

doi: 10.13241/j.cnki.pmb.2022.12.030

急性 ST 段抬高型心肌梗死介入手术时间窗 与血清 FGF21 水平的相关性*

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摘要 目的:探讨急性 ST 段抬高型心肌梗死介入手术时间窗与血清成纤维细胞生长因子 21(FGF21)水平的相关性。**方法:**选择本院 2019 年 1 月-2021 年 1 月收治的急性 ST 段抬高型心肌梗死患者 120 例作为研究对象,根据随机 1:1 抽签法把患者分为研究组与对照组各 60 例。所有患者都给予急诊经皮冠脉介入手术治疗,对照组在发病后 7-12 h 进行介入治疗,研究组在发病后 ≤ 6 h 进行介入治疗,检测、记录血清 FGF21 表达变化情况并进行相关性分析。**结果:**两组治疗后 1 周的血清心肌钙蛋白 T(cTnT)、心肌钙蛋白 I(cTnI)含量低于治疗前,研究组低于对照组($P<0.05$)。两组治疗后 1 周的血清 FGF21 水平高于治疗前,研究组高于对照组($P<0.05$)。治疗后随访 6 个月,研究组的心律失常、心力衰竭、心绞痛、心源性休克等不良心血管事件发生率为 3.3%,低于对照组的 26.7%($P<0.05$)。在两组 120 例患者中,发病后 ≤ 6 h 进行介入治疗为影响患者治疗后血清 FGF21 水平、近期疗效与随访不良心血管事件的重要因素($P<0.05$)。**结论:**发病后 ≤ 6 h 介入治疗急性 ST 段抬高型心肌梗死可促进血清 FGF21 的释放,提高治疗近期疗效,改善心功能,也可降低远期不良心血管事件的发生,介入手术时间窗与血清 FGF21 的表达存在相关性。

关键词:手术时间窗;急性 ST 段抬高型心肌梗死;成纤维细胞生长因子 21

中图分类号:R542.22 文献标识码:A 文章编号:1673-6273(2022)12-2347-05

Correlation between the Time Window of Interventional Surgery for Acute ST-segment Elevation Myocardial Infarction and Serum FGF21 Levels*

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ABSTRACT Objective: To investigate the correlation between the time window of interventional surgery for acute ST-segment elevation myocardial infarction and serum fibroblast growth factor 21 (FGF21) levels. **Methods:** From January 2019 to January 2021, 120 cases of patients with acute ST-segment elevation myocardial infarction admitted to our hospital were selected as the research objects, and the patients were divided into research group and control group with 60 patients in each groups accorded to a random 1:1 lottery method. All patients were treated with emergency percutaneous coronary intervention. The control group were received interventional treatment 7-12 h after the onset of the disease, and the research group were received interventional treatment ≤ 6 h after the onset of the disease. The changes in serum FGF21 expression were detected and recorded and correlation analysis were performed. **Results:** The serum cardiac troponin T (cTnT) and cardiac troponin I (cTnI) levels in the two groups were lower than before treatment, and the research group were lower than the control group ($P<0.05$). Serum FGF21 level 1 week after treatment in both groups was higher than that before treatment, and that in the study group was higher than that in the control group ($P<0.05$). Followed-up for 6 months after treatment, The incidence of adverse cardiovascular events such as arrhythmia, heart failure, angina, and cardiogenic shock in the research group were 3.3 %, which were lower than 26.7 % in the control group ($P<0.05$). In the two groups of 120 patients, interventional therapy ≤ 6 h after the onset of the disease were an important factor affecting the serum FGF21 level, short-term efficacy and follow-up adverse cardiovascular events ($P<0.05$). **Conclusion:** Interventional treatment of ACUTE ST-segment elevation myocardial infarction ≤ 6 h after onset can promote the release of serum FGF21, improve the short-term therapeutic effect, improve cardiac function, and reduce the occurrence of long-term adverse cardiovascular events. The time window of interventional surgery is correlated with the expression of serum FGF21.

