华北理工大学
NORTH CHINA UNIVERSITY OF SCIENCE AND TECHNOLOGY

申请专业学位研究生校内指导教师佐证材料

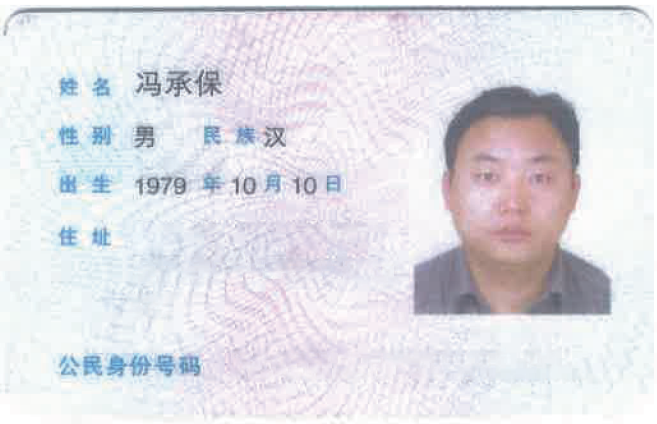
申请人姓名：冯承保

专业学位类别：临床医学

专业学位领域：肿瘤学

工作单位：保定市第二医院

2025 年 5 月


姓 名 冯承保
性 别 男 民 族 汉
出 生 1979 年 10 月 10 日
住 址
公民身份号码


中华人民共和国
居民身份证
签发机关 保定市公安局北市分局
有效期限 2008.11.07-2028.11.07

目　录

身份证复印件

学历、资历

一、毕业证书复印件.....1 页

二、学位证书复印件.....2 页

三、现专业技术职务任职资格证书复印件.....3 页

科研课题

一、科研立项、科研成果鉴定复印件，效益证明原件

1、结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究复印件....4-56 页

2、结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究效益证明原件.....57 页

论文、著作

一、论文复印件及论文收录检索报告

1、Clinical value of circulating tumour cells in evaluating the efficacy of continuous hepatic arterial infusion among colorectal cancer patients　J Chemother. 2025 Feb;37（1）:76-84 通讯作者.....58-70

2、The mechanisms of tumor necrosis factor α in regulating Krüpple-like factor 4 expression in SK-BR-3 breast cancer cells　Asia Pac J Clin Oncol. 2025 Feb;21（1）:123-128 并列第一作者.....71-79 页

3、Clinical effect and safety analysis of long-round needle usage in treating cervical spondylotic radiotelegraphy and its effect on pain and functional recovery 2023.07　J　Back Musculoskelet Rehabil 并列第一作者 .....80-89 页

普通高等学校

毕业证书

中华人民共和国教育部监制

No. 02135519

学生 冯承保 性别 男，

一九七九年十 月 十日生，于一九九七年

九 月至二〇〇二年 七 月在本校

临床医学 专业

五 年制本科学习，修完教学计划规定的全部课程，成绩合格，准予毕业。

校(院)长：

校 名：承德医学院

二〇〇二 年七 月一 日

学校编号：10093120020500034

学士学位证书

（普通高等教育本科毕业生）

冯承保 男，

1979 年10 月生。自1997

年9 月至 2002 年 7 月

在 临床医学 专业

完成了 五 年制本科学习计划，业已毕业。

经审核符合《中华人民共和国学位条例》

的规定，授予 医 学学士学位。

学位评定委员会主席

二〇〇二 年七 月一 日

证书编号：10093120020500034

河北省专业技术职务任职资格证书

姓　　名 Name：冯承保

性　　别 Gender：男性

证件类型 Certification Type：居民身份证（户口簿）

证件号码 Certification No.：13080219791010101X

系　　列 Category：卫生系列-内科

专　　业 Specialism：肿瘤内科

资格名称 Title of Qualification：主任医师（省市级）

批 文 号 Approval No.：冀职改办函〔2023〕19号

授予时间 Date of Conferment：2023年11月24日

工作单位 Place of Work：保定市第二医院

管 理 号 File No.：2023A107432

颁证机关：

河北省高级职称医疗卫生技术专业评审委员会 评审委员会

证书可通过“河北省专业技术职称申报评审信息系统”

网址：http://111.63.208.196:8080 查询核验

（二维码核验）

保定市科学技术局文件

保市政科字〔2019〕20号　　签发人：刘铁英

保定市科学技术局
关于下达2019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2019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30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《保定市市级科学技术研究与发展计划项目管理办法》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：2019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

