

## THE ROLE OF VIRGIN COCONUT OIL IN REDUCING LIPIDS AND INFLAMMATION POST-ACS

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### **Abstract:**

*The incidence of Acute Coronary Syndrome (ACS) is on the rise, making it a pressing global health concern. In Malaysia, cardiovascular diseases have consistently ranked as the leading cause of mortality for several decades, with cardiovascular disease contributing significantly to the non-communicable disease-related deaths. Statins, a class of prescription drugs designed to lower cholesterol levels, play a pivotal role in preventing ACS. However, they are associated with statin-related side effects, primarily muscle-related issues, including pain, lethargy, weakness, and myopathy. Observational studies have reported muscle problems in a substantial proportion of patients, ranging from 10% to 30%, while randomized controlled trials have indicated a lower but still significant incidence, affecting up to 5% of patients. Given the increasing significance of ACS, it is crucial to critically identify effective management and treatment strategies for this condition.*

**Keywords:** Acute Coronary Syndrome (ACS), Statins, Cardiovascular Disease, Muscle-Related Side Effects, Medication Management

### **1.0 INTRODUCTION**

Acute Coronary Syndrome (ACS) is a growing health problem with statistics showing an increasing trend of ACS incidence yearly. According to the Ministry of Health Malaysia (2017), cardiovascular disease has been the number one cause of death since the early 1980s. In 2017, MOH estimated 73% of death in Malaysians was from non-communicable diseases, and cardiovascular disease was one of them (Ministry of Health Malaysia, 2017a,b). ACS was announced by WHO to be an important worldwide health problem. Thus, it is necessary to critically identify strategies for the effective management and treatment of ACS. In Malaysia, the medication for lowering lipid levels to prevent ACS is statins. A class of prescription drugs, statins are designed to lower cholesterol levels (Newman et al, 2019). The most common statin-related side effects are muscle-related issues including pain, lethargy, weakness, and myopathy (Deichmann et al, 2010 ; QuMin et al, 2018).

There were reported muscle problems in 10% to 30% of patients in observational studies and up to 5% of patients in randomized controlled trials (RCTs) (Toth et al, 2018).

Realizing these side effects of statins, there is needs for a new solution to overcome them. Without denying the major contribution(s) of statins in ACS management, the negative side effects also cannot be neglected. Apart from the side effects, ACS patients have also reported developing certain mental illnesses which decrease their quality of life. The introduction of a natural product as supplemental management alongside statins could give patients' better outcomes.

There is a need to determine a new solution to increase patients' quality of life (QOL). A natural product may give a better impact on health and thus increase QOL. VCO, a Malaysian product, has been reported to be a good health supplement (Zakaria et al., 2010; Zakaria et al., 2011; Zakaria et al., 2015; Law et al., 2014). Currently, there is a lack of research on patients' QOL with supplement consumption. Hence, this study contributes insight into the abilities of VCO as a natural local product that influences the QOL of ACS patients. This research hopes to provide scientific

data that can be used for future protocols in ACS treatment in Malaysia. Therefore, this study seeks to verify the effect of VCO on QOL, serum lipid profile, glucose level, and hs-CRP level among ACS patients.

Virgin coconut oil (VCO) is an example of a natural product that is currently widely used as a supplement in Malaysia as antioxidant and treating metabolic disorder (Ibrahim et al, 2020). Introducing VCO as an innovative supplementary treatment alongside standard medical care for ACS patients could improve their health condition. The current study focuses on examining the effects of VCO as such evidence are still lacking. There requires further research to accurately determine the effects of VCO (Dela Paz et al, 2018; Liauet al, 2011; Praagman et al, 2016). Available studies about the effects of VCO on the human subject are limited as those published concern the animal subject. Further research using the human subject is much needed to confirm the effects of VCO on ACS patients. The objective of this study is to investigate the effect of VCO on the quality of life of ACS patients and to improve the clinical outcomes of ACS patients such as serum lipid profile, glucose level, and hs-C-reactive protein level.

## **2.0 METHODOLOGY**

The initial phase of the study involves quantitative research of a randomized controlled trial (RCT) with a crossover design. This is a uni-centre, randomized, parallel-group study conducted at the medical cardiac ward and the medical clinic in University Malaya Medical Center (UMMC), Malaysia. This crossover RCT follows the recommendations of the Consolidated Standards of Reporting Trials (CONSORT) Statement. This study included patients from the age of 25 to 65, of either gender, diagnosed with ACS (unstable angina, Non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI), who can understand the Malay and English languages, and who are willing to ingest soft gels. This study excluded patients who are pregnant, with uncontrolled hypothyroidism, with renal failure with creatinine >2mg/dL, and with liver failure. Only patients who met the inclusion criteria were randomized into the study. After consent was obtained, block randomization (1:1) and random number table were employed for the allocation of treatment.

Randomization and allocation concealment were conducted after obtaining informed consent. The participants were randomized using block randomization (1:1). The author developed a list of the participants randomly numbered from 1 to 400, generated by Stat Trek's Random Number Generator. There were 20 rows and 20 columns, and each column consisted of 20 random numbers. 200 numbers were randomly selected from the 400 numbers. The random numbers were each placed into an envelope. The envelopes were then distributed to the participants based on a first come first serve basis during recruitment. Participants with a number from column one received bottle A containing Virgin coconut oil (VCO) whereas participants with a number from column two received bottle B containing Virgin olive oil (VOO) as a positive control. A total of 160 patients were initially expected for this study, but 40 were excluded for failing to meet the inclusion criteria, and 18 declined participation. In the end, a total of 120 patients were randomized, with 60 in the intervention group and 60 in the control group, using a random number table generated by Stat Trek's Random Number Generator.

