CPD BULLETIN
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Foreword

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Recent reports on the impact of the SARS-CoV-2 and the effects of COVID-19 vaccination on the heart have brought to attention the risk of myocarditis in these 2 groups of patients. As knowledge on this matter is evolving, it is timely that an article is included in this issue which looks at the incidence of myocarditis in young athletes who were recovering from the coronavirus infection.

This issue also covers some of the guidelines on frequently encountered clinical problems such as the latest American guidelines on the management of hypertrophic cardiomyopathy and valvular heart disease. Hypertrophic cardiomyopathy remains an important cause of sudden death in the young. While it is uncommon to see rheumatic heart disease, in present day Singapore, a higher life expectancy will mean that there will be more degenerative valvular heart disease. This issue also includes other topics which are related to an aging society such as atrial fibrillation and transcatheter aortic valve replacement therapy.

For those who are advocates of preventive medicine, articles on diet and the all-in-one polypill are also available in this issue.

Together with the Academy's Deanery, we hope that you will find the articles in this issue both enjoyable and beneficial. Should you have views about what topics you would like to see included in future issues, please do let us know.

TABLE OF CONTENTS

COVID-19

ARTICLE

1 **Evaluation for Myocarditis in Competitive Student Athletes Recovering from Coronavirus Disease 2019 With Cardiac Magnetic Resonance Imaging** FULL ARTICLE ACCESS

Starekova J, Bluemke DA, Bradham WS, Eckhardt LL, Grist TM, Kusmirek JE, Purtell CS, Schiebler ML, Reeder SB.
JAMA Cardiol. 2021 Aug 1;6(8):945-950.
PMID: 33443537

The utility of cardiac magnetic resonance imaging (MRI) as a screening tool for myocarditis in competitive student athletes returning to training after recovering from coronavirus disease 2019 (COVID-19) infection is unknown. The objective is to describe the prevalence and severity of cardiac MRI findings of myocarditis in a population of competitive student athletes recovering from COVID-19.

In this case series, an electronic health record search was performed at our institution (University of Wisconsin) to identify all competitive athletes (a consecutive sample) recovering from COVID-19, who underwent gadolinium-enhanced cardiac MRI between January 1, 2020, and November 29, 2020. The MRI findings were reviewed by 2 radiologists experienced in cardiac imaging, using the updated Lake Louise criteria. Serum markers of myocardial injury and inflammation (troponin-I, B-type natriuretic peptide, C-reactive protein, and erythrocyte sedimentation rate), an electrocardiogram, transthoracic echocardiography, and relevant clinical data were obtained. COVID-19 infection was confirmed using reverse transcription-polymerase chain reaction testing. Prevalence and severity of MRI findings are consistent with myocarditis among young competitive athletes recovering from COVID-19. A total of 145 competitive student athletes (108 male and 37 female individuals; mean age, 20 years; range, 17-23 years) recovering from COVID-19 were included. Most patients had mild (71 [49.0%]) or moderate (40 [27.6%]) symptoms during the acute infection or were asymptomatic (24 [16.6%]). Symptoms were not specified or documented in 10 patients (6.9%). No patients required hospitalization. Cardiac MRIs were performed a median of 15 days (range, 11-194 days) after patients tested positive for COVID-19. Two patients had MRI findings consistent with myocarditis (1.4% [95% CI, 0.4%-4.9%]). Of these, 1 patient had marked nonischaemic late gadolinium enhancement and T2-weighted signal abnormalities over multiple segments, along with an abnormal serum troponin-I level; the second patient had 1-cm nonischaemic mild late gadolinium enhancement and mild T2-weighted signal abnormalities, with normal laboratory values.

In this case series study, based on MRI findings, there was a low prevalence of myocarditis (1.4%) among student athletes recovering from COVID-19 with no or mild to moderate symptoms. Thus, the utility of cardiac MRI as a screening tool for myocarditis in this patient population is questionable.

PRACTICE-CHANGING UPDATES

ARTICLES

1 **2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines** FULL ARTICLE ACCESS

Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A, Toly C.

Circulation. 2021 Feb 2;143(5):e35-e71.

PMID: 33332149

This executive summary of the valvular heart disease guideline provides recommendations for clinicians to diagnose and manage valvular heart disease as well as supporting documentation to encourage their use.

