計 畫 編 號：NHRI-EX96-9531PI

國家衛生研究院整合性醫藥衛生科技研究計畫

少年高血壓危險因子及後續影響

計畫名稱

96年度成果報告

執 行 機 構： 中國醫藥大學

計 畫 主 持 人： 宋鴻樟 教授

本年度執行期間 96 年 1 月 1 日 至 96 年 12 月 31 日

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壹、96年度計畫研究成果摘要

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計 畫 編 號：NHRI-EX96-9531PI

執 行 機 構：中國醫藥大學

計畫主持人：宋鴻樟

研 究 人 員：李源德、王主科、許秀卿、簡國龍、蘇大成、林瑞雄、劉秋松、林文元、周碧瑟

關 鍵 字：青少年、高血壓、危險因子、追蹤研究

成 果 分 類：
- ☐ 癌症基礎與臨床研究(可複選，最多三項)
- ☐ 分子與基因醫學研究
- ☐ 臨床研究
- ☐ 生物技術與藥物研究
- ☐ 生物統計與生物資訊研究
- ☑ 醫療保健政策研究
- ☐ 環境衛生與職業醫學研究
- ☐ 醫學工程研究
- ☐ 老年醫學研究
- ☐ 精神醫學與藥物濫用研究
- ☐ 疫苗研究
- ☐ 幹細胞研究
- ☐ 奈米醫學研究
- ☑ 其他重要疾病或醫藥衛生問題研究

（1）中文摘要

中風是台灣地區排名第二的主要死因，中風族群中最盛行的共病為高血壓和糖尿病。雖然高血壓盛行情況在孩童中相對較低。但是，有高血壓方面疾病的孩童仍為數不少。在台灣，估計每年有 60-100 名 20 歲青年死於中風。1992-2000 年台灣地區高、中、小學大規模的尿液篩檢結果，被定義為高血壓者有 5,792 名。有高血壓的學生較可能有蛋白尿和尿糖。本計畫根據這些尿液篩檢結果，選取蛋白尿、血尿或尿糖為陽性反應者，並分別建立高血壓學生及非高血壓學生世代。

我們期望了解孩童高血壓、家庭聚集、治療效果、不同程度之血壓控制進展至心血管疾病、腎臟疾病及其他共生疾病之相關危險因子。這計畫可能達成以下目標：

1. 建置執行本研究和資料收集的方式。
2. 從小學生尿液篩檢結果建立高血壓孩童與正常血壓孩童（對照）的世代。
3. 利用問卷訪視與健康檢查的方式，進行高血壓孩童族群與對照族群的比較，以探討孩童高血壓之可能相關因子 。
4. 評估病人遵醫囑的情形，包括臨床診斷過程、用藥情況及其他等。
5. 在 3 年的研究期間觀察任何短期的不良反應。
6. 評估高血壓青少年的共病問題。
7. 比較有無新共生疾病孩童的血液/尿液生化值及生活型態之差異。

本研究對象之選取是以大規模尿液之尿蛋白、尿糖篩檢結果為依據，有選取誤差之限制。血壓情況可能不能代表一般孩童。然而，這些孩童有高的風險產生心血管及腎臟方面的共生疾病，需要受到立即的重視。本計畫將探討高血壓、尿糖和尿蛋白是否有交互作用之危險，並且提出預防發

展出共生疾病之方法。根據過去金山社區心血管世代研究之經驗，本研究計畫在國家衛生研究院的資助結束後，仍將繼續追蹤。在此過程，所有的研究對象將持續接受適當的照護及諮詢。本研究希望能正確的估計可能的危險因子。

主持人與台大醫院參與過金山社區世代研究的人員有長期的合作。於本計畫，我們以台灣地區孩童為收案目標，以期能建立標準的過程與規範。

我們審視基線資料，將沒有身份證字號、身份證字號重複、沒有血壓值資料及血壓值超過正常範圍者、血壓值超過平均值±2 標準差者刪除。根據美國心臟病學會的孩童血壓分類標準，有 5,792 名孩童被定義為高血壓。對照組是依據性別、年齡做頻數配對選取，共 5,792 名。於刪除沒有地址及電話資料者後，有 3,418 名為合適本研究之高血壓學生。這些學生中，有 732 名在台北地區，279 位在台中地區。

國家衛生研究院於 2006 年 4 月正式資助本計畫，我們即開始招收和訓練研究助理及研究生。我們透先過信件聯絡研究對象的父母親，解釋此研究計畫，並且以電訪的方式來確定會面及健康檢查的時間，健康檢查則在台大醫院進行，今年九月開始在台中收案。問卷為自填式問卷，填寫完後由訪員做再次確認。問卷內容包括學生及父母親的人口社經、生活形態資料和健康史。

健康調查的項目包括血壓、理學檢查、尿液和血液樣本的測量。另外還有頸動脈和心臟踝部血管指數的檢查，並分析這些青少年高血壓患者是否有動脈硬化的現象，合計有 30 項。全部的檢查大約花費 1.5 至 2 個小時。從 2006 年 5 月至 2007 年 10 月期間，我們總共完成了 188 位高血壓患者及 274 位對照組的測量。我們期待到 2007 年 12 月底會有 500 人完成檢查。

目前所分析的資料是根據到 2007 年 10 月底前完成檢查的 462 人的追蹤資料。病例組較對照組年輕(19.87±3.11 對 21.31±3.55 歲，$p<0.0001$)，且較多人仍為學生（69.7 %對 52.7%，$p=0.0003$）。生活型態和飲食習慣在病例與對照之間很相似，但病例組目前較對照組多做運動(34.4%對 22.2%，$p=0.013$)。分析健康史資料可見病例組有糖尿病、高血壓、腎臟病及痛風病史的百分比都高於對照組。

病例組與對照組的平均血壓都是男孩的較女孩的高，男孩病例組血壓較對照組高（收縮壓：121.1±17.94 對 110.9±9.89 mmHg，$p=0.0001$；舒張壓：79.2±15.0 對 70.1±9.90 mmHg，$p<0.0001$ mmHg），女孩病例的平均舒張壓亦較對照組高(67.9±11.8 對 64.1±8.58 mmHg，$p=0.0006$）。我們也發現病例組的 BMI 平均值高於對照組(23.3±5.28 對 20.9±3.13 kg/m^2，$p<0.0001$)，且平均腰圍和腰臀比也是病例組顯著高於對照組。血液檢查項目多，病例組與對照組之間大多無顯著的不同，但是病例組的高密度脂蛋白膽固醇平均值低於對照組(48.52±10.28 對 51.45±10.07 mg/dL, $p=0.0003$)，胰島素則是病例組較對照組高（8.37±9.34 對 6.44±6.57μU/mL, $p=0.0067$）。在尿液檢查方面，病例組白蛋白排出率高於對照組(56.08±233.12 對 34.21±175.19 mg/g, $p=0.0458$)。

動脈粥樣化的相關檢測顯示，心臟-頸動脈波速度(hcPWV)、心臟-踝部

脈波速度(haPWV)、臂踝部脈波速度(baPWV)、及踝部肱部指標(ABI)在兩組間無顯著差異。但病例組頸動脈的 RCCA (0.524±0.072 對 0.433±0.043 mm，$p<0.0001$)及 LCCA(0.527±0.073 對 0.431±0.053 mm，$p<0.0001$)的平均值是病例組較對照組高。在逐步羅吉斯迴歸分析中，經控制了相關因子後，我們發現有少年高血壓、男性、血小板過高、白蛋白過高、三酸甘油脂過高及 baPWV≧90 百分比，都與高血壓前期(prehypertension)有關。我們也觀察到，年齡≧20 歲(OR=3.66，95%CI=1.55-8.65)、男性(OR=3.73，95%CI=1.76-7.91)、有高血壓前期(OR=4.80，95%CI=2.20-10.5)、總蛋白量(OR=5.23，95%CI=1.30-21.1)、及飯前血糖過高(OR=4.95，95%CI=1.34-18.3))都是 baPWV≧90 百分比的危險因子。在動脈粥樣化(IMT≧75 百分比)與相關因子的逐步羅吉斯迴歸分析中，有少年高血壓(OR=36.6，95%CI=18.6-72.0)、母親年齡≧50 歲(OR=4.49，95%CI=1.94-10.4)、血小板(OR=2.33，95%CI=1.03-5.25)過高及尿酸過高(≧5 mg/dL) (OR=2.93，95%CI=1.28-6.74)都是動脈粥樣化(IMT≧75 百分比)的危險因子，但父親年齡≧50 歲是保護因子(OR=0.40，95%CI=0.19-0.82)。

以上所探討的大部分是單變項的分析，多變項分析較少，我們試圖來證明影響高血壓的潛在因子。我們期待有較多的樣本數，才進行更詳細的分層及多變項分析。不過，第一年及第二年的初步資料分析已可認出肥胖

是青少年高血壓的重要危險因子，青少年時期的高血壓與後來的動脈硬化有關。有了兩年的經驗，如果儀器問題能夠解決，我們期望能在第三年同時於台中及台南持續招收研究的個案。

基線資料的研究

另外，我們也使用篩檢基線資料進行分析研究。我們因此在第二年參加了 2 個國際研討會發表我們的發現。一個是本計畫主持人參加在中國北京舉行的第 6 屆亞太高血壓年會，報告"Risk of Hypertension among Children with Urinary Screening Positive for Proteinuria, Glucosuria, and Hematuria"。另一個是由參加本計畫的博士班研究生出席在 2007 年七月在新加坡舉行的世界家庭醫師研討會，以口頭報告"Body Mass Index, Cholesterol, and Hypertension among School Children in Taiwan: Results of National Mass Urine Screening Program"。這兩篇摘要分別附在附錄一和二。

另外我們完成了一篇期刊論文「Childhood hypertension in association with obesity and hyperlipidemia in the mass urine screening in Taiwan」投稿到 SCI 期刊。

（2）英文摘要

Hypertension is the most prevalent disease in our population with stroke the second leading cause of deaths. Hypertension has a relatively low prevalence in children. But, there are a number of children being suffered from this problem in significance. There were 60-100 deaths annually from stroke before the age of 20 years in Taiwan. In the mass urine screening between 1992 and 2000 for all elementary, junior and senior high schools students in Taiwan Province, 5,792 students with hypertension had been identified. Students with hypertension were more likely to have proteinuria and glucosuria. This proposed study has established in the year one a cohort, based on these hypertensive students (n=600-800) and students without hypertension (n=600-800). Both groups of students have been found to be glucosuria, hematuria, and/or proteinuria positive in a urine screening program conducted by the Chinese Foundation of Health.

We proposed to investigate the risk factors associated with childhood hypertension, family cluster and the treatment effectiveness and different levels of blood pressure (BP) control in showing the progression of cardiovascular disease (CVD) and renal diseases and other comobidity in hypertensive children. This study as a feasibility study has the following aims.

1. To create a protocol, an operation procedure and data collection form.
2. To establish a cohort consists of hypertensive children and normotensive children (controls) identified from mass urine screening for elementary students.
3. To conduct a questionnaire investigation and health examination for factors that may associate with childhood hypertension by comparing hypertensive group and control group.
4. To assess patient compliance with their treatment protocol, including clinic visit schedules, medications and other procedures.
5. To observe any short-term adverse effects in the 3-year study period.

6. To obtain risks within patient variation in comobidity during the baseline and follow-up period.
7. To compare differences in blood/urine chemistry and lifestyle between children with and with no new comobidity.

This study population based on a mass urine screening for glucosuria or/and proteinuria in children may have limitations generated from selection bias. The BP status may not represent general children. However, these children are at elevated risk of developing comobidity in cardiovascular and renal systems, they are a group children deserve immediate attention. This project may provide a prominent approach for identifying risks in the interaction of hypertension, glucosuria and proteinuria, and identifying ways to prevent the development of comobidity. Based on the past experience in Chin-Shan Community Cardiovascular Cohort Study, the investigators conducted a follow-up task for children of hypertension with the NHRI support. In doing so, all study subjects may continue to receive adequate care and consultation, the investigators will be able to precisely estimate the risk may occur in the treatment effectiveness.

The PI has a long term collaboration experience with faculty members at the National Taiwan University Hospital who have been involved in the Chin-Shan Community Cardiovascular Cohort study. In this study, we therefore started the study subjects recruitment effort targeting children in Taipei area, attempting to establish the study standard process and protocol, presently we have also started recruit study subjects in the Taichung area.

We reviewed the baseline data to exclude those with no ID or duplicated ID and those with blood pressure data missing or exceeding normal range. Blood pressures exceeding mean±2 standard deviation were also excluded. After 5792 students with hypertensives were identified based on the American Heart

Association criteria of blood pressure classification for children, 5792 controls were also selected using frequency match with sex and age. After excluding those with no consistent address and/or telephone number, 3418 students were considered eligible for this study as hypertensive students. Among them, 732 students were in Taipei area, and 279 hypertensive students in Taichung area.

The NHRI funds were finalized and available in April 2006. We started to recruited and train research assistants and graduated students for this projects. Parents of potential subjects were contacted with a letter to explain this study project and followed by telephone calls to make appointments for interviews and check-up at National Taiwan University Hospital. The questionnaire was self-completed in Chinese and checked by an interviewer for the completion. Specific cautious measures about the questionnaires were the life style recall and health histories of the student and parents.

Element health examinations included the original 30 items on blood pressure, anthropometry, and measurements of urine and blood specimens of fasting. In addition, ultra sound measurements for common carotid artery and cardiac-ankle vascular index were performed to verify whether there is atherosclerosis development in young hypertensives. The whole examination procedure may take 1.5 to 2.0 hours. With parental and students consent, we have completed the procedure for 188 hypertensive cases and 274 controls between May 2006 and October 2007. We expected to complete 500 persons by the end of December 2007.

Data analysis was based on the data of these 462 persons who had completed the follow-up check up as of the end of October 2007. Cases were younger than

controls (19.87±3.11 vs. 21.31±3.55 years, $p<0.0001$) and more likely still at school (69.7% vs. 52.7%, p=0.0003). Both cases and controls were similar for life style and dietary behavior, although 34.4% of cases and 22.2% of controls had habits of exercise (p=0.013). Analysis for health history showed that cases were more prevalent than controls for diabetics, hypertension, kidney illness, and gout.

The average blood pressures were higher in cases than in controls with greater differences in males (systolic blood pressure [SBP]: 121.1±17.94 vs. 110.9±9.89 mmHg, p=0.0001; diastolic blood pressure [DBP]: 79.2±15.0 vs. 70.1±9.90 mmHg, $p<0.0001$) than in females (DBP: 67.7±12.2 vs. 60.3±10.7 mmHg, p=0.0006). We also found a higher average BMI, waist circumference, and waist to hip ratio (WHR) in cases than in controls. There were no significant differences in averages between cases and controls for most items in the blood examination. But, cases did have higher average values than controls in high density lipoprotein cholesterol (HDL) (48.52±10.28 vs. 51.45±10.07, p=0.0003) and insulin (8.37±9.34 vs. 6.44±6.57μU/mL, p=0.0067). The average values in urinary examinations were higher in cases than in controls and significant for the albumin excretion (56.1±233.1 vs.34.2±175.2 mg/g, p=0.046).

The ultrasound measurements for the common carotid artery showed that cases had higher average RCCA (0.524±0.072 vs. 0.433±0.043 mm, $p<0.0001$) and LCCA (0.527±0.073 vs. 0.431±0.053 mm, $p<0.0001$) than controls. Among results of analysis in pulse wave velocity (PWV), there was no significant difference between cases and controls in the average of heart-carotid

PWV (hcPWV), heart-ankle PVW (haPWV), and ABI (ankle-brachial index). We found ≧20 years of age (OR=3.66), being boys (OR=3.73), with prehypertensive status, high total protein (OR=5.23), and high blood glucose (OR=4.95) were associated with high baPWV. Hypertensive children were 36.6 times more likely than controls to have an IMT at ≧75 percentile.

The above referred results were all derived from univariate analyses, with few multivariate analyses, attempting to identify potential factors associated with hypertension for the participants in years one and two follow-up study. We expect to have a larger sample size in year three of this study and to perform the analyses using stratification and multivariate models with more representative outcomes. As of the years one and two preliminary data, we were already able to identify obesity as an important anthropometry indicator associated with blood pressure for adolescent and young persons and adolescent hypertension was associated with atherosclerosis. With the years one and two experience, we will be able to recruit study subjects simultaneously in Taipei and Taichung areas in year three, and possibly in Taichung and Tainan area if instruments are available.

Baseline Data Study

In addition, we also conducted studies by analyzing the baseline data. This year, we have participated in two international conferences to present our findings. One poster presented at the 18th meeting of Asia-Pacific Society of Hypertension entitled "Risk of Hypertension among Children with Urinary Screening Positive for Proteinuria, Glucosuria, and Hematuria" in November 2007, Beijing, China. The other poster entitled "Body Mass Index, Cholesterol, and Hypertension among School Children in Taiwan: Results of National Mass

Urine Screening Program" was presented at the 18th WONCA World Conference (World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians, WONCA), in July 2007, Singapore. The latter article was presented by the doctoral student with this study. Both posters are attached as appendixes I and Ⅱ.

We also completed a manuscript developed from the baseline screening data, entitled "Childhood hypertension in association with obesity and hyperlipidemia in the mass urine screening in Taiwan". This article has been submitted to a prestigious journal.

