JACC: CARDIOVASCULAR IMAGING VOL. 7, NO. 1, 2014

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcmg.2013.08.012

Acute Mortality in Critically Ill Patients Undergoing Echocardiography With or Without an Ultrasound Contrast Agent

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OBJECTIVES The objective of this observational study was to compare 48-h all-cause mortality (as well as hospital stay mortality) among critically ill patients who underwent echocardiography either with or without an ultrasound contrast agent (UCA).

BACKGROUND The safety of perflutren-based UCAs has been questioned by the U.S. Food and Drug Administration (particularly when administered to critically ill patients) following rare reports of deaths or life-threatening adverse reactions that occurred in close temporal relationship to UCA administration.

METHODS This was a retrospective observational outcome study conducted in critically ill patients to compare all-cause 48-h and hospital stay mortality subsequent to echocardiography procedures performed either with or without a UCA. The study utilized discharge data from a database maintained by Premier, Inc. (Charlotte, North Carolina). Premier's database is the largest U.S. hospital–based, service-level comparative database for quality and outcomes research, and provides detailed resource utilization data along with patients' primary and secondary diagnoses and procedure billing codes. A propensity score–matching algorithm between UCA-enhanced echocardiography patients and non–contrast-enhanced echocardiography patients was utilized to reduce the potential for imbalance in covariates of selected patients in the comparison of mortality between groups.

RESULTS Patients undergoing echocardiography with a UCA had lower mortality at 48 h compared with patients undergoing non–contrast-enhanced echocardiography (1.70% vs. 2.50%), with an odds ratio = 0.66 (95% confidence interval [CI]: 0.54 to 0.80). Patients undergoing echocardiography with a UCA had lower hospital stay mortality compared with patients undergoing noncontrast echocardiography (14.85% vs. 15.66%), with an odds ratio = 0.89 (95% CI: 0.84 to 0.96).

CONCLUSIONS In critically ill, propensity-matched hospitalized patients undergoing echocardiography, use of a UCA is associated with a 28% lower mortality at 48 h in comparison with patients undergoing non–contrast-enhanced echocardiography. These results are reassuring, given previous reports suggesting an association between UCAs and increased mortality in critically ill patients. (J Am Coll Cardiol Img 2014;7:40–8) © 2014 by the American College of Cardiology Foundation

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Manuscript received April 18, 2013; revised manuscript received August 9, 2013, accepted August 16, 2013.

Transthoracic echocardiography (TTE) is an inexpensive, portable, safe, and reliable imaging tool used to evaluate cardiac structure and function. In critically ill patients, echocardiographic imaging is an essential component of care and provides data that alter immediate patient management. In the intensive care unit (ICU), echocardiograms are limited in quality in over 30% of studies because of obesity, severe pulmonary disease, and mechanical ventilation (1). However, most nondiagnostic echocardiography studies can be salvaged with ultrasound contrast agents (UCA) (1,2). As a result, judicious UCA use is now recommended by the American Society of Echocardiography and the combined specialty Appropriate Use Criteria for Echocardiography (3,4). The objective of this observational study was to compare 48-h all-cause mortality (as well as hospital stay mortality) among critically ill patients who underwent echocardiography either with or without a UCA.

Table 1. Demographics and Other Baseline Characteristics Collected for Each Patient

Patient characteristics (age, sex, race)
Hospital characteristics (Northeast, Midwest, South, and West)
Population served (urban and rural)
Teaching status (teaching, nonteaching)
Hospital size (006–099, 100–199, 200–299, 300–499, 500+)
Hospital length of stay
Admission type (emergency, elective, trauma, or urgent)
Discharge status (discharged, expired)
48-h all-cause mortality defined as a discharge code of deceased within 48 h of echocardiography
Major comorbid conditions
Myocardial infarction (410 series)
Congestive heart failure (428 series)
Acute coronary syndromes (411 series)
Ventricular arrhythmias (426.82, 427.1, 427.4, or 427.5 series)
Pulmonary hypertension (415 series, 416.0 series, 416.8 series, or 416.9 series)
Hypertension (401 series)
Intra-aortic balloon pump (97.44)
Cardiogenic shock (785.51)
Renal failure (584 series, 585 series, or 586 series)
Venous catheterization for renal dialysis (38.95)
Hemodiafiltration, hemofiltration (extracorporeal) (39.95)
Peritoneal dialysis (54.98)
Diabetes (250 series)
Chronic obstructive lung disease (490.00 and 496.99)
Pneumonia (480.00 and 486.00)
Mechanical ventilation (96.7 series)
Continuous positive airway pressure (93.90)
Stroke (430.00 and 435.99) cerebrovascular disease includes TIA
Sepsis (995.91)
Septic shock (785.52)
Anaphylactic shock (995.0)
Gastrointestinal hemorrhage (578 series)
Transfusion procedure (99.00 and 99.05)

TIA = transient ischemic attack.

METHODS

This was a retrospective observational outcome study conducted in critically ill patients to compare all-cause 48-h and hospital stay mortality subsequent to echocardiography procedures performed either with or without a UCA. The study used a propensity score–matching algorithm between UCA-enhanced echocardiography patients and nonenhanced echocardiography patients to reduce the potential for imbalance in covariates of selected patients in the comparison of mortality between groups. The study tested the primary hypothesis that there is no difference in 48-h all-cause mortality between the non–contrast-enhanced and UCA-enhanced groups using an odds ratio obtained from a mortality analysis of the propensity-matched study population.

ABBREVIATIONS AND ACRONYMS

APR-DRG = All Patient Refined Diagnosis Related Group

CI = confidence interval

cTTE = contrast-enhanced transthoracic echocardiography

FDA = Food and Drug Administration

ICU = intensive care unit

nTTE = non–contrast-enhanced transthoracic echocardiography

TTE = transthoracic echocardiography

UCA = ultrasound contrast agent

The study utilized discharge data from a database maintained by Premier, Inc. (Charlotte, North Carolina). Premier's database is the largest U.S. hospital-based, service-level comparative database for quality and outcomes research, and provides detailed resource utilization data along with patients' primary and secondary diagnoses and procedure billing codes. Patient diagnoses and procedures in the Premier database are coded using the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) classification system. The Premier database contains over 2.5 billion daily service records of patients from 750 geographically diverse hospitals, and about 45 million records are added each month. This is approximately 1 in every 4 discharges (26%) from U.S. hospitals. The demographics and baseline patient and hospital characteristics collected from the Premier database for use in this study are listed in Table 1.

A previous large retrospective study of 4,300,966 consecutive patients, using the Premier database,