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## 女性冠心病患者胆红素血脂综合指数、ApoB 水平 与冠状动脉病变程度的相关性研究 \*

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**摘要 目的:**研究女性冠心病患者胆红素血脂综合指数、ApoB 水平与冠脉病变程度的关系。**方法:**选取 2016 年 1 月-2016 年 12 月于我院行冠状动脉造影检查的女性患者共 246 例,按照两种不同方法分组:(1)按照冠状动脉造影结果分为冠心病组( $n=105$ )和正常对照组( $n=141$ );(2)按照 Gensini 评分系统定量评估所有冠心病患者的冠状动脉病变程度,分为第 1 四分位组( $n=35$ )、第 2 四分位组( $n=32$ )、第 3 四分位组( $n=39$ )及第 4 四分位组( $n=35$ )。测定所有患者的血清总胆红素(TBIL)、直接胆红素(DBIL)、间接胆红素(IBIL)、总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)、载脂蛋白 A/B(Apo A/B)水平,计算胆红素血脂综合指数 $[TC/(HDL-C+TBIL)$ 、 $LDL-C/(HDL-C+TBIL)]$ 。**结果:**(1)冠心病组 TC、TG、LDL-C、ApoB 较正常组高, HDL-C、ApoA、TBIL、DBIL、IBIL 较正常组低,差异有统计学意义 ( $P<0.05$ );与正常组相比,冠心病组胆红素血脂综合指数 $[TC/(HDL-C+TBIL)$ 、 $LDL-C/(HDL-C+TBIL)]$ 升高,差异有统计学意义( $P<0.05$ )。(2)在不同 Gensini 评分四分位组中,TC、LDL-C、Apo B、TBIL、DBIL、IBIL、TC/ (HDL-C+TBIL)、LDL-C/ (HDL-C+TBIL) 的差异均有统计学意义 ( $P<0.05$ )。(3)相关性分析显示:TC/ (HDL-C+TBIL)、LDL-C/ (HDL-C+TBIL)、ApoB 均与冠脉不同 Gensini 评分呈正相关( $r=0.538, P<0.05$ ;  $r=0.670, P<0.05$ ;  $r=0.462, P<0.05$ );TBIL、DBIL、IBIL 与冠脉不同 Gensini 评分呈负相关( $r=-0.485, P<0.05$ ;  $r=-0.564, P<0.05$ ;  $r=-0.359, P<0.05$ )。**结论:**(1)女性冠心病患者胆红素血脂综合指数、ApoB 较正常对照组患者显著升高,而 TBIL、DBIL、IBIL 降低;(2)女性冠心病患者胆红素血脂综合指数、ApoB 水平与其冠脉病变程度呈显著正相关。

**关键词:**胆红素血脂综合指数;ApoB;女性;冠心病

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## Correlation of the Bilirubin Blood Lipid Comprehensive Index and Apolipoprotein B with the Severity of Coronary Lesions in Female Patients with Coronary Artery Disease\*

