

Relationship of Thickness of Carotid Artery according to Smoking and Drinking in University Students

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대학생들의 흡연 및 음주에 따른 목동맥 두께의 상관성

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This study examined the associations of smoking, alcohol drinking habits and both with the carotid intima-media thickness (CIMT) in university students. This study was performed using a CAGE (test for alcohol: cutting down, annoyance by criticism, guilty feeling, and eye-openers) questionnaire, FTND (the Fagerstrom test for nicotine dependence) questionnaire, and CIMT of university students. No statistically significant differences were observed among the CIMT results according to each CAGE level classified into 3 groups. The results of CIMT according to the FTND smoking categorization showed that the smoking group was higher than nonsmoking group ($P < 0.01$). A statistically significant difference was observed between the left and right CIMT regarding smoking and drinking ($P < 0.01$). In the only drink risk group, the left CIMT (19.84 rank) showed a low-ranking. The CIMT on the left (42.38 rank) and right (42.81 rank) showed high scores in the group with only the risk of smoking ($P < 0.01$). These results suggested that there are distinct differences in CIMT and relevant risk factors between smokers and drinkers, particularly among those with a high smoking status. This study had several limitations: the study population was small; the relatively young age of the study subjects; and limited of focus on smoking, drinking and CIMT. In conclusion, cigarette smoking significantly exacerbates the adverse effects and higher CIMT on the subclinical atherosclerosis risk in young adults, which underscores the importance of prevention and cessation of cigarette smoking in young adults.

Key words: Carotid Intima-Media Thickness, Drinking, Smoking

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INTRODUCTION

Numerous studies have shown the serious adverse effects of lifelong smoking, increased mortality rates from chronic heavy drinking [1]. Most people perceive the combined effects on health of smoking and drinking. Cigarette smoking is also known to increase the risk of

cardiovascular diseases. Cigarette smoking has been well-documented as a risk factor for ischemic stroke in general [2]. It is also well-reported that smoking degrades carotid IMT, a well-known marker for atherosclerosis [3, 4]. Suggested chronic effects of alcohol on the vascular system include favorable changes in lipid profile and other cardiovascular biomarkers, as well as deleterious changes

in arterial hypertension, peripheral artery disease and atherosclerosis [5-7]. Ischemic heart disease (IHD) and ischemic stroke (IS) are posing major burdens to global health [8]. Atherosclerosis is an important pathologic cause of cardiovascular (CV) and cerebrovascular diseases. Additionally, CV and cerebrovascular diseases are the leading causes of mortality in humans and can have significant impacts on morbidity. Therefore, the early prevention of CV and cerebrovascular diseases has become a focus of current research. Preclinical atherosclerosis has been related to higher coronary heart disease and stroke rates [9]. Cardiovascular disease (CVD) is the leading cause of death and a major cause of disability worldwide. A growing body of evidence indicates that the process of atherosclerosis begins at young age [10, 11]. In similar studies, modifiable lifestyle factors, such as nonsmoking, moderate alcohol consumption, have been consistently linked to a reduced cardiovascular risk [12, 13]. CIMT is a simple and non-invasive method of the assessment of subclinical atherosclerosis and has been shown to be an independent predictor of cardiovascular (CV) disease risk [14]. In this reason, carotid intima-media thickness (CIMT) ultrasonography may represent an accessible and reliable method to detect subclinical atherosclerosis [15]. Measuring carotid artery intima-media thickness (CIMT) is currently a standard diagnostic procedure in assessing cardiovascular risk (CVR) in adults [16]. Additionally, CIMT was positively associated with smoking and alcohol consumption in men [17, 18]. The purpose of the study was to investigate the associations among smoking habits, alcohol drinking habits and both by the carotid intima-media thickness (IMT) in a university student. However, the limitations of this study have been limited studies focusing on the association among smoking, drinking and CIMT. Even so, identifying risk factors associated with CIMT will be contributed for the prevention and treatment of early atherosclerosis.

