Effects of Dietary Fish Oil on Myocardial Ischemia and Reperfusion in Isolated Guinea Pig Heart

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Guinea Pig 심장에서 식이성 생선유가 심근의 허혈상태와 재관류에 미치는 영향

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=국 문 초 록=

정상적인 관류상태에서 또는 심근의 허혈-재관류의 기간동안에, 식이지방의 급원을 달리한 실험식이가 심장의 기능과 심근의 산소대사에 미치는 영향을 분리 관류시킨 guinea pig의 심장을 사용하여 조사하였다. 이유기를 바로 끝낸 guinea pig을 chow식이로 사육하던지, 또는 식이지방의 종류로 10% 옥수수유, 10% 생선유, 또는 10% 생선유에 1% cholesterol이 각각 첨가된 인공적인 반순수식이를 공급하여 4주 동안 사육하였다. 정상적인 관류상태에서 chow식이를 한 실험동물의 심장에 비하여 옥수수유와,생선유를 첨가한 식이로 사육한 동물의 심장에서 그것의 심근 수축력과 심박동수는 유의적으로 감소하였다. 게다가, 생선유의 식이지방으로 사육한 동물에서의 관상 관류량은 옥수수유 또는 생선유에 cholesterol을 첨가한 실험식이로 사육한 동물에 비해서 훨씬 낮았고, 그 반면에 심근의 산소 추출량은 높았다. chow식이를 한 실험동물과 비교할 때에, 심근의 산소 소비량은 식이지방이 첨가된 실험식이로 사육된 동물에서 훨씬 저하되었다. 심장을 8분 동안 심근의 허혈상태에 놓이게 한 후에 측정된 심장의 기능과 관상 관류량 및 심근의 산소 소비량은 각각의 모든 실험식이군에서 서로 비슷한 수준으로 감소하였다. 5분 동안의 재관류 기간이 경과하면서 이러한 심장의 반응효과들은 향상되었지만, 허혈상태 이전의 정상적인 관류시에 관찰된 심장의 반응효과에 비해서 여전히 저하된 상태로 유지되었다. 10 분간의 재관류 기간이 끝나는 무렵에서, 생선유가 첨가된 실험식이로 사육된 동물의 심장에서만 심장기능과 관상 관류량이 정상적인 관류시의 반응상태로 완전히 회복되었다. 이와같이 심장기능이 생선유가 첨가된 실험식이로 사육된 실험동물군에서만 허혈상태로 부터 완전히 회복되어지는 것을 보여 주었기 때문에, 본 연구의 실험결과는 생선유의 식이지방은 허혈에 의해 유발된 심근의 손상을 감소시키는 데에 그 역활을 담당한다는 사실을 제시하고 있다.

KEY WORDS : Fish oil · Corn oil · Cholesterol · Contractility · Coronary flow · Myocardial oxygen consumption.

Introduction

Epidemiological studies have revealed that populations consuming diets rich in fish oils have lower incidences of coronary heart disease[1-4]. Such findings have been explained on the basis that dietary n−3 fatty acids, found in fish oils, reduce plasma lipids[4-6] and exert antithrombotic effects[6-8]. It has been shown that these polyunsaturated fatty acids are incorporated into cellular membranes of the myocardium, and might therefore induce alterations in cardiac function and the responses of the heart to stress[9-12]. Other studies[13,14] have shown that dietary modifications of membrane phospholipids results in a noticeable reduction in ischemic myocardial damages, and in alterations in β-adrenoceptor-mediated changes in cardiac inotropy in rat hearts. However, the effect of dietary fish oil on cardiovascular function is controversial[15-17]. According to Hartog et al.[17], although prolonged feeding of fish oil induced significant changes in membrane fatty acid composition, recovery of cardiac function and the incidence of cardiac arrhythmias during acute recurrent ischemia were not affected.

Little information is available, however, concerning the physiological effects of fish oils on mammalian cardiac function, coronary circulation and myocardial oxygen consumption. Accordingly, the present study was performed to investigate the effects of dietary lipids on these variables during transient ischemia and reperfusion in the isolated perfused guinea pig hearts.

