行政院國家科學委員會專題研究計畫　期中進度報告

身體活動功能、血清炎症反應指標與代謝症候群相關系列研究(1/2)

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英文摘要

The metabolic syndrome, a collection of multiple problem including hypertension, dyslipidemia, glucose intolerance and insulin resistance, has been paid much attention for its high risk of developing cardiovascular disease and type 2 diabetes. Although physical activity is showed to prevent cardiovascular risk factors such as type 2 diabetes, hypertension, hyperlipidemia, the effect of exercise training on the reduction of risk for individuals who are at high risk for metabolic diseases is unknown. A two-year study is proposed to reveal the relationships among physical capacity, inflammation state, and components of the metabolic syndrome, so that, the possible mechanism of exercise training effect on components of the metabolic syndrome may be enlightened for further disease prevention and treatment accordingly.

The main purposes of the first year study are to describe physical capacity, inflammation condition, and components of the metabolic syndrome; and to determine the intensity, duration and frequency of exercise training for treating individuals with metabolic syndrome. The eligible participants were assigned randomly into either exercise or control group. The exercise group participated in a 12-week moderate-intensity aerobic exercise program. The functional capacity and biomedical data were collected at baseline, and the 12^{th} weeks of the program.

During the first year of the study, 22 subjects completed the 12-week data collection. Of these, 11 subjects participated the exercise training program. These exercise participants show significant improvements in hip circumference, waist to hip ratio, physical capacity, systolic & diastolic blood pressure, levels of triglycerides, interlenkin-6 and MCP-1 following the training program. However, the changes in metabolic syndrome indicators and inflammatory markers between exercise and control groups were not significantly different. This is probably due to a small

sample size. Further investigation with a larger sample size is needed to explore the effectiveness and mechanism of physical exercise on inflammatory markers and metabolic syndrome.

Keyword: metabolic syndrome, exercise training, physical capacity, inflammation

中文摘要

代謝症候群是指包括高血壓、血脂異常、葡萄糖耐受性異常和胰島素阻抗之症候群，由於代謝症候群為糖尿病和心血管疾病發生的主要危險因素，故臨床上越來越被重視。研究亦發現代謝症候群與動脈粥狀硬化有相同形態的炎症反應。雖然規律運動訓練能有效改善心血管疾病和相關危險因子，但運動對代謝症候群危險性之影響並未被明確探討。本研究第一年針對代謝症候群個案之身體活動功能、血清炎症指標及代謝症候群症狀加以分析，並確立代謝症候群個案之運動強度、運動持續時間和頻率，並進行個案之運動訓練計劃。

第二年計劃探討規律運動訓練對代謝症候群個案之症狀、身體活動功能、及血清炎症反應之影響，並分析代謝症候群個體運動訓練成效之可能機轉，合乎收案之對象將依隨機方式分配至規律運動組及控制組，所有個案於計劃進行前接受身體活動功能、血清炎症指標以及代謝症候群症狀之評估。運動組隨即參與為期 12 週，每週三次，每次 30 分鐘之有氧運動訓練計劃，控制組則維持其原有生活型態，本研究將於計劃第 12 週再次進行資料之收案與分析。

第一年計劃由 94 年 9 月至 95 年 5 月止，共有 22 位個案完成 12 週之資料分析，其中運動組及控制組各 11 名，個案年齡介於 38 至 62 歲之間，平均為 49.3±7.0 歲。分析運動組個案代謝症候群危險因子於 12 週計劃前後之變化，結果在腰圍、腰臀圍比、身體活動功能、靜態收縮壓及舒張壓、及血清三酸甘油脂濃度，均有顯著下降情形，然於控制組則未觀察到顯著變化。進一步檢定兩組個案於計劃前後變化之差異，並未發現顯著之差異。在血清濃度 Cytokines 濃度變化方面，運動組經 12 週之運動計劃後，平均 IL-6 及 MCP-1 濃度顯著下降，但在控制組則未觀察到任何 Cytokines 之變化，而兩組各 Cytokines 平均濃度於計劃前後之改變，並無顯著差異。

關鍵字：代謝症候群、運動訓練、身體活動耐力、炎症指標

一、研究背景與目的

代謝症候群（Metabolic Syndrome; MS）是許多心血管疾病危險因素聚集的現象，是指同一個人身上，同時聚集肥胖、高血壓、血脂異常及血糖偏高的情形，發生的原因可能是遺傳或環境影響，而使個體產生胰島素阻抗而造成生理異常的現象。這些異常的現象包括：加速人體血管粥樣硬化，及增加心血管疾病發生之危險性等（The National Cholesterol Education Program's Adult Treatment Panel III; NCEP ATP III, 2001）。