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**ABSTRACT Objective:** To investigate the relationship between Bilirubin blood lipid Comprehensive index and apolipoprotein B and the severity of coronary lesions of female patients with coronary artery disease (CAD). **Methods:** A total of 246 cases of female patients with coronary angiography were divided into 2 sets of groups. ① According to the results of coronary angiography, the female patients were divided into the CAD group ( $n=141$ ) and normal control group ( $n=105$ ); ② By Gensini scoring system, the female patients were divided into 4 quartile groups: 1st quartile group( $n=35$ ), 2nd quartile group( $n=32$ ), 3rd quartile group( $n=39$ ) and 4th quartile group ( $n=35$ ). The blood level of total bilirubin(TBIL), direct bilirubin(DBIL), indirect bilirubin(IBIL), total cholesterol(TC), triglyceride(TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), apolipoprotein A/B (Apo A/B) level were measured. Bilirubin blood lipid Comprehensive index $[TC/(HDL-C+TBIL)$ ,  $LDL-C/(HDL-C+TBIL)]$  were calculated. **Results:** ① The levels of TC, TG, LDL-C and ApoB in CAD group were higher than those of the normal control group; the HDL-C, ApoA, TBIL, DBIL and IBIL were lower than those of the normal control group( $P<0.05$ ); Compared with the normal group, the ratios of TC/(HDL-C+TBIL) and LDL-C/(HDL-C+TBIL) were increased( $P<0.05$ ). ② By Gensini scoring system, the level of TC, LDL-C, ApoB, TBIL, DBIL, IBIL, ratios of TC/ (HDL-C+TBIL) and LDL-C/ (HDL-C+TBIL) were different among 4 groups ( $P<0.05$ ). ③ Correlation analysis showed that TC/(HDL-C+TBIL), LDL-C/ (HDL-C+TBIL) and ApoB were positively related to Gensini scoring system( $r=0.538, P<0.05$ ;  $r=0.670, P<0.05$  and  $r=0.462, P<0.05$ ). But TBIL, DBIL, IBIL were negatively related to Gensini scoring system ( $r=-0.485, P<0.05$ ;  $r=-0.564, P<0.05$  and  $r=-0.359, P<0.05$ ). **Conclusions:** ① Bilirubin blood lipid Comprehensive index and apolipoprotein B were significantly higher than the control group, while TBIL, DBIL, IBIL decreased. ② Bilirubin blood lipid Comprehensive index and apolipoprotein B were positively

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related to the severity of coronary artery lesions of female CAD patients.

**Key words:** Bilirubin blood lipid comprehensive index; Apolipoprotein B; Female; Coronary artery disease

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## 前言

动脉粥样硬化是心血管疾病的病理基础,目前关于动脉粥样硬化发病机制的学说有炎症反应学说、脂质浸润学说、巨噬细胞受体缺失学说、致平滑肌突变学说、损伤应答学说、血流动力学学说、免疫应答学说等,而越来越多的证据表明动脉粥样硬化是一种慢性炎症疾病<sup>[1]</sup>。胆红素具有抗氧化作用,能抑制血脂和脂蛋白氧化,从而发挥保护心血管的作用,是冠心病(Coronary artery disease, CAD)的一个重要而独立的危险因素<sup>[2]</sup>。本研究主要探讨了女性冠状动脉造影患者的胆红素血脂综合征指数和 ApoB 水平及其与冠状动脉病变程度的关系。

## 1 资料与方法

### 1.1 研究对象

选择 2016 年 1 月-2016 年 12 月于西南医科大学附属医院心内科行冠状动脉造影检查的女性患者共 246 例。所有患者按照两种不同的方法进行分组:(1)以首次诊断为冠心病的女性患者 141 例为冠心病组,平均年龄  $65.09 \pm 7.97$  岁;冠状动脉未见异常的女性患者 105 例为正常组,平均年龄  $64.14 \pm 5.46$  岁。(2)应用 Gensini 评分系统评价冠心病患者的冠状动脉病变程度,得出所有患者的 Gensini 评分,再根据分值结果得出四分位数:P25=13.5, P50=30, P75=54。第 1 四分位组:Gensini 分值小于 13.5;第 2 四分位组:Gensini 分值大于等于 13.5 且小于 30;第 3 四分位组:Gensini 分值大于等于 30 且小于 54;第 4 四分位组:Gensini 分值大于等于 54。排除标准:(1)心脏瓣膜疾病、心肌病、心肌炎、心包炎;(2)先天性冠状动脉畸形、既往有经皮冠状动脉介入治疗(PCI)或冠状动脉旁路移植术(CABG)史;(3)甲状腺疾病;(4)肝肾功能不全;(5)急慢性感染性疾病;(6)主动

