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RESEARCH NEWS

Troponin levels make a difference

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***JGP* study reveals that lower troponin expression in the right ventricle underlies interventricular differences in excitation–contraction coupling.**

The right ventricle of the heart pumps blood into the pulmonary circulation, and therefore experiences lower afterload pressure than the left ventricle, which pushes blood around the entire rest of the body. This functional difference is reflected not only at the anatomical level—the right ventricular wall is thinner than the left—but also at the cellular level, where cardiomyocytes in the left and right ventricles are thought to demonstrate differences in excitation–contraction (E–C) coupling. In this issue of *JGP*, Jeon et al. carefully characterize these interventricular differences and show that they arise, in part, from lower troponin expression in the right ventricle (1).

E–C coupling is the process by which an action potential triggers a transient rise in cytosolic Ca^{2+} that initiates myofibril sliding and cardiomyocyte contraction. Previous studies have shown that action potential duration is shorter in right ventricular cardiomyocytes (RVCM) than in left ventricular cells (LVCM; 2, 3). "However, experimental findings on the differences in Ca^{2+} transients and sarcomere shortening kinetics are not consistent and demand a more rigorous approach," explains Sung Joon Kim, a professor at Seoul National University College of Medicine.

Kim and colleagues, including co-first authors Young Keul Jeon and Jae Won Kwon, and co-corresponding author Yin Hua Zhang, isolated cardiomyocytes from the left and right ventricles of rats and subjected them to a variety of assays (1).

Whole-cell patch clamping confirmed that action potential duration is shorter in RVCMs and that this is largely because a higher density of transient outward K^+ current drives faster repolarization. This, in turn, reduces the influx of Ca^{2+} into RVCMs.

Young Keul Jeon, Jae Won Kwon, Yin Hua Zhang, Sung Joon Kim (left to right), and colleagues reveal that E–C coupling differs between the right and left ventricles, partly because troponin complex expression is lower in RVCMs. For example, even though action potential duration is shorter in RVCMs, Ca^{2+} transients have a similar amplitude in both LVCMs and RVCMs, while the transient decay rate is slower in RVCMs.

"Surprisingly, despite the shorter action potential duration in RVCM, the amplitude of the Ca^{2+} transient was not different, while the decay of the Ca^{2+} transient was slower in RVCM than LVCM," Kim says.

The slower decay of cytosolic Ca^{2+} levels in RVCMs is mainly due to a 60% reduction in the activity of the SERCA ATPase that pumps Ca^{2+} back into the SR. But why do cytosolic Ca^{2+} levels show similar peaks in RVCMs and LVCMs? Kim and colleagues found that, compared with LVCMs, RVCMs express lower levels of the cardiac troponin complex that regulates the interaction between actin and myosin filaments in the sarcomere. Decreased expression of the Ca^{2+}-binding troponin subunit TnC appears to reduce the Ca^{2+} buffering capacity of RVCMs, allowing cytosolic Ca^{2+} levels to reach similar peaks to those seen in LVCMs, despite the interventricular differences in action potential duration.

However, though Ca^{2+} transients show similar amplitudes in RVCMs and LVCMs, Kim and colleagues found that contractility—as measured by changes in sarcomere length—is reduced in RVCMs. "We suggest that this phenomenon might be caused by the lower expression of the troponin complex," Kim says.

Indeed, when the researchers introduced the specific features of RVCMs—higher transient outward K^+ current, lower SERCA activity, and reduced troponin expression—into computational models previously developed for LVCMs (4, 5), they were able to recapitulate all of their experimental measurements obtained from RVCMs, including the shorter action potential duration, the amplitude and decay rate of the Ca^{2+} transient, and the reduction in contractility.

Lower troponin expression therefore significantly alters E–C coupling in RVCMs. Kim and colleagues note that the reduced Ca^{2+} buffering capacity of RVCMs may make the right ventricle more susceptible to arrhythmias, something they now plan to investigate using an animal model of pulmonary arterial hypertension and right ventricular failure.

References

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