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Ischemic Evaluation in Patients Presenting with Hypertensive Emergency / Urgency and Acute Systolic Heart Failure: Is Coronary Angiography Required for all?☆

Jared W. Davis [a], Muhannad Almubarak [a], Amrita Mukherjee [b], Samuel K. McElwee [c], Massoud A. Leesar [c], Arka Chatterjee [c,*]

[a] Department of Internal Medicine, University of Alabama at Birmingham, Birmingham, AL, United States
[b] Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, United States
[c] Division of Cardiovascular Disease, University of Alabama at Birmingham, Birmingham, AL, United States

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ABSTRACT

Background: Patients presenting with hypertensive urgency / emergency (HUE) often have systolic heart failure (SHF). Coronary angiography is routinely done for these patients to rule out obstructive coronary artery disease (Obs-CAD). We performed a retrospective study to investigate predictors of ObsCAD in this population.
Methods: Patients who underwent angiography to investigate SHF and had hospital admission(s) for HUE in the preceding 6 months were included in the study. Chart review was performed to obtain demographic, clinical and imaging / angiographic data. A risk score was formulated based on multivariable logistic regression analysis.
Results: 205 patients [age 58.9 ± 14.4 years; 62.4% male; 39.5% diabetic; median EF 25% (Inter Quartile Range: 11)] were included in the study. 33.1% patients ($n = 68$) had obs-CAD. Patients with obs-CAD were older, diabetic, more likely to have a history of stroke, echocardiographic regional wall motion abnormalities (RWMA) while African Americans were less likely to have obs-CAD. On multivariable analysis, only non-African American race (OR: 2.18; CI: 1.08–4.4) and RWMA (OR: 5.62; CI: 2.47–12.81) remained significant predictors of obs-CAD. A risk score (RANDS) from 0 to 9 was formulated which had a c-statistic of 0.75 with a sensitivity and specificity of 84% and 53% for predicting obsCAD respectively.
Conclusion: Our results suggest that only a minority of patients with HUE and SHF have obs-CAD. A simple risk score may be used to stratify this population and lower risk individuals may be screened with non-invasive testing instead of invasive catheterization. These results should be validated in large registry populations.

Introduction

Coronary angiography has been an integral component in the algorithm used to investigate the cause of newly diagnosed systolic heart failure (SHF) to identify whether new SHF is caused by ischemic cardiomyopathy and, if so, whether intervention would be beneficial [1–3]. Previous studies have examined the use and appropriateness of coronary angiography in SHF [4,5]. Current guidelines on coronary angiography are clear for those presenting with SHF and angina pectoris or a history of ventricular arrhythmias [3,6]. Uncontrolled hypertension (HTN) is a common cause for systolic heart failure, especially amongst African-Americans [7,8]. However, patients presenting with hypertensive urgency/emergency (HUE) often have chest pain and positive biomarkers mimicking coronary syndromes. Thus, it is hard to distinguish patients with SHF related to uncontrolled HTN from ischemic heart disease. It remains unclear as to who may benefit from immediate coronary angiography and who should undergo risk stratification with non-invasive imaging, prior to cardiac catheterization.

Our study set out to investigate patients who presented to our institution with new onset systolic heart failure and either a recent history of or current HUE to determine which factors were associated with an ischemic cause of the heart failure and thereby predict which patients will benefit from coronary angiography and who can be stratified to non-invasive imaging. Previous studies have suggested that African American patients are less likely to have an ischemic cause of cardiomyopathy [8,9]. Instead, African Americans have been described to be at a higher risk of non-ischemic and dilated cardiomyopathy. As part of this study, we were interested in further examining this correlation also.

Materials and methods

All coronary angiographies performed between January 2007 and May 2017 for the indication of “CHF”, “Acute CHF”, “Hypertensive

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* Corresponding author at: 510 20th St S FOT 920, Birmingham, AL 35294.
E-mail address: achatterjee@uabmc.edu (A. Chatterjee).

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Table 1
Demographic and clinical parameters of the study population.

	Obstructive CAD ($n = 68$)	Non-obstructive CAD ($n = 137$)	*P* value
Median Age (years)	63 (17.5)	57 (19)	0.002
Male Sex	70.6% (48)	58.4% (80)	0.09
African American	48.5% (33)	68.6% (94)	0.005
Smoker	61.2% (41)	55.5% (76)	0.44
Diabetes mellitus	51.5% (35)	33.6% (46)	0.013
FH of CAD	34.3% (23)	31.4% (43)	0.67
h/o Stroke	16.2% [11]	6.6% [9]	0.029
Typical angina	33.3% (22)	30.4% (41)	0.67
Systolic BP (mm Hg): Median (IQR)	185 (20)	181 (23)	0.07
Diastolic BP (mm Hg): Median (IQR)	109.5 (23)	110 (19)	0.36
Ejection fraction	25% (15%)	25% (10%)	0.073
Regional wall motion abnormalities	39.7% (27)	8.2% [11]	<0.001
Positive Troponin (I)	74.6% (41)	70.4% (81)	0.58

