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世别 女 医单汉

出 生 1972 年 3 月 21 日

the Mr. Common of the Mary



公民身份粤码



中华人民共和国 居 民 身 份 证

益发机关 北京市公安局朝阳分局

有效期限 2008.11.03-2028.11.03

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東京のGNOSIS OF PATTENTS // 次次
東第一作者 SCI 位系
COMPLICATED CORONARY HEART DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND THE
PROGNOSIS OF PATIENTS》检索报告
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月二十一四生,于 性別、女、一九七二年三 研究生 刘梅

内料學 月在 二00三年 九 月至二00七年 六 专业学习,学制 三年,修完硕士研究生培养计划规定的全部课程,成绩合格,

毕业论文答辨通过、准予毕业。

培养单位: 河北医科大学

证书编号: 100891200702000561

校(院、所)长: 🔏

二00七年 六 月三十

回

中华人民共和国教育亦学历证书查询网址: http://www.chsi.com.cn



领土学位通书

剑 格奈河北省保定市 人,一九七二年 三 月 中一日生。在我 核

營 士宗 區 $\widetilde{\Xi}$ 试和论文答辩 THAT 根据《中华人民共和 MA 学科(专) 被交 学位的课程考 例》的机 西世布 0 茶品 **V**I 山 文示 士兵 生原

爾煮胺霧大擊 撥长 学位评定委员会主席 二00七 年次 月11六日

证书编号 1008932007000561

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本证书表明特证人通过专业技术职务任职资格评审委员会评审具有的任职资格

This is to certify the qualification level of speciality and technology of the bearer who has passed the enaluation of the evaluating commission of a technical or professional post.

高级专业技术职务任职



Qualification Certificate

of Senior Professional Technical Position



The Title Reform Leading Group Office of Hebei Province

	(加盖审批部门钢即有效)	是名 文	出生年月 1972 年 Date of Birth 编号 0055707	
专业技术系列 Prifessuibak Series	专业名称 Name of Speciality 资格名称	和 文 子 子 Approval No Approv	Ax 子 P P P P P P P P P P P P P P P P P P	

保定市科学技术局文件

保科发〔2020〕16号

签发人: 刘铁英

保定市科学技术局 关于下达 2020 年保定市科技计划自筹 经费项目(第一批)的通知

有关县(市、区)科技局,有关单位:

现将 2020 年保定市科技计划自筹经费项目(第一批)下达给你们,请于 8 月 15 日前组织项目承担单位与市科技局签订项目任务书,尽快落实研究任务,并按照《保定市科技计划自筹经费项目管理办法》(保科发 [2020] 15 号)的有关规定,加强对项目的组织与管理,确保计划项目的顺利实施。

附件: 2020 年保定市科技计划自筹经费项目表 (第一批)

保定市科学技术局 2020年7月29日

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(此件不宜公开)

	2041ZF005	77.5	安国市医院		2020. 06-2021. 07	安国 市
	2041ZF006	进骨关节炎软骨细胞增殖和减轻氧	安国市中医院		2020. 02-2021. 12	安国市
-	2041ZF007	E肝脏外科精准	保定市第二医院		2020, 04-2022, 04	保定市第二医院
16	2041ZF008	(S)联合品管圈 (QCC) 在肝内的用研究	保定市第二医院		2020. 04-2022. 12	保定市第二医院
	2041ZF009	炎纤维蛋白原、脂 开究	保定市第二医院		2020, 05-2022, 03	保定市第二医院
	2041ZF010	F-a 检测在急	保定市第二医院		2020. 02-2021. 06	保定市第二医院
	2041ZF011	宮颈癌中的表达及	保定市第二医院		2020. 05-2022. 12	保定市第二医院
20	2041ZF012	2动图对高龄孕妇	保定市第二医院		2020. 05-2022. 05	保定市第二医院
	2041ZF013	STZ诱导的糖尿病大鼠早期肾损伤 及除压活性研究	保定市第二医院	首都医科大学三博 脑科医院	2020. 05-2021. 06	保定市第二医院
22	2041ZF014	AFI基因与结肠癌 研究	保定市第二医院	4	2020, 05-2022, 05	保定市第二医院
R	2041ZF015	的分子机制	保定市第二医院		2020. 05-2022. 05	保定市第二医院
24	2041ZF016	血式开放性有创动脉导管采集动脉血气的方法研究	保定市第二医院		2020. 01-2023. 01	保定市第二医院
25	2041ZF017	ERK/MAPK信号通路并影响胶 3条的全验研究	保定市第二医院	首医大三博脑科医 院	2020. 06-2022. 06	保定市第二医院
26	2041ZF018	//超重2型糖	保定市第二医院		2020. 06-2021. 12	保定市第二医院
	2041ZF019	mey.	保定市第二医院		2020. 05-2023. 05	保定市第二医院
28	2041ZF020	-	保定市第二医院		2020. 06-2022. 06	保定市第二医院
83	2041ZF021	Ki-67在膀胱尿路上皮癌中含义	保定市第二医院		2020, 05-2023, 05	保定市第二医院
	2041ZF022	"效相关因素分析	保定市第二医院	保定市儿童医院	2020, 01-2022, 05	_
31	2041ZF023	流松性骨折	保定市第二中心医院		2020. 06-2022. 12	保定市第二中心医院
32	2041ZF024		保定市第二中心医院		2020.02-2022.02	保定市第二中心医 院
33	2041ZF025	及血清炎性因	保定市第二中心医院		2020, 07-2022, 07	保定市第二中心医 院

保定市社发类项目申请书

(医疗卫生)

其它

冠心病合并2型糖尿病者血浆纤维蛋白原 危险因素研究 脂蛋白a、D-二聚体

项目依托单位:

加单位:

刘梅 目组长: 顶

完全自筹式 申请资助方式:

其他 申报项目类别:

保定市第二医院 项目主管单位:

2020年 申请计划年度:

2020, 05-2022, 03 项目起止年月:

2020-05-19 报 目 期: [1]

保定市科学技术局制

	名称	冠心病合并2型物	原尿病者血浆纤维	蛋白原、脂蛋白:	a. D-二聚体危险[因素研究	
	地址	保定市东风西路	338号				
頻	法人代码	40188830-3		E-mail			
	法人代表	葛长青	电话		曲路編	071051	
E	开户名称	保定市第二医院	1	开户银行	保定银行向阳支	ff	
目衣毛角立既	开户行行号	313134000038	1	银行账号	860070201050110	074	
II.	员工总数	1400 人	技术人员数	人	中高级技术 人员数	入	
1	1 1	性质]模	其他特征		
	医院	其他 ————————————————————————————————————					
	病的关系。将 ,分别测定四	组的Fg、Lp(a)、	前组、12型相尿病 0-0,所又受检青 F據尿病组,切床	合并冠心病组, 均空腹12h以上 病组鼻手冠心病	冠心病组,与健康 抽取静脉血。结果 组、且以上三组为	2型糖尿病合并冠 这对原组进行比较 4,2型糖尿病合并 均高于健康对照组。 译血一纤溶系统的	

衝失调。冠心病组较正常对照组有较高水平的Fg、Lp(a)、D-D,而2型糖尿病组较冠心病组水平更高,其与炎症刺激Ⅱ6释放增加、高脂血症加速压合成而减慢其降解及胰岛素抵抗所致高胰岛素血症有关。通过对2型糖尿病合并冠心病患者的多种相关因素指标进行分析,加深对2型糖尿病并发冠心病患者的多种相关因素指标进行分析,加深对2型糖尿病并发冠心病高危因

素的认识,为2型簡尿病并发冠心病的预测、评估病情及防治提供理论依据。

项目内容摘要

应用行业	专科疾病防治活动	创新类型	知识创新
技术领域	医疗卫生技术		
学科分类	心血管病学		
科技活动 类型	基础研究		
	随着我国社会经济的发展,生活水平的	提高以及人口的老	. 於此,糖尿病、冠心病的发病率和病

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随着我国社会经济的发展生活水平的提高以及人口的老龄化,糖尿病、冠心病的发病率和病死率呈上升趋势。糖尿病和心血管疾病已成为人类健康的最大、最严重威胁,是日益严重的公共卫生问题。糖尿病患者发生心血管疾病的风险是非糖尿病人群的二到四倍。糖尿病患者如果合并活心病,无疑具有"双重危险",更应该积极采取措施,降低心血管事件的风险。2型糖尿病患者80%死于心血管疾病,其中75%死于冠心病,心肌梗死发生率高,预后差。识别和阻断糖尿病、冠心病的危险因素可以使其得到早期的预防和治疗。Fg、Lp(a)、D-D从多环节参与动脉粥样硬化、凝血一纤溶系结的平衡失调。有研究发现显著增高的Lp(a)预示着急性心肌梗死的风险率增加3~4倍。Fg和D-D作为凝血和纤溶系统的两个常用指标,Fg水平反映体内凝血状态,是糖尿病、冠心病血管病变独立的危险医子。而DD是体内处于高凝状态和继发纤溶增强的分子标志物之一,与血栓形成也有着密切的关系。Fg在血管内膜与Lp(a)结合,可能强化纤维斑块的细胞外脂质沉积,增加斑块的不稳定性。Lp(a)可致内皮损伤,激活内外源凝血途径使下g升高,血液高凝;而Fg转变为Fb在血管内膜与Lp(a)有效交联强化了斑块的细胞脂质堆积,两者共同参与致病过程。因此,联合监测Lp(a)、FIB和DD水平有助于评估糖尿病及冠心病的风险。为今后进一步探究其协同机制,切断致病链条,以及2型糖尿病合并冠心病的预防和早期诊断及动态监测有着十分重要的临床价值。

二、国内外现状及发展趋势

糖尿病是一种全身性代谢紊乱性疾病,易合并冠心病这一事实已被国内外学者所公认。糖尿病和冠心病存在许多共同的危险因素。早在1992年哥本哈根心脏流行病学调查发现心肌梗死危险随Lp(a)的升高逐渐增加。LP(a)是冠心病的独立危险因素,并与动脉粥样硬化的形成和发展密切相关。高水平的LP(a)可通过促进动脉粥样硬化及抗纤溶作用使糖尿病患者更易并发高血压、冠心病,及大血管和微血管的并发症,并在其发生发展中起重要作用。Fg与冠心病的相关性,早在50年代即已被学者们所注意,经过多年的临床研究及流行病学调定证实,降低Fg水平可以预防冠心病及改善其预后。Fg是糖尿病血浆高凝状态形成的重要原因,目前被认为是糖尿病血管病变发生的重要机制。D-D在临床上已被视为体内高凝状态和纤溶亢进的分子标志物。近年来凝血一纤溶系统的平衡失调在糖尿病、冠心病中的作用日益得到重视,动脉粥样硬化斑块的产生和发展系由血栓形成或纤溶功能缺陷所导致。它与糖尿病、心血管疾病及其急性临床事件的发生密切相关。

随着我国老龄化社会的进程,2型糖尿病合并冠心病的发病率逐年上升。有研究表明突发的糖尿病,其中有46%已经合并了冠心病。患2型糖尿病5年以上的患者。一半左右有并发冠心病的可能,并且糖尿病有80%的病人都死于冠心病。鉴于以上原因,2型糖尿病合并冠心病的危险因素的研究已经刻不容缓。目前已经有大量研究证明Fg、Lp(a)、D-D既是冠状动脉血管病变独立的危险因子、也是糖尿病大血管及微血管病变的危险因子。但国内外尚未有关于糖尿病合并冠心病的情况下,对Fg、Lp(a)、D-D的浓度变化进行的系统研究的报道,亦未有Fg、Lp(a)、D-D在糖尿病合并冠心病的疾病发展、转归中起何种作用的报道。本研究填补了国际及国内在此领域的空白,为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路,对于降低病人致死率、致残率,提高生活质量具有重大意义。

三、项目依托单位、参加单位现有工作基础、特色及优势

保定市第二医院始建于1920年,为保定市心血管病医院,是一所拥有百年历史,集医疗、科研、教学、预防、保健和康复功能为一体的三级甲等综合医院。目前医院有总院、妇产儿科院区两个院区,总占地面积33373平方米,建筑面积96321平方米,职工1737人,开发床位1398张。年门诊量53万人次,住院病人4万人次。医院另设有天威分院、农大分院及朝阳社区、韩南社区等5家卫生服务中心。医院拥有多种先进医疗设备,如磁共振大型医疗设备200余件。我院心内科是保定市重点发展科室,分两大病区,共有床位100余张。年至划进行冠状动脉介入手术1000余例。而康复医学科是我院的龙头科室,共有床位40余张,科室医生均为硕士研究生、本科以上学历,基础知识扎实,工作作风严谨,具有较强的科研创新能力。康复医学科面向一人多病的老年病患,对于此类复杂病症的治疗及预防有丰富临床经验。