Materials and Methods

1. Experimental animals and diets

Forty three post-weanling guinea pigs of either sex, weighing 180~220g were divided arbitrarily into four groups, and fed one of the following diets for a period of four weeks : 1) regular commercial chow(n=9, CH), 2) 10%(w/w) corn oil(n=12, CO), 3) 10% fish oil(n=10, FO), and 4) 10% fish oil with 1% cholesterol(n=12, FC). The guinea pigs were housed in a room maintained at constant temperature on a 12 : 12 hour light/dark cycle. Fresh water and food were provided ad libitum daily and uneaten food portions were discarded. Body weights were obtained three times per week.

The composition of the semi-purified fat-free diet contained(g/kg diet) : soy protein 200, DL-methionine 5, corn starch 150, sucrose 333, cellulose 100, guar gum 25, salt mix 75, vitamin mix 10, and choline bitartrate 2. The semi-purified fat-free diet met specified dietary requirements for the guinea pigs, which was formulated by the U.S. National Research Diets. Either CO or FO was added to the powdered fat-free diet to provide 10% of the dietary weight. One additional treatment group received 10 % FO diet plus 1% cholesterol. A control group was fed commercially available guinea pig/rat chow containg 4% crude fat by weight.

The fatty acid composition of the three different dietary oils is presented in Table 1. The CO diet is rich in linoleic acid(18 : 2, n−6), while the FO diet is deficient in this fatty acid and instead rich in eicosapentaenoic(20 : 5, n−3) and docosahexaenoic acids(20 : 6, n−3). Accordingly, the FO diet had a significantly higher n−3/n−6 ratio than the CO diet. One percent cholesterol did not affect the total fatty acid composition of the FO diet and thus maintained a similar n−3/n−6 ratio to that in the FO diet.

2. Perfusion of the isolated heart

An isolated perfused guinea pig heart preparation described previously was used in the present study[18-20]. After four weeks on their respective diets, guinea pigs were sacrified. Hearts were quickly excised and mounted in a Langendorff perfusion apparatus within 2~3 minutes. Hearts were cannulated in situ with a polyethylene catheter(PE240) via the ascending aorta and retrogradely perfused at a constant pressure of 65cmH_2O with oxygenated(95% O_2, 5%

Table 1. Fatty acid composition of dietary oils

Fatty acid	Corn oil	Fish oil	Fish oil+Cholesterol
14 : 0	ND	8.0	8.0
16 : 0	10.3	18.6	18.4
16 : 1 (n−7)	0.3	12.4	12.4
18 : 0	1.7	3.5	3.5
18 : 1 (n−9)	25.1	4.4	4.4
18 : 2 (n−6)	60.7	1.2	1.3
18 : 3 (n−3)	1.1	1.2	1.3
18 : 4 (n−3)	ND	3.8	3.8
20 : 1 (n−9)	ND	2.0	2.0
20 : 4 (n−6)	ND	1.2	1.1
20 : 5 (n−3)	ND	17.4	16.9
22 : 4 (n−6)	ND	1.3	1.2
22 : 5 (n−3)	ND	2.6	2.5
22 : 6 (n−3)	ND	8.6	8.0
n−3 / n−6	0.02	9.08	8.97

Values represent weight % of total fatty acids in dietary oils. Fatty acids are expressed by chain length : number of double bonds with the number in parentheses representing the cabon atoms between the terminal bond and the methyl group. ND, nondetectable.

CO_2, pH 7.43±0.02) Krebs-Ringer bicarbonate solution containing(mM) : glucose 5.5, pyruvate 2.0, NaCl 127.5, KCl 4.7, $CaCl_2$ 2.5, KH_2PO_4 1.2, $MgSO_4$ $7H_2O$ 1.2, and $NaHCO_3$ 24.9. Gentle squeezing of hearts prior to suspending them from a non-recirculating extracorporeal perfusion circuit prevented air from entering the aorta upon cannulation. Retrograde aortic inflow(arterial perfusate) was monitored electromagnetically by Empco Bloodflow Transducer 300AP connected to a Carolina Medical Electronics(Model 501 Flowmeter, King, North Carolina, U.S.A), in order to measure coronary flow (CF, ml/min/g) Additionally, CF was manually measured by collecting venous perfusates with a graduated cylinder and stopwatch from the pulmonary artery cannulated with a short wide-bore polyethylene catheter(PE240). Global left ventricular performance(left ventricular dP/dt_{max}) was measured with a pressure-probe tipped intraventricular catheter(Millar, Model TC500, Houston, Texas, U.S.A) by passing the catheter across the mitral valve and into the left ventricle. Coronary perfusion pressure(CPP) was continuously monitored by connecting a pressure transducer(Gould/Statham, Model P23D, Oxnard, California, U.S.A) to the perfusion circuit just proximal to the heart.