有關運動計劃對冠狀動脈心臟疾病（Coronary Heart Disease）危險因子的改善已有相當文獻的探討，運動訓練成效包括：改善個體 BMI、血管動脈壓等。最近亦有研究指出，增加健康成人身體活動量與其血清炎症指標（inflammatory makers）的降低有關。有鑑於炎症指標異常對心血管疾病及代謝症候群的發生扮演著重要角色，然而有關身體活動量、血清炎症指標及代謝症候群危險因子之相關性，目前仍缺乏研究加以探討。因此，本研究擬進行系列研究，第一年先探討代謝症候群患者身體活動功能、血清炎症指標，及其代謝症候群危險因子；第二年則分析規律運動訓練對代謝症候群改善之成效及可能機轉。

二、文獻查證

代謝症候群患者之特徵包括：血脂異常（dyslipidemia）、胰島素阻抗（insulin resistance）、高血壓、腹部肥胖（abdominal obesity）及凝血異常（pro-thrombotic state）。這些異常現象會加速血管粥樣硬化，一旦這些現象成為群聚狀態（clustered status），更會顯著增加心血管疾病的發生率及死亡率。近來美國 NCEP ATP III 提出治療性生活型態改善計劃（Therapeutic Lifestyle Changes）來降低代謝症候群的盛行率，其中包括調整飲食習慣及規律運動。

在一些研究中發現，在沒有飲食介入情況下，進行運動訓練，可改善個體身體脂肪（percent body fat），及內臟脂肪（visceral adipose tissue），因此，建議增加身體活動量，可改善心血管疾病危險因子（Kang et al., 2002）。另 Ritsavos 等

學者發現，新陳代謝症候群病患中，規律運動者，相較於靜態生活之患者，其體內 C-reactive proein（CRP）、interlenkin（IL）-6、及 tumour nerosis factor (TNF-α) 顯著的低（所有 $p < 0.05$）。因此，身體活動量及血清炎症指標與代謝症候群患者之間，應有其重要之相關性，然經由系統性文獻之查證，發現並無實證之資料，宜有進一步之研究加以探討。

三、研究方法

（一）研究個案及場所

本計劃第一年於 94 年 9 月至 95 年 5 月止，在某醫學大學附設醫學中心之心臟內科、家醫科及新陳代謝科門診，招募代謝症候群受試者，經醫師評估及同意後轉介。代謝症候群之診斷標準是採美國 the Adult Treatment Panel III of the National Cholesterol Education Program (NCEP ATP III, 2001)之指引，同時參考國內國民健康局（2004）之建議，取樣標準如下：

1. 選樣條件：

(1) 年齡介於 18 至 64 歲；目前未服降血壓、降血糖、或降血脂藥物者。

(2) 400mg/dl ≧ TG ≧ 150mg/dl；HDL-C：男≦ 40mg/dl，女≦ 50mg/dl；160/100mmHg ≧ BP ≧ 130/85mmHg；200 mg/dl ≧ fasting blood sugar ≧ 110 mg/dl，腰圍：男 ≧ 90cm，女 ≧ 80cm，以上五項符合三項者。