医院设医疗专业49个,肝胆外科为省级重点专科,口腔颌面外科、普通外科、医学影像科、心血管内科、神经内科、肿瘤内科、血管外科、耳鼻喉科头颈外科为市级医学重点学科,中西医结合老年病科室是市级医院重点发展学科,皮肤科、康复医学科为市级重点中医专科。在人才、设备和基础设施上形成明显的竞争优势,某些项目达到省内领先和国内先进水平。为充分发挥优势和特色,医院按阶梯性人才培养规化,选拔学有成就,卓有建树的专科技术尖子,担任学科带头人。近十年医院每年选派数十名治学严谨,德才兼备的技术骨干到国外和国内大医院进修或进行学术交流,培养了一批研究生和学科带头人,孕育了新世纪的优秀人才,目前各科有专家,科科有新秀。

四、项目主要实施内容(包括实施方案、工艺技术路线、创新点及技术关键)

本研究旨在探讨血浆纤维蛋白原(Fg)、脂蛋白a(Lp(a))、D-二聚体(D-D)与2型糖尿病合并冠心病的 关系,糖尿病、冠心病及2型糖尿病合并冠心病患者Fg、Lp(a)、D-D的浓度变化及其临床意义。

本研究拟将证实Fg、Lp(a)、D-D不但是糖尿病、冠心病的高危因素,同时对于2型糖尿病合并冠心病者Fg、Lp(a)、D-D显著升高,相互促进,互为因果,造成恶性循环,加重2型糖尿病合并冠心病者冠状血管及大血管、微血管的病变。这将为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路,

拟入选2018年1月-2022年4月在我院心内科及康复医学科科就诊的冠心病及糖尿病病人180人。将病人分为三组,每组各60人:组1为2型糖尿病组、组II为冠心病组,组III为2型糖尿病合并冠心病组,组间进行两两比较,并将同期来我院门诊健康体检的人群设为健康对照组进行比较,分别测定四组的Fg、Lp(a)、D-D,所有受检者均空腹12 h 以上抽取静脉血。采用日立7180全自动生化分析仪测定Lp(a),CA-1500全自动血凝分析仪测定Fg、D-D。应用SPSS统计分析软件进行统计学处理。分析三组病人Fg、Lp(a)、D-D的浓度变化及其临床意义。

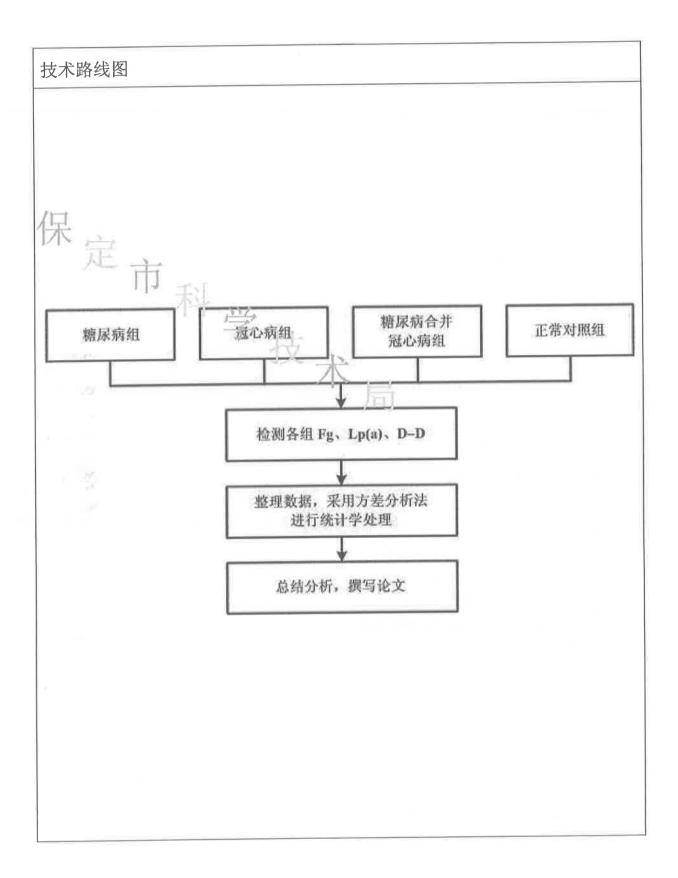
基于: 1、国内外学者已经对Fg、Lp(a)、D-D进行了深入研究,其研究方法已经成熟并公开报道; 2、已与我院检验科联系,我院检验仪器日立7180全自动生化分析仪、CA-1500全自动血凝分析仪及检验人员能够保证所测数据的准确性。3、本课题组成员具有丰富的临床经验及科研经验,故预期该研究过程会非常顺利,如遇技术困难,可随时求助于北京阜外医院及北京大学附属第三医院(本课题组成员与其保持着良好工作关系)

主要创新点:

本研究对象经冠状动脉造影证实为冠心病患者,分析四组的Fg、Lp(a)、D-D含量水平及其相互间的作用。国内外尚未有关于糖尿病合并冠心病的情况下,对Fg、Lp(a)、D-D的浓度变化进行的系统研究的报道,亦未有Fg、Lp(a)、D-D在糖尿病合并冠心病的疾病发展、转归中起何种作用的报道。本研究填补了国际及国内在此领域的空白,为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路,对于降低病人致死率、致残率,提高生活质量具有重大意义。

技术关键:

- 1、根据不同的疾病严格筛选病人,建立实验组及对照组。研究糖尿病、冠心病与Fg、Lp(a)、D-D的关系,以及糖尿病合并冠心病者Fg、Lp(a)、D-D浓度变化,并进行两两比较。
- 2、所有受检者均空腹12 h 以上抽取静脉血,采用日立7180全自动生化分析仪测定Lp(a), C A-1500全自动血凝分析仪测定Fg、D-D。
- 3、应用SPSS统计分析软件进行统计学处理,比较各组间Fg、Lp(a)、D-D浓度差异,为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路、新方法。
- 通过该课题的研究,详细了解了Fg、Lp(a)、D-D做为高危因素在冠心病、糖尿病以及的糖尿病合并冠心病发生、发展的过程中所起到的重要作用,这将为人类预防和治疗糖尿病及冠心病提供新的理论基础。



知识	项目扩	支术来源	国内技术	是否形成 标准	无	是否运用5 技术进一次	步开发研	是
产权情况	项目5	完成后技 有权是否 主知识产 权	是	项目完成 后,是否 申请国家 专利	否			
×	预期/	成果形式	论文论著		预计技术	成果水平	国际领先	
保	遠	工业。	年产量 単位:	年产值 (万元)	年销售额收入(万元)	年利润 (万元)	年税金 (万元)	年创汇 (万美 元)
	477 344	TIJ	-x* . I	0	0	0	0	0
预计成果水平及效益	经济 效益	农业	试验(或推广 应用)面积 (公顷)	年产值 (万元)	年人均产值 (万元)	年亩产 (Kg)	年纯收 入(万 元)	年人均 纯收入 (万元)
水			0	0 -	0	0	0	0
	括耗健、	效益(包 保节能、 医疗 就业等)	联合监测Lp(a)、F 探究其协同机制, 动态监测有着十分 2型糖尿病人预防 思路,对于降低病	为人致死平、3	以汉平,证同王	[[] (以里) 代刊 里	ухлах 2 °	
			为:2020.05-2022.03 本安排如下:					
	2020年5月-2020年7月病历搜集							
電	2020年7月-2020年9月资料整理分析							
项目实施进度安排			3月论文完成					

五、	项目经费来源与支出	预算	N4 12+	下二 / 归匆西台	: .l.
序号	预算科目名称	合计	专项经费	万元(保留两位 自筹经费	小致力 配套经费
1	一、经费来源	5	0	5	0
-71	二、经费支出	5	0	5	0
约	1			5	0
3	(一) 直接経費	5	0		
4	1、设备费	0.9	0	0.9	0
5	(1) 购置设备费	0.1	0	0.4	0
6	(2) 试制设备费	0.3	0-	0.3	0
7	(3)设备改造与租赁费	0.2	0	0.2	0
8	2、材料费	0.3	0	0.3	0
9	3、测试化验加工费	0.3	0	0.3	0
10	4、燃料动力费	0	0	0	0
11	5、差旅费	0.2	0	0.2	0
12	6、会议费	0.3	0	0.3	0
13	7、国际合作与交流费	0	0	0	0
14	8、出版/文献/信息传播/知识产权事务费	2	0	2	0
15	9、劳务费	0	0	0	0
16	10、专家咨询费	1	0	1	0
17	11、其他支出	0	0	0	0
18	(二) 间接经费	0	0	0	0
19	其中: 绩效支出	0	0	0	0

	_	1	- H - T - T - T - T - T - T - T - T - T - T	~		批	专项经费	白箜灰弗	配存级费
单位名称 甲位	甲位类型	任务分工 	州	<u> </u>		小计	其中:间接费用	日本江风	田林丹太
本担単			2 本	5.0	0.0		0.0	5.0	0.0
1	承担事		负责人		负责人	负责人 刘梅 5.0	负责人 刘梅 5.0	<u>负责人</u> 刘梅 5.0 0.0	负责人 刘梅 5.0 0.0 0.0

性中	姓名	性别	年龄	证件号码	职称	学历	学位	现从事专业	所学专业	所在单位	承担任务 (分工)	工作时间
1	刘梅	¥	48	130602197203210021	副主任医师	研究生	愛 十	内科学其他学科	心血管病学	保定市第二医院	项目负责人	18月
2	韩天云	¥	34	130522198604238025	主治医药师	本科	十 計	药学其他学科	药学其他学科	保定市第二医院	资料收集整理	12月
က	解冬干		39	130603198103230931	王治医药师	本科	光	药学其他学科	药学其他学科	保定市第二医院	资料收集整理	12月
4	刘绮	¥	37	130631198209080869	其他中级	本科	小十	基础护理学	基础护理学	解放军总院第七医学中心	资料收集整理	12
2	と数型	¥	54	130703196607040329	主任医师	本科	干款	内科学其他学科	临床医学其他学科	保定市第二医院	资料整理	12
9	范多娇	¥	37	13063219831122524X	主治医师	研究生	優十	小血管病学	心血管病学	保定市第二医院	收集资料,撰 写论文	12月

				यामा न्यं या		绩效标准	标准	
中	绩效目标	绩效指标		沿你描述	优	良	4	業
降低病治疗治疗	人的致死率和致残率,为预防和 心病及糖尿病提供新思路、发表	降低患病率、致死率和致残率, 刊论文。	发表核心期	发表论文被核心期刊收录,或被SCI收录	发表SCI文章 章1篇以上	发表核心期 刊4篇	发表3篇核 心期刊	小于3篇核心期刊

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上左座	年销售	馬收入 元)	年创汇 (万美元)		激税金 ī元)	年利润 (万元)
上年度 (2019)年 项目承	400	000	0		0	0
担 単位整 体 效益	研究开发 (或推广应 用)规模	年农业总产 值(万元)	年人均产值 (万元)	年亩产 (kg)	年农业纯收 入(万元)	年人均纯收 入(万元)
效益	0	0	0	0	0	0

(成立时间、资质、注册资金、主导产品、技术力量、承担项目情况、业绩及其他情况)

保定市第二医院始建于1920年,为保定市心血管病医院,是一所拥有百年历史,集医疗、科研、教学、预防、保健和康复功能为一体的三级甲等综合医院。目前医院有总院、妇产儿科院区两个院区,总占地面积33373平方米,建筑面积96321平方米,职工1737人,开发床位1398张。年门诊量53万人次,住院病人4万人次。医院另设有天威分际、农大分院及朝阳社区、韩南社区等5家卫生服务中心。医院拥有多种先进医疗设备,如磁共振大型医疗设备200余件。

我院心内科是保定市重点发展科室,分两大病区,共有床立100余张。年平均进行冠状动脉介入手术 1000余例。而康复医学科是我院的龙头科室,共有床位40余张,科室医生均为硕士研究生、本科以上 学历,基础知识扎实,工作作风严谨,具有较强的科研创新能力。康复医学科面向一人多病的老年病 患,对于此类复杂病症的治疗及预防有丰富临床经验。