During the first intervention, Group A received one bottle of VCO (120 pieces of (VCO soft gel) and was to ingest four pieces of VCO soft gels consisting of 1.84g of lauric acid (C:12) twice per day for 90 days while Group B received one bottle of (VOO) (120 pieces of VOO soft gel) and was to ingest four pieces VOO soft gels consisting of 1.84g of oleic acid (C18:1) as a positive control twice per day for 90 days. After 90 days, all participants from both groups stopped consuming any treatment for 90 days (washout period). After the washout period, the crossover took place, where Group A received one bottle of VOO and was to ingest four pieces of VOO soft gels and Group B received one bottle of VCO and was to ingest four pieces of VCO soft gels. The second intervention also lasted for 90 days. Both types of soft gels were prepared and provided by a local company. To maintain allocation concealment, both soft gels were made to appear similar (bottle type, bottle size, bottle colour, amount of soft gel, and colour of soft gel). The only exception is the label (code) attached to the bottom of the bottles, A for VCO and B for VOO. The study spent 90 days for the first intervention (participants were randomised and received either VCO or VOO), 90 days for the washout period, and another 90 days for the second intervention. Participants were required to come to the hospital for follow-ups every four weeks, where blood sample and anthropometric measurements were taken. This was a

double-blind study where both participants and experimenters were not exposed to the code, that includes the nurses who took the blood samples.

According to the CONSORT statement (2010), the intention-to-treat (ITT) analysis is a more appropriate analysis to reflect the whole picture of the intervention effect. Therefore, this study included a total of 60 participants in each arm for the ITT analysis. An ITT population is used to fulfil primary outcomes.

The ITT analysis is a method for analysing results in a prospective randomized study where all randomized participants are included in the statistical analysis and analysed according to the group they were originally assigned, regardless of what treatment they received (Eric, 2017). According to Eric (2017), this method allows the investigator to draw accurate (unbiased) conclusions regarding the effectiveness of an intervention.

### 2.1 Nutritics – a nutrition analysis software

The authors employed Nutritics for dietary analysis, where the patients' daily diet was calculated for total energy, total calories, and percentage of all nutrition components such as saturated fat, carbohydrate, protein, vitamin, and alcohol. Besides, the author also employed Nutritics to calculate the patients' level of activities to prevent a confounder from affecting the results. The 120 participants in this study were required to record their daily diet and level of activities. The purpose was to identify and to ensure that their total energy, total calories, and level of activities remain similar across the study. These parameters are important to prevent a confounder from affecting the results. By monitoring their diet intake and level of activities, the author could justify that the results are because of the intervention introduced.

### 2.2 Ethical consideration

The approvals from the Head of Medical Department, Head of Cardiac Unit, Medical Ethics Committee (MREC 2017528-5276), and the National Medical Research Register (NMRR 17-169537433SI) were obtained before conducting the study. This study was also registered in April 2018 with Australia New Zealand Clinical Trial Registry (ANZCTR) with a unique number (ACTRN12618000752268).

### 3.0 RESULTS

Figure 1 shows the flow chart of the study design and response rates based on the CONSORT statement. It shows the enrolment of participants in this study. During the study period, the researcher daily screened all ACS patients who attended the ward for eligibility, according to the inclusion criteria. In relation to data analysis, the per-protocol analysis was performed on the 44 participants from Group A and 46 participants from Group B.

#### 3.1 Demographic characteristics

Table 1 shows the demographic and clinical characteristics of the participants in the study. Overall, most participants were male, Group A with 43 (71.7%) and Group B with 38 (63.3%). The participants' mean age for Group A was  $51.2 \pm 9.3$  and for Group B,  $52.7 \pm 10.1$ . There was no significant difference in demographic and clinical characteristics between the two groups, suggesting that they were homogenous and hence comparable.

**Table 1: Demographic and Clinical Characteristic of Participant**

Characteristics	Group A (Start with VCO) n = 60	Group B (Start with VOO) n = 60	stat.	p-value
	n (%) or mean $\pm$ SD		t/ $\chi^2$	
<b>Age (year)</b>				
	51.2 $\pm$ (9.3)	52.7 $\pm$ (10.1)	-.85 <sup>a</sup>	0.3
<b>Gender</b>				
Male	43 (71.7%)	38 (63.3%)	0.95 <sup>b</sup>	0.33
Female	17 (28.3%)	22 (36.7%)		

<b>Race</b>				
Malay	39 (65%)	35 (58.3%)		
Chinese	7 (11.7%)	8 (13.3%)	0.57	0.751
Indian	14 (23.3%)	17 (28.7%)		
<b>ACS classification</b>				
UA	13 (22%)	17 (28%)		
NSTEMI	32 (53%)	29 (48%)	0.71	0.74
STEMI	15 (25%)	14 (24%)		
<b>ACS management</b>				
PCI	55 (92%)	48 (80%)		
CABG	2 (3%)	2 (3%)	4.28	0.13
MEDICATIONS	3 (5%)	10 (7%)		
<b>Comorbidities</b>				
ACS with HPT	14 (23.3%)	13 (21.7%)		
ACS with DM	7 (11.7%)	8 (13.3%)	1.55	0.98
ACS with HPT & DM	21 (35%)	20 (33.3%)		
ACS with hyperlipidemia	18 (30%)	19 (31.7%)		
<b>Medications</b>				
Statin, anti-HPT, & antiplatelet	20 (37.3%)	19 (31.7%)		
Statin, OAD, & antiplatelet	5 (8.3%)	5 (8.3%)	0.056	0.99
Statin, anti-HPT, OAD, & antiplatelet	19 (31.7%)	19 (31.7%)		
Statin & antiplatelet	16 (26.7%)	17 (28.3%)		
<b>Education level</b>				
Primary	7 (11.7%)	10 (16%)		
Secondary	20 (33.3%)	18 (30%)	0.63	0.8
College (Diploma level)	27 (45%)	25 (42%)		

