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INSIDE

Transcatheter Aortic Valve Implantation for Aortic Stenosis

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

Assistant Professor of Medicine, Interventional Cardiology, University of California, San Francisco

Dr. Boyle reports no financial relationships relevant to this field of study.

This article originally appeared in the November 2010 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Ethan Weiss, MD. Dr. Crawford is Professor of Medicine, Chief of Cardiology, University of California, San Francisco, and Dr. Weiss is Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Crawford is on the speaker's bureau for Pfizer, and Dr. Weiss reports no financial relationships relevant to this field of study.*

Sources: Leon MB, et al. Transcatheter aortic valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010; online pre-print; Gurvitch R, et al. Transcatheter aortic valve implantation. Durability of clinical and hemodynamic outcomes beyond 3 years in a large patient cohort. *Circulation*. 2010;122:1319-1327.

THERE IS NO MEDICAL THERAPY FOR AORTIC STENOSIS (AS), AND BALLOON aortic valvuloplasty (BAV) has sub-optimal long-term results. The incidence of AS increases with age and, thus, many patients have significant comorbidities. These patients are often denied surgical aortic valve replacement (AVR) because of the high risk of surgery when serious comorbidities are present, and there has been no other treatment option for them. Percutaneous transcatheter aortic valve implantation (TAVI) may represent an alternative treatment option for patients at prohibitively high risk to undergo surgical AVR. Recently, the results of the PARTNER trial were presented at the Transcatheter Cardiovascular Therapeutics meeting, and the longer-term results from a Canadian registry also were released. These studies provide data to support the use of TAVI in patients with severe AS who have are too high risk to undergo surgical AVR.

The PARTNER trial was a randomized, controlled trial performed at 21 centers (17 in the United States) of TAVI vs. standard

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care in patients with symptomatic severe AS who were not candidates for surgical AVR. Inclusion criteria were New York Heart Association class II-IV symptoms and an aortic valve area of < 0.8 cm^2, a mean aortic valve gradient of > 40 mmHg, or a peak aortic valve velocity of > 4.0 m/sec. All were considered too high risk for surgical AVR by at least two cardiac surgeons. Exclusion criteria included a bicuspid or non-calcified aortic valve, reduced left ventricular ejection fraction (< 20%), acute myocardial infarction (MI), coronary artery disease requiring revascularization, severe mitral or aortic regurgitation, stroke or transient ischemic attack (TIA) in the prior six months, severe peripheral vascular disease, and aortic valve diameter that was not between 18 and 25 mm (therefore unsuitable for the currently available valve sizes). The trial was sponsored by Edwards, which manufacture the valve. The valve was implanted via the femoral artery after standard BAV in either the operating room or the cardiac catheterization laboratory. The valve consists of a bovine pericardial trileaflet valve mounted on a stainless steel frame that is balloon-expanded inside the existing aortic valve.

The baseline characteristics of the two treatment groups were similar, but the standard-care group had slightly higher rates of COPD (52.5% vs. 41.3%; $p = 0.04$), atrial fibrillation (48.8% vs. 32.9%; $p = 0.04$), and a higher logistic Euroscore (30.4 ± 19.1 vs. 26.4±17.2; $p = 0.04$). The mean age was 83 years in each group and the STS score (Society of Thoracic Surgeons score), a predictor of surgical mortality, was similar between groups (12.1 ± 6.1 vs. 11.2 ± 5.8, $p = 0.14$). TAVI resulted in immediate improvement in aortic valve area from 0.6 ± 0.2 cm^2 to 1.5 ± 0.5 cm^2, as well as a reduction in aortic mean valve gradient from 44.5 ± 15.7 mmHg to 11.1 ± 6.9 mmHg, and these improvements were maintained at one-year follow-up.

