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This manuscript describes the coronary artery patterns in 64 consecutive patients undergoing repair of PA/VSD/MAPCA. Twenty-seven percent of the patients had an anomalous origin and course of their coronary arteries. The most frequently observed anomalous course was a LAD originating from the right coronary and accounted for 15% of all anomalous patterns.

This prevalence of coronary arterial anomalies in PA/VSD/MAPCA is at the high end of the spectrum compared with other forms of conotruncal defects.

There was a 91% correlation between the coronary artery patterns identified at surgery and the findings described by cardiac catheterization. The 9% of patients who were not correctly identified at catheterization were all false negatives. The specificity of cardiac catheterization was 100% and the sensitivity was 65%. Five of the 6 false negatives had 2 separate coronary ostia, emphasizing the need to exclude all 4 anomalous coronary patterns.

Recognition of coronary artery anomalies is important in PA/VSD/MAPCA due to the need for placement of a conduit from the right ventricle to the reconstructed pulmonary arteries. The surface anatomy of the coronary system is discernible at the time of the first surgical procedure, and this is why this is a requirement for inclusion in this study. The ability to see the coronary arterial pattern at first surgery allows safe placement of the proximal end of the conduit regardless of the presence or absence of anomalous coronaries. The surface anatomy is obscured in subsequent re-operations, and during these subsequent conduit changes, injury to coronary arteries can occur. In view of the relatively high prevalence of anomalous coronaries in PA/VSD/MAPCA, it is imperative to identify the coronary artery pattern prior to contemplating re-operations for conduit replacement.

In summary, this study has documented a 27% incidence of anomalous coronary arteries in patients with PA/VSD/MAPCA. This information is clinically important to avoid coronary injuries during conduit re-operations.

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Ashok Muralidaran, MD
***Richard D. Mainwaring, MD**
V. Mohan Reddy, MD
Frank L. Hanley, MD

*Division of Pediatric Cardiac Surgery
Lucile Packard Children's Hospital
Stanford University School of Medicine
300 Pasteur Drive, Falk CVRC
Stanford, California 94305
E-mail: mainwaring@stanford.edu

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From the Division of Pediatric Cardiac Surgery, Lucile Packard Children's Hospital, Stanford University School of Medicine, Stanford, California.

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Letters to the Editor

All Vasodilators Are Not Equal

We read with interest the paper published by Naya et al. (1), in which they suggest that global coronary flow reserve (CFR), and not coronary artery calcium, as assessed by positron emission tomographic (PET) myocardial perfusion imaging (MPI), provides significant incremental improved risk stratification over clinical risk scores for prediction of major adverse cardiac events (1). However, we feel the results should be interpreted with caution for the following reasons.

This large study (n = 901) permitted the use of 4 different types of vasodilators to assess CFR: dipyridamole (52% of patients), regadenoson (38%), adenosine (5%), and dobutamine (5%). The investigators assumed that each pharmacological agent would produce an equivalent vasodilator effect, and therefore, allow collective comparison of CFR with outcome variables. However, this assumption is unproven and unlikely to be correct given their different modes of action. As such, this could have a profound effect on the study endpoints. Previous comparative studies that have involved small numbers of patients have demonstrated that these pharmacological agents produce significantly different magnitudes of hemodynamic and vasodilator effects. Importantly, where differences have not been shown, this does not mean they do not exist, and may be due to the limited numbers of patients studied.

Vasu et al. (2) used stress cardiac magnetic resonance imaging (MRI) in 40 patients and showed that regadenoson had a 20% significantly greater vasodilator effect than dipyridamole on myocardial blood flow reserve. In 20 healthy volunteers, dobutamine-atropine infusion caused a 40% greater increase in peak myocardial blood flow as measured by PET MPI in comparison to dipyridamole (3). In a separate study, adenosine was shown to produce a significantly greater decrease in mean arterial blood pressure than dipyridamole, and although myocardial blood flow reserve was numerically greater with adenosine, it did not reach statistical significance (4). This study involved just 15 patients.

The investigators also attempted to exclude patients with obstructive coronary artery disease from the study on the basis of an abnormal PET MPI. As a result, almost a quarter of the 1,240 patients screened were rejected. Unfortunately, an inherent methodological problem, known as incorporation bias, arises when the same technique is used both as a gatekeeper for "abnormal patients" and also acts as the diagnostic test. This problem is further compounded when no criteria are given as to how an "abnormal PET MPI" was defined. For example, readers would wish to know whether all 1,240 PET MPI scans had flows quantitatively assessed. In which case, what cutoff values for blood flow were used to define obstructive disease? Clearly, inadvertent exclusion of scans presumed to be abnormal due to obstructive coronary artery disease, but which were due to microvascular dysfunction, could significantly affect the outcome of the study.

We look forward to the authors' reply.

Karen Nel, B. Tech
***Kim Greaves, BSc, MD**

*Poole Hospital NHS Foundation Trust
and Bournemouth University
Department of Cardiology
Longfleet Road
BH15 2JB Poole, Dorset
United Kingdom
E-mail: kim.greaves@poole.nhs.uk

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Reply

All Vasodilators Are Not Equal

We appreciate the commentary by Ms. Nel and Greaves regarding our study (1). Previous studies have demonstrated that dipyridamole, regadenoson, and adenosine all achieve maximal coronary hyperemic flow via endothelial-independent vasodilation of the microvasculature (2–4). Although dobutamine stress has a different mechanism of action, the resulting hyperemia is similar in magnitude to adenosine (5). More important, in both the larger cohort from which this study was derived (6) and in other large cohorts (7), the stressor used was not informative to the multivariable model for predicting cardiac events. Accordingly, we do not believe that the use of multiple stress agents is likely to have resulted in a type 1 error or a false-positive association between CFR and outcomes.

In response to concerns raised by Nel and Greaves regarding incorporation bias, this problem occurs in diagnostic studies in which the test being evaluated is available to referring clinicians, and thus, may influence the diagnostic endpoint. In our study of prognosis, CFR was not available to referring clinicians, and consequently, could not have influenced clinical decision making. Furthermore, the clinical endpoints were adjudicated blinded to CFR values. Finally, for inclusion in this study, normal PET myocardial perfusion imaging was defined not on the basis of CFR, but rather on semiquantitative interpretation of myocardial perfusion scans.

Masanao Naya, MD, PhD
Venkatesh L. Murthy, MD, PhD
***Marcelo F. Di Carli, MD**

*Brigham and Women's Hospital
ASB L1-037C
75 Francis Street
Boston, Massachusetts 02115
E-mail: mdicarli@partners.org

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A Randomized Comparison of Pulmonary Vein Isolation With Versus Without Concomitant Renal Artery Denervation in Patients With Refractory Symptomatic Atrial Fibrillation and Resistant Hypertension

With the advent of renal artery denervation, numerous publications have been forthcoming. Previously, we petitioned the *Journal* as well as other publications about the lack of citation of our earlier studies (1–6) using intravascular electrode catheters to ablate autonomic nerves on the outside of blood vessels. We can appreciate the reluctance of the *Journal* to include these citations at that time based on the difference between the intravascular ablation of nerves in the renal arteries affecting blood pressure (7,8) rather than intravascular ablation of nerves outside of blood vessels affecting heart rate and cardiac arrhythmias (9). However, recent reports have documented the consistent and independent effects of renal sympathetic denervation (RSD) on heart rate reduction (10,11). More conclusive evidence supporting our contention is based on the experimental studies of Zhao et al. (12) and the recent clinical study by Pokushalov et al. (13), which have shown that RSD can be used to reduce the