To measure global myocardial oxygen consumption(MVO_2), perfusate(arterial and venous) pO_2 was recorded with a blood pH/gases Analyzer (Corning Medical Instruments, Model 165, Medfield, Massachusetts, U.S.A) by collecting samples anaerobically(1ml) at selected time intervals as indicated below. The perfusate oxygen contents of samples were calculated as the product of pO_2 and the solubility of oxygen in the perfusate at 37℃($k=2.82\times10^{-2}$ μl/O_2 ml/mmHg). Global MVO_2, expressed in μl/min/g wet weight of myocardium, was calculated as the product of CF times the arterio-venous difference in O_2 contents, $(a\text{-}v)O_2$(μl/ml).

Preparation usefulness was tested before and after each experiment in order to determine which hearts should be included in final data analysis[18,19]. Treatment with 100~200μg of adenosine produced transient cardiac arrest in diastole accompaied by a 2~3 fold increase in peak coronary flow. Hearts not displaying post-experimental responses which

were quantitatively similar to the pre-experimental responses were discarded[18,19].

3. Experimental protocol

After excision and instrumentation, hearts were allowed 20~25 minutes to achieve the steady state for all monitored variables(post-extraction stabilization period). Baseline control data were then recorded and designated *Pre-ischemia*. Subsequently, CPP was lowered to 40 cmH_2O. This is just outside the lower limit for pressure-flow autoregulation in this preparation[18]. The reduction in CPP decreased CF and ensured initiation of hypoperfusion myocardial ischemia. The hypoperfusion ischemia was maintained for 8 minutes. All measured variables were continuously monitored during ischemia. During the last 30 seconds of ischemia, when hearts were in the steady state, perfusate samples and monitored data were collected(designed *Ischemia*). This enabled us to compare the effects of different dietary lipids on the magnitude of cardiac dysfunction, and on the change in coronary circulation during ischemia. Thereafter, normal perfusion was restored by elevating CPP to 65 cmH_2O. Post-ischemia reperfusion data were collected at 5 and 10 minutes and designated *5' Reperfusion* and *10' Reperfusion*, respectively. Both the rate of recovery and the extent of recovery of cardiac function and coronary circulation were compared among the different dietary groups.

4. Statistical analysis

All values are expressed as mean± SE. The present study was designed statistically to permit comparison both within and between dietary groups. Statistical significance for between-group comparisons was determined using a two-way Analysis of Variance[21]. Least significant Difference and Tukey's test were used to compare means amongst the various groups[21]. For within-group comparisons, all data were compared with the corresponding pre-ischemic control data using Students t-test. Significance was established at $p<0.05$ throughout.

Results

Before the start of the dietary period, the body weights of the four groups were similar. After the dietary period of four weeks the body weights of the groups fed with the CO, FO and FC diets were significantly less when compared to the CH diet-fed group. However, the ratio of heart weight to body weight was not significantly different in any of the groups(data not shown).

1. Comparative effects of dietary lipids under pre-ischemic condition

Table 2 shows the effects of dietary lipids on cardiac function and myocardial oxygen metabolism under pre-ischemic condition. In the FO-fed group heart rate(HR) was significantly lower when compared to that seen in the other dietary groups. Left ventricular contractility(dP/dt_{max}) was significantly lower in the FO- and CO-fed groups than that of the CH-fed group. In the FC-fed group,

Table 2. Effect of dietary lipids on cardiac function and myocardial oxygen metabolism under pre-ischemic conditions