The primary endpoint was all-cause mortality at one year. Patients randomized to standard care (n = 358) had a higher one-year mortality of 50.7%, patients randomized to TAVI had a lower mortality (30.7%; hazard ratio 0.55, $p < 0.001$). Patients randomized to TAVI also had lower rates of cardiovascular death (20.5% vs. 44.6%, $p < 0.001$), death or repeat hospitalization ($p < 0.001$), and death or major stroke (33.1% vs. 51.3%, $p < 0.001$). Patients randomized to TAVI had improvement in symptoms and six-minute walk test. However, the improved mortality comes at a price. Patients randomized to TAVI had a higher rate of stroke or TIA (10.6% vs. 4.5%, $p = 0.04$), driven mainly by an increase in major stroke in the first 30 days (5.0% vs. 1.1%, $p = 0.06$). There was a higher incidence of vascular complications (32.4% vs. 7.3%, $p < 0.001$) and major bleeding (22.3% vs. 11.2%, $p < 0.001$) in the TAVI group. Importantly, there were no differences between groups in the rates of acute kidney injury, new atrial fibrillation, MI, new pacemaker requirement, or endocarditis. Despite all being considered unsuitable for surgical AVR, 17 patients in the standard-care group and two patients in the TAVI group underwent surgical AVR during the study. The authors concluded that in patients with severe AS who were not suitable for surgical AVR, TAVI significantly reduced the rates of death, the composite of death or repeat hospitalization, and cardiac symptoms, despite the higher incidence of strokes and major vascular events.

Gurvitch and colleagues present their data on a 3-year follow-up of patients undergoing TAVI in Canada. Unlike the PARTNER trial, this is not a randomized, controlled trial; it is a registry of 70 patients undergoing TAVI who were considered unsuitable for surgical AVR. The patients had a STS score 9.6 ± 3.5% and a mean age 80.7 ± 7.6 years, indicating a high-risk population. The patients received either the Edwards Sapien balloon expandable valve or the earlier generation Cribier-Edwards valve; 78.6% of cases were performed by the trans-femoral route and 21.4% via the trans-apical route. Patients were routinely prescribed aspirin for life and clopidogrel for six months after the procedure. All patients were followed for at least three years. The researchers excluded from their analysis those patients who died in the first 30 days, because these were thought to be due to procedural difficulties and the initial learning curve rather than problems with the device.

In those patients who survived the first 30 days after TAVI, survival at one, two, and three years was 81%, 74%, and 61%, respectively. One patient required re-operation from endocarditis, but no patients required re-operation for valve dysfunction. The aortic valve gradient decreased from

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45 mmHg to 10 mmHg after the procedure ($p < 0.01$) and increased slightly to 12.1 mmHg after three years ($p = 0.03$). Valve area increased from 0.6 ± 0.2 cm^2 to 1.7 ± 0.4 cm^2 after the procedure ($p < 0.01$) and reduced to 1.4 ± 0.3 cm^2 after three years ($p < 0.01$). At baseline, 1%, 3%, 69%, and 17% were in NYHA class I, II, III, and IV, respectively. At one-year follow-up, 93% of patients were in NYHA class I or II. This improvement was sustained with no change from 1-3 years post-procedure. After TAVI, aortic regurgitation (AR) was common: it was trivial in 40%, mild in 44%, and moderate in 6%; no patients had severe AR. One patient with mild AR worsened to moderate; of the patients with moderate AR, two improved to mild and two remained unchanged. This suggests that the degree of AR seen immediately post-procedure remains largely unchanged over three years. There were no cases of valve thrombosis, deterioration, or embolization. The authors conclude that TAVI demonstrates good medium- to long-term durability and preserved hemodynamic function, with no evidence of structural failure.

■ **COMMENTARY**

Surgical AVR remains the gold-standard treatment for severe symptomatic AS. However, there remain a group of patients who are at high surgical risk due to other comorbidities, who are unable to undergo surgical AVR. As our population ages, this patient group is likely to increase in size substantially, and there is currently a very high mortality (50% at one year) and no definitive therapy for this group. The randomized, controlled PARTNER trial demonstrated a 20% absolute reduction (40% relative risk reduction) in mortality if these patients undergo TAVI instead of medical therapy. This is a staggering improvement in all-cause mortality compared to most cardiology trials. Importantly, quality of life also is improved. The additional three-year data from Gurvitch and colleagues shows us that this early benefit is likely to be sustained. Their cohort maintained their hemodynamic and symptomatic improvement for over three years.