Master PhD	6 (10%)	7 (12%)		
<b>Occupation</b>				
Civil servant	29 (48.3%)	23 (38.3%)		
Private sector	19 (31.7%)	23 (38.3%)	0.63	0.5
Unemployed	12 (20%)	14 (23.3%)		
<b>Income</b>				
RM1000 – RM3999	7 (11.7%)	8 (13.3%)		
RM4000 – RM6999	18 (30%)	20 (33.3%)	0.32	0.95
RM7000 – RM10,000	28 (46.7%)	26 (43.3%)		
> RM10,000	7 (11.7%)	6 (10%)		
<b>Marital status</b>				
Single	53 (88.3%)	55 (91.7%)	0.37	0.5
Married	7 (11.7%)	5 (8.3%)		
<b>Anthropometry</b>				
Weight (kg)	76 ± (15)	72 ± (11)	1.62	0.93
Height (cm)	166 ± (6.9)	165 ± (8.6)	0.90	0.36
BMI (kg/m <sup>2</sup> )	27 ± (5)	26 ± (3.8)	1.27	0.2
Blood pressure (mmg/Hg)	131/75 ± (15/10)	127/76 ± (15/9)	0.63/-0.45	0.53/0.65
<b>Baseline of nutrition analysis using Nutritics</b>				
Total calories %	2089.7 ± (403)	2139.8 ± (392)	-0.089	0.49
Total energy %	9944 ± (3873)	9091 ± (2425)	1.44	0.15
Total carbohydrate %	52 ± (5.3)	50 ± (7.0)	2.2	0.65
Total protein %	18 ± (2.2)	17.8 ± (3.4)	-0.315	0.75
Total saturated fat %	12.2 ± (1.3)	11.5 ± (2.1)	-0.12	0.89
Total alcohol %	0.8 ± (1.7)	1.1 ± (1.9)	-0.92	0.35

<b>Level of activities</b>				
None – little or no regular exercise	6 (10%)	2 (3.3%)		
Light – 1 to 3 days per week	25 (42%)	22 (36.7%)	2.96	0.41
Moderate – 1 to 3 days per week (light) or 5 days per week (hard)	23 (38%)	29 (48.3%)		
Very active – 6 days week (hard)	6 (10%)	7 (11.7%)		
<b>Baseline data of QOL &amp; clinical measure</b>				
QOL				
Emotional	6.05 ± (0.25)	6.07 ± (0.26)	-.358	0.72
Global	6.13 ± (0.18)	6.17 ± (0.20)	-.104	0.9
Physical	6.19 ± (0.24)	6.21 ± (0.19)	-.623	0.53
Social	6.25 ± (0.23)	6.22 ± (0.25)	-.587	0.55
<b>Serum lipid profile (mg/L) and HS Crp</b>				
Total cholesterol	5 ± (1.1)	4.7 ± (1.03)	1.01	0.31
Triglyceride	1.64 ± (0.98)	1.77 ± (0.83)	-.15	0.87
HDL	1.13 ± (0.3)	1.21 ± (0.27)	0.23	0.81
LDL	2.75 ± (1.02)	2.69 ± (0.90)	0.35	0.72
HS C-reactive protein (mg/dL)	2.1 ± (4.5)	1.5 ± (3.9)	-.73	0.46

### 3.2 VCO's effect on serum lipid profile

Table 2 shows the results of the effect of the VCO effect on the serum lipid profile parameters namely HDL, LDL, triglycerides, and total cholesterol. There were 13.4%, 1%, and 4% reductions in total cholesterol level from baseline to 1st, 2nd, and 3rd follow-up respectively. However, Group B that received VOO showed a stable trend with no reduction from baseline to follow-ups. After 90 days of washout, both groups switched intervention (crossover).

There was a significant effect of time on Group B that received VCO with a reduction of total cholesterol level from baseline to 3<sup>rd</sup> follow-up at 2.5%, 3%, and 0.2 % respectively. The result of the VCO effect on HDL showed no significant difference from baseline until the last follow-up in both groups. However, after 90 days of washout period, Group B who received VCO for 90 days showed improvement in HDL level. There was an increase of about 1% to 3% in the HDL level of Group B from baseline to 6th follow-up. In LDL level, Group A that received VCO for the first 90 days showed LDL level reduced about 14% from baseline to 1st follow-up and continued to reduce about 3% from 1st to 3rd follow-up. On the other hand, Group B experienced no significant effect by VOO intake. However, after 90 days of washout, both groups experienced no statistically significant effect on LDL level at baseline and 4th, 5th, and 6th follow-up.

Repeated measure ANOVA (RM ANOVA) compared the effect of VCO on triglyceride level between Group A and B. Group A that received VCO in the first intervention showed a 14% reduction in triglycerides from baseline to 1st follow-up and subsequently, a 3% reduction from 2nd to 3rd followup, a small effect size. On the other hand, there was no reduction in Group B (received VOO). After 90 days of washout, both groups completed another three follow-ups and results showed a statistically significant mean score from baseline to 3rd follow-up. Group A that received VOO with Wilks' Lambda = 0.79,  $F(3,57) = 5.04$ ,  $p < 0.05$  and Cohen's  $d = 0.21$  and Group B (received VCO) with Wilks' Lambda = 0.87,  $F(3, 57) = 2.86$ ,  $p < 0.05$ . Both groups had a statistically significant difference in mean triglyceride level from baseline to 6th follow-up. Group B (received VCO) experienced a 9%, 1%, and 3% reduction from baseline to 4th, 5th, and 6th follow-up respectively. It proves that VCO can reduce the triglyceride level.

### **3.3 VCO's effect on hs-CRP level**

RM ANOVA compared the effect of VCO on the hs-CRP level between Group A and Group B. There was a significant effect of time on Group A from baseline to 1st, 2nd, and 3rd follow-up with a medium effect size of Cohen's  $d$ . On the contrary, Group B that consumed VOO did not show any difference from baseline until the last follow up. The results revealed a 7% reduction in hs-CRP level by VCO from baseline to 1st follow-up, a 3% reduction from 1st to 2nd follow-up, and a 46% reduction from 2nd to 3rd follow-up. However, the hs-CRP results after the washout period of 90 days showed no statistically significant effect of time on both groups from baseline to 6th follow-up.