Groups	dP/dt_{max} (mmHg/sec)	HR (bpm)	$(a\text{-}v)O_2$ (μl/ml)	MVO_2 (μl/min/g)
CH (n= 8)	847± 36[a]	213± 10[a]	7.4± 0.6[a]	55± 4[a]
CO (n=12)	769± 34[b]	217± 9[a]	6.5± 0.5[b]	51± 4[b]
FO (n= 9)	794± 34[b]	189± 15[b]	7.2± 0.6[a]	46± 2[c]
FC (n=10)	823± 60[a]	204± 11[a]	6.2± 0.6[b]	49± 4[b,c]

All values are mean± SE for the number of animals indicated beside each diet type. CH, chow ; CO, corn oil ; FO, fish oil ; FC, fish oil plus cholesterol ; dP/dt_{max}, rate of left ventricular pressure development ; HR, heart rate ; $(a\text{-}v)O_2$, difference of arteriovenous oxygen content ; MVO_2, global myocardial oxygen consumption. Values in a column with common superscripts are not significantly different at $p<0.05$.

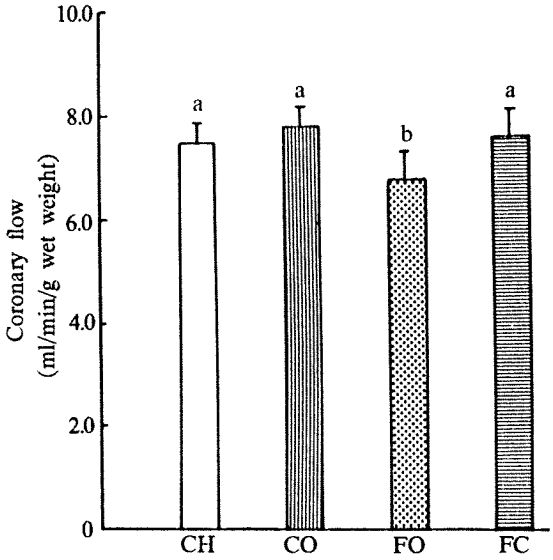

Fig. 1. Comparative effects of dietary lipids on coronary flow under pre-ischemic conditions. All values are mean± SE for the number of animals indicated beside each diet type. CH, chow ; CO, corn oil ; FO, fish oil ; FC, fish oil plus cholesterol. Value in a bar with common superscripts are not significantly different at $p<0.05$.

dP/dt_{max} was not significantly different from that of the CH-fed group.

Coronary flow was significantly lower in the FO-fed group when compared to the other dietary groups(Fig. 1), while myocardial oxygen extraction was not significantly different from that of the CH-fed group(Table 2). In contrast, oxygen extraction was significantly lower($p<0.05$) in the CO- and FC-fed groups than in the CH-fed group. As shown in Table 2, global MVO_2 was significantly decreased in all the dietary lipid groups when compared to that of the CH diet group. Moreover, MVO_2 in the FO diet group was lower than both the CO- and CH-fed animals.

2. Comparative effects of dietary lipids on cardiac function and coronary circulation during ischemia and reperfusion

As expected, cardiac function was significantly decreased in all the dietary groups during acute hypoperfusion ischemia(Table 3). After 8 minutes of ischemia, the magnitude of decrease in contractility was not significantly different between the groups(Table 3). Hearts of animals fed the FO diet showed a significantly smaller change(17± 7, $p<0.05$) in HR, whereas hearts of animals fed the FC diet had a significantly higher change(52± 14, $p<0.05$) when compared to values observed in the CH diet group(Table 3). Coronary flow decreased by 46~53% depending on the dietary group and were all significantly lower than pre-ischemic values(Fig. 2). Compared to the pre-ischemic value for myocardial oxygen extraction(%, EO_2), none of the dietary groups showed a significant change during ischemia (Table 4). Therefore, the significant decrease in

Table 3. Comparative effect of dietary lipids on cardiac function during ischemia and reperfusion

Groups	Pre-ischemia		Ischemia		5' Reperfusion		10' Reperfusion	
	dP/dt_{max} (mmHg/sec)	HR (bpm)	dP/dt_{max} (mmHg/sec)	HR (bpm)	dP/dt_{max} (mmHg/sec)	HR (bpm)	dP/dt_{max} (mmHg/sec)	HR (bpm)
CH (n= 8)	847± 36	213± 10	316± 30*	176± 11*	622± 58*	213± 8	606± 58*	219± 8
CO (n=12)	769± 34	217± 9	298± 27*	173± 14*	600± 60*	215± 11	605± 41*	224± 10
FO (n= 9)	794± 34	189± 15	314± 22*	172± 13*	614± 35*	200± 7	758± 65	222± 17*
FC (n=10)	823± 60	204± 11	307± 28*	152± 9*	618± 30*	194± 10*	753± 53*	205± 8