However, this is no free lunch. It is important to note the significant procedural risks involved with TAVI. The procedure requires large arterial sheaths that can cause significant vascular complications and bleeding. Furthermore, there is a significant peri-procedural risk of stroke. Notably, over 80% of the standard-therapy patients received BAV, which is not usually the standard of care. BAV may have increased the rate of early stroke and vascular complications in the standard-therapy group, thus underestimating the difference between the groups. We should, thus, look at the absolute rates of stroke and vascular access site complications. Interestingly, many of the late complications in the Canadian registry occurred due to combination anti-platelet therapy and warfarin, or over-anti-coagulation. In future, it will be important to define the optimal anti-thrombotic therapy in this group. TAVI is not FDA-approved for use in the United States, but is already on the market in other countries, as well as Europe. This is a promising new treatment strategy, reducing the high mortality in this very high-risk population, but its benefits must be weighed against its early risks. ■

Neurological Complications of H1N1 Influenza in Children

ABSTRACT & COMMENTARY

By Sotirios Keros, MD, PhD, and Steven Weinstein, MD

Dr. Keros is Fellow, Child Neurology, Weill Cornell Medical College, New York Presbyterian Hospital; and Dr. Weinstein is Director, Pediatric Comprehensive Epilepsy Program, Weill Cornell Medical School, New York Presbyterian Hospital

Drs. Keros and Weinstein report no financial relationships relevant to this field of study.

This article originally appeared in the November 2010 issue of Neurology Alert. *It was edited by Matthew E. Fink, MD, and peer reviewed by M. Flint Beal, MD. Dr. Fink is Interim Chair and Neurologist in Chief, Department of Neurology and Neuroscience, Weill Cornell Medical College, NewYork Presbyterian Hospital, and Dr. Beal is Anne Parrish Titzel Professor, Department of Neurology and Neuroscience, Weill Cornell Medical Center. Drs. Fink and Beal both report no financial relationships relevant to this field of study.*

Synopsis: *Children with H1N1 influenza are more likely to have neurologic complications compared to those with non-N1H1 seasonal influenza.*

Source: Ekstrand J, et al. Heightened neurological complications in children with pandemic H1N1 influenza. *Ann Neurol* DOI: 10.1002/ana.22184

INFLUENZA LONG HAS BEEN KNOWN TO CAUSE NEUROLOGIC disorders, including encephalitis, encephalopathy, and seizures. Case reports of neurologic complications published during the 2009 H1N1 pandemic hinted at an increased incidence and severity of these complications when compared to previous years' non-H1N1 (seasonal) influenza A, particularly in children.

A single-center, retrospective study of children hospitalized at Primary Children's Hospital in Salt Lake City conducted by Ekstrand et al compared neurologic complications of H1N1 to seasonal influenza infections. Patients were all hospitalized, were younger than 19 years, had direct fluorescent antibody confirmed influenza A, and had new neurologic symptoms not attributable to another systemic problem. The 2009 H1N1 group was identified

between April 1 and November 30, 2009, whereas the seasonal influenza group was admitted from summer 2004 to 2008. The H1N1 cases were further divided into two waves (April 1-July 31 and Aug 1-Nov 30). Qualifying neurologic disorders were seizures, including febrile seizures and status epilepticus, encephalopathy, encephalitis, headache, myositis, myalgia, aphasia, neuropathy, Guillain-Barré, and other focal neurologic signs.

In the 2004-2008 group, 234 hospitalized children were diagnosed with season influenza, with 16 meeting inclusion criteria. Of 303 children with 2009 H1N1, 18 met inclusion criteria, 9 in each wave. The H1N1 influenza group was older (mean 6.5 years vs. 2.4 years) and more likely to have an underlying medical or neurologic condition (83% vs. 25%) that included epilepsy, febrile seizures, neuromuscular disease, developmental delay, or a combination. The demographic characteristics were similar between wave 1 and wave 2.

The incidence of seizures (63% and 67%) and status epilepticus (39% and 37%) was similar between the groups. However, the H1N1 group had a statistically significant increased incidence of other neurologic symptoms including encephalopathy (n = 9), focal neurological findings (n = 5), and aphasia (n = 6).