(3) 近 3 週內未規律運動

(4) 同意參與本研究計劃共持續 12 週者

2. 排除條件：

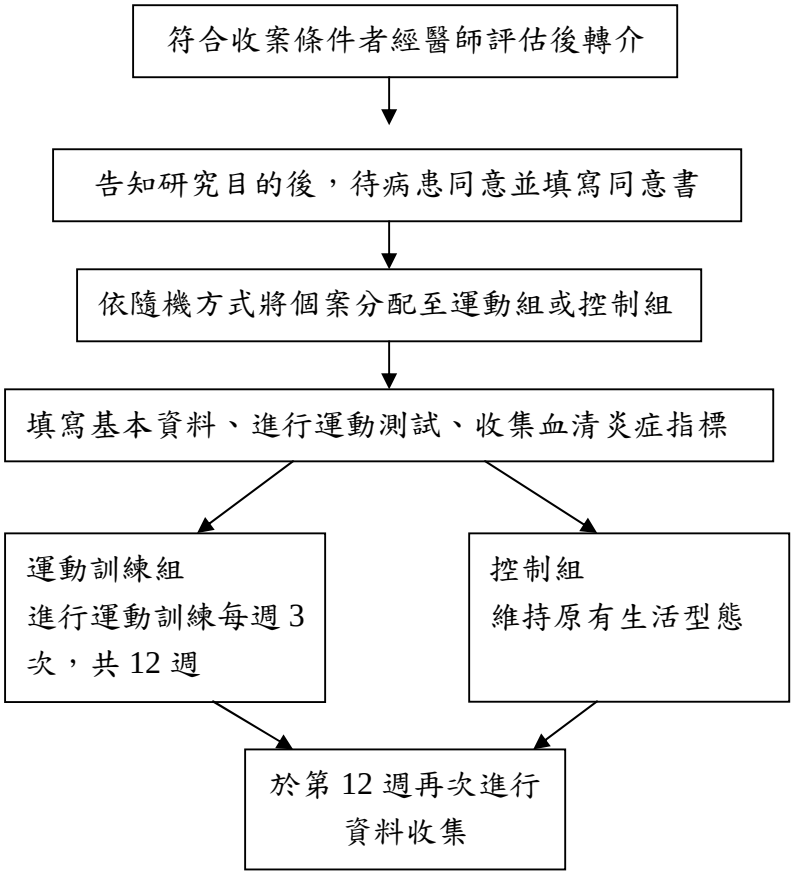
(1) 有精神疾病個案

(2) 肌肉骨骼疾病無法執行運動訓練者

(3) 經醫師診斷為癌症、冠狀動脈疾病、慢性覆發性呼吸道疾病

（二）研究設計及進行方法

在研究計劃進行期間，經個案同意並填寫同意書後再進行收案，並依隨機方式將個案分配至運動組或控制組。運動組以 60-80%儲備心率（heart rate reserve）為強度，進行跑步機運動訓練，每週 3 次，每次 30 分鐘，共 12 週。研究進行流程如下：



在血液資料之收集方面，每位個案至少禁食 8 小時，每次收集血液樣本 12^{cc}，個案血清炎症指標（IL-1, IL-6, IL-10, TNF-α 及 MCP-1）之分析採酵素連結免疫吸附法（General ELISA Protocol），另採全自動生化分析儀以酵素分析法（enzymatic methods）測量血液生化值，包括：總膽固醇、HDL-C 及三酸甘油酯，而 LDL-C 濃度在三酸甘油酯≦ 400 mg/dl 情況下，以 Friedewald 公式計算之。

（三）資料分析方法

本研究以 SPSS 11.0（Chicago, IL, USA）統計軟體進行資料分析，以百分比、平均值及標準差了解個案基本屬性分佈情形。再以 Unpaired t-test 及 Mann-Whitney U test 等方法，比較兩組代謝症候群危險因子、身體活動功能及血清炎症指標濃度之差異。而兩組個案於研究計劃前後代謝症候群危險因子、身體活動功能與血清炎症指標之變化，則以 dependent t-test、Mann-Whitney U test、或 Wilcoxon signed ranks test 來分析。

四、結果與討論

本研究至 95 年 5 月止，共有 22 位個案完成 12 週之資料分析，其中運動組及控制組各 11 名，個案年齡介於 38 至 62 歲之間，平均為 49.3±7.0 歲，個案資料詳列於表一。進一步以 Mann-Whitney U test 分析兩組個案基本資料之間並無顯著差異（表二）。

在血清 Cytokine 濃度方面，所有個案平均 IL-6、IL-10、MCP-1 及 TNF-α 濃度分別為 5.4±2.6、3.4±7.1、381.7±154.0 及 3.5±1.9 pl/ml（表三），而兩組個案 Cytokines 濃度於計劃前後亦無顯著差異（表四）。

分析運動組個案代謝症候群危險因子於 12 週計劃前後之變化，結果在腰圍、腰臀圍比、心肺適能、靜態收縮壓及舒張壓、及血清三酸甘油脂濃度，均有顯著下降情形（表五），然控制組方面則未觀察到顯著變化（表六）。進一步以 Mann-Whitney U test 檢定兩組個案於計劃前後變化之差異，並未發現顯著之差異（表七）。

在血清濃度 Cytokines 濃度變化方面，運動組經 12 週之運動計劃後，IL-6 及 MCP-1 濃度顯著下降（表八），在控制組則尚未觀察到顯著 Cytokines 之變化（表九），而兩組 Cytokines 於計劃前後之改變，並無顯著差異（表十）。