医院设医疗专业49个,肝胆外科为省级重点专科,口腔颌面外科、普通外科、医学影像科、心血管内科、神经内科、肿瘤内科、血管外科、耳鼻喉科头颈外科为市级医学重点学科,中西医结合老年病科室是市级医院重点发展学科,皮肤科、康复医学科为市级重点中医专科。在人才、设备和基础设施上形成明显的竞争优势,某些项目达到省内领先和国内先进水平。为充分发挥优势和特色,医院按阶梯性人才培养规化,选拔学有成就,卓有建树的专科技术尖子,担任学科带头人。近十年医院每年选派数十名治学严谨,德才兼备的技术骨干到国外和国内大医院进修或进行学术交流,培养了一批研究生和学科带头人,孕育了新世纪的优秀人才。

姓名	性别	出生 年月	学历	职务、职称	所学专业	现从事专业	
刘梅			研究生	研究生 副主任医师		内科学其他学科	
所在单 位	保定市	保定市第二医院					
联系电话	0312-3099716		手机	17733221600	E-Mail	liu_m mei@163.com	
	通讯地址 保定市 学科		西路338号保定	路338号保定市第二医院康复医		071000	

个人经历与业绩

刘梅,48岁,心血管内科硕士,副主任医师。1994年于承德医学院临床医学系毕业后一直在我院特诊科从事临床医疗工作,2007年毕业于河北医科大学研究生学院。有较深厚而扎实的基础知识,能熟练查阅英文文献,掌握本学科最新动态,在三年硕士研究生学习阶段,在河北省著名心血管专家、河北省老年病学会秘书长、导师郭艺芳教授的指导一,从事老年病及心脑血管病的研究,对老年病人同时患有糖尿病、脑血管病、心脏病、肾病等一人多病的复杂情况均能正确分析处理,具有很强的综合分析处理能力。与老年病学同仁联合编著了《老年病学》一书。曾多次发表有价值的学术论文共十余篇,其中《肾素-血管紧张素-醛固酮系统对血压近日节律的影响》发表于国家级核心期刊《心血管病学进展》;《年龄性别对肾素-血管紧张素系统的近日节律的影响》发表于国家级核心期刊《实用内科学》;《衰老大鼠肾素-血管紧张素系统的近日节律的变化》发表在《中华临床医学实践杂志》上等等。在科研方面《健脾补肾活血化瘀法对老年性激素的影响及对心脑血管病的疗效观察》,以及科研《代谢综合征与糖尿病心脑血管病的相关性研究》,均获市二等奖。

在专业技能方面:掌握现代心血管病学,熟知各种常见疾病的病理生理学特征,具备紧急应变和处理 危重、疑难病例的能力。能正确识别各种复杂心电图,并予以正确处理。掌握了多种医学数据库的应 用,如Medline、OVIDE、CHKD等等,能通过Internet与国内外医学专家进行交流。掌握本学科动态及 前沿,熟练掌握SAS、SPSS、NCSS等统计软件的操作,以处理实验数据。

保定市市级科技计划项目申报诚信承诺书

(申报单位部分)

本单位依据市级科技计划项目指南的任务需求,严格履行法人负责制,自愿提交申报书,在此郑重承诺:本单位已就所中报材料内容的真实性和完整性进行审核,不存在违背《关于加强科研诚信建设的实施意见》(冀办字〔2019〕1号〕和其它科研诚信要求的行为,申报材料符合《中华人民共和国保守国家秘密法》和《科学技术保密规定》等相关法律法规,在参与项目申报和评审活动全过程中,遵守有关评审规则和工作纪律,杜绝以下行为:

- (一)组织或协助、包庇、纵容项目团队以不正当方式影响项目评审公正,获 /1:11 取市级科技计划项目承担资格;
- (二)在申报书中以高指标通过评审,在任务书签订时故意篡改降低任务书中相应指标:
 - (三) 其它违反财经纪律和相关管理规定的行为。

如有违反,本单位愿接受项目管理机构和相关部门做出的各项处理决定,包括但 不限于停拨或核减经费,追回项目经费,取消一定期限市级科技计划项目申报资格,

记入科研诚信严重失信行为数据库以及主要负责人接受相应党纪政纪处理等。



保定市市级科技计划项目申报诚信承诺书

(申请人部分)

本人根据市级科技计划项目申报指南的要求自愿提交项目申报书,在此郑重承诺:严格落实《关于加强科研诚信建设的实施意见》(冀办字〔2019〕1号)有关要求,所申报材料和相关内容真实有效,不存在违背科研诚信要求的行为;申报材料符合、中华人民共和国保守国家秘密法》和《科学技术保密规定》等相关法律法规;在参与市级科技计划项目申报、评审和实施全过程中,恪守职业规范和科学道德,遵守评审规则和工作纪律,杜绝以下行为:

- (一) 采取贿赂或变相贿赂、造假、故意重复申报等不正当手段获取科技计划项目承担资格;
 - (二) 抄袭、剽窃他人科研成果或者伪造、篡改研究数据、研究结论;
 - (三)购买、代写、代投论文,虚构同行评议专家及评议意见;
 - (四) 违反论文署名规范,擅自标注或虚假标注获得科技计划等资助;
- (五)在申报书中以高指标通过评审,在任务书签订时故意篡改降低任务书中相应指标;
- (六)违反市级科技计划项目管理要求,不按规定提交项目过程管理和验收资料、办理项目结题验收手续;遇不可抗力导致项目无法执行时,不按要求履行项目变更、中止和撤销手续等。
 - (七) 其它违反财经纪律和相关管理规定的行为。

如有违反,本人愿接受项目管理机构和相关部门做出的各项处理决定,包括但不限于取消项目承担资格,追回项目经费,在一定范围内通报违规情况,取消一定期限市级科技计划项目申报资格,记入科研诚信严重失信行为数据库以及接受相应的党纪政纪处理等。

签字: 3 / 18 日期: >0>0、5、19

九、项目依托单位意见 十、项目主管单位意见 年 月 十一、市科技局意见 备 淮

保

市科学技术局

18

保定市科技计划项目任务书

项目起止年月: 2020.05-2022.03 士

食 修 稳 位:

项 目 负 债 人: 刘梅 联 系 电 话: 17738221600

开 户 名 称:保定市第二医院

开 户 银 行:保定银行向阳支行

开户银行行号: 3J3I34000038

号: 86007020105011074

归口管理部门(丙方): 保定市第二医院

保定市科学技术局制

填报说明

一、本项目任务书是市科技局对保定市科技计划项目全程管理的基本文件之一。要求 承担单位登录保定市科技计划项目管理平台在线填写、提交,逐级审核并经科技局同意后 在线打印书面任务书一式四份,报归口管理部门审查盖章,并将书面文件报市科技局分管 业务处室审查确认。本项目任务书的电子数据文件不要求盖章。

一、本任务书的甲方是指市科技计划项目任务下达单位,即市科技局; 乙方是指项目第一承担单位; 丙方(归口管理部门)指市直有关部门、各县(市)、区科技局及市科技局投收或委托的其他机构。

三、"项目名称"才项目编号"、"项目起止年月"等必须与市科学技术研究与发展计划下达的内容一致。

四、开户名称与承担单位一致 采用集直支付方式的单位除外)。

五、本任**务书**要求打印。涉及到外文名称, 事写清全称和缩写字母, 第一次出现时要注意中文。

六、木任务书一式四份,分存甲方两份,乙方一份,丙方一份。本项目任务书打印书 面文件要求盖章,其中乙方盖所在单位公章,丙方盖科技计划管理章。

一、主要研究开发内容、技术路线及创新点(推广类包括规模、地点等)

本研究旨在探讨血浆纤维蛋白原(Fg)、脂蛋白a(Lp(a))、D-二聚体(D-D)与2型糖尿病合并冠心病的 关系,糖尿病、冠心病及2型糖尿病合并冠心病患者Fg、Lp(a)、D-D的浓度变化及其临床意义。

本研究拟将证实Fg、Lp(a)、D-D不但是糖尿病、冠心病的高危因素,同时对于2型糖尿病合并冠心病者Fg、Lp(a)、D-D显著升高、相互促进、互为因果、造成恶性循环、加重2型糖尿病合并冠心病者冠状血管及大血管、微血管的病变。这将为2型糖尿病人预防冠心病提供理论基础、对预防和治疗糖尿病合并冠心病提供了

拟入选2019年10月-8020年10月在我院就诊的冠心病及糖尿病病人180人。将病人分为三组、每组各60人、组 1 为2型糖尿病组 2011为冠心病组、组111为2型糖尿病合并冠心病组、组间进行两两比较、并将同期来我院 门诊健康体检的人群设为健康对照组进行比较,分别测定四组的Fg、Lp(a)、D-D,所有受检者均空腹12h以上抽取静脉血。采用目立7180全目对生化分析仪测定Lp(a)、CA-1500全自动血凝分析仪测定Fg、D-D。应用 SPSS统计分析软件进行统计学处理。分析了处态人Fg、Lp(a)、D-D的浓度变化及其临床意义。

基于: 1、国内外学者已经对Fg、Lp(a)、D-D进行了深入研究。其研究方法已经成熟并公开报道: 2、已与我院检验科联系,我院检验仪器日立7180全自动生化分析权。500全自动血凝分析仪及检验人员能够保证所测数据的准确性。3、本课题组成员具有丰富的临床经验及科研经验,故预期该研究过程会非常顺利,如遇技术困难,可随时求助于北京阜外医院及北京大学附属第三医院(本课题组成员与其保持着良好工作关系、

主要创新点:

本研究对象经临床确诊为冠心病患者,分析四组的Fg、Lp(a)、D-D含量水平及其相互间的作用。国内外尚未有关于糖尿病合并冠心病的情况下,对Fg、Lp(a)。D-D的浓度变化进行的系统研究的报道,亦未有Fg、Lp(a)、D-D在糖尿病合并冠心病的疾病发展、转归中起何种作用的报道。本研究填补了国际及国内在此领域的空白,为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路,对于降低病人致死率、致残率,提高生活质量具有重大意义。

二、项目验收的考核指标(技术指标、经济指标、技术创新能力及社会效益

技术指标:

- 1、根据不同的疾病严格筛选病人,建立实验组及对照组。研究糖尿病、冠心病与Fg、Lp(a)、b-b的关系。以及糖尿病合并冠心病者Fg、Lp(a)、b-b浓度变化、并进行两两比较。
- 2、所有受稅者均空腹12h以上抽取静脉血、采用自立7180全負动生化分析仪测定Lp(a), EA-1500全自动血凝分析仪测定Fg、D-D。

了一家用SP9S统计分析软件进行统计学处理,比较各组同Fg、Lp(a)、D-D浓度差异。

经济指标上 一十

降低了病人的致死率、致艰率、减少再住院率、减少了医疗保险支出。

技术创新能力:

本研究分析四组的Fg、Lp(a)、D-D含量水平及其相互间的作用。国内外尚未有关于糖尿滴合并冠心病的情况下,对Fg、Lp(a)、D-D的浓度变化进行的系统研究的限道。亦未有Fg、Lp(a)、D-D在糖尿病含并冠心病的疾病发展、转归中起何种作用的报道。本研究填补了国际及国内在此领域的空白。为2型糖尿病人预防笼心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新恩路、对于降低病人致死率、致残率,提高生活质量具有重大意义。

社会效益:

联合监测Lp(a)、F1B和DD水平有助于评估糖尿病及冠心病的风险。为今后进一步探究其协同机制,切断致病链条,以及2型糖尿病合并冠心病的顶防和早期诊断及动态监测有着十分重要的临床价值。本研究填补了国际及国内在此领域的空白,为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路,对于降低病人致死率、致残率、提高生活质量具有重大意义。

发表论文1-3篇。

三、进度、安排和阶段目标

本项目起止时间为:2020,05-2022.03 项目实施进度具体和阶段目标安排如下: 2020年5月-2020年10月病历搜集 2020年10月-2020年11月资料整理分析 2020年11月~2021年1月撰写论文

42年1月-2022年3月论文发表。

是作和学技术局

四、项目承担单位、合作单位任务分工、知识产权归属

项目承担单位为保定市第二医院,负责该科研项目的具体实施,已联系上级医院例如河北省人民医院,解放 军总院第七医学中心,北京阜外医院等,遇到困难可随时给予帮助,单无合作关系。 知识产权归属保定市第二医院。

保定市科学技术局

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25	二、经费支出	5	0	5	0
3	(一) 直接经费	5	0	5	0
4	1、设备费	0.9	0	0.9	0
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11	流質	0.3	0	0.3	0
12	6、出版/文献/信息传播/知识 产权事务费	2	0	2	0
13	7、劳务费	0	0	0	0
14	8、专家咨询费	1	0	1	0
15	9、其他支出	0	0	o	0
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八、承诺条款

签约各方共遵守市科技计划管理有关规定前提下,承诺如下;

乙方:

