

# CHEST<sup>®</sup>

Official publication of the American College of Chest Physicians



## Right-Sided Heart Catheterization :

Daniel A. Culver and Richard A. Krasuski

*Chest* 2010;138:1030-1032  
DOI 10.1378/chest.10-1241

The online version of this article, along with updated information and services can be found online on the World Wide Web at:  
<http://chestjournal.chestpubs.org/content/138/5/1030.full.html>

*Chest* is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 2010 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook, IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder.  
(<http://chestjournal.chestpubs.org/site/misc/reprints.xhtml>)  
ISSN:0012-3692

A M E R I C A N C O L L E G E O F



P H Y S I C I A N S<sup>®</sup>

## REFERENCES

1. Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G. The use of continuous IV sedation is associated with prolongation of mechanical ventilation. *Chest*. 1998;114(2):541-548.
2. Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med*. 1999;27(12):2609-2615.
3. Carson SS, Kress JP, Rodgers JE, et al. A randomized trial of intermittent lorazepam versus propofol with daily interruption in mechanically ventilated patients. *Crit Care Med*. 2006;34(5):1326-1332.
4. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet*. 2008;371(9607):126-134.
5. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med*. 2000;342(20):1471-1477.
6. De Jonghe B, Bastuji-Garin S, Fangio P, et al. Sedation algorithm in critically ill patients without acute brain injury. *Crit Care Med*. 2005;33(1):120-127.
7. Strøm T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet*. 2010;375(9713):475-480.
8. Chlan LL, Weinert CR, Skaar DJ, Tracy MF. Patient-controlled sedation: a novel approach to sedation management for mechanically ventilated patients. *Chest*. 2010;138(5):1045-1053.
9. Riker RR, Shehabi Y, Bokesch PM, et al; SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA*. 2009;301(5):489-499.
10. Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. *JAMA*. 2007;298(22):2644-2653.

## Right-Sided Heart Catheterization

### De Rigueur in Sarcoidosis?

Cardiac impairment in sarcoidosis was first described by Mitchell Bernstein in 1929,<sup>1</sup> the same year that Werner Forssman<sup>2</sup> demonstrated the feasibility of cardiac catheterization. By the late 1940s, the effect of advanced sarcoidosis on the pulmonary vasculature and right side of the heart was recognized, and the first documented elevation of pulmonary artery pressure (PAP) was reported by Austrian et al<sup>3</sup>

in 1951. Nearly 60 years later, the interactions among the heart, lungs, and pulmonary vasculature in sarcoidosis remain a conundrum.

Over the ensuing decades, studies of the pulmonary hemodynamics in sarcoidosis were sporadic at best largely because of the lack of viable therapeutic options. Another reason for the relative paucity of early interest may be the complex pathophysiology of sarcoidosis-associated pulmonary hypertension (PH), which may be due to destruction of pulmonary venous and arterial vascular beds by granulomas or fibrosis, pulmonary arterial vasoconstriction, and intrinsic cardiac dysfunction.<sup>4</sup> A third factor is the tendency among physicians to ascribe dyspnea to pulmonary parenchymal involvement. A telling observation in this regard was made by Shorr et al,<sup>5</sup> who noted that the mean PAP in US patients awaiting lung transplantation was 9 mm Hg higher (34.4 vs 25.6 mm Hg) in sarcoidosis than in idiopathic pulmonary fibrosis, despite similar spirometric severity.

Today, we have available both diagnostic tools and potential options for treatment, including specific pharmacologic therapies and transplantation. Interest in sarcoidosis-associated PH, as well as a host of other nonidiopathic causes of elevated PAPs, has burgeoned. Despite the increased attention, a frequent rejoinder has been that mild elevations of PAPs are just a reflection of advanced disease. Thus, the findings reported by Baughman et al<sup>6</sup> in this issue of *CHEST* (see page 1078) represent an extremely provocative step forward in our understanding of the significance of sarcoidosis-associated PH. Beyond its obvious prognostic implications, the study invites consideration of the possibility of screening subsets of patients with sarcoidosis for sarcoidosis-associated PH. Further, it suggests that invasive testing, not echocardiography, is necessary when sarcoidosis-associated PH is suspected. Finally, by linking prognosis to physiology, this article implies that mechanisms leading to pulmonary vascular pathology in sarcoidosis may be important therapeutic targets.