A comprehensive literature search was conducted from January 1, 2010, to March 1, 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from PubMed, EMBASE, Cochrane, Agency for Healthcare Research and Quality Reports, and other selected database relevant to this guideline. Structure: Many recommendations from the earlier valvular heart disease guidelines have been updated with new evidence and provides newer options for diagnosis and treatment of valvular heart disease.

This summary includes only the recommendations from the full guideline which focus on diagnostic work-up, the timing and choice of surgical and catheter interventions, and recommendations for medical therapy. The reader is referred to the full guideline for graphical flow charts, text, and tables with additional details about the rationale for and implementation of each recommendation, and the evidence tables detailing the data considered in developing these guidelines.

2 **2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines**

FULL ARTICLE ACCESS

Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, Evanovich LL, Hung J, Joglar JA, Kantor P, Kimmelstiel C, Kittleson M, Link MS, Maron MS, Martinez MW, Miyake CY, Schaff HV, Semsarian C, Sorajja P.
J Am Coll Cardiol. 2020 Dec 22;76(25):3022-3055.
PMID: 33229115

This executive summary of the hypertrophic cardiomyopathy clinical practice guideline provides recommendations and algorithms for clinicians to diagnose and manage hypertrophic cardiomyopathy in adult and paediatric patients as well as supporting documentation to encourage their use.

A comprehensive literature search was conducted from January 1, 2010, to April 30, 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from PubMed, EMBASE, the Cochrane Collaboration, Agency for Healthcare Research and Quality reports, and other relevant databases. Many recommendations from the earlier hypertrophic cardiomyopathy guidelines have been updated with new evidence or a better understanding of earlier evidence.

This summary operationalizes the recommendations from the full guideline and presents a combination of diagnostic work-up, genetic and family screening, risk stratification approaches, lifestyle modifications, surgical and catheter interventions, and medications that constitute components of guideline directed medical therapy. For both guideline-directed medical therapy and other recommended drug treatment regimens, the reader is advised to follow dosing, contraindications and drug-drug interactions based on product insert materials.

FEATURED ARTICLES

ARTICLES

1 **TAVR Patients Requiring Anticoagulation: Direct Oral Anticoagulant or Vitamin K Antagonist?** FULL ARTICLE ACCESS

Didier R, Lhermusier T, Auffret V, Eltchaninoff H, Le Breton H, Cayla G, Commeau P, Collet JP, Cuisset T, Dumonteil N, Verhoye JP, Beurtheret S, Lefèvre T, Teiger E, Carrié D, Himbert D, Albat B, Cribier A, Sudre A, Blanchard D, Bar O, Rioufol G, Collet F, Houel R, Labrousse L, Meneveau N, Ghostine S, Manigold T, Guyon P, Delepine S, Favereau X, Souteyrand G, Ohlmann P, Doisy V, Beygui F, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Iung B, Gilard M; STOP-AS and France-TAVI.

JACC Cardiovasc Interv. 2021 Aug 9;14(15):1704-1713.

PMID: 34274294

Using French transcatheter aortic valve replacement (TAVR) registries linked with the nationwide administrative databases, the study compared the rates of long-term mortality, bleeding, and ischemic events after TAVR in patients requiring oral anticoagulation with direct oral anticoagulants (DOACs) or vitamin K antagonists (VKAs).

The choice of optimal drug for anticoagulation after TAVR remains debated. Data from the France-TAVI and FRANCE-2 registries were linked to the French national health single-payer claims database, from 2010 to 2017. Propensity score matching was used to reduce treatment-selection bias. Two primary endpoints were death from any cause (efficacy) and major bleeding (safety).

A total of 24,581 patients who underwent TAVR were included and 8,962 (36.4%) were treated with OAC. Among anticoagulated patients, 2,180 (24.3%) were on DOACs. After propensity matching, at 3 years, mortality (hazard ratio [HR]: 1.37; 95% confidence interval [CI]: 1.12-1.67; $P < 0.005$) and major bleeding including haemorrhagic stroke (HR: 1.64; 95% CI: 1.17-2.29; $P < 0.005$) were lower in patients on DOACs compared with those on VKAs. The rates of ischemic stroke (HR: 1.32; 95% CI: 0.81-2.15; $P = 0.27$) and acute coronary syndrome (HR: 1.17; 95% CI: 0.68-1.99; $P = 0.57$) did not differ among groups. In these large multicentre French TAVR registries with an exhaustive clinical follow-up, the long-term mortality and major bleeding were lower with DOACs than VKAs at discharge.

