AHC Media

Clinical Cardiology

Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

Vol. 35, Issue 11, November 2016
AHCMedia.com

ABSTRACT & COMMENTARY

Stent Complexity Matters When Choosing Dual Antiplatelet Therapy Duration

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco; Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

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

SYNOPSIS: A new study shows that increased percutaneous coronary intervention procedural complexity helps risk stratify patients and correlates with the benefit of longer-term dual antiplatelet therapy.

SOURCE: Giustino G, Chieffo A, Palmerini T, et al. Efficacy and safety of dual antiplatelet therapy after complex PCI. *J Am Coll Cardiol* 2016 Aug 25. pii: S0735-1097(16)34935-X. doi: 10.1016/j.jacc.2016.07.760. [Epub ahead of print].

Choosing an appropriate duration of dual antiplatelet therapy (DAPT) following coronary intervention with drug-eluting stents (DES) involves weighing competing risks of ischemic and thrombotic events with those of serious bleeding. Over the past several years, a bevy of trials has examined this issue at both the short and the long ends of the scale. Multiple studies, including ISAR SAFE, ITALIC, and OPTIMIZE, have investigated the minimum DAPT duration, comparing one year of DAPT with shorter durations of therapy in the range of three to six months. These individual studies have, for the most part, confirmed the safety of newer DES, and led to the recent change in U.S. guidelines reducing the DAPT duration for non-acute coronary syndrome, post-percutaneous coronary intervention patients to six months. At the opposite pole, the DAPT, DES LATE, and PEGASUS TIMI 54 trials have assessed the results of DAPT duration beyond 12 months, demonstrating a tradeoff between reductions in stent thrombosis and ischemic endpoints and an increase in clinically significant bleeding. Tools such as the DAPT score have attempted to individualize therapy by applying event- and patient-level characteristics to the risk-benefit equation.

The recent study by Giustino et al takes this indi-

Financial Disclosure: *Clinical Cardiology Alert*'s Physician Editor Michael H. Crawford, MD, Peer Reviewer Susan Zhao, MD, Nurse Planner Aurelia Macabasco-O'Connell, PhD, ACNP-BC, RN, PHN, FAHA, Assistant Editor Jonathan Springston, and Executive Editor Leslie Coplin report no financial relationships relevant to this field of study.

Clinical Cardiology
Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

Clinical Cardiology Alert,
ISSN 0741-4218, is published monthly by AHC Media LLC, One Atlanta Plaza, 950 East Paces Ferry Road NE, Suite 2850 Atlanta, GA 30326.

GST Registration Number: R128870672. Periodicals Postage Paid at Atlanta, GA, and at additional mailing offices.

POSTMASTER: Send address changes to *Clinical Cardiology Alert*, P.O. Box 550669, Atlanta, GA 30355.

SUBSCRIBER INFORMATION
(800) 688-2421
Customer.Service@AHCMedia.com
AHCMedia.com

Questions & Comments:
Please contact Assistant Editor
Jonathan Springston
at Jonathan.Springston@AHCMedia.com

Subscription Prices
United States
Print: 1 year with ***free*** *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.
Online only, single user: with ***free*** *AMA PRA Category 1 Credits™*: $299

Back issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. AHC Media designates this enduring material for a maximum of 2.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AHC Media is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. This activity has been approved for 2.25 nursing contact hour using a 60-minute contact hour. Provider approved by the California Board of Registered Nursing. Provider #CEP14749 for 27 Contact Hours.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.25 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

This activity is intended for the cardiologist. It is in effect for 36 months from the date of the publication.

AHC Media

vidualized approach one step further, linking PCI complexity with downstream events and with the potential benefits of longer-term DAPT. The authors combined patient-level data from six randomized, controlled trials comparing short (three or six months) and long (≥ 12 months) post-PCI DAPT duration. They developed and operationalized the definition of "complex" PCI, which includes any of the following: treatment of three or more lesions, treatment of three or more vessels, use of at least three stents or a total stent length > 60 mm, stenting of a chronic total occlusion, or treatment of a bifurcation with two stents. Of the 9,577 patients from the pooled trials, 1,680 (17.5%) presented with characteristics of complex PCI. Newer-generation stents were used in approximately 86% of the study population.