Key words: Operating window; Acute ST-segment elevation myocardial infarction; Fibroblast growth factor 21

Chinese Library Classification(CLC): R542.22 **Document code:** A

Article ID:1673-6273(2022)12-2347-05

* 基金项目:山东省中医药科技发展计划项目(2019-0509)

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(收稿日期:2021-11-02 接受日期:2021-11-26)

前言

急性心肌梗死为临床上较常见心血管疾病,其中急性 ST 段抬高型心肌梗死占 50.0 % 以上,具有伤害性大、病情严重、起病快等特点,具有极高死亡率^[1,2]。急性 ST 段抬高型心肌梗死可在短时间内损害心肌组织,导致心脏骤停,若不及时诊治,可增加患者的致残率与致死率^[3]。随着医学技术的发展与提高,当前已有多种方法应用于急性 ST 段抬高型心肌梗死的诊治,也已取得很好效果^[4]。经皮冠脉介入手术是当前急性 ST 段抬高型心肌梗死的标准性治疗方法,能避免梗死心肌组织加速扩大,还可重建冠脉血流,能降低患者的致死率与残疾病^[5,6]。但其治疗时间窗在临床上的应用还存在一定商榷之地,特别是不同时间窗治疗的患者,其预后也存在一定的不同^[7]。心肌损伤标志物在急性 ST 段抬高型心肌梗死的诊断、评估和预后中发挥重要的作用。发生急性 ST 段抬高型心肌梗死时,患者的血清心肌肌钙蛋白 T (Cardiac troponin T, cTnT)、心肌肌钙蛋白 I (Cardiac Troponin I, cTn I) 均呈高表达^[8]。现代研究表明:脂质代谢和动脉粥样硬化斑块形成在急性 ST 段抬高型心肌梗死的发病中占据重要地位,特别是脂肪组织可分泌多种活性脂肪因子,后者可加速动脉粥样硬化,从而引发急性 ST 段抬高型心肌梗死的发生^[9,10]。成纤维细胞生长因子 21 (Fibroblast growth factor 21, FGF21) 是 FGF 家族的重要成员,可在脂肪细胞、肝脏中分

泌与表达,改善体内糖脂代谢情况,具有抗血管动脉粥样硬化、抑制凋亡等作用,为急性 ST 段抬高型心肌梗死的独立诊断因子,也为开发治疗急性 ST 段抬高型心肌梗死的重要标志物因子^[11,12]。本研究具体探讨了急性 ST 段抬高型心肌梗死介入手术时间窗与血清 FGF21 水平的相关性,并明确手术时间窗的应用效果及其对 FGF21 表达的影响。现报道如下。

1 资料与方法

1.1 研究对象

选择本院 2019 年 1 月 -2021 年 1 月收治的急性 ST 段抬高型心肌梗死患者 120 例作为研究对象。

纳入标准:符合急性 ST 段抬高型心肌梗死的诊断标准;冠脉造影显示冠脉完全闭塞的患者;本院伦理委员会批准了此次研究;患者或患者家属在自愿条件下签署了知情同意书;发病至救治时间 ≤ 12 h。

排除标准:血液系统疾病的患者;药物过敏体质的患者;肝肾功能不全的患者;合并感染性或传染性疾病的患者;不能配合完成研究或调查的患者。

根据随机 1:1 抽签法把患者分为研究组与对照组各 60 例,两组患者的血压、肝功能、疾病史等资料对比无差异 ($P>0.05$)。见表 1。

表 1 两组一般资料对比

Table 1 Comparison of general data between the two groups

Groups	n	Gender (Male/female)	Age (years)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Aspartate Transferase (U/L)	Alanine transferase (U/L)	History of diabetes (n)	History of hypertension (n)
The research group	60	33/27	60.18 $\pm$ 1.55	144.22 $\pm$ 6.87	84.98 $\pm$ 5.55	20.87 $\pm$ 2.11	21.33 $\pm$ 1.47	13(21.7 %)	22(36.7 %)
The control group	60	31/29	60.28 $\pm$ 1.74	144.02 $\pm$ 7.11	84.76 $\pm$ 6.10	20.58 $\pm$ 1.29	21.87 $\pm$ 2.72	12(20.0 %)	23(38.3 %)

1.2 治疗方法

所有患者均给予急诊经皮冠脉介入手术治疗,对照组在发病后 7-12h 进行介入治疗,研究组在发病后 ≤ 6 h 进行介入治疗。

术前口服替格瑞洛 180 mg (AstraZeneca AB 公司,国药准字 J20130020) 与阿司匹林 300 mg (湖南中南制药有限责任公司,国药准字 H43021055)。对患者进行冠状动脉造影检查,了解患者的血管壁病变、冠脉狭窄程度等情况。皮肤消毒后采用经皮冠脉介入手术,使梗死血管复通,密切关注患者的生命体征变化并持续进行心电监护。介入术后患者口服阿司匹林 100 mg 与替格瑞洛 90 mg 治疗,2 次/d。

1.3 观察指标

(1) 在治疗前与治疗后 1 周抽取患者的空腹静脉血 2 mL,室温静置 20 min 后,3000 rpm 离心 20 min,取上层血清分为两管。第一管采用全自动生化分析仪 (罗氏公司, Cobas c702) 检测血清 cTnT、cTn I 含量,另外一管采用酶联免疫法 (试剂盒购自赛默飞公司) 检测血清 FGF21 水平。