2019年7月30日

2019年保定市科技计划自筹经费项目表（第一批）

归口管理部门	合作单位	承担单位

（此件不宜公开）

保定市科学技术局　　2019年7月30日印

2019年保定市科技计划自筹经费项目表（第一批）

序号	项目编号	项目名称	起止年月	承担单位	合作单位	归口管理部门
		一、科技攻关计划				
		（一）工业高新技术				
1	1911ZG001	台钻改制为自动攻丝机的研究与实践	2019.06-2020.08	保定职业技术学院		保定职业技术学院
2	1911ZG002	基于JavaEE的企业级快速开发框架研究	2019.05-2019.08	保定职业技术学院		保定职业技术学院
3	1911ZG003	装配式桥涵结构铰接技术与节点灌浆材料开发研究	2019.06-2021.06	河北大学	汇通路桥建设集团有限公司	河北大学
4	1911ZG004	冠梁支撑梁支护体系的研究	2019.02-2019.06	河北建设集团股份有限公司		市科技局
5	1911ZG005	大数据态势感知与运维可视化平台的研究与实现	2019.06-2020.05	河北金融学院		河北金融学院
6	1911ZG006	人社大数据平台的建设与应用研究	2019.06-2020.06	河北农业大学		河北农业大学
7	1911ZG007	多无人机农业喷洒编队控制方法研究	2019.06-2021.06	河北农业大学	河北翔拓航空科技有限公司	河北农业大学
8	1911ZG008	保定高新技术企业计算机辅助设计与制造技术培训体系研究	2019.07-2020.12	河北农业大学		河北农业大学
9	1911ZG009	数据挖掘技术在数字图书馆个性化服务中的应用设计研究	2019.05-2020.05	河北软件职业技术学院		河北软件职业技术学院
10	1911ZG010	基于关联规则的水资源监测与污染防治	2019.04-2021.04	河北省保定环境监测中心		市科技局
		（二）农业（畜牧业）新技术				
11	1911ZN001	保定市大球盖菇栽培技术创新研究与示范	2019.06-2020.12	保定市农业科学院	保定市恩鹏农业科技有限公	市科技局
12	1911ZN002	保定市旱涝时空特征演变研究	2019.07-2020.06	保定市气象局		市科技局
13	1911ZN003	保定市人工影响天气信息管理系统研究	2019.06-2020.10	保定市气象局		市科技局

14	1911ZN004	保定市苹果气象科技示范区建设	2019.05-2020.12	保定市气象局		市科技局
15	1911ZN005	保定市农业气象灾害特征及防御技术体系研究	2019.05-2021.05	保定市气象局	保定市农业技术推广工作站	市科技局
16	1911ZN006	基于GIS的保定市气候舒适度评价及预报方法研究	2019.07-2020.05	保定市气象局		市科技局
		（三）社会发展新技术				
17	1941ZF001	C-erbB-2、Bcl-1和COX-2在大肠癌组织中的表达及其临床意义	2019.06-2021.06	保定市第二医院		保定市第二医院
18	1941ZF002	胃癌术后采用不同方式联合免疫增强型营养支持治疗效果对比研究	2019.01-2020.12	保定市第二医院	保定市第一中心医院	保定市第二医院
19	1941ZF003	结直肠癌肝转移患者肝动脉前置化疗前后循环肿瘤细胞检测的临床研究	2019.01-2020.07	保定市第二医院		保定市第二医院
20	1941ZF004	CYP2C19基因型指导急性冠脉综合征患者抗血小板药物选择研究	2019.01-2020.06	保定市第二医院		保定市第二医院
21	1941ZF005	血清糖类抗原125对射血分数保留的慢性房颤心衰的诊断、疗效	2019.01-2020.06	保定市第二医院		保定市第二医院
22	1941ZF006	通脉养心丸治疗冠心病房性心律失常的临床研究	2019.01-2020.05	保定市第二医院		保定市第二医院
23	1941ZF007	加减附红八珍方配合喹普普酶及普罗非诺治疗老年急性心肌梗死的治疗效果观察	2019.02-2019.03	保定市第二医院	望都县医院	保定市第二医院
24	1941ZF008	脑梗死患者血清尿酸、炎性因子、神经元特异性烯醇化酶、同型半胱氨酸水平与病情及预后的关系研究	2019.06-2021.06	保定市第二医院		保定市第二医院
25	1941ZF009	安宫牛黄丸对高血压病合并2型糖尿病患者心脑血管疾病预防作用的临床研究	2019.06-2021.06	保定市第二医院		保定市第二医院
26	1941ZF010	Semaphorin分子在胃癌侵袭和转移过程中作用的研究	2019.07-2020.05	保定市第二医院		保定市第二医院
27	1941ZF011	十二指肠镜联合保胆手术治疗胆囊结石合并胆总管结石的临床研究	2019.07-2020.06	保定市第二医院		保定市第二医院
28	1941ZF012	不同手术方式介入治疗大隐静脉曲张疗效差异的临床研究	2019.05-2021.05	保定市第二医院		保定市第二医院
29	1941ZF013	两种窝沟封闭剂对于预防正畸术后龋齿发生的疗效差异的研究	2019.05-2021.05	保定市第二医院		保定市第二医院
30	1941ZF014	BT主导规范化健康教育对二胎产后压力性尿失禁者生活质量的研究	2019.01-2020.03	保定市第二医院		保定市第二医院

保定市社发类项目申请书

(医疗卫生)