本研究第一年研究結果發現，運動組於規律運動訓練後，代謝症候群危險因子及血清 IL-6 及 MCP-1 濃度有顯著下降，因此，運動訓練對改善代謝症候群可能扮演重要的角色，但可能限於樣本數，因此，兩組個案於計劃前後之血清炎症指標及代謝症候群危險因子之變化，並未觀察到顯著差異情形。本計劃目前仍持續進行收案，預計兩組各完成 25 位個案之資料收集，以增加本研究結果之推論性。未來將進一步分析資料，並探討運動訓練對代謝症候群改善成效之可能機轉，期望能對代謝症候群患者運動介入措施及成效提出具體建議。

表一、個案代謝症候群危險因子描述統計（*N* = 22）

變項	最小值	最大值	M±SD
年齡 (歲)	38	62	49.3±7.0
身體組成			
體重 (kg)	55.0	93.0	73.9±11.4
身體質量指數 (kg/m^2)	25.5	35.2	29.1±2.8
腰圍 (cm)	78.0	108.5	93.0±7.0
腰臀圍比	0.8	0.9	0.9±0.0
身體活動功能			
VO2max (ml/kg/min)	24.5	43.1	32.9±4.4
靜態血壓 (mmHg)			
靜態收縮壓	113	157	135.5±10.7
靜態舒張壓	68	108	86.6±10.1
血脂肪 (mg/dL)			
總膽固醇	163	321	219.3±41.3
高密度脂蛋白膽固醇	31	55	41.0±8.0
低密度脂蛋白膽固醇	75	227	139.3±39.7
三酸甘油酯	60	464	195.0±108.9

表二、運動組與控制組代謝症候群危險因子之檢定（*N* = 22）

項目	運動組 (n = 11) M±SD	控制組 (n = 11) M±SD	*U* 值	*P*
年齡 (歲)	50.8±7.4	47.8±6.6	46.00	.37
身體組成				
體重 (kg)	72.0±8.1	74.7±10.1	18.00	.08
身體質量指數 (kg/m^2)	28.5±3.2	29.7±2.4	38.50	.15
腰圍 (cm)	92.0±6.7	94.0±6.2	30.50	.08
腰臀圍比	0.87±0.03	0.89±0.03	32.00	.07
身體活動功能				
VO2max (ml/kg/min)	32.9±5.0	32.9±4.0	50.50	.52
靜態血壓 (mmHg)				
靜態收縮壓	133.0±12.6	138.0±8.2	48.50	.44
靜態舒張壓	83.6±12.0	89.6±7.1	37.00	.13
血脂肪 (mg/dL)				
總膽固醇	209.7±21.1	228.9±54.2	54.00	.70
高密度脂蛋白膽固醇	40.2±6.9	41.8±9.3	53.00	.65
低密度脂蛋白膽固醇	134.1±30.9	144.5±47.9	52.50	.61
三酸甘油酯	177.0±102.5	212.9±117.0	48.00	.44

表三、代謝症候群個案血清 Cytokines 濃度（*N* = 22）

項目	最小值	最大值	M±SD
IL-6	2.81	13.90	5.42±2.55
IL-10	1.00	32.30	3.37±7.08
MCP-1	155.00	792.00	381.70±153.95
TNF-α	2.16	10.60	3.46±1.86

表四、運動組與控制組血清 Cytokines 之比較（*N* = 22）

項目	運動組 (n = 11) M±SD	控制組 (n = 11) M±SD	*U*	*P*
IL-6	5.47±2.95	5.15±1.11	19.50	.20
IL-10	3.64±9.54	2.81±0.73	21.00	.30
MCP-1	353.64±78.74	416.33±214.67	45.00	.77
TNF-α	3.33±0.98	3.60±2.63	32.00	.20

表五、運動組於研究計畫前後代謝症候群危險因子之變化（*N* = 11）

項目	研究計畫前 (n = 11) M±SD	研究計畫後 (n = 11) M±SD	*U* 值	*P*
身體組成				
體重 (kg)	72.0±8.1	66.0±9.1	-1.20	.23
身體質量指數 (kg/m^2)	28.5±3.2	28.1±3.1	-1.12	.26
腰圍 (cm)	92.0±6.7	87.7±6.6	-2.94	.00*
腰臀圍比	0.87±0.03	0.85±0.04	-2.41	.02*
身體活動功能				
VO2max (ml/kg/min)	32.9±5.0	38.2±5.8	-2.54	.01*
靜態血壓 (mmHg)				
靜態收縮壓	133.0±12.6	127.0±11.9	-2.04	.04*
靜態舒張壓	83.6±12.0	78.3±11.0	-2.38	.02*
血脂肪 (mg/dL)				
總膽固醇	209.7±21.1	209.3±28.1	-0.53	.59
高密度脂蛋白膽固醇	40.2±6.9	42.0±9.5	-0.85	.40
低密度脂蛋白膽固醇	134.1±30.9	140.1±32.1	-0.76	.45
三酸甘油酯	177.0±102.5	136.0±64.3	-2.22	.03*