Compared with the non-complex population, patients in the complex PCI category experienced significantly higher rates of major adverse cardiac events (MACE), as well as of coronary thrombotic events, myocardial infarction (MI), and stent thrombosis. Patients with higher numbers of complex PCI characteristics experienced higher MACE rates; among these characteristics, bifurcation PCI with two stents was most strongly associated with increased ischemic risk.

In the complex PCI group, long-term DAPT showed a significant reduction in MACE (adjusted hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.35-0.89) that was not evident in the non-complex PCI group (adjusted HR, 1.01; 95% CI, 0.75-1.35; *P* for interaction = 0.01). Furthermore, the magnitude of this benefit increased with the number of high-risk procedural features. As expected, the risk for significant bleeding was higher in the long-term DAPT group, regardless of PCI complexity.

The authors concluded that DAPT for ≥ 1 year carried a significant benefit in terms of risk of cardiac ischemic events, compared with three or six months of DAPT, specifically in patients who underwent complex PCI. The perceived benefits of longer-term DAPT were greater as the degree of procedural complexity increased.

■ COMMENTARY

Much of the discussion of DAPT in the past year has focused on the safety of shorter duration of therapy with newer DES platforms. Identifying patients who will benefit from longer-term treatment has been limited to tools such as the DAPT score, which uses patient age, diabetes status, recent smoking history, PCI or MI history, presence of chronic heart failure or reduced ejection fraction, and index procedural characteristics, including MI at presentation, vein-graft PCI, and stent diameter. Overall, these are relatively blunt instruments and ignore most of the characteristics of the procedure itself.

Here, the authors convincingly identified PCI procedural complexity as a predictor of both downstream adverse events and of concrete benefit to long-term DAPT. This validates a strategy that many interventionalists have followed instinctively for some time, identifying a population for whom the risk-benefit ratio favors longer-duration antiplatelet therapy.

These anatomic and procedural characteristics provide a better surrogate for identifying risk compared with clinical factors such as age and diabetes and temper the enthusiasm for across-the-board shorter durations of therapy with concrete data. Most of all, this study demonstrates the need to fully understand a patient's stent anatomy before making recommendations regarding duration of therapy. ■

ABSTRACT & COMMENTARY

Indications for Prophylactic Surgery in Dilated Ascending Aortas Revisited

By Michael Crawford, MD, Editor

SYNOPSIS: An observational study of patients with dilated ascending aortas not due to inflammatory or syndromic conditions supports the current guideline recommending clinicians consider prophylactic surgery at ≥ 5.5 cm in diameter, and the risk of dissection or rupture is not greater in those with bicuspid aortic valves.

SOURCES: Kim JB, Spotnitz M, Lindsay ME, et al. Risk of aortic dissection in the moderately dilated ascending aorta. *J Am Coll Cardiol* 2016;68:1209-1219.

Pape LA. Aortic risk redux. *J Am Coll Cardiol* 2016;68:1220-1222.

Current guidelines recommend elective repair of the ascending aorta when the diameter reaches 5.5 cm to prevent acute dissection or rupture. However, recent observations have shown that dissection often occurs in smaller ascending aortas, especially in patients with bicuspid valves. Thus, some have proposed lowering the surgical diameter cut point. To explore this further, investigators analyzed the echocardiography database at the Massachusetts General Hospital and identified those with ascending aortic diameters between 4.0 and 5.5 cm. Patients with connective tissue disorders, inflammatory aortic diseases, or a history of aortic surgery were excluded. Medical records were assessed to identify subsequent aortic dissection or rupture for up to five years (median 3.4) from the index echo. The study group included 4,654 adults, of whom 586 (13%) had bicuspid valves. Aortic dissection or rupture occurred in 13 and one patients, respectively, which represented a 0.1% per patient-year incidence. On multivariate analysis, aortic dissection/rupture was associated with age (hazard ratio [HR], 1.06; 95% confidence interval [CI], 1.01-1.12; $P = 0.024$) and baseline aortic diameter (HR, 1.2; 95% CI, 1.05-1.36; $P = 0.006$), but not a bicuspid valve (HR, 0.94; 95% CI, 0.10-8.4; $P = 0.95$). Dissection or rupture rates within five years were: 0.4% at a diameter of 4.5 cm; 1.1% at 5.0 cm; and 2.9% at 5.5 cm. The authors concluded that in subjects with moderate dilation of the ascending aorta, the risk of dissection or rupture was low at diameters < 5.0 cm and this risk was not increased in patients with bicuspid aortic valves.