社 发 类 别： 肿瘤科

项 目 名 称： 结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究

项目依托单位： 保定市第二医院

参 加 单 位：

项 目 组 长： 冯承保

申请资助方式： 完全自筹式

申报项目类别： 应用

项目主管单位： 保定市第二医院

申请计划年度： 2019年

项目起止年月： 2019.01-2020.07

申 报 日 期： 2019-05-24

保定市科学技术局制

项目依托单位概况	名称	结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究				
	地址	保定市东风西路338号				
	法人代码	40188830-3		E-mail		
	法人代表	葛长青	电话		邮编	071051
	开户名称	保定市第二医院		开户银行	保定银行向阳支行	
	开户行行号	313134000038		银行账号	86007020105011074	
	员工总数	1400人	技术人员数	人	中高级技术人员数	人
	性质		规模		其他特征	
	医院		其他			

项目内容摘要

对于患有结直肠肿瘤的病人，肝是远处器官转移最常见的部位。结直肠癌肝转移后自然生存期很短，其中位存活期为5～10个月，调查发现仅有15～25% 的结、直肠癌肝转移的患者可以接受外科手术治疗，但是，至少有一半施行了肝转移灶切除的结、直肠癌患者仍会复发。

由于肝转移癌的生物学特性，单纯手术切除的残肝复发率相当高。全身化疗仍然是标准的一线治疗。肝动脉区域化疗在内科化疗失败或耐药后，常常可作为补救治疗方案作为三线选择。当肝脏是唯一的转移部位时，肝动脉化疗是一种直接的治疗方法。另外，肝脏的转移灶几乎全部由肝动脉供血，某些药物的肝脏清除率很高，这就使得肝脏局部的药物浓度高而全身的毒副作用降低。

循环肿瘤细胞(CTCs)是指自发或因诊疗操作从肿瘤原发灶或转移灶脱落进入外周血液的肿瘤细胞。美国食品与药品管理局已批准将计数分析CTCs的CellSearch系统应用于临床监控乳腺癌、前列腺癌和结直肠癌根治术后肿瘤复发。

本研究的目的主要是检测结直肠癌肝转移患者肝动脉留管化疗前后循环细胞计数，以期为结直肠癌肝转移患者动脉化疗疗效提供一种理论依据。

应用行业	医院	创新类型	其它
技术领域	医疗卫生技术		
学科分类	肿瘤治疗学		
科技活动类型	应用研究		

一、项目的立项背景和意义

结、直肠癌是最常见的恶性肿瘤之一，全球每年大约有40万人死于结、直肠癌，被诊断为结、直肠癌的新发病例有70万。对于患有结直肠肿瘤的病人，肝是远处器官转移最常见的部位。据尸解材料分析，结直肠癌死亡的病人肝转移高达60~71% 。结直肠癌肝转移后自然生存期很短，其中位存活期为5~10个月，调查发现仅有15~25% 的结、直肠癌肝转移的患者可以接受外科手术治疗，但是，至少有一半施行了肝转移灶切除的结、直肠癌患者仍会复发。因此，如何处理肝转移成为延长结直肠癌病人生存期的关键之一。目前结直肠癌肝转移的治疗尚无金标准，多以个体化的综合治疗为主要趋势。

由于肝转移癌的生物学特性，单纯手术切除的残肝复发率相当高。全身化疗仍然是标准的一线治疗。大多数患者最终会进展。尤其是在肝转移局部客观反应率低。肝动脉区域化疗在内科化疗失败或耐药后，常常可作为补救治疗方案作为三线选择。肝动脉灌注化疗提高了到达肿瘤处的药物浓度，而正常的肝组织由于其门静脉和肝动脉的双重血供仅接受相对较少量的化疗药物，因此肝外组织仅暴露于较低的药物水平，从而降低了全身毒性。

循环肿瘤细胞(CTCs)是指自发或因诊疗操作从肿瘤原发灶或转移灶脱落进入外周血液的肿瘤细胞。CTCs与肿瘤转移、复发相关性的研究在近年亦取得较大进展。同时，CTCs检测具有无创、方便、可重复等特点，可作为一种“液相活检”技术应用于临床实践。

本研究的目的主要是检测结直肠癌肝转移患者肝动脉留管化疗前后循环细胞计数，以期为结直肠癌肝转移患者动脉化疗疗效提供一种理论依据。

二、国内外现状及发展趋势

全球每年大约有40万人死于结、直肠癌，被诊断为结、直肠癌的新发病例有70万。对于患有结直肠肿瘤的病人，肝是远处器官转移最常见的部位。据尸解材料分析，结直肠癌死亡的病人肝转移高达60～71% 。结直肠癌肝转移后自然生存期很短，其中位存活期为5～10个月，调查发现仅有15～25% 的结、直肠癌肝转移的患者可以接受外科手术治疗，但是，至少有一半施行了肝转移灶切除的结、直肠癌患者仍会复发。因此，如何处理肝转移成为延长结直肠癌病人生存期的关键之一。目前结直肠癌肝转移的治疗尚无金标准，多以个体化的综合治疗为主要趋势。

