Serum HCV RNA Level Is Not Associated with Insulin Resistance and Metabolic Syndrome in Chronic Hepatitis C Patients with Genotype 1 or 2 Infection

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Background: Previous reports have indicated that insulin resistance (IR) is associated with chronic hepatits C virus (HCV) infection. However, the correlations between IR, metabolic syndrome (MS), and serum HCV RNA levels are still controversial. The aim of this study was to determine the relationships between IR, MS, and HCV RNA in patients with chronic genotype 1 or 2 HCV infection.

Methods: One hundred and twenty subjects with chronic genotype 1 or 2 HCV infection with complete clinical data were prospectively enrolled. Baseline and laboratory data were collected and analyzed. IR was defined as a homeostatic model assessment- IR (HOMA-IR) score > 2.5.

Results: Of the 120 patients, 47 (39.2%) had a HOMA-IR > 2.5, and 42 (35%) met the criteria for MS. IR was significantly associated with a high body mass index ($p < 0.0001$), high waist circumference ($p < 0.0001$) and high triglyceride level ($p = 0.025$). IR was an independent predictor of MS. However, in multivariate linear regression analysis, the serum HCV RNA level was not significantly different in chronic hepatitis C patients with or without IR ($p = 0.761$), and with or without MS ($p = 0.292$).

Conclusions: IR and MS are not uncommon in patients with chronic hepatitis C. The serum HCV RNA level is not associated with the presence of IR or MS in chronic hepatitis C patients with genotype 1 or 2 infection. The impact of hepatitis C virus on IR is not dose responsive.

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Key words: hepatitis C virus (HCV), RNA level, insulin resistance, metabolic syndrome

Hepatitis C virus (HCV), which infects approximately 200 million people worldwide, is a major cause of liver disease, ranging from hepatitis and cirrhosis to hepatocellular carcinoma. Chronic HCV infection not only affects the liver, but can involve many other organs and systems. Several extra-hepatic diseases, including dermatologic, hematologic, autoimmune, and metabolic disorders, have been associated with chronic HCV infection.[1] A systematic review and meta-analysis pointed out

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that there is an increased risk of diabetes mellitus (DM) in patients with HCV infection compared with non-infected controls, suggesting that HCV has a potential direct role in promoting the development of DM.[2] Many studies also have indicated that patients with chronic HCV infection are at an increased risk of developing insulin resistance (IR) and DM compared with non-infected individuals or patients with hepatitis B virus infection.[3-5] Chronic HCV infection represents an entity of metabolic diseases that induce insulin resistance.[6,7]

IR is defined as cells becoming resistant to the action of insulin. It provides a protective mechanism to maintain a normal insulin level. Previous studies had shown that IR is an early regulatory event in chronic HCV infection that accelerates liver fibrosis,[8,9] and results in an impaired response to antiviral treatment in some genotypes.[10,11] Some research has suggested IR is correlated with higher serum HCV RNA levels, age, gender, and body mass index.[9,12] However, other investigations have provided contradictory results.[13,14] Metabolic syndrome (MS) is characterized by central obesity, elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure, and elevated fasting plasma glucose. It has also been shown to be correlated with chronic HCV infection, and plays an important role in chronic hepatitis C.[14] The aim of the present study was to clarify the relationships among IR, MS, and HCV RNA level in patients with chronic hepatitis C (CHC) genotype 1 or 2 infection.

