Dietary and Free n-3 Polyunsaturated Fatty Acids Modify Calcium Handling Mechanisms in the Heart

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TABLE OF CONTENTS

ABSTRACT

It is well recognized that the consumption of fish correlates with a reduction in mortality due to cardiovascular disease. Whole heart studies have identified that dietary fish oil confers protection from cardiac arrhythmias. Many studies have shown that the acute application of the polyunsaturated fatty acids present in fish oil, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) to cardiac myocytes significantly reduce the amplitude of the various sarcolemmal ion currents responsible for the cardiac action potential. It is believed that this reduction in electrical excitability is the mechanism by which fish oil confers protection from cardiac arrhythmias. However not all arrhythmias arise from disturbances in membrane electrical excitability, a class of arrhythmias arise from calcium mishandling.

The aim of this thesis was to determine whether the antiarrhythmic actions of polyunsaturated fatty acids present in fish oil are due to modulation of calcium handling. Using fast line scan confocal microscopy, calcium sparks, transients and waves were studied.

These studies show that in rats supplemented with 10% dietary fish oil, the width and duration of spontaneous calcium sparks was significantly reduced in both atrial and ventricular myocytes compared to myocytes from lard supplemented rats. This was also found in rat ventricular myocytes incubated with 15 μM EPA compared to the controls. Calcium transients in ventricular myocytes from rats supplemented with fish oil displayed a reduced doubling time of the rising phase of the transient without altering the

decaying phase compared to myocytes from lard supplemented rats. This was also found in ventricular myocytes incubated with 15 μM EPA compared to the controls.

Dietary fish oil supplementation was not found to alter the properties of calcium waves in rat ventricular myocytes.

When added to isolated ryanodine receptors in artificial bilayers, 50 μM EPA was found to significantly reduce the open probability of the channel compared to the controls.

The reduction in spark size and ryanodine receptor open probability may indicate that the polyunsaturated fatty acids may provide protection against arrhythmias by reducing spontaneous calcium release thereby reducing spontaneous membrane depolarization resulting from calcium extrusion from the cytosol by the Na^{+}-Ca^{2+} exchanger.