■ COMMENTARY

Given the high morbidity and mortality rates associated with ascending aortic dissections, there has been considerable interest in indicators for prophylactic surgical replacement. Current guidelines recommend ≥ 5.5 cm (class I) and this observational study supports this cutpoint. Also, even at > 5.5 cm, the risk of dissection or rupture is low (2.9%). Prophylactic surgery makes the most sense when the risk of dissection rupture is higher than the risk of death or major morbidity from surgery. Contemporary data suggest elective ascending aortic replacement surgery has a 2-3% mortality, a 2-3% stroke rate, and a 0.5% risk of paraplegia. So even operating at 5.5 cm seems aggressive based on the dissection/rupture rates in this study.

Patients with bicuspid valves in this study had larger ascending aortic diameters and more rapid expansion rates in the subgroup (30%) with serial echoes. However, a bicuspid valve was not a predictor of dissection/rupture. This contradicts the American College of Cardiology/American Heart Association guidelines, which call for consideration of surgery at smaller diameters in bicuspid aortic valve patients (4.5-5.5 cm, class IIa). However, they updated the guidelines this year to eliminate this clause but kept the class I recommendation for surgery at 5.5 cm. Thus, surgery at < 5.5 cm is only recommended now for patients with aortic syndromic disease such as Marfan syndrome. Such patients were excluded from this study.

There are limitations to this study. The most obvious is that it is observational, but randomized trials in this area are unlikely to ever be conducted. Also, this isn't a true population study since it is biased by referral to echo, which would include more patients with cardiovascular disease. Rates of aortic dissection or rupture likely are lower in a true community population. In addition, there were only 14 events, which makes determining predictors difficult. Finally, some patients were removed from the population for elective surgery based on a more aggressive approach to prophylactic surgery than the 5.5 cm cutoff or the need for aortic valve surgery.

The editorial accompanying this article noted that aortic size is related to age, sex, and body size, increasing with age, male sex, and larger bodies. The latter has prompted some to use aortic diameter in-

dexed to body surface area. But others have pointed out that body surface area is heavily influenced by weight, and the typical weight gain with age may have little influence on aortic size. They have suggested indexing for height, which often changes less with aging. Thus, Pape suggested that future guidelines on prophylactic surgery for ascending aortic dilation should appropriate norms based on age, sex, and height. Until this happens, perhaps we should factor in extremes of age and body size into our decision making. ■

ABSTRACT & COMMENTARY

Coronary CT Angiography Prior to Heart Valve Surgery

By Michael Crawford, MD, Editor

SYNOPSIS: A meta-analysis of available studies of coronary CT angiography compared to invasive angiography demonstrates that coronary CT angiography is a reasonable substitute for invasive angiography in patients with low- to intermediate-risk for coronary artery disease and without aortic stenosis undergoing valve surgery.

SOURCES: Opolski MP, Staruch AD, Jakubczyk M, et al. CT angiography for the detection of coronary artery stenoses in patients referred for cardiac valve surgery: Systematic review and meta-analysis. *JACC Cardiovasc Imaging* 2016;9:1059-1070.

Dewey M, Schlattmann P. Investigating patients for CAD before cardiac valve surgery: Is CT angiography enough? *JACC Cardiovasc Imaging* 2016;9:1071-1073.

