Heydari et al. Journal of Cardiovascular Magnetic Resonance 2015, 17(Suppl 1):O7
http://www.jcmr-online.com/content/17/S1/O7

Journal of Cardiovascular Magnetic Resonance

ORAL PRESENTATION Open Access

Effect of purified omega-3 fatty acids on reducing left ventricular remodeling after acute myocardial infarction (OMEGA-REMODEL study): a double-blind randomized clinical trial)

Bobby Heydari[2,1*], Siddique A Abbasi[2], Ravi Shah[2], Shuaib Abdullah[6], Jiazuo Feng[2], William Harris[5], Joe McConnell[5], Evan Appelbaum[4], Udo Hoffmann[3], Michael Steigner[2], Ron Blankstein[2], Elliott A Antman[2], Michael Jerosch-Herold[2], Raymond Y Kwong[2]

From 18th Annual SCMR Scientific Sessions
Nice, France. 4-7 February 2015

Background

Acute myocardial infarction (MI) remains a leading cause of patient death and morbidity. Prognosis following MI has been shown to be strongly associated with small changes in left ventricular remodeling. Omega-3 fatty acid (PUFAs) supplementation may have a number of beneficial pleiotropic effects, including enhancement of myocardial relaxation[1] and reduction of vascular tone.[2] One prospective, randomized trial demonstrated significant survival benefit for PUFAs following acute MI.[3] However, the mechanism and potential myocardial changes during the convalescent phase post MI from PUFAs have not been well described.

Methods

The OMEGA-REMODEL study was a randomized, double-blinded, placebo controlled trial of PUFA supplementation post acute MI. A total of 358 patients were randomized to study therapy with PUFAs (n=180) or matching placebo (n=178) and underwent baseline assessment by CMR 4-28 days following MI, with follow-up after 6 months of randomized therapy. The primary endpoint was changes in left ventricular end-systolic volume indexed to body surface area (LVESVI). Secondary outcomes included a) change in total infarct size, b) expansion of MECVF within noninfarcted myocardium, and c) changes in systemic biomarkers.

Results

Baseline demographics for the entire cohort and both treatment arms are shown in Table 1. CMR characteristics, PUFAs levels, and biomarkers for baseline and 6-month post-treatment values of each treatment arm are shown in Table 2 and Figure 1. There were no significant differences for any ventricular parameters, infarct size or MECVF at baseline. After 6 months of therapy, follow-up CMR revealed a significant difference for percent change of LVESVI (-5.4±16.6 PUFAs versus 0.75±21.0 Placebo, p=0.01) and MECVF (-1.3±14.9 PUFAs versus 3.8±18.0 Placebo, p=<0.05) between the treatment arms. In addition, the inflammatory biomarkers, hsCRP and myeloperoxidase, were substantially reduced in the PUFAs treated arm as compared with the placebo arm (-98.2±243.6% versus -30.5±221.5% p<0.01, and -0.8±6.7 versus +0.8±5.3 p=<0.05, respectively). Finally, the percent reduction in ST2 after 6 months, a biomarker of myocardial fibrosis, was significantly greater in the PUFAs treated arm (-1.35±8.0 versus +0.92±7.5, p=0.03). Adjusted multivariable analysis demonstrated an independent association for change in PUFAs levels with adverse LV remodeling.

Conclusions

The results of this study demonstrated a significant reduction in LVESVI and MECVF for patients treated with high-dose PUFAs as compared to placebo. Further assessment of systemic biomarkers demonstrated a substantial reduction in biomarkers of inflammation, and

[2]Cardiology, Brigham and Women's Hospital, Boston, MA, USA
Full list of author information is available at the end of the article