The present study supports preferential use of DOACs rather than VKAs in patients requiring oral anticoagulation therapy after TAVR.

2

Plant-Centred Diet and Risk of Incident Cardiovascular Disease During Young to Middle Adulthood FULL ARTICLE ACCESS

Choi Y, Larson N, Steffen LM, Schreiner PJ, Gallaher DD, Duprez DA, Shikany JM, Rana JS, Jacobs DR Jr.
J Am Heart Assoc. 2021 Aug 4:e020718.
PMID: 34344159

The association between diets that focus on plant foods and restrict animal products and cardiovascular disease (CVD) is inconclusive.

We investigated whether cumulative intake of a plant-centred diet and shifting toward such a diet are associated with incident CVD. Participants were 4946 adults in the CARDIA (Coronary Artery Risk Development in Young Adults) prospective study. They were initially 18 to 30 years old and free of CVD (1985-1986, exam year [year 0]) and followed until 2018. Diet was assessed by an interviewer-administered, validated diet history. Plant-centred diet quality was assessed using the A Priori Diet Quality Score (APDQS), in which higher scores indicate higher consumption of nutritionally rich plant foods and limited consumption of high-fat meat products and less healthy plant foods.

Proportional hazards models estimated hazard ratios of CVD associated with both time-varying average APDQS and a 13-year change in APDQS score (difference between the year 7 and year 20 assessments). During the 32-year follow-up, 289 incident CVD cases were identified. Both long-term consumption and a change toward such a diet were associated with a lower risk of CVD. Multivariable-adjusted hazard ratio was 0.48 (95% CI, 0.28-0.81) when comparing the highest quintile of the time-varying average ADPQS with lowest quintiles. The 13-year change in APDQS was associated with a lower subsequent risk of CVD, with a hazard ratio of 0.39 (95% CI, 0.19-0.81) comparing the extreme quintiles. Similarly, strong inverse associations were found for coronary heart disease and hypertension-related CVD with either the time-varying average or change APDQS.

Consumption of a plant-centred, high-quality diet starting in young adulthood is associated with a lower risk of CVD by middle age.

3

Effect of Long-term Continuous Cardiac Monitoring vs Usual Care on Detection of Atrial Fibrillation in Patients With Stroke Attributed to Large- or Small-Vessel Disease: The STROKE-AF Randomized Clinical Trial

FULL ARTICLE ACCESS

Bernstein RA, Kamel H, Granger CB, Piccini JP, Sethi PP, Katz JM, Vives CA, Ziegler PD, Franco NC, Schwamm LH; STROKE-AF Investigators.

JAMA. 2021 Jun 1;325(21):2169-2177.

PMID: 34061145

Patients with ischemic stroke attributed to large- or small-vessel disease are not considered at high risk for atrial fibrillation (AF), and the AF incidence rate in this population is unknown. The objective was to determine whether long-term cardiac monitoring is more effective than usual care for AF detection in patients with stroke attributed to large- or small-vessel disease through 12 months of follow-up.

The STROKE-AF trial was a randomized (1:1), multicentre (33 sites in the US) clinical trial that enrolled 496 patients between April 2016 and July 2019, with primary end point follow-up through August 2020. Eligible patients were aged 60 years or older or aged 50 to 59 years with at least 1 additional stroke risk factor and had an index stroke attributed to large- or small-vessel disease within 10 days prior to insertable cardiac monitor (ICM) insertion.

Patients randomized to the intervention group (n = 242) received ICM insertion within 10 days of the index stroke; patients in the control group (n = 250) received site-specific usual care consisting of external cardiac monitoring, such as 12-lead electrocardiograms, Holter monitoring, telemetry, or event recorders. The main outcome and measure were incident AF lasting more than 30 seconds through 12 months. Among 492 patients who were randomized (mean [SD] age, 67.1 [9.4] years; 185 [37.6%] women), 417 (84.8%) completed 12 months of follow-up. The median (interquartile range) CHA2DS2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category) score was 5 (4-6). AF detection at 12 months was significantly higher in the ICM group vs the control group (27 patients [12.1%] vs 4 patients [1.8%]; hazard ratio, 7.4 [95% CI, 2.6-21.3]; P < .001). Among the 221 patients in the ICM group who received an ICM, 4 (1.8%) had ICM procedure-related adverse events (1 site infection, 2 incision site haemorrhages, and 1 implant site pain). Among patients with stroke attributed to large- or small-vessel disease, monitoring with an ICM compared with usual care detected significantly more AF over 12 months.