Small single-center studies have suggested that coronary computed tomography angiography (CCTA) may be a suitable replacement for invasive coronary angiography (ICA) to detect coronary artery disease (CAD) in patients scheduled for valve surgery. Thus, an international group of investigators performed a meta-analysis of English-language studies published in peer-reviewed journals up to July 2015 that used ≥ 16 slice CCTA to evaluate adult patients for heart valve surgery and had absolute numbers of patients from which the accuracy of the technique could be calculated. Patients referred for transcatheter aortic valve replacement were excluded. A total of 17 studies involving 1,153 patients were included in the analysis. All studies used a 50% diameter narrowing cutoff for significant CAD. In the per patient analysis, 313 of 1,107 patients (28%) had at least one significant stenosis by ICA. In these patients, the sensitivity of CCTA was 93%, specificity was 89%, positive likelihood ratio (LR) was 8.44, negative LR was 0.07, and the diagnostic odds ratio was 113. Studies that excluded patients with aortic stenosis when pooled had better specificity (96%) and positive LR (21). Also, 64 slice CT scanners had better specificity (90%) and positive LR (9.5). In addition, male sex was the only covariate with a negative effect on sensitivity. The authors concluded that CCTA is a reliable alternative to ICA with excellent sensitivity and negative LR for the detection of significant CAD in patients undergoing heart valve surgery. The use of CCTA in aortic stenosis reduces its specificity.

■ COMMENTARY

It makes sense to evaluate patients undergoing valve surgery for CAD. Stress testing is not a good option since it is not 100% accurate and its accuracy has not been tested in valve disease patients who need surgery. Also, there are several reasons to believe that it may be less accurate in such patients. Consequently, ICA is recommended for these patients if they have angina or objective evidence of myocardial ischemia; have reduced left ventricular function; are men > 40 years of age; or women who are either postmenopausal or premenopausal with risk factors of CAD (Level of evidence = C). With the exception of aortic stenosis patients, most valve disease patients don't have significant CAD. Thus, exposing them to the risk, cost, and inconvenience of ICA doesn't make much sense. These considerations make CCTA seem attractive, but there are no robust studies on which to base firm recommendations. Consequently, this meta-analysis is worth considering.

Population studies employing CCTA have shown that it can accurately exclude CAD in low-to intermediate-risk subjects. CCTA in these population studies has a high negative predictive value (> 95%) and a low negative likelihood ratio (< 0.1). This meta-analysis shows similar results in presurgical valve disease patients with a negative likelihood ratio of (0.07). Thus, CCTA in valve disease patients is excellent for excluding the presence of significant CAD with only a 3% false negative rate. In the meta-analysis, a negative CCTA would mean about two-thirds of patients could avoid ICA. The positive likelihood ratio of CCTA for identifying CAD (8.4) is more modest and in older aortic stenosis patients is even lower (7.4). Of course, aortic stenosis patients have more risk factors for CAD. The

specificity of CCTA for CAD in aortic stenosis patients also is lower (87%). If CCTA is positive for CAD, ICA should be performed to confirm the results and decide if coronary artery bypass also must be performed. Thus, CCTA could serve as a gatekeeper for ICA in presurgical valve disease patients.

CCTA has other uses in valve disease. It can determine the amount or location of valve calcifications; valve area can be measured; and aortic arch atherosclerosis and coronary anomalies can be detected. Currently, the radiation and contrast agent exposure are higher than with ICA, but this is improving with better equipment. Also, in the meta-analysis, the positive LR was not good using scanners with < 64 detectors. In addition, not all patients can undergo CCTA because of arrhythmias, contrast allergy, chronic kidney disease, and hemodynamic instability. This causes a selection bias in CCTA studies.

In conclusion, until better data are available, CCTA makes sense in low- to moderate-risk patients undergoing valve surgery who do not have aortic stenosis. Those with a high risk of CAD or aortic stenosis should undergo ICA. ■

ABSTRACT & COMMENTARY

Is the Wearable Cardioverter-defibrillator Ready for Prime Time?

By Michael Crawford, MD, Editor

SYNOPSIS: A large German experience with the wearable cardioverter-defibrillator confirms the finding of U.S. registry studies and suggests that the device is useful for patients with reduced left ventricular function at high risk of sudden cardiac death who are not currently good candidates for an implantable cardioverter-defibrillator.

