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Stable Ischemic Heart Disease

RANOLAZINE RELIEVES ISCHEMIA BY DECREASING MYOCARDIAL WORK WITHOUT ALTERING MYOCARDIAL BLOOD FLOW: INSIGHTS FROM AN EXPERIMENTAL MODEL

Moderated Poster Contributions
Hall C
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Background: Ranolazine (RAN) increases exercise duration and time to angina onset and decreases angina frequency in patients with chronic angina without effect on heart rate and aortic blood pressure. We hypothesized that RAN relieves myocardial ischemia by decreasing cardiac work through its negative inotropic effect.

Methods: Non-flow limiting stenosis was created in the left anterior descending coronary artery (LAD) in 17 open-chest dogs. The left circumflex bed was the normal control region. We compared changes in hemodynamic measurements, global myocardial function (peak LV dP/dt), regional myocardial function (radial strain using speckle-tracking echocardiography), and regional myocardial blood flow (contrast echocardiography) in the absence and presence of intravenous RAN at rest and during dobutamine stress.

Results: In the presence of a non-critical coronary stenosis, RAN significantly reduced mean aortic blood pressure, rate pressure product, peak LV dP/dt, and LAD coronary artery pressure, but had no effect on myocardial blood flow both at rest and during dobutamine stress. While radial strain was not different with RAN in absolute terms, the magnitude of LAD radial strain increase was significantly greater in the presence of RAN. (Table 1).

Conclusion: Ranolazine acutely decreased myocardial work by decreasing global contractility and rate-pressure product without altering myocardial blood flow. This resulted in beneficial effect on regional function during ischemia.

Table 1. Hemodynamics, Myocardial Function, Myocardial Perfusion Data

Parameter	Stenosis	Stenosis+Ran	Stenosis+Dob	Stenosis+Ran+Dob
HEMODYNAMICS				
Heart Rate (beats/min)	102±2	99±2	158±4 †	155±4 §
Mean Aortic Pressure (mmHg)	99±3	83±2 †	153±9 †	112±7 §#
RPP (beats/min•mmHg)	12,070±521	10,580±481 *	30,015±1,989 †	24,513±1,908 §
LAD Artery Pressure (mmHg)	81±3	65±3 *	101±6 *	76±5 §#
LAD Blood Flow (mL/min)	20±1	17±1	44±4 †	36±3 §
LCX Blood Flow (mL/min)	35±2	41±4	100±8 †	90±6 §
MYOCARDIAL FUNCTION				
Peak LV dP/dt (mmHg/s)	7,400±1,226	6,293±945 *	24,911±3,938 †	18,784±3,038 §
LAD Strain (%)	21.01±2.66	15.39±1.78	23.08±3.54	24.98±3.68
LCX Strain (%)	21.66±2.43	23.53±2.40	31.49±4.04	31.20±3.10
MYOCARDIAL BLOOD FLOW				
LAD Myocardial Blood Volume (A)	75.9±3.0	64.5±4.8	70.9±3.6	76.0±4.1
LAD Velocity (Beta)	0.68±0.09	0.64±0.10	1.15±0.17 *	0.94±0.11
LAD Myocardial Blood Flow (A*B)	55.9±7.3	43.0±6.4	78.5±10.8	72.5±9.5 ‡
MYOCARDIAL STRAIN				
	Stenosis *versus* Stenosis+Dob		**Stenosis+Ran *versus* Stenosis+Ran+Dob**	**p Value**
LAD Percent Change	2.07±2.74		9.74±4.47	0.046
LCX Percent Change	9.83±3.35		9.81±4.24	0.996

* p<0.05 vs. stenosis; † p<0.001 vs. stenosis;
‡ p<0.05 vs. stenosis+ranolazine; §p<0.001 vs. stenosis+ranolazine;
# p<0.05 vs. stenosis+dobutamine
Ran=ranolazine; Dob=dobutamine; RRP=rate pressure product; LAD=left anterior descending; LCX=left circumflex; LV=left ventricular; ESWS=end-systolic wall stress