The risk score must be validated with a different population.

Table 3. Demographic and medical variables associated with true and false ST-elevation myocardial infarction among patients with positive cocaine findings

Variable	True STEMI (n = 34)[a]	False STEMI (n = 29)[a]	p value χ^2
Age (SD)	54.6 (11.5)	51.3 (10.8)	0.24
Sex (men)	28 (82.4)	22 (75.9)	0.53
Length of stay in days (SD)	4.7 (4.0)	3.1(3.6)	0.13
Death in hospital	1 (2.9)	0	1
Race			0.36
African American	30 (88.2)	28 (96.6)	
White	4 (11.8)	1 (3.4)	
Married	9 (26.5)	9 (31.0)	0.78
Self-pay (uninsured)	21 (61.8)	10 (34.5)	0.03
Diabetes mellitus	6 (17.6)	6 (21.4)	0.71
Hypertension	22 (64.7)	18 (64.3)	0.97
Hyperlipidemia	10 (29.4)	6 (21.4)	0.48
Prior myocardial infarction	6 (17.6)	6 (21.4)	0.76
Family history of CAD	12 (35.3)	5 (17.9)	0.16
CHF	2 (5.9)	1 (3.6)	1
CKD	0	2 (7.1)	0.2
ESRD	0	1 (3.6)	0.45
Smoking	31 (91.2)	23 (82.1)	0.29
Alcohol use	17 (50.0)	14 (50.0)	1
Chest pain	32 (94.1)	27 (93.1)	0.87
Hypotension	3 (9.1)	2 (6.9)	1
Transferred	11 (32.4)	8 (27.6)	0.68
IABP	3 (9.1)	2 (7.1)	1
Intubation	4 (12.1)	1 (3.4)	0.36
CABG	3 (9.1)	3 (10.3)	1
Medical management	1 (3.0)	21 (72.4)	< 0.01
Troponin at admission (SD)	2.70 (7.2)	0.89 (3.1)	0.24
Troponin at peak (SD)	21.2 (30.9)	2.12 (5.8)	< 0.01
Hemoglobin (SD)	13.5 (2.2)	13.1 (2.0)	0.47
RDW (SD)	14.9 (2.7)	14.8 (2.3)	0.83
Creatinine level (SD)	1.23 (0.4)	1.82 (2.9)	0.24
LV ejection fraction by ECHO % (SD)	42.9 (13.6)	46.9 (11.1)	0.43
LV ejection fraction by angiography % (SD)	43.1 (11.8)	54.8 (10.9)	< 0.01
LVEDP (SD)	23.2 (7.6)	20.8 (7.6)	0.24

[a] Responses are no. (%) unless otherwise indicated.

CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; DM = diabetes mellitus; ECHO = echocardiogram; ESRD = end-stage renal disease; IABP = intra-aortic balloon pump; LV = left ventricle; LVEDP = left ventricular end-diastolic pressure; RDW = red blood cell distribution width; SD = standard deviation.

CONCLUSION

In patients with suspected STEMI, cocaine positivity leads to a higher incidence of false STEMI. A better risk prediction tool is needed to provide a more educated informed consent process before cardiac catheterization. The combination of age older than 65 years, lack of health insurance, and troponin levels outside of defined limits was associated with true STEMI for our patients. ❖

Disclosure Statement

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References

1. Ward MJ, Kripalani S, Zhu Y, et al. Incidence of Emergency Department visits for ST-elevation myocardial infarction in a recent six-year period in the United States. Am J Cardiol 2015 Jan 15;115(2):167-70. DOI: https://doi.org/10.1016/j.amjcard.2014.10.020.
2. Finkel JB, Marhefka GD. Rethinking cocaine-associated chest pain and acute coronary syndromes. Mayo Clin Proc 2011 Dec;86(12):1198-207. DOI: https://doi.org/10.4065/mcp.2011.0338.
3. O'Gara PT, Kushner FG, Ascheim DD, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013 Jan 29;127(4):e362-425. DOI: https://doi.org/10.1161/CIR.0b013e3182742cf6. Erratum in: Circulation 2013 Dec 24;128(25):e481.
4. McCabe JM, Armstrong EJ, Kulkarni A, et al. Prevalence and factors associated with false-positive ST-segment elevation myocardial infarction diagnoses at primary percutaneous coronary intervention-capable centers: A report from the Activate-SF registry. Arch Intern Med 2012 Jun 11;172(11):864-71. DOI: https://doi.org/10.1001/archinternmed.2012.945.
5. Nfor T, Kostopoulos L, Hashim H, et al. Identifying false-positive ST-elevation myocardial infarction in Emergency Department patients. J Emerg Med 2012 Oct;43(4):561-7. DOI: https://doi.org/10.1016/j.jemermed.2011.09.027.
6. Pavlou M, Ambler G, Seaman SR, et al. How to develop a more accurate risk prediction model when there are few events. BMJ 2015 Aug 11;351:h3868.

