*Charlotte E. Mills, PhD
Virginia Govoni, MPhil
Luca Faconti, MBBS
Maria-Linda Casagrande, MBBS
Steven V. Morant, PhD
Andrew J. Webb, MBBS, PhD
J. Kennedy Cruickshank, MD, MBChB

*Cardiovascular Medicine Group
Division of Diabetes and Nutritional Sciences
King's College London
4.103, Franklin Wilkins Building
150 Stamford Street
London, SE1 9NH
United Kingdom
E-mail: charlotte.1.mills@kcl.ac.uk

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REFERENCES

1. Cruickshank JK, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? Circulation 2002;106:2085–90.

2. Mills CE, Govoni V, Casagrande ML, Faconti L, Webb AJ, Cruickshank JK. Design and progress of a factorial trial testing the effect of spironolactone and inorganic nitrate on arterial function in people at risk of or with type 2 diabetes. Artery Res 2015;12:48–53.

3. Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Arterial stiffness index beta and cardio-ankle vascular index inherently depend on blood pressure but can be readily corrected. J Hypertens 2017;35:98–104.

4. Edwards NC, Steeds RP, Stewart PM, Ferro CJ, Townend JN. Effect of spironolactone on left ventricular mass and aortic stiffness in early-stage chronic kidney disease: a randomized controlled trial. J Am Coll Cardiol 2009;54:505–12.

5. Omar SA, Fok H, Tilgner KD, et al. Paradoxical normoxia-dependent selective actions of inorganic nitrite in human muscular conduit arteries and related selective actions on central blood pressures. Circulation 2015;131:381–9.

Outcomes of TAVR in Bicuspid Aortic Valve Stenosis

The study by Yoon et al. (1) provides the largest series to date evaluating the role of transcatheter aortic valve replacement (TAVR) in bicuspid valve morphology. The authors concluded that although there was no difference in all-cause mortality at 2 years in patients undergoing TAVR for bicuspid valve aortic stenosis compared with tricuspid valve stenosis, the incidence of periprocedural complications was significantly higher with TAVR for bicuspid morphology. This effect was no longer evident with the use of newer generation valves. Compared with tricuspid valves, stenotic bicuspid patients receiving the Sapien XT (Edwards Lifesciences, Irvine, California) had significantly higher aortic root injury, whereas patients receiving Core Valve (Medtronic, Minneapolis, Minnesota) had higher rates of procedural failure, moderate-to-severe aortic regurgitation, and the need for a second valve.

Although appropriate sizing takes on added significance with bicuspid valve on account of multiple anatomic factors including the elliptical shape of the annulus, aortopathy, and eccentricity of calcium distribution (2), the use of valvuloplasty before TAVR appears to be an important variable that seems unaccounted for in the current report. As pointed out by the editorialist, valvuloplasty before TAVR may help in accurate sizing of the valve, particularly so in bicuspid morphology; still others have raised concern about the potential hazards of pre-TAVR valvuloplasty in bicuspid morphology. Similarly, the size of the ascending aorta and baseline aortic regurgitation seem to be likely determinants of TAVR outcomes. In this context, it would be important to study the interaction between use of valvuloplasty and procedural success and outcomes between: 1) TAVR in general and valve morphology (bicuspid vs. tricuspid valve); 2) older versus newer generation valves; and 3) balloon expandable versus self-expanding valves.

Yoon et al. (1) are to be congratulated for comprehensively evaluating this important aspect of what is still considered an off-label use for TAVR.

*Abdul Hakeem, MD
Mehmet Cilingiroglu, MD

*Division of Cardiovascular Medicine
University of Arkansas for Medical Sciences
Central Arkansas VA Health System
4301 West Markham Street
UAMS
Little Rock, Arkansas 72205
E-mail: ahakeem@gmail.com

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REFERENCES

1. Yoon SH, Bleiziffer S, De Backer O, et al. Outcomes in transcatheter aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis. J Am Coll Cardiol 2017;69:2579–89.