- 1、保证项目实施所必需的场所、仪器、设备等支撑条件。
- -2、严格按照国家、省和市有关规定及本任务书要求使用科技局拨款。
- 3、按任务书要求完成市科技局下达的计划任务,接受科技局及其授权或委托机构的监督 和评估。
 - 4、项目实行验收结题制,项目验收后向甲方、乙方填报验收证书。

芮方:

- 1、协助甲方组织和实施项目,监督和检验乙方对任务书的执行。
- 2、负责初审任务书内容,向甲方报告项目进展情况和经费决算。
- 3、受甲方委托组织项目的验收工作。

甲方:

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- 1、 定期对项目进度监督检验和验收, 协调解决项目进行中出现的问题。
- 2、 接任务书规定的用款计划拨给乙方当年的科研经费。
- 3、对于不能恰当履行任务书义务的乙方、丙方,应通报批评,并视情况终止或撤消项目。此款将作为对承担单位和项目负责人信誉评估的重要依据。

本任务书所协议的其它条款如下

九、任务书签订各方签章

甲方: 保定市科学技术局

主管业务处处长:

主管局长:



东季即毙

乙方(承担单位):保定市第二医院

项目负责人: 31200

合作单位:





(公章)

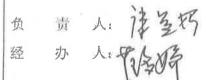
旦期:

丙方(归口管理单位),保定市第二医院

(科研计划专用章)

日期:

日期:





保定市科技计划项目验收证书

保

保科验字 (2023)03-068 号

14

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项目编号: 2041/2E009第

项 目 名 称: 冠心病合并2型糖尿病者血浆纤维蛋白原、脂蛋白a、D-二聚体危险因素

研究

承 担 单 位: 保定市第二医院

合作单位:解放军总院第七医学中心

验收主持部门: 市科技局

验 收 方 式: 函审验收

验 收 日 期: 2023-03-30

保定市科学技术局制

填写说明

- 1.《保定市科技计划项目验收证书》:本表格规格为标准 A4 纸,竖装,必须打印。本证书为保定市科技局制定的标准格式,任何部门、单位、个人均不得擅自改变内容、增减证书中栏目。
- 3. 证书编号: 指市科技局按年度组织验收的生成的顺序编号, 必须与申请表中一致。
- 3. 项目编号: 指项目计划编号, 必须与计划下达时一致。
- 4. 项目名称: 与计划下达文件中项目名称一致。
- 5. 承担单位:与计划下达文件中单位名称一致
- 6. 验收方式:指该项目验收所采用的验收方式,即会议验收、函审验收或书面验收。
- 7. 验收日期: 指该项目通过专家验收的再期。
- 8. 项目基本信息表:由项目单位如实填写,对不实填写引起的后果,由项目单位负全部责任。
- 9. 技术资料目录:指按照规定应由项目单位提供的主要文件和技术资料。
- 10. 主要研究人员名单:由项目单位填写,应与任务合同书的内容一致。
- 11. 验收专家名单:采用会议验收时,由参加验收会的专家亲自填写;采用函审验收时,由项目承担单位填写,同时附验收专家验收函审表;采用书面审核验收时,此页不用填写。
- 12. 验收意见:会议验收是验收专家组形成的验收意见;函审验收是函审专家组组长根据函审专家验收意见表汇总形成的意见;采用书面审核验收时,此页不用填写。
- 13. 验收单位意见:由项目单位填写,经领导签字后,加盖单位公章。
- 14. 项目归口管理部门意见:由项目归口管理部门填写,经负责人签字后,加盖科研管理章。
- 15. 市科技局意见:由项目主管处室负责人签字,加盖保定市科技计划项目验收专用章。

一、项目基本信息

项目名称	冠心病合并	2型糖尿病者血线	浆纤维蛋白原、 周	旨蛋白a、D-二聚	体危险因素研			
第一承担 单位名称	保定市第二	二医院		单位性质		医院		
项目	姓名	刘梅	联系电话	17733221600	电子邮箱	liu_m m	ei@163.com	
负责人	坐 历	研究生	学位	硕士	职称	副主	上任医师	
	24 I W	ili i	安专业技术职务	分布		按学位分		
ATT I F	总人数 (人)	高级职称	中级 初级职称 职称		博士	硕士 学	:士 其它	
参研人员情况	0	0	0	* O	0	0	0	
	累计投入项目研究的工作量(人月)			0.15	吸引省	外人才(人)	0	
所属 领域	其它			'				
产学研联	主要合作单位名称	E	第七医学中心	合作单位性质		医防	Š.	
合	合作形式	其他						
累计经费	总投入	省科技厅拨款	市科技局拨	市县匹配款 资金	単位自筹	银行贷款	其他	
筹集情况 (万元)	5.5			0	5	0	0.5	
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	新产品、新材料(种)	0	新工艺、		C)	出版科技著作 (万字)			0
	科技论文、 报告(篇)	7	其中: 发 论文	(篇)	4		其中:被EI、SCI ISTP、ISR收录(篇			3
保	动植物部 开发个数		0		动		h种推广面积或 性(亩或头)			0
P.C. E. 3	累计建立试 (基地)		0				(试验示范区 (亩或头)			0
累计实现的直接社	专利申请 数(项)	发明	英用 新型	外观设计	专利授	权数(项) 发明	实		外观 设计
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- 1	培养人才数	获博士:	获博士学位人数		获硕士学位人数			培训专业技术人员 (人次)		员
	0		0		0			0		
累计环保	节 煤 (万吨)		0	节电(万度))	0	节 水 (万吨)			0
节能效益	减排废气 (万立方米)		0	减排废力 (万吨)	1	0	减排废物 (万吨)			0

注: 1、本表由完成单位如实填写, 无填报内容可空缺;

- 2、累计情况请填报自项目开始实施至结题的合计数;
- 3、本表数据做为项目绩效评价的参考依据。

二、项目概述实施内容

本研究选择河北省保定市第二医院2017年1月至2022年4月期间诊治的冠心病合并2型糖尿病患者280例(糖尿病冠心病组)为研究对象,将受试人群分为三组,组 I 为冠心病合并2型糖尿病患者,组 II 为单纯冠心病患者(单纯冠心病组,n=240),组III为同期来我院门诊健康体检者(对照组,n=260),分析患者血浆纤维蛋白原、D二聚体及脂蛋白a水平变化。通过此课题的研究,详细了解了Fg、Lp(a)、D-D做为高危因素在冠心病、糖尿病以及的糖尿病合并冠心病发生、发展的过程中所起到的重要作用,这将为人类预防和治疗糖尿病及冠心病提供,新的理论基础。本研究证实Pg、Lp(a)、D-D不但是糖尿病、冠心病的高危因素,同时对于冠心病合并2型糖尿病者Fg、Lp(a)、D-D显著升高,相互促进、互为因果,造成恶性循环,加重2型糖尿病合并冠心病者冠状血管及大血微血管的病变。这将为2型糖尿病人预防冠心病提供理论基础,对预防和治疗糖尿病合并冠心病提供了新思路。对于降低病人致死率、致残率,提高生活质量具有重大意义。在临床工作中,该方案操作简单,安全性高,具有很好的应用前景。

创新性简介

随着全球人口的老龄化及生活水平提高,糖尿病、冠心病的发病率和病死率呈上升趋势。本研究探讨了冠心病合并2型糖尿病者发生急性心脑血管事件的危险因素研究,能为解决减少病死率,减缓疾病进程的问题提供参考和借鉴作用。冠心病合并2型糖尿病患者血浆纤维蛋白原、D二聚体、脂蛋白a、白细胞介素2、降钙素原及hs-CRP水平均明显升高,与2型糖尿病合并冠心病患者血管病变支数及Censini评分均有明显的正相关性(P<0.05)。提示控制以上三项指标的水平,可以降低糖尿病及心血管事件的风险,控制其协同机制,切断致病链条,对冠心病合并2型糖尿病的预防及动态监测有着十分重要的临床价值。

项目在提升产业技术进步、推动经济社会发展等方面对我市的促进和带动作用

糖尿病和心血管疾病已成为人类健康的最大、最严重威胁,是日益严重的公共卫生问题。糖尿病患者发生心血管疾病的风险是非糖尿病人群的二到四倍。糖尿病患者如果合并冠心病,无疑具有"双重危险",更应该积极采取措施,降低心血管事件的风险。联合监测血浆纤维蛋白原、D二聚体和脂蛋白a水平,有助于评估糖尿病及冠心病的风险,切断致病链条。对于降低致残率、致死率,提高人民健康水平,减少医保支出有重大意义。

三、主要技术文件目录及来源

- 一、工作报告
- 二、技术报告
- 三、鉴定大纲
- 四、论文
- 1、《ANALYSIS ON THE CORRELATION OF PLASM A FIBRIN OGEN, LIPOPROTEIN (A), AND D-DIMER WITH DISEASE STATE AND PROGNOSIS OF PATIENTS WITH CORONARY HEART DISEASE》发表于《ACTA MEDICA MEDITERRANEA》 2020年第36卷第6期 SCI检索。
- 2、《PLASM A FIBRIN O GEN, LIP O PROTEIN A, AND D-DIMER IN PREDICTING THE OCCURRENCE OF COMPLICATED CORONARY HEART DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND THE PROGNOSIS OF PATIENTS》 发表于《ACTA MEDICA JEDITERRANEA》 2021年第37卷第1期SCIJ检索
- 3、《2型糖尿病合并冠心病患者血浆纤维蛋白原、D二聚体及脂蛋白a水平的临床分析》发表于《中南医学科学杂志》,2019年第47卷,第2期,核心期刊。
- 4、《Effect of Metformin ntervention on Pancreatic β-Cell Apoptosis》发表于《Journal of Biomaterials and TissueEngineering》2022年第12卷第1-5期 SCI检索。
- 5、《2型糖尿病合并冠心病患者血浆纤维蛋白原、D二聚体及脂蛋白a检测的临床应用价值》发表于《世界最新医学信息文摘》,2021年第21卷,第91期,
- 6、《格列齐特对冠心病合并2型糖尿病患者心功能及血浆FIB、D-D、LP(a)水平的影响》发表于《现代医学与健康研究》2021年第4卷第16期。
- 7、《达格列净联合吲哚布芬治疗 2 型糖尿病合并冠心病患者中的疗效及对血浆纤维蛋白原、D 二聚体及脂蛋白 a 水平的影响》发表于《健康之友》2021年2月下。
- 8、《吲哚布芬治疗冠心病的临床效果及对血浆纤维蛋白原(Fg)、脂蛋白 a (Lp (a))、D -二聚体(D-D)的影响》发表于《健康之友》2021年3月上。

要研制、	1人员名	東							
姓名	体别	年龄	即称	李历	学位	现从事专业	单位名称	分工	本人签名
刘泰	A	88	副主任医师	研究生	硕士	内科学其他学科	保定市第二医院	项目负责人	ツ多く
韩天云	赵	34/1	主治医药师	李蓉	*	药学其他学科	保定市第二張院	资料收集整理	\$43
解冬千	眠	39	主治医药师	本科	光	药学其他学科	保定市第二医院	资料收集整理	的大大
刘娟	*	37	其他中级	本	计帐	基础护理学	解故军总院第七医学中心,	资料收集整理	心衛
2を描	*	25	主任医师	本科	小小	内科学其他学科	保定市第二医院	资料整理	をなる
范多娇	X	37	主治医师	研究生	0年	心血管病學	保定市第二医院	收集资料, 撰写论文	松文学

本人物名 を治路 资料收集整 理撰写论文 资料收集整 资料收集整 理撰写论文 理撰写论文 资料整理 收集资料 负责 H A Ш 图 医院 驱 些 驱 4 盤 Ѭ 凩 郷 HK! 困 心中 单位名称 11 11 业 11 11 11 定市第二 定市第一 搬 瓣 無 刘 姚 汝平 作 柜 化 胀 保定 是 恨 账 虚 账 账 账 内科学及其他专业 哲学其他学科 核学其他字科 内科学及其他 十十 基础护理学 心由衛施學 + 川川 现从事专 相等 位盖章、管 多种 41 4 + +1 4 无 赤 姚 洲 李 恩 歐 奸究生 # 本科 本幹 本科 本科 压 张 排 出 本 辰 些 衛塔斯 管塔师 任医师 北北 主治医师 H (项目 职業 和 1Jun -14 -14 4 -14 -111 iiiii 要研制人员名单 年粉 40 40 42 37 57 51 iii; X 駅 X X X X 和 以友斯 抗多娇 韩无宏 解冬千 好 刘皓 沙衛 数 1 ulp ŝ 4 D 9 S 11 世