由于肝转移癌的生物学特性，单纯手术切除的残肝复发率相当高。全身化疗（FO LFO X/FO LFIRI）仍然是标准的一线治疗，大多数患者最终会进展。尤其是在肝转移局部客观反应率低。肝动脉区域化疗在内科化疗失败或耐药后，常常可作为补救治疗方案作为三线选择。其理论基础如下：因为已经证明肿瘤直径大于3cm时，血供大部分来自肝动脉，只有微小转移灶的血供来自门静脉，故对于不能切除或有残留的病人往往进行术后的动脉区域化疗。而门静脉化疗可以消灭游离癌细胞和镜下转移灶，减少延迟性肝转移发生率及残肝病灶再发。当肝脏是唯一的转移部位时，肝动脉化疗是一种直接的治疗方法。另外，肝脏的转移灶几乎全部由肝动脉供血，某些药物的肝脏清除率很高，这就使得肝脏局部的药物浓度高而全身的毒副作用降低。这种现象应用FU D R表现得最为显著，其肝脏的首过清除率为94% ~99% 而5-Fu只有19~55% 。肝动脉灌注化疗提高了到达肿瘤处的药物浓度，而正常的肝组织由于其门静脉和肝动脉的双重血供仅接受相对较少量的化疗药物，因此肝外组织仅暴露于较低的药物水平，从而降低了全身毒性。

经肝动脉灌注化疗治疗结直肠癌肝转移最常用的药物是5-FU 和FU D R，这两种药物的浓度一疗效曲线都很陡峭，而且全身清除率很高。根据不同的给药方式，肝脏对FU D R的摄取率是90% ，对5-FU 的摄取率是19-90% 。5-FU 的药代动力学是非线性的。全身清除和肝脏在高浓度时摄取速率的下降会降低5-FU 的选择性局部疗效。当药物浓度过高时，肝脏对药物的摄取和代谢达到饱和。因此，要想获得最佳的局部效果，经肝动脉持续灌注化疗药是最好的方法。

新药应用日益受到重视，V an R ie等人2002年报道，对20例结直肠癌伴肝转移的患者使用依立替康进行H A I，作了药物代谢动力学和临床I期的研究。患者接受了每3周进行一次连续五天的依立替康H A I。第一疗程通过选择性H A I给药，第二疗程全身静脉给药，随后的疗程为H A I给药。M TD （平均总剂量）为25m /m²/天，剂量限制性毒性为腹泻和中性白细胞减少。H A I给药与静脉内给药相比，依立替康的代谢率显著增高，P=0.015。M D Anderson癌中心和意大利也进行了类似使用依立替康H A I治疗结肠直肠癌伴肝转移的研究，显示肿瘤减少，癌胚抗原（CEA ）和乳酸脱氢酶（LD H ）水平降低。

循环肿瘤细胞(CTCs)是指外周血中的肿瘤细胞，一般情况下来自肿瘤原发灶或者转移灶。CTC 主要表达上皮源性的表面标志，广泛存在于乳腺癌、结直肠癌、前列腺癌等多种不同类型的癌症患者中，用于监控乳腺癌、前列腺癌和结直肠癌根治术后肿瘤复发。

研究表明，外周血CTCs在肿瘤发生阶段发挥重要作用。K im 等的研究显示，CTCs不仅可脱离原发肿瘤灶转移至其他器官，同时亦能重新返回并逆向渗透进原发瘤灶，促进肿瘤增殖和生长，增强原发瘤灶的侵袭性

，此过程称为肿瘤自我播种(tum orself-seeding)。该过程为探索恶性肿瘤的生长机制以及开发相应的肿瘤靶向治疗提供了新思路。

继发性肿瘤转移主要包括CTCs脱落入血以及CTCs对远隔器官环境再适应两个过程。不同来源的CTCs转移潜能有所不同。外周血CTCs既可能是直接从病灶脱落入血的上皮特征CTCs，亦可能是经历上皮-间质转化(EM T)脱落并存活于血液中的CTCs。研究表明，发生EM T 的乳腺癌细胞不仅获得了自我更新能力，同时亦具备一定的抗凋亡能力，此可能是肿瘤患者对化学疗法产生耐药性的原因之一。

CTC 的检测将会为肿瘤患者的个体化治疗带来进一步的突破，相当具有前景。CTC 作为一种无创性液体活检，摆脱了肿瘤组织标本活检及影像学多次检查的限制，可以允许进行实时、微创的监测，具有较好的重复性。综合以上优点使得关于 CTC 在结直肠癌领域中的临床研究成为热门。

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，是一所集医疗、教学、科研、预防、保健和康复功能为一体的三级甲等综合性医院。目前医院有总院、妇产儿科院区两个院区，总占地面积33370平方米，建筑面积57800平方米，职工1613人，其中卫生技术人员1454人，副高职称以上327人，博士、硕士研究生132人，编制床位1250张，年门诊量45万人次，收住院3万人次。医院另设有天威分院、农大分院及包括朝阳社区、韩南社区等5家卫生服务中心（站）。

