Alpha-Adrenergic Coronary Vasoconstriction in Humans

I read with interest the study of Jensen et al. (1) and the accompanying editorial (2). Jensen et al. demonstrated the abundance of the α1D-adrenoceptor subtype on the mRNA and by radioligand binding on the protein level in epicardial coronary arteries of explanted healthy and diseased human hearts. This information is novel and potentially important for the development of more specific α-adrenoceptor blockers to treat hypertension and/or prostate hyperplasia. The accompanying editorial correctly emphasizes the importance of studies in human rather than animal tissue. The original study and the editorial, however, do not acknowledge the limitations of the in vitro nature of the study. Specifically, no information on the morphological and/or functional status of the analyzed coronary arterial segment with respect to its underlying atherosclerosis is provided. In fact, mRNA and radioligand binding of an adrenoceptor in vitro are one thing, but their functional contribution to coronary blood flow in vivo is a different thing. The original study and the editorial do not acknowledge that: 1) coronary blood flow in humans is tightly regulated by redundant mechanisms such that α-adrenergic vasoconstriction has little impact under physiological conditions; and 2) microvascular α2-adrenoceptors are of greater importance than epicardial α1-adrenoceptors, particularly in the presence of coronary stenoses (3). The functional importance of α2-adrenergic coronary vasoconstriction was first demonstrated in dogs (4,5) and subsequently confirmed in humans in relevant clinical settings such as percutaneous coronary intervention (6–9). Thus, in the context of α-adrenergic coronary vasoconstriction, the “in vivo over in vitro” may outweigh the “human over animal” preference; studies in dogs are particularly suited because their coronary vascular α-adrenoceptor distribution is largely identical to that of humans (5,6). The original study and the editorial contrast human only to mouse and rat tissue. Clearly, studies in humans in vivo are preferable, notably with respect to polymorphisms (7) and also feasible with current imaging modalities (3).

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REFERENCES


We appreciate Dr. Heusch for calling attention to our paper (1) and for his generous praise.

We do, however, disagree with some comments in his letter. His letter says that we do not acknowledge the distinction between α2-adrenergic receptors (ARs) (microvascular) and α1-ARs (epicardial coronaries), the fact that α-vasoconstriction is limited to arteries with coronary artery disease, and that α2-mediated coronary vasoconstriction is more important than α1-mediated.

In fact, in our introduction, we state: “The α1-ARs constrict primarily epicardial coronary arteries and large arterioles, whereas α2-ARs act mostly on the coronary microcirculation. Stimulation of α1-ARs by endogenous catecholamines produces little constriction of normal coronary arteries, but causes pronounced vasoconstriction in coronary arteries with atherosclerotic endothelium” (1). In making these statements, we cite Dr. Heusch’s group (references 3 and 6 in his letter).

In addition, in his reference 6, α1- and α2-agonists appear to reduce coronary blood flow to a similar extent in patients with coronary artery disease (Figs. 3 and 5 in Baumgart et al. [2]), suggesting similar α1- and α2-mediated effects in humans.

Furthermore, his letter also states that no information is provided “on the morphological and/or functional status of the analyzed coronary arterial segment with respect to its underlying atherosclerosis.” On the contrary, we did analyze α1-AR subtype mRNAs according to the presence or absence of coronary artery disease, as determined by coronary angiography and direct observation, and found no significant differences (Fig. 5A in Jensen et al. [1]).

We do agree fully that in vivo coronary physiology is most important. In this regard, it is highly pertinent that the α1D...