MATERIALS AND METHODS

1. Sample and setting

All datas were from the questionnaire, an individual participant data analysis established to determine the incremental value of CIMT in finding smoking and drinking habits. This study was performed of CAGE (Cutting down, Annoyance by criticism, Guilty feeling and Eye-openers) questionnaire [19], FTND (The Fagerstrom Test for Nicotine Dependence) questionnaire [20], CIMT and general characterizes of university students at Suwon-si, Gyeonggi-do, Korea. In this paper, by using the survey data were completed from 2015 to December 2016. The participants in this study were 127 (male: 40, female: 87) university students without the other disease. The questionnaire to assess was administered on students in class room setting. The purpose of this study was to explain the purpose of the study to all participants, to inform the participants about the research method, duration, side effects, risk factors, personal information and confidentiality. Written informed consent was obtained from all participants of this study.

2. CAGE

The CAGE questionnaire was developed in 1968 at North Carolina Memorial Hospital to combat the paucity of screening measures to detect problem drinking behaviors [19].

The CAGE questionnaire asks the following questions:

- 1) Have you ever felt you needed to cut down on your drinking?
- 2) Have people annoyed you by criticizing your drinking?
- 3) Have you ever felt guilty about drinking?
- 4) Have you ever felt you needed a drink first thing in the morning (Eye-opener) to steady your nerves or to get rid of a hangover?

Choose "Yes", Score 1, Choose "No", Score 0, calculate all numbers and record into "Total"

If "Yes" to one: drinking at a risk level, if "Yes" to 2 or more: drinking at a problematic level.

3. FTND

The current version includes self-administered questionnaire consists of 6 questions, and examines nicotine consumption and intake habits in those that smoke cigarettes. It is used as a screening instrument that assesses nicotine dependence in adults who are currently smokers or have been in the past two years. Level of nicotine dependence is scored on a scale from 0~10, with 0~2: very low dependence and 8~10: very high dependence [20].

The FTND questionnaire asks the following questions:

- 1) How soon after you wake up do you smoke your first cigarette?
 "Within 5 minutes": score 3, "6~30 minutes": score 2, "31~60 minutes": score 1, "After 60 minutes": score 0
- 2) Do you find it difficult to refrain from smoking in places where it is forbidden such as church, the library, or movie theatres?
 "Yes": score 1, "No": score 0
- 3) Which cigarette would you hate most to give up?
 "the first in the morning": score 1, "No": score 0
- 4) How many cigarettes do you smoke? (20 cigarettes are in a pack)
 "31 or more": score 3, "21~30": score 2, "11~20": score 1, "10 or less": score 0
- 5) Do you smoke more frequently during the first hours after waking than the rest of the day?
 "Yes": score 1, "No": score 0
- 6) Do you smoke if you are so ill that you are in bed most of the day?
 "Yes": score 1, "No": score 0

Add up the scores from the questionnaire;

1~2: low dependence, 3~4: low to mod dependence, 5~7: moderate dependence, 8+: high dependence

4. Carotid ultrasonography test

The ultrasound machine (Medison Accuvix V20 Prestige 3D Live Ultrasound Scanner; MEDISON, South Korea) equipped with 7.5 MHz linear transducer was used to measure the CIMT. CIMT was measured by B mode

ultrasound having an electric transducer on both the right and left extra cranial carotid arteries. Study subjects were facing the left side and laid down comfortably to set the probe around the central part of the sternocleidomastoid, which is below the thyroid cartilage. On a longitudinal, two-dimensional ultrasound image of the carotid artery, the anterior (near) and posterior (far) walls of the carotid artery are displayed as two bright white lines separated by a hypo echogenic space. We assessed the common carotid arterial structures at a point 1 cm proximal to the carotid bifurcation bulb region using longitudinal images. Plaque score was the sum of the maximum IMT measured at each of 3 locations: the distal common carotid region 2 cm proximal to the bifurcation bulb region; the bifurcation bulb region; and the proximal internal carotid artery region 1 cm distal to the bifurcation bulb region, including both near and far sides of the carotid arteries and CIMT was measured in centimeter (cm).