Baughman et al<sup>6</sup> retrospectively analyzed survival among 130 patients who had a right-sided heart catheterization for the indication of moderate to severe persistent dyspnea at a single large referral center. Similar to their prior reports,<sup>7</sup> they found a high prevalence of elevated PAPs and noted that 29% of the cohort with PAP  $\geq$  25 mm Hg had elevated pulmonary capillary wedge pressure, suggesting intrinsic cardiac disease. It is interesting that unsuspected occult cardiac involvement by sarcoidosis has been reported previously in approximately one-fourth of the US population,<sup>8</sup> which suggests a major weakness of routine echocardiography: the inability to reliably distinguish pulmonary hypertension due to left atrial hypertension from that due to isolated pulmonary

vascular disease. Newer echocardiographic techniques may be helpful in this regard, but their use remains far from universal, and their application in patients with parenchymal lung disease is largely unstudied.<sup>9</sup> It is unclear whether there were other signs of diastolic dysfunction in the current population, such as abnormal mitral inflow velocity, left atrial enlargement, or left ventricular hypertrophy.

The authors found that the presence of any elevation of PAP  $\geq 25$  mm Hg with normal pulmonary capillary wedge pressure conferred independent risk of death over a meaningful follow-up period. A strength and potential weakness of these data are that all the hemodynamic characterizations were performed by a single investigator with an interest in the subject, assuring consistency of interpretation, but this raises the issue of whether equally useful hemodynamic measurements would be obtained with more widespread adoption in other centers. For now, it seems prudent to interpret any hemodynamic data in the context of the patient's individual symptoms, functional status, and clinical course over time.

It is well established that the clinical manifestations and course of sarcoidosis are profoundly influenced by the geographic location.<sup>10</sup> The biggest limitation of this study may be the difficulty of applying it to various clinical settings to determine eligibility for catheterization. The absence of generalizable prospective indications for right-sided heart catheterization and the inability to account for patients who refused catheterization are also limitations, as the authors acknowledge.

The authors also point out that the time is ripe for a prospective trial of screening for sarcoidosis-associated PH. We agree. However, the question is raised of whether earlier or more frequent identification of sarcoidosis-associated PH is beneficial. The current data accord with analysis of US patients listed for lung transplantation, where race, amount of supplemental oxygen, and mean PAP independently predicted mortality.<sup>11</sup> It seems evident that identifying pulmonary hypertension in a patient with sarcoidosis with substantial functional impairment should trigger consideration of referral to a lung transplantation center prior to deterioration that would obviate the possibility of transplantation. However, a trial of more widespread screening for sarcoidosis-associated PH will need to be informed by the lung cancer screening experience. For example, there are issues of lead-time bias (earlier diagnosis of sarcoidosis-associated PH not changing the outcome due to the failure of therapies to alter the course), length-time bias (diagnosing slowly progressive sarcoidosis-associated PH earlier), and overdiagnosis bias (diagnosing increased numbers of patients with sarcoidosis-associated PH but whose clinical trajectory is benign).

Is direct measurement of the pulmonary hemodynamics now *de rigueur* in patients with persistent dyspneic sarcoidosis? The data here suggest that it almost certainly is needed prior to initiation of any specific therapy, especially given the high costs of most medications and the not-insignificant rate of complications from vasodilators in this population.<sup>12</sup> Whether the additional risk stratification that can be obtained from invasive hemodynamic measurements warrant the costs and risks associated with that information remains to be seen. Until either the effectiveness and efficacy of specific pulmonary hypertension therapy in sarcoidosis-associated PH are determined or a benefit for screening is demonstrated, clinicians will continue to struggle with the decision about when to send patients for invasive testing.

Daniel A. Culver, DO, FCCP  
Richard A. Krasuski, MD  
Cleveland, OH

**Affiliations:** From the Respiratory Institute (Dr Culver) and Cardiovascular Medicine (Dr Krasuski), The Cleveland Clinic.

