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THE PHYSICIAN AS TEACHER: EMPOWERING PATIENTS IN PRIMARY HEALTHCARE SETTINGS

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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;Liau*et 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-elevationmyocardial infarction (NSTEMI), and STelevation 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

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Group A was 51.2±9.3 and for Group B, 52.7±10.1. There was no significant difference in demographic and clinical charcharacteristicsween 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 ± SD		t/□2	
Age (year)				
	51.2 ± (9.3)	52.7 ± (10.1)	-.85[a]	0.3
Gender				
Male	43 (71.7%)	38 (63.3%)	0.95[b]	0.33
Female	17 (28.3%)	22 (36.7%)		
Race				
Malay	39 (65%)	35 (58.3%)		
Chinese	7 (11.7%)	8 (13.3%)	0.57	0.751
Indian	14 (23.3%)	17 (28.7%)		
ACS classification				
UA	13 (22%)	17 (28%)		
NSTEMI	32 (53%)	29 (48%)	0.71	0.74
STEMI	15 (25%)	14 (24%)		
ACS management				
PCI	55 (92%)	48 (80%)		
CABG	2 (3%)	2 (3%)	4.28	0.13
MEDICATIONS	3 (5%)	10 (7%)		
Comorbidities				
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%)		
Medications				

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%)		
Education level				
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%)		
Occupation				
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%)		
Income				
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%)		
Marital status				
Single	53 (88.3%)	55 (91.7%)	0.37	0.5
Married	7 (11.7%)	5 (8.3%)		
Anthropometry				
Weight (kg)	76 ± (15)	72 ± (11)	1.62	0.93
Height (cm)	166 ± (6.9)	165 ± (8.6)	0.90	0.36
BMI (kg/m2)	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
Baseline of nutrition analysis usi ng Nutritics				
Total calories %	2089.7 ± (403)	2139.8 ± (392)	-.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)	-.315	0.75
Total saturated fat %	12.2 ± (1.3)	11.5 ± (2.1)	-.12	0.89
Total alcohol %	0.8 ± (1.7)	1.1 ± (1.9)	-.92	0.35
Level of activities				
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%)		
Baseline data of QOL & clinical measure				
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
Serum lipid profile (mg/L) and HS Crp				
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 3rd 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
TOTAL CHOLESTEROL							
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		
HDL							
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		
L DL							
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		
TRIGY CERIDE							
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		
H S Crp							
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		
WASHOUT PERIOD FOR 90 DAYS							

*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
TOTAL CH OLESTEROL							
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		
HDL							

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		
L DL							
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		
TRIGY CERIDE							
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		
H S Crp							
Baseline hs-CRP after waahout	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		
6rd 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; Khaw*et al.*, 2018; Vijayakumar *et al*., 2016). Those previous studies only reported changes in HDL (Khaw *et al*, 2018 ; Chinwong*et 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 αtocopherol 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 α-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 Khaw*et 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; Chinwong*et al*., 2017; Khaw*et 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:O) 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; Liau*et 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 Ca2þ influx and mobilization of Ca2þ 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 ;Chinwong*et 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 Chinwong*et 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 Liau*et 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 (Hamsi*et al*. 2015). Previous studies found VCO to mitigate oxidative stress,

Dr. Eleni Semertzidou dyslipidemia, and inflammation in organs of animals and humans via antioxidant activitie (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 decadeand 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 (Makki*et 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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