5. Statistical analysis

All statistical analyses were performed using SPSS, PC, and Version 21.0 (SPSS, Chicago, USA) program for windows. We used the Kolmogorov-Smirnov test to evaluate normal distribution. Descriptive statistics (n, minimum, maximum, mean, standard deviation) outlined the variables used within the study. Every analysis was performed on observed data. A single categorical variable is described by frequency distribution. A cross tabulation with Pearson (Chi) test was used to measure differences in two categorical variables between two groups for stressed group and stress free groups. Differences in baseline characteristics between general characteristics and personal variables were tested for significance using the t-test, ANOVA or chi-square test, Mann-Whitney, Wilcoxon rank sum test. In addition, the Spearman correlation analysis was performed according to the correlation. All statistical significance level was presented as proportions and mean with 95% confidence intervals (set as $P < 0.05$).

RESULTS

1. General characteristics

The subjects were 147 [males 60 (40.8%) and females 87 (59.2%)]. Their total average age was 22.14 ± 2.15 (males ages 23.28 ± 2.12 years, females 21.34 ± 1.78 years). Their average height was 167.73 ± 8.77 cm, the average weight was 59.12 ± 11.40 kg, the average BMI of the subjects was 20.86 ± 2.65 . All variable was significant difference between male and female groups ($P < 0.01$). The subjects' height, weight and BMI showed an irregular distribution and age was normal distribution (Table 1).

2. CAGE questionnaire results

The distribution of the participants by the CAGE and its level was tabulated as shown in Table 2. There was a

statistically significant difference between male and female in "Have people annoyed you by criticizing your drinking?" There was no significantly difference between male and female according to the other three questions. The drinking classification according to the score was described in Table 2. As a result of drinking classification, 32 (21.8%) were normal, drinking at a risk level (55; 38.1%), drinking at a problematic level (24; 16.4%). There was no significantly difference among normal, drinking at a risk level and drinking at a problematic level results according to CAGE level.

3. FTND questionnaire results

The distribution of the participants by the FTND and its level was tabulated as shown in Table 3. There was no statistically significant difference between male and

Table 1. General characteristics of study

Variable	Total N=147	Male	Female	Z/U [†] , F/t ^{††}
		N=60 (40.8%)	N=87 (59.2%)	
M±SD				
Age	22.14±2.15	23.28±2.12	21.34±1.78	2.48**/1100.50** [†]
Height (cm)	167.73±8.77	176.02±5.53	162.02±5.36	0.00/15.36** ^{††}
Weight (kg)	59.12±11.40	68.98±9.47	52.41±6.62	8.64**/11.34** [†]
BMI (kg/m ²)	20.86±2.65	22.17±2.61	19.95±2.28	2.47/5.45** ^{††}

** $P < 0.01$, [†] P -values were calculated by Kolmogorov-Smirnov, Mann-Whitney, ^{††} P -values were calculated by t-test. Abbreviations: BMI, body mass index; Z, Kolmogorov-Smirnov value; U, Mann-Whitney value; F, Fisher distribution value; t, student-t value.

Table 2. CAGE questionnaire results of study

N=147, N (%)

Questionnaire	Yes			No			χ^2
	Male	Female	Total	Male	Female	Total	
Have you ever felt you needed to cut down on your drinking?	24 (16.3)	37 (25.2)	61 (41.5)	36 (24.5)	50 (34.0)	86 (58.5)	0.76
Have people annoyed you by criticizing your drinking?	11 (7.5)	33 (22.4)	44 (29.9)	49 (33.3)	54 (36.7)	103 (70.1)	6.50*
Have you ever felt guilty about drinking?	13 (8.8)	27 (18.4)	40 (27.2)	47 (32.0)	60 (40.8)	107 (72.8)	1.57
Have you ever felt you needed a drink first thing in the morning (Eye-opener) to steady your nerves or to get rid of a hangover?	3 (2.0)	3 (2.0)	6 (4.1)	57 (38.8)	84 (57.1)	141 (95.9)	0.18

Level	Score	Male	Female	Total	χ^2
Normal	Total score "0"	67 (45.6)	35 (23.8)	32 (21.8)	3.46
Drinking at a risk level	Total score "1"	14 (9.5)	21 (14.3)	35 (23.8)	
	Total score "2"	6 (4.1)	15 (10.2)	20 (14.3)	
	Total score "3"	7 (4.8)	15 (10.2)	22 (15.0)	
Drinking at a problematic level	Total score "4"	1 (0.7)	1 (0.7)	2 (1.4)	

P -values were calculated by chi-square test.