**Financial/nonfinancial disclosures:** The authors have reported to CHEST the following conflicts of interest: Dr Culver is a site investigator for a trial sponsored by Actelion (Dr Baughman, principal investigator). Dr Krasuski has served as a consultant to Actelion and is on the speakers bureau of Actelion and United Therapeutics. He also has been a coinvestigator for trials sponsored by Actelion.

**Correspondence to:** Daniel A. Culver, DO, FCCP, Respiratory Institute, The Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195; e-mail: culverd@ccf.org

© 2010 American College of Chest Physicians. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (<http://www.chestpubs.org/site/misc/reprints.xhtml>).

DOI: 10.1378/chest.10-1241

## REFERENCES

- Bernstein M, Konzleemann FW, Sidlick DM. Boeck's sarcoid: report of a case with visceral involvement. *Arch Intern Med.* 1929;44(5):721-734.
- Forssmann W. Die sonderung des rechten herzens. *Klin Wochenschr.* 1929;8:2085-2087.
- Austrian R, McClement JH, Renzetti AD Jr, Donald KW, Riley RL, Courmand A. Clinical and physiologic features of some types of pulmonary diseases with impairment of alveolar-capillary diffusion; the syndrome of "alveolar-capillary block". *Am J Med.* 1951;11(6):667-685.
- Diaz-Guzman E, Farver C, Parambil J, Culver DA. Pulmonary hypertension caused by sarcoidosis. *Clin Chest Med.* 2008;29(3):549-563.
- Shorr AF, Davies DB, Nathan SD. Outcomes for patients with sarcoidosis awaiting lung transplantation. *Chest.* 2002; 122(1):233-238.
- Baughman RP, Engel PJ, Taylor L, Lower EE. Survival in sarcoidosis-associated pulmonary hypertension: the importance of hemodynamic evaluation. *Chest.* 2010;138(5):1078-1085.
- Baughman RP, Engel PJ, Meyer CA, Barrett AB, Lower EE. Pulmonary hypertension in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis.* 2006;23(2):108-116.
- Silverman KJ, Hutchins GM, Bulkley BH. Cardiac sarcoid: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. *Circulation.* 1978;58(6):1204-1211.

9. Milan A, Magnino C, Veglio F. Echocardiographic indexes for the non-invasive evaluation of pulmonary hemodynamics. *J Am Soc Echocardiogr.* 2010;23(3):225-239, quiz 332-334.
10. Siltzbach LE, James DG, Neville E, et al. Course and prognosis of sarcoidosis around the world. *Am J Med.* 1974;57(6):847-852.
11. Shorr AF, Davies DB, Nathan SD. Predicting mortality in patients with sarcoidosis awaiting lung transplantation. *Chest.* 2003;124(3):922-928.
12. Heresi GA, Dweik RA. Sarcoidosis-associated pulmonary hypertension. One size does not fit all. *Chest.* 2009;135(6):1410-1412.

## Balancing the Risk of Hemorrhage vs Thromboembolism in Patients With Atrial Fibrillation

### How To Navigate Between Scylla and Charybdis?

According to mythology, Scylla and Charybdis were two sea monsters placed on opposite sides of the Strait of Messina, between Calabria and Sicily in Italy. Sailors' navigation was extremely difficult since these monsters were very close to each other and attempts to avoid Scylla implied passing very closely to Charybdis and vice versa. This imaginary scenario well depicts the difficulties that a practicing physician may encounter when deciding on the intriguing trade-off between benefits and risks of antithrombotic prophylaxis in the challenging and complex setting of "real-world" patients affected by nonvalvular atrial fibrillation (AF).<sup>1</sup>

In this issue of *CHEST* (see page 1093), Pisters et al<sup>2</sup> report on the development of a novel, easy, and practical risk score to estimate the 1-year risk for major bleeding, which uses the acronym HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (> 65 years), Drugs/alcohol concomitantly). The authors tested this score (also called the Birmingham AF Bleeding Risk Schema) on a cohort of 3,678 real-world patients enrolled in the Euro Heart Survey on AF. At discharge, around 65% of patients were on oral anticoagulation (OAC) treatment (13% of them also taking aspirin and/or clopidogrel), 24% on antiplatelet therapy alone, and 10% without any antithrombotic therapy, with unadjusted bleeding rates of 1.75%, 0.97%, and 1.42% per year, respectively.