貳、96年度計畫著作一覽表

Journal

序號	計畫產出名稱	產出型式	Impact factor	致謝對象
1	Chien-Chang Liao, Ta-Chen Su, Kuo-Liong Chien, Chu-Ko Wang, Chuan-Chi Chiang, Chau-Ching Lin, Ruey S Lin, Yuan-Teh Lee, Fung-Chang Sung Childhood hypertension in association with obesity and hyperlipidemia in the mass urine screening in Taiwan. 2007; (SCI) Submitted	Domestic		NHRI

Patent

序號	計畫產出名稱
	無

Book

序號	計畫產出名稱
	無

Conference Paper

序號	計畫產出名稱
1	少年高血壓危險因子及後續影響 2007

Technical Report

序號	計畫產出名稱
	無

參、96年度計畫重要研究成果產出統計表

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

（係指執行96年度計畫之所有研究產出結果）

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〔註〕：

期刊論文：指在學術性期刊上刊登之文章，其本文部份一般包含引言、方法、結果、及討論，並且一定有參考文獻部份，未在學術性期刊上刊登之文章（研究報告等）與博士或碩士論文，則不包括在內。

研討會論文：指參加學術性會議所發表之論文，且尚未在學術性期刊上發表者。

專　　著：為對某項學術進行專門性探討之純學術性作品。

技術報告：指從事某項技術之創新、設計及製程等研究發展活動所獲致的技術性報告且未公開發表者。

技術移轉：指技術由某個單位被另一個單位所擁有的過程。我國目前之技術轉移包括下列三項：一、技術輸入。二、技術輸出。三、技術擴散。

技術輸入：藉僑外投資、與外國技術合作、投資國外高科技事業等方式取得先進之技術引進國內者。

技術輸出：指直接供應國外買主具生產能力之應用技術、設計、顧問服務及專利等。我國技術輸出方包括整廠輸出、對外投資、對外技術合作及顧問服務等四種。

技術擴散：指政府引導式的技術移轉方式，即由財團法人、國營事業或政府研究機構將其開發之技術擴散至民間企業之一種單向移轉（政府移轉民間）。

技術創新：指研究執行中產生的技術，且有詳實技術資料文件者。

技術服務：凡有關各項研究計畫之規劃與評審、技術督察與指導及專業技術服務事項等。

肆、96年度計畫重要研究成果

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

計畫之新發現、新發明或對學術界、產業界具衝擊性(impact)之研究成果，請依性質勾選下列項目。

☐1. 研發或改良國人重要疾病及癌症的早期診斷方式及治療技術

☐2. 發展新的臨床治療方式

☐3. 發展新生物製劑、篩檢試劑及新藥品

☐4. 瞭解常見疾病及癌症之分子遺傳機轉

☐5. 瞭解抗癌藥劑對癌細胞之作用機制

☑6. 提供有效的疾病預防策略

☐7. 利用生物統計與生物資訊研究，推動台灣生技醫藥研究，促進生物技術與基因體醫學之發展

☐8. 醫療保健政策相關研究

☐9. 瞭解環境毒理機制及重金屬對人體健康的影響

☐10. 研發適合臨床使用的人造器官及生醫材料

☐11. 縮短復健流程並增加復健效果的醫療輔助方式或器材之研究應用

☐12. 改進現有醫療器材的功能或增加檢驗影像的解析能力

☑13. 其他重要疾病或醫藥衛生問題研究

解析青少年高血壓相關因子

96 年計畫重要研究成果

一、計畫之新發現、新發明或對學術界、產業界具衝擊性（impact）之研究成果，請敘述其執行情形。

這是三年計畫的第二年收案，到年底可完成約 500 名樣本。根據截止今年 10 月底的資料分析，我們已經可以很清楚看出青少年的高血壓和動脈粥樣硬化、肥胖等有關，以腰圍或腰臀比計算的相關最精準，這是國內較完整的青少年相關記載。這些資料亦顯示粥樣硬化現象即可在青少年時期出現，是過去未曾報告過的發現。相信本計畫將可為心血管疾病防治研究及政策決定之依據。

二、計畫對民眾具教育宣導之研究成果（此部份將為規劃對一般民眾教育或宣導研究成果之依據，請以淺顯易懂之文字簡述研究成果，內容以不超過 300 字為原則）

目前雖有初步成果，但由於樣本仍在收案，數值持續變動，不宜做此宣示。第三年資料夠多時則有可能。

三、簡述年度計畫成果之討論與結論，如有技術移轉、技術推廣或業界合作，請概述情形及成效

本年度除了可完成 500 個案調查，已完成二次國際研討會壁報論文報告。另外完成一篇基線資料論文稿投到 SCI 期刊。本計畫的執行雖需有許多人力支援，但相當順利。

四、成效評估（技術面、經濟面、社會面、整合綜效）

真正成效有待整個計畫完成才能評估得較精準，但至少已經達成（一）所述的成果。

五、下年度工作構想及重點之妥適性

我們在下年度將會使個案收集面由台北及台中地區逐漸南移至南部地區。利用第一年及第二年所建立之模式，健康檢查部分可分區執行，但血液及尿液等檢體分析宜以由第一年團隊人員執行，以免產生人為及儀器偏差。

六、檢討與展望

由於第二年度在台中收案的執行起點稍晚，取樣點分散，加上研究對象遷居多，地址和電話不適用，增加聯絡所耗之人力及時間。我們預期第三年將收集面擴大時會有類似型情發生，但依據第一年及第二年之經驗，我們仍有信心邀得青少年參加本研究追蹤，希望在台灣北、中、南收案使我們預期可達成夠代表性的資料。

伍、96年度計畫所培訓之研究人員

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

種類				人數	備註
專任人員	1.	博士後研究人員	訓練中	0	
			已結訓	0	
	2.	碩士級研究人員	訓練中	2	
			已結訓	0	
	3.	學士級研究人員	訓練中	1	
			已結訓	0	
	4.	其他	訓練中	0	
			已結訓	0	
兼任人員	1.	博士班研究生	訓練中	1	
			已結訓	0	
	2.	碩士班研究生	訓練中	1	
			已結訓	0	
醫師			訓練中	0	
			已結訓	0	

特殊訓練課程（請於備註欄說明所訓練課程名稱）

陸、參與96年度計畫所有人力之職級分析

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

職級	所含職級類別	參與人次
第一級	研究員、教授、主治醫師	10 人
第二級	副研究員、副教授、總醫師、助教授	0 人
第三級	助理研究員、講師、住院醫師	0 人
第四級	研究助理、助教、實習醫師	4 人
第五級	技術人員	2 人
第六級	支援人員	3 人
合計		19 人

〔註〕：

第一級：研究員、教授、主治醫師、簡任技正，若非以上職稱則相當於博士滿三年、碩士滿六年、或學士滿九年之研究經驗者。

第二級：副研究員、副教授、助研究員、助教授、總醫師、薦任技正，若非以上職稱則相當於博士、碩士滿三年、學士滿六年以上之研究經驗者。

第三級：助理研究員、講師、住院醫師、技士，若非以上職稱則相當於碩士、或學士滿三年以上之研究經驗者。

第四級：研究助理、助教、實習醫師，若非以上職稱則相當於學士、或專科滿三年以上之研究經驗者。

第五級：指目前在研究人員之監督下從事與研究發展有關之技術性工作，且具備下列資格之一者屬之：具初（國）中、高中（職）、大專以上畢業者，或專科畢業目前從事研究發展，經驗未滿三年者。

第六級：指在研究發展執行部門參與研究發展有關之事務性及雜項工作者，如人事、會計、秘書、事務人員及維修、機電人員等。

柒、參與96年度計畫所有人力之學歷分析

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

類別	學　歷　別	參與人次
1	博士	8 人
2	碩士	4 人
3	學士	3 人
4	專科	0 人
5	博士班研究生	1 人
6	碩士班研究生	2 人
7	其他	1 人
合計		19 人

捌、參與96年度計畫所有協同合作之研究室

註：群體/中心計畫者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

機構	研究室名稱	研究室負責人
中國醫藥大學環境醫學研究所	宋鴻樟教授辦公室	宋鴻樟教授
中國醫藥大學附設醫院家醫科		劉秋松主任、林文元醫師
台大醫院小兒科		王主科教授

台大醫院內科		李源德教授、許秀卿博士、蘇大成助理教授
台大醫院	醫學檢驗部	
台大公共衛生學院		林瑞雄教授、簡國龍副教授
陽明大學		周碧瑟教授

玖、九十六年度計畫執行情形

註：群體計畫(PPG)者，不論是否提出各子計畫資料，都必須提出總計畫整合之資料

一、請簡述原計畫書中，九十六年預計達成之研究內容

本計畫為三年計畫，期盼在這期間達成下述目標：

1.建置執行本研究和資料收集方式。

2.從小學生尿液篩檢結果建立高血壓孩童與正常血壓孩童(對照)的世代。

3.利用問卷訪視與健檢的方式，進行高血壓孩童族群與對照族群的比較，以探討孩童高血壓之可能相關因子。

4.評估病人遵醫囑的情形，包括臨床診斷過程、用藥情況及其他等。

5.在 3 年的研究期間觀察任何短期的不良反應。

6.評估高血壓青少年的共病問題。

7.比較有無共生疾病孩童的血液/尿液生化值及生活型態之差異。

由於這是三年連續性計畫，病例組和對照組需持續邀請青少年參加，才做最後的評估，並未分年做研究內容的分配。但其中建立研究、操作及資料收集程序，和建立經由尿液檢鑑知的高血壓和正常血壓組成追蹤組二項，為第一年的任務，已經完成並開始個案調查，收集資料；其餘五項是整個計畫需要達成的，均為問卷及追蹤檢查的項目。我們另外嘗試將 1992-2000 年間的基本資料加以整理並分析，探究尿液篩檢初期的高血壓問題及相關因子。本計畫的資料收集除了以問卷收集人口、社經、生活型態、健康史資料之外，主要還是執行一系列的健康檢查，原訂即有 30 項。我們後來增加了用兩種儀器做血管彈性檢查。

二、請詳述九十六年度計畫執行情形，並評估是否已達到原預期目標（請註明達成率）

本年度已清理中小學尿液篩檢資料，將預計達成工作的第一、二項。第三、六、七項的目標，以目前分析的資料已經看出，若明年的收案過程順利，這三項目標應可達成。其他兩項目標目前有短期不良反應的現象尚未見，可能要在本三年計畫完成後或更久，才可進行更明確評估。但參與本計畫的醫師在追蹤時均給予青少年健康教育，以預防有害因子。本研究計畫到今年十月底的收案數為 462 位，但相關青少年高血壓危險因子的分析已可看出相當重要的未曾報導過的發現。除了 BMI 和高血壓的相關，更重要的是我們發現高血壓前期的孩子有血管彈性的變化及頸動脈粥樣化的現象。預計到今年底應可達成 500 位追蹤個案，寒假期間可再加強。我們有信心明年同時在中、南部進行收案工作，樣本數再大些時，會呈現更多獨特顯著結果。

此外，我們做了一些基線資料分析。完成了兩個國際研討會論文發表。一個是本計畫主持人參加在中國北京舉行的第 6 屆亞太高血壓年會，報告 "Risk of Hypertension among Children with Urinary Screening Positive for Proteinuria, Glucosuria, and Hematuria"。另一個是由參加本計畫的博士班研究生出席在 2007 年七月在新加坡舉行的世界家庭醫師研討會，以口頭報告 "Body Mass Index, Cholesterol, and Hypertension among School Children in Taiwan: Results of National Mass Urine Screening Program"。這兩篇摘要分別附在附錄一和二。

另外我們完成了一篇期刊論文「Childhood hypertension in association with obesity and hyperlipidemia in the mass urine screening in Taiwan」投稿到 SCI 期刊。

拾、附錄

一、研討會論文 poster

二、研討會論文

三、第二年度資料分析報告

附錄一、研討會論文 poster

(I) 2007 年 11 月中國北京第 6 屆亞太高血壓年會

Risk of Hypertension among Children with Urinary Screening Positive for Proteinuria, Glucosuria, and Hematuria

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Objective

An annual mass urine screening for proteinuria, glucosuria, and hematuria among approximately 3 million school children 6-18 years of age was conducted in 1992-2000. The authors compared the hypertension risk among the three types of screening positive students.

Methods

Children with consecutive urinary screening positive received the third screening including examinations of blood pressure and lipid, etc. Present study subjects were 103,840 children with known blood pressure conditions after excluding data with no identification (n=63,800) and no blood pressure measures (n=24,561). Hypertension was classified by age established by the 1987 US Task Force.

Results

The prevalence of hypertension was 5.58 per 100 among all urine screened positive children. Compared with children with hematuria, children at higher risk of hypertension were those with proteinuria (odds ratio [OR]=1.16, 95% confidence interval [CI]=1.08-1.26) or with glucosuria (OR=4.27, 95%CI=3.29-5.54). The multivariate logistic regression analyses showed that body mass index (BMI) had strong inverse association with hypertension in all three types of urine test positive children. Compared with children with BMI less than 18 kg/m2, students with BMI of 27 kg/m2 and above had the ORs increased to 13.7 for glucosuria positive students, 6.89 for hematuria positive students and 6.22 for proteinuria positive students. Associations also were inversed for cholesterol and blood urine nitrogen levels among proteinuria positive students.

Table 1 Risk of hypertension in the multivariate logistic regression

	Proteinuria N=6,676 OR (95%CI)	Glucosuria N=358 OR (95%CI)	Hematuria N=4,542 OR (95%CI)
Sex			
Female	Reference	Reference	Reference
Male	0.98 (0.88-1.09)	0.45 (0.24-0.82)	0.88 (0.76-1.01)
Grade, years			
≤3	Reference	Reference	Reference
4-6	0.86 (0.73-1.01)	1.10 (0.39-3.15)	0.75 (0.63-0.89)
7-9	0.77 (0.66-0.89)	1.36 (0.51-3.73)	0.64 (0.54-0.75)
10-12	0.57 (0.44-0.74)	1.13 (0.32-3.99)	0.39 (0.27-0.56)
BMI, kg/m²			
BMI<18	Reference	Reference	Reference
18≤ BMI<24	1.45 (1.30-1.63)	4.01 (1.61-9.98)	1.51 (1.41-1.85)
24≤ BMI<27	3.11 (2.44-3.98)	7.12 (2.41-21.0)	2.95 (2.29-3.81)
BMI ≥27	6.22 (4.86-7.97)	13.7 (5.32-35.1)	6.89 (5.06-9.39)
Cholesterol, mg/dL			
<200	Reference	Reference	Reference
200-249	1.25 (1.06-1.47)	2.01 (1.04-3.88)	1.13 (0.93-1.38)
≥250	2.20 (1.64-2.97)	2.01 (0.77-5.300	1.36 (0.75-2.49)
Albumin, g/dL			
<4.5	Reference	Reference	Reference
4.5-4.9	1.10 (0.99-1.23)	0.78 (0.40-1.52)	1.25 (1.08-1.40)
≥5.0	1.14 (0.92-1.430	1.25 (0.31-4.98)	1.41 (1.08-1.85)
BUN, mg/dL			
<23	Reference	Reference	Reference
≥23	2.16 (1.39-3.35)	0.22 (0.05-0.94)	1.26 (0.57-2.78)
Creatinine, mg/dL			
<1.3	Reference	Reference	Reference
≥1.3	0.99 (0.87-1.14)	1.69 (0.81-3.52)	1.05 (0.89-1.29)

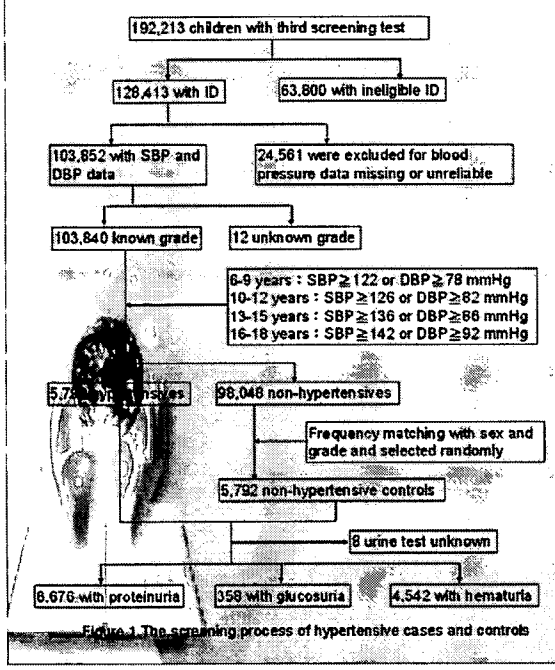

Figure 1.The screening process of hypertensive cases and controls

Table 2.Risk of hypertension in the multivariate logistic regression

	OR (95%CI)
Sex	
Female	Reference
Male	0.97 (0.90-1.05)
Grade, years	
≤3	Reference
4-6	0.97 (0.87-1.08)
7-9	0.98 (0.87-1.05)
10-12	0.90 (0.75-1.07)
BMI, kg/m²	
BMI<18	Reference
18≤ BMI<24	1.53 (1.40-1.67)
24≤ BMI<27	3.06 (2.58-3.63)
BMI ≥27	6.60 (5.48-7.96)
Urine Test	
Hematuria	Reference
Proteinuria	1.16 (1.08-1.26)
Glucosuria	4.27 (3.29-5.54)

Conclusion

Obesity is the strongest risk factor associated with hypertension for students with positive tests of proteinuria, glucosuria and even hematuria.

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附錄二、 研討會論文

(Ⅰ) 2007 年 11 月中國北京第 6 屆亞太高血壓年會

INTRODUCTION

An annual mass urine screening for proteinuria, glucosuria, and hematuria among approximately 3 million school children 6-18 years of age was conducted in 1992-2000. The authors compared the hypertension risk among the three types of screening positive students.

METHODS and MATERIALS

Subjects were 103,840 children with known blood pressure conditions after excluding data with no identification (n=63,800) and no blood pressure measures (n=24,561). Hypertension was classified by age established by the 1987 US Task Force.

RESULTS

The prevalence of hypertension was 5.58 per 100 among all screened children. Compared with children with hematuria, children at higher risk of hypertension were those with proteinuria (odds ratio [OR]=1.16, 95% confidence interval [CI]=1.08-1.26) or with glucosuria (OR=4.27, 95%CI=3.29-5.54). The multivariate logistic regression analyses showed that body mass index (BMI) had strong inverse association with hypertension in all three types of urine test positive children. Compared with children with BMI less than 18 kg/m^2, students with BMI of 27 kg/m^2 and above had the ORs increased to 13.7 for glucosuria positive students, 6.89 for hematuria positive students and 6.22 for proteinuria positive students. Associations also were inverse for cholesterol and blood urine nitrogen levels among proteinuria positive students.

CONCLUSIONS

Obesity may increase the risk of hypertension for students with positive test for proteinuria, glucosuria and even hematuria.