**Table II: Result on the Effect of VCO on Serum Lipid Profile and HS CRP (Intervention 1)**  
**INTERVENTION ONE**

Group A (received VCO)	M±SD	P-value	Cohen d	Group B (received VOO)	M±SD	P-value	Cohen d
<b>TOTAL CHOLESTEROL</b>							
Baseline TC	5.0 ± 1.15		0.67	Baseline TC	4.7±1.03	0.10	0.10
1st follow-up TC	4.33 ± 1.0	<0.001		1st follow-up TC	4.6± 0.99		
2nd follow-up TC	4.28± 0.95			2nd follow-up TC	4.7±0.95		
3rd follow-up TC	4.11 ±0.93			3rd follow-up TC	4.7 ± 0.93		
<b>HDL</b>							
Baseline HDL	1.13± 0.31		-0.18	Baseline HDL	1.12 ± 0.27		
1st follow-up HDL	1.18 ± 0.27	0.51		1st follow-up HDL	1.17±0.30	0.77	-0.16
2nd follow-up HDL	1.16 ± 0.30			2nd follow-up HDL	1.14 ± 0.28		
3rd follow-up HDL	1.18 ± 0.28			3rd follow-up HDL	1.12 ± 0.26		
<b>L DL</b>							
Baseline LDL	2.75± 1.0		0.47	Baseline LDL	2.69 ± 0.91		
1st follow-up LDL	2.37±0.8	<0.001		1st follow-up LDL	2.58 ± 1.07		0.10
2nd follow-up LDL	2.37 ± 0.79			2nd follow-up LDL	2.72±0.99	0.58	
3rd follow-up LDL	2.31±0.85			3rd follow-up LDL	2.73±0.90		
<b>TRIGY CERIDE</b>							
Baseline TG	1.74 ± 0.98		0.30	Baseline TG	1.77 ± 0.83		0.15
1st follow-up TG	1.50 ± 0.78	0.04		1st follow-up TG	1.64 ± 0.83	0.10	
2nd follow-up TG	1.57 ± 0.87			2nd follow-up TG	1.90 ± 0.94		
3rd follow-up TG	1.47 ± 0.80			3rd follow-up TG	1.80 ± 0.98		
<b>H S Crp</b>							
Baseline hs-CRP	2.15±4.5		0.04	Baseline hs-CRP	1.58 ± 3.94		-0.06
1st follow-up hs-CRP	2.00 ± 3.59	<0.001		1st follow-up hs-CRP	1.85 ± 4.26	0.33	
2nd follow-up hs-CRP	1.98 ± 3.99			2nd follow-up hs-CRP	1.12 ± 2.44		
3rd follow-up hs-CRP	1.07 ± 3.13			3rd follow-up hs-CRP	1.06 ± 2.36		
<b>WASHOUT PERIOD FOR 90 DAYS</b>							

\*Repeated measure ANOVA

**Table III: Result on The Effect of VCO on Serum Lipid Profile and HS CRP (Intervention 2)INTERVENTION TWO (After washout period)**

Group A (received VOO)	M±SD	P-value	Cohen d	Group B (received VCO)	M±SD	P-value	Cohen d
<b>TOTAL CH OLESTEROL</b>							
Baseline TC after washout	4.48±1.12		0.02	Baseline TC after washout	4.73±0.86		0.10
4th follow-up TC	4.45±1.01	0.63		4th follow-up TC	4.61±0.79	0.35	
5th follow-up TC	4.50 ± 1.12			5th follow-up TC	4.47±0.81		
6th follow-up TC	4.55 ± 1.15			6th follow-up TC	4.46 ± 0.81		
<b>HDL</b>							
Baseline HDL after washout	1.11±0.26		-0.09	Baseline HDL after washout	1.22±0.33		-0.21
4th follow-up HDL	1.14 ± 0.33	0.30		4th follow-up HDL	1.23 ± 0.28	0.02*	-0.16
5th follow-up HDL	1.13±0.32			5th follow-up HDL	1.25 ± 0.29		
6th follow-up HDL	1.16 ± 0.37			6th follow-up HDL	1.29 ± 0.33		
<b>L DL</b>							



Baseline LDL after washout	2.50±0.91		0.00	Baseline LDL after washout	2.56 ± 0.88		
4th follow-up LDL	2.50 ± 0.80	0.98		4th follow-up LDL	2.43 ± 0.90		0.14
5th follow-up LDL	2.51±0.84			5th follow-up LDL	2.32 ± 0.82	0.06	
6th follow-up LDL	2.48±0.83			6th follow-up LDL	2.31 ± 0.88		
<b>TRIGY CERIDE</b>							
Baseline TG after washout	1.69±0.84		0.09	Baseline TG after washout	1.83±0.95		0.30
4th follow-up TG	1.62±0.76	0.004		4th follow-up TG	1.66 ± 0.76	0.045*	
5th follow-up TG	1.54 ± 0.75			5th follow-up TG	1.65 ± 0.71		
6th follow-up TG	1.60 ± 0.73			6th follow-up TG	1.63 ± 0.67		
<b>H S Crp</b>							
Baseline hs-CRP after washout	0.87 ± 2.97		-0.16	Baseline hs-CRP after washout	1.45 ± 4.0		0.53
4th follow-up hs-CRP	1.04 ± 3.30	0.304		4th follow-up hs-CRP	0.60±1.60	0.116	
5th follow-up hs-CRP	0.94 ± 3.21			5th follow-up hs-CRP	0.97 ± 3.24		
6th follow-up hs-CRP	0.90±2.99			6th follow-up hs-CRP	0.82 ± 3.08		

\*Repeated measure ANOVA

#### 4.0 DISCUSSION

The current study revealed a 13% reduction in total cholesterol (TC) from baseline to the first follow-up. However, through pairwise comparison, there was no further significant reduction. The 60 participants in Group A who received VCO as the first intervention showed a statistically significant difference in mean TC from baseline to the first follow-up. After the washout period where both groups switched intervention, Group B reported a similar result. These findings confirmed that VCO can reduce TC. Only this current study proved a reduction in TC from using VCO for 90 days, none of the previous studies proved likewise (Cardoso et al., 2015; Chinwong et al., 2017; Cecille de la Paz et al., 2010; Harris et al., 2017; Khawet al., 2018; Vijayakumar et al., 2016). Those previous studies only reported changes in HDL (Khaw et al, 2018 ; Chinwonget al. 2017a and Harris et al. 2017). Once a lipid parameter has changed, TC would remain unchanged because its calculation depends on other parameters.