Urgency or Emergency", "Systolic Heart Failure" at a single large academic center were reviewed by study investigators. A retrospective chart review was conducted for each patient. Patients were included in the analysis if records revealed presentation with new SHF (LVEF ≤40%) and a presentation with HUE (SBP ≥ 170 and/or diastolic blood pressure ≥ 110 mmHg) either during the HF admission or within the prior 6 months. Patients with known coronary artery disease, defined as prior surgical or percutaneous revascularization, were excluded. In total, 205 patients were included in the study. The IRB of the University of Alabama at Birmingham approved the study. Detailed chart reviews were conducted for each patient meeting the inclusion criteria to extract demographic and clinical parameters. Imaging and angiographic data, transthoracic echocardiograms, and coronary angiograms were individually reviewed by experienced cardiologists. Echocardiograms were evaluated for left ventricular dysfunction defined as an ejection fraction ≤ 40% calculated using Simpson's Biplane method and presence or absence of regional wall motion abnormalities (RWMA) noted. Echocardiograms were evaluated by a cardiologist (SKM) blinded to results of coronary angiograms and clinical data. Obstructive coronary artery disease (obs-CAD) was defined as the presence of greater than or equal to 50% stenosis of the left main coronary artery or greater than or equal to 70% stenosis of any major epicardial artery determined by quantitative coronary analysis (QCA) using CAAS system. Two experienced interventional cardiologists (ML, AC) performed QCA in a blinded fashion.

Statistical analysis

Statistical analysis was carried out using SAS 9.4 software (SAS Institute, Cary, NC). Continuous variables are depicted as mean / median depending upon whether their distribution was normal or not. Categorical variables are depicted as percentages. Univariate logistic regression analysis was used to ascertain relationships of the following variables: age, sex, race, Diabetes Mellitus, tobacco use, chronic kidney disease, family history of CAD, prior stroke, and RWMA. Multivariate logistic regression was then used to further extrapolate significant associations between these variables. A risk score was created using the multivariable beta regression coefficients to assign weights for each variable. A Receiver Operating Characteristic Curve was then computed for the risk score.

Results

A total of 205 patients undergoing coronary angiography for acute SHF and HUE were included in the study. 199 patients met our blood pressure criteria for HUE at the time of presentation whereas 6 patients had been admitted with HUE within the preceding six months. Median systolic and diastolic blood pressure at presentation for the sample was 182 (IQR 23) and 110 (IQR 20) mm Hg respectively. 30.7% ($n = 63$) patients were deemed to have typical angina at presentation. 33.2% ($n = 68$) patients were found to have Obs-CAD. Demographic and clinical characteristics of the patient population were broken down into two groups depending on the presence or absence of Obs-CAD. This is shown in Table 1. The median age for patients with Obs-CAD was higher [63 (IQR 17.5) v 57 (IQR 19) years; $p = 0.002$]. Other statistically significant findings included African American race (protective for Obs-CAD), diabetes, history of stroke, and regional wall motion abnormalities on echocardiography. Using these variables, a multivariable analysis was then run. Only African American race (protective) and RWMA still remained significant predictors of Obs-CAD in our study population. We used the multivariable regression coefficients for each factor as weights to create a risk score between 0 and 9 (Acronym: RANDS; Table 2). Using a cutoff of ≥2 identifies Obs-CAD with a sensitivity of 84% and a specificity of 53%. Distribution of the study population stratified by the risk score is depicted in Table 3. Use of the RANDS score in this study population would avoid an initial coronary angiogram in 41% ($n = 84$) patients with only 11 patients mis-classified as low risk. Thus, a total of 35.6% patients ($n = 73$) may be spared an invasive coronary angiogram. The receiver operating characteristic curve for this risk score gives a c statistic of 0.75 suggesting a good fit. (Fig. 1).