Of those with lumbar punctures, none had CSF pleocytosis or significantly elevated protein, and one CSF sample tested for viral DNA by PCR was negative. The H1N1 group was more likely to be treated with antibiotics, antivirals, IVIG, and steroids, none with reported benefit. MRI was performed in seven children with H1N1 with three (17%) abnormal, and in five children with seasonal influenza, all of which were normal. EEG abnormalities were present in eight of 11 patients tested in the H1N1 group, compared to one of 12 in the seasonal group. Abnormal findings included burst-suppression, diffuse slowing, and spike-and-wave discharges. Four patients had persistent neurologic deficits, of which two of three for whom follow-up was available recovered after 6 months.

There was a trend toward increased severity of illness in wave 1 vs. wave 2 of the 2009 H1N1 pandemic, with longer hospital stay, more cases of encephalopathy, focal findings, persistent neurological symptoms, and MRI and EEG abnormalities.

■ COMMENTARY

This is the largest study to date directly comparing the neurologic complications of the 2009 pandemic H1N1 influenza virus with non-H1N1 infections from previous years. A significant strength of the study is the large catchment area of Primary Children's Hospital that spans several states, but given the large distances to be traveled, may have led to an underestimate of complications with exclusion of milder cases not leading to hospitalization. The case ascertainment could have been alternatively skewed by the massive media coverage with multiple medical alerts for children with pre-existing neurologic and other underlying medical conditions, leading to increased community awareness and hospital stays (median hospitalization stays were only 1-3 days). Although some conclusions are limited by the relatively small sample size and the retrospective design of the study, the data suggest that H1N1 infections are more likely to result in neurologic complications compared to seasonal influenza. But, are children with pre-existing neurologic conditions more likely to be infected and hospitalized with H1N1 in the first place, or of those hospitalized with influenza, is it those with neurologic and other illness who are more likely to have neurologic complications? The authors did not provide the baseline characteristics of the population of children hospitalized with influenza, and thus that question cannot be answered from the data provided.

This study emphasizes the potential severity of influenza infections in children, particularly the H1N1 subtype, and reinforces the need for vaccinations, especially in those with pre-existing medical and neurologic illness. ■

Is Hyperoxia Harmful After Resuscitation from Cardiac Arrest?

ABSTRACT & COMMENTARY

By David J. Pierson, MD

Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle

Dr. Pierson reports no financial relationships relevant to this field of study.

This article originally appeared in the November 2010 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. Dr. Thompson is Associate Professor of Medicine, University of Washington. Dr. Thompson reports no financial relationships relevant to this field of study.*

Synopsis: *In this study from 120 hospitals in the Project IMPACT database, the presence of hyperoxia (arterial PO_2 300 mm Hg or higher) in the first 24 hours after resuscitation from cardiac arrest was associated with a worse in-hospital mortality than either normoxia or hypoxia.*

Source: Kilgannon JH, et al; for the Emergency Medicine Shock Research Network (EMShockNet) Investigators. Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality. *JAMA*. 2010;303:2165-2171.

Project IMPACT, a proprietary database originally created by the Society for Critical Care Medicine and now

maintained by Cerner Corp., collects data from a voluntary consortium of ICUs across America. In this study, Kilgannon et al used data collected from 120 Project IMPACT hospitals between 2001 and 2005 to look for associations between initial arterial PO_2 obtained in the ICU and patient outcome following resuscitation from cardiac arrest.

Data from adult patients with non-traumatic cardiac arrest, either out-of-hospital or occurring in hospitalized patients, within 24 hours of ICU admission were examined. The presence of hyperoxia, normoxia, or hypoxia according to the first PO_2 entered into the database during the initial 24 hours in the ICU was correlated with in-hospital mortality. Hyperoxia was defined as a PO_2 of 300 mm Hg or higher; hypoxia was either a $PO_2 < 60$ mm Hg or PaO_2/FIO_2 (P/F) < 300 mm Hg; normoxia was either a $PO_2 > 60$ mm Hg or a P/F > 300 mm Hg with $PO_2 < 300$ mm Hg. Statistical attempts were made to control for potential confounders such as age, pre-admission functional status, comorbid conditions, and vital signs.