脉夹层、肺栓塞、下肢动静脉血栓形成等;(7)恶性肿瘤;(8)血液系统疾病;(9)自身免疫性疾病、结缔组织疾病等。

### 1.2 研究方法

**1.2.1 基线资料** 收集所有入选患者的基线资料,如年龄、吸烟史、高血压病史、糖尿病病史、体质指数(BMI, BMI= 体重/身高<sup>2</sup>, kg/m<sup>2</sup>)、冠心病阳性家族史等。

**1.2.2 临床资料** 抽取所有入选患者次日清晨空腹肘静脉血,测定血清总胆固醇(Total cholesterol, TC)、甘油三酯(Triglyceride, TG)、低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(High density lipoprotein cholesterol, HDL-C)、载脂蛋白 A/B(Apolipoprotein A/B, Apo A/B)、总胆红素(Total bilirubin, TBIL)、直接胆红素(Direct bilirubin, DBIL)、间接胆红素(Indirect bilirubin, IBIL)等指标水平。

**1.2.3 冠脉造影** 经桡动脉或股动脉路径行左右冠状动脉造影,造影结果至少由两位专业心血管介入医师确定。冠心病诊断标准为:造影显示左主干、左前降支、左回旋支或右冠状动脉至少有 1 支血管管腔直径狭窄 $\geq 50\%$ 。

### 1.3 统计学处理

采用 SPSS19.0 统计软件处理数据,符合正态分布的计量资料用均值 $\pm$ 标准差( $\bar{x} \pm s$ )表示,两组间比较采用独立样本 t 检验,多组间比较采用单因素方差分析;计数资料组间比较采用 $\chi^2$ 检验;相关性分析采用 Pearson 相关分析。以  $P < 0.05$  为差异有统计学意义。

## 2 结果

女性冠心病组与正常组年龄、吸烟、家族史、BMI、及合并高血压、糖尿病等差异无统计学意义( $P > 0.05$ ),见表 1。

表 1 女性正常组与冠心病组基线资料的比较( $\bar{x} \pm s$ )

Table 1 Comparison of the baseline data between the normal group and the CAD group in female

| Project                 | The normal group<br>(n=105) | The CAD group<br>(n=141) | P     |
|-------------------------|-----------------------------|--------------------------|-------|
| Age(Year)               | 64.14 $\pm$ 5.46            | 65.09 $\pm$ 7.97         | 0.273 |
| Smoke                   | 2(1.90)                     | 3(2.13)                  | 1.000 |
| Hypertension            | 63(60.00)                   | 92(65.25)                | 0.399 |
| Diabetes                | 15(14.29)                   | 31(20.99)                | 0.126 |
| Family history          | 7(6.67)                     | 6(4.26)                  | 0.403 |
| BMI(kg/m <sup>2</sup> ) | 24.36 $\pm$ 3.54            | 24.28 $\pm$ 3.41         | 0.861 |
| Obesity                 | 12(11.43)                   | 20(14.18)                | 0.525 |

Notes: Obesity: BMI $\geq 28$  kg/m<sup>2</sup>.

冠心病组 TC、TG、LDL-C、ApoB 较正常组升高,差异有统计学意义( $P < 0.05$ );HDL-C、ApoA、TBIL、DBIL、IBIL 较正常组显著降低,差异有统计学意义( $P < 0.05$ );与正常组相比,冠心病

组胆红素血脂综合征指数 [TC/(HDL-C+TBIL)、LDL-C/(HDL-C+TBIL)]显著升高( $P < 0.05$ ),见表 2。

女性冠心病组不同 Gensini 评分四分位组基线资料的比

较:四组在年龄、BMI、肥胖例数及合并高血压、糖尿病方面,差异无统计学意义( $P>0.05$ ),见表3。

表2 女性正常组与冠心病组生化指标的比较( $\bar{x}\pm s$ )