Table 3. FTND questionnaire results of study

N=127, N (%)

Questionnaire	Male				Female				χ^2
	60 m <	31~60 m	5~30 m	Within 5 m	60 m <	31~60 m	5~30 m	Within 5 m	
How soon after you wake up do you smoke your first cigarette?	38 (25.9)	13 (8.8)	6 (4.1)	3 (2.0)	87 (59.2)	0 (0.0)	0 (0.0)	0 (0.0)	37.51**
Do you find it difficult to refrain from smoking in places where it is forbidden such as church, the library, or movie theatres?	No		Yes		No		Yes		10.66**
	53 (36.1)		7 (4.8)		87 (59.2)		0 (0.0)		
Which cigarette would you hate most to give up?	The first in the morning		Any other		The first in the morning		Any other		15.56**
	50 (34.0)		10 (6.8)		87 (59.2)		0 (0.0)		
How many cigarettes do you smoke? (20 cigarettes are in a pack)	<10	11~20	21~30	31<	<10	11~20	21~30	31<	24.22**
	45 (30.6)	15 (10.2)	0 (0.0)	0 (0.0)	87 (59.2)	0 (0.0)	0 (0.0)	0 (0.0)	
Do you smoke more frequently during the first hours after waking than the rest of the day?	No		Yes		No		Yes		1.46
	59 (40.1)		1 (0.7)		87 (59.2)		0 (0.0)		
Do you smoke if you are so ill that you are in bed most of the day?	No		Yes		No		Yes		20.68**
	57 (32.0)		13 (8.9)		87 (59.2)		0 (0.0)		
Nicotine dependence									
None	34 (23.1)				87 (68.5)				
Low dependence	Total score "1~2"	12 (8.2)				0 (0.0)			
Low to moderate dependence	Total score "3~4"	7 (4.7)				0 (0.0)		45.80**	
Moderate dependence	Total score "5~7"	6 (4.1)				0 (0.0)			
High dependence	Total score "8+"	1 (0.7)				0 (59.2)			

** $P < 0.01$.

P -values were calculated by chi-square test.

Table 4. Measurement of CIMT according to study

Classified	Total	Male	Female	$Z/U/W$
		N=60 (40.8%)	N=87 (59.2%)	
		M±SD (Rank)		
Left CIMT (cm)	0.046±0.045	0.055±0.013 (104.96)	0.039±0.006 (52.65)	-7.54/752.50/4580.50**
Right CIMT (cm)	0.051±0.051	0.066±0.103 (100.25)	0.040±0.006 (55.90)	-6.32/1035.00/4863.00**

** $P < 0.01$.

P -values were calculated by Kolmogorov-Smirnov, Mann-Whitney, Wilcoxon test.

Abbreviation: CIMT, carotid artery intima-media thickness; See Table 1.

female in "Do you smoke more frequently during the one hour after waking up than the rest of the day?" There was significantly difference between male and female according to the other five questions ($P < 0.01$). The smoking dependence classification according to the score was described in Table 3. As a result of smoking dependence classification, only male (34; 23.1%) were none, low dependence (12; 8.2%), low to moderate dependence (7; 4.7%), moderate dependence (6; 4.1%), high dependence

(1; 0.7%). There was significantly difference among dependence level to FTND ($P < 0.01$).

4. Measurement of CIMT

As a result, the right CIMT (0.051±0.051 cm) was higher than the left CIMT (0.046±0.045 cm) in the subject, and the male (left: 104.96 rank, Right: 100.05 rank) was higher in all CIMT side than the female (left: 52.65 rank, Right: 55.90 rank), and statistically significant ($P < 0.01$). The

descriptive statistics for CIMT are presented in Table 4.

5. Differences by CIMT according to CAGE and FTND total score

The results of the CIMT according to the CAGE classification are shown in Table 5. There was no statistically significant difference among CIMT results according to each CAGE level classified into 3 stages. The results of the CIMT according to the FTND classification are shown in Table 6. The results of CIMT according to FTND smoking categorization showed that smoking group was higher than none smoking group ($P < 0.01$). The results of the CIMT according to the drinking and smoking classification are shown in Table 7. There was significantly difference between left and right CIMT regarding smoking

and drinking. In the only drink risk group, the left CIMT (19.84 rank) showed a low-ranking. The CIMT on the left (42.38 rank) and right (42.81 rank) showed high scores in the group with only the risk of smoking. There were significantly difference in the CIMT results between the subjects who were not at risk of smoking and drinking, only had the risk of drinking, only had the risk of smoking and who were at risk of both smoking and drinking ($P < 0.01$).