医院设临床、医技科室54个，肝胆外科为省级医学重点发展学科，口腔科、普外科、医学影像科、心血管内科、神经内科、肿瘤内科、血管外科、耳鼻咽喉科为市级医学重点学科；中西医结合科老年病科为市级医学重点发展学科；耳鼻咽喉科、皮肤科、康复医学科门诊为市级重点中医专科。

我院拥有当今世界上先进的德国西门子3.0T超导磁共振成像系统、飞利浦造影系统及德国西门子V B30EC臂造影系统、64排128层螺旋CT、口腔CT等大型医疗设备200余台（件），能够为患者提供全面、快捷、准确的诊断检查报告。

我院肿瘤内科是保定市市属医院最早成立的肿瘤临床科室之一，历经十余年的发展，现已成为集医疗、教学、科研于一体，能够开展肿瘤个体化治疗、靶向治疗、肿瘤微创介入治疗，并在保定市有一定知名度的肿瘤学科，现为保定市重点学科，目前承担着河北大学、华北理工大学、承德医学院等多所院校的理论和实践教学任务。本学科目前能开展恶性肿瘤的化疗、靶向、微创等多种治疗手段，部分治疗达手段达到市内先进水平。

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）

本项目具体实施细则：

一、研究对象

入组标准：

1.年满18～80周岁，男女均可

2.经病理或临床诊断证实的结直肠癌肝转移患者

3.全身化疗进展或者不能耐受全身化疗者，或者拒绝全身化疗者

4.（M）RECIST 1.0标准下肝内可测量病灶数≥1个，各病灶长径≥1.5 cm 且≤20cm，

5.ECOG PS评分为≤2

6.预计生存时间≥12周

7.化验结果须满足以下要求：

血红蛋白≥ 90 g/L

绝对中性粒细胞数（ANC）>1,500/mm3

血小板数≥ 50x109/L

血清谷丙转氨酶（ALT）和谷草转氨酶（AST）< 5倍正常值上限(UNL)

总胆红素<2UNL

血肌酐<1.5UNL

PT或INR、PPT<1.5UNL(对于正在接受华法令或肝素抗凝治疗的患者,如果没有证据证明上述参数存在异常,则可以入组,但须进行严密监测,至少每周检测一次直至INR稳定)

排除标准：

严重心、肺疾病

其他肿瘤病史

恶病质

二、研究方法：

1、外周血循环肿瘤细胞（Circulating tumor cell, CTC）检测

①样本采集：每例患者于每周期化疗前抽取外周静脉血5-10mL

②CTC检测：本研究应用Leica DM 4B&DM 6B Life Science Research系统进行CTC检测。

③CTC判定标准及阳性定义

检出CD45阴性，同时肿瘤特异性细胞核抗原DAPI、细胞质抗原CK-FITC阳性的细胞，判定为CTC，CTC阳性定义：本研究以见到CTC≥5即为CTC阳性结果。

2、临床操作：常规股动脉入路，患者仰卧位，腹股沟及会阴部消毒、铺巾、局部浸润麻醉。采用Seldinger技术，经皮穿刺股动脉（穿刺点一般选择腹股沟韧带下1.0~1.5 cm，股动脉搏动明显处），置入导管鞘，插入导管置于腹腔动脉或肝总动脉造影。采集包括动脉期、实质期及静脉期图像。若发现肝脏某区域血管稀少

或缺乏，则可能存在供养肿瘤的侧支循环，需探查相应的动脉（包括肠系膜上动脉、下位肋间动脉、膈下动脉、肾动脉发出的肾上腺下动脉、肾上腺中动脉、胃左动脉、腰动脉、内乳动脉等），以发现异位起源的肝动脉或侧支供养血管。留置导管于肝固有动脉或肝左、右动脉分支内（靶病灶所在区域），给予肝动脉留管化疗。常选用方案为：奥沙利铂（伊立替康、洛铂）、亚叶酸钙、氟尿嘧啶土贝伐珠单抗/西妥昔单抗，肝动脉化疗结束后拔除导管和导管鞘，压迫穿刺部位止血，包扎伤口。拔管前注意患者血压的变化和纠正。患者仰卧，穿刺侧下肢伸直、制动6~12h。