In this study, VCO also proved its ability to reduce other lipid parameters such as LDL and TG. Therefore, the result of TC is statistically significant as its calculation depends on the other parameters. TC is calculated by adding HDL level and LDL level, plus 20 percent of triglyceride level (American Heart Association, 2020).

#### 4.1 Effect of VCO on triglycerides

This study proved that VCO can reduce triglycerides among ACS patients. As opposed by all available studies, none reported any effect of VCO on triglyceride levels. These conflicting results may be due to the amount of coconut oil used in the different studies.

Besides, the difference in the quality of VCO used also contributes to conflicting results. VCO with higher polyphenol content and minor constituents such as Vitamin E would lead to better outcomes. Moreover, the different methods of extracting virgin coconut oil (the chilling method) compared with the refined, bleached, and deodorized coconut oil may influence phenolic compounds and antioxidant activity (Marina et al. 2009). The wet extraction conducted in the dark and at a controlled temperature may be responsible for retaining the biological activities of the minor components in the oil. In this context, it is important to remember that  $\alpha$ -tocopherol concentration is greatly affected by the storage conditions of the oil, including temperature and light exposure (Srivastava et al. 2016). Studies have also shown that  $\alpha$ -tocopherol has a synergistic effect in association with some phenolic compounds having a significant antioxidant activity (El Yamani et al, 2019 ; Kim et al, 2018) . Although the fatty acid composition of coconut oil is well established, relatively little is known about the minor constituents and their biological effects (Pehowich,, 2000). Another possible reason that could be an obstacle in capturing reduction in triglycerides may be

the lack of compliance from the participants. As mentioned by Khawet al.(2018), lack of compliance with consuming the dietary fat would lead to no differences between groups and hence explain the lack of differences in LDL-C between coconut oil and olive oil groups.

#### **4.2 Effect of VCO on high-density lipoproteins**

The researcher found that HDL level increased significantly in the VCO group during the second intervention, though the first intervention had no significant difference. A lack of compliance could explain this discrepancy in findings. However, reported compliance was high during both interventions, hence dismisses the theory.

It was found that consuming 4ml of VCO twice daily for 90 days was associated with a significant increase in HDL level, reflecting the claim by recent studies that VCO is potentially beneficial for increasing HDL levels (Cardoso et al., 2015; Chinwonget al., 2017; Khawet al., 2018). A possible explanation for the increase in HDL-C observed in the study may be due to the high proportion of lauric acid and myristic acid in VCO. In principle, diets high in saturated fat raise HDL level, whereas diets high in polyunsaturated or monounsaturated fat lowers HDL levels (Mensink,2016).

A meta-analysis of 27 trials evaluated the effects of three classes of fatty acids, that is, saturated, monounsaturated, and polyunsaturated fatty acids on serum lipid and lipoprotein levels.

Among these three classes of fatty acids, saturated fatty acid had the greatest raising effect on HDL-C, total cholesterol, and LDL-C. On the other hand, monounsaturated and polyunsaturated fatty acids lowered total cholesterol and LDL-C levels (Mensink, 2016). Furthermore, the study also compared the effects of diets high in caprylic acid (C8:0) and capric acid (C10:0) and diets high in lauric acid (C12:0) on lipid metabolism. It was shown that the total HDL level significantly increased in diets rich in lauric acid, whereas remained unchanged in diets rich in caprylic acid and capric acid.

Several previous studies were not in favour of coconut oil lowering serum lipid profile (Dela Paz et al,2018; Liauet al, 2011). These studies reported on the effect of coconut oil instead of VCO. As mentioned earlier, VCO and regular coconut oil are different in their fatty acid compositions. A study in India among 100 stable CAD patients revealed that there were no changes in serum lipid profile using coconut oil as compared to sunflower oil in their two-year study (Vijayakumar et al, 2016a). In their study, they stated that coconut oil is not VCO, hence their result could not capture the differences in the two-year intervention as coconut oil does not contain lauric acid and other MCT components as VCO does. Furthermore, the doses of oils were not standardized and could be used in various amounts, leading to outcome bias. As reported in their study, there were several confounding factors like eating out, duration of consumption, and physical activities which could not be assessed accurately since the study was conducted on free-living subjects (Vijayakumar et al. 2016a). The difference in population, research methodology, and VCO dosage are the main factors which contribute to the different findings across VCO studies.

#### **4.3 VCO's effect on low-density lipoproteins**

Several studies have consistently demonstrated that consumption of VCO elevates LDL and thus may cause adverse cardiovascular health conditions despite it being a healthy oil with a relatively high concentration of medium-chain triglycerides (MCT). However, in the current study, participants who consumed about 5ml of VCO were able to reduce LDL in the first and second interventions.

As reported by Nevin and Rajamohan in 2004, VCO contains appreciable amounts of many biologically active components viz. polyphenols (80mg/ 100g oil) and antioxidant vitamins (30mg/ 100g oil),which may affect blood coagulation ((Nevin et al. 2004). Besides, the MCT component of coconut oil reduced fat accumulation, serum and tissue cholesterol, and linoleate requirement (Laurence, 2014). In vitro studies have proved that polyphenols inhibit platelet aggregation, as well as increase the Ca<sup>2+</sup> influx and mobilization of Ca<sup>2+</sup> in endothelial cells. These compounds are also reported to suppress adhesion molecules and inhibit experimental atherosclerosis (Zeng et al. 2016).In vitro studies also showed VCO as effective in reducing the concentrations of total cholesterol, triglycerides, and low-density lipoproteins (Nevin et al. 2008).