DISCUSSION

This study was the research to investigate the association between CIMT and non-health behaviors including smoking and drinking in Korean young students

Table 5. Differences by CIMT and general characteristics according to CAGE (cm)

Classified level	N (%)	M±SD (Rank)		χ^2
		Left CIMT [†]	Right CIMT ^{††}	
Normal	67 (45.6)	0.047±0.012 (79.59)	0.048±0.012 (79.28)	2.316 [†] /2.322 ^{††}
Drinking at a risk level	35 (23.8)	0.044±0.012 (67.90)	0.044±0.011 (66.61)	
Drinking at a problematic level	45 (30.6)	0.044±0.012 (70.44)	0.061±0.012 (71.88)	

[†]Left CIMT, ^{††}Right CIMT.

No statistically significant difference by Kruskal-Wallis one-way analysis of variance.

Abbreviation: See Table 3.

Table 6. Differences by CIMT and general characteristics according to FTND

Classified	N (%)			$Z/U/W$
	Total 60 (100.0)	None smoking 34 (56.7)	Smoking 26 (43.3)	
	M±SD (Rank)			
Left CIMT (cm)	0.055±0.013	0.048±0.010 (22.94)	0.062±0.013 (40.38)	-3.88/185.00/780.00**
Right CIMT (cm)	0.067±0.103	0.071±0.137 (24.26)	0.060±0.014 (38.65)	-3.226/230.00/825.00**

* $P < 0.05$, ** $P < 0.01$.

P -values were calculated by Kolmogorov-Smirnov, Mann-Whitney, Wilcoxon test.

Abbreviation: See Table 1, 3.

Table 7. Differences by CIMT and general characteristics according to drinking and smoking risk

Classified	N (%)				χ^2
	None 19 (31.7)	Only drinking 16 (26.7)	Only smoking 13 (21.7)	Both 12 (20.0)	
	M±SD (Rank)				
Left CIMT(cm)	0.050±0.008 (26.24)	0.047±0.011 (19.84)	0.064±0.014 (42.38)	0.060±0.013 (38.58)	16.057**
Right CIMT (cm)	0.050±0.008 (27.21)	0.094±0.201 (20.63)	0.064±0.013 (42.81)	0.058±0.016 (35.54)	13.784**

** $P < 0.01$.

No statistically significant difference by Kruskal-Wallis one-way analysis of variance.

Abbreviation: See Table 3.

from a one university. The principal finding of our study was that CIMT found difference with related to smoking and drinking. This is consistent with previous researches [3, 4, 21]. Much of the existing literature uses data with alcohol or smoking measured at only single variable but we had taken a mixed group of “drinking and smoking” as the subjects group. Ours is the first study to look at non-health behavior of drinking and smoking and risk of CIMT, which makes drawing comparisons between our work and others difficult. Smoking status and drinking were collected from self-reported questionnaires. For this study, CIMT was compared using a smoking dependence questionnaire and a drinking questionnaire. The CAGE questionnaire is a series of four questions that doctors can use to check for signs of possible alcohol dependency. The CAGE questionnaire, among other methods, has been extensively validated for use in identifying alcoholism [19]. The FTND is a standard instrument for assessing the intensity of physical addiction to nicotine. The test was designed to provide an ordinal measure of nicotine dependence related to cigarette smoking [20].