Of the 8736 eligible patients, 2410 did not have an arterial blood gas recorded within the first 24 hours in the ICU. Among the other 6326 patients, 1156 (18%) had hyperoxia, 3999 (63%) hypoxia, and 1171 (19%) normoxia on the initial ICU blood gas specimen. Hyperoxia was associated with higher in-hospital mortality (63%; 95% confidence interval [CI], 60%-66%) as compared to the normoxia group (45%; 95% CI, 43%-48%) and the hypoxia group (57%; 95% CI, 56%-59%). After correcting for the potential confounders, initial hyperoxia had an odds ratio for death of 1.8 (95% CI, 1.5-2.2). The authors conclude that exposure to hyperoxia following cardiac arrest is an independent predictor of a worse outcome in the form of in-hospital mortality.

■ COMMENTARY

The findings of this study support the notion that exposure of the brain and other tissues to hyperoxia following return of spontaneous circulation after cardiac arrest is harmful, perhaps through the generation of free oxygen radicals. Based on these findings, the authors call for clinical trials of controlled reoxygenation during the post-resuscitation period. While the results fit nicely with our concept of pathophysiology, there are a couple of troubling issues with the study with respect to its design and the potential generalizability of the findings.

The first issue is how exposure to the variable of interest was identified — both in terms of definition and with respect to duration of exposure. The 3 categories of arterial oxygenation, as determined on the first arterial blood specimen recorded after the patient arrived in the ICU, do not correspond to any physiologic categorization I can figure out. Presumably, oxygen free radicals are generated in some relation to tissue oxygen exposure — that is, to the number of oxygen molecules to which vulnerable cells are exposed. This should correlate with tissue PO_2, which would be approximated most closely by capillary oxygen content, and next best (in the absence of hemoglobin concentration) by arterial PO_2 — but not the concentration of inspired oxygen or the alveolar-to-arterial PO_2 gradient, for which P/F is a surrogate. One would expect that arterial PO_2 and not P/F would best assess the variable of interest. In the present study, however, according to the criteria used, patients in the normoxia and hypoxia groups could both have PO_2 values as high as 299 mm Hg (PO_2 between 60 and 299 mm Hg in the former, and PO_2 up to 299 mm Hg in the latter).

This concern could be addressed if the paper reported actual PO_2 values in the 3 groups, but it does not. Thus, the magnitude of differences in the variable of greatest interest among the groups, in relation to the reported outcome, is unknown. In addition, in keeping with the hypothesis being investigated, the duration of exposure to hyperoxia would be expected to be an important variable. As it is, the time from resuscitation to identification of oxygenation status is unknown, other than the patient entered the ICU within 24 hours after resuscitation and the blood gas was obtained within 24 hours after that. Presumably, the reasons for this, and for the unusual definitions used with respect to oxygenation, have to do with what was available in the database.

A second concern relates to the potential generalizability of the findings beyond the hospitals that furnished the data. Project IMPACT collects data from a voluntary consortium of ICUs rather than from a defined subset of U.S. ICUs selected by specified criteria. According to the authors, the 120 hospitals furnishing data for the present study were mainly large non-academic community hospitals. How the results of this study might apply to patients and their management in institutions with different demographics is unknown.

These concerns notwithstanding, the findings of the present study support the concept that, after resuscitation from cardiac arrest, adequate oxygenation should be provided to avoid the adverse effects of tissue hypoxia, but excessive exposure to oxygen beyond that necessary for adequate arterial oxygenation should be avoided. The study's results are consistent with the most recent recommendations of the International Liaison Committee on Resuscitation that arterial saturation be maintained between 94% and 96% following resuscitation from cardiac arrest.[1] ■

Reference

1. Neumar RW, et al. Post-cardiac arrest syndrome: Epidemiology, pathophysiology, treatment, and prognostication. *Circulation*. 2008;118:2452-2483.

Type B Aortic Dissection

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

This article originally appeared in the November 2010 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Ethan Weiss, MD.*

Source: Trimarchi S, et al. Importance of refractory pain and hypertension in acute type B aortic dissection. Insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation*. 2010;122:1283-1289.

Indications for surgical or interventional management in acute type B aortic dissection (ABAD) include malperfusion syndromes, progression of dissection, and aneurysm expansion. The prognostic significance of refractory pain and high blood pressure (BP) are not completely understood. Accordingly, Trimarchi and colleagues examined the IRAD database to determine the effects of ongoing pain and incomplete blood pressure control on in-hospital outcomes.