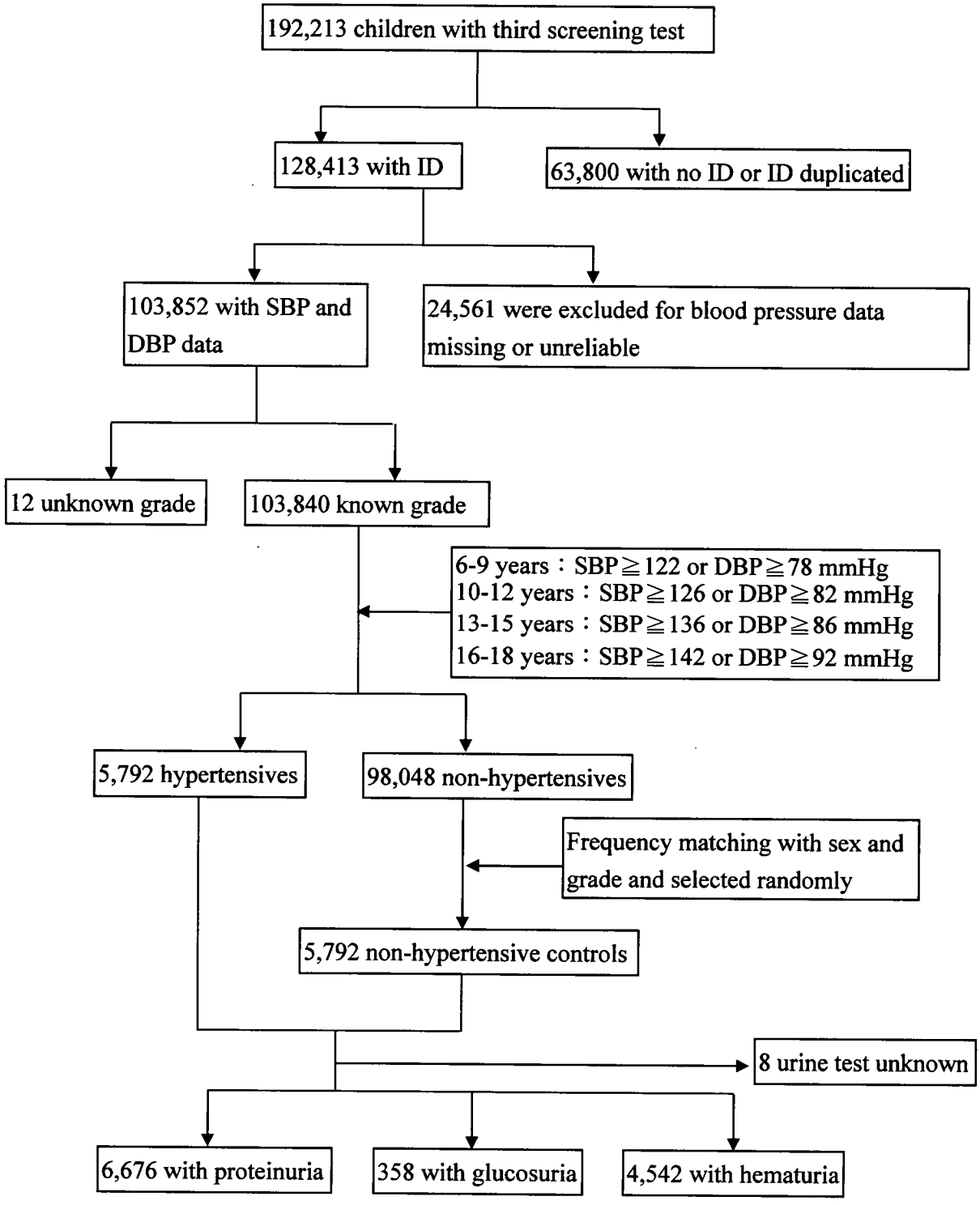

Figure 1.The screening process of hypertensive cases and controls

Table 1.Risk of hypertension in the multivariate logistic regression

	Proteinuria N=6,676	Glucosuria N=358	Hematuria N=4,542
	OR (95%CI)	OR (95%CI)	OR (95%CI)
Sex			
Female	Reference	Reference	Reference
Male	0.98 (0.88-1.09)	0.45 (0.24-0.82)	0.88 (0.76-1.01)
Grade, years			
≦3	Reference	Reference	Reference
4-6	0.86 (0.73-1.01)	1.10 (0.39-3.15)	0.75 (0.63-0.89)
7-9	0.77 (0.66-0.89)	1.38 (0.51-3.73)	0.64 (0.54-0.75)
10-12	0.57 (0.44-0.74)	1.13 (0.32-3.99)	0.39 (0.27-0.56)
BMI, kg/m^3			
BMI＜18	Reference	Reference	Reference
18≦ BMI＜24	1.45 (1.30-1.63)	4.01 (1.61-9.98)	1.61 (1.41-1.85)
24≦ BMI＜27	3.11 (2.44-3.98)	7.12 (2.41-21.0)	2.95 (2.29-3.81)
BMI ≧27	6.22 (4.86-7.97)	13.7 (5.32-35.1)	6.89 (5.05-9.39)
Cholesterol, mg/dL			
＜200	Reference	Reference	Reference
200-249	1.25 (1.06-1.47)	2.01 (1.04-3.88)	1.13 (0.93-1.38)
≧250	2.20 (1.64-2.97)	2.01 (0.77-5.300	1.36 (0.75-2.49)
Albumin, g/dL			
＜4.5	Reference	Reference	Reference
4.5-4.9	1.10 (0.99-1.23)	0.78 (0.40-1.52)	1.23 (1.08-1.40)
≧5.0	1.14 (0.92-1.430	1.25 (0.31-4.96)	1.41 (1.08-1.85)
BUN, mg/dL			
＜23	Reference	Reference	Reference
≧23	2.16 (1.39-3.35)	0.22 (0.05-0.94)	1.26 (0.57-2.78)
Creatinine, mg/dL			
＜1.3	Reference	Reference	Reference
≧1.3	0.99 (0.87-1.14)	1.69 (0.81-3.52)	1.05 (0.86-1.29)

Risk of hypertension in the multivariate logistic regression

	OR (95%CI)
Sex	
Female	Reference
Male	0.97 (0.90-1.05)
Grade, years	
≦3	Reference
4-6	0.97 (0.87-1.08)
7-9	0.96 (0.87-1.05)
10-12	0.90 (0.75-1.07)
Urine test	
Hematuria	Reference
Proteinuria	1.16 (1.08-1.26)
Glucosuria	4.27 (3.29-5.54)

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Body Mass Index, Cholesterol, and Hypertension among School Children in Taiwan: Results of National Mass Urine Screening Program

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Background: This study investigated factors associated with the childhood hypertension among students with urinary screening positive hematuria, proteinuria or glucosuria in Taiwan. **Methods:** Between 1992 and 2000, a national wide mass urine screening program for hematuria, proteinuria, and glucosuria was conducted annually for approximately 3,000,000 students aged 6-18 years. About 103,756 school children found to be two times positive of proteinuria, glucosuria, and/or hematuria, and consequently receiving a third urine screening test and a health check-up for blood pressure and blood biochemistry measures. **Results:** Among 103,756 students, 42793 were hematuria, 58060 were proteinuria, and 1573 were glucosuria. The prevalence of hypertension increased as body mass index (BMI) ($p<0.0001$) and as cholesterol ($p<0.0001$) increased. Students with glucosuria positive and at BMI $\geqq 27$ mg/dL had a highest prevalence of hypertension (32.25%). The multivariate logistic regression analysis revealed that hypertension had much stronger association with BMI than with cholesterol with a significant dose-response relationship particularly among students with glucosuria. Among students with glucosuria, the odds ratio (OR) of hypertension was 11.8 (95% CI=6.40-21.8) for those with BMI $\geqq 27$ kg/m^2 compared with those with BMI < 18 kg/m^2 in the multivariate logistic regression. There was also significant dose-response relationship between hypertension and BMI among students with hematuria or proteinuria, but with smaller odds ratio. **Conclusion:** Our findings show that the childhood hypertension has a strong association with BMI among students with urine screening positive.

Table 1. The characteristics of school children with hematuria, proteinuria, and glucosuria

	Grade, years				Total
	1-3	4-6	7-9	10-12	
Boys	N=5,585	N= 8,595	N= 18,987	N=5,691	N=38,858
Hypertension, n (%)†	*457 (8.18)	432 (5.03)	*1306 (6.88)	*195 (3.43)	*2390 (6.15)
Hematuria, %	51.17	37.85	19.09	17.40	27.60
Proteinuria (light), %	24.73	34.01	49.54	49.04	42.47
Proteinuria (moderate), %	14.32	17.39	19.04	17.61	17.79
Proteinuria (heavy), %	8.56	9.35	10.71	12.97	10.43
Glucosuria, %	1.22	1.40	1.62	2.99	1.71
All, %	100	100	100	100	100
Girls	N=11,012	N=20,366	N=25,946	N=7,574	N=64,898
Hypertension, n (%)†	712 (6.47)	1035 (5.08)	1527 (5.89)	124 (1.64)	3398 (5.24)
Hematuria, %	54.63	44.07	51.10	57.41	50.23
Proteinuria (light), %	24.39	28.72	24.99	20.78	25.57
Proteinuria (moderate), %	14.20	18.64	15.07	12.07	15.69
Proteinuria (heavy), %	5.90	7.26	7.31	7.39	7.06
Glucosuria, %	0.87	1.31	1.53	2.35	1.44
All, %	100	100	100	100	100

*$p < 0.0001$ for Chi-square test compared with girls

†$p < 0.0001$ for Chi-square test between grade

Table 2. Hypertension prevalence (%) between body mass index and cholesterol among school children with hematuria, proteinuria, and glucosuria

	Hematuria	Light Proteinuria	Moderate Proteinuria	Heavy Proteinuria	Glucosuria
	N=42,793	N=32,657	N=16,878	N=8,525	N=1,573
BMI, kg/m^3	Cases (%)	Cases (%)	Cases (%)	Cases (%)	Cases (%)
BMI<18	666 (3.67)	622 (4.18)	322 (3.96)	214 (5.38)	15 (4.63)
18≦BMI<24	1028 (4.89)	826 (5.32)	422 (5.45)	277 (7.15)	50 (10.4)
24≦BMI<27	196 (8.68)	132 (10.9)	54 (9.71)	58 (16.3)	43 (17.3)
BMI≧27	222 (16.2)	226 (21.2)	112 (24.7)	62 (19.5)	168 (32.3)
p for trend	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Cholesterol, mg/dL					
<200	1833 (4.79)	1566 (5.30)	749 (5.01)	425 (6.15)	115 (12.3)
200-249	255 (5.85)	199 (6.85)	134 (8.14)	97 (9.36)	123 (25.6)
250-299	24 (6.59)	32 (11.0)	24 (10.1)	31 (12.1)	34 (24.5)
≧300	3 (5.36)	9 (15.3)	11 (15.3)	64 (16.6)	10 (22.7)
p for trend	0.0010	<0.0001	<0.0001	<0.0001	<0.0001

Table 3. Risk of hypertension for body mass index and cholesterol among school children with hematuria, proteinuria, and glucosuria in the multivariate logistic regression analysis‡

	Hematuria	Low Proteinuria	Moderate Proteinuria	Heavy Proteinuria	Glucosuria
	N=42,793	N=32,657	N=16,878	N=8,525	N=1,573
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
BMI, kg/m^3					
BMI<18	Reference	Reference	Reference	Reference	Reference
18≦BMI<24	1.80 (1.62-2.01)	1.60 (1.43-1.80)	1.70 (1.45-1.99)	1.57 (1.29-1.92)	2.79 (1.48-5.24)
24≦BMI<27	3.37 (2.83-4.00)	3.55 (2.88-4.36)	3.00 (2.18-4.11)	3.92 (2.82-5.45)	5.13 (2.62-10.0)
BMI≧27	7.17 (6.02-8.53)	8.33 (6.94-10.0)	10.3 (7.94-13.3)	5.02 (3.59-7.02)	11.8 (6.40-21.8)
p for trend	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Cholesterol, mg/dL					
<200	Reference	Reference	Reference	Reference	Reference
200-249	1.08 (0.94-1.24)	1.11 (0.94-1.30)	1.54 (1.27-1.88)	1.35 (1.06-1.72)	2.23 (1.64-3.04)
250-299	1.23 (0.81-1.89)	1.63 (1.10-2.41)	1.81 (1.16-2.81)	1.78 (1.19-2.66)	2.06 (1.28-3.33)
≧300	1.02 (0.31-3.34)	2.56 (1.21-5.42)	2.89 (1.46-5.71)	2.33 (1.69-3.21)	2.03 (0.90-4.60)
p trend	0.1407	0.0001	<0.0001	<0.0001	<0.0001

‡Adjusted for sex, grade, albumin, creatinine, blood urea nitrogen, C3 complement, and Antistreptolysin O

BMI=body mass index

附錄三、第二年度資料分析報告

少年高血壓危險因子及後續影響

第二年資料分析結果

壹、前言

2003 年高血壓仍為國人第十大死因後，台灣每年約有 1800 人死於高血壓。但仔細分析國人的十大死因，排名第三位的心臟病及第二位的中風皆與高血壓有很強的相關；與正常血壓相較，有高血壓的人的中風勝算比高達 9.0，心臟病危險也有 2.8 倍[R1, R18]。另外第四位的糖尿病及第八位的腎臟病也往往是高血壓的共生病。相對於癌症是多部位的疾病；因此，就單一死因而言，把高血壓視為國人的相關第一死因一點也不為過[R2]。有關心血管疾病的探討越多，對粥狀硬化衍生中風和心臟病的機制就更清楚，高血壓即是造成粥樣硬化的重要原因之一[R3]。研究也指出，成人的高血壓源於青少年時期[R4, R19]。

高血壓是台灣的重要健康問題，影響著 40%的老年人口且一直被衛生單位視為中老年人疾病防治的主要項目，衛生當局也積極於此。但鑑於青少年中風病例逐漸增加，顯示兒科高血壓也不容忽視，需先期預防，並界定相關危險因子。

更重要的是青少年的中風和成年人的型態不相同，醫療費用也相差很大。我們曾分析 1996-2003 年健保資料，發現青少年多出血性中風，成年人則相反。出血性中風尤其是蜘蛛網膜下腔出血(subarachnoid hemorrhage)的第一次住院平均費用約為 198,000 元，比

ischemic stroke(平均 50,500 元)約為 4 倍貴，比 transient cerebral ischemia(平均 16,000 元)更達 12 倍之多。由於青少年多出血性，因此 10 歲以下小孩的平均費用(114,000 元)比成人(61,600 元)貴約 5 萬元以上[R30]. 更應探討青少年高血壓的問題，雖然青少年的中風危險因子有更多先天問題，高血壓的角色更應釐清。

肥胖是高血壓的重要危險因子，相較於不胖的孩子，胖的孩子會有高血壓的危險，Chu et al. [R5] 發現男孩是 2.7 倍，女孩是 3.5 倍，高膽固醇的危險也分別為 2.5 和 1.4 倍。隨著飲食型態的西化、運動量不足及久坐的習慣增加等，台灣兒童及青少年肥胖的盛行率也有逐年增加的趨勢[R5, R6]。文獻指出台北市學童(12-15 歲)肥胖盛行率從 1982 年的 10.1%，上升至 1988 年及 1996 年的 11.1%[R6]，而根據較新的研究，2002 年台灣地區 6-18 歲兒童及青少年肥胖盛行率高達 16.8%(男性：18.5%，女性：15.0%)[R1]。相較於西方國家，兒童與青少年的肥胖盛行率也有逐年增加的趨勢[R7]。1999-2000 的美國健康與營養調查(National Health and Nutrition Examination Survey, NHANES)顯示 6-11 歲的孩童肥胖盛行率為 15%[R8]，2003 年美國紐約市國小學童肥胖盛行率有 24%，加拿大 7-13 歲兒童肥胖盛行率也從 1981 年的 5%升高到 1996 年男孩的 17%及女孩的 15%，快速增加了 3 倍[R9]。

隨著學童肥胖盛行率增加，高血壓病患也有年輕化的趨勢[R4, R10]。美國分別在 1988-1994 及 1999-2000 年[R8]做過兩次的國家衛生調查(NHANES)，發現 8-17 歲學童的平均收縮壓經過年齡、性別及種族校正之後升高了 1.4 mmHg(95%可信限為 0.6-2.2 mmHg)，而舒張壓也升高了 3.3 mmHg(95%可信限為 2.1-4.5 mmHg)。而根據 2002 年的調查，美國休斯頓 10-19 歲學童高血壓盛行率高達 4.5%[R10, R11]。因此我們相信兒童及青少年高血壓與肥胖有一定的關係，但不限於此。例如 Lin et al.[R12]研究 136 位次發性高血壓孩子，主動脈狹窄(coarctation of aorta)和全身性紅班狼瘡(systemic lupus)是高血壓的主因，具高死亡危險。

過去的研究也曾經指出高血壓與很多因子相關，如：身體質量指數(body mass index, BMI)、總膽固醇、高密度膽固醇、低密度膽固醇及肌酸酐等。預防措施應直接針對兒童及青少年族群，尤其是高危險的兒童族群。而找出危險因子更是當務之急。有關青少年高血壓的研究國內並不多見。

財團法人中華民國衛生保健基金會(The Chinese Foundation of Health, CFH)在 1992-2000 年間曾進行台灣省中小學生尿液篩檢，檢測尿蛋白、尿糖和潛血。連續陽性兩次以上的孩子，在第三次時進行較詳細的檢查，包括身高、體重等人體量測學檢查、血壓量測及血液

生化分析等。因此檢測出 12630 名學生有高血壓的傾向。這些孩子多數是原發性高血壓(essential hypertension)和少數次發性高血壓(secondary hypertension)，後者有較高的生命危害。前者的心血管疾病危害較緩和，但仍須密切注意其發展，並做適當防治工作。

本研究利用這些的台灣省中小學學童尿液篩檢資料，依照高血壓標準分類，進行青少年高血壓追蹤，目的在探討兒童及青少年高血壓的危險因子以及青少年高血壓的後續影響，以提供疾病預防之參考。

貳、研究方法

一、研究對象、資料收集及檢測

中華衛生保健基金會於 1992 至 1999 年期間，每學期實施一次全國性的尿液篩檢，對象為台灣省中小學(國小 1 年級至高中三年級)的學生。1992 年每學期有 2,615,207 人接受篩檢，1993 年之後每學期約有 2,932,000 左右接受篩檢[R13, R14]。結果有 128,413 位學生至少有二次尿液檢查呈陽性反應(圖一)。基金會針對這些兩次蛋白尿、尿糖或潛血陽性反應的學生再進行的一次做較詳細的理學、血液及尿液檢查，包括血壓及生化檢測。

經排除不正確的血壓及年級的資料或缺失值後，以美國心臟學會的標準[R15]對不同年齡的血壓分級(如下表)，在 103,840 位學生中辨識出 5,792 人有高血壓。我們經由衛生署死亡資料檔(至 2004 年 4 月)剔除部分資料，再將姓名、地址或電話資料不全的學生排除，最後滿足條件的高血壓學生有 3,418 位。在 103,840 位學生中，有 98,048 位不具高血壓，其中住在台北縣的 5,384 位無高血壓對照組為本研究第二年的少年高血壓追蹤對象。我們在第二年加上台中地區的個案進行追蹤。

Age	SBP (mmHg)		DBP(mmHg)
6-9	≧122	或	≧78
10-12	≧126	或	≧82
13-15	≧136	或	≧86
16-18	≧142	或	≧92