三、有效性评价指标

1.治疗前1周内

测量生命体征。

ECOG体能状态评分和child pugh评分

肿瘤标记物检测：CEA，CA199，CA125，CA72.4

实验室检查：

-血常规：白细胞计数（WBC）、血红蛋白（Hb）、血小板计数（PLT）

-血生化：白蛋白（ALB）、丙氨酸氨基转移酶（ALT）、天门冬氨酸氨基转移酶（AST）、胆红素、血清肌酐（Scr）等

-凝血试验

-对育龄妇女进行检查尿或血清妊娠试验：（结果必须为阴性）

-循环肿瘤细胞检测

心电图、腹部盆腔平扫+增强CT检查、胸部CT检查

2.治疗后

ECOG体能状态评分；Child-pugh评分

肿瘤标记物检测；

实验室指标评价：包括全血细胞计数、血生化、凝血试验；

循环肿瘤细胞检测。

每八周或必要时进行肿瘤评估：

腹部CT检查所有的扫描应与基线时使用的技术相同。

3.主要疗效指标

①肝转移灶局部客观反应率（PR＋SD）

②无进展生存时间（PFS）

4.次要疗效指标

总生存时间（OS）

四、统计处理方法

①统计软件

研究方案确定后，采用SPSS 17.0统计软件进行统计分析。

②统计分析内容

实际入选数量，脱落和剔除病例情况，人口统计学和其他基线特征，疗效分析及安全性分析。

③统计方法

所有的统计检验均采用双侧检验，P值≤0.05将被认为所检验的差别有意义。

定量指标的描述将计算均值、标准差、中位数、最小值、最大值，下四分位数（Q1），上四分位数（Q3），分类指标描述各类的例数及百分数。

对两组一般情况的比较将根据指标的类型采用适当的方法进行分析，分类数据采用卡方检验或精确概率法，应用Kaplan-Meier曲线进行生存分析，Log-rank检验比较生存差异。

创新点：

1、肝动脉留管化疗对结直肠癌肝转移患者治疗优势：改变化疗给药的模式及肝脏局部药物浓度高。

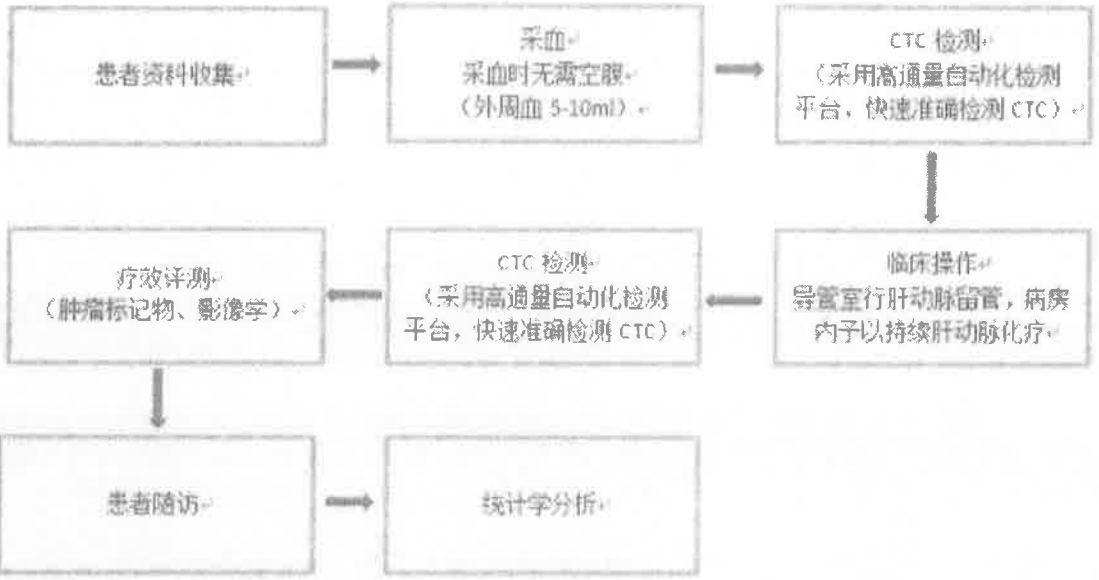
2、通过与肿瘤标记物、影像学检测对比，显示CTC评估结直肠癌肝转移患者肝动脉留管化疗的化疗疗效及预后的优势。

技术关键：

1.肝动脉留管：保证全肝的灌注；如遇血管变异情况存在，则应行血流再分布。

2.CTC检测：抽取外周血时防止静脉穿刺过程中皮肤上皮细胞污染；应用Leica DM 4B& DM 6B Life Science Research系统进行CTC检测。

技术路线图


患者资料收集
采血
采血时无需空腹
（外周血 5-10ml）
CTC 检测
（采用高通量自动化检测平台，快速准确检测 CTC）
临床操作
导管室行肝动脉留管，病房内予以持续肝动脉化疗
CTC 检测
（采用高通量自动化检测平台，快速准确检测 CTC）
疗效评测
（肿瘤标记物、影像学）
患者随访
统计学分析

<table>
<tr><td rowspan="2">知识产权情况</td><td colspan="2">项目技术来源</td><td>国内技术</td><td>是否形成标准</td><td>国家标准</td><td colspan="2">是否运用现有专利技术进一步开发研究</td><td>否</td></tr>
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<tr><td rowspan="6">预计成果水平及效益</td><td colspan="2">预期成果形式</td><td colspan="2">研究(咨询)报告</td><td colspan="2">预计技术成果水平</td><td colspan="2">国内领先</td></tr>
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单位：</td><td>年产值（万元）</td><td>年销售额收入（万元）</td><td>年利润（万元）</td><td>年税金（万元）</td><td>年创汇（万美元）</td></tr>
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<tr><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td colspan="2">社会效益（包括环保节能、降耗、医疗保健、就业等）</td><td colspan="6">本课题的研究为结直肠癌肝转移患者动脉留管化疗疗效提供简单、快捷的监测手段，及早预测肿瘤复发。</td></tr>
<tr><td>项目实施进度安排</td><td colspan="8">本项目起止时间为2019.01-2020.07
项目实施进度具体安排如下：
2019.1-2019.5 阅读相关文献，进行实验设计
2019.5-2020.5 收集病例资料
2020.5-2020.7 数据统计分析、结题</td></tr>
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五、项目经费来源与支出预算