Table 2 Comparison of the biochemical index between the normal group and the CAD group in female

| Project            | The normal group<br>(n=105) | The CAD group<br>(n=141) | P     |
|--------------------|-----------------------------|--------------------------|-------|
| TC(mmol/L)         | 4.46± 1.10                  | 4.87± 1.232              | 0.008 |
| TG(mmol/L)         | 1.63± 1.00                  | 1.97± 1.23               | 0.019 |
| HDL-C(mmol/L)      | 1.33± 0.34                  | 1.18± 0.33               | 0.001 |
| LDL-C(mmol/L)      | 2.61± 0.93                  | 2.89± 1.05               | 0.029 |
| ApoA(g/L)          | 1.64± 0.29                  | 1.51± 0.27               | 0.000 |
| ApoB(g/L)          | 0.83± 0.26                  | 0.94± 0.27               | 0.003 |
| TBIL( $\mu$ mol/L) | 14.05± 3.16                 | 12.54± 4.04              | 0.001 |
| DBIL( $\mu$ mol/L) | 5.08± 1.57                  | 4.50± 1.67               | 0.006 |
| IBIL( $\mu$ mol/L) | 8.98± 2.01                  | 8.03± 2.82               | 0.002 |
| TC/(HDL-C+TBIL)    | 0.30± 0.10                  | 0.39± 0.15               | 0.000 |
| LDL-C/(HDL-C+TBIL) | 0.18± 0.08                  | 0.23± 0.10               | 0.000 |

表3 女性冠心病不同 Gensini 评分四分位组基线资料比较( $\bar{x}\pm s$ )

Table 3 Different Gensini scores of four quartile groups comparison of basical data in female

| Project                 | 1 <sup>st</sup> quartile group(n=35) | 2 <sup>nd</sup> quartile group(n=32) | 3 <sup>rd</sup> quartile group(n=39) | 4 <sup>th</sup> quartile group(n=35) | P     |
|-------------------------|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|-------|
| Age(Year)               | 64.46± 9.66                          | 66.34± 8.00                          | 65.23± 6.71                          | 64.40± 7.55                          | 0.736 |
| Project                 | 26(74.29)                            | 24(75.00)                            | 24(66.67)                            | 18(51.43)                            | 0.122 |
| Diabetes                | 9(25.71)                             | 4(12.50)                             | 9(23.08)                             | 8(22.86)                             | 0.570 |
| BMI(kg/m <sup>2</sup> ) | 24.73± 3.24                          | 24.23± 4.00                          | 23.41± 2.85                          | 24.83± 3.50                          | 0.256 |
| Obesity                 | 5(14.29)                             | 6(18.75)                             | 3(7.69)                              | 6(17.14)                             | 0.542 |

女性冠心病组不同 Gensini 评分四分位组的生化指标的比较:不同 Gensini 评分四分位组组间,TC、LDL-C、Apo B、TBIL、DBIL、IBIL 水平的差异有统计学意义( $P<0.05$ );TC 在第3四分位组和第4四分位组均明显升高,与第1四分位组和第2四分位组比较差异有统计学意义( $P<0.05$ );LDL-C、Apo B 在第2四分位组和第3四分位组比较差异无统计学意义( $P>0.05$ ),在其他四分位组两两比较中差异均有统计学意义( $P<0.05$ );TC/(HDL-C+TBIL)、LDL-C/(HDL-C+TBIL)的比值在四分位组各组间两两比较,差异均有统计学意义( $P<0.05$ ),见表4。

相关性分析显示:TC/(HDL-C+TBIL)、LDL-C/(HDL-C+TBIL) 均与冠脉不同 Gensini 评分呈正相关( $r=0.538$ ,  $P<0.05$ ;  $r=0.670$ ,  $P<0.05$ );TC、LDL-C、ApoB 与冠脉不同 Gensini 评分呈正相关 ( $r=0.275$ ,  $P<0.05$ ;  $r=0.433$ ,  $P<0.05$ ;  $r=0.462$ ,  $P<0.05$ )。TBIL、DBIL、IBIL 与冠脉不同 Gensini 评分呈负相关 ( $r=-0.485$ ,  $P<0.05$ ;  $r=-0.564$ ,  $P<0.05$ ;  $r=-0.359$ ,  $P<0.05$ )。