首先我們將少年高血壓追蹤檢查的邀請函依照學生資料上的地址寄出，在邀請函寄出三天後，經過訓練的研究助理及臨時工依照資料上的電話號碼撥打，以確認學生或其家長是否收到邀請函。若學生沒到邀請函，我們經過詢問學生或其父母正確地址後補寄邀請函，同時並進行少年高血壓追蹤檢查的電話問卷訪問及邀請。受訪者若願意參加少年高血壓追蹤檢查，我們即安排時間進行檢查。青少年接受檢查後的兩星期內，我們以電話與青少年約定時間，請他們回來醫院由醫師向青少年解釋檢驗報告內容，並將報告提供受檢者。在青少年回院為他們說明檢驗結果的同時，我們除了邀請原先篩檢時無高血壓的同學做為對照進行追蹤，也請這些青少年邀請同儕來醫院做少年高血壓檢查，作為本研究的另一項對照，年齡差距不超過兩歲。

在諮詢專家及兩位心臟科醫師進行各項檢查時，我們同時檢視少年心血管健康問卷。問卷內容包括人口社會經濟狀況資料、居家及工作環境、個人生活習慣、個人疾病史、父母親的生活習慣、父母疾病史及家族疾病史。人口學變項包括性別、年齡、身高、體重、出生體重、2-5 歲的體型、教育程度、職業、婚姻狀態、家庭收入、兄弟姊妹人數及排行等。居家工作環境包括住家附近是否有工廠、機場、機

車行、汽車修配場、平交道、中大型醫院、夜市和大型卡車經過等設施或建築物，以及住所居住年數、是否有噪音暴露、工作年數、是否有化學物質暴露等。個人生活習慣包括是否抽菸、喝酒、嚼檳榔、運動、吃素，飲食調查包括牛奶或乳酪、海鮮類、蔬菜、水果、甜食、飲料、硝酸製品、肥肉、速食、咖啡等攝取頻率。個人疾病史包括糖尿病、高血壓、腦中風、心絞痛、心肌梗塞、腎臟病、痛風、脊椎側彎等疾病。父母親資料包括年齡、身高、體重、教育程度、職業、是否抽菸、是否喝酒、是否嚼檳榔、運動習慣、是否為素食者等。父母疾病史及家族疾病史調查的疾病包括糖尿病、高血壓、腦中風、冠心病、腎臟病、痛風、癌症等。

本計畫的第二年，我們在國立台灣大學附設醫院進行少年高血壓追蹤檢查。另外在 2007 年 9 月開始，我們也在中國醫藥大學附設醫院進行中部地區少年高血壓追蹤檢查，對象是居住在台中市過去有尿液篩檢異常的學生，包括病例組(有高血壓)與對照組(無高血壓)，總計共 279 位高血壓病例，追蹤方式與在台大醫院進行的方式類似，至 2007 年 10 月，已有 13 位來醫院接受追蹤檢查，但受限於研究資源，無法進行頸動脈超音波的檢查。

我們先以信函向家長說明本計畫的目的和程序及功能等，接著以電話聯絡約定檢查時間。在檢查之前，我們會先向受檢者說明檢查的

內容及項目，再請受檢者填寫檢查同意書，之後再進行檢查。少年高血壓追蹤檢查的內容包括：理學檢查(包括身高、體重、腰圍及臀圍等)、生化檢查(空腹血液及尿液)、Dynapulse 血壓量測、頸動脈超音波及 colin 血管彈性等。

1.理學檢查：

包括身高、體重、腰圍、臀圍、收縮壓、舒張壓等。

2.尿液檢查：

尿液檢查包括總蛋白量(total protein, TP)、微白蛋白尿(microalbumine)、肌酸酐(creatinine, CRE)、白蛋白排出率(albumin excretion rates, AER)、鈉離子(Na^+)、鉀離子(K^+)、氯離子(Cl^-)、尿糖(urine glucose)、尿蛋白(urine protein)等檢查。

3.抽血檢查：

血液檢查項目包括白血球(white blood cell, WBC)、紅血球(red blood cell, RBC)、血色素(hemoglobin, HB)、血小板(platelet)、嗜中性球(neutrophil)、嗜酸性球(eosinophil, eosin)、嗜鹼性球(basophil, baso)、淋巴球(lymphocyte)、單核球(monocyte)、總膽固醇(total cholesterol, TCHO)、高密度膽固醇(high-density lipoproteins, HDL)、低密度膽固醇(low-density lipoproteins, LDL)、三酸甘油脂(triglyceride, TG)、鈉離子(Na^+)、鉀離子(K^+)、氯離子(Cl^-)、總蛋白量(total protein, TP)、白蛋

白(albumin)、球蛋白(globulin)、尿酸(uric acid, UA)、尿素氮(Blood urea nitrogen, BUN)、肌酸酐(creatinine)、glutamic-oxalacetic-transaminase(GOT)、alulamic-pyruvic-transaminase(GPT)、血糖(glucose)、胰島素(insulin)等。

4. Dynapulse 及血壓量測：

血壓是由Dynapulse(電腦血壓心脈儀)(Company: PMI，SanDiago)及水銀血壓計兩種工具測量取得。Dynapulse是使用一般量血壓的氣袋(Cuff)，把脈波信息經過放大、數字化，然後傳送到個人電腦去分析處理，並顯示脈波及血壓數值。當氣袋壓力超過縮收壓時，氣袋把動脈血管壓住，血液無法流過，脈波信息較小。當氣袋壓力逐漸減少，血液開始衝過氣袋壓住的血管部位，脈波信息隨血流之衝擊之增高而加大。Dynapulse的精確性（±2 mmHg）高於傳統的水銀柱血壓計與電子血壓計，並以非侵入性的方式，取得了近似心導管所測得完整脈動波形，有助於瞭解血壓在心臟血管疾病上的詳細作用機轉。而當氣袋內壓力再降低到舒張測得的縮收壓和舒張壓，以及相關的特有波形。受測者進入檢查室，平躺在檢查床上2分鐘後，開始進行測量血壓，測量以非慣用手為主。兩種工具均測量兩次，每次間隔至少2分鐘。

5.頸動脈超音波檢查：

頸動脈超音波所使用的儀器為 Sonosite Titan (Sonosite，Bothell, WA)，測量項目包括：總頸動脈(Common carotid artery, CCA)的平均厚度與最大厚度、內頸動脈(Internal carotid artery, ICA) 的平均厚度與最大厚度、頸動脈球體部動脈(bulb) 的平均厚度與最大厚度、頸動脈硬化塊分數(plaque score)、頸動脈血管內中皮層厚度(intima-mediate thickness, IMT)等。IMT 的評估根據 RCCA1(右頸動脈 0-1 cm 處的 IMT)、RCCA2(右頸動脈 1-2 cm 處的 IMT)、LCCA1(左頸動脈 0-1 cm 處的 IMT)、LCCA2 (左頸動脈 1-2 cm 處的 IMT)、RCCA (為 RCCA1 及 RCCA2 的平均值)及 LCCA (為 RCCA1 及 RCCA2 的平均值)。

6.Colin 血管彈性量測：

受測者進入檢查室後，以仰臥姿勢(supine)平躺在診察床上，五分鐘後進行量測。檢查室的溫度保持在 22-25˚C。檢查前預先讓受測者排尿。在測量前請受測者做 2-3 次深呼吸。受測者穿著厚重衣物時請其脫掉，只留一件薄衣，穿著襪子時請其脫下，或拖至露出後腳跟的程度。測量時間約 3 分鐘。第一次體驗下肢血壓測量時受測者容易緊張，我們先說明測量方法以緩和受測者的心情。測量前告知受測者請勿移動身體並暫時不要說話。若數值與波形產生左右極大差異時，必須判斷是自於受檢者本身生理狀況或是測量者技術的問題。再決定

是否需要從新測量。

二、資料處理及分析

我們將收集好的問卷資料及少年高血壓檢查資料輸入Excel軟體中，為確定電腦資料輸入無誤，每一變項都經過頻數分布(frequency distribution)檢查，檢視不合理的數值，有誤即加以校正。我們將過去中小學時代有高血壓及無高血壓的青少年分別視為病例組及對照組，進行病例對照研究。我們先以單變項分析比較病例和對照的異同。利用卡方檢定來分析問卷資料及少年高血壓檢查資料中的類別變項(categorical variable)，比較病例組與對照組之間各變項的分布差異。連續性的測值再依照臨床的標準分類，如SBP≧140 mmHg為高血壓、舒張壓≧90 mmHg為高血壓、BMI≧27 kg/m^2為肥胖、腰圍(男性≧90 cm，女性≧80 cm)為肥胖、腰臀比(男性≧0.9，女性≧0.8)為肥胖等。以t檢定(t-test)來比較病例組與對照組之間的連續性變項(如血壓、BMI及總膽固醇等)的平均數之差異。最後再以多變項逐步羅吉斯回歸分析與高血壓、脈波速度≧90百分比及IMT≧75百分比的相關因子，並計算其危險比(odds ratio, OR)及95%信賴區間(confidence interval, CI)。所有檢定方法皆以p值＜0.05為檢定水準。

參、結果

一、青少年心血管健康問卷資料

(一)青少年個人資料

至 2007 年 10 月，我們成功追蹤了 462 人接受少年高血壓追蹤檢查，其中病例組有 188 位(40.7%)(表 1)，平均年齡為 19.9±3.1 歲，較對照組(274 人)的 21.3±3.6 歲年輕($p<0.0001$)。病例組受過大學以上教育的百分比較對照組小(56.%對 65.9%，$p=0.034$)，病例組仍就學的的百分比較對照組高(69.7%對 52.8%，$p=0.0003$)，家庭收入大於 7 萬元的百分比則是對照組較病例組高(44.1%對 31.8%，$p=0.02$)。出生體重、2-5 歲時的體型、婚姻狀態以及住家是否有固定噪音來源在兩組間均無顯著差異。

(二) 生活型態、飲食習慣與過去病史

病例組目前較對照組多做運動(34.4 對 22.2%，$p=0.013$)，吃素、抽菸、喝酒與嚼檳榔的習慣則無顯著差異(表 2 及表 3)。乳製品、海鮮魚蝦貝類、蔬菜、水果、甜食、醃製品、肥肉速食、汽水飲料、咖啡等的攝取使用，亦無顯著的差異。

表 4 比較兩組的疾病史，病例組有糖尿病、高血壓、腎臟病及痛風病史的百分比都高於對照組，但脊椎側彎病在兩組間無顯著差異，而兩組皆無人有中風及心肌梗塞的病史。

(二) 父親的人口學資料、生活型態和健康史比較

相較於對照組，病例組的父親較年輕，較多為白領階級，而身高、體重及 BMI 以及教育程度在兩組間則無顯著差異(表 5)。生活型態的分析顯示，病例組的父親目前仍有抽菸習慣的百分比較對照組的高，喝酒、嚼檳榔、運動習慣以及吃素在兩組間則無顯著差異(表 6)。兩組父親的糖尿病與高血壓病史也無顯著差異。

(三) 母親的人口學資料、生活型態和健康史比較

相較於對照組，病例組的母親也較年輕(表 7)，多從事白領工作，而身高、體重及 BMI 以及教育程度在兩組間則無顯著差異。在生活型態方面，抽菸、喝酒、嚼檳榔、運動習慣以及吃素在兩組間無顯著差異(表 8)。而兩組母親的糖尿病與高血壓病史也無顯著差異。

二、理學檢查

表 9 說明病例組與對照組的理學檢查結果的比較。病例組與對照組在平均身高無顯著差異，但病例組比對照組有較高的平均體重(62.5±16.1 對 56.6±10.8 kg，$p<0.0001$)、BMI(23.3±5.28 對 20.9±3.13 kg/m^2，$p<0.0001$)、腰圍(75.2±15.4 對 67.0±8.88 cm，$p<0.0001$)、臀圍(96.2±9.56 對 90.8±6.41 cm，$p<0.0001$)、腰臀比(0.78±0.11 對 0.74±0.06，$p<0.0001$)、收縮壓(110.6±17.2 對 106.3±9.98 mmHg，$p=0.01$)以及舒張壓(72.0±14.1 對 66.3±9.51 mmHg，$p<0.0001$)。

男性、女性分別分析：男病例組比對照組有較低的平均身高(167.0±7.08 對 172.5±6.27 cm，p=0.0337)、但較高的平均體重(73.3±17.2 對 64.3±10.4 kg，p＜0.0001)、BMI (25.4±6.08 對 21.6±3.08 kg/m^2，p＜0.0001)、腰圍(83.1±14.2 對 72.4±9.88 cm，p＜0.0001)、臀圍(99.9±10.77 對 93.5±5.9 cm，p＜0.0001)、腰臀比(0.83±0.074 對 0.77±0.08，p＜0.0001)、收縮壓(121.1±17.94 對 110.9±9.89 mmHg，p=0.0001)以及舒張壓(79.2±15.0 對 70.1±9.90 mmHg，p＜0.0001)的平均值。在女性中，病例組相對於對照組的身高相近，但也有較高的平均體重(56.2±11.5 對 52.2±8.31 kg，p=0.004)、BMI (22.1±4.33 對 20.6±3.11 kg/m^2，p=0.002)、腰圍(70.6±14.2 對 63.8±6.45 cm，p＜0.0001)、臀圍(94.1±8.09 對 89.3±6.21 cm，p＜0.0001)、腰臀比(0.75±0.12 對 0.71±0.04，p=0.013)以及舒張壓(67.9±11.8 對 64.1±8.58 mmHg，p=0.0006)等；但收縮壓在兩組間無顯著差異。

將血壓分布分為高血壓、高血壓前期及正常血壓，BMI 分為＜18、18-23.9、24-26.9 及 27 kg/m^2，腰圍、臀圍及腰臀比做類別比較，表 10 顯示病例組的高血壓盛行率明顯高於對照組(9.04%對 1.09%，p＜0.0001)，高收縮壓(≧130 mmHg) (10.64%對 2.19%，p=0.0001)及高舒張壓(≧80 mmHg) (26.06%對 7.66%，p＜0.0001)的盛行率也是病例組高於對照組。病例組也比對照組有較高百分比的腰圍過大(21.8%對

4.36%，$p<0.0001$)、腰臀比過高(18.09%對 1.82%，$p<0.0001$)和 BMI≧27 kg/m^2 (19.2%對 4.73%，$p<0.0001$)。

依照 BMI 分層，腰圍是否過大及腰臀比是否過高，比較對照組和病例組的各階層血壓平均值顯示，病例組的平均收縮壓都較對照組的高，但其中具統計顯著的只有 BMI=24.0-26.9 kg/m^2 時的收縮壓(111.1±12.5 對 105.6±8.97 mmHg，$p=0.0109$) (表 11)。在舒張壓的分層分析中，當 BMI 介於 18-23.9 kg/m^2 (70.5±14.0 對 66.2±9.66 mmHg，$p=0.001$)及 BMI 介於 24-26.9 (71.4±10.2 對 64.9±99.0 mmHg，$p=0.006$)時，病例組的平均舒張壓較對照組的高。而不管腰圍過大(80.8±15.4 對 71.0±10.2 mmHg，$p=0.035$)或不過大(69.6±12.8 對 66.1±9.44 mmHg，$p<0.002$)，不管腰臀圍比有過大(76.6±14.0 對 63.2±8.07 mmHg，$p=0.02$)或不過大(71.0±14.0 對 63.4±9.54 mmHg，$p<0.0001$)，病例組的平均舒張壓皆較較對照組來得高。

三、生化檢查

(一)血液檢查

表 12 比較兩組的血液成分平均值。在所有的分析中，病例組顯著較高的項目只有血小板平均值(275.7±60.1 對 257.4±52.1 k/μL，$p=0.0008$)、平均紅血球容積(86.8±6.91 對 88.2±7.88 fL，$p=0.0009$)和平均血球血紅素(28.5±2.75 對 28.9±2.43 pg，$p=0.038$)及都高於對照

組，RDWSD(41.2±2.57 對 41.8±2.77 fL，p=0.025)則是病例組較對照組低。其餘白血球、紅血球、血紅色素等其他測量在兩組間皆無顯著差異。

在血液生化檢查中(表 13)，相較對照組，病例組的平均值較低的有 HDL (48.5±10.3 對 51.4±10.1 mg/dL，p=0.0003)、鈉離子(140.2±2.65 對 144.6±3.70 mmol/L，p＜0.0001)、鉀離子(4.16±0.31 對 4.31±0.37 mmol/L，p＜0.0001)、氯離子(103.7±7.93 對 107.7±3.04 mmol/L，p＜0.0001)、總蛋白量(7.65±0.49 對 7.87±0.46 g/dL，p＜0.0001)、白蛋白(4.85±0.29 對 5.01±0.25 g/dL，p＜0.0001)、球蛋白(2.80±0.32 對 2.86±0.33 g/dL，p=0.023)以及尿素氮(12.0±4.20 對 12.5±3.21 mg/dL，p=0.0294)，而胰島素平均值則是病例組較對照組高(8.37±9.34 對 6.44±6.57 μU/mL，p=0.007)。

(二)尿液檢查

在尿液分析中，病例組的白蛋白排出率平均值較對照組高(56.08±233.12 對 34.21±175.19 mg/g，p=0.0458）(表 14)。而病例組的尿中微白蛋白、肌酸酐及氯離子濃度雖比對照組高，但無統計上的顯著。鈉離子及鉀離子濃度之平均值則是對照組較病例組高，但也無統計上的顯著。

四、儀器檢查

(一)血管彈性檢查

表 15 說明血管彈性檢查結果，病例組的左心室血液噴出時間少於對照組(296.47±21.28 對 302.32±17.65 ms，p=0.0055)，心臟-頸動脈波速度(hcPWV)、心臟-右踝部脈波速度(hRaPWV)、右臂-踝部脈波速度(RbaPWV)、右踝部肱部指標(RABI)、心臟-左踝部脈波速度(hLaPWV)、左臂-踝部脈波速度(LbaPWV)及左踝部肱部指標(LABI)在兩組間無顯著差異。

(二)頸動脈超音波檢查

右頸動脈檢測資料分析顯示，病例組的 RCCA1 (0.525±0.080 對 0.439±0.056 mm，p＜0.0001)、RCCA2 (0.523±0.076 對 0.427±0.044 mm，p＜0.0001)及 RCCA (0.524±0.072 對 0.433±0.043 mm，p＜0.0001)的平均值都較對照組來的高(表 16)。以左頸動脈來看，LCCA1 (0.525±0.075 對 0.430±0.062 mm，p＜0.0001)、LCCA2(0.530±0.082 對 0.432±0.074 mm，p＜0.0001)及 LCCA(0.527±0.073 對 0.431±0.053 mm，p＜0.0001)的平均值也是病例組較對照組高。