Table 1. Baseline Demographics

Characteristics	All patients (n=358)	Treatment PUFAs (n=180)	Placebo (n=178)	P value
Age (years)	58.9±10.5	59.6±10.4	58.3±10.4	0.25
Female, *n* (%)	69 (19)	31 (17)	38 (21)	0.42
Body surface area, m^2	1.99±0.2	1.99±0.2	2.0±0.2	0.71
Heart rate (beats/min)	66.1±12.0	65.3±10.0	67.0±13.4	0.19
Systolic blood pressure (mm Hg)	121 ±16	121 ±15	120 ±16	0.75
Diastolic blood pressure (mm Hg)	70 ±10	70 ±10	70 ±11	0.62
Ethnicity				
White, *n* (%)	289 (81)	143 (79)	146 (82)	0.78
CAD History				
CHF, *n* (%)	10 (3)	4 (2)	6 (3)	0.75
MI, *n* (%)	36 (10)	22 (12)	14 (8)	0.99
PCI, *n* (%)	40 (11)	21 (12)	19 (11)	0.73
CABG, *n* (%)	35 (10)	24 (14)	11 (6)	<0.05
Cardiac risk factors, *n* (%)				
Hypercholesterolemia	253 (71)	133 (74)	120 (67)	0.13
Diabetes mellitus	90 (25)	45 (25)	45 (25)	0.99
Hypertension	229 (64)	117 (65)	112 (63)	0.58
Smoking	177 (49)	85 (47)	92 (52)	0.52
Medications, *n* (%)				
Aspirin	356 (99)	179 (99)	177 (99)	0.99
β-adrenergic blockers	326 (91)	162 (90)	162 (92)	0.85
Statin	342 (96)	171 (95)	171 (96)	0.99
Calcium channel blockers	26 (7)	17 (9)	9 (5)	0.23
ACE inhibitor/ARB	260 (73)	133 (74)	127 (71)	0.47
Insulin	33 (9)	18 (10)	15 (8)	0.59
Type MI				
STEMI	203 (57)	100 (56)	103 (58)	0.83
Anterior	96 (27)	48 (27)	48 (27)	0.99
TIMI 3 Flow Achieved	327 (91)	164 (92)	163 (92)	0.99
Laboratory				
Hematocrit, %	39.0±26.4	39.4±36.8	38.7±7.9	0.79
AST, μmol/L	42.7±78.2	48.3±76.0	37.3±80.1	0.20
Creatinine, μmol/L	0.93±0.24	0.95±0.26	0.91±0.22	0.14
Glucose, mg/dl	124.9±63.4	124.6±67.3	125.1±59.7	0.90
Peak troponin (T), μmol/L	20 ± 62	26 ± 81	15 ± 34	0.12
Peak creatine kinase, U/L	1166 ±1269	1139 ±1067	1193 ±1450	0.72
Peak creatine kinase MB, U/L	98 ± 97	98 ± 95	97 ±100	0.98

Data listed where available. Abbreviations: ACE = angiotensin converting enzyme, ARB = angiotensinx receptor blocker, AST = aspartate aminotransferase, CAD = coronary artery disease, CABG = coronary artery bypass grafting, CHF = congestive heart failure, MI = myocardial infarction, PCI = percutaneous coronary intervention, PUFA = purified omega-3 fatty acids, STEMI = ST elevation myocardial infarction, TIMI = 'thrombolysis in myocardial infarction'

Figure 1 Baseline demographics

Table 2. Baseline and 6-month Post Treatment Results.

	PLACEBO (n=178)			Treatment PUFAs (n=180)			*Comparison of Baseline (pre-therapy)	%Change post-therapy for Placebo and Treatment Group		
	Baseline (pre-therapy)	6-month (post-therapy)	P Value	Baseline (pre-therapy)	6-month (post-therapy)	P Value	P Value	Placebo (n=128)	PUFAs (n=133)	P Value
Fatty Acids (RBC %)										
EPA	0.8 ± 0.4	0.9 ± 0.6	0.02	0.8 ± 0.6	2.3 ± 1.2	0.0001	NS	+10.98 ± 46.02	+254.94 ± 234.86	<0.0001
DPA	2.9 ± 0.4	2.9 ± 0.5	0.08	2.9 ± 0.5	3.8 ± 0.7	0.0001	NS	-1.95 ± 14.67	+32.32 ± 25.10	<0.0001
DHA	4.9 ± 1.4	5.1 ± 1.5	NS	4.7 ± 1.3	7.1 ± 1.4	0.0001	NS	+2.58 ± 18.04	+58.48 ± 45.84	<0.0001
Omega-3-Index	5.7 ± 1.7	5.9 ± 2.0	NS	5.5 ± 1.8	9.4 ± 2.5	0.0001	NS	+3.34 ± 19.41	+80.86 ± 60.86	<0.0001
Inflammatory index	27.5 ± 12.0	26.5 ± 14.7	NS	28.0 ± 12.4	9.4 ± 7.7	0.0001	NS	+1.35 ± 41.37	-62.09 ± 31.45	<0.0001
CMR Characteristics										
LVESVI, ml/m^2	38.6 ± 17.2	36.1 ± 12.4	NS	39.8 ± 16.0	36.8 ± 14.1	0.0001	NS	+0.75 ± 20.99	-5.41 ± 16.61	0.01
LVEDVI, ml/m^2	82.4 ± 21.0	82.1 ± 18.3	NS	84.0 ± 20.0	82.9 ± 20.1	NS	NS	+1.46 ± 15.60	-0.77 ± 14.66	NS
LV ejection fraction, %	54.3 ± 9.8	56.7 ± 7.6	NS	53.6 ± 9.2	56.4 ± 8.6	0.0001	NS	+2.25 ± 12.22	+4.81 ± 11.30	NS
LV mass index, g/m^2	58.8 ± 70.4	56.1 ± 13.2	0.01	60.3 ± 14.4	58.6 ± 12.9	0.06	NS	-2.07 ± 18.65	-1.08 ± 16.62	NS
LV mass to volume ratio	0.74 ± 0.2	0.70 ± 0.17	0.03	0.74 ± 0.2	0.74 ± 0.2	NS	NS	-1.46 ± 24.53	+2.10 ± 22.57	NS
RV ejection fraction, %	53.3 ± 7.8	52.8 ± 7.0	NS	53.2 ± 6.0	53.3 ± 6.7	NS	NS	+0.59 ± 14.98	+0.23 ± 13.47	NS
RVESVI, ml/m^2	33.8 ± 11.4	34.4 ± 10.3	NS	33.1 ± 9.1	34.7 ± 10.2	0.04	NS	+4.20 ± 25.25	7.05 ± 26.01	NS
LGE mass (g)	17.7 ± 17.7	13.9 ± 12.6	0.008	17.8 ± 17.2	15.0 ± 15.0	0.05	NS	-2.91 ± 57.31	-8.81 ± 39.93	NS
MECVF	0.33 ± 0.05	0.35 ± 0.06	NS	0.34 ± 0.05	0.34 ± 77.1	0.09	NS	+3.79 ± 17.99	-1.35 ± 14.90	<0.05
Biomarkers										
Cholesterol										
Total Cholesterol	132 ± 37	144 ± 37	0.0001	132 ± 30	144 ± 41	0.004	NS	15.1 ± 28.3	6.8 ± 25.3	NS
LDL	72 ± 28	76 ± 30	0.004	74 ± 24	76 ± 31	NS	NS	18.8 ± 53.7	21.2 ± 46.0	NS
HDL	44 ± 11	50± 13	0.0001	44 ± 11	52 ± 15	0.0001	NS	12.8 ± 19.9	11.3 ± 18.1	NS
Triglycerides	144 ± 79	151 ± 87	NS	130 ± 60	136 ± 110	NS	NS	-9.0 ± 23.0	-7.0 ± 22.5	NS
Neurohormonal (log)										
NT-proBNP	6.09 ± 1.13	4.92 ± 1.11	0.0001	6.24 ± 1.05	5.01 ± 1.09	0.0001	0.0001	-18.76 ± 13.50	-19.39 ± 11.71	NS
Inflammation (log)										
hsCRP	1.06 ± 1.46	0.30 ± 1.14	0.0001	1.25 ± 1.43	0.22 ± 1.04	0.0001	0.0001	-30.50 ± 221.49	-98.16 ± 243.61	0.03
Myeloperoxidase	5.78 ± 0.32	5.81 ± 0.40	NS	5.81 ± 0.39	5.77 ± 0.42	NS	NS	+0.80 ± 5.32	-0.80 ± 6.68	<0.05
Cardiac fibrosis (log)										
ST2	3.59 ± 0.35	3.61 ± 0.37	NS	3.54 ± 0.37	3.49 ± 0.37	0.047	NS	+0.92 ± 7.47	-1.35 ± 8.03	0.03
Galectin-3	2.75 ± 0.36	2.74 ± 0.38	NS	2.75 ± 0.38	2.68 ± 0.30	0.04	NS	+0.31 ± 7.43	-1.22 ± 8.85	NS