METHODS

We initially focused on 156 consecutive patients with HCV genotype 1 or 2 infections who were regularly followed at the gastroenterology clinics of Chang Gung Memorial Hospital, Chia-Yi, Taiwan, between April 2008 and May 2010. Chronic HCV infection was defined as anti-HCV antibody positivity and elevated alanine transaminase (ALT) for more than 6 months. Patients with the following were excluded: (1) positive results for hepatitis B surface antigen (HBsAg) or HIV antibody; (2) undetectable HCV RNA level; (3) evidence of liver cirrhosis or HCC; (4) history of antiviral treatment; (5) known history or serological evidence of autoimmune liver disease or inheritable disorders such as hemochromatosis or Wilson's disease; (6) excessive alcohol intake (daily alcohol consumption > 30 g), or drug abuse; and (7) DM, defined as a known history of anti-diabetic treatment. In total, 36 patients were excluded, 18 because of undetectable HCV RNA levels, 2 because of sonographic evidence of liver cirrhosis, 1 because of positive HBsAg, 5 because of DM, 9 because of withdrawal from the study for personal reasons, and 1 who died before the HCV RNA level was obtained. Finally, a total of 120 patients were prospectively enrolled and included in the analysis. Data regarding sex, age, waist circumference (WC), body mass index (BMI), platelet count (PLT), and serum fasting blood glucose, total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), ALT, aspartate transaminase (AST), and insulin levels were collected. The BMI was calculated as the weight in kilograms (kg) divided by the height in square meters. Blood samples were collected in the morning after 12 hours fasting, and measured by standard laboratory techniques. HBsAg and anti-HCV antibody were analyzed with commercial enzyme-linked immunosorbent assay kits (Abbott Laboratories, North Chicago, IL, U.S.A.). The serum insulin level was measured by an immunometric assay (Diagnostic Products Co., Los Angeles, CA, U.S.A.). Serum fasting blood glucose, TG, TC, LDL, HDL, AST, and ALT were measured by an auto-analyzer (Hitachi 7250, Special; Hitachi, Tokyo, Japan).

The pretreatment IR index was determined using homeostasis model assessment (HOMA). Insulin resistance (HOMA-IR) = fasting insulin (μU/mL) x fasting glucose (mg/dL) / 405, and an index value of > 2.5 was defined as IR. This cutoff value was chosen because recent studies have suggested that a HOMA-IR of 2.4-3.0 is probably suitable to define IR in CHC patients, and the HOMA-IR value for the first quartile of the Taiwanese population.[15]

MS was defined according to the 2004 International Diabetes Federation criteria, i.e., WC (Men ≥ 90 cm; Women ≥ 80 cm) plus any two of the following: (1) triglycerides > 150 mg/dL (1.7 mmol/L), (2) HDL cholesterol < 40 mg/dL (1.03 mmol/l) in men or < 50 mg/dL (1.29 mmol/l) in women, (3) systolic blood pressure > 130 mm Hg, diastolic blood pressure > 85 mm Hg, or treatment for hypertension, and (4) fasting plasma glucose > 100 mg/dL (5.6 mmol/L).

Quantitative HCV RNA was assayed by a real-time polymerase chain reaction (Q-PCR) assay (Abbott m2000rt-Real time PCR; Abbott Molecular Inc., Des Plaines, IL, U.S.A.) on the day that metabolic profiles were assessed. Genotyping was performed by reverse transcription PCR with type-specific primers (Tru-Gene HCV 5'NC Genotyping Kit). Informed consent was obtained from each patient at the time of enrollment, and the hospital Ethics Committee approved the study protocol.

Statistical analysis

The association of HCV RNA levels, IR, and MS were analyzed. Baseline features and metabolic factors were compared between patients with and without IR/MS using the χ^2 test for categorical variables and the *t*-test for continuous variables. Odds ratios (ORs) and 95% confidence intervals (CIs), as well as *p* values, were estimated for each variable by unconditional logistic regression. The correlation between HCV RNA and IR/MS was estimated by multiple linear regression. All tests were two sided, and $p < 0.05$ was considered statistically significant. All data were analyzed using Statistical Package for the Social Sciences software, version 13.0 (SPSS Inc., Chicago, IL, U.S.A.).

RESULTS

Baseline characteristics of the study subjects are shown in Table 1. There were 55 men (45.8%) and 65 women (54.2%), with a mean age of 57.3 ± 1.0 years and a mean BMI of 25.24 ± 0.30 kg/m^2. Of the subjects, 68 (56.7%) were infected with genotype 1 HCV and 52 (43.3%) with genotype 2. The mean serum HCV RNA level was 5.67 ± 0.15 $\log_{10}$ IU/ml. Forty-seven (39.2%) of the subjects had a HOMA-IR > 2.5, and 42 (35%) met the criteria for MS.