### 3 讨论

随着人民生活水平的提高、人口老龄化的进展、社会经济的发展,我国冠心病的死亡人数在逐年上升,已成为危害人类健康、影响生活质量的最常见心血管疾病<sup>[3]</sup>。多年来,男性冠心

病患者一直占据主要地位,而随着冠心病知识的宣传普及以及大众对冠心病的重视普遍加深,男性冠心病的发病率及死亡率已呈现下降趋势,然而女性冠心病的发病率及病死率却呈上升趋势。

载脂蛋白作为冠心病的独立危险因素,对冠状动脉粥样硬化程度具体预测作用<sup>[4]</sup>。ApoB 是 LDL-C 的主要成分,在 LDL-C 代谢中发挥着重要作用。流行病学调查表明 ApoB 预测心血管事件风险和心血管疾病进展的作用优于 LDL-C<sup>[5,6]</sup>。高水平的 ApoB 易促进血管的炎症反应和斑块的形成,从而导致动脉粥样硬化<sup>[7]</sup>。ApoB 是通过刺激炎症反应、产生炎症细胞因子及抑制纤溶系统而增加动脉粥样硬化的发生<sup>[8,9]</sup>。Westerveld 等人研究发现 ApoB 水平与冠状动脉病变程度存在相关性,ApoB 水平越高,则冠状动脉病变程度越严重<sup>[10]</sup>。本研究结果也显示冠心病组 ApoB 水平高于正常组,不同 Gensini 评分四分位组间 ApoB 水平的差异有统计学意义,且与 Gensini 评分呈正相关。

胆红素是一种内源性抗氧化分子,能抑制低密度脂蛋白的氧化作用,延缓动脉粥样硬化的进展,在动脉粥样硬化形成中起着关键的作用<sup>[11-13]</sup>。与血红素降解有关的胆红素氧合酶是一种应激诱导酶,具有抗氧化作用。胆红素氧合酶催化血红素生成一氧化碳、游离铁、胆绿素。此后,胆绿素迅速转化为胆红素、

表 4 女性冠心病 Gensini 四分位组间生化指标比较( $\bar{x} \pm s$ )

Table 4 Comparison of the biochemical index between Different Gensini scores of four quartile groups in female

| Project            | 1 <sup>st</sup> quartile group(n=35) | 2 <sup>nd</sup> quartile group(n=32) | 3 <sup>rd</sup> quartile group(n=39) | 4 <sup>th</sup> quartile group(n=35) | P     |
|--------------------|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|-------|
| TC(mmol/L)         | 4.41± 1.01                           | 4.35± 1.08                           | 5.14± 1.07 <sup>a</sup> ▲            | 5.49± 1.35 <sup>a</sup> ▲            | 0.000 |
| TG(mmol/L)         | 1.76± 1.25                           | 1.73± 0.87                           | 2.02± 1.22                           | 2.35± 1.42                           | 0.131 |
| HDL-C(mmol/L)      | 1.18± 0.43                           | 1.18± 0.29                           | 1.22± 0.33                           | 1.13± 0.23                           | 0.751 |
| LDL-C(mmol/L)      | 2.28± 0.95                           | 2.77± 0.99 <sup>a</sup>              | 2.97± 0.79 <sup>a</sup>              | 3.52± 1.14 <sup>a</sup> ▲            | 0.000 |
| Apo A(g/L)         | 1.47± 0.33                           | 1.54± 0.28                           | 1.52± 0.26                           | 1.50± 0.23                           | 0.748 |
| Apo B(g/L)         | 0.78± 0.21                           | 0.89± 0.27                           | 0.95± 0.21 <sup>a</sup>              | 1.12± 0.28 <sup>a</sup> ▲            | 0.000 |
| TBIL(μmol/L)       | 16.59± 4.58                          | 12.71± 2.97 <sup>a</sup>             | 11.26± 2.22 <sup>a</sup>             | 9.75± 2.46 <sup>a</sup> ▲            | 0.000 |
| DBIL(μmol/L)       | 6.36± 1.75                           | 4.78± 1.02 <sup>a</sup>              | 3.75± 0.89 <sup>a</sup> ▲            | 3.21± 0.79 <sup>a</sup> ▲            | 0.000 |
| IBIL(μmol/L)       | 10.19± 3.47                          | 7.94± 2.38 <sup>a</sup>              | 7.52± 1.85 <sup>a</sup>              | 6.51± 2.09 <sup>a</sup> ▲            | 0.000 |
| TC/(HDL-C+TBIL)    | 0.26± 0.07                           | 0.32± 0.07 <sup>a</sup>              | 0.42± 0.10 <sup>a</sup> ▲            | 0.53± 0.18 <sup>a</sup> ▲            | 0.000 |
| LDL-C/(HDL-C+TBIL) | 0.13± 0.04                           | 0.20± 0.05 <sup>a</sup>              | 0.25± 0.09 <sup>a</sup> ▲            | 0.33± 0.09 <sup>a</sup> ▲            | 0.000 |