This study is particularly interesting because the risk of bleeding was assessed on real-world patients with AF included in a registry, thus in a much-less-selected population than that represented in randomized clinical trials on OACs, where, quite often, up

to one-third of patients with AF were not enrolled, mainly because they were judged to be at high risk of bleeding.<sup>3</sup> During treatment with OACs, the absolute risk of major bleeding complications for patients followed by specialized anticoagulation services ranges from 0.32% to 2.1% per year, with a risk of fatal bleeding ranging from 0% to 0.25% per year, and this implies that the risk of major bleeding and the risk of intracranial hemorrhage are increased by 0.3% to 0.5% per year and by 0.2% per year, respectively, in comparison with controls.<sup>3,4</sup>

However, these data cannot necessarily be extrapolated to real-world clinical practice, where patients' care may be less accurate and rigorous.<sup>4</sup> A series of bleeding-risk stratification schemes have been previously developed and proposed to estimate the risk of major bleeding during OAC treatment,<sup>3,4</sup> but most of them were not necessarily specific for patients with AF, were derived from historic cohorts without subsequent prospective validation, and did not appear to be user friendly.<sup>2-4</sup> The study by Pisters et al<sup>2</sup> indicates that a very simple risk score, HAS-BLED, is able to predict the bleeding risk with consistent accuracy, performing better than the more complicated HEMOR<sub>2</sub>RAGES (Hepatic or renal disease, Ethanol abuse, Malignancy, Older age [> 75 years], Rebleeding, Reduced platelet count or function, Hypertension [uncontrolled], Anemia, Genetic factors, Excessive fall risk, and Stroke) scheme (which also requires genetic assessment<sup>4</sup>) when tested in the overall population and in all the subgroups of patients, apart from those receiving both OAC and antiplatelet treatments.<sup>2</sup>

While the HAS-BLED score is a very simple and useful tool to be applied in daily practice, the article also stimulates questions about how to further improve our prediction of the risk of bleeding. In our view, and according to what the authors reported, assessment of the bleeding risk in the elderly will merit further evaluation. Indeed, the use of antithrombotic treatments in the elderly is quite problematic but relevant given the increasing prevalence of AF with age.<sup>1</sup> However, biologic age is perhaps more relevant than chronological age. For example, a frail 60-year-old patient with multiple comorbidities and polypharmacy would be at greater bleeding risk than a fit, healthy 90-year-old subject with no previous illnesses who still goes ballroom dancing.

The risk of bleeding, and specifically the risk of intracranial hemorrhage, is particularly increased in the elderly.<sup>3-6</sup> Whereas the prevalence of bleeding is reported to be 0.2% to 1.0% patient-years overall among patients who are anticoagulated, this rate increases to 1.1% patient-years in patients aged  $\geq 75$  years.<sup>3</sup> Fang et al<sup>5</sup> reported an adjusted odds ratio of 2.5 for intracranial hemorrhage in patients aged

**Right-Sided Heart Catheterization :**  
Daniel A. Culver and Richard A. Krasuski  
*Chest* 2010;138; 1030-1032  
DOI 10.1378/chest.10-1241

**This information is current as of November 24, 2010**

**Updated Information & Services**

Updated Information and services can be found at:  
<http://chestjournal.chestpubs.org/content/138/5/1030.full.html>

**References**

This article cites 12 articles, 6 of which can be accessed free at:  
<http://chestjournal.chestpubs.org/content/138/5/1030.full.html#ref-list-1>

**Permissions & Licensing**

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<http://www.chestpubs.org/site/misc/reprints.xhtml>

**Reprints**

Information about ordering reprints can be found online:  
<http://www.chestpubs.org/site/misc/reprints.xhtml>

**Citation Alerts**

Receive free e-mail alerts when new articles cite this article. To sign up, select the "Services" link to the right of the online article.

**Images in PowerPoint format**

Figures that appear in *CHEST* articles can be downloaded for teaching purposes in PowerPoint slide format. See any online figure for directions.