单位：万元（保留两位小数）

序号	预算科目名称	合计	专项经费	自筹经费	配套经费
1	一、经费来源	0	0	0	0
2	二、经费支出	0	0	0	0
3	（一）直接经费	0	0	0	0
4	1、设备费	0	0	0	0
5	（1）购置设备费	0	0	0	0
6	（2）试制设备费	0	0	0	0
7	（3）设备改造与租赁费	0	0	0	0
8	2、材料费	0	0	0	0
9	3、测试化验加工费	0	0	0	0
10	4、燃料动力费	0	0	0	0
11	5、差旅费	0	0	0	0
12	6、会议费	0	0	0	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	0	0	0	0
15	9、劳务费	0	0	0	0
16	10、专家咨询费	0	0	0	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

六、承担单位、合作单位经费预算明细表

序号	单位名称	单位类型	任务分工	研究任务负责人	合计	专项经费		自筹经费	配套经费
						小计	其中:间接费用		
1	保定市第二医院	承担单位	项目负责	冯承保	0.0	0.0	0.0	0.0	0.0

七、参加人员及分工

序号	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	冯承保	男	39	130802197910101011X	副主任医师	本科	学士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	项目负责人	18
2	刘锦燕	女	50	130604196903180626	主任医师	本科	学士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集、CTC检测	18
3	王晶晶	女	37	130604198202160621	其他中级	本科	无	基础护理学	基础护理学	保定市第二医院	资料收集	18
4	杨雪	女	37	130603198112180622	其他中级	本科	无	基础护理学	基础护理学	保定市儿童医院	资料收集	18
5	臧雪芳	女	44	130603197408011241	其他中级	本科	无	基础护理学	基础护理学	保定市第二医院	资料收集	18
6	周海坤	女	36	13068119830412582X	其他中级	本科	学士	专科护理学	专科护理学	保定市第二医院	资料收集	18
7	张二蓉	女	30	130628198805024224	医师	研究生	硕士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集、CTC检测、数据分析	18
8	李海飞	女	34	130982198406131625	副主任药师	研究生	硕士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集、数据分析	18
9	刘博	男	37	130631198204150215	主治医师	本科	学士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集	18
10	陈淑敏	女	52	130602196701020349	主任药师	本科	无	药剂学	药剂学	保定市第二医院	资料收集	18
11	王颖	男	41	130603197801130925	副主任医师	本科	硕士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集	18
12	王鹏	男	40	130602197811070616	副主任医师	研究生	硕士	肿瘤治疗学	肿瘤治疗学	保定市第二医院	资料收集、数据分析	18

八、保定市市级预算项目绩效说明书							
序号	绩效目标	绩效指标	指标描述	绩效标准			
				优	良	中	差

项目承担单位基本情况简介							
	上年度(2018)年项目承担单位整体效益	年销售收入（万元）		年创汇（万美元）	年上缴税金（万元）		年利润（万元）
		0		0	0		0
		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）
		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，是一所集医疗、教学、科研、预防、保健和康复功能为一体的三级甲等综合性医院。目前医院有总院、妇产儿科院区两个院区，总占地面积33370平方米，建筑面积57800平方米，职工1613人，其中卫生技术人员1454人，副高职称以上327人，博士、硕士研究生132人，编制床位1250张，年门诊量45万人次，收住院3万人次。医院另设有天威分院、农大分院及包括朝阳社区、韩南社区等5家卫生服务中心（站）。

医院设临床、医技科室54个，肝胆外科为省级医学重点发展学科，口腔科、普外科、医学影像科、心血管内科、神经内科、肿瘤内科、血管外科、耳鼻咽喉科为市级医学重点学科；中西医结合科老年病科为市级医学重点发展学科；耳鼻咽喉科、皮肤科、康复医学科门诊为市级重点中医专科。我院拥有当今世界上先进的德国西门子3.0T超导磁共振成像系统、飞利浦造影系统及德国西门子V B30E C臂造影系统、64排128层螺旋CT、口腔CT等大型医疗设备200余台（件），能够为患者提供全面、快捷、准确的诊断检查报告。

肿瘤内科是保定市市属医院最早成立的肿瘤临床科室之一，历经十余年的发展，现已成为集医疗、教学、科研于一体，能够开展肿瘤个体化治疗、靶向治疗、肿瘤微创介入治疗，并在保定市有一定知名度的肿瘤学科，现为保定市重点学科，目前承担着河北大学、华北理工大学、承德医学院等多所院校的理论和实践教学任务。本学科目前能开展恶性肿瘤的化疗、靶向、微创等多种治疗手段，部分治疗达手段达到市内先进水平。