注: 本表由承担单位如实填写。

四、验收专家名单

本人签名	Month.	1839 A	The state of	光路	MA SE
职务/职称	主任医师	主任医师	主任医师	主任医师	開主任检验技
现从事学科	心血管内科	心血管内科	心血管内科	心血管內科	医学检验
所学专业	なとう	本五分	本区分	本内や	医学检验
工作单位	河北医科大学第一医院	河北医科大学第四医院	河北大学附属医院	保定市第一中心医院	保定市第一中心医院
姓名	郑明奇	日暑游	贾辛未	张回乐	常文龙
中中	-	2	3	4	2

六、验收意见

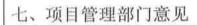
由保定市第二医院承担的2020年保定市科学技术研究与发展指导计划项目《冠心病合并2型糖尿病者血浆纤维蛋白原、脂蛋白a、D-二聚体危险因素研究》(编号: 2041ZF009)已按项目申报书或任务书完成, 经审查, 提供的技术资料完整、规范,符合验收要求。综合其他委员一件,形成验收意见如下:

该课题旨在研究血浆纤维蛋白原、脂蛋白a、D-二聚体的水平与冠心病合并2型糖尿病者预后的关系,来探讨如何降低糖尿痰及心血管事件的风险,探究其协同机制,切断致病链条。排除性别、年龄等因素的干扰,分析冠心病合并2型糖尿病患者、单纯冠心病患者、健康体检者血浆纤维蛋白原、D二聚体及脂蛋白a水平变化。临床研究得出结论:冠心病合并2型糖尿病患者血浆纤维蛋白原、D二聚体、脂蛋白a、白细胞介素2、降钙素原及hs-CRP水平均明显升高;上述指标与2型糖尿病合并冠心病患者血管病变支数及Censni评分均有明显的正相关性。

该课题选题新颖、贴近临床,研究方法得当,资料齐全,统计方法正确,结论可靠,具有科学性、先进性及创新性,易于在临床推广,且有较好的社会效益。

综上所述,承担单位完成了项目申报书或任务书规定的各项指标,具有显著的社会效益,推广应用前景广阔。验收组一致同意通过验收。

建议:可以进一步深入研究糖尿病合并急性冠脉综合征,或糖尿病泛血管病患者的上述指标情况,也可将瘦素、白细胞介素2、降钙素原及hs-CRP水平纳入进一步研究中,对于疾病预后的预测、评估病情及防治提供更多的理论依据



项目承担单位意见









项目归口管理部门意见



(科研管理章)

E

市科技局意见

项目主管处室负责人签



验收文件和资料目录

序号	附件名称	附件说明
	验收专家组成员签字扫描图片	验收专家组成员签字扫描图片
2	验收专家组长意见	验收专家组长意见
3	专家签字的函审表	专家签字的函审表郑明奇
	专家签字的函审表	专家签字的函审表马景涛
/ In	专家签字的函审表	专家签字的函审表贾辛未
	专家签字的函审表	专家签字的函审表张同乐
17	专家签字的函审表	专家签字的函审表常文龙
}	延期心均申请表	延期验收申请表
)	科研参加人员签名表	科研参加人员签名表
	科学技	Ž_b.



由保气市第>限院承担的2000年(保气市科学技术研究与发展计划 吸目《图心和分类2型猪股和使者的烧红竹馆后原、的麦白a.D.源丰 危险周季研究》(维考2041年009)已接项目中报书或政治实践、 经布查. 提供的指其资料完整. 概范. 特分验收受水。保含其他

委员见,形成的收费.况如下:

说课题首在研究血浆纤维蛋白原,脸蛋白a, D.一颗本的小学 冠心病病之型佛际病饮后的贫氧,来操注如何断纸糖的病及 心血管部件的风险,探究其相同机制。竹叶研系结论找示、此些 风险圆季在经心和分省>到防心和考古的图等者:如为一直的这

支数及censini i等为是耐量正相美。

该, 得, 段道, 数新数, 家, 团、田、致好, 研克方法得当, 资和合金. 谷泊而靠,具有较好的科学性、先电性及创新性、易于和城市

推介,是有效好的社会效益。

得少的过,完成了项目中报书刊会书的和处理个具有 图者的和全效益, 转了应用新拿广阔。给你祖一致门走通过

建议:进步浮入研究护师的合并急性运搬给在或被 医多种外的性体特色。

_2023年__3__月_24__日

成果名称: 远心病合并2型糖尿病患者血浆纤维蛋白期、脂蛋白。 D 二聚体危险因研究

完成人: 刘梅(第雲完成人)

所在单位: 保定市第二医院

河北省科学技术成果

第一完成单位:保定市第二医院

省级登记号: 20231143



河北省科学技术厅

半点

冠心病合并2型糖尿病患者血浆纤维蛋白原、脂蛋白a、D-二聚体危险因研究 於 竹 眯 出

二医院 位: 保定市第 珊 完成

解冬千 輔 表 新 新 多 娇 人: 刘 梅 刘林瑶 出 完

河北省科学技术成果

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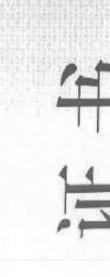
省级登记号: 20231143





日十

技成展登记专用章



河北省科学技术厅



篇号: Hbsyxh-01220240203-001

为了表彰您在促进医药科学技术进步工作中 山資米區 特领此证, 出的突出自被。 級

获奖者: 刘梅

冠心病合并2型糖尿病者血浆纤维蛋白原 项目名称:

脂蛋白a、D-二聚体危险因素研究

奖励等级: 科学技术奖(应用研究类)二等奖

附表 1

应用证明

项目名称	冠心病合并 2 型糖尿病者血浆纤维蛋白原、脂蛋白 a、D-二聚体 危险因素研究					
应用单位	保定	市第二医院				
单位注册地址	河北省保定	市东风西路 338 号				
应用起止时间	2020年5月至2023年3月					
	经济效益 (万元)					
自然年	新增销售额	新增利润				
2018年						
2019 年						
2020年						
累计						

所列经济效益的有关说明及计算依据:

应用单位财务章

年 月 日

具体应用情况:

本研究通过对冠心病合并 2 型糖尿病者血浆纤维蛋白原、脂蛋白(a)、D-二聚体水平的测定,有助于评估糖尿病及冠心病的风险。明确了控制以上三项指标的水平,可以降低糖尿病及心血管事件的风险,控制其协同机制,切断致病链条,对冠心病合并 2 型糖尿病的预防及动态监测有着十分重要的临床价值。对于降低病人致死率、致残率,提高生活质量具有重大意义。

应用单位法定代表人签名:

年 月 日



注: 无经济效益的项目, 可不填经济效益相关栏目、不加盖应用单位财务章

ANALYSIS ON THE CORRELATION OF PLASMA FIBRINOGEN, LIPOPROTEIN (A), AND D-DIMER WITH DISEASE STATE AND PROGNOSIS OF PATIENTS WITH CORONARY HEART DISEASE

MEI LIU^{1*}, TIANYUN HAN², DONGQIAN XIE²

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ABSTRACT

Introduction: To analyze the correlation of plasma fibrinogen (FIB), lipoprotein (a) ((Lp (a)), and D-dimer with disease state and prognosis of patients with coronary heart disease (CHD).

Methods: Altogether 148 patients with CHD in our hospital were selected and assigned to a research group (res group), and 150 healthy individuals who received physical examination in our hospital were selected and assigned to a control group (con group). The levels of FIB, Lp (a), and D-Dimer between the two groups was compared, and the correlation of them with disease

development and prognosis of patients with CHD was analyzed.

Results: The levels of FIB, Lp (a), and D-Dimer in the res group were greatly higher than those in the con group (all P<0.05), and the levels of them in patients with acute myocardial infarction were greatly higher than those in patients with unstable angina pectoris or stable angina pectoris (all P<0.05). Additionally, the levels of FIB, Lp (a), and D-Dimer in patients in stage III (according to Canadian Cardiovascular Society classification (CCSC)) were greatly higher than those in patients in stage II or stage I (all P<0.05). In the res group, the angina pectoris grade was positively linked to FIB (r=0.53, P<0.05), Lp (a) (r=0.68, P<0.05), as well as D-Dimer (r=0.70, P<0.05), and Gensini score was also positively related to FIB (r=0.44, P<0.05), Lp (a) (r=0.47, P<0.05), as well as D-Dimer (r=0.43, P<0.05). In addition, the levels of FIB, Lp (a), and D-Dimer in the major adverse cardiovascular event (MACE) group were greatly higher than those in the non-MACCE group (all P<0.05), and the prognosis of patients was negatively linked to FIB (r=-0.64, P<0.05), Lp(A) (r=-0.73, P<0.05), as well as D-Dimer (r=-0.45, P<0.05).

Conclusion: The levels of FIB, Lp (a), and D-Dimer in patients suffering from CHD increase significantly, and the levels of them are positively related to the disease state of the patients, and negatively correlated with the prognosis of them, so FIB, Lp (a)

and D-Dimer can be adopted to predict the disease development and prognosis of patients with CHD.

Key words: Sepsis-3, C-reactive protein, Procalcitonin, CD64, diagnosis.

DOI: DOI: 10.19193/0393-6384_2020_6_605

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Introduction

Coronary heart disease (CHD) is a malady that seriously endangers human health worldwide⁽¹⁾. CHD is the most familiar cause of death for patients with cardiovascular diseases, and cardiovascular diseases account for one third of all deaths worldwide⁽²⁾. With the continuous development of social economy in developing countries, measured by human development index, the prevalence rate of CHD is on the rise⁽³⁾.

According to the China Statistical Yearbook on Health and Family Planning (2013-2017), in China, the number of patients with CHD is increasing and the mortality of them is also on the rise, which seriously affects the health of Chinese⁽⁴⁾. CHD is the primary cause of development of cardiovascular disease and cardiovascular disease-related deaths not only in China, but also in North American and western European countries⁽⁵⁾.

Chest distress and chest pain are typical symptoms of CHD, which would aggravate after

Mei Liu, Tianyun Han et Al

exercise⁽⁶⁾. At present, a great progress has been achieved in common treatment for CHD. There are various treatments for CHD, including operations such as percutaneous coronary intervention and coronary artery bypass grafting(7,8), conventional drugs including cyclooxygenase inhibitor, nitrate preparations, β receptor antagonist, and calcium channel blockers(9), and cardiac rehabilitation treatment that can significantly enhance the physical strength of patients and help delay and prevent the development of CHD(10). The progress in these treatments effectively increases the long-term survival rate of patients suffering from CHD, but also brings many new challenges to patients, their families, and professional medical personnel(11). It is especially important to evaluate the development and prognosis of patients suffering from CHD.

This study compared the levels of fibrinogen (FIB), lipoprotein (a) ((Lp(a)), and D-dimer between the two groups to explore the correlation of them with disease state and prognosis of patients with CHD.

Materials and methods

General data

Altogether 148 patients suffering from CHD treated in our hospital were selected and assigned to a research group (res group), including 86 males and 62 females, with an average age of (64.53±9.84) years, and 150 healthy individuals who received physical examination in our hospital over the same period were selected and assigned to a control group (con group), including 84 males and 66 females, with an average age of (65.42±10.21) years.

The inclusion criteria of patients: Patients accompanied by family members at admission, patients diagnosed with CHD according to coronary angiography, and those with complete clinical pathological data. The exclusion criteria of patients: Patients with a history of mental disease or a family history of psychosis, patients with a history of autoimmune system deficiency, patients with a history of drug dependence, and those who were unable to cooperate with examination due to aphasia, dysphoria, unconsciousness, or communication obstacle.

This study was carried out with permission from the Ethics Committee of our hospital and informed consent forms signed by all participants and their families after understanding the detailed content of the study.

Methods

Venous blood (10 mL) was extracted from every study participant in the two groups after 12 hours of fasting, and transferred to anticoagulant tubes for coagulation for 60 min (20-25°C). Subsequently, the blood was centrifuged at 1369.55xp and 4°C for 15 with a centrifuge (TG 112, Shuke Instrument Co., Ltd., Sichuan, China) to isolate the upper serum, and the upper serum was stored in a refrigerator at -70°C. The level of FIB in each participant was quantified through an automatic coagulometer (58151, Stago Diagnostic Products Trading Co., Ltd., Beijing, China) and auxiliary reagent, and the level of Lp (a) in them was quantified using an automatic biochemistry analyzer (H293KH, Yuduo Biotechnology Co., Ltd., Shanghai, China), and auxiliary reagent. In addition, the level of D-Dimer in the serum of each participant was quantified via an enzyme-linked immuno-sorbent assay (ELI-SA) with a Human D-Dimer ELISA kit (HM10865, MultiSciences (Lianke) Biotech Co., Ltd., Wuhan, China). All the quantification operations were carried out in strict accordance with kit instructions.