Discussion

Many patients presenting with acute SHF have accompanying HUE. Over the last decade, studies have examined the acute heart failure population but have been unable to reach a firm conclusion on the exact role and timing of coronary angiography [10]. Therefore, whether a patient undergoes coronary angiography has been largely physician dependent and many patients with non-ischemic cardiomyopathy undergo cardiac catheterization without gaining measurable benefit. We hypothesized that only a minority of patients presenting with acute SHF and HUE have significant obstructive coronary artery disease at time of presentation. Because African American patients have been suggested to have a lower incidence of obs-CAD, we expected to find a similar association in this patient population. It is important to understand which patients are at higher risk of obstructive coronary artery disease from both a procedural risk stand-point and from a viewpoint of providing cost-effective care. By accurately predicting which patients with acute SHF and HUE have obstructive coronary artery disease, we can provide higher value care to our patients. The majority of patients included had severe SHF indicated by the median LVEF of 25%. Although the sample size in our study is small, the population is similar to those in landmark HF trials such as VMAC trial OPTIME trials in age and LVEF [11,12]. However, majority of patients in our study were African-

Table 2
Odds ratios for multivariable analysis and assignment of points for risk score.

Factor	OR (95%CI)	β Regression coefficient	Points for risk score
Regional wall motion abnormalities (R)	5.62 (2.47–12.81)	1.73	3
Age ≥ 60 years (A)	1.66 (0.84–3.30)	0.51	1
Non African-American race (N)	2.18 (1.08–4.4)	0.78	2
Diabetes mellitus (D)	1.71 (0.86–3.39)	0.54	1
H/o stroke (S)	2.40 (0.85–6.8)	0.88	2

Table 3
Distribution of study population based on RANDS score.

RANDS score	Patients with obstructive CAD	Total patients
0	4	45
1	7	39
2	14	29
3	10	40
4	7	17
5	9	15
6	9	11
7	5	6
8	3	3
9	0	0
Total	68	205

American which is in stark contrast to most HF trials [11,12–14]. This is likely due to our focus on hypertension in combination with acute heart failure. As described earlier, African-Americans are more likely to have hypertension induced heart failure [9,14,15]. In our study population, the traditional risk factors of age, Diabetes mellitus and prior history of stroke predicted Obs-CAD. RWMA on echocardiography was a strong predictor of Obs-CAD also. Our data is also in line with studies supporting less incidence of Obs-CAD in African Americans [8,9,15]. The RANDS risk score we provide is simple to use and may be of help in deciding who needs to undergo coronary angiography after presenting with HF and uncontrolled HTN. It can be hypothesized that patients at low risk of Obs-CAD can be screened with computed tomography (CT), which is considered to be much more cost effective [16]. One could argue that a CT coronary angiogram would likely avoid the diagnosis of Obs-CAD being missed in even the small number of patients who would be mis-classified by use of the RANDS score.

Limitations.

Our study carries all the limitations expected of a retrospective analysis and the inherent biases. We attempted to correct for these biases through careful data acquisition, exclusion of potential confounders, and accurate statistical analysis. Our study was conducted at a single large center and after exclusions contains a relative small sample size. Although our study size is small, as outlined above, characteristically it correlates well with large multicenter trials and therefore its results may generalize well. Although classically, hypertensive urgency/emergency has been characterized by a higher blood pressure cutoff, we used >170/110 mmHg as our cutoff since patients with systolic heart failure are more sensitive to elevated afterload and carry a higher morbidity and mortality from this when compared to non-heart failure populations [17–20]. However, the median systolic and diastolic blood pressure values for our study population is similar to the standard definition of 180 and 110 mmHg. Only variables which reach statistical significance on multivariable analysis should be included in the risk score. However, since our sample size is small, and the univariate predictors are historically well-established risk factors for Obs-CAD, hence they were incorporated in the risk score. Also, presence of Obs-CAD does not imply an ischemic etiology of SHF in every patient.

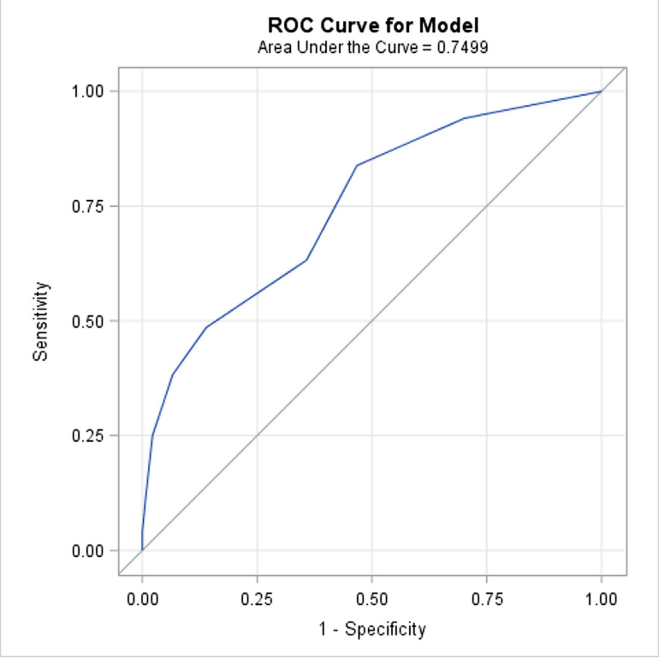

Fig. 1. ROC curve for RANDS risk score in prediction of obstructive CAD in patients presenting with systolic heart failure and hypertensive urgency / emergency.