Abbreviations: ApoA1 = apolipoprotein A1, ApoB = apolipoprotein B, CMR = cardiac magnetic resonance imaging (contrast enhanced), DHA = docosahexaenoic acid, DPA = docosapentaenoic acid, EPA = eicosapentaenoic acid, HDL = high-density lipoprotein, hsCRP = high-sensitivity C-reactive protein, LDL = low-density lipoprotein, LP(a) = lipoprotein(a), LGE = late gadolinium enhancement, LV = left ventricular, LVEDVI = left ventricular end-diastolic volume index, LVESVI = left ventricular end-systolic volume index, MECVF = myocardial extracellular volume fraction, NT-proBNP = N-terminal prohormone of brain natriuretic peptide, PUFA = purified omega-3 fatty acids, SA = stearic acid, RV = right ventricular, RVESVI = right ventricular end-systolic volume index, sdLDL = small dense low-density lipoprotein cholesterol
*P-values are for comparisons between baseline (pre-treatment) values for Placebo and PUFAs Treatment groups

Figure 2 Baseline and 6-month post treatment results

fibrosis for the PUFAs treated arm. These findings represent the first description of the effect of PUFAs on myocardial tissue phenotypes during the convalescent phase post MI and may suggest potentially important pathophysiological pathways for their pleiotropic effects.

Funding

National Institutes of Health Heart, Lung and Blood Institute (NHLBI).

Authors' details

[1]Cardiology, University of Calgary, Calgary, AB, Canada. [2]Cardiology, Brigham and Women's Hospital, Boston, MA, USA. [3]Radiology, Massachusetts General Hospital, Boston, MA, USA. [4]Cardiology, BIDMC, Boston, MA, USA. [5]Health Diagnostic Laboratory, Richmond, VA, USA. [6]Cardiology, UT Southwestern, Dallas, TX, USA.

Published: 3 February 2015

doi:10.1186/1532-429X-17-S1-O7
Cite this article as: Heydari *et al.*: Effect of purified omega-3 fatty acids on reducing left ventricular remodeling after acute myocardial infarction (OMEGA-REMODEL study): a double-blind randomized clinical trial). *Journal of Cardiovascular Magnetic Resonance* 2015 **17**(Suppl 1):O7.