五、綜合分析

表 17 為病例組與對照組的血液生化之卡方檢定，病例組的血小板過高(≧320 k/μL)、(20.2%對 12.0%，p=0.016)飯前血糖過高(≧100 mg/dL) (7.98%對 2.55%，p=0.0072)、HDL 過低(男＜50mg/dL，女＜

40mg/dL) (44.2%對 28.4%，p=0.0005)的百分比較對照組高，白蛋白過高(≧5.0 mg/dL) (19.2%對 44.9%，p＜0.0001)的百分比則是病例組較對照組低。

以 PWV≧90 百分比來分，病例組的 PWV 過高(15.5%對 6.25%，p=0.0012)百分比較對照組高(表 18)。在 IMT 的檢測結果中，以 CCA (Common carotid artery, CCA)≧90 百分比來分，病例組的 RCCA≧0.510 mm (54.8%對 5.24%，p＜0.0001)及 LCCA≧0.508 mm (54.1%對 6.37%，p＜0.0001)的百分比都比對照組高很多。

我們將腰圍過大(男≧90 cm，女≧80 cm)、血壓過高(收縮壓≧130 mmHg 或舒張壓≧80 mmHg)、血糖過高(≧100 mg/dL)、總膽固醇過高(≧200 mg/dL)、HDL 過低(男＜50mg/dL，女＜40mg/dL)、LDL 過高(≧130 mg/dL)、TG 過高(≧150 mg/dL)當做是心血管疾病危險因子，病例組有 3 個以上危險因子的百分比較對照組高(23.4%對 7.66%，p＜0.0001)。相較於對照組，病例組有一個危險因子、兩個危險因子及三個以上危險因子的勝算比分別為 1.95(95%CI=1.23-3.09)、2.07(95%CI=1.15-3.73)及 5.53(95%CI=2.98-10.3) (表 19)。

在多變項迴歸分析中，不論是收縮壓或舒張壓，BMI、血中肌酸酐及 RbaPWV 都會影響血壓(表 20)。在逐步羅吉斯迴歸分析中，經

控制了人口地理社經因子、過去病史、父母親人口社經因子、生化檢查相關因子及血管彈性等發現，有少年高血壓、男性、血小板過高、白蛋白過高、三酸甘油脂過高及 baPWV≧90 百分比，都與高血壓前期 (prehypertension) 有關 (表 21) 。若以 baPWV≧90 百分比為 outcome(表 22) ，年齡≧20 歲(OR=3.66，95%CI=1.55-8.65)、男性 (OR=3.73 ， 95%CI=1.76-7.91) 、有高血壓前期 (OR=4.80 ， 95%CI=2.20-10.5)、總蛋白量(OR=5.23，95%CI=1.30-21.1)、及飯前血糖過高(OR=4.95 ，95%CI=1.34-18.3))都是危險因子。在動脈硬化 (IMT≧75 百分比)與相關因子的逐步羅吉斯迴歸分析中(表 23)，有少年高血壓(OR=36.6，95%CI=18.6-72.0)、母親年齡≧50 歲(OR=4.49，95%CI=1.94-10.4)、血小板(OR=2.33，95%CI=1.03-5.25)過高及尿酸過高(≧5 mg/dL) (OR=2.93，95%CI=1.28-6.74)都是動脈硬化的危險因子，但父親年齡≧50 歲是保護因子(OR=0.40，95%CI=0.19-0.82)。

肆、討論

從兒童到老年，年齡與性別一直是影響血壓的重要因素[R20, R21]，通常年齡越大其血壓值越高。本研究目前所收集的病例組約較對照組年輕一歲多，且病例組的收縮壓與舒張壓平均值都較對照組高。本研究的收縮壓與舒張壓的多變項回歸分析的中，性別顯著與收

縮壓(p＜0.0001)及舒張壓(p＜0.0001)有關。在逐步多變項羅吉斯回歸中，相較於女性，男性有高血壓前期(prehypertension)的危險比為女性的 6.26 (95%CI=2.87-13.66)。文獻指出教育程度和社經因子與高血壓有一定的相關[R17]，而本研究也觀察到病例組受過大學教育的百分比較對照組低(56.25%對 65.93%，p=0.0342)，家庭收入≧7 萬的比例也是病例組較對照組低(31.82%對 44.11%，p=0.0200)。文獻指出噪音的暴露也與血壓有關[R16]，但在本研究中住家有無固定噪音來源在兩組間無顯著差異。不健康的生活型態會增加高血壓的危險[R17]，但病例組與對照組在抽菸、喝酒及嚼檳榔習慣無顯著差異，可能是因為青少年的抽菸及喝酒盛行率仍低，因此目前看不出明顯的差別。

在 188 位病例組中，問卷訪問的糖尿病史、高血壓病史腎臟病史及痛風病史的盛行率，都是病例組較對照組高。可見青少年時期有高血壓的人其成年後的疾病率會比青少年時期無高血壓的人還要高。在本研究中，相較於無少年高血壓的人，少年時期有高血壓的人目前具有高血壓的危險比為 3.54 (95%CI=1.68-7.44)。

肥胖是高血壓的危險因子之一，而對於兒童及青少年的高血壓來說，兒童肥胖影響更是重要，且少年肥胖與成年後的肥胖也有相關[R23]，肥胖甚至會影響從青少年至老年的動脈硬化[R22]。在本研究的人體測量學的比較中，可以看出肥胖或體重過重的狀態是青少年高

血壓的重要相關因子，不論是從平均值比較，分層分析、相關係數或是多變項迴歸觀查，腰圍、腰臀比及 BMI 都是影響血壓的重要因素。無論是腰臀比的過胖(18.09%對 1.82%，$p<0.0001$)、腰圍過大的肥胖(21.81%對 4.36%，$p<0.0001$)或是 BMI≧27 kg/m^2 的肥胖(19.15%對 4.73%，$p<0.0001$)，都是病例組顯著高於對照組。在多變項迴歸分析中，BMI 也顯著影響收縮壓($\beta=0.7243$，$p<0.0001$)與舒張壓($\beta=0.5957$，$p<0.0001$)。這些結果顯示肥胖與高血壓的強烈相關性。

三酸甘油脂(triglyceride, TG)與少年高血壓的相關已被許多研究證實[R24-26]。在本文研究中，病例組的 TG 平均值較對照組的高，但不顯著。但在逐步羅吉斯迴歸中，相較於 TG＜150 mg/dL 的人，TG≧150 mg/dL 的人其高血壓的危險比為 3.46 (1.14-10.5)。

文獻指出，血管彈性檢測中的脈波速度(PWV)與心血管疾病有密切相關[R27, R28]。在本研究中相較於對照組，病例組 baPWV (brachial-ankle pulse wave velocity) ≧90 百分比的比例較高(15.51%對 6.25%，$p=0.0012$)。在逐步羅吉斯迴歸中，相較於無 baPWV≧90 百分比的人，有 baPWV≧90 百分比的人其高血壓前期的危險比為 3.98 (95%CI=1.76-8.99)。此證據顯示年輕人的 PWV 與高血壓的重要性。這個發現尚未在青少年的相關研究中報導過。

根據台灣的金山社區心血管世代研究(the CCCC study)的結果，

高血壓及心血管疾病可由頸動脈硬化表現出來[R29]。在本研究中，無論是左頸動脈或右頸動脈，病例組的 IMT 都較對照組嚴重。在逐步羅吉斯迴歸中，相較於對照組，病例組有 IMT≧75 百分比(頸動脈硬化程度較高)的危險比高達 36.60 (95%CI=18.6-72.0)，顯示有少年高血壓的人其發生動脈硬化的情況較無少年高血壓的人顯著嚴重，值得重視。這個發現也是青少年心血管健康研究中的重要發現。

伍、建議

依據到 2007 年 10 月底完成建檔的資料分析，樣本數仍不夠大，尤其是對照組的收案較不易。雖然如此，但我們可以從目前的資料看出，尚不能進一步執行過多的分層分析。我們應加強對照收案。

這是一個相當困難執行的工作，牽涉到許多聯絡的作業，不僅是和研究對象聯絡，也和分析檢驗及資料處理分析等的繁多項目有關。從學生時代的資料，到目前經過了約十年的時間，許多學生的地址、電話都已無法聯絡，加上社會風氣不良，詐騙集團甚多，我們在與個案聯絡時，增加了不少困擾，在研究的執行上確實不容易。工作人員有時需親自到 subjects 家中去訪視取樣，負擔相當重，實驗室的工作更是需要支持，幸好過去金山工作伙伴的協力，尤其是協同主持人蘇大成和簡國龍醫師的協助。蘇醫師不僅每次收案都到場，協助督導各種檢查工作並向青少年解釋檢查結果，適時給予教育，甚至邀請了了

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表 1. 病例組與對照組的人口及社經因子比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
性別	n	(%)	n	(%)	n	(%)	0.9640
女	174	(63.5)	119	(63.3)	293	(63.4)	
男	100	(36.5)	69	(36.7)	169	(36.6)	
年齡，歲							0.0521
＜20	99	(36.1)	84	(45.2)	183	(39.8)	
≧20	175	(63.9)	102	(54.8)	277	(60.2)	
教育程度							0.0342
國中/高中(職)	93	(34.1)	84	(43.7)	177	(38.1)	
大學以上	180	(65.9)	108	(56.3)	288	(61.9)	
職業							0.0003
非學生	127	(47.2)	56	(30.3)	183	(40.3)	
學生	142	(52.7)	129	(69.7)	271	(59.7)	
婚姻狀態							0.6076
未婚	265	(97.1)	182	(97.8)	447	(97.4)	
已婚	8	(2.93)	4	(2.15)	12	(2.61)	
家庭收入							0.0200
＜5 萬	95	(36.1)	70	(39.8)	165	(37.6)	
5-6.9 萬	52	(19.8)	50	(28.4)	102	(23.2)	
≧7 萬	116	(44.1)	56	(31.8)	172	(39.2)	
出生體重，克							0.6873
≧2500	252	(95.4)	176	(94.6)	428	(95.1)	
＜2500	12	(4.55)	10	(5.38)	22	(4.89)	
2-5 歲時體型							0.5348
瘦小	58	(21.6)	35	(18.2)	93	(20.2)	
中等	189	(70.3)	137	(71.3)	326	(70.7)	
寬胖	22	(8.18)	20	(10.4)	42	(9.11)	
住家有固定噪音來源							0.7368
無	130	(48.3)	93	(50.0)	223	(49.0)	
一項	90	(33.5)	56	(30.1)	146	(32.1)	
兩項以上	49	(18.2)	37	(19.9)	86	(18.9)	
合計							

Missing data：年齡=2、出生體重=12、2-5 歲時體型=7、教育程度=3、職業=8、婚姻狀態=3、家庭收入=23、噪音來源=7

表 2. 病例組與對照組的生活型態及飲食習慣比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
抽菸習慣	n	(%)	n	(%)	n	(%)	0.3316
無	227	(83.2)	166	(86.5)	393	(84.5)	
有/已戒	46	(16.8)	26	(13.5)	72	(15.5)	
喝酒習慣							0.3552
無	237	(87.8)	172	(90.5)	409	(88.9)	
有	33	(12.2)	18	(9.47)	51	(11.1)	
嚼檳榔習慣#							0.9287
無	266	(97.8)	188	(97.9)	454	(97.8)	
有/已戒	6	(2.21)	4	(2.08)	10	(2.16)	
運動習慣							0.0126
從來沒有	79	(29.3)	43	(22.4)	122	(26.4)	
過去有	131	(48.5)	83	(43.2)	214	(46.3)	
目前有	60	(22.2)	66	(34.4)	126	(27.3)	
素食者							0.8292
不是	259	(94.9)	183	(95.3)	442	(95.1)	
是/早齋或偶而	14	(5.13)	9	(4.69)	23	(4.95)	
乳製品的攝食							0.2781
幾乎沒有/不知道	69	(25.4)	55	(28.6)	124	(26.7)	
每週 1-2 次	128	(47.1)	76	(39.6)	204	(44.0)	
每週 3 次以上	75	(27.6)	61	(31.8)	136	(29.3)	
海鮮魚蝦貝類的攝食							0.2860
幾乎沒有/不知道	52	(19.1)	34	(17.7)	86	(18.5)	
每週 1-2 次	157	(57.7)	101	(52.6)	258	(55.6)	
每週 3 次以上	63	(23.2)	57	(29.7)	120	(25.9)	
蔬菜的攝食							0.4881
幾乎沒有/不知道	6	(2.20)	2	(1.04)	8	(1.04)	
每週 1-2 次	33	(12.1)	28	(14.58)	61	(14.6)	
每週 3 次以上	234	(85.7)	162	(84.38)	396	(84.4)	
水果的攝食							0.1695
幾乎沒有/不知道	26	(9.59)	17	(8.85)	43	(9.29)	
每週 1-2 次	109	(40.2)	62	(32.29)	171	(36.9)	
每週 3 次以上	136	(50.2)	113	(58.85)	249	(53.8)	

Missing data：抽菸=3、喝酒=8、嚼檳榔=4、運動=6、素食者=3、乳製品=4、海鮮=4、蔬菜=3、水果=5

Fisher's Exact Test

表 3. 病例組與對照組的生活型態及飲食習慣比較(續)

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
甜食的攝食	n	(%)	n	(%)	n	(%)	0.5666
幾乎沒有/不知道	40	(14.8)	28	(14.6)	68	(14.7)	
每週 1-2 次	96	(35.4)	77	(40.1)	173	(37.4)	
每週 3 次以上	135	(49.8)	87	(45.3)	222	(47.9)	
可樂、汽水等飲料							0.5249
幾乎沒有/不知道	99	(36.4)	69	(36.1)	168	(36.3)	
每週 1-2 次	91	(33.5)	56	(29.3)	147	(31.8)	
每週 3 次以上	82	(30.2)	66	(34.6)	148	(31.9)	
香腸/臘肉/火腿/培根等							0.8007
幾乎沒有/不知道	66	(24.2)	43	(22.5)	109	(23.5)	
每週 1-2 次	137	(50.2)	94	(49.2)	231	(49.8)	
每週 3 次以上	70	(25.6)	54	(28.3)	124	(26.7)	
肥肉的攝食							0.1723
幾乎沒有/不知道	180	(66.2)	129	(67.5)	309	(66.7)	
每週 1-2 次	67	(24.6)	53	(27.8)	120	(25.9)	
每週 3 次以上	25	(9.19)	9	(4.7)	34	(7.34)	
麥當勞/肯得基等速食							0.6667
幾乎沒有/不知道	157	(57.9)	117	(61.3)	274	(59.3)	
每週 1-2 次	102	(37.6)	68	(35.6)	170	(36.8)	
每週 3 次以上	12	(4.4)	6	(3.1)	18	(3.90)	
喝咖啡							0.3994
幾乎沒有/不知道	171	(62.6)	125	(65.5)	296	(63.8)	
每週 1-2 次	65	(23.8)	48	(25.1)	113	(24.3)	
每週 3 次以上	37	(13.6)	18	(9.42)	55	(11.9)	

Missing data：甜食=5、可樂=5、香腸=4、肥肉=5、麥當勞=6、喝咖啡=4

表 4. 病例組與對照組的個人自我陳述之病史比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
糖尿病	n	(%)	n	(%)	n	(%)	0.0006
無	271	(99.6)	176	(94.6)	447	(97.6)	
有	1	(0.37)	10	(5.38)	11	(2.40)	
高血壓							0.0179
無	270	(99.3)	178	(95.7)	448	(97.8)	
有	2	(0.74)	8	(4.30)	10	(2.18)	
腎臟病							0.0198
無	264	(96.7)	170	(91.4)	434	(94.5)	
有	9	(3.30)	16	(8.60)	25	(5.45)	
痛風[#]							0.0042
無	273	(100)	180	(96.8)	453	(98.7)	
有	0	(0.00)	6	(3.23)	6	(1.31)	
脊椎測灣							0.2026
無	206	(76.3)	154	(82.8)	360	(79.0)	
輕微	57	(21.1)	27	(14.5)	84	(18.4)	
嚴重	7	(2.59)	5	(2.69)	12	(2.63)	

Missing data：糖尿病=4、高血壓=4、腎臟病=3、痛風=3、脊椎測灣=6

[#] Fisher's Exact Test

表 5. 病例組與對照組的父親人口學資料比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
年齡，歲	n	(%)	n	(%)	n	(%)	0.0020
＜50	97	(38.3)	95	(53.4)	192	(44.6)	
≧50	156	(61.7)	83	(46.6)	239	(55.4)	
身高，公分							0.0941
＜170	120	(47.4)	99	(55.6)	219	(50.8)	
≧170	133	(52.6)	79	(44.4)	212	(49.2)	
體重，公斤							0.8092
＜70	122	(48.8)	85	(50.0)	207	(49.3)	
≧70	128	(51.2)	85	(50.0)	213	(50.7)	
BMI，kg/m^3							0.4207
＜24	111	(44.4)	75	(44.1)	186	(44.3)	
24-26.9	95	(38.0)	57	(33.5)	152	(36.2)	
≧27	44	(17.6)	38	(22.4)	82	(19.5)	
教育程度							0.5228
國小	41	(15.9)	37	(20.9)	78	(18.0)	
國中	59	(23.0)	36	(20.3)	95	(21.9)	
高中(職)	92	(35.8)	65	(36.7)	157	(36.2)	
大學以上	65	(25.3)	39	(22.0)	104	(24.0)	
職業							＜0.0001
白領	64	(26.1)	86	(49.7)	150	(35.9)	
藍領	143	(58.4)	74	(42.8)	217	(51.9)	
其他	38	(15.5)	13	(7.51)	51	(12.2)	

遺漏值：年齡=31、身高=31、體重=42、BMI=42、教育程度＝28、職業＝44

表 6. 病例組與對照組的父親生活型態及病史比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
抽菸習慣	n	(%)	n	(%)	n	(%)	0.0052
無	104	(40.2)	59	(32.6)	163	(37.0)	
已戒除	57	(22.0)	26	(14.4)	83	(18.9)	
有	98	(37.8)	96	(53.0)	194	(44.1)	
喝酒習慣							0.4249
無	137	(54.2)	101	(56.1)	238	(55.0)	
已戒除	31	(12.1)	15	(8.33)	46	(10.6)	
有	85	(33.6)	64	(35.6)	149	(34.4)	
嚼檳榔習慣#							0.1670
無	267	(100)	183	(98.9)	450	(99.6)	
有	0	(0)	2	(1.08)	2	(0.44)	
運動習慣							0.1320
從來沒有	90	(35.9)	70	(38.9)	160	(37.1)	
過去有	56	(22.3)	51	(28.3)	107	(24.8)	
目前有	105	(41.8)	59	(32.8)	164	(38.1)	
素食者							0.5920
否	245	(94.6)	169	(93.4)	414	(94.1)	
是	14	(5.41)	12	(6.63)	26	(5.91)	
糖尿病病史							0.6166
無	231	(89.9)	158	(91.3)	389	(90.5)	
有	26	(10.1)	15	(8.67)	41	(9.53)	
高血壓病史							0.6714
無	217	(84.1)	142	(82.6)	359	(83.5)	
有	41	(15.9)	30	(17.4)	71	(16.5)	