(2) 所有患者介入后随访 6 个月,记录与观察患者心律失常、心力衰竭、心绞痛、心源性休克等不良心血管事件发作情况。

1.4 统计方法

本次研究统计软件为 SPSS27.00,计数数据与计量数据以百分比、均数 $\pm$ 标准差表示,对比为卡方 χ^2 检验与 t 检验,采用 Spearman 方法与多元 logistic 回归模型分析相关性。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 血清 cTnT、cTn I 含量变化对比

两组治疗后 1 周的血清 cTnT、cTn I 含量低于治疗前,研究组低于对照组 ($P<0.05$)。见表 2。

2.2 血清 FGF21 水平变化对比

两组治疗后 1 周的血清 FGF21 水平高于治疗前,研究组高于对照组 ($P<0.05$)。见表 3。

2.3 随访疗效对比

治疗后随访 6 个月,研究组的心律失常、心力衰竭、心绞痛、心源性休克等不良心血管事件发生率为 3.3 %,低于对照组的 26.7 % ($P<0.05$)。见表 4。

2.4 相关性分析

在两组 120 例患者中,发病后 ≤ 6 h 进行介入治疗为影响患者治疗后血清 FGF21 水平、近期疗效与随访不良心血管事

表 2 两组治疗前后血清 cTnT、cTn I 含量变化对比($\mu\text{g/mL}$, 均数 $\pm$ 标准差)Table 2 Comparison of serum cTnT and cTnI contents between the two groups before and after treatment ($\mu\text{g/mL}$, mean $\pm$ standard deviation)

Groups	n	cTnT		cTn I	
		Before the treatment	1 week after treatment	Before the treatment	1 week after treatment
The research group	60	3.49 $\pm$ 0.18	0.45 $\pm$ 0.04* [#]	1.68 $\pm$ 0.23	0.12 $\pm$ 0.02* [#]
The control group	60	3.50 $\pm$ 0.13	1.45 $\pm$ 0.12 [#]	1.69 $\pm$ 0.13	0.67 $\pm$ 0.04 [#]

Note: Compared with control group, * $P<0.05$; Compared with before the treatment, [#] $P<0.05$.

表 3 两组治疗前后血清 FGF21 水平变化对比(pg/mL , 均数 $\pm$ 标准差)Table 3 Comparison of serum FGF21 levels between the two groups before and after treatment (PG /mL, mean $\pm$ standard deviation)

Groups	n	Before the treatment	1 week after treatment
The research group	60	20.92 $\pm$ 2.44	51.48 $\pm$ 3.22* [#]
The control group	60	20.28 $\pm$ 2.10	31.74 $\pm$ 4.19 [#]

Note: Compared with control group, * $P<0.05$; Compared with before the treatment, [#] $P<0.05$.

表 4 两组随访不良心血管事件发生情况对比(n)

Table 4 Comparison of adverse cardiovascular events between the two groups during follow-up (n)

Groups	n	Arrhythmia	Cardiac failure	Stenocardia	Cardiogenic shock	Summation
The research group	60	1	0	1	0	2(3.3 %)*
The control group	60	6	3	4	3	16(26.7 %)

Note: Compared with control group, * $P<0.05$.

表 5 急性 ST 段抬高型心肌梗死介入手术时间窗与治疗前后血清 FGF21 水平的相关性(n=120)

Table 5 Correlation between the time window of interventional surgery and serum FGF21 level after treatment in ACUTE ST-segment elevation myocardial infarction (n=120)

Indexs	FGF21	Short-term curative effect	Adverse cardiovascular events
<i>r</i>	0.644	0.598	0.652
<i>P</i>	0.000	0.001	0.000

表 6 影响急性 ST 段抬高型心肌梗死患者治疗后血清 FGF21 水平的多因素分析(n=120)

Table 6 Multivariate analysis of serum FGF21 level in patients with acute ST-segment elevation myocardial infarction after treatment (n=120)

Indexs	OR	95%CI	<i>P</i>
Time window for interventional surgery	1.865	1.113-3.908	0.013

3 讨论

急性 ST 段抬高型心肌梗死的早期介入治疗的原则为:重建冠状动脉血流与开通梗死相关动脉。其中经皮冠脉介入手术能缩小梗死心肌组织的面积,还可改善冠脉血流。且经皮冠脉介入手术技术的成熟发展,使其治疗成功率逐渐升高^[13,14]。但该手术的最大关键因素是时间,患者发病至经皮冠脉介入手术的时间越短,救治的成功性越高,同时也越有利于患者的预后康复^[15]。两组治疗后 1 周的血清 cTnT、cTn I 含量低于治疗前,研究组低于对照组,表明发病后 ≤ 6 h 介入治疗急性 ST 段抬高型心肌梗死能提高治疗近期疗效,改善患者的心功能。同时本研