Conclusion

Our study shows that patients presenting with acute systolic heart failure and hypertensive urgency / emergency are less likely to have Obs-CAD. Patient risk for Obs-CAD can be stratified using a simple risk score and those at low risk may be screened with non-invasive modalities instead. Validation of the risk score is needed in large populations.

References

[1] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey Jr DE, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. J Am Coll Cardiol 2013;62(16):e147–239.
[2] Lindenfeld J, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, et al. HFSA 2010 comprehensive heart failure practice guideline. J Card Fail 2010;16(6):e1-94.
[3] McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the task force for the diagnosis and treatment of acute and chronic heart failure 2012 of the European Society of Cardiology. Developed in collaboration with the heart failure association (HFA) of the ESC. Eur J Heart Fail 2012;14(8):803–69.
[4] Flaherty JD, Rossi JS, Fonarow GC, Nunez E, Stough WG, Abraham WT, et al. Influence of coronary angiography on the utilization of therapies in patients with acute heart failure syndromes: findings from organized program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF). Am Heart J 2009;157(6):1018–25.
[5] Ferreira JP, Rossignol P, Demissei B, Sharma A, Girerd N, Anker SD, et al. Coronary angiography in worsening heart failure: determinants, findings and prognostic implications. Heart 2018 Apr;104(7):606–13.
[6] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC); developed with the special contribution of the heart failure association (HFA) of the ESC. Eur Heart J 2016;37(27):2129–200.
[7] Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke Statistics-2017 update: a report from the American Heart Association. Circulation 2017;135(10):e146–603.
[8] Peacock F, Amin A, Granger CB, Pollack CV, Levy P, Nowak R, et al. Hypertensive heart failure: patient characteristics, treatment, and outcomes. Am J Emerg Med 2011;29(8):855–62.
[9] Mathew J, Davidson S, Narra L, Hafeez T, Garg R. Etiology and characteristics of congestive heart failure in blacks. Am J Cardiol 1996;78(12):1447–50.
[10] Doukky R, Shih MJ, Rahaby M, Alyousef T, Abusin S, Ansari NH, et al. A simple validated clinical tool to predict the absence of coronary artery disease in patients with systolic heart failure of unclear etiology. Am J Cardiol 2013;112(8):1165–70.
[11] Abraham WT, Cheng ML, Smoluk G. Clinical and hemodynamic effects of nesiritide (B type natriuretic peptide) in patients with decompensated heart failure receiving beta blockers. Congest Heart Fail 2005;11(2):59–64.
[12] Klein L, Massie BM, Leimberger JD, O'Connor CM, Pina IL, Adams KF, et al. Admission or changes in renal function during hospitalization for worsening heart failure predict postdischarge survival: results from the outcomes of a prospective trial of intravenous Milrinone for exacerbations of chronic heart failure (OPTIME-CHF). Circ Heart Fail 2008;1(1):25–33.
[13] Adams Jr KF, Fonarow GC, Emerman CL, Lejemtel TH, Costanzo MR, Abraham WT, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the acute decompensated heart failure National Registry (ADHERE). Am Heart J 2005;149(2):209–16.
[14] Yancy CW, Abraham WT, Albert NM, Clare R, Stough WG, Gheorghiade M. Quality of care of and outcomes for African Americans hospitalized with heart failure: findings

from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol 2008;51(17):1675–84.
[15] Yancy CW. Heart failure in African Americans: a cardiovascular engima. J Card Fail 2000;6(3):183–6.
[16] Halpern EJ, Savage MP, Fischman DL, Levin DC. Cost-effectiveness of coronary CT angiography in evaluation of patients without symptoms who have positive stress test results. AJR Am J Roentgenol 2010;194(5):1257–62.
[17] Miller RR, Awan N, Amsterdam EA, Mason DT. Afterload reduction in congestive heart failure. Adv Cardiol 1978;22:199–204.
[18] Mason DT. Afterload reduction and cardiac performance. Physiologic basis of systemic vasodilators as a new approach in treatment of congestive heart failure. Am J Med 1978;65(1):106–25.
[19] Cole RT, Kalogeropoulos AP, Georgiopoulou VV, Gheorghiade M, Quyyumi A, Yancy C, et al. Hydralazine and isosorbide dinitrate in heart failure: historical perspective, mechanisms, and future directions. Circulation 2011;123(21):2414–22.
[20] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey Jr DE, Colvin MM, et al. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2016;68(13):1476–88.