遺漏值：抽菸＝22；喝酒＝29；嚼檳榔＝24；運動＝31；素食者＝22；糖尿病＝32；高血壓＝32

Fisher's Exact Test

表 7. 病例組與對照組的母親人口學資料比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
年齡，歲	n	(%)	n	(%)	n	(%)	0.0135
＜50	168	(63.6)	136	(74.7)	304	(68.2)	
≧50	96	(36.4)	46	(25.3)	142	(31.8)	
身高，公分							0.5513
＜160	167	(63.0)	121	(65.8)	288	(64.1)	
≧160	98	(37.0)	63	(34.2)	161	(35.9)	
體重，公斤							0.5671
＜60	166	(63.1)	110	(60.4)	276	(62.0)	
≧60	97	(36.9)	72	(39.6)	169	(38.0)	
BMI，kg/m^3							0.4207
＜24	111	(44.4)	116	(44.1)	186	(44.3)	
24-26.9	95	(38.0)	36	(33.5)	152	(36.2)	
≧27	44	(17.6)	30	(22.4)	82	(19.5)	
教育程度							0.2291
國小	62	(23.9)	51	(27.6)	113	(25.4)	
國中	48	(18.5)	44	(23.8)	92	(20.7)	
高中(職)	101	(38.8)	65	(35.1)	166	(37.3)	
大學以上	49	(18.8)	25	(13.5)	74	(16.6)	
職業							＜0.0001
白領	14	(5.47)	45	(25.3)	59	(13.6)	
藍領	116	(45.3)	54	(30.3)	170	(39.2)	
家管	112	(43.8)	72	(40.5)	184	(42.4)	
其他	14	(5.45)	7	(3.93)	21	(4.84)	

遺漏值：年齡=16、身高=13、體重=17、BMI=17、教育程度＝17、職業＝28

表 8. 病例組與對照組的母親生活型態及病史比較

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
抽菸習慣	n	(%)	n	(%)	n	(%)	0.3023
無	252	(94.7)	169	(91.4)	421	(93.4)	
已戒	3	(1.13)	5	(2.70)	8	(1.77)	
目前有	11	(4.14)	11	(5.95)	22	(4.88)	
喝酒習慣							0.7924
無	244	(91.7)	165	(90.2)	409	(91.1)	
已戒	6	(2.26)	4	(2.19)	10	(2.23)	
目前有	16	(6.02)	14	(7.65)	30	(6.68)	
嚼檳榔習慣#							0.0886
無	267	(100)	183	(98.9)	450	(99.6)	
有	0	(0)	2	(1.08)	2	(0.44)	
運動習慣							0.2328
從來沒有	105	(40.1)	74	(40.2)	179	(40.1)	
過去有	47	(17.9)	44	(23.9)	91	(20.4)	
目前有	110	(42.0)	66	(35.9)	176	(39.4)	
素食者							0.6722
否	217	(81.6)	155	(83.8)	372	(82.5)	
只有初一、十五	33	(12.4)	18	(9.73)	51	(11.3)	
是	16	(6.02)	12	(6.49)	28	(6.21)	
糖尿病病史							0.1094
無	256	(97.0)	167	(93.8)	423	(95.7)	
有	8	(3.03)	11	(6.18)	19	(4.30)	
高血壓病史							0.1207
無	240	(90.2)	152	(85.4)	392	(88.3)	
有	26	(9.77)	26	(14.6)	52	(11.7)	

遺漏值：抽菸＝11、喝酒＝13、嚼檳榔＝10、運動＝16、素食者＝11、糖尿病＝20、高血壓＝18

Fisher's Exact Test

表 9. 病例組與對照組人體量測及血壓資料比較

	對照組 N=274	病例組 N=188	合計 N=462
	平均值 ± 標準差	平均值 ± 標準差	*p* 值
年齡，歲	21.31 ± 3.55	19.87 ± 3.11	<0.0001
身高，cm	164.13 ± 8.52	163.28 ± 8.10	0.5607
體重，kg	56.64 ± 10.84	62.49 ± 16.10	<0.0001
BMI，kg/m^2	20.94 ± 3.13	23.33 ± 5.28	<0.0001
腰圍，cm	66.97 ± 8.88	75.19 ± 15.38	<0.0001
臀圍，cm	90.84 ± 6.41	96.24 ± 9.56	<0.0001
腰臀比	0.74 ± 0.06	0.78 ± 0.11	<0.0001
收縮壓，mmHg	106.34 ± 9.89	110.60 ± 17.22	0.0098
舒張壓，mmHg	66.33 ± 9.51	72.02 ± 14.11	<0.0001
男性(N=170)	N=100	N=69	
年齡，歲	21.37 ± 3.43	20.27 ± 3.42	0.0455
身高，cm	172.51 ± 6.27	169.97 ± 7.08	0.0337
體重，kg	64.34 ± 10.38	73.29 ± 17.15	<0.0001
BMI，kg/m^2	21.59 ± 3.08	25.44 ± 6.08	<0.0001
腰圍，cm	72.36 ± 9.88	83.08 ± 14.17	<0.0001
臀圍，cm	93.46 ± 5.92	99.93 ± 10.77	<0.0001
腰臀比	0.77 ± 0.08	0.83 ± 0.074	<0.0001
收縮壓，mmHg	110.86 ± 9.89	121.06 ± 17.94	0.0001
舒張壓，mmHg	70.09 ± 9.90	79.17 ± 14.99	<0.0001
女性(N=293)	N=174	N=119	
年齡，歲	21.28 ± 3.62	19.64 ± 2.91	<0.0001
身高，cm	159.26 ± 5.23	159.40 ± 5.81	0.3697
體重，kg	52.17 ± 8.31	56.23 ± 11.53	0.0035
BMI，kg/m^2	20.56 ± 3.11	22.11 ± 4.33	0.0016
腰圍，cm	63.84 ± 6.45	70.62 ± 14.19	<0.0001
臀圍，cm	89.31 ± 6.21	94.10 ± 8.09	<0.0001
腰臀比	0.71 ± 0.04	0.75 ± 0.12	0.0125
收縮壓，mmHg	103.71 ± 8.91	104.54 ± 13.54	0.4780
舒張壓，mmHg	64.14 ± 8.58	67.87 ± 11.78	0.0006

表 10. 病例組與對照組的血壓及人體量測比較之卡方檢定

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
高血壓分類	n	(%)	n	(%)	n	(%)	<0.0001
正常血壓	250	(91.2)	134	(71.3)	384	(83.1)	
高血壓前期	21	(7.66)	37	(19.7)	58	(12.6)	
高血壓	3	(1.09)	17	(9.04)	20	(4.33)	
收縮壓，mmHg							0.0001
<130	268	(97.8)	168	(89.4)	436	(94.4)	
≧130	6	(2.19)	20	(10.6)	26	(5.63)	
舒張壓，mmHg							<0.0001
<80	253	(92.3)	139	(73.9)	392	(84.8)	
≧80	21	(7.66)	49	(26.1)	70	(15.2)	
BMI，kg/m^2							<0.0001
<18	33	(12.0)	16	(8.51)	49	(10.6)	
18-23.9	203	(73.8)	110	(58.5)	313	(67.6)	
24-26.9	26	(9.45)	26	(13.8)	52	(11.2)	
≧27	13	(4.73)	36	(19.2)	49	(10.6)	
腰圍過大的肥胖							<0.0001
無	263	(95.6)	147	(78.2)	410	(88.5)	
有	12	(4.36)	41	(21.8)	53	(11.5)	
腰臀比過高的肥胖							<0.0001
無	270	(98.2)	154	(81.9)	424	(91.6)	
有	5	(1.82)	34	(18.1)	39	(8.42)	

Ψ根據衛生署血壓標準定義

腰圍過大的肥胖：男≧90 cm，女≧80 cm

腰臀比過高的肥胖：男≧0.9，女≧0.8

表 11. 病例組與對照組的血壓平均值依 BMI、腰圍過大肥胖、及腰臀比過大肥胖之分層分析

	對照組 N=274		病例組 N=188		合計 N=462
	n	平均值±標準差	n	平均值±標準差	*p* 值
收縮壓，mmHg					
BMI，kg/m^2					
＜18	33	103.33± 9.88	16	104.63±10.37	0.6385
18-23.9	203	106.34± 9.84	110	108.81±17.91	0.4940
24-26.9	26	105.58± 8.97	26	111.15±12.46	0.0109
≧27	13	115.38± 7.82	36	118.33±18.45	0.7508
腰圍過大					
無	263	106.02± 9.81	147	108.36±15.93	0.1908
有	12	113.25± 9.52	41	118.63±19.37	0.6396
腰臀比過高的					
無	270	106.34± 9.95	154	109.87±17.02	0.0605
有	5	106.40± 6.39	34	113.90±18.00	0.2835
舒張壓，mmHg					
BMI，kg/m^2					
＜18	33	65.30± 8.26	16	64.31±10.49	0.5784
18-23.9	203	66.16± 9.66	110	70.54±13.99	0.0013
24-26.9	26	64.88± 8.99	26	71.42±10.16	0.0060
≧27	13	74.38± 8.04	36	80.38±15.08	0.2039
腰圍過大					
無	263	66.11± 9.44	147	69.58±12.77	0.0017
有	12	71.00±10.19	41	80.76±15.35	0.0350
腰臀比過高					
無	270	66.39± 9.54	154	71.02±13.99	0.0001
有	5	63.20± 8.07	34	76.56±13.99	0.0195

表 12. 病例組與對照組血液檢查平均值比較

	對照組 N=274	病例組 N=188	合計 N=462
	平均值 ± 標準差	平均值 ± 標準差	*p* 值
紅血球，M/μL	6.25 ± 1.58	6.55 ± 1.71	0.0445
白血球，k/μL	4.86 ± 0.51	4.91 ± 0.49	0.2069
血小板，k/μL	257.36 ± 52.10	275.75 ± 60.08	0.0008
血紅色素，g/dL	14.00 ± 1.46	13.92 ± 1.67	0.6083
血球容積比，%	42.79 ± 3.83	42.42 ± 4.14	0.3960
平均紅血球容積，fL	88.15 ± 7.88	86.80 ± 6.91	0.0009
平均血球血紅素，pg	28.92 ± 2.43	28.46 ± 2.75	0.0379
平均血色素濃度，g/dL	32.68 ± 0.92	32.75 ± 1.12	0.3237
RDWSD，fL	41.85 ± 2.77	41.23 ± 2.57	0.0070
紅血球分佈寬度，%	13.01 ± 0.89	13.10 ± 1.15	0.9357
血小板分佈寬度，fL	12.31 ± 1.59	12.42 ± 1.51	0.2804
平均血小板容積，fL	10.44 ± 0.77	10.49 ± 0.78	0.5468
巨大血小板	28.19 ± 6.84	28.76 ± 6.48	0.3778
嗜中性球百分比	55.61 ± 9.32	56.11 ± 8.69	0.5860
淋巴球百分比	35.71 ± 8.47	35.36 ± 8.02	0.5414
單核球百分比	5.33 ± 1.17	5.10 ± 1.33	0.0671
嗜酸性球百分比	2.91 ± 2.13	2.97 ± 2.02	0.5633
嗜鹼性球百分比	0.51 ± 0.33	0.45 ± 0.27	0.0535
嗜中性球計數(k/μL)	3.55 ± 1.32	3.76 ± 1.42	0.0634
淋巴球計數(k/μL)	2.17 ± 0.59	2.27 ± 0.61	0.0693
單核球計數(k/μL)	0.33 ± 0.10	0.34 ± 0.11	0.4787
嗜酸性計數(k/μL)	0.18 ± 0.14	0.19 ± 0.14	0.1860
嗜鹼性計數(k/μL)	0.03 ± 0.02	0.03 ± 0.02	0.2399

表 13. 病例組與對照組血液生化檢查平均值比較

	對照組 N=274	病例組 N=188	合計 N=462
	平均值 ± 標準差	平均值 ± 標準差	*p* 值
總膽固醇，mg/dL	175.79 ± 36.63	177.62 ± 37.87	0.7014
高密度膽固醇，mg/dL	51.45 ± 10.07	48.52 ± 10.28	0.0003
低密度膽固醇，mg/dL	102.18 ± 32.94	105.94 ± 33.74	0.2376
三酸甘油脂，mg/dL	78.35 ± 38.34	96.71 ± 116.29	0.6488
鈉離子，mmol/L	144.62 ± 3.70	140.22 ± 2.65	＜0.0001
鉀離子，mmol/L	4.31 ± 0.37	4.16 ± 0.31	＜0.0001
氯離子，mmol/L	107.66 ± 3.04	103.71 ± 7.93	＜0.0001
總蛋白量，g/dL	7.87 ± 0.46	7.65 ± 0.49	＜0.0001
白蛋白，g/dL	5.01 ± 0.25	4.85 ± 0.29	＜0.0001
球蛋白，g/dL	2.86 ± 0.33	2.80 ± 0.32	0.0231
蛋白比值，	1.77 ± 0.20	1.75 ± 0.19	0.6041
尿酸，mg/dL	5.87 ± 1.47	5.90 ± 1.56	0.8545
尿素氮，mg/dL	12.50 ± 3.21	12.02 ± 4.20	0.0294
肌酸酐，mg/dL	0.97 ± 0.19	1.00 ± 0.76	0.2022
GOT，U/L	18.08 ± 6.43	19.27 ± 8.80	0.3268
GPT，U/L	16.42 ± 11.16	20.96 ± 22.91	0.2265
CRP	0.08 0.12	0.12 0.30	0.2983
飯前血糖，mg/dL	85.82 ± 8.32	92.06 ± 34.80	0.5434
胰島素，μU/mL	6.44 ± 6.57	8.37 ± 9.34	0.0067

表 14. 病例組與對照組尿液檢查平均值比較

	對照組 N=274	病例組 N=188	合計 N=462
	平均值 ± 標準差	平均值 ± 標準差	*p* 值
尿中微白蛋白，mg/L	43.36 ± 153.67	67.74 ± 218.80	0.2421
肌酸酐，mg/dL	174.96 ± 89.62	176.43 ± 90.36	0.8913
白蛋白排出率，mg/g	34.21 ± 175.19	56.08 ± 233.12	0.0458
鈉離子，mmol/L	115.25 ± 56.45	113.72 ± 55.68	0.8027
鉀離子，mmol/L	39.35 ± 23.14	38.84 ± 23.18	0.7106
氯離子，mmol/L	92.18 ± 44.54	93.10 ± 40.89	0.6360

表 15.以 Colin 血管彈性檢測儀檢測病例組與對照組的脈波速度(PWV)檢查結果平均值比較

	對照組 N=274		病例組 N=188		合計 N=462
	平均值	標準差	平均值	標準差	*p* 值
hcPWV, cm/s	500.55	63.24	505.81	71.92	0.7913
hRaPWV, cm/s	730.18	60.62	745.82	80.49	0.1184
RbaPWV, cm/s	1105.58	136.97	1141.00	165.68	0.1175
RABI	1.08	0.07	1.09	0.07	0.4474
hLaPWV, cm/s	733.99	65.80	752.67	80.40	0.0621
LbaPWV, cm/s	1124.01	134.54	1162.26	167.12	0.0573
LABI	1.08	0.07	1.08	0.06	0.2695
左心室血液噴出時間	302.32	17.65	296.47	21.28	0.0055

PWV=脈波速度 (pulse wave velocity)

hcPWV=心臟-頸動脈波速度、hRaPWV=心臟-右踝部脈波速度、RbaPWV=右臂-踝部脈波速度、RABI=右踝部肱部指標、hLaPWV=心臟-左踝部 PWV、LbaPWV=左臂-踝部脈波速度、LABI=左踝部肱部指標

表 16.病例組與對照組的頸動脈超音波檢查結果平均值比較

	對照組 N=274	病例組 N=188	合計 N=462
	平均值± 標準差	平均值± 標準差	*p* 值
RCCA1, mm	0.439± 0.056	0.525± 0.080	<0.0001
RCCA2, mm	0.427± 0.044	0.523± 0.076	<0.0001
RCCA, mm	0.433± 0.043	0.524± 0.072	<0.0001
LCCA1, mm	0.430± 0.062	0.525± 0.075	<0.0001
LCCA2, mm	0.432± 0.074	0.530± 0.082	<0.0001
LCCA, mm	0.431± 0.053	0.527± 0.073	<0.0001

表 17. 病例組與對照組的血壓及人體量測比較之卡方檢定

	對照組 N=274		病例組 N=188		合計 N=462		*p* 值
血小板，k/μL	n	(%)	n	(%)	n	(%)	0.0160
＜320	242	(88.0)	150	(79.8)	392	(84.7)	
≧320	33	(12.0)	38	(20.2)	71	(15.3)	
飯前血糖，mg/dL							0.0072
＜100	267	(97.4)	173	(92.0)	440	(95.2)	
≧100	7	(2.55)	15	(7.98)	22	(4.76)	
白蛋白，mg/dL							＜0.0001
＜5.0	151	(55.1)	152	(80.8)	303	(65.6)	
≧5.0	123	(44.9)	36	(19.2)	159	(34.4)	
總膽固醇，mg/dL							0.8859
＜200	212	(77.1)	146	(77.7)	358	(77.3)	
≧200	63	(22.9)	42	(22.3)	105	(22.7)	
HDL，mg/dL							0.0005
正常	197	(71.6)	105	(55.8)	302	(65.2)	
過低	78	(28.4)	83	(44.2)	161	(34.8)	
LDL，mg/dL							0.1592
＜130	228	(82.9)	146	(77.7)	374	(80.8)	
≧130	47	(17.1)	42	(22.3)	89	(19.2)	
三酸甘油脂，mg/dL							0.1281
＜150	259	(94.2)	170	(90.4)	429	(92.7)	
≧150	16	(5.82)	18	(9.57)	34	(7.34)	