All values are mean± SE. CH, chow ; CO, corn oil ; FO, fish oil ; FC, fish oil plus cholesterol ; dP/dt_{max}, rate of left ventricular pressure development ; HR, heart rate. *$p<0.05$, relative to corresponding pre-ischemic values.

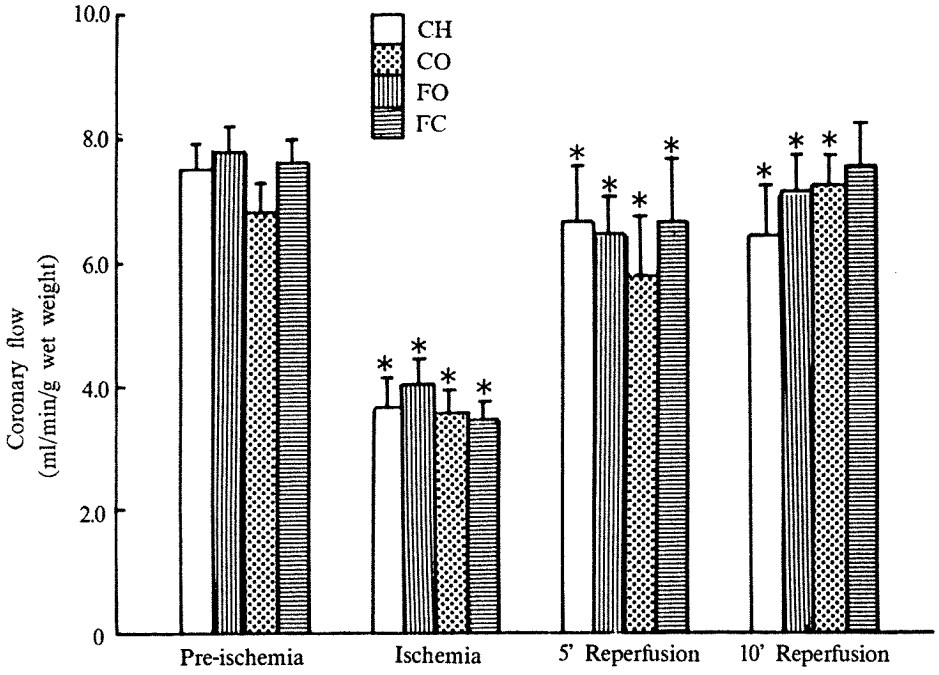

Fig. 2. Comparative effect of dietary lipids on coronary flow during ischemia and reperfusion. All values are mean± SE. CH, chow ; CO, corn oil ; FO, fish oil ; FC, fish oil plus cholesterol. *$p<0.05$, relative to corresponding pre-ischemic values.

Table 4. Comparative effect of dietary lipids on coronary flow and myocardial oxygen metabolism during ischemia and reperfusion

Groups	Pre-ischemia		Ischemia		5' Reperfusion		10' Reperfusion	
	EO_2	MVO_2	EO_2	MVO_2	EO_2	MVO_2	EO_2	MVO_2
CH (n= 8)	56± 2	55± 4	57± 4	25± 4*	58± 5	48± 6*	57± 4	47± 6*
CO (n=12)	50± 2	51± 4	51± 2	24± 2*	51± 3	42± 6*	53± 4	47± 4*
FO (n= 9)	53± 3	46± 2	53± 2	18± 2*	55± 2	36± 6*	53± 2	49± 2*
FC (n=10)	48± 4	49± 4	51± 3	17± 2*	49± 2	36± 5*	50± 4	47± 3

All values are mean± SE. CH, chow ; CO, corn oil ; FO, fish oil ; FC, fish oil plus cholesterol ; EO_2, myocardial oxygen extraction ; MVO_2, global myocardial oxygen consumption ; Units of EO_2 : %. Units of MVO_2 : μl/min/g. *$p<0.05$, relative to corresponding pre-ischemic values.