Outcome measures

The levels of FIB, Lp (a), and D-Dimer were compared between the two groups and among subgroups, and the correlation of angina pectoris grade, coronary artery lesion degree, and prognosis with the levels of FIB, Lp (a), and D-Dimer in the res group was studied. The coronary artery lesion degree of patients in the res group was scored using the Gensini scoring system according to the stenosis of each coronary artery with lesion: 1 point for stenosis ≤25%, 2 points for stenosis≤25% but ≤50%, 3 points for stenosis≤50% but ≤75, and 4 points for stenosis≤75% but ≤100%. Patients in the res group were followed up for 2 years by telephone and reexamination, and the major adverse cardiovascular events (MACE) such as unstable angina pectoris (UAP), severe arrhythmia, acute myocardial infarction (AMI), heart failure, revascularization as well as all-cause death in them were recorded. Prognosis of participants in the res group: The prognosis of patients without CHD-related clinical symptoms and with electrocardiogram (ECG) within the normal range was considered excellent; the prognosis of patients whose CHD-related symptoms was relieved and ECG were improved was considered good, and the prognosis of patients whose CHD-related symptoms and ECG had no changes was considered poor.

Statistical analysis

In this study, SPSS20.0 (IBM Corp, Armonk, NY, USA) was adopted for statistical analyses, and GraphPad Prism 7 (San Diego Graphpad Software Co., Ltd., USA) for figure drawing. Enumeration data were expressed as (n(%)), and inter-group comparison was carried out through the chi-square test. Measurement data were presented as $(x^-\pm s)$, and inter-group comparison was carried out using the t test. In addition, Pearson correlation coefficient was adopted for analyzing correlation. P<0.05 suggests a remarkable difference.

Results

Comparison of general data

According to the comparison of general data between the res group and the con group (Table 1), there was no remarkable difference between them in general data including sex, age, as well as body mass index (all P>0.05).

According to comparison of the levels of FIB, Lp (a), and D-Dimer between the res group and the con group, in contrast to the con group, the res group showed greatly increased FIB, Lp (a), and D-Dimer (all P<0.05). Figure 1.

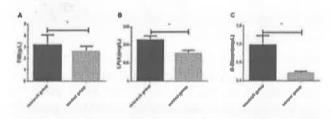


Figure 1: Comparison of the levels of FIB, Lp (a), and D-Dimer between the two groups. Figure 1A, Compared with the con group, the res group showed significantly increased FIB. Figure 1B, Compared with the con group, the res group showed significantly increased Lp (a). Figure 1C, Compared with the con group, the res group showed significantly increased D-Dimer.

Note: * indicates that in comparison between the two groups, P < 0.05.

Comparison of the levels of FIB, Lp (a), and D-Dimer among different types of patients in the res group

Comparison of the levels of FIB, Lp (a), as well as D-Dimer among different types of patients in the res group showed that the levels of them in patients with AMI were greatly higher than those in patients with UAP or stable angina pectoris (SAP) (all P<0.05), and the levels of them in patients with

UAP were greatly higher than those in patients with SAP (all P<0.05). Figure 2.

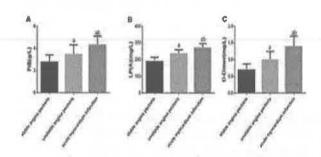


Figure 2: Comparison of the levels of FIB, Lp (a), and D-Dimer among different types of patients in the res group. Figure 2A, The FIB level in patients with AMI was significantly higher than that in patients with UAP or SAP, and the FIB level in patients with UAP was significantly higher than that in patients with SAP. Figure 2B, The Lp (a) level in patients with AMI was significantly higher than that in patients with UAP or SAP (P<0.05), and the Lp (a) level in patients with UAP was significantly higher than that in patients with SAP. Figure 2C, The D-Dimer level in patients with AMI was significantly higher than that in patients with UAP or SAP, and the D-Dimer level in patients with UAP was significantly higher than that in patients with UAP was significantly higher than that in patients with SAP.

Note: aP<0.05 vs. patients with SAP; bP<0.05 vs. patients with UAP.

Correlation between angina pectoris grade and the levels of FIB, Lp (a), and D-Dimer in patients in the res group

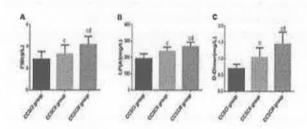


Figure 3: Comparison of the levels of FIB, Lp (a), and D-Dimer among three subgroups. Figure 3A, the FIB level in the class III group was significantly higher than that in the class II group and the class I group, and the FIB level in the class II group was significantly higher than that in the class I group. Figure 3B, the Lp (a) level in the class III group was significantly higher than that in the class II group and the class I group, and the Lp (a) level in the class I group was significantly higher than that in the class I group. Figure 3C, the D-Dimer level in the class III group was significantly higher than that in the class II group and the class I group, and the D-Dimer level in the class II group was significantly higher than that in the class I group.

Notes: cP < 0.05 vs. patients in the class I group; dP < 0.05 vs. patients in the class II group.

According to the Canadian Cardiovascular Society classification (CCSC), patients in the res group were assigned to a class I group (n=42), class II group (n=69), as well as class III group (n=37).

Comparison of the levels of FIB, Lp (a), and D-Dimer among the three subgroups showed that the levels of them in the class III group were greatly higher than those in therest two groups (all P<0.05), and the levels of them in the class II group were greatly higher than those in the class I group (all P<0.05) (Figure 3).

Analysis on the correlation between angina pectoris grade and the levels of FIB, Lp (a), and D-Dimer in patients in the res group revealed that angina pectoris grade was positively related to FIB (r=0.53, P<0.05), Lp (a) (r=0.68, P<0.05), as well as D-Dimer (r=0.70, P<0.05) in the patients. Figure 4.

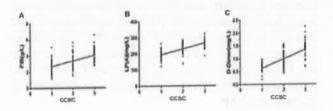


Figure 4: Correlation between angina pectoris grade and the levels of FIB, Lp (a), and D-Dimer in patients in the res group. Figure 4A, Angina pectoris grade was positively correlated with FIB level in patients in the res group. Figure 4B, Angina pectoris grade was positively correlated with Lp (a) level in patients in the res group. Figure 4C, Angina pectoris grade was positively correlated with D-Dimer level in patients in the res group.

Notes: I indicates class I in CCSC; 2 indicates class II in CCSC;

Correlation between Gensini score and the levels of FIB, Lp(a) and D-Dimer in patients in the res group

Analysis on the relationship between Gensini score and the levels of FIB, Lp (a), and D-Dimer in patients in the res group revealed a positive correlation between Gensini score and FIB (r=0.44, P<0.05, Lp (a) (r=0.47, P<0.05), as well as D-Dimer (r=0.43, P<0.05) in the patients. Figure 5.

Comparison of the levels of FIB, Lp (a), and D-Dimer between the MACE group and the non-MACE group

All 148 patients in the res group were followed up successfully, and they were assigned to MACE group (n=33) and non-MACE group (n=115) based on the occurrence of MACE. Comparison of the levels of FIB, Lp(a), and D-Dimer between the two subgroups showed that the levels of them in the

MACE group were greatly higher than those in the other group (all P<0.05). Figure 6.

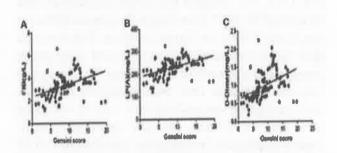


Figure 5: Correlation between Gensini score and the levels of FIB, Lp (a) and D-Dimer in patients in the res group. Figure 5A, Gensini score was positively correlated with FIB level in patients in the res group. Figure 5B, Gensini score was positively correlated with Lp (a) level in patients in the res group. Figure 5C, Gensini score was positively correlated with D-Dimer level in patients in the res group.

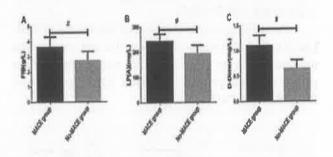


Figure 6: Comparison of the levels of FIB, Lp (a), and D-Dimer between the MACE group and the non-MACE group. Figure 6A, The FIB level in the MACE group was significantly higher than that in the non-MACE group. Figure 6B, The Lp (a) level in the MACE group was significantly higher than that in the non-MACE group. Figure 6C, The D-Dimer level in the MACE group was significantly higher than that in the non-MACE group.

Note: "P<0.05 vs. the MACE group.

Correlation between the prognosis and the levels of FIB, Lp(a) and D-Dimer in patients in the res group

In the res group, there were 61 patients with excellent prognosis, 72 patients with good prognosis, as well as 15 patients with poor prognosis. Analysis on the correlation between prognosis and the levels of FIB, Lp (a), and D-Dimer in patients in the res group revealed that the prognosis was negatively related to FIB (r=-0.64, P<0.05), Lp (a) (r=-0.73, P<0.05), as well as D-Dimer (r=-0.45, P<0.05). Namely, better prognosis of patients indicates lower levels of FIB, Lp (a), and D-Dimer in them. Figure 7.

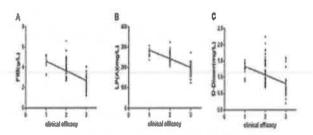


Figure 7: Correlation between prognosis and the levels of FIB, Lp (a), and D-Dimer in patients in the res group. Figure 7A, Prognosis was negatively correlated with FIB level in patients in the res group. Figure 7B, Prognosis was negatively correlated with Lp (a) level in patients in the res group. Figure 7C, Prognosis was negatively correlated with D-Dimer level in patients in the res group.

Notes: 1 indicates poor prognosis; 2 indicates good prognosis; 3 indicates excellent prognosis.

Discussion

CHD has become a serious common disease in the modern society(12). One study has pointed out that the level of FIB is linked to CHD and can be adopted to predict the severity of the disease(13). Lp (a) is one risk factor for the development of cardiovascular disease, which has special influence on the development of CHD (14). A high level of Lp (a) increases the risk of suffering from CHD by two or three times(15). D-Dimer is a degradation product of cross linked fibrin and a marker of hypercoagulable state and thrombotic events. Moderately elevated D-Dimer is related to the risk of venous and arterial events in cases with vascular diseases(16). In addition, CHD is a chronic disease, and the period of treatment and recurrence of the disease is relatively long after the acute phase of the disease, so it is particularly important to evaluate the development and prognosis of CHD.

According to some studies, FIB and D-Dimer in patients with CHD are up-regulated⁽¹⁷⁾, and the serum D-Dimer in patients with coronary artery lesions increases significantly⁽¹⁸⁾. In addition, Lp (a) in patients with stable coronary disease also increases⁽¹⁹⁾. These findings are consistent with the results of our study. In our study, the levels of FIB, Lp (a), and D-Dimer in the res group were greatly higher than those in the con group, indicating that the levels of them are closely linked to the progression of CHD and can be adopted as indicators for detection of early CHD. Additionally, according to some other studies, FIB is an effective tool to distinguish from patients with stable CHD⁽²⁰⁾, and as FIB increases,

the mortality of patients with SAP or UAP also increases⁽²¹⁾.

Therefore, this study further compared the levels of FIB, Lp(a), and D-Dimer among different types of patients in the res group, finding that the levels of them in patients with AMI were greatly higher than those in patients with UAP or SAP, and the levels of them in patients with UAP were greatly higher than those in patients with SAP. Moreover, one study has indicated that the concentration of Lp (a) is linked to cardiovascular risk, and the aggravation of CHD is linked to the increase of Lp (a) concentration(22). According to this study and our study, FIB, Lp(a), and D-Dimer can adopted as indicators of the severity and classification of CHD. In our study, the levels of FIB, Lp (a), and D-Dimer in the class III group were greatly higher than the other two groups, and levels of them in the class II group were greatly higher than those in the class I group, implying that the levels of FIB, Lp (a), and D-Dimer are helpful to the diagnosis of CHD. In addition, in patients from the res group, the angina pectoris grade was positively related to the levels of FIB, Lp (a), and D-Dimer, which further suggests that the levels of FIB, Lp (a), and D-Dimer have an important reference value in the diagnosis of early CHD. According to some studies, the level of Lp (a) is positively related to Gensini score⁽²³⁾, and strongly linked to the severity of CHD(24), and FIB is also positively linked to Gensini score, and linked to the stenosis of coronary artery in patients with myocardial infarction⁽²⁵⁾, which are consistent with conclusion of our study that Gensini score is positively related to the levels of FIB, Lp (s), as well as D-Dimer in patients with CHD. Follow-up results of this study revealed that the levels of FIB, Lp (a), as well as D-Dimer in the MACE group were greatly higher than those in the corresponding non-MACE group. Earlier studies have concluded that FIB is a risk factor of MACE for patients with CHD⁽²⁶⁾, and significantly related to MACE(27). These results suggest that FIB, Lp (a), and D-Dimer can be adopted to evaluate the prognosis of patients with CHD. Our study analyzed the prognosis of patients suffering from CHD, and found that the prognosis of patients with CHD was negatively correlated with the levels of FIB, Lp (a), and D-Dimer. Namely, better prognosis of patients indicated lower levels of FIB, Lp (a), and D-Dimer in them, which is also consistent with the results in one study that among patients with CHD, the prognosis of patients with a D-Dimer level higher than the normal level is the worst⁽²⁸⁾, indicating that the levels of FIB, Lp (a), and D-Dimer can be adopted to evaluate the prognosis of patients suffering from CHD⁽²⁹⁻⁴⁴⁾.