SOURCES: Wäßnig NK, Günther M, Quick S, et al. Experience with the wearable cardioverter-defibrillator in patients at high risk for sudden cardiac death. *Circulation* 2016;134:635-643.

Lee BK, Olgin JE. The wearable cardioverter-defibrillator: Is it now the standard of care? *Circulation* 2016;134:644-646.

After considerable research in the United States, the FDA approved the wearable cardioverter-defibrillator (WCD) in 2001, and an American Heart Association (AHA) scientific advisory panel rated it a class II indication in several specific patient categories in which a temporary external cardioverter-defibrillator would be preferable to an implantable cardioverter-defibrillator (ICD). This retrospective observational study from Germany is the first large report of WCD use outside the United States. This report of all registered WCD users in Germany from 2010 to 2013 includes 6,043 patients from 404 centers with eight indications for its use: ICD explantation (12%), heart failure (0.4%), awaiting heart transplant (0.7%), immediate post-myocardial infarction (MI) or coronary artery bypass graft (27%), newly diagnosed dilated cardiomyopathy (37%), newly diagnosed nonischemic cardiomyopathy (12%), acute myocarditis (10%), and familial sudden cardiac death syndromes (1.4%). All patients who experienced WCD shocks were fully investigated. Most of the patients were men (79%). In 120 patients, one to five shocks were delivered per episode for a grand total of 163 shocks. In 94 patients (1.6%), the shocks were delivered for ventricular tachycardia (VT)/ventricular fibrillation (VF). Eleven percent of these episodes required more than one shock to terminate the arrhythmia. The WCD detected 242 VT episodes in 70 patients who remained conscious and manually withheld the shocks for these self-terminating episodes. Successful cardioversion occurred in 88 patients (94%), and 87 survived for 24 hours post-shock. There were seven deaths within 24 hours of treatment: four with unresponsive monomorphic VT and three with VF. One patient who was not shocked died of sustained asystole. One-half of the deaths occurred in ICD explant patients. Inappropriate shocks occurred in 26 patients (0.4%) and were due to artifact, rapid supraventricular tachycardia (SVT), or failure of the patient to press the hold button. None resulted in harm to the patient. The authors concluded that the German experience confirms the value of the WCD outside the United States.

■ COMMENTARY

These days, it is unusual for a new medical device to move from the United States to Europe rather than the reverse. However, despite FDA approval in 2001, guidelines for WCD use did not appear until the European Society of Cardiology guidelines on the management of ventricular arrhythmias and the prevention of sudden death in 2015 and the AHA scientific advisory in 2016. The recommendations of both organizations are very similar and can be summarized as follows. Specifically, both organizations recommended class IIa for patients post-ICD explantation until another can be implanted, as a bridge to transplant, and in the first

90 days post-MI in patients with ejection fraction (EF) < 35%. Also, patients with acute myocarditis, patients post-revascularization with low EF, and patients with new dilated or non-ischemic cardiomyopathy, in whom recovery of left ventricular function (LVF) is expected with optimal medical or device therapy, received a IIb recommendation. There are no class I indications for a WCD because there are no completed randomized trials showing efficacy. Although the WCD has been shown to effectively treat VT/VF, only a randomized, controlled trial can verify a survival benefit. This may sound nuts, but remember the ICD was not associated with improved survival in patients with low EF early after acute MI, despite being very effective at treating ventricular arrhythmias. So as Drs. Lee and Olgin opined in their editorial, the WCD is not considered the standard of care for any situation yet. Ongoing randomized trials, such as the VEST study, hopefully will help clarify the role of the WCD in the near future.

There are some other interesting aspects of this German study. There were fewer inappropriate shocks in their experience (0.4%) compared to 1-2% in the two large U.S. registry studies. Presumably, this was due to patient selection difference. The German study included a wider range of indications, and some of their patients may have been at lower risk of SVT. For example, the German study included more patients with acute myocarditis. Also, adherence was much better in Germany. Only 3% of German patients discontinued the device in less than three days. In the U.S. registry, 14% stopped using the WCD due to discomfort or adverse reactions. One problem with the German registry is that we do not have data on comorbid conditions, left ventricular ejection fraction, or medical treatment strategies. This makes using the data to guide individual patient decisions difficult.