究显示治疗后随访 6 个月,研究组的心律失常、心力衰竭、心绞痛、心源性休克等不良心血管事件发生率低于对照组,表明发病后 ≤ 6 h 介入治疗急性 ST 段抬高型心肌梗死能改善患者的远期预后。这一结果与 Rodríguez-Jiménez A E 等人^[16]以及 Chiesa M 等人^[17]的研究具有一致性。分析可知:急性 ST 段抬高型心肌梗死可导致患者的心脏供血血管被阻塞,诱发心肌缺血的发生,特别是在 12 h 后多数患者的心肌将完全坏死,且随着时间的迁移,心肌的存活率越低。越早进行经皮冠脉介入手术,就越有可能开通闭塞的血管,降低心肌损伤,实现心肌水平的有效灌注,有效抑制炎症反应,进而促进患者临床症状的快速恢复,从而延缓心肌坏死进程^[18,19]。

急性 ST 段抬高型心肌梗死是心血管内科常见危急重症之一,目前经皮冠脉介入手术是促使冠脉再通的重要途径,但也需进行早期预测患者的预后。相关研究显示:心血管疾病患者的血清 FGF21 的表达高于非心血管疾病患者,为心血管疾病的独立预测因子^[20]。本研究显示两组治疗后的血清 FGF21 水平高于治疗前,研究组高于对照组,表明发病后 ≤ 6 h 介入治疗急性 ST 段抬高型心肌梗死能促进血清 FGF21 的释放。这一结果与 Geng L 等人^[21]以及 Pan X 等人^[22]的报道具有一致性。分析可知:FGF 家族成员是一种具有多种分泌功能(内分泌、自分泌、旁分泌)的多肽链,其可通过与由 FGF 受体结合而发挥生物学作用^[23]。在病理状态下 FGF21 可与受体结合形成复合体,使得成纤维细胞受体亚基-2 α 发生磷酸化,诱发旁分泌作用,从而发挥抗炎反应、抗细胞凋亡、改善心肌重构、抗氧化应激等多种作用^[24]。该物质也可抑制内皮细胞凋亡和对抗炎症,抑制氧化应激反应,保护内皮细胞,以减缓冠心病血管疾病的发展速度。FGF21 对多种心血管疾病具有保护作用,抑制动脉粥样硬化斑块的形成,可作为治疗因子参与心血管疾病的发展,以降低心血管疾病的发生几率。越早期进行经皮冠脉介入手术,能缩小梗死面积,能越早期改善患者的血流状况,使得缺血心肌组织得到血液灌注,提高患者的心功能,从而促进 FGF21 的表达^[25]。

急性 ST 段抬高型心肌梗死是中老年人发病率极高的危重症疾病,在临床上可持续表现为胸痛持续疼痛,在很短的时间内引发心律失常,导致患者出现心肌细胞损伤,具有极高心脏猝死率^[26]。经皮冠脉介入手术可抑制心肌梗死,使缺血心肌组织得到血液灌注,改善心肌缺血现象,利于恢复血流进而有利于患者预后^[27]。本研究显示在两组 120 例患者中,发病后 ≤ 6 h 进行介入治疗为影响患者治疗后血清 FGF21 水平、近期疗效与随访不良心血管事件的重要因素。这一结果与 Mindur JE 等人^[28]的报道具有一致性。从机制上分析,FGF21 在脂肪分化、生长中发挥重要作用,与心血管疾病的危险因素具有相关性,血清 FGF21 水平降低可导致机体出现全身炎反应,诱发机体出现胰岛素抵抗及高脂血症^[29]。早期进行经皮冠脉介入手术不仅可缩小梗死面积,还对心肌予以再灌注,也能延缓心肌坏死时间,促进 FGF21 的表达,从而促进改善患者的预后^[30]。但本文存在一定不足,如本研究样本量相对较小,无正常人群,且是一个横断面研究,相关性分析还不够深入,将在后续研究中探讨。

总之,发病后 ≤ 6 h 介入治疗急性 ST 段抬高型心肌梗死能促进血清 FGF21 的释放,能提高治疗近期疗效,改善患者的心功能,也能降低远期不良心血管事件的发生,研究表明,介入手术时间窗与血清 FGF21 的表达存在相关性。

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