However, further research is needed to understand whether identifying AF in these patients is of clinical importance.

4 **Effect of Implantable vs Prolonged External Electrocardiographic Monitoring on Atrial Fibrillation Detection in Patients With Ischemic Stroke: The PER DIEM Randomized Clinical Trials** FULL ARTICLE ACCESS

Buck BH, Hill MD, Quinn FR, Butcher KS, Menon BK, Gulamhusein S, Siddiqui M, Coutts SB, Jeerakathil T, Smith EE, Khan K, Barber PA, Jickling G, Reyes L, Save S, Fairall P, Piquette L, Kamal N, Chew DS, Demchuk AM, Shuaib A, Exner DV.

JAMA. 2021 Jun 1;325(21):2160-2168.

PMID: 34061146

The relative rates of detection of atrial fibrillation (AF) or atrial flutter from evaluating patients with prolonged electrocardiographic monitoring with an external loop recorder or implantable loop recorder after an ischemic stroke are unknown. The objective was to determine, in patients with a recent ischemic stroke, whether 12 months of implantable loop recorder monitoring detects more occurrences of AF compared with conventional external loop recorder monitoring for 30 days.

Investigator-initiated, open-label, randomized clinical trial conducted at 2 university hospitals and 1 community hospital in Alberta, Canada, including 300 patients within 6 months of ischemic stroke and without known AF from May 2015 through November 2017; final follow-up was in December 2018. Participants were randomly assigned 1:1 to prolonged electrocardiographic monitoring with either an implantable loop recorder (n = 150) or an external loop recorder (n = 150) with follow-up visits at 30 days, 6 months, and 12 months. The primary outcome was the development of definite AF or highly probable AF (adjudicated new AF lasting ≥2 minutes within 12 months of randomization). There were 8 prespecified secondary outcomes including time to event analysis of new AF, recurrent ischemic stroke, intracerebral haemorrhage, death, and device-related serious adverse events within 12 months. Among the 300 patients who were randomized (median age, 64.1 years [interquartile range, 56.1 to 73.7 years]; 121 were women [40.3%]; and 66.3% had a stroke of undetermined etiology with a median CHA2DS2-VASc [congestive heart failure, hypertension, age ≥75 years, diabetes, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category] score of 4 [interquartile range, 3 to 5]), 273 (91.0%) completed cardiac monitoring lasting 24 hours or longer and 259 (86.3%) completed both the assigned monitoring and 12-month follow-up visit. The primary outcome was observed in 15.3% (23/150) of patients in the implantable loop recorder group and 4.7% (7/150) of patients in the external loop recorder group (between-group difference, 10.7% [95% CI, 4.0% to 17.3%]; risk ratio, 3.29 [95% CI, 1.45 to 7.42]; P = .003). Of the 8 specified secondary outcomes, 6 were not significantly different. There were 5 patients (3.3%) in the implantable loop recorder group who had recurrent ischemic stroke vs 8 patients (5.3%) in the external loop recorder group (between-group difference, -2.0% [95% CI, -6.6% to 2.6%]), 1 (0.7%) vs 1 (0.7%), respectively, who had intracerebral haemorrhage (between-group difference, 0% [95% CI, -1.8% to 1.8%]), 3 (2.0%) vs 3 (2.0%) who died (between-group difference, 0% [95% CI, -3.2% to 3.2%]), and 1 (0.7%) vs 0 (0%) who had device-related serious adverse events. Among patients with ischemic stroke and no prior evidence of AF, implantable electrocardiographic monitoring for 12 months, compared with prolonged external monitoring for 30 days, resulted in a significantly greater proportion of patients with AF detected over 12 months.

Further research is needed to compare clinical outcomes associated with these monitoring strategies and relative cost-effectiveness.

5

Prevention of Viridians Group Streptococcal Infective Endocarditis: A Scientific Statement From the American Heart Association FULL ARTICLE ACCESS

Wilson WR, Gewitz M, Lockhart PB, Bolger AF, DeSimone DC, Kazi DS, Couper DJ, Beaton A, Kilmartin C, Miro JM, Sable C, Jackson MA, Baddour LM; American Heart Association Young Hearts Rheumatic Fever, Endocarditis and Kawasaki Disease Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Cardiovascular and Stroke Nursing; and the Council on Quality of Care and Outcomes Research.

Circulation. 2021 May 18;143(20):e963-e978.