So what should clinicians do now? Consider a WCD for patients with poor left ventricular ejection fraction at risk for sudden cardiac death who currently are not candidates for an ICD. However, discuss the risks and potential benefits with patients. Make patients aware that there is no conclusive scientific data on whether the WCD will prolong life. ■

ABSTRACT & COMMENTARY

Right Ventricular Function Predicts Outcomes in Dilated Cardiomyopathy

By Van Selby, MD

Assistant Professor of Medicine, University of California, San Francisco, Cardiology Division, Advanced Heart Failure Section

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

SYNOPSIS: Right ventricular dysfunction is common in dilated cardiomyopathy and frequently recovers with medical therapy for heart failure. Recovery of right ventricular function predicts subsequent improvement in left ventricular function and is associated with better outcomes.

SOURCE: Merlo M, Gobbo M, Stolfo D, et al. The prognostic impact of the evolution of RV function in idiopathic DCM. *JACC Cardiovasc Imaging* 2016;9:1034-1042.

Although dilated cardiomyopathy (DCM) is defined by left ventricular (LV) systolic dysfunction, right ventricular (RV) dysfunction also has been identified as an important prognostic marker. No study to date has evaluated changes in RV function over time and the association with survival in patients being treated for DCM.

Merlo et al retrospectively analyzed RV function at baseline and at least one follow-up assessment in 512 patients with recently diagnosed idiopathic DCM who were enrolled in the Trieste Heart Muscle Disease Registry between 1993 and 2008. All patients featured LV ejection fraction (EF) < 50%, and coronary artery disease was ruled out with angiography in all patients > 35 years of age and those with risk factors. At baseline, 95% of patients were treated with angiotensin-converting enzyme inhibitors and 84% with beta-blockers. RV function was evaluated using the RV fractional area change (RV-FAC: end-diastolic area - end-systolic area/end-diastolic area x 100). The primary outcome was a composite of death or heart transplantation.

At baseline, 20% of the cohort experienced RV dysfunction, defined as RV-FAC < 35%. Subjects with RV dysfunction demonstrated more advanced New York Heart Association functional class, worse LV systolic function, and higher pulmonary artery systolic pressure. Baseline RV dysfunction was associated independently with increased rates of death or heart transplant (hazard ratio, 1.71; $P = 0.0413$).

During follow-up, 86% of patients with RV dysfunction at baseline recovered RV function, with a median time to recovery of six months. Recovery of RV function was associated with subsequent LV reverse remodeling (LVRR, defined as an improvement in EF ≥ 10%), occurring at a median time of 24 months (odds ratio, 2.49; $P = 0.018$). Subjects with RV dysfunction at baseline who subsequently recovered RV function on follow-up evaluation demonstrated similar overall survival compared to those with normal RV function ($P = 0.205$). On the other hand, those with persistent RV dysfunction or those who developed RV dysfunction on subsequent evaluations experienced significantly worse survival ($P = 0.003$ for the global comparison). The authors concluded that systematic serial evaluation of RV function may assist clinical decision making, and RV reverse remodeling should be considered an important target in the early management of DCM.

■ COMMENTARY

This is among the first studies to report the natural history of RV function in a large cohort of DCM, with several important findings. RV dysfunction was common, present in 20% of subjects at baseline, and is associated with worse outcomes independent of other clinical or echocardiographic predictors. However, the majority of subjects with baseline RV dysfunction recover function, and this recovery occurs relatively quickly. Those with recovery of RV function demonstrated long-term survival that was similar to those with normal RV function, highlighting the importance of serial echocardiograms when using RV function as a prognostic marker in idiopathic DCM.