The IRAD registry is an international multi-center registry of patients presenting with acute aortic dissection. This study presents data on patients presenting between 1996 and 2004 with ABAD. They included patients with ABAD and patients with intramural hematoma. ABAD was defined as an aortic dissection involving the descending aorta with no tear in the ascending aorta or arch, and intramural hematoma was defined as a regionally thickened aortic wall with no double lumen or entry flap. The patients were separated into group 1 (intermediate risk) with recurrent or refractory pain and/or refractory hypertension but no other clinical complications; group 2 (low risk) with no refractory pain or hypertension and no other clinical complications; and group 3 (high risk) with one or more of the following complications: shock, peri-aortic hematoma, spinal cord ischemia, pre-operative mesenteric ischemia/infarction, acute renal failure, or limb ischemia. Group 3 were excluded from this analysis, as they were considered to have indications for surgery and analysis was confined to the 365 patients in groups 1 and 2.

The mean age of patients was 63.5 years, 5% had diabetes and 33% were female. Intramural hematoma was present in 11.4%. Baseline characteristics were well matched between groups, except for a higher prevalence of Marfan syndrome in group 1 (7.3% vs. 2.1%, $p = 0.03$), as well as higher rates of abrupt pain onset (92.2% vs. 81.3%, $p = 0.03$), migrating pain (35.5% vs. 16.6%, $p = 0.0008$), and radiating pain (51.6% vs. 33.6%, $p = 0.007$). Patients in group 1 (n = 69) were more likely to undergo surgical (36.2% vs. 8.4%, $p < 0.001$) or endovascular therapy (39.1% vs. 3.7%, $p < 0.001$) than patients in group 2 (n = 296). There was longer time to invasive treatment in group 1 than in group 2 (240 hrs vs. 99 hrs, $p < 0.01$). Overall in-hospital mortality in patients with recurrent/refractory pain or refractory hypertension (group 1) was higher than in those without (group 2) [17.4% vs. 4.0%, $p < 0.001$]. In those managed medically, group 1 also had a higher mortality (35.6% vs. 1.5%, $p < 0.001$). Multivariable analysis showed that refractory/recurrent pain or refractory hypertension are associated with higher risk of in-hospital mortality (odds ratio 3.3, $p = 0.04$), as are age > 70 years (OR 5.1, $p < 0.01$) and absence of chest pain (OR 3.5, $p = 0.05$). The authors conclude that in uncomplicated ABAD patients, medical therapy was associated with excellent in-hospital outcomes. By contrast, the presence of recurrent pain and/or refractory hypertension was associated with increased in-hospital mortality, particularly in those patients managed medically. These observations suggest that aortic interventions, such as by an endovascular approach, may be indicated in this intermediate-risk group.

■ COMMENTARY

Type B aortic dissections traditionally have been managed medically, as advised in the ACC/AHA guidelines, with surgery or endovascular therapy being reserved for cases of impending aortic rupture or side-branch compromise. The current study reinforces the importance of strict BP and pain control in patients managed medically. Although this is a retrospective, observational study, rather than a prospective, randomized trial, it appears that inadequate pain or BP control is associated with higher in-hospital mortality, especially in the patients managed medically. Whether these patients should undergo more invasive therapy remains unknown, and the authors' conclusion that an endovascular approach may be warranted is probably somewhat overzealous. With the rapid evolution of endovascular therapies and the variation in regional practice patterns and experience with these technologies, it is difficult to make any conclusions from this data set. Furthermore, the equipment used in 1996 is already obsolete, and endovascular therapy was only used in the minority (38 patients; 10.4% of the cohort). Thus, the most appropriate conclusion from this study is to underscore the importance of strict BP and pain control in patients with acute type B aortic dissection. ■

Unilateral Pulmonary Edema

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

Professor of Medicine, Chief of Cardiology,

University of California, San Francisco

Dr. Crawford reports no financial relationships relevant to this field of study.

This article originally appeared in the November 2010 issue of Clinical Cardiology Alert. *It was peer reviewed by Ethan Weiss, MD.*

Source: Attias D, et al. Prevalence, characteristics, and outcomes of patients presenting with cardiogenic unilateral pulmonary edema. *Circulation*. 2010;122:1109-1115.