HDL 過低：男＜50 mg/dL，女＜40 mg/dL

表 18. 病例組與對照組的血壓及人體量測比較之卡方檢定

	對照組 N=274		病例組 N=188		合計 N=462		*P* 值
hcPWV, ms	n	(%)	n	(%)	n	(%)	0.2495
＜574	248	(91.2)	151	(87.8)	399	(89.7)	
≧574	24	(8.82)	21	(12.2)	45	(10.1)	
RhaPWV, ms							0.0885
＜822	250	(91.9)	161	(87.0)	411	(89.9)	
≧822	22	(8.09)	24	(13.0)	46	(10.1)	
RbaPWV, ms							0.0090
＜1314	253	(93.0)	160	(85.6)	413	(89.0)	
≧1314	19	(6.99)	27	(14.4)	46	(10.0)	
LhaPWV, ms							0.1655
＜828	249	(91.5)	162	(87.6)	411	(89.9)	
≧828	23	(8.46)	23	(12.4)	46	(10.1)	
LbaPWV, ms							0.0477
＜1314	251	(92.3)	162	(86.6)	413	(89.0)	
≧1314	21	(7.72)	25	(13.4)	46	(10.0)	
baPWV, ms							0.0012
＜1307	255	(93.7)	158	(84.5)	413	(89.0)	
≧1307	17	(6.25)	29	(15.5)	46	(10.0)	
RCCA, mm							＜0.0001
＜0.510	253	(94.8)	81	(45.2)	334	(74.9)	
≧0.510	14	(5.24)	98	(54.8)	112	(25.1)	
LCCA, mm							＜0.0001
＜0.508	250	(93.6)	83	(45.9)	333	(74.3)	
≧0.508	17	(6.37)	98	(54.1)	115	(25.7)	

PWV 以≧90 百分比為切點，RCCA 及 LCCA 以≧75 百分比

遺漏值：hcPWV=18，RhaPWV=5，RbaPWV=3，LhaPWV=5，LbaPWV=3，baPWV=3，RCCA=15，LCCA=14

表 19.心血管危險因子之盛行狀況

	單變項	對照組	病例組	合計	*p* 值
	OR (95%CI)	N=274	N=188	N=462	
危險因子		n (%)	n (%)	n (%)	<0.0001
0 個	1.00 -	124 (45.3)	47 (25.0)	171 (37.0)	
1 個	1.95 (1.23-3.09)	91 (33.2)	68 (36.2)	159 (34.4)	
2 個	2.07 (1.15-3.73)	38 (13.8)	29 (15.4)	67 (14.5)	
3 個以上	5.53 (2.98-10.3)	21 (7.66)	44 (23.4)	65 (14.1)	

心血管危險因子：腰圍過大(男≧90 cm，女≧80 cm)、血壓過高(收縮壓≧130 mmHg 或舒張壓≧80 mmHg)、血糖過高(≧100 mg/dL)、總膽固醇過高(≧200 mg/dL)、HDL 過低、LDL 過高、TG 過高

表 20.收縮壓與舒張壓的單變項及多變項回歸分析

變項	收縮壓		舒張壓	
	單變項	多變項	單變項	多變項
	β	β	β	β
截距項		56.3744		25.5165
年齡	0.2276	- 0.2805	0.2663	0.0817
性別	11.3102***	4.3740**	7.5454***	2.0878
病例或對照	4.2262**	0.0319	5.9083***	2.8918*
運動習慣	2.0523*	0.0587	1.5491*	0.2065
BMI	1.0559***	0.7243***	1.0112***	0.5957***
血中尿素氮	0.9055***	- 0.1216	0.4600*	- 0.2404
血中肌酸酐	10.4670***	7.4524***	6.9003***	5.5778***
GOT	0.3098**	- 0.1632	0.3184***	- 0.0714
GPT	0.2140***	0.1037	0.2109***	0.0772
總膽固醇	0.0298	0.1407*	0.0203	0.0308
HDL	- 0.3143***	- 0.2537*	- 0.2595***	- 0.0836
LDL	0.0627**	- 0.1255*	0.0410*	- 0.0410
三酸甘油脂	0.0269**	- 0.0296**	0.0338***	- 0.0042
飯前血糖	0.0888**	0.0462	0.0907***	0.0376
RbaPWV	0.0443***	0.0358***	0.0320***	0.0198*
LbaPWV	0.0406***	- 0.0044	0.0303***	0.0012
CRP	6.5173*	- 2.9914	6.6887*	- 2.3314

*$p<0.05$，**$p<0.001$，***$p<0.0001$

表 21.高血壓前期與相關因子的逐步羅吉斯回歸分析

	逐步分析 OR (95%CI)	逐步分析# OR (95%CI)
少年高血壓		
無	1.00 -	- -
有	3.54 (1.68-7.44)	- -
性別		
女	1.00 -	1.00 -
男	6.26 (2.87-13.66)	5.72 (2.67-12.2)
BMI，kg/m^2		
＜18	1.00 -	1.00 -
18-23.9	0.69 (0.21-2.32)	0.77 (0.23-2.59)
24-26.9	0.53 (0.12-2.37)	0.79 (0.18-3.39)
≧27	2.20 (0.57-8.55)	3.37 (0.88-12.9)
血小板，k/μL		
＜320	1.00 -	1.00 -
≧320	3.54 (1.47-8.52)	3.49 (1.48-8.22)
白蛋白，mg/dL		
＜5.0	1.00 -	1.00 -
≧5.0	0.42 (0.18-0.96)	0.31 (0.14-0.67)
三酸甘油脂，mg/dL		
＜150	1.00 -	1.00 -
≧150	3.46 (1.14-10.49)	3.28 (1.13-9.52)
baPWV≧90 百分比		
否	1.00 -	1.00 -
是	3.98 (1.76-8.99)	4.23 (1.91-9.35)

考慮了少年高血壓狀態、年齡、性別、BMI、教育程度、職業、家庭收入、運動習慣、糖尿病史、高血壓病史、腎臟病史、痛風病史、父親年齡、父親職業、父親抽菸習慣、母親年齡、母親職業、血小板、總蛋白量、白蛋白、尿酸、肌酸酐、GOT、GPT、飯前血糖、總膽固醇、高密度脂蛋白膽固醇、低密度脂蛋白膽固醇、三酸甘油脂、baPWV及IMT

#不考慮少年高血壓狀態

表 22.baPWV≧90 百分比與相關因子的逐步羅吉斯回歸分析

	逐步分析 OR (95%CI)
年齡，歲	
＜20	Reference
≧20	3.66 (1.55-8.65)
性別	
女	Reference
男	3.73 (1.76-7.91)
高血壓前期	
否	Reference
是	4.80 (2.20-10.5)
總蛋白量，g/dL	
＜8.7	Reference
≧8.7	5.23 (1.30-21.1)
飯前血糖，mg/dL	
＜100	Reference
≧100	4.95 (1.34-18.3)

考慮了少年高血壓狀態、年齡、性別、BMI、教育程度、職業、家庭收入、運動習慣、糖尿病史、高血壓病史、腎臟病史、痛風病史、父親年齡、父親職業、父親抽菸習慣、母親年齡、母親職業、血小板、總蛋白量、白蛋白、尿酸、肌酸酐、GOT、GPT、飯前血糖、總膽固醇、高密度脂蛋白膽固醇、低密度脂蛋白膽固醇、三酸甘油脂、baPWV 及 IMT

表23.IMT≧75百分比與相關因子的逐步羅吉斯回歸分析

	逐步分析 OR (95%CI)
少年高血壓	
無	Reference
有	36.60 (18.6-72.0)
父親年齡，歲	
＜50	Reference
≧50	0.40 (0.19-0.82)
母親年齡，歲	
＜50	Reference
≧50	4.49 (1.94-10.4)
血小板，k/μL	
＜320	Reference
≧320	2.33 (1.03-5.25)
尿酸，mg/dL	
＜5.0	Reference
≧5.0	2.93 (1.28-6.74)

考慮了少年高血壓狀態、年齡、性別、BMI、教育程度、職業、家庭收入、運動習慣、糖尿病史、高血壓病史、腎臟病史、痛風病史、父親年齡、父親職業、父親抽菸習慣、母親年齡、母親職業、血小板、總蛋白量、白蛋白、尿酸、肌酸酐、GOT、GPT、飯前血糖、總膽固醇、高密度脂蛋白膽固醇、低密度脂蛋白膽固醇、三酸甘油脂、baPWV及IMT

拾壹、本年度之著作抽印本或手稿

Childhood hypertension in association with obesity and hyperlipidemia in the mass urine screening in Taiwan

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Summary

Background This study investigated childhood hypertension risk by body mass index (BMI) among children urine screened positive for proteinuria and/or glucosuria and/or hematuria.

Methods Between 1992 and 2000, an islandwide mass urine screening for glucosuria and proteinuria was conducted annually for near 3,000,000 students aged 6-18 years in Taiwan. Among 103,840 students identified urine test positive, further examinations found 5,792 students of hypertensive. A nested case-control analysis was performed with randomly selected 5,792 non-hypertensive controls frequency matched with sex and grade. We examined the hypertension risk associated with BMI controlling for potential covariates.

Findings The multivariate logistic regression analysis showed the odds ratio (OR) of hypertension for students of BMI$\geqq$27 kg/m^2 was 7.04 (95% confidence interval [CI] 5.87-8.46), compared with students of BMI$<$18 kg/m^2. High cholesterol (OR 2.54, 95% CI 1.71-3.79), high blood urine nitrogen (BUN) (OR 1.73, 95% CI 1.20-2.49), and high albumin (OR 1.24, 95% CI 1.05-1.47) also elevated the risk. The hypertension odds ratio increased to 23.3 (95% CI 8.42-64.6) for students with total cholesterol (TCOL)$\geqq$250 mg/dL and BMI$\geqq$27 kg/m^2, compared with students with TCOL$<$200 mg/dL and BMI$<$18 kg/m^2. The risk was 16.8 times higher (95% CI 2.12-133) for students with BUN$\geqq$23 mg/dL and BMI$\geqq$27 kg/m^2 than those with BUN$<$23 mg/dL and BMI$<$18 kg/m^2.

Interpretation Our findings show that the childhood hypertension is strongly associated with BMI and other BMI related factors.

Key Words: Body mass index, Childhood hypertension, Urine screening, Stratified analysis

Introduction

Cerebrovascular disease is the second leading cause of death in Taiwan and the heart disease the fifth. Both diseases are strongly associated with hypertension. Hypertension has also become the tenth lethal cause in Taiwan since 2003.[1] Diabetes mellitus and renal disease are common comorbidity of hypertension. As a result, hypertension can be considered as the most important attributable cause of deaths for population in Taiwan.[2] Consequently, efforts to identify the risk of hypertension and to control hypertension are crucial in cardiovascular diseases control. The vital statistics in Taiwan has shown that childhood mortalities from cerebrovascular disease and other hypertension related diseases are increasing.[3] This has attracted attention to investigate whether factors associated with childhood hypertension similar to that with adult hypertension.

The prevalence of childhood hypertension varies among populations, 4.5% among school children of 10-19 years in Houston in 2002,[4] and 5.8% among school children of 11-17 years in India in 2004.[5] Hypertension has become an important medical problem in children and adolescents in the U.S.[6,7] Muntner et al. compared NHANES data of 1999-2000 with that of 1988-1994 and found significant increases in both the mean systolic blood pressure (SBP) (1.4 mmHg) and the mean diastolic blood pressure (DBP) (3.3 mmHg) among school children aged 8-17 years.[8]

Obesity is a well known important factor leading to hypertension among middle-aged and elderly people.[9] Some studies have also demonstrated the effect of obesity with respect

to hypertension for children.[10,11] Studies show that childhood obesity has become prevalent among populations worldwide.[7,12] Ogden et al. found from the National Health and Nutrition Examination Survey (NHANES) in 1999-2000 that 15% children aged 6-11 years in the U.S. were obese.[13] The prevalence was even greater in New York City with 24% children considered as obese in 2003.[12] The prevalence rates of obesity among children aged 7-13 years in Canada increased drastically from 5% in 1981 to 17% for boys and 15% for girls in 1996.[14] Studies in Taiwan also show an increasing trend of obesity in children.[15-17] The prevalence rates of obesity in school children of 12-15 years were 10.1% in 1982 and 11.1% in 1996.[16] A later study in 2002 found that the prevalence among these school children increased to 18.5% in boys and 15.0% in girls.[18] The risk of hypertension is 3 times higher for children with BMI $\geqq$ 95th percentile than for children with BMI $<$ 90th percentile.[7]

The urine screening campaign in Taiwan has found that childhood diabetes is strongly related to obesity.[19] Compared with children of BMI $<$ 50th percentile, children of BMI $\geqq$ 95th percentile were 25.9 times more likely to be diabetic. Based on the similar population based data, this study investigated the risk of hypertension by BMI among these school children who had participated in the mass urine screening program in Taiwan with positive results for proteinuria, glucosuria, and/or hematuria.

Methods

In 1992-2000, Chinese Foundation of Health in Taipei, Taiwan, conducted an annual mass urine screening campaign for all school children of 1-12 grades in the whole Taiwan Province. Approximately 2,615,000 school students in 1992 and 2,932,000 in 1993-2000 were enrolled annually in this mass screening. Details of this screening project have been described in previous reports.[19-24] A urine strip (Hemscomistix III urine strip, Ames Division, Miles lab Ltd, Elkhnrt, Ind) was used for the screening. School children with tests two times positive of proteinuria, glucosuria, or hematuria using consequently received a third urine screening test and a general health check-up, including the fasting blood test for total cholesterol (TCOL), creatinine (CRE), blood urea nitrogen (BUN), C3 complement, albumin and antistreptolysin O (ASLO). The check-up also included anthropometry measures and blood pressure. All positive students in the third screening test were referred to their physicians for further follow-up cares. The original screening program was conducted as a public policy supported by the Taiwan Provincial Department of Health and approved by the Provincial Education Board. A letter was sent to parents to explain the program and invite the participation. The provision of the urine sample was taken as consent for the program.

Childhood hypertension was defined by age using the American Heart Association criteria of blood pressure classification for children.[25] Figure 1 shows the procedure to select hypertensive cases and controls for the present study. After excluding missing data and unreliable data, 103,840 school children were legible for this study among 192,213 students

who had received the third screening tests and the check-up, 5,792 were hypertensives. Controls were randomly selected from non-hypertensive school children frequency matched with sex and grade.

We used weight (kg) divided by the square of height (m^2) to calculated body mass index (BMI). After consulting with two cardiac physicians and with the criteria of the Taiwan Department of Health, students were stratified by BMI as underweight (BMI $<$ 18 kg/m^2), normal weight (BMI=18-23.9 kg/m^2), overweight (BMI=24-26.9 kg/m^2) and obesity (BMI $\geqq$ 27 kg/m^2).[15] Other categorical variables were TCOL ($<$200, 200-249, 250-299, and $\geqq$300 mg/dL), BUN ($<$23 and $\geqq$23 mg/dL), and CRE($<$1.3 and $\geqq$1.3 mg/dL).

We compare the means of SBP, DBP, TCOL, BUN, CRE, albumin, and ASLO between cases and controls by BMI group. Kruskal-Wallis test was used whether these factors varied by BMI level. Comparisons between hypertension cases and controls were also performed for the categorical distributions of sex, grade, BMI, TCOL, CRE, and BUN among BMI groups. We calculated adjusted odds ratios (aORs) and 95% confidence intervals (CI) for the risk of hypertension associated with all these factors using both univariate analysis and multivariate analysis. Further analyses attempted to identify whether BMI had interactions with sex, grade, TCOL, BUN, and CRE, and albumin in the hypertension risk using BMI $<$ 18 kg/m^2 as the reference group.

All analyses were performed with SAS software, version 8.0 (SAS Institute Inc., Carey, NC). Two-sided probability values <0.05 were considered statistically significant.

Role of founding source

The study sponsor did not have the role in the study design, data collection and analysis, in the writing of the report and in the decision to submit the paper for publication.

Results

The mean values of SBP, DBP, TCOL, BUN, CRE, and ASLO increased as BMI increased for both cases and controls (Table 1). The mean SBP, DBP, and TCOL levels were consistently higher in cases than in controls and significant at $\leqq 0.0002$ levels. For the BMI$\geqq$27 kg/m^2 group, cases to controls differences in SBP, DBP, and TCOL were significantly greater than for thinner groups. No significant differences were found for BUN among BMI groups, and between cases and controls.

Both the univariate and multivariate logistic regression analyses showed that students with higher BMI, cholesterol, BUN, creatinine, and albumin were at higher risk of hypertension compared controls (Table 2). The hypertension children were more prevalent in obesity than controls (13.8% vs. 3.1%, $p<0.0001$). The multivariate logistic regression showed that BMI had the strongest association with hypertension risk and followed by cholesterol, both with strong dose-response relationship ($p < 0.0001$). Albumin levels also had a significant dose-response association with the hypertension risk ($p=0.0016$). However, the risk of hypertension decreased with the increasing grade. High school students were more likely than young primary graders to become none hypertensives.

Table 3 demonstrates the estimated risk of childhood hypertension by the interaction terms between BMI and covariates in the multivariate logistic regression analysis. The odds ratio of hypertension increased as BMI increased for both girls and boys in a similar pattern. The younger children tend to have a greater association with BMI for the risk of hypertension.

Compared with 1-3 graders with the BMI $<$ 18 kg/m^2, those with the BMI of $\geqq$27 kg/m^2 had the highest risk of hypertension (OR 13.2, 95% CI 4.70-37.1). In the same BMI strata, the odds ratio decreased to 4.60 (95% CI 3.21-6.57) for 4-6 graders with BMI$\geqq$27 kg/m^2 and rose again to 7.21 (95% CI 4.52-11.5) for 10-12 graders. There was an apparent interaction between BMI and TCOL and BUN for the risk of hypertension, the risk generally increased with increasing TCOL and BUN. Compared with students at TCOL $<$ 200 mg/dL and BMI $<$ 18 kg/m^2, the risk increased to the highest for students at 250-299 mg/dL of TCOL and BMI$\geqq$27 (OR 25.1, 95% CI 7.77-81.3).

Discussion

In this mass urinary screening for grade school children, 103,840 students had at least two times of abnormal urine tests and 5792 (5.6%) of them were found to be hypertensives in the subsequent health check-up. Among significant factors associated with the adolescent hypertension, BMI was of greater importance than TCOL, BUN and albumin, particularly BMI in younger children.

Obesity is a known leading public health concern associated with hypertension.[4, 7, 11, 13, 26-30] The prevalence of obesity was higher in hypertensives than in controls in this study, contrast with those previous studies. However, our study demonstrated a much greater association, indicating the mass urine screening program has found a high risk hypertensive group among urinary test positives.