Interestingly, recovery of RV function was a strong predictor of subsequent LVRR. When LVRR occurred, it did so after a median follow-up of 24 months. The authors hypothesized the different time to recovery in RV and LV function may be related to the effects of neurohormonal antagonist therapy on each ventricle. Changes in RV function appear to reflect the early hemodynamic benefits of treatment such as lowering vascular resistance and left-sided filling pressures. Among patients with baseline RV dysfunction, those who subsequently recovered experienced a significant reduction in pulmonary artery systolic pressure, whereas those with persistent dysfunction did not. Subjects who recovered function also had a marked reduction in the prevalence of LV diastolic dysfunction on follow-up evaluation, compared to no significant change in those who did not recover. On the other hand, the LV response to neurohormonal blockade therapy depends on structural changes to the LV, which occur at a slower pace. Early after initial diagnosis, assessment of RV function may be more important than LV function when determining prognosis, although this requires

United States Postal Service

Statement of Ownership, Management, and Circulation

1. Publication Title	2. Publication Number	3. Filing Date
Clinical Cardiology Alert	0 7 4 1 _ 4 2 1 8	10/1/16
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price
Monthly	12	$349.00

7. Complete Mailing Address of Known Office of Publication *(Not printer) (Street, city, county, state, and ZIP+4)*
950 East Paces Ferry Road NE, Ste. 2850, Atlanta
Fulton County, GA 30326-1180

Contact Person: Regenia Sims
Telephone: 404-262-5473

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not printer)*
950 East Paces Ferry Road NE, Ste. 2850, Atlanta, GA 30326-1180

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do not leave blank)*

Publisher *(Name and complete mailing address)*
AHC Media LLC, David Fournier, President and CEO
950 East Paces Ferry Road NE, Ste. 2850, Atlanta, GA 30326-1180

Editor *(Name and complete mailing address)*
Leslie Coplin, same as above

Managing Editor *(Name and complete mailing address)*
Jonathan Springston, same as above

10. Owner *(Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual owner. If the publication is published by a nonprofit organization, give its name and address.)*

Full Name	Complete Mailing Address
AHC Media LLC	950 East Paces Ferry Road NE, Ste 2850, Atlanta, GA 30326-1180
David Fournier	950 East Paces Ferry Road NE, Ste 2850, Atlanta, GA 30326-1180
~~Bethany Schilling~~	~~950 East Paces Ferry Road NE, Ste 2850, Atlanta, GA 30326-1180~~
Lone Peak Capital Group, LLC	79 West Paces Ferry Road, Suite 200-A, Atlanta, GA 30305

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box → ☒ None

Full Name	Complete Mailing Address

12. Tax Status *(For completion by nonprofit organizations authorized to mail at nonprofit rates) (Check one)*
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☑ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months *(Publisher must submit explanation of change with this statement)*

PS Form **3526,** October 1999 *(See Instructions on Reverse)*

13. Publication Title: Clinical Cardiology Alert			14. Issue Date for Circulation Data Below: September 2016	
15.		Extent and Nature of Circulation	Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
a.		Total Number of Copies *(Net press run)*	305	290
b. Paid and/or Requested Circulation	(1)	Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. *(Include advertiser's proof and exchange copies)*	260	252
	(2)	Paid In-County Subscriptions Stated on Form 3541 *(Include advertiser's proof and exchange copies)*	0	0
	(3)	Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution	12	11
	(4)	Other Classes Mailed Through the USPS	8	2
c.		Total Paid and/or Requested Circulation *[Sum of 15b. (1), (2),(3),and (4)]* ▶	280	265
d. Free Distribution by Mail *(Samples, compliment ary, and other free)*	(1)	Outside-County as Stated on Form 3541	10	10
	(2)	In-County as Stated on Form 3541	0	0
	(3)	Other Classes Mailed Through the USPS	0	0
e.		Free Distribution Outside the Mail *(Carriers or other means)*	5	5
f.		Total Free Distribution *(Sum of 15d. and 15e.)* ▶	15	15
g.		Total Distribution *(Sum of 15c. and 15f)* ▶	295	280
h.		Copies not Distributed	10	10
i.		Total *(Sum of 15g. and h.)* ▶	305	290
j.		Percent Paid and/or Requested Circulation *(15c. divided by 15g. times 100)*	95%	95%

16. Publication of Statement of Ownership
☑ Publication required. Will be printed in the November 2016 issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: *David R. Fournier* Publisher & CEO — Date: 09/12/2016

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties).