Table 4. Multivariate analysis of troponin level and insurance status

Significant variables	b (variable)	Exp(b) (95% confidence interval)	Significance
Age > 65 y	2.958	19.261 (1.166-318.261)	0.039
Troponin level > 0.05	3.178	23.959 (2.648-216.804)	0.005
Uninsured	1.595	4.929 (1.240-19.596)	0.024
Constant	-3.375	0.034	0.004

Exp(b) = odds ratio for predictors.

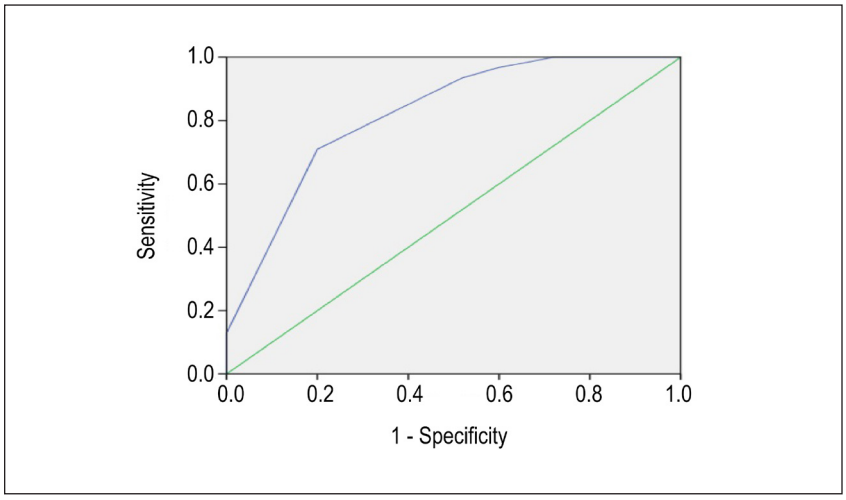

Figure 1. Receiver operating characteristics (ROC) curve showing a C-statistic of 82% (95% confidence interval = 71-93) for true ST-elevation myocardial infarction prediction when factoring in older than age 65 years, lack of health insurance, and troponin value higher than 0.05.

DOI: https://doi.org/10.1136/bmj.h3868. Erratum in: BMJ 2016 Jun 8;353:i3235. DOI: https://doi.org/10.1136/bmj.i3235.

7. West R, Ellis G, Brooks N, Joint Audit Committee of the British Cardiac Society and Royal College of Physicians of London. Complications of diagnostic cardiac catheterisation: Results from a confidential inquiry into cardiac catheter complications. Heart 2006 Jun;92(6):810-4. DOI: https://doi.org/10.1136/hrt.2005.073890.
8. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. N Engl J Med 2003 Nov 27;349(22):2128-35. DOI: https://doi.org/10.1056/NEJMra022580.
9. Singh V, Rodriguez AP, Thakkar B, et al. Hospital admissions for chest pain associated with cocaine use in the United States. Am J Med 2017 Jun;130(6):688-98. DOI: https://doi.org/10.1016/j.amjmed.2016.12.003.
10. McCord J, Jneid H, Hollander JE, et al; American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Management of cocaine-associated chest pain and myocardial infarction: A scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Circulation 2008 Apr 8;117(14):1897-907. DOI: https://doi.org/10.1161/CIRCULATIONAHA.107.188950.
11. Gupta N, Washam JB, Mountantonakis SE, et al. Characteristics, management, and outcomes of cocaine-positive patients with acute coronary syndrome (from the National Cardiovascular Data Registry). Am J Cardiol 2014 Mar 1;113(5):749-56. DOI: https://doi.org/10.1016/j.amjcard.2013.11.023.
12. Shitole SG, Kayo N, Srinivas V, et al. Clinical profile, acute care, and middle-term outcomes of cocaine-associated ST-segment elevation myocardial infarction in an inner-city community. Am J Cardiol 2016 Apr 15;117(8):1224-30. DOI: https://doi.org/10.1016/j.amjcard.2016.01.019.

Daily Encounters

The method … which proceeds by means of reason admonishes us to study the nature of the body which one tries to heal and the forces of all the causes which the body encounters daily. For it is as a result of these that it becomes healthier or sicker than it was before.

— Galen of Pergamon, 130 AD-210 AD, prominent Greek physician, surgeon, and philosopher in the Roman Empire