The CIMT can be used as a surrogate marker for cardiovascular health, also drinking and smoking are risk factor for cardiovascular disease. The CIMT is a simple and non-invasive method of the assessment of subclinical atherosclerosis and has been shown to be an independent predictor of cardiovascular disease risk [22, 23]. The results of this study showed that there was no difference between men and women. However, the answer frequency of “Have people annoyed you by criticizing your drinking?” question was 70.1% for female students, which was higher than male students and statistically significant ($P<0.05$). Numerous studies have demonstrated that patients with drinking relative have increased CIMT and flow-mediated dilation, which are early markers of atherosclerosis and are associated with an increased risk of cardiovascular disease. Drinking causes hepatic steatosis which plays an important role in the increased risk for cardiovascular disease. A lot of studies have demonstrated that patients with drinking relative have increased CIMT and flow-mediated dilation, which are early markers of

atherosclerosis and are associated with an increased risk of cardiovascular disease [24-26]. However, the relation between drinking and CIMT has not been proven in this study. Probably the cause, relatively young of the study subjects may lead to these results. Cigarette smoking significantly exacerbates the adverse effects of age and metabolic syndrome on subclinical atherosclerosis in young adults, which underscores the importance of prevention and cessation of cigarette smoking behavior in the young [27]. These results are consistent with this study. This study, cigarette smokers (left CIMT: 40.38 rank, right CIMT: 38.65 rank) had greater CIMT than nonsmokers (left CIMT: 22.94 rank, right CIMT: 24.26 rank), indicating that these cigarette smokers had increased atherosclerosis risk. However, smoking and drinking condition variable and CIMT are very few previous studies, makes researching comparisons between our work and others difficult. As a result, it can be easily inferred that cigarette smokers not only have increased CIMT. Further, the inclusive effect variable of smoking and drinking on CIMT was vastly increased from only smoking (left: 42.38 rank, right: 42.81 rank) in only drinking to (left: 19.84 rank, right: 20.63 rank). This study has currently shown cigarette smokers have higher CIMT than alcohol drinkers and also, shown smoker have higher CIMT than both smoking and drinking.

These findings suggest that there are distinct differences in mean CIMT and relevant risk factors between smokers and drinkers, especially among those with a high smoking status. There were several limitations in this study. First, this study population was small and from university students in Korea, so the findings may not be generalized to the Korea population. Second, relatively young of the study subjects may lead to a selection bias. Third, the limitations of this study have been a limited studies focusing on the association among smoking, drinking and CIMT.

However, measuring CIMT and measuring the subjects' smoking and drinking habits were not an easy task. The reason why drinking students have higher CIMT than healthy habits students remains to be studied further.

In conclusion, cigarette smoking significantly exacerbates the adverse effects and higher CIMT on subclinical atherosclerosis risk in young adults, which underscores the importance of prevention and cessation of cigarette smoking behavior in the young. Futures continuous studies should be conducted to variety experiment the influences of smoking and generalized drinking on CIMT when these are many continuous variables.

요약

이 연구의 목적은 대학생의 CIMT (목동맥 내막-중막 두께)와 흡연 습관, 음주 습관 및 두 가지 연관성을 조사하는 것이다. 이 연구는 CAGE (음주 관련: 절주, 비판에 대한 반감, 죄책감, 해장) 설문지, FTND (Fagerstrom Test for Nicotine Dependence) 설문지, 대학생들의 CIMT에 대하여 수행되었다. 세 군으로 분류된 각 음주 수준에 따른 CIMT 결과 간에는 통계적으로 유의한 차이가 없었다. FTND 흡연 분류에 따른 CIMT의 결과는 흡연 군이 비 흡연 군보다 높았다($P < 0.01$). 흡연과 음주는 좌우 CIMT 간에는 통계적으로 유의한 차이가 있었다($P < 0.01$). 음주의 위험만 있는 군에서 왼쪽 CIMT (19.84 순위)는 낮은 순위를 보였다. 왼쪽(42.38 순위)과 오른쪽(42.81 순위)의 CIMT는 흡연 위험만 있는 집단에서 높은 순서를 보였다($P < 0.01$). 이 연구 결과 흡연자와 음주자 사이의 평균 CIMT, 특히 흡연 상태가 높은 사람들 사이에 뚜렷한 차이가 있음을 시사한다. 이 연구에는 몇 가지 제한 점이 있다. 첫째, 작은 연구 대상 두 번째, 대상자가 어리고, 셋째, 흡연, 음주 및 CIMT에만 중점을 두었다. 결론적으로, 흡연은 젊은 성인에서 무증상 아테롬성 동맥 경화 위험인자에 대한 부작용과 CIMT를 현저하게 악화시키며 젊은 성인에서 금연의 중요성이 강화되어야 한다.

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Conflict of interest: None

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