Diet supplemented with polyphenolic compounds improved lipid metabolism and increased plasma antioxidant potential especially in rats fed with added cholesterol (Nevin et al. 2008). According to Nevin et al.(2008) in their animal study, they reported that VCO polyphenols can prevent the oxidation of LDL in vitro. They can trap reactive oxygen species from aqueous media such as plasma and interstitial fluid of arterial wall thereby inhibiting the oxidation of LDL and showing atherosclerosis activity (Hoak, 1997). Thus, the proportion of MCT and polyphenolic compounds in VCO may explain the reduction in LDL in our study.

In a total of seven human studies, none reported the effect of VCO to reduce LDL. All studies showed a neutral effect with no changes in LDL level from baseline to the last follow-up, in various populations and settings (Cardoso et al, 2015 ;Chinwonget al. 2017a). This finding could be due to the different VCO dosage and the different population and settings between each study. The VCO dosage for most studies ranged between 15ml to 30ml, though one study did not specify the dosage(Cardoso et al,2015 and Chinwonget al. 2017a). They had only instructed the participants to use VCO as a cooking medium (Vijayakumar et al. 2016a)

This study showed an improvement in all clinical parameters namely serum lipid profile, serum glucose, and serum hs-CRP with only 5ml of VCO with 1.13gm of lauric acid. Other human studies which used various dosage of VCO ranging from 15ml to 30ml could have led to the different findings across all studies. In a study by Chinwong et al. in Thailand (2017), they instructed the participants to consume 15ml of VCO twice daily for 8 weeks which led to an increase in HDL level. However, the Malaysian study by Liauet al. (2011) among 20 obese participants which gave a similar dosage of VCO in three separate times in 4 weeks showed no change in serum lipid profile, except for the reduction in waist circumference. Another study from the USA which used 30ml of VCO for 28 days in their crossover design found VCO increased total cholesterol and LDL levels (Harris et al. 2017). These three studies, albeit using a similar dosage, had differing results.

#### **4.4 Effect of VCO on hs-CRP**

High sensitivity C-reactive protein (hs-CRP) is a risk assessment tool in ACS. Increased hs-CRP means increased risk for inflammation in the arteries caused by lipid accumulation. This study found that serum hs-CRP level reduced during the first intervention where participants consumed VCO for 90 days. However, after crossover during the second intervention, there was no change. A possible explanation of the reduction is the polyphenols in VCO. Moreover, a phytochemical analysis found that coumaric and ferulic acids are the major potent phenolics in VCO (Hamsiet al. 2015). Previous studies found VCO to mitigate oxidative stress, Dr. Eleni Semertzidou dyslipidemia, and inflammation in organs of animals and humans via antioxidant activities (Famurewa et al. 2018 and Zhang et al. 2019).

Apart from that, the effect of lauric acid on metabolism that leads to satiety and a reduction in body weight could also explain the reduction of hs-CRP in this study. In this current study, participants' body weight significantly reduced from baseline to the final follow-up.

A randomized trial of four weight reduction diets observed the association between weight loss and substantial reductions in hs-CRP, an effect independent of macronutrient composition. Further, those randomized into the study observed that the per cent reduction in hs-CRP correlated similarly with changes in all measures of body fat including total fat, abdominal fat, and intrahepatic fat (Nicklas et al. 2013). This study is consistent with prior smaller studies which demonstrated that diet-induced weight-loss substantially reduces hsCRP (Selvin et al. 2007; Shai et al. 2008). In a systematic review of 28 lifestyle weight loss studies ranging from 14 to 90 participants, the weighted correlation between change in hs-CRP and change in weight was 0.30 by Selvin et al.(2007), similar to Nicklas et al.(2013) with their 6-month correlation coefficient of 0.31. The decrease in hs-CRP with weight loss in this study is also similar to that observed among participants with impaired glucose tolerance in the Diabetes Prevention Program (DPP), where a 6.7% reduction in body mass was associated with a 30% reduction in hs-CRP ( American Diabetes Association, 2005). This study found that VCO reduced serum hs-CRP however, this did not correlate with weight loss.

The decrease in hs-CRP could be due to the mechanism of adipose tissue. Adipose tissues may be directly involved in the production and regulation of inflammatory cytokines that induce CRP production, and it has been suggested that inflammation may represent one of the mechanisms by which lifestyle changes and weight loss reduce the risk of cardiovascular disease (Pietraszek et al. 2011). Several findings over the last decade and recently suggest that weight loss could directly lead to reductions in CRP levels (Yatsuya et al. 2011 ; Van Gemert, 2016)

Adipocytes produce cytokines that regulate CRP production (Makkiet al. 2013). Interleukin 6, a key proinflammatory cytokine and principal regulator of hepatic CRP production may be particularly important in mediating the increases in CRP levels associated with greater adiposity (Van Gemert, 2016). Thus, a reduction in body weight is likely to have important consequences for circulating levels of CRP.

Based on the results presented, VCO proved effective during the first intervention but was unstable during the second intervention. The author concluded that VCO is only able to deliver health effects when free interaction with other medications. The findings suggested that VCO can be taken before the patient begins taking other medications. Further, they proposed VCO administration as first-line management in preventing ACS. Results also showed that the effect of VCO was unstable after switching supplements to VOO. Furthermore, the participants who received VCO

in the second intervention showed no significant difference in all biomarkers except for body weight and BMI. This could be due to the effect of concomitant statins on the biomarkers as participants would have been exposed to them longer by that time, which would have nullified the effect of VCO. VCO may have had positive effects on biomarkers after angioplasty before the effects of other concomitant medications. The above would explain the findings in this study, where VCO had significant effects only during the first intervention. Improvement in biomarkers could be achieved if VCO was administered to the patients earlier, compared to receiving statins alone.