Table 1. Baseline Characteristics and Metabolic Factors in 120 Chronic Hepatitis C Patients with Genotype 1 or 2 Infection

Age (years)	18 – 81 (57.32 ± 1.04)
Male	55
Female	65
BMI (kg/m^2)	17.6 – 34.2 (25.24 ± 0.30)
WC (cm)	66 – 106 (83.73 ± 0.71)
Genotype 1	68 (56.7%)
Genotype 2	52 (43.3%)
With IR	47 (39.2%)
Without IR	73 (60.8%)
With MS	42 (35%)
Without MS	78 (65%)
Sugar AC (mg/dl)	115.74 ± 5.15
ALT (IU/L)	74.06 ± 6.60
AST (IU/L)	109.15 ± 11.89
PLT (1000/uL)	181.04 ± 9.92
HDL (mg/dl)	50.34 ± 1.90
TG (mg/dl)	110.19 ± 5.55
Log_{10}HCV RNA (IU/ml)	5.67 ± 0.15
APRI	0.71 ± 0.08
AAR	1.47 ± 0.06

Abbreviations: BMI: body mass index; WC: waist circumference; IR: insulin resistance; ALT: alanine transaminase; AST: aspartate transaminase; PLT: platelets; HDL: high-density lipoprotein; TG: triglycerides; HCV: hepatits C virus; APRI: AST: PLT ratio index; AAR: AST: ALT ratio; MS: metabolic syndrome.
Data shown are number (%) or mean ± standard deviation.

Insulin resistance, metabolic syndrome and serum HCV RNA

In univariate analysis, HOMA-IR > 2.5 was associated with a high BMI ($p < 0.00001$), WC ($p < 0.0001$), fasting blood glucose ($p < 0.0001$), and TG ($p = 0.025$), but was not associated with HDL, ALT, or AST levels, or the PLT count. There was no association between a HOMA-IR > 2.5 and the serum HCV RNA level (Table 2). This lack of association persisted even when a cutoff of 3.0 was used for the HOMA-IR, when different cutoff values for defining a high viral load were examined, and when the viral load was analyzed as a continuous variable.

Forty-two (35%) subjects met the criteria for MS, and they had higher BMI ($p < 0.0001$), WC ($p < 0.0001$), fasting blood glucose ($p < 0.0001$), HDL ($p = 0.004$), TG ($p = 0.001$) and HOMA-IR scores ($p < 0.0001$). There were no significant differences in the ALT and AST levels, PLT count, or serum HCV RNA level between subjects with and without MS in univariate analyses (Table 2). However, the Pearson product-moment correlation coefficient indicated a strong correlation between IR and MS (r = 0.656, 95% CI 0.62-0.75, $p < 0.0001$). Multiple linear regression analysis showed there were no associations among the serum HCV RNA level, IR, and MS after adjustment for age, gender, BMI, AST, ALT, PLT count, and other metabolic factors (Table 3).

Table 2. Comparison of Baseline Characteristics and Metabolic Factors between Patients with/without Insulin Resistance and with/without Metabolic Syndrome

	HOMA-IR > 2.5 (n = 47)	HOMA-IR ≦ 2.5 (n = 73)	*p* value	MS (n = 42)	No MS (n = 78)	*p* value
Age (years)	58.85 ± 1.72	56.34 ± 1.30	0.247	59.71 ± 1.58	56.04 ± 1.34	0.079
Male (%)	51.1	41.1	0.288	42.9	47.4	0.732
BMI (kg/m^2)	26.59 ± 0.35	24.37 ± 0.41	< 0.0001*	26.96 ± 0.43	24.31 ± 0.35	< 0.0001*
WC (cm)	87.56 ± 0.79	81.26 ± 0.95	< 0.0001*	89.44 ± 0.76	80.65 ± 0.83	< 0.0001*
SugarAC (mg/dl)	115.74 ± 5.15	95.36 ± 1.87	< 0.0001*	119.76 ± 5.40	94.50 ± 1.83	< 0.0001*
ALT (IU/L)	74.06 ± 6.60	75.75 ± 8.70	0.877	67.71 ± 5.92	79.06 ± 8.44	0.273
AST (IU/L)	109.15 ± 11.89	103.52 ± 12.72	0.747	96.95 ± 9.92	110.45 ± 12.79	0.406
PLT (1000/uL)	181.04 ± 9.92	175.52 ± 8.39	0.672	174.31 ± 10.94	179.50 ± 7.92	0.702
HDL (mg/dl)	50.34 ± 1.90	52.94 ± 1.84	0.326	47.05 ± 1.87	54.57 ± 1.73	0.004*
TG (mg/dl)	110.19 ± 5.55	93.22 ± 4.96	0.025*	118.55 ± 7.78	89.77 ± 3.55	0.001*
Genotype 1 (%)	44.1	55.9	0.276	39.7	60.3	0.167
Genotype 2 (%)	32.7	67.3	0.128	28.8	71.2	0.093
Log_{10}HCV RNA (IU/ml)	5.67 ± 0.15	5.61 ± 0.13	0.761	5.77 ± 0.15	5.56 ± 0.13	0.292
APRI	0.71 ± 0.08	0.69 ± 0.08	0.839	0.79 ± 0.12	0.73 ± 0.10	0.715
AAR	1.47 ± 0.06	1.38 ± 0.07	0.353	1.44 ± 0.08	1.45 ± 0.06	0.87
HOMA-IR index				4.53 ± 0.55	1.87 ± 0.18	< 0.0001*