Note: Comparison with 1<sup>st</sup> quartile group <sup>a</sup>  $P<0.05$ ; Comparison with 2<sup>nd</sup> quartile group ▲  $P<0.05$ ; Comparison with 3<sup>rd</sup> quartile group <sup>a</sup>  $P<0.05$ .

游离铁转化为螯合铁。众所周知,底物血红素具有高度的活性和细胞毒性,但胆红素是活性氧的清除剂。Zhu KF 等人发现血清总胆红素水平与冠状动脉斑块易损性呈负相关<sup>[14]</sup>。总胆红素水平可独立预测行经皮冠状动脉介入治疗的急性 ST 段抬高型心肌梗死的远期心脏不良事件<sup>[15]</sup>,但与远期死亡率无关。Schwertner HA 等人研究发现低水平的血清胆红素浓度与冠心病的发病风险密切相关<sup>[2]</sup>。胆红素水平与罹患心血管疾病风险呈 U 型曲线,意味着胆红素能起到保护作用,但过高浓度的胆红素亦可能产生有害的影响<sup>[16]</sup>。低血清胆红素浓度已被证明是一个独立的、与冠心病风险增加成负相关的危险因素。不同于传统危险因素,如胆固醇、高密度脂蛋白、胆固醇 / 高密度脂蛋白、甘油三酯、年龄、吸烟和收缩压,TC/ (HDL-C+TBIL)及 LDL-C/(HDL-C+TBIL)是一个诊断灵敏度优于上述指标的独立的危险预测因子<sup>[17]</sup>。本研究结果显示与正常组相比,冠心病组血清胆红素显著降低,胆红素血脂综合指数 [TC/ (HDL-C+TBIL)、LDL-C/(HDL-C+TBIL)]升高。Turfan M 等人研究表明胆红素与冠状动脉疾病的存在有关,且冠心病的严重程度与总胆红素降低水平的关系<sup>[18,19]</sup>。余亚仁等研究发现胆红素血脂综合指数与冠状动脉的病变呈正相关<sup>[20]</sup>。本研究结果也显示冠脉不同 Gensini 评分的四分位组间 TC、LDL-C、Apo B、TBIL、DBIL、IBIL、TC/(HDL-C+TBIL)及 LDL-C/(HDL-C+TBIL)水平的差异有统计学意义,相关性分析显示 TC/(HDL-C+TBIL)、LDL-C/(HDL-C+TBIL)及 Apo B 与冠脉 Gensini 评分呈正相关,而 TBIL、DBIL、IBIL 与冠脉 Gensini 评分呈负相关。

综上所述,胆红素血脂综合指数是一个综合血脂及胆红素的评价指标,较单纯地使用血脂、胆红素评价冠心病风险更全面、灵敏度更高,TC/(HDL-C+TBIL)及 LDL-C/(HDL-C+TBIL)可能作为临床评价冠心病罹患风险的指标,为临床综合评估冠心病提供参考依据。

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