This study compared the levels of FIB, Lp (a), and D-Dimer between the two groups and among subgroups and analyzed the correlation of the disease state and prognosis with the levels o them to explore the value of FIB, Lp (a), and D-Dimer in predicting the disease state and prognosis of patients with CHD, with the goal of providing reference for clinical diagnosis and treatment of CHD. However, there are still some limitations in this study. This study has not explored the diagnostic value of FIB combined with Lp (a) and D-Dimer, and the exact mechanism of action of FIB, Lp (a) and D-Dimer in the whole process of CHD remains to be further studied. We will continuously improve the study in the future to provide more scientific reference for clinical diagnosis and treatment of CHD.

To sum up, the levels of FIB, Lp (a), and D-Dimer in patients with CHD increase significantly, and the levels of them are positively linked to the disease state of the patients, and negatively correlated with the prognosis of them, so FIB, Lp(a) and D-Dimer can be adopted to predict the disease development and prognosis of patients with CHD.

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ANALYSIS ON THE CORRELATION OF PLASMA FIBRINOGEN, LIPOPROTEIN (A),
AND D-DIMER WITH DISEASE STATE AND PROGNOSIS OF PATIENTS WITH CORONARY
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By: 刘梅 (Liu, Mei; 第一作者)

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Abstract

ANALYSIS ON THE CORRELATION OF PLASMA FIBRINOGEN, LIPOPROTEIN (A), AND D-DIMER WITH DISEASE STATE

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AND PROGNOSIS OF PATIENTS WITH CORONARY HEART DISLAS Dongqian)[2]

By:Liu, M (Liu, Mei)[1] ; Han, TY (Han, Tianyan)[11] Mig

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Introduction: To analyze the correlation of plasma fibringen (FIB), lipoprotein (a) ((Lp (a)), and D-dimer with disease state and prognosis of patients with coronary heart disease (CHD).

Methods: Altogether 148 patients with CHD in our hospital were selected and assigned to a research group (res group), and 150 healthy individuals who received physical examination in our hospital were selected and assigned to a control group (con group). The levels of FIB, Lp (a), and D-Diener between the two groups was compared, and the correlation of them with disease development and prognosis of patients with CHD was analyzed.

Results: The levels of FIB, Lp (a), and D-Diener in the res group were greatly higher than those in the con group (all P<0.05), and the levels of them in patients with acute myocardial infarction were greatly higher than those in patients with unstable angina pectoris or stable angina pectoris (all P<0.05). Additionally, the levels of FIB, Lp (a), and D-Dimer in patients in stage III (according to Canadian Cardiovascular Society classification (CCSC)) were greatly higher than those in patients in stage II or stage 1 (all P < 0.05). In the res group, the angina pectoris grade was positively linked to FIB (r=0.53, P <0.05), Lp (a) (r=0.68 P<0.05), as well as D-Diener (r=0.70, P<0.05), and Gensini score was also positively related to FIB (r=0.44, P<0.05), Lp (a) (r=0.47, P<0.05), as well as D-Diener (r=0.43, P<0.05). In addition, the levels of FIB, Lp (a), and D-Diener in the major adverse cardiovascular event (MACE) group were greatly higher than those in the non-MACCE group (all P<0.05), and the prognosis of patients was negatively linked to FIB (r=-0.64, P<0.05), Lp(A) (r=-0.73, P<0.05), as well as D-Dimer (r=-0.45, P<0.05).

Conclusion: The levels of FIB, Lp (a), and D-Dimer in patients suffering . from CHD increase significantly, and the levels of them are positively related to the disease state of the patients, and negatively correlated with the prognosis of them, so FIB, Lp (a) and D-Diener can be adopted to predict the disease development and prognosis of patients with CHD.

Keywords

Author Keywords: Sepsis-3; C-reactive protein; Procalcitonin; CD64; diagnosis

KeyWords Plus:ARTERY-DISEASE; METABOLITES

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ISSN: 0393-6384 eISSN: 2283-9720 PLASMA FIBRINOGEN, LIPOPROTEIN A, AND D-DIMER IN PREDICTING THE OCCURRENCE OF COMPLICATED CORONARY HEART DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND THE PROGNOSIS OF PATIENTS

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ABSTRACT

Aim: This study aims to explore the roles of plasma fibrinogen (FIB), lipoprotein a (Lp (A)), and D-dimer (D-D) in predicting the occurrence of complicated coronary heart disease (CHD) in patients with type 2 diabetes mellitus (T2DM) and the prognosis of patients.

Methods: We enrolled 86 patients with T2DM (the control group, CG) and 72 patients with T2DM complicated by CHD (the observation group, OG) admitted to our hospital over the same period in this study. We tested the concentrations of FIB, D-D, and Lp (A) in the two groups of patients to analyze their correlations with cardiac troponin (cTn) and their value in predicting the occurrence of CHD in patients with T2DM. We also tested the concentrations of FIB, D-D, and Lp (A) in patients before and after treatment to explore their value in predicting the disease recurrence and assessing the prognosis of patients.

Results: We detected higher concentrations of FIB, D-D, and Lp (A) in OG than in CG (P<0.05). FIB, D-D, and Lp (A) levels were positively correlated with cTn in OG (P<0.05). FIB, D-D, and Lp (A) all showed good efficiency in predicting the occurrence of CHD in patients with T2DM, especially when the three genes were jointly tested. In OG, levels of FIB, D-D, and Lp (A) were lower after treatment than before treatment (P<0.05), and lower in patients without recurrence than in patients with recurrence (P<0.05).

Conclusion: FIB, D-D, and Lp (A) are highly expressed in patients with T2DM complicated by CHD. FIB, D-D, Lp (A) levels can be used to predict the occurrence and progression of CHD in patients with T2DM, which are expected to become accurate markers for CHD.

Keywords: Plasma fibrinogen, lipoprotein a, D-dimer, type 2 diabetes mellitus complicated by coronary heart disease.

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Introduction

Diabetes mellitus (DM) is a series of metabolic diseases featuring high blood glucose⁽¹⁾. Type 2 DM (T2DM) is the most common type of diabetes, resulting from a continuous increase in blood glucose levels due to insufficient insulin secretion in the body or poor insulin utilization, triggered by various factors^(2, 3). T2DM, life-threatening and costly, is becoming more common and frequent and seeing a year-by-year increase in its incidence recently because of the aging of the population and changed lifestyles⁽⁴⁾. T2DM is a progressive disease that can

be treated with oral monotherapy at the primary stage but eventually requires other oral drugs, and even requires insulin therapy to control the blood glucose levels^(5, 6). It is suggested by 12 prospective studies that high blood glucose levels can induce cardiovascular complications in patients with T2DM⁽⁷⁾. Coronary heart disease (CHD) is a frequent comorbidity of T2DM and the main cause of death for most patients with T2DM⁽⁸⁾. The inconspicuous onset of CHD aggravates the risk of death.

Intensive blood glucose control can effectively reduce microvascular complications in patients with T2DM, but its role in preventing cardiovascu-

lar complications is limited⁽⁹⁾. None of the existing treatment regimens is markedly effective for lowering blood glucose⁽¹⁰⁾. Therefore, early diagnosis of CHD is very crucial for the treatment of T2DM complicated by CHD. In short of accurate specific markers, T2DM complicated by CHD is generally diagnosed by multiple examination methods⁽¹¹⁾. Fibrinogen (FIB) is a protein present in plasma and has a strong influence on coagulation function⁽¹²⁾. A former study revealed that FIB is abnormally expressed during the occurrence of CHD⁽¹³⁾.

Lipoprotein a (Lp (A)), mainly synthesized in the liver, can promote the formation of atherosclerosis⁽¹⁴⁾. D-dimer (D-D) is currently recognized as the simplest fibrin degradation product, which reflects the hypercoagulable state and secondary fibrinolysis⁽¹⁵⁾. The above-mentioned three markers can affect the progression of T2DM⁽¹⁶⁾ and are involved in CHD. So we speculate that the three genes may be effective in predicting the occurrence of CHD in patients with T2DM. To confirm our conjecture, here we conducted related experiments to provide a reliable theoretical experimental basis for future clinical treatment of T2DM complicated by CHD.

Materials and methods

Basic information of participants

A prospective analysis was performed on 86 T2DM patients (the control group, CG) and 72 patients with T2DM complicated by CHD (the observation group, OG) admitted to our hospital from May 2017 to May 2018. This study has been approved by the ethics committee of our hospital and obtained informed consent from all participants.

Inclusion and exclusion criteria

Inclusion criteria:

- Patients diagnosed with T2DM complicated by CHD (OG) by the results of laboratory and imaging tests and treated in our hospital for the first time;
 - Patients diagnosed with T2DM (CG);
 - Patients with complete medical data;
- Patients with no previous history of major diseases;
- Patients who agreed to cooperate with this study.

Exclusion criteria:

Patients with tumors, cardiovascular and cerebrovascular diseases, previous history of hyperlipidemia, autoimmune diseases, mental diseases, or language communication disorders;

- Patients with low treatment compliance;
- Patients during pregnancy.

Sample collection and test

We collected 4 mL of fasting venous blood from each participant with a special vacutainer blood collection tube, exposed the sample to room air for 30 minutes, and then centrifuged for 10 minutes (400×g) to separate the plasma. Plasma FIB and D-D levels were tested by the latex agglutination assay on the automatic hemagglutination analyzer (ALC9000, USA). Lp (A) levels were tested by the immunoturbidimetry and the kits were from Guangzhou Improve Medical Instruments Co., Ltd. All test procedures followed the kit instructions strictly.

Outcome measures

We tested the concentrations of FIB, D-D, and Lp (A) in the two groups of patients to analyze their correlations with cardiac troponin (cTn) and their value in predicting the occurrence of CHD in patients with T2DM. We also tested the concentrations of FIB, D-D, and Lp (A) in patients before and after treatment to explore their value in predicting the disease recurrence and assessing the prognosis of patients.

Statistical analysis

Statistical analysis was performed on SPSS22.0. The count data were represented by the percentage (%) and their intergroup comparison was analyzed by the chi-square test.

The measurement data were represented by the mean \pm standard deviation and their intergroup comparison was analyzed by the t-test. The Pearson correlation coefficient was used for the correlation analysis. The predictive value of genes was analyzed on the receiver operating characteristic (ROC) curve. P<0.05 indicates a statistical difference.

Results

Comparison of basic information

The comparison between the two groups showed no differences in age, sex, BMI, living environment, smoking, drinking, family medical history, ethnicity (P>0.05). More details are shown in Table 1.

FIB, D-D, and Lp (A) levels in the two groups We detected higher levels of FIB, D-D, and Lp (A) in OG than in CG (P<0.05). More details are shown in Figure 1.

	OG (n = 72)	CG (n = 86)	t or χ²	P
Age (year)			0.793	0,42
	46.3±6.6	47.2±7.5		
BMI (KG/cm²)			1.454	0.14
	23,52±3.05	24.46±4.72		
Sex			0.125	0.72
Male	39 (54.17)	49 (56,98)		
Female	33 (45.83)	37 (43,02)		
Living environment			0,562	0.45
Urban area	58 (80.56)	65 (75.58)		
Rural area	14 (19.44)	21 (24,42)		
Smoking			0.013	0.90
Yes	32 (44.44)	39 (45.35)		
No	40 (55.56)	47 (54.65)		
Drinking			0.055	0.81
Yes	38 (52.78)	47 (54.65)		
No	34 (47.22)	39 (45.35)		
Family history			0.080	0.77
Yes	5 (6.94)	7 (8.14)		
No	67 (93.06)	79 (91.86)		
Ethnicity			0.384	0.53
Han nationality	67 (93.06)	82 (95,35)		
Minority nationality	5 (6.94)	4 (4.65)		

Table 1: Basic information of participants.