Abbreviations: BMI: body mass index; WC: waist circumference; ALT: alanine transaminase; AST: aspartate transaminase: PLT: platelets; HDL: high-density lipoprotein; TG: triglycerides; HCV: hepatits C virus; APRI: AST: PLT ratio index; AAR: AST: ALT ratio; HOMA: homeostasis model assessment; IR: insulin resistance.

Data shown are mean ± standard deviation.

IRwas determined using HOMA, with a HOMA-IR > 2.5 indicating the presence of IR. Metabolic syndrome (MS) was defined according to the International Diabetes Federation 20004 criteria.

*: $p < 0.05$ was considered statistically significant.

Table 3. Parameter Estimates Gained from Multiple Linear Regression Identifying Factors Associated with Insulin Resistance and Metabolic Syndrome in 120 Chronic Hepatitis C Patients with Genotype 1 or 2 Infection

	Insulin resistance (IR)			Metabolic syndrome (MS)		
	Parameter estimate	Standard error	*p* value	Parameter estimate	Standard error	*p* value
Age (years)	–0.003	0.004	0.438	–0.002	0.003	0.47
BMI (kg/m^2)	–0.036	0.013	0.008*	–0.04	0.012	0.001*
WC (cm)	0.003	0.002	0.003*	0.001	0.002	0.001*
SugarAC (mg/dl)	0.001	0.001	0.001*	0.001	0.001	0.001*
TG (mg/dl)	–0.001	0.001	0.033*	–0.002	0.001	0.001*
HDL (mg/dl)	0.004	0.003	0.891	0.0001	0.003	0.005*
Genotype 1 (%)	0.023	0.016	0.089	0.017	0.009	0.063
Genotype 2 (%)	0.037	0.045	0.174	–0.012	0.005	0.077
Log_{10}HCV RNA (IU/ml)	–0.005	0.039	0.889	–0.042	0.035	0.23
APRI	–0.06	0.175	0.731	–0.044	0.155	0.775
AAR	0.139	0.136	0.309	–0.021	0.12	0.865

Abbreviations: BMI: body mass index; WC: waist circumference; ALT: alanine transaminase; AST: aspartate transaminase: HDL: high-density lipoprotein; TG: triglycerides; HCV: hepatits C virus; HOMA: homeostasis model assessment. APRI: AST: PLT ratio index; AAR: AST: ALT ratio; HOMA: homeostasis model assessment; IR: insulin resistance; MS: metabolic syndrome.

Multiple linear regression model using IR as the dependent variable and age, gender, triglyceride, body mass index, ALT, AST and log_{10}HCV RNA as independent variables. HOMA was used to determine IR with a HOMA-IR > 2.5 indicating the presence of IR. MS was defined according to the International Diabetes Federation 2004 criteria.

*: $p < 0.05$ was considered statistically significant.

HCV genotypes and insulin resistance

Based on unadjusted analysis, patients with type 1 HCV infection had slightly higher serum HCV RNA titers than those infected with type 2 (5.79 ± 0.13 $\log_{10}$ IU/ml vs. 5.44 ± 0.15 $\log_{10}$ IU/ml, p = 0.09, Table 4). After adjustment for age, gender, BMI, AST, ALT, PLT, and other metabolic factors, multiple logistic regression analyses showed that subjects infected with type 1 HCV did not have significantly higher HOMA-IR scores than those infected with type 2 HCV (OR = 1.954, 95% CI 0.57-6.71, p = 0.287).

Insulin resistance, metabolic syndrome, and non-invasive markers of liver fibrosis

As the majority of subjects did not have a liver biopsy, histological evaluation for fibrosis was impossible. Instead, we used the AST: ALT ratio (AAR) and AST: PLT ratio index (APRI) as non-invasive markers of liver fibrosis to determine the relationships between IR, MS, and fibrosis severity.