Cardiogenic unilateral pulmonary edema is unusual and, if it is the presenting manifestation of heart failure, diagnosis and appropriate treatment may be delayed. Thus, these investigators from France reviewed 869 cases of cardiogenic pulmonary edema admitted over eight years to assess the prevalence and clinical features of unilateral pulmonary edema. Echocardiograms were obtained within 48 hours in 96% of the patients.

Results: Bilateral edema was present in 851 (98%) and unilateral in 18 (2%). Severe mitral regurgitation (MR) was found in 71 (8%). Unilateral edema was right-sided in most (89%). All patients with unilateral edema had severe MR, and the radiological location of the edema in the lungs was related to the direction of the MR jet. Only 6% of the patients with bilateral edema had severe MR. A murmur was heard in about two-thirds of patients with severe MR, but it was more likely in those with organic MR (83%) vs. functional MR (43%). Delay in treatment (> 6 hours from presentation) was more common in unilateral edema as compared to bilateral edema patients (33 vs. 4%, $p < 0.003$). Total in-hospital mortality was 9%, and was higher in those with unilateral edema as compared to bilateral edema (39% vs. 8%, OR 6.9, 95% CI 2.6-18, $p < 0.001$). Multivariate analysis for clinical factors associated with death showed that unilateral edema was the most predictive variable. The authors concluded that unilateral pulmonary edema is infrequent (2% of pulmonary edema cases), usually involves the right lung, and is almost always associated with acute severe MR. The presence of unilateral edema delays treatment and is associated with greater mortality.

■ COMMENTARY

Unilateral pulmonary edema in this series was unusual (2% of cardiac pulmonary edema), but was always associated with severe mitral regurgitation (MR). Among their patients presenting with pulmonary edema due to severe MR, unilateral edema was seen in 25%. Their series demonstrates that the diagnosis of cardiac edema was often delayed when unilateral edema was present. In fact, pneumonia was often suspected, and 61% were treated with antibiotics even though only 11% had fever. Unfortunately, you cannot rely on the presence of a murmur to help you arrive at the correct diagnosis. Although over 80% of those with organic MR had murmurs, less than half of those with functional murmurs did. Also, an elevated leukocyte count was frequent (72%) in those with unilateral edema. Thus, if you suspect a cardiac cause, an echocardiogram should be done.

Echocardiography suggested that unilateral edema is due to the regurgitant jet preferentially impacting the pulmonary veins from one lung. Prior invasive studies of patients with severe MR and eccentric jets have confirmed that pulmonary capillary wedge pressures can be higher in one lung vs. the other. Interestingly, involvement of the right lung is more common perhaps because the more common posterior leaflet prolapse usually directs the MR jet toward the right pulmonary veins. Anterior leaflet prolapse often is directed toward the left pulmonary veins. Whether the observed increase in mortality in patients with unilateral edema is due to the delay in diagnosis is unclear. In this series, these patients had lower blood pressures and were more likely to be on mechanical ventilation and pressors. Also, all patients with unilateral edema had severe MR, whereas only 6% of those with bilateral edema did. Thus, it appears that delaying the diagnosis of severe MR is detrimental to survival. ■

CME Questions

10. Based on the study by the Kilgannon and the Emergency Medicine Shock Research Network, what level of PaO_2 was associated with the best outcome after cardiac arrest?

a. PaO_2 > 300 mm Hg

b. PaO_2 < 60 mm Hg

c. PaO_2 > 60 and < 300 mm Hg

d. PaO_2 did not correlate with survival after cardiac arrest

11. According to the report by Trimarchi and colleagues of patients with acute type B aortic dissection, lack of control of which set of clinical features led to the worst outcomes?

a. Blood pressure and heart rate

b. Blood pressure and recurrent pain

c. Heart rate and urine output

d. Blood pressure and urine output

12. Based on the recent case series by Attias et al, patients who present with unilateral pulmonary edema usually have which of the following?

a. Pneumonia

b. Chronic mitral stenosis

c. Diastolic heart failure

d. Acute severe mitral regurgitation

Answers: 10. (c); 11. (b); 12. (d)

CME / Objectives

Upon completion of this educational activity, participants should be able to:

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems. ■