* $p < 0.05$

表六、控制組於研究計畫前後代謝症候群危險因子之變化（*N* = 11）

項目	研究計畫前 (n = 11) M±SD	研究計畫後 (n = 11) M±SD	*U* 值	*P*
身體組成				
體重 (kg)	74.7±10.1	78.4±9.4	0.60	.55
身體質量指數 (kg/m^2)	29.7±2.4	29.5±2.7	-1.24	.21
腰圍 (cm)	94.0±6.2	93.1±5.1	-0.66	.51
腰臀圍比	0.89±0.03	0.89±0.03	-1.22	.22
身體活動功能				
VO2max (ml/kg/min)	32.9±4.0	32.0±5.9	-0.59	.55
靜態血壓 (mmHg)				
靜態收縮壓	138.0±8.2	139.2±8.8	-0.65	.51
靜態舒張壓	89.6±7.1	84.4±5.6	-1.82	.07
血脂肪 (mg/dL)				
總膽固醇	228.9±54.2	219.8±43.1	-0.24	.81
高密度脂蛋白膽固醇	41.8±9.3	41.9±9.4	-0.94	.35
低密度脂蛋白膽固醇	144.5±47.9	143.9±37.2	-0.53	.59
三酸甘油酯	212.9±117.0	169.4±87.3	-1.60	.11

表七、兩組個案於研究計畫前後代謝症候群危險因子變化之差異（*N* = 22）

項目	運動組 (n = 11) M±SD	控制組 (n = 11) M±SD	*U* 值	*P*
身體組成				
體重 (kg)	5.8±2.7	4.3±1.4	45.50	.77
身體質量指數 (kg/m^2)	0.5±1.4	0.2±0.4	45.00	.77
腰圍 (cm)	2.3±1.5	0.8±2.4	28.00	.11
腰臀圍比	0.02±0.02	0.01±0.02	34.00	.26
身體活動功能				
VO2max (ml/kg/min)	-5.3±5.9	0.8±5.2	24.00	.06
靜態血壓 (mmHg)				
靜態收縮壓	6.0±7.9	-2.3±8.0	25.50	.07
靜態舒張壓	5.4±5.9	5.4±6.9	48.50	.94
血脂肪 (mg/dL)				
總膽固醇	0.5±19.7	-1.0±25.0	41.00	.84
高密度脂蛋白膽固醇	-1.8±5.6	-0.5±3.4	33.50	.40
低密度脂蛋白膽固醇	-6.0±20.6	-4.6±22.2	43.00	.97
三酸甘油酯	41.0±50.6	20.5±39.0	35.00	.49

表八、運動組計劃前後血清 Cytokines 之變化（*N* = 11）

項目	研究計畫前 (n = 11) M±SD	研究計畫後 (n = 11) M±SD	*U*	*P*
IL-6	6.47±2.95	4.73±2.02	-2.05	.04*
IL-10	4.64±9.54	1.09±0.26	- .18	.85
MCP-1	353.36±78.74	317.73±61.02	-1.87	.04*
TNF-α	3.33±0.98	3.08±0.36	- .45	.65

* $p < .05$

表九、控制組於計劃前後血清 Cytokines 之變化（*N* = 11）

項目	研究計畫前 (n = 11) M±SD	研究計畫後 (n = 11) M±SD	*Z*	*P*
IL-6	4.15±1.11	3.86±1.60	- .18	.86
IL-10	1.81±0.73	1.12±0.20	-2.10	.06
MCP-1	416.33±214.67	420.33±225.35	- .89	.37
TNF-α	3.60±2.63	2.96±0.61	- .66	.51

表十、兩組個案於計劃前後血清 Cytokines 變化之比較（*N* = 22）

項目	研究計畫前 (n = 11) M±SD	研究計畫後 (n = 11) M±SD	*U*	*P*
IL-6	1.74±3.31	0.29±2.15	33.00	.23
IL-10	3.55±9.29	0.69±0.75	31.00	.18
MCP-1	35.64±61.70	-4.00±209.29	26.00	.08
TNF-α	0.25±1.09	.65±2.50	47.50	.88

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