Table 4. Comparison of Baseline Characteristics and Metabolic Factors between Patients with Hepatitis C Virus Genotype 1 and Those with Genotype 2

	Genotype 1 (n = 68)	Genotype 2 (n = 52)	p value
Age (years)	56.56 ± 1.28	58.33 ± 1.72	0.412
Male (%)	44.1	46.2	0.826
BMI (kg/m^2)	25.64 ± 0.43	24.71 ± 0.38	0.107
ALT (IU/L)	69.66 ± 4.44	82.19 ± 12.24	0.34
AST (IU/L)	97.91 ± 8.04	115.94 ± 17.93	0.362
PLT (1000/uL)	187.66 ± 9.75	164.63 ± 7.14	0.062
SugarAC (mg/dl)	100.71 ± 2.58	106.79 ± 4.61	0.253
HDL (mg/dl)	52.51 ± 2.32	48.83 ± 2.74	0.381
TG (mg/dl)	102.38 ± 6.05	97.71 ± 6.65	0.701
$\log_{10}$HCV RNA (IU/ml)	5.79 ± 0.13	5.44 ± 0.15	0.09
HOMA-IR index	2.98 ± 0.37	2.40 ± 0.34	0.256
APRI	0.69 ± 0.09	0.87 ± 0.14	0.403
AAR	1.45 ± 0.06	1.45 ± 0.07	0.659

Abbreviations: BMI: body mass index; IR: insulin resistance; ALT: alanine transaminase; AST: aspartate transaminase: PLT: platelets; HDL: high-density lipoprotein; TG: triglycerides; HCV: hepatits C virus; HOMA: homeostasis model assessment; APRI: AST: PLT ratio index; AAR: AST: ALT ratio.

Data shown are mean ± standard deviation

HOMA was used to determine IR. A HOMA-IR > 2.5 indicated IR.

An AAR ≥ 1 or APRI ≥ 1.4 was regarded as significant liver fibrosis.[16,17] Multiple linear regression analyses adjusted by age, gender, BMI, WC, AST, ALT, PLT, and other metabolic factors revealed that there was no significant association between IR and the AAR (r = 0.0089, 95% CI 0.12-2.77, p = 0.470), or between IR and the APRI (r = 0.0052, 95% CI 0.29-5.87, p = 0.582).

DISCUSSION

In this study, we explored the predictors of IR, and its role in disease progression in a well-defined cohort of 120 treatment-naïve CHC patients with genotype 1 or 2 HCV infection. To eliminate confounding factors, we excluded subjects with pre-existing DM, alcohol abuse, and cirrhosis. Our data showed that the emergence of IR and MS is not associated with the serum HCV RNA level, while IR is an independent predictor of MS. The HCV RNA level was really not a good parameter for insulin resistance or metabolic syndrome because the variation was very small with a small standard deviation.

IR and type II DM have been associated with HCV infection more often than with other chronic inflammatory liver diseases.[18] CHC patients have been estimated to have a 3-fold increased risk of IR and impairment of glucose metabolism.[19] In addition, different sources have indicated that roughly 50% of patients with CHC exhibit some evidence of IR.[9,10,12-14] In the current study, 39.2% of CHC patients were found to be insulin resistant, which is compatible with figures reported by two recent series,[9,13] but much lower than the rate of 56.1% reported by Hsu et al.[12] In the latter study, subjects with cirrhosis were not excluded. The different composition of the patient population might explain this discrepancy, as many studies have shown that IR is more prevalent in subjects with advanced fibrosis or cirrhosis.[20-22]

The term MS has been coined to indicate a cluster of diseases that are correlated with each other, have IR as the common pathogenic determinant, and carry a high risk of cardiovascular disease. This explains why the percentage of subjects with IR (39.3%) and MS (35%) were similar in this study, and indicates that IR is an independent predictor of MS. The rate of MS in our study was higher than that in the general population in Taiwan (13-20%)[23] and

that reported in the National Health and Nutrition Examination Survey III (22%).[24] This finding supports the notion that chronic genotype 1 or 2 HCV infection promotes the development of MS, possibly through inducing IR.