Instructions to Publishers

1. Complete and file one copy of this form with your postmaster annually on or before October 1. Keep a copy of the completed form for your records.
2. In cases where the stockholder or security holder is a trustee, include in items 10 and 11 the name of the person or corporation for whom the trustee is acting. Also include the names and addresses of individuals who are stockholders who own or hold 1 percent or more of the total amount of bonds, mortgages, or other securities of the publishing corporation. In item 11, if none, check the box. Use blank sheets if more space is required.
3. Be sure to furnish all circulation information called for in item 15. Free circulation must be shown in items 15d, e, and f.
4. Item 15h., Copies not Distributed, must include (1) newsstand copies originally stated on Form 3541, and returned to the publisher, (2) estimated returns from news agents, and (3), copies for office use, leftovers, spoiled, and all other copies not distributed.
5. If the publication had Periodicals authorization as a general or requester publication, this Statement of Ownership, Management, and Circulation must be published; it must be printed in any issue in October or, if the publication is not published during October, the first issue printed after October.
6. In item 16, indicate the date of the issue in which this Statement of Ownership will be published.
7. Item 17 must be signed.

Failure to file or publish a statement of ownership may lead to suspension of Periodicals authorization.

PS Form **3526,** October 1999 *(Reverse)*

validation in further studies.

This was a retrospective study, limited only to patients with idiopathic DCM. Whether the findings extend to patients with ischemic or other cardiomyopathies is unknown. RV function only was evaluated using RV-FAC. Accurate measurement of RV-FAC requires adequate echocardiographic windows. In everyday practice, simpler methods, such as the tricuspid annular plane systolic excursion, often are used. Whether the same prognostic significance holds for alternate measures of RV function is unknown.

The left ventricle, especially systolic function, measured by EF, often is the primary focus of follow-up echocardiograms in patients with systolic heart failure. The findings of Merlo et al emphasize the importance of comprehensive evaluations, including RV function. Future studies will help clarify the role of monitoring changes in RV function when assessing response to therapy for heart failure. ■

CME/CE INSTRUCTIONS

To earn credit for this activity, please follow these instructions:
1. Read and study the activity, using the provided references for further research.
2. Log on to **AHCMedia.com** and click on My Account. First-time users will have to register on the site using the eight-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the test, a credit letter will be emailed to you instantly.
5. Twice yearly after the test, your browser will be directed to an activity evaluation form, which must be completed to receive your credit letter.

CME/CE QUESTIONS

1. **The wearable cardioverter-defibrillator now has a class IIa recommendation for which patient group with a left ventricular ejection fraction < 35%?**
   a. Acute myocarditis
   b. Implantable cardio-defibrillator explanted waiting re-implant
   c. New non-ischemic cardiomyopathy
   d. Long QT syndrome

2. **Surgical repair of ascending aortic aneurysms with diameters between 4.5-5.5 cm to prevent dissection or rupture is recommended for which patients?**
   a. Marfan syndrome
   b. Syphilis
   c. Bicuspid aortic valve
   d. Both a and c

3. **The use of coronary CT angiography to evaluate patients for coronary artery disease prior to heart valve surgery is highly accurate in all of the following *except*:**
   a. women.
   b. low-risk patients.
   c. aortic stenosis patients.
   d. those studied on ≥ 64 detector scanners.

4. **Which of the following procedural characteristics is most strongly associated with post-percutaneous coronary intervention ischemic events risk?**
   a. Three or more lesions stented
   b. Stenting all three major vessels
   c. Stenting a complete occlusion
   d. Two stent bifurcation lesion

5. **Which dilated cardiomyopathy patients have the worst prognosis?**
   a. Right ventricular function recovers with therapy.
   b. Right ventricular function does not recover.
   c. Right ventricular function worsens.
   d. Both b and c