MVO_2 in each of the dietary groups resulted from a significant decrease in CF(Table 4, Fig. 2).

After 5 minutes of reperfusion, contractility in each of the dietary groups was still depressed relative to corresponding pre-ischemic values(Table 3). In contrast, the recovery for HR was already seen after 5 minutes of reperfusion with the exception of the FC group(Table 3). At the end of 10 minutes of reperfusion, there was a marked increase in HR of the FO diet group relative to its pre-ischemic value(Table 3). Moreover, only FO-fed animals showed full recovery of contractility after 10 minutes of reperfusion. In each of the dietary groups CF and MVO_2 were still significantly less than corres-

ponding pre-ischemic values at the end of 5 minutes of reperfusion(Table 4, Fig. 2). Unlike those of any other group, CF and MVO_2 in the FO-fed group increased above their pre-ischemic values after 10 minutes of reperfusion(Table 4, Fig. 2). In animals fed the FC diet CF and MVO_2 were not significantly different from corresponding pre-ischemic values. Myocardial oxygen extraction did not change in any of the diet groups during reperfusion(Table 4).

Discussion

Myocardial activity following acute ischemia is characterized by immediate mechanical dysfunction. Globally, it is characteized by a decrease in left ventricular pressure and contractility. However, the time course of cardiac mechanical changes during coronary reperfusion has not been well studied. Thus, it is not yet clear whether a period of reperfusion, equal to that of myocardial ischemia, can restore the ischemic myocardium to normal. Epidemiologic data[1-4] and biochemical studies[4-6,22] have suggested that dietary manipulations influence the myocardial membrane fatty acid composition and cardiovascular function. Accordingly, one might assume that different dietary interventions can affect the magnitude of cardiac dysfunction during ischemia, and might also affect the rates of recovery and the extent of recovery of cardiac function and coronary circulation during reperfusion. McLennan et al.[12] reported that alterations in the fatty acid composition of dietary lipids can affect the responses of the heart to ischemic stress. Accordingly, the main objective of the current study was to investigate the comparative effects of different lipid diets on cardiac function, coronary circulation and myocardial oxygen metabolism during ischemia and reperfusion.

1. Dietary lipids and cardiac function under pre-ischemic basal condition

The present results show that dietary lipids can influence cardiac mechanical function, coronary circulation, and myocardial oxygen metabolism after just four weeks of dietary alteration. This finding is consistent with other reports that dietary manipulation can alter cardiac function and coronary circulation[9-11]. For example, decreased left ventricular contractility and heart rate were observed in hearts of guniea pigs fed FO versus CH diet. In contrast, supplementation of FO with 1% cholesterol compromised these beneficial effects. It has previously been reported that dietary cholesterol compromises cardiac and coronary function, and decreases myocardial repsonsiveness to adrenergic agents[23-25]. Cholesterol is incorporated into sarcoplamic reticulum, and alters membrane fluidity[26]. Afterations in membrane fluidity may affect cellular transport processes or membrane-bound enzyme activities[9,27]. Swanson et al.[28] have reported that modification of fatty acid composition of cardiac sarcoplasmic reticulum phosphoglycerides, induced by dietary lipid alters the activity of Ca^{2+}-Mg^{2+} ATPase. It is conceivable that the difference in cardiac function between the two FO-fed groups of guinea pigs might have been due to changes in membrane ATPase activity, or in sarcoplasmic calcium transport, both of which influence cardiac function.

Previous studies have shown that alterations in cardiac function or in the response to stress, induced by dietary manipulation are associated with alterations in myocyte membrane phospholipid composition[9-11,13]. The present study did not examine the effects of diets on membrane phospholipid composition. However, it is assumed from other works that four weeks of dietary manipulation would have altered the membrane phospholipid fatty acid composition of the hearts employed in the present study [9-11,13,29]. It is also known that alterations in the phospholipid composition of membranes can affect lipid metabolism and the formation of cardiac prostaglandins and thromboxanes[30-32].