The relationship between IR and HCV infection is complex and bidirectional, and the exact pathogenesis is still unknown. Some clinical observations support a "fat independent" mechanism in the development of IR in HCV -infected subjects.[14] Koike demonstrated in an animal model that HCV can induce IR itself by disturbing the insulin signaling pathway.[7] The author found that an elevated level of tumor necrosis factor-α might inhibit tyrosine phosphorylation of insulin receptor substrate-1 in the liver, suppress intracellular transduction of insulin signals, and lead to IR in mice transgenic for the HCV core gene. HCV has also been reported to mediate dysfunction of insulin signaling pathways by upregulating the expression of suppressor of cytokine signaling 3 or attenuating signal transducer and activator of transcription 3.[25-27]

Two previous studies have claimed a dose-response relationship between the serum HCV RNA titer and IR;[9,12] however, a recent multicenter study provided contradictory data.[13] Our data, consistent with the latter, indicated that the serum HCV RNA level was not a predictor of IR in subjects with genotype 1 and 2 HCV infection. This discordance raises important questions regarding the pathogenesis of IR in CHC, and suggests that the exact pathways need further exploration. The regulation of insulin is a complex interplay between the liver, adipose tissue, and muscle.[28] Many factors affect insulin resistance, such as age, sex, obesity, cytokines, hepatic fibrosis and steatosis. HCV infection is just one of the contributing factors. Perhaps, intrahepatic replication, not the serum viral load, is a more sensitive HCV replication marker to predict the development of IR.

Although genotype has been shown to be the strongest predictor of response to standard treatments in patients with CHC, IR and MS have also been proven to have a negative impact on the outcome of antiviral therapy.[29,30] Since HCV infection induces their development, IR and MS would be expected to improve after eradication of HCV. We did not evaluate changes in IR and MS after antiviral therapy, but several previous studies have shown that IR and MS improve after HCV eradication.[31-36]

A consistent finding among published studies is that IR has a close relationship with the HCV genotype. A number of studies have reported that IR is independently associated with genotypes 1/4 CHC, and ethnicity is not associated with metabolic disorders.[30,37,38] In this study, we observed that IR and MS seemed more prevalent in genotype 1 than genotype 2 subjects, although there was no statistical difference.

Conclusions

Our results indicate that IR and MS are frequent events in subjects with chronic genotype 1 and 2 HCV infection. IR was correlated with the presence of MS. The serum HCV RNA level was not associated with the presence of IR or MS. The impact of HCV on IR or MS was not dose responsive. Some non-viral factors might modulate the relationships of HCV, IR, and MS.

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基因 1 或 2 型慢性 C 型肝炎患者之胰島素抗性及代謝症候群與血清病毒量不相關

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背 景： 過去的報告指出，慢性 C 型肝炎病毒感染與胰島素抗性有關。但胰島素抗性，代謝症候群以及血清 C 型肝炎病毒量的相關性則尚未有定論。本研究希望能探討基因 1 或 2 型慢性 C 型肝炎患者中之此議題。

方 法： 一百二十位第一或第二基因型慢性 C 型肝炎患者的臨床資料完整地被收錄於此前瞻性研究。我們使用 HOMA-IR 指數作爲胰島素抗性評估指標，指數大於 2.5 則認定爲具胰島素抗性。代謝症候群的定義則是根據 2004 年的國際糖尿病聯合會標準。

結 果： 在第一或第二基因型慢性 C 型肝炎患者中，胰島素抗性伴隨著較高的身體質量指數 ($p < 0.0001$)，較大的腰圍 ($p < 0.0001$) 和較高的三酸甘油酯 ($p = 0.025$)。然而，多元線性回歸分析顯示，患者有無胰島素抗性，在 C 型肝炎病毒量沒有統計上顯著差異 ($p = 0.761$)，而有無代謝症候群，同樣在 C 型肝炎病毒量沒有統計上顯著差異 ($p = 0.292$)。

結 論： 在基因 1 或 2 型慢性 C 型肝炎患者中，胰島素抗性及代謝症候群並不罕見，但 C 型肝炎病毒量與胰島素抗性及代謝症候群之有無不相關。C 型肝炎病毒感染對胰島素抗性及代謝症候群的影響與病毒量多寡無關，某些非病毒因素可能會調節慢性 C 型肝炎、胰島素抗性及代謝症候群之間的關係。

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關鍵詞：C 型肝炎病毒，病毒量，胰島素抗性，代謝症候群

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