Definition of obesity affects the measure of association with blood pressure. The nature of anthropometric measures are different between Chinese and Caucasian populations. We considered a BMI ranging 18-23.9 kg/m^2 as normal and a BMI of $\geqq 27$ kg/m^2 as obesity. In the present study, the average blood pressures were higher for cases than for controls among the four BMI levels. The average SBP was 12.4 mmHg higher for obese hypertensive cases than normal weight cases while the average DBP was 4.5 mmHg higher. The corresponding differences were 10.0 mmHg and 4.1 mmHg for controls. In a Spanish study, both SBP (112.6±6.6 vs. 107.8±6.9 mmHg) and DBP (65.9±4.4 vs. 64.2±4.2 mmHg) are higher in obese children than in non-obese children of 6-16 years old.[26]

Among students aged 5-18 years in Netherlands, the hypertensive students have higher average BMI than non-hypertensive students had (22.7±3.85 vs. 20.2±2.67 kg/m^2, $p < 0.001$).[27] Among children 2-18 years in a Delaware weight management program, the hypertensive children also have higher BMI than non-hypertensive children (36.4±9.3 vs. 32.1±7.1 kg/m^2, $p<0.001$).[28] These studies are consistent that the obese children have higher SBP and DBP than normal-weight children have. A previous study in a Taiwan cross-sectional study showed that the correlation coefficients were 0.379 ($p<0.001$) between BMI and SBP and 0.252 ($p<0.001$) between BMI and DBP among 1,265 children aged 12-16 years.[11]

After reviewing 74 articles, Sorof and Daniel concluded that obese children are at a risk approximately 3-fold higher for hypertension than nonobese children.[7] Among school children ages 10-19 years in Houston, the overweight children are 3.26 times more likely than none- overweight children to be hypertensive.[4] In this study, we found that the estimated risk of hypertension for overweight children is 7.04 times as great as underweight children. The dose-response association indicates a strong effect of BMI in childhood hypertension. Neter et al. conducted a meta-analysis and indicated that blood pressure reductions were -1.05 mmHg in systolic and -0.92 mmHg in diastolic for per kilogram of body weight loss.[31] This also indicated the relationship between BMI and hypertension. Obesity often increases the risk of cardiovascular disease among adults while childhood obesity increases the risk of adulthood obesity.[29]

Hypercholesterol is also a known risk factor of hypertension.[6,27] Among students of 5-18

years age in Netherlands, the hypertensive students had higher TCOL than non-hypertensive students had (4.3±0.8 vs. 3.9±0.6 mmol/L, $p<0.01$).[27] In this study, children with higher TCOL levels are at elevated risk of hypertension. We even demonstrated an apparent interaction between BMI and TCOL for the hypertension risk. Compared with students with the lowest TCOL and BMI, students with the highest TCOL and BMI had the estimated hypertension risk increased for 23 folds. This strong dose-response interaction phenomenon has not been reported in previous studies.

High blood urea nitrogen is also a risk factor associated with high blood pressure as well. Klag et al. have demonstrated that both systolic blood pressure and diastolic blood pressure are associated with urea nitrogen for African American.[32] This study showed an addictive effect of higher BUN level in the risk of hypertension. For obese children with BMI of ≧27 kg/m^2, the OR of hypertension may aggravated from 7.03 in those with an BUN of <23 mg/dL to 16.8 in those with BUN≧23 mg/dL.

Urinary creatinine is an important marker in urine screening for kidney function which is also associated with hypertension and CVD.[33,34] The hazard risks of mortality from cardiovascular disease (CVD) and stroke increase as creatinine level increases.[35] Among students ages 5-18 years in the Netherlands study, hypertensive students have higher creatinine than non-hypertensive students have.[27] Two folds increase in hypercreatininemia can be associated with a 20 mmHg increment in blood pressure among community residents.[36] The US NHNES study also showed the prevalence of elevated creatinine level

($\geqq$1.6 mg/dL) is approximately 9 times higher in hypertensives than in nonhypertensives among American aged 17 years and older.[34] In this study, we failed to find significant association between urinary creatinine and hypertension risk, except for obese children. The elevated urinary creatinine has an addition effect on hypertension risk for these children.

Several studies have found a positive association between serum albumin and blood pressure.[37,38] The US NHNES cohort study of 7,690 men aged 40-59 years showed that the increased serum albumin is associated with not only systolic blood pressure ($p<0.0001$) but also the risk of stroke and coronary heart disease.[38] A Norwegian population study of 5071 men and women aged between 30-75 years found that the systolic blood pressure increased for 5-11 mmHg in males and 6-17 mmHg in females as the albumin levels increased for 4-5 g/dL.[39] Our study observed a significant dose-response relationship between albumin concentration and the hypertension risk. This relationship was enhanced for obese children.

The effect of sex on blood pressure could not be well observed in this study because controls were frequency matched with cases. In contrast, the older students tend to have a lowered hypertension risk. Older students were less likely obese than younger students (data not shown). Furthermore, the results of this study could not be generalized because cases and controls were selected from children positive with proteinuria, hematuria and/or glucosuria in this mass urine screening campaign. We believe that the measured odds ratios of hypertension would be greater if we compared cases with healthy controls.

In summary, our study proved a strong evidence from the strong dose-response relationship

between hypertension and BMI among school children positive in urine screening. Total cholesterol, urea nitrogen, and creatinine also appear to be independent predictors having interaction effect with BMI for hypertension risk. In this study population, obesity is the most important marker in the association with the hypertension, followed by hyperlipidemia, and elevated urea nitrogen, creatinine and albumin.

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Conflict of interest: none declared.

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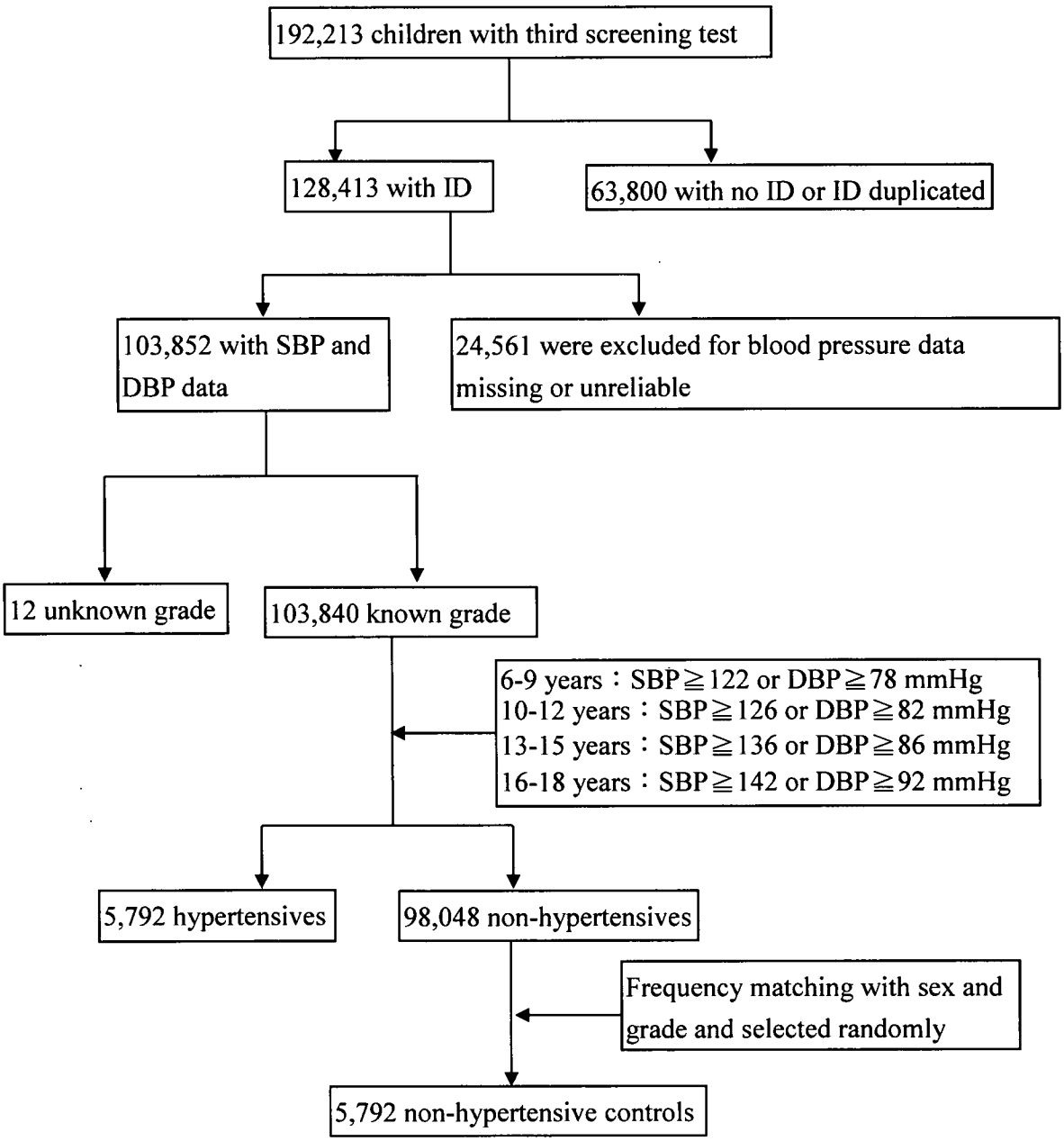

Figure 1.Procedure to select hypertensive cases and controls

Table 1: Comparison in means for factors associated with body mass index between cases and controls†

Variable	Body mass index, kg/m^2				*p* for trend
	<18 n=4,461 Mean ± SD	18-23.9 n=5,292 Mean ± SD	24-26.9 n=724 Mean ± SD	≧27 n=967 Mean ± SD	
SBP (mmHg)					
Cases	118.3 ± 12.6	125.3 ± 12.5	129.4 ± 12.6	137.7 ± 15.1	<0.0001
Controls	102.2 ± 12.8	109.9 ± 12.5	113.6 ± 12.3	119.9 ± 15.4	<0.0001
Difference	16.17	15.40	15.74	17.82	0.5589‡
*p***	<0.0001	<0.0001	<0.0001	<0.0001	
DBP (mmHg)					
Cases	86.6 ± 6.55	88.8 ± 6.13	89.8 ± 5.93	93.3 ± 8.10	<0.0001
Controls	63.9 ± 9.28	68.4 ± 8.91	69.6 ± 8.40	72.5 ± 8.57	<0.0001
Difference	22.65	20.38	20.13	20.79	<0.0001‡
*p***	<0.0001	<0.0001	<0.0001	<0.0001	
TCOL (mg/dL)					
Cases	172.0 ± 47.0	168.1 ± 48.3	181.1 ± 49.4	189.0 ± 53.9	<0.0001
Controls	164.6 ± 34.3	161.2 ± 37.6	167.5 ± 51.1	173.9 ± 35.5	0.4248
Difference	7.395	6.892	13.65	15.08	<0.0001‡
*p***	<0.0001	<0.0001	<0.0001	0.0002	
BUN (mg/dL)					
Cases	12.8 ± 7.19	12.4 ± 6.17	12.7 ± 4.02	12.6 ± 3.53	0.5674
Controls	12.6 ± 18.3	12.3 ± 4.03	12.6 ± 3.31	12.5 ± 3.77	0.6128
Difference	0.137	0.115	0.078	0.075	0.7495‡
*p***	0.9452	0.3983	0.8506	0.9342	
CRE (mg/dL)					
Cases	1.02 ± 0.54	1.08 ± 0.42	1.09 ± 0.24	1.12 ± 0.25	<0.0001
Controls	0.98 ± 0.21	1.07 ± 0.24	1.09 ± 0.23	1.11 ± 0.23	<0.0001
Difference	0.038	0.007	-0.0008	0.01	0.0005‡
*p***	0.2877	0.6863	0.9794	0.6853	
Albumin					
Cases	4.29 ± 0.46	4.37 ± 1.08	4.33 ± 0.49	4.40 ± 0.42	0.0039
Controls	4.42 ± 6.00	4.34 ± 0.41	4.36 ± 0.41	4.35 ± 0.39	0.5550
Difference	-0.1306	0.033	-0.0323	0.046	0.2604‡
*p***	0.1876	0.0802	0.7076	0.2755	
ASLO					
Cases	145.5 ± 107.2	161.0 ± 105.0	161.5 ± 102.8	168.3 ± 103.6	<0.0001
Controls	151.9 ± 109.7	156.8 ± 106.2	160.0 ± 109.4	179.8 ± 105.9	<0.0011
Difference	-6.4295	4.213	1.468	-11.545	0.7154‡
*p***	0.0529	0.1084	0.7622	0.2217	

Abbreviation: SBP=systolic blood pressure, DBP=diastolic blood pressure, TCOL=total cholesterol, BUN=blood urea nitrogen, CRE=creatinine, ASLO=Antistreptolysin O

*Kruskal-Wallis test of BMI groups, **Wilcoxon rank sum test between cases and controls

†140 BMI data missing

‡Test for interaction between difference and BMI status

Table 2: The comparison between cases and controls by sex, grade, body mass index and selected physiological examinations with univariate and multivariate logistic regression

Factors	Cases N=5,792	Controls N=5,792	Univariate	Multivariate
Sex	(%)	(%)	OR (95%CI)	OR (95%CI)
Female	(58.7)	(58.7)	Reference	Reference
Male	(41.3)	(41.3)	1.00 -	0.97 (0.89-1.05)
Grade, years				
≦3	(20.2)	(20.2)	Reference	Reference
4-6	(25.4)	(25.4)	1.00 -	0.83 (0.74-0.93)
7-9	(48.9)	(48.9)	1.00 -	0.74 (0.66-0.82)
10-12	(5.5)	(5.5)	1.00 -	0.53 (0.43-0.64)
p for trend			1	<0.0001
BMI, kg/m^3				
BMI<18	(32.2)	(45.8)	Reference	Reference
18≦ BMI<24	(45.6)	(46.9)	1.38 (1.27-1.50)	1.51 (1.38-1.64)
24≦ BMI<27	(8.5)	(4.2)	2.86 (2.42-3.37)	3.06 (2.58-3.63)
BMI ≧27	(13.8)	(3.1)	6.40 (5.38-7.62)	7.04 (5.87-6.46)
p for trend			<0.0001	<0.0001
Cholesterol, mg/dL				
<200	(81.7)	(88.5)	Reference	Reference
200-249	(14.1)	(9.8)	1.56 (1.39-1.75)	1.28 (1.13-1.45)
≧250	(4.2)	(1.6)	2.71 (2.13-3.44)	2.17 (1.69-2.79)
p for trend			<0.0001	<0.0001
C3 complement				
>67	(99.4)	(99.5)	Reference	Reference
≦67	(0.6)	(0.5)	1.22 (0.74-2.01)	1.24 (0.73-2.11)
BUN, mg/dL				
<23	(98.4)	(99.1)	Reference	Reference
≧23	(1.6)	(0.9)	1.90 (1.35-2.68)	1.73 (1.20-2.49)
Creatinine, mg/dL				
<1.3	(82.3)	(83.9)	Reference	Reference
≧1.3	(17.7)	(16.1)	1.12 (1.01-1.23)	1.04 (0.93-1.16)
Albumin, g/dL				
<4.5	(59.9)	(63.5)	Reference	Reference
4.5-4.9	(33.9)	(31.4)	1.15 (1.06-1.24)	1.13 (1.04-1.23)
≧5.0	(6.3)	(5.1)	1.29 (1.10-1.52)	1.24 (1.05-1.47)
p for trend			0.0001	0.0016
ASLO, IU/mL				
<200	(56.3)	(56.6)	Reference	Reference
≧200	(43.7)	(43.4)	1.01 (0.94-1.09)	0.99 (0.92-1.07)

Missing data: 140 in BMI, 85 in cholesterol, 91 in C3 complement, 86 in BUN, 87 in creatinine, 92 in albumin, 89 in ASLO.

BMI=body mass index, BUN=blood urea nitrogen, ASLO=Antistreptolysin O

Tables 3: Odds ratios and 95% confidence intervals for the risk of hypertension associated with body mass index by sex, grade, total cholesterol, blood urea nitrogen, creatinine, and albumin

	Body mass index, kg/m^2			
	<18	18-23.9	24-26.9	≧27
	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)
Sex				
Female	1 -	1.48 (1.32-1.65)	3.46 (2.75-4.34)	6.94 (5.42-8.90)
Male	0.96 (0.84-1.08)	1.49 (1.32-1.68)	2.51 (1.96-3.22)	6.85 (5.31-8.85)
Combined	1 -	1.51 (1.38-1.64)	3.06 (2.58-3.63)	7.04 (5.87-8.46)
Grade, years				
≦3	1 -	2.07 (1.71-2.52)	6.76 (3.51-12.0)	13.2 (4.70-37.1)
4-6	0.91 (0.78-1.06)	1.48 (1,27-1.71)	2.48 (1.81-3.41)	4.60 (3.21-6.57)
7-9	0.91 (0.78-1.05)	1.18 (1.04-1.34)	2.55 (2.03-3.21)	5.44 (4.30-6.89)
10-12	0.91 (0.56-1.47)	0.73 (0.57-0.93)	1.25 (0.70-2.22)	7.21 (4.52-11.5)
Total cholesterol, mg/dL				
<200	1 -	1.52 (1.39-1.66)	2.93 (2.43-3.53)	6.71 (5.46-8.24)
200-249	1.23 1.01-1.49	1.89 (1.57-2.28)	4.70 (3.08-7.17)	9.84 (6.86-14.1)
≧250	2.40 1.60-3.59	2.70 (1.87-3.90)	8.23 (3.41-19.9)	23.3 (8.42-64.6)
Urea nitrogen, mg/dL				
<23	1 -	1.51 (1.39-1.65)	3.04 (2.56-3.61)	7.03 (5.85-8.44)
≧23	1.81 (1.08-3.02)	2.21 (1.25-3.89)	12.2 (1.53-97.3)	16.8 (2.12-133)
Creatinine, mg/dL				
<1.3	1 -	1.54 (1.41-1.69)	3.15 (2.61-3.81)	6.92 (5.63-8.49)
≧1.3	1.15 (0.94-1.40)	1.52 (1.31-1.76)	3.00 (2.11-4.28)	8.10 (5.69-11.5)
Albumin, g/dL				
<5.0	1 -	1.54 (1.41-1.68)	3.06 (2.57-3.65)	6.81 (5.41-8.57)
≧5.0	1.40 (1.07-1.84)	1.54 (1.22-1.95)	4.31 (2.14-8.66)	7.21 (5.42-9.59)

aOR, adjusted odds ratio; CI, confidence interval