PMID: 33853363

In 2007, the American Heart Association published updated evidence-based guidelines on the recommended use of antibiotic prophylaxis to prevent viridians group streptococcal (VGS) infective endocarditis (IE) in cardiac patients undergoing invasive procedures. The 2007 guidelines significantly scaled back the underlying conditions for which antibiotic prophylaxis was recommended, leaving only 4 categories thought to confer the highest risk of adverse outcome. The purpose of this update is to examine interval evidence of the acceptance and impact of the 2007 recommendations on VGS IE and, if needed, to make revisions based on this evidence.

A writing group was formed consisting of experts in prevention and treatment of infective endocarditis including members of the American Dental Association, the Infectious Diseases Society of America, and the American Academy of Paediatrics, in addition to the American Heart Association. MEDLINE database searches were done for English language articles on compliance with the recommendations in the 2007 guidelines and the frequency of and morbidity or mortality from VGS IE after publication of the 2007 guidelines.

Overall, there was good general awareness of the 2007 guidelines but variable compliance with recommendations. There was no convincing evidence that VGS IE frequency, morbidity, or mortality has increased since 2007. Based on a review of the available evidence, there are no recommended changes to the 2007 VGS IE prevention guidelines.

We continue to recommend VGS IE prophylaxis only for categories of patients at highest risk for adverse outcome while emphasizing the critical role of good oral health and regular access to dental care for all. Randomized controlled studies to determine whether antibiotic prophylaxis is effective against VGS IE are needed to further refine recommendations.

6 **Polypill with or without Aspirin in Persons without Cardiovascular Disease** FULL ARTICLE ACCESS

Yusuf S, Joseph P, Dans A, Gao P, Teo K, Xavier D, López-Jaramillo P, Yusoff K, Santoso A, Gamra H, Talukder S, Christou C, Girish P, Yeates K, Xavier F, Dagenais G, Rocha C, McCready T, Tyrwhitt J, Bosch J, Pais P; International Polycap Study 3 Investigators.

N Engl J Med. 2021 Jan 21;384(3):216-228.

PMID: 33186492

A polypill comprising statins, multiple blood-pressure-lowering drugs, and aspirin has been proposed to reduce the risk of cardiovascular disease. Using a 2-by-2-by-2 factorial design, we randomly assigned participants without cardiovascular disease who had an elevated INTERHEART Risk Score to receive a polypill (containing 40 mg of simvastatin, 100 mg of atenolol, 25 mg of hydrochlorothiazide, and 10 mg of ramipril) or placebo daily, aspirin (75 mg) or placebo daily, and vitamin D or placebo monthly.

We report here the outcomes for the polypill alone as compared with matching placebo, for aspirin alone as compared with matching placebo, and for the polypill plus aspirin as compared with double placebo. For the polypill-alone and polypill-plus-aspirin comparisons, the primary outcome was death from cardiovascular causes, myocardial infarction, stroke, resuscitated cardiac arrest, heart failure, or revascularization. For the aspirin comparison, the primary outcome was death from cardiovascular causes, myocardial infarction, or stroke. Safety was also assessed. A total of 5713 participants underwent randomization, and the mean follow-up was 4.6 years. The low-density lipoprotein cholesterol level was lower by approximately 19 mg per decilitre and systolic blood pressure was lower by approximately 5.8 mm Hg with the polypill and with combination therapy than with placebo. The primary outcome for the polypill comparison occurred in 126 participants (4.4%) in the polypill group and in 157 (5.5%) in the placebo group (hazard ratio, 0.79; 95% confidence interval [CI], 0.63 to 1.00). The primary outcome for the aspirin comparison occurred in 116 participants (4.1%) in the aspirin group and in 134 (4.7%) in the placebo group (hazard ratio, 0.86; 95% CI, 0.67 to 1.10). The primary outcome for the polypill-plus-aspirin comparison occurred in 59 participants (4.1%) in the combined-treatment group and in 83 (5.8%) in the double-placebo group (hazard ratio, 0.69; 95% CI, 0.50 to 0.97). The incidence of hypotension or dizziness was higher in groups that received the polypill than in their respective placebo groups. Combined treatment with a polypill plus aspirin led to a lower incidence of cardiovascular events than did placebo among participants without cardiovascular disease who were at intermediate cardiovascular risk. (Funded by the Wellcome Trust and others; TIPS-3 ClinicalTrials.gov number, NCT01646437.).

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