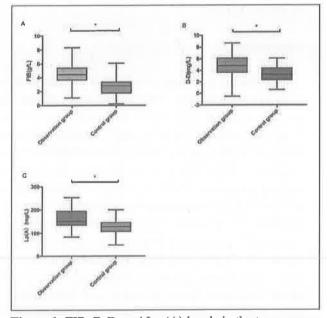


Figure 1: FIB, D-D, and Lp (A) levels in the two groups. A. Comparison of the FIB levels between the two groups. B. Comparison of the D-D levels between the two groups. C. Comparison of the Lp (A) levels between the two groups.

Correlation of FIB, D-D, and Lp (A) with cTn in OG

We noted that FIB, D-D, and Lp (A) levels were positively correlated with cTn levels in OG (P = 0.712, P = 0.709, P = 0.655, P < 0.05). More details are shown in Figure 2.

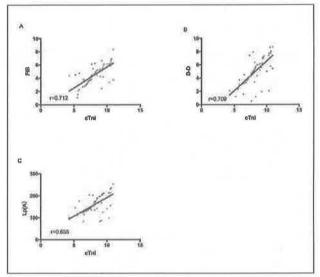


Figure 2: Correlation of FIB, D-D, and Lp (A) with cTn in OG. A. Correlation between FIB levels and cTn levels in OG. B. Correlation between D-D levels and cTn levels in OG. C. Correlation between Lp (A) levels and cTn levels in OG.

Value of FIB, D-D, and Lp (A) in predicting the occurrence of CHD in patients with T2DM

According to ROC curve analysis, the diagnostic sensitivity of FIB for predicting the occurrence of CHD in patients with T2DM was 75.58% and the specificity was 83.33% when the cut-off value was 3.355; the diagnostic sensitivity of DD was 88.37% and the specificity was 56.94% when the cut-off value was 4.540; the diagnostic sensitivity of Lp (A) was 60.47% and the specificity was 75.00% when the cut-off value was 134.700. We performed the binary regression analysis on the SPSS software and obtained the formula of the joint test of the three genes: Log(P) = 9.739 + (-1.106 * FIB) + (-0.531 * D-D) +(-0.024 * Lp (A)). The diagnostic sensitivity of the joint test for predicting the occurrence of CHD in patients with T2DM was 82.56% and the specificity was 86.11% when the cut-off value was 0.599. More details are shown in Table 2 and Figure 3.

Levels of FIB, D-D, and Lp (A) in OG before and after treatment

In OG, levels of FIB, D-D, and Lp (A) were lower after treatment than before treatment (P<0.05). More details are shown in Figure 4.

	FIB	D-D	Lp (A)	Joint test
AUC	0.847	0.754	0.737	0.910
Std.Error	0,031	0.040	0.040	0.023
95% CI	0.785±0.908	0.676±0.832	0.660±0.815	0.866±0.955
Cut-off	< 3.355	< 4.540	< 134,700	> 0,599
Sensitivity (%)	75,58	88,37	60.47	82.56
Specificity (%)	83,33	56.94	75.00	86.11
Youden index (%)	58.91	45.31	35.47	68.67
P	< 0.001	< 0.001	< 0.001	< 0,001

Table 2: Value of FIB, D-D, and Lp (A) in predicting the occurrence of CHD in patients with T2DM.

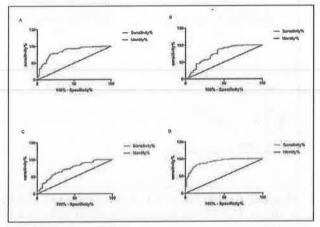


Figure 3: Value of FIB, D-D, and Lp (A) in predicting the occurrence of CHD in patients with T2DM. A. The ROC curve demonstrating the efficiency of FIB in predicting the occurrence of CHD in patients with T2DM. B. The ROC curve demonstrating the efficiency of D-D in predicting the occurrence of CHD in patients with T2DM. C. The ROC curve demonstrating the efficiency of Lp (A) in predicting the occurrence of CHD in patients with T2DM. D. The ROC curve demonstrating the efficiency of the joint test in predicting the occurrence of CHD in patients with T2DM.

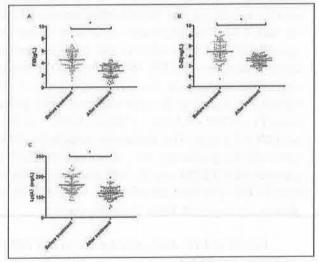


Figure 4: Levels of FIB, D-D, and Lp (A) in OG before and after treatment. A. FIB I evels in OG before and after treatment. B. D-D levels in OG before and after treatment. C. Lp (A) levels in OG before and after treatment.

Levels of FIB, D-D, and Lp (A) after treatment in patients with recurrence and patients without recurrence in OG

Among the 72 patients in OG, 13 cases reported recurrence and 59 reported no recurrence. Levels of FIB, D-D, and Lp (A) were lower in patients without recurrence than in patients with recurrence (P<0.05). More details are shown in Figure 5.

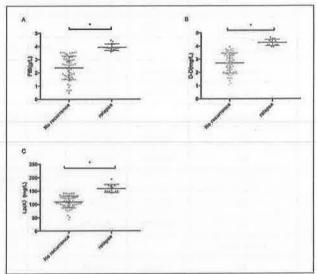


Figure 5: Levels of FIB, D-D, and Lp (A) after treatment in patients with recurrence and patients without recurrence in OG. A. FIB levels after treatment in patients with recurrence and patients without recurrence in OG. B. D-D levels after treatment in patients with recurrence and patients without recurrence in OG. C. Lp (A) levels after treatment in patients with recurrence and patients without recurrence in OG.

Discussion

T2DM is a common endocrine chronic disease with high incidence, which seriously affects the quality of life of patients(17). DM itself does not directly threaten the life of patients; however, diseases induced by DM are important causes of death of DM patients(18). Most DM patients die from cardiovascular complications. CHD is a frequent complication of DM⁽¹⁹⁾. CHD is caused by myocardial ischemia, hypoxia, and necrosis triggered by coronary atherosclerosis(20). According to clinical research, the main causes of T2DM complicated by CHD include glucose metabolism disorders, abnormal lipid metabolism, increased blood pressure, and insulin resistance. However, due to poor prognosis, single-target drugs, individual differences between patients, and adverse drug reactions, the overall clinical treatment efficacy for T2DM is poor(21). In addition to the active control of blood glucose, the strict monitoring of

the occurrence of complications is crucial in treating T2DM. Here we investigated the role of FIB, D-D, and Lp (A) in predicting the occurrence of CHD in patients with T2DM and their prognosis, aiming to provide reference and guidance for the future clinical prediction of T2DM complicated by CHD.

In this study, we detected higher levels of FIB, D-D, and Lp (A) in patients with T2DM complicated by CHD than in patients with simple T2DM, suggesting that FIB, D-D, and Lp (A) are not only abnormally expressed in T2DM but also have marked abnormal expression levels in CHD. FIB, a blood coagulation factor present in plasma synthesized and secreted by liver cells, is directly involved in the blood coagulation process and becomes soluble by the action of thrombin cleavage, which encapsulates the visible components in the blood and forms a solid thrombus, leading to enhanced coagulation function and increased FIB levels during the pre-thrombotic state and in thrombotic diseases(22). A large number of studies have confirmed that FIB levels are elevated in diseases such as acute myocardial infarction, DM, hypertension, and malignant tumors⁽²³⁾.

The above-mentioned studies all support the results of this study. D-D, a small peptide that is the degradation product produced by plasmin-mediated hydrolysis of cross-linked FIB, can reflect abnormal coagulation and fibrinolysis, and the increased plasma D-D levels can indicate activated thrombus or fibrin degradation in the blood vessels⁽²⁴⁾.

Elevated D-D levels can increase the risk of thrombosis⁽²⁵⁾. Also, an increase in D-D levels leads to enhanced tumor aggressiveness⁽²⁶⁾. Lp (A) is mainly synthesized in the liver and can be deposited on the walls of blood vessels to promote the formation of atherosclerotic plates⁽²⁷⁾. Lp (A) can inhibit the hydrolysis of FIB. Studies at home and abroad have confirmed that the continuous increase in Lp (A) levels can induce angina, myocardial infarction, and cerebral hemorrhage⁽²⁸⁾.

Previous data suggest that FIB, D-D, and Lp (A) levels are higher in cardiovascular diseases⁽²⁹⁾, which is similar to our results. CTn is a regulator of myocardial muscle contraction, commonly used in the diagnosis of cardiovascular diseases⁽³⁰⁾. We suspect that the convenient and fast test of FIB, D-D, and Lp (A) levels can greatly enhance the diagnosis rate of T2DM complicated by CHD, improve the prognosis of patients, and can be used to diagnose complications of T2DM in the future. We analyzed the correlation of FIB, D-D, and Lp (A) with cTn and noted that FIB, D-D, and Lp (A) levels were

positively correlated with cTn levels in OG. Such results suggest that FIB, D-D, and Lp (A) are closely related to T2DM complicated by CHD. According to the ROC curve analysis, FIB, D-D, and Lp (A) all showed good efficiency in predicting the occurrence of CHD in patients with T2DM, especially when the three genes were jointly tested. Such results suggest that FIB, D-D, and Lp (A) are important in predicting the occurrence of CHD in patients with T2DM and preventing complications, enlightening new directions for the future diagnosis of T2DM complicated by CHD. Inconspicuous at its early stage, DM is already at the middle stage at the time of diagnosis, facing a higher risk of complications. In this study, levels of FIB, D-D, and Lp (A) were lower after treatment than before treatment in OG, which supports our speculation. In order to further determine the clinical significance of FIB, D-D, and Lp (A) for T2DM complicated by CHD, we recorded cases with recurrence in OG. Among the 72 patients in OG, 13 cases reported recurrence and 59 reported no recurrence, and the FIB, D-D, and Lp (A) levels were lower in patients without recurrence than in patients with recurrence.

Such results confirm the specific roles of FIB, D-D, and Lp (A) in T2DM complicated by CHD. As suggested by other studies, these three markers can stimulate the occurrence and progression of CHD through different mechanisms of action, so they may be effective markers for T2DM complicated by CHD in the future.

In summary, FIB, D-D, and Lp (A) are highly expressed in patients with T2DM complicated by CHD. FIB, D-D, Lp (A) levels can be used to predict the occurrence and development of CHD in patients with T2DM, which are expected to become accurate markers for CHD.

Of course, this study is subject to some deficiencies. For example, we did not conduct basic experiments to identify the specific mechanism of action of FIB, D-D, and Lp (A). Besides, we did not explore the influence of FIB, D-D, and Lp (A) on the long-term prognosis of patients with T2DM complicated by CHD due to the short time duration of this study. We will address those deficiencies to perfect this study and obtain the most accurate results.

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Abstract

Aim: This study aims to explore the roles of plasma fibringen (B), lipoprotein a (Lp (A)), and D-dimer (D-D) in predicting the occurrence of complicated coronary heart disease (CHD) in patients with type 2 diabetes mellitus (12DM) and the prognosis of patients.

Methods: We enrolled 86 patients with T2DM (the control group, CG) and 72 patients with T2DM complicated by CHD (the observation group, OG) admitted to our hospital over the same period in this study. We tested the concentrations of FIB, D-D, and Lp (A) in the two groups of patients to analyze their correlations with cardiac troponin (cTn) and their value in predicting the occurrence of CHD in patients with T2DM. We also tested the concentrations of FIB, D-D, and Lp (A) in patients before and after treatment to explore their value in predicting the disease recurrence and assessing the prognosis of patients.

Results: We detected higher concentrations of FIB, D-D, and Lp (A) in OG than in CG (P<0.05). FIB, D-D, and Lp (A) levels were positively correlated with cTn in OG (P<0.05). FIB, D-D, and Lp (A) all showed good efficiency in predicting the occurrence of CHD in patients with T2DM, especially when the three genes were jointly tested. In OG, levels of FIB, D-D, and Lp (A) were lower after treatment than before treatment (P<0.05), and lower in patients without recurrence than in patients with recurrence (P<0.05).

Conclusion: FIB, D-D, and Lp (A) are highly expressed in patients with T2DM complicated by CHD. FIB, D-D, Lp (A) levels can be used to predict the occurrence and progression of CHD in patients with T2DM, which are expected to become accurate markers f or CHD.

Keywords

Author Keywords:Plasma fibrinogen; lipoprotein a; D-dither; type 2 diabetes mellitus complicated by coronary heart disease

KeyWords Plus:CARDIOVASCULAR-DISEASE; RISK; SCORE; ASSOCIATION; OUTCOMES; JOINT

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