In contrast to reports that a diet rich in linoleic acid increases contractility in isolated perfused rat

hearts[9-11], the present study found a decrease in contractility in hearts of CO-fed guinea pigs. The mechanisms by which dietary lipids affect cardiac contractility are not well understood. One possibility to explain the decrease in contractility produced by the CO diet, might be a lipid-induced alteration in the formation of cardiac prostaglandins. Endoh [33] found that exogenous arachidonic acid or prostaglandin E_1 inhibits the positive inotropic effect of the catecholamines. In addition, changes in membrane lipid composition and/or fluidity associated with these changes in membrane enzyme activity, or receptor function, cannot be ruled out as explanations for the decreased contractility[27,30]. These results are not able to identify the mechanisms which caused negative cardiac inotropy in these hearts. It can only be assumed that CO and FO diets might have affected cardiac contractility via different molecular mechanism.

The results show that the type of dietary lipid can also affect coronary circulation and myocardial oxygen metabolism. The FO diet resulted in a decrease in coronary flow under basal conditions. Myocardial oxygen consumption was decreased by either a reduction in coronary flow or myocardial oxygen extraction. Since the CO and FO diets reduced cardiac function to the similar extent, the decrease in myocardial oxygen consumption in these hearts is not surprising. Even in the absence of a decrease in cardiac function, both myocardial oxygen extraction and myocardial oxygen consumption were reduced in FC-fed animals. In this case, an imbalance between oxygen demand and supply might have resulted. The decrease in coronary flow in FO-fed animals relative to FC-fed animals was compensated by an increase in myocardial oxygen extraction. This allowed oxygen supply, hence myocardial oxygen consumption to normalize. Consequently, oxygen became more dependent on oxygen extraction in the hearts of animals fed the FO diet. Other studies have demonstrated the effects of dietary n−3 fatty acids on vascular reactivity[30,32]. For example, Scherhag et al.[32] found a significant increase in arterial blood pressure an inhibition of prostacyclin release by vascular tissues in rats receiving dietary EPA or linolenic acid supplements. It is also known that EPA-supplemented diets inhibit production of thromboxanes[34].

2. Dietary lipids, cardiac function and coronary circulation during ischemia and reperfusion

The results also demonstrate that four weeks of dietary manipulation affect the rate of recovery and the magnitude of cardiac and coronary function during post-ischemic reperfusion. When considered collectively, these data reveal no remarkable differential effects of dietary lipids on the extent of decrease in cardiac function and coronary circulation during ischemia. In a related in vivo study Hartog et al.[17] compared the cardiac responses to intermittent myocardial ischemia in pigs fed mackerel oil diet or lard-fat diet for eight weeks. The changes in cardiac mechanical function due to ischemia were similar in both groups. Moreover, there were no differences in basal cardiac performance between the mackerel oil and lard-fat dietary groups, even though there were major differences between the two groups in fatty acid composition of platelet and cardiac membranes[17]. Conversely, McLennan et al.[12] found that dietary intervention affected the risk for arrhythmias and infarct size after prolonged coronary artery ligation.

The temporal recovery of cardiac fnction and myocardial oxygen consumption following reperfusion in the present study is note worthy. The decrease in cardiac funciton, coronary flow and myocardial oxygen consumption during ischemia was followed by partial recovery during the first five minutes of reperfusion in all dietary groups. However, at the end of ten minutes of reperfusion, a fully-recovered coronary flow response resulted only in the FO-fed group. Hartog et al.[17] also showed that mackerel oil feeding induced a hyperemic flow response during the post-ischemic reperfusion period.

They found that mackerel oil feeding reduced the levels of the vasoconstrictor thromboxane A_2, and that the thromboxane A_2/prostaglandin I_2 ratio was significantly decreased in mackerel oil-fed animals. It is conceivable, therefore, that full recovery of coronary flow in the FO-fed group resulted from an effect of this diet on the formation and release of prostaglandin I_2 and thromboxane A_3[32,34]. Further studies are needed to confirm this speculation.

In summary, the results suggest that dietary lipids differentially affect pre-ischemic basal cardiac function and myocardial oxygen metabolism, and that after ten minutes of reperfusion, hearts of animals fed a fish oil diet are respored to normal function. While clarification of specific mechanisms must await further investigation, it is conceivable that both structural and functional changes in vascular and myocardial membranes play important roles.

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