2. Philip F, Faza NN, Schoenhagen P, et al. Aortic annulus and root characteristics in severe aortic stenosis due to bicuspid aortic valve and tricuspid aortic valves: implications for transcatheter aortic valve therapies. Catheter Cardiovasc Interv 2015;86:E88–98.

β-Blockers and Outcome After Acute Myocardial Infarction

The paper by Dondo et al. (1) published in the *Journal* describing the effect of β-blockers among survivors of acute myocardial infarction within the MINAP (Myocardial Infarction National Audit Project) study elicited great interest among members of our research working group. The authors found no beneficial effect of β-blockers in patients with acute myocardial infarction without heart failure. In this regard, the authors defined heart failure as a history of heart failure, use of a loop diuretic on or during hospitalization, and/or a left ventricular ejection fraction <30% as recorded in the hospital.

The limitation of the MINAP study is that the final diagnosis of acute coronary syndrome (ACS) was based on the patient history or electrocardiographic or biochemical marker (2). We would like to bring the authors' attention to the fact that Takotsubo syndrome mimics ACS and could not be distinguished by the overselected criteria at admission. However, the large International Takotsubo Registry reported a 5.6% mortality per patient year (3); the use of β-blockers did not affect the survival rate of these patients. The diagnosis of the culprit lesion was not required in the MINAP study and therefore it is possible that a high proportion of cases could be in fact reasonably be explained by Takotsubo syndrome. Consequently, more information about the coronary status is required before the final conclusion can be made regarding the absence of beneficial effects of β-blockers in ACS patients.

***Ibrahim El-Battrawy, MD**
Martin Borggrefe, MD
Ibrahim Akin, MD

*First Department of Medicine
University Medical Centre Mannheim
Theodor-Kutzer-Ufer 1-3
68167 Mannheim
Germany
E-mail: Ibrahim.El-battrawy@medma.uni-heidelberg.de

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REFERENCES

1. Dondo TB, Hall M, West RM, et al. β-Blockers and mortality after acute myocardial infarction in patients without heart failure or ventricular dysfunction. J Am Coll Cardiol 2017;69:2710–20.

2. Raffel OC, White HD. Practising what is preached: the MINAP study. Heart 2004;90:969–71.

3. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. N Engl J Med 2015;373:929–38.

Should Beta-Blockers Be Routinely Prescribed for Myocardial Infarction Without Heart Failure or Ventricular Dysfunction?

We read with great interest the recent paper by Dondo et al. (1), who studied the association between beta-blocker use and all-cause mortality in acute myocardial infarction (AMI) without heart failure or left ventricular systolic dysfunction (LVSD). The investigators found that the use of beta-blockers in patients with AMI without HF or LVSD was not associated with reduced mortality risk at any time point up to 1 year and therefore declared that the routine prescription of beta-blockers in this setting might not be recommended anymore in modern era. However, their analysis and declaration raise concerns.

First of all, the beta-blocker dose actually used by patients in this observational study may at least partly account for the lack of survival benefits of beta-blockers because underdosing of beta-blockers is quite common in daily clinical practice (2) and therefore in observational study, whereas most randomized clinical trials demonstrating improved survival in post-AMI patients used the large target dose. Besides, post hoc analysis of a beta-blocker trial in HF patients indicated better survival rates with greater dose (3). Therefore, although the authors stated information on beta-blocker dose after discharge was missing, they should at least incorporate the dose used at discharge into analysis because up-titration of beta-blocker dose during outpatient follow-up occurred quite infrequently (2).

Second, although there is a lack of evidence that beta-blockers improve survival in AMI without HF or LVSD in the modern era, beta-blockers should still be routinely prescribed for this group of patients for other cardiovascular benefits such as recurrent myocardial infarction (4), which also add great economic and social burdens to patients.