## **5.0 CONCLUSION**

The study findings conclude that VCO is more effective when prescribed earlier, before other medications. This current study also revealed that 4ml of VCO (1.84gm of lauric acid) can improve biomarkers such as serum lipid profile, glucose level, and hs-CRP level. This study also emphasized that only MCTs with a certain chain length were beneficial to health, they are C6 to C12, predominant in VCO. Hence, when addressing the health benefits of MCT, the chain length should be specified to avoid misinformation.

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## **7.0 AUTHOR CONTRIBUTIONS**

All the authors, Sharifah Shafinaz, Mei Chan Chong, Khatijah Lim, Imran, and Yap Bee Wah have contributed to this study from its design to the manuscript preparation through data collection, analysis of results and presentation.

## **8.0 CONFLICT OF INTEREST**

The authors declare that there are no conflicts of interest regarding the publication of this article

## **9.0 AUTHOR DECLARATION STATEMENT**

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## **10.0 REFERENCES**

- American Diabetes Association. (2005). Intensive lifestyle intervention or metformin on inflammation and coagulation in participants with impaired glucose tolerance. *Diabetes*, 54(5), 1566-1572
- American Heart Association. (2013). What your cholesterol levels mean. Retrieved from American Heart Association website: [http://www.heart.org/HEARTORG/Conditions/Cholesterol/AboutCholesterol/What-Your-CholesterolLevels-Mean\\_UCM\\_305562\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/Cholesterol/AboutCholesterol/What-Your-CholesterolLevels-Mean_UCM_305562_Article.jsp).
- Cardoso, D. A., Moreira, A. S., de Oliveira, G. M., Luiz, R. R., & Rosa, G. (2015). A coconut extra virgin oil-rich diet increases HDL cholesterol and decreases waist circumference and body mass in coronary artery disease patients. *Nutricionhospitalaria*, 32(5), 2144-2152.
- Chinwong, S., Chinwong, D., & Mangklabruks, A. (2017). Daily consumption of virgin coconut oil increases highdensity lipoprotein cholesterol levels in healthy volunteers: a randomized crossover trial. *Evidence-Based Complementary and Alternative Medicine*, 2017.
- Deichmann, R., Lavie, C., & Andrews, S. (2010). Coenzyme q10 and statin-induced mitochondrial dysfunction. *Ochsner Journal*, 10(1), 16-21.
- Dela Paz, C., Jimeno, C., Sy, R., Eduardo, F., Punzalan, M. D., & dela Pena, P. (2010). The effect of virgin coconut oil on lipid profile and fasting blood sugar: A phase I clinical trial. *Philippine journal of internal medicine*, 48(2).
- Eyres, L. (2014). Coconut oil and the heart. Heart Foundation Evidence Paper.
- Famurewa, A. C., Folawiyo, A. M., Enohnyaket, E. B., Azubuike-Osu, S. O., Abi, I., Obaje, S. G., & Famurewa, O. A. (2018). Beneficial role of virgin coconut oil supplementation against acute methotrexate chemotherapy-induced oxidative toxicity and inflammation in rats. *Integrative medicine research*, 7(3), 257-263.

- Hamsi, M. A., Othman, F., Das, S., Kamisah, Y., Thent, Z. C., Qodriyah, H. M. S., ... & Jaarin, K. (2015). Effect of consumption of fresh and heated virgin coconut oil on the blood pressure and inflammatory biomarkers: an experimental study in Sprague Dawley rats. *Alexandria Journal of Medicine*, 51(1), 53-63.
- Harris, M., Hutchins, A., & Fryda, L. (2017). The impact of virgin coconut oil and high-oleic safflower oil on body composition, lipids, and inflammatory markers in postmenopausal women. *Journal of medicinal food*, 20(4), 345-351.
- Hoak, J. C. (1997). Fatty acids in animals: thrombosis and hemostasis. *The American journal of clinical nutrition*, 65(5), 1683S-1686S.
- Ibrahim, M. A., Ghazali, M. F., Mustafa, F. F., Tengku Muhammad, T. S. (2020). Virgin coconut oil as antioxidant and treatment on metabolic disorders: a short review *international journal of allied health sciences*, 4(4), 1602-1607.
- Khaw, K. T., Sharp, S. J., Finikarides, L., Afzal, I., Lentjes, M., Luben, R., & Forouhi, N. G. (2018). Randomised trial of coconut oil, olive oil or butter on blood lipids and other cardiovascular risk factors in healthy men and women. *BMJ open*, 8(3).
- Law, K. S., Azman, N., Omar, E. A., Musa, M. Y., Yusoff, N. M., Sulaiman, S. A., & Hussain, N. H. N. (2014). The effects of virgin coconut oil (VCO) as supplementation on quality of life (QOL) among breast cancer patients. *Lipids in Health and Disease*, 13(1), 139. <https://doi.org/10.1186/1476-511X-13-139>
- Liau, K. M., Lee, Y. Y., Chen, C. K., & Rasool, A. H. G. (2011). An open-label pilot study to assess the efficacy and safety of virgin coconut oil in reducing visceral adiposity. *International Scholarly Research Notices*, 2011.
- Ma, Z. F., & Lee, Y. Y. (2016). Virgin coconut oil and its cardiovascular health benefits. *Natural Product Communications*, 11(8), 1934578X1601100829.
- Makki, K., Froguel, P., & Wolowczuk, I. (2013). Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. *International Scholarly Research Notices*, 2013.
- Marina, A. M., Che Man, Y. B., Nazimah, S. A. H., & Amin, I. (2009). Antioxidant capacity and phenolic acids of virgin coconut oil. *International journal of food sciences and nutrition*, 60(sup2), 114-123.
- Mensink, R. P., & World Health Organization. (2016). Effects of saturated fatty acids on serum lipids and lipoproteins: a systematic review and regression analysis.
- Ministry of Health Malaysia. (2017a). Primary & Secondary Prevention of Cardiovascular Disease 2017.
- Ministry of Health Malaysia. (2017b). Management of Dyslipidaemia 2017, 5th Edition Clinical Practice Guidelines (Vol. 17, Issue July).
- Nevin, K. G., & Rajamohan, T. (2004). Beneficial effects of virgin coconut oil on lipid parameters and in vitro LDL oxidation. *Clinical biochemistry*, 37(9), 830-835.
- Nevin, K. G., & Rajamohan, T. (2008). Influence of virgin coconut oil on blood coagulation factors, lipid levels and LDL oxidation in cholesterol fed Sprague-Dawley rats. *e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism*, 3(1), e1-e8.
- Newman, C. B., Preiss, D., Tobert, J. A., Jacobson, T. A., Page, R. L., Goldstein, L. B., ... & Welty, F. K. (2019). Statin safety and associated adverse events: a scientific statement from the American Heart



Association. Arteriosclerosis, thrombosis, and vascular biology, 39(2), e38-e81.

Nicklas, J. M., Sacks, F. M., Smith, S. R., LeBoff, M. S., Rood, J. C., Bray, G. A., & Ridker, P. M. (2013). Effect of dietary composition of weight loss diets on high sensitivity C reactive protein: the Randomized POUNDS LOST trial. *Obesity*, 21(4), 681-689.

Noakes, M., Foster, P. R., Keogh, J. B., James, A. P., Mamo, J. C., & Clifton, P. M. (2006). Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. *Nutrition & metabolism*, 3(1), 1-13.

Pehowich, D. J., Gomes, A. V., & Barnes, J. A. (2000). Fatty acid composition and possible health effects of coconut constituents. *West Indian Medical Journal*, 49(2), 128-133.

Pietraszek, A., Gregersen, S., & Hermansen, K. (2011). Acute effects of dietary fat on inflammatory markers and gene expression in first-degree relatives of type 2 diabetes patients. *The review of diabetic studies: RDS*, 8(4), 477.

Praagman, J., Beulens, J. W., Alsema, M., Zock, P. L., Wanders, A. J., Sluijs, I., & Van Der Schouw, Y. T. (2016). The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition–Netherlands cohort, 2. *The American journal of clinical nutrition*, 103(2), 356-365.

Qu, H., Guo, M., Chai, H., Wang, W. T., Gao, Z. Y., & Shi, D. Z. (2018). Effects of coenzyme Q10 on statin induced myopathy: an updated meta analysis of randomized controlled trials. *Journal of the American Heart Association*, 7(19), e009835.

Selvin, E., Paynter, N. P., & Erlinger, T. P. (2007). The effect of weight loss on C-reactive protein: a systematic review. *Archives of internal medicine*, 167(1), 31-39.

Shai, I., Schwarzfuchs, D., Henkin, Y., Shahar, D. R., Witkow, S., Greenberg, I., ... & Stampfer, M. J. (2008). Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *New England Journal of Medicine*, 359(3), 229-241.

Srivastava, Y., Semwal, A. D., & Majumdar, A. (2016). Quantitative and qualitative analysis of bioactive components present in virgin coconut oil. *Cogent Food & Agriculture*, 2(1), 1164929.

Toth, P. P., Patti, A. M., Giglio, R. V., Nikolic, D., Castellino, G., Rizzo, M., & Banach, M. (2018). Management of statin intolerance in 2018: still more questions than answers. *American Journal of Cardiovascular Drugs*, 18(3), 157-173.

Vijayakumar, M., Vasudevan, D. M., Sundaram, K. R., Krishnan, S., Vaidyanathan, K., Nandakumar, S., ... & Mathew, N. (2016). A randomized study of coconut oil versus sunflower oil on cardiovascular risk factors in patients with stable coronary heart disease. *Indian Heart Journal*, 68(4), 498-506.

Van Gemert, W. A., May, A. M., Schuit, A. J., Oosterhof, B. Y., Peeters, P. H., & Monninkhof, E. M. (2016). Effect of weight loss with or without exercise on inflammatory markers and adipokines in postmenopausal women: the SHAPE-2 trial, a randomized controlled trial. *Cancer Epidemiology and Prevention Biomarkers*, 25(5), 799-806.

Yamani, M. E., Sakar, E. H., Boussakouran, A., Benali, T., & Rharrabti, Y. (2019). Antioxidant activity of phenolic extracts from olive mill wastewater and their influence on virgin olive oil stability. *Moroccan Journal of Chemistry*, 7(1), 7-1.

- Yatsuya, H., Jeffery, R. W., Langer, S. L., Mitchell, N., Flood, A. P., Welsh, E. M., ... & Levy, R. L. (2011). Changes in C-reactive protein during weight loss and the association with changes in anthropometric variables in men and women: LIFE Study. *International journal of obesity*, 35(5), 684-691.
- Zakaria, Z. A., Ahmad, Z., Somchit, M., Arifah, A., Khairi, H., Sulaiman, M., Teh, L., Salleh, M., & Long, K. (2010). Antihypercholesterolemia property and fatty acid composition of madi-produced virgin coconut oils. *African Journal of Pharmacy and Pharmacology*, 4(September), 636-644. wos:000285688300004
- Zakaria, Z. A., Somchit, M. N., Mat Jais, A. M., Teh, L. K., Salleh, M. Z., & Long, K. (2011). In vivo antinociceptive and anti-inflammatory activities of dried and fermented processed virgin coconut oil. *Medical Principles and Practice*, 20(3), 231-236. <https://doi.org/10.1159/000323756>
- Zakaria, Z., Emran, A., Subermaniam, K., & Jaarin, K. (2015). Effect of consumption of fresh and heated virgin coconut oil on the blood pressure and inflammatory biomarkers: An experimental study in Sprague Dawley rats. *Alexandria Journal of Medicine*, 51(1), 53-63. <https://doi.org/10.1016/j.ajme.2014.02.002>
- Zhang, X., Xue, C., Xu, Q., Zhang, Y., Li, H., Li, F., ... & Guo, C. (2019). Caprylic acid suppresses inflammation via TLR4/NF- $\kappa$ B signaling and improves atherosclerosis in ApoE-deficient mice. *Nutrition & metabolism*, 16(1), 1-16.