项目组长简介

姓名	性别	出生年月	学历	职务、职称	所学专业	现从事专业
冯承保	男	1979.10	本科	副主任医师	肿瘤治疗学	肿瘤治疗学
所在单位	保定市第二医院					
联系电话	0312-3099722		手机	15603123011	E-M ail	m ovingw ind@ sina.co m
通讯地址	东风西路338号保定市第二医院肿瘤内科				邮政编码	071000

个人资历与业绩

2002年毕业于承德医学院，现工作于保定市第二医院肿瘤内科，从事临床工作17年余，2006年于中国人民解放军总医院进修介入放射学，2016年于北京大学肿瘤医院介入治疗科学习。现主要工作方向为：常见肿瘤的诊断及治疗，尤其擅长肿瘤的介入治疗，包括：1、影像学引导下的肿瘤穿刺活检、射频（微波、冷冻））消融术、粒子植入术；2、血管介入治疗，动脉栓塞术、靶血管区域内化疗、改良动脉泵治疗；3、输液港植入术、经皮穿刺胆道引流术等技术。主持并参与多项科研课题，多次获得省市级科技进步奖，并发表著作及论文数篇。目前为中国抗癌协会肿瘤介入专业委员会化疗与免疫治疗专家委员会委员，中国抗癌协会肿瘤微创治疗专业委员会、胆道肿瘤专业委员会、肿瘤介入学专业委员会及癌症康复与姑息治疗专业委员会委员，中国医疗保健国际交流促进会肺癌预防与控制分会肺癌微创诊断与治疗专业委员会委员，河北省抗癌协会会员，河北省抗癌协会青年理事会常务理事，北京健康促进会中青年专家委员会胸部疾病精准活检分委会委员，河北省预防医学会食管癌专委会委员，保定市医学会肿瘤分会胸部肿瘤学组委员。

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**：本单位已就所申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。

申报单位签章：

日期：

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：冯承保

日期：2019-8-1

九、项目依托单位意见 同意申报 年 月 日（公章）
十、项目主管单位意见 同意申报 年 月 日（计划专用章）
十一、市科技局意见 年 月 日（计划专用章）
备注

附件目录：		
序号	附件名称	附件说明

保定市科技计划项目任务书

项　目　名　称：结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究

项　目　编　号：1941ZF003

签　订　年　度：2019　　年

项目起止年月：2019.01-2020.07

承担单位（乙方）：保定市第二医院

合　作　单　位：

项　目　负　责　人：冯承保　　联系电话：15603123011

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：313134000038

账　　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。

二、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授权或委托的其他机构。

三、“项目名称”、“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（采用集中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，要写清全称和缩写字母，第一次出现时要注意中文。

六、本任务书一式四份，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）

本研究的目的主要是检测结直肠癌肝转移患者肝动脉留管化疗前后循环细胞计数，以期为结直肠癌肝转移患者动脉化疗疗效提供一种理论依据。根据入组标准及排除标准选择研究对象。并进行外周血循环肿瘤细胞（Circulating tumor cell，CTC）检测，同时行肝动脉留管化疗，常规股动脉入路，患者仰卧位，腹股沟及会阴部消毒、铺巾、局部浸润麻醉。采用Seldinger技术，经皮穿刺股动脉（穿刺点一般选择腹股沟韧带下1.0～1.5 cm，股动脉搏动明显处），置入导管鞘，插入导管置于腹腔动脉或肝总动脉造影。采集包括动脉期、实质期及静脉期图像。若发现肝脏某区域血管稀少或缺乏，则可能存在供养肿瘤的侧支循环，需探查相应的动脉（包括肠系膜上动脉、下位肋间动脉、膈下动脉、肾动脉发出的肾上腺下动脉、肾上腺中动脉、胃左动脉、腰动脉、内乳动脉等），以发现异位起源的肝动脉或侧支供养血管。留置导管于肝固有动脉或肝左、右动脉分支内（靶病灶所在区域）常选用方案为：奥沙利铂（伊立替康、喜铂）、亚叶酸钙、氟尿嘧啶土贝伐珠单抗/西妥昔单抗，肝动脉化疗结束后拔除导管和导管鞘，压迫穿刺部位止血，包扎伤口。拔管前注意患者血压的变化和纠正。患者仰卧，穿刺侧下肢伸直、制动6～12 h。本研究有效性评价指标1.主要疗效指标①肝转移灶局部客观反应率（PR＋SD）；②无进展生存时间（PFS）2.次要疗效指标总生存时间（OS）。采用SPSS 17.0统计软件进行统计分析，所有的统计检验均采用双侧检验，P值≤0.05将被认为所检验的差别有意义。定量指标的描述将计算均值、标准差、中位数、最小值、最大值，下四分位数（Q1），上四分位数（Q3），分类指标描述各类的例数及百分数。对两组一般情况的比较将根据指标的类型采用适当的方法进行分析，分类数据采用卡方检验或精确概率法，应用Kaplan Meier曲线进行生存分析，Log-rank检验比较生存差异。

技术路线

查阅资料、实验设计、论证——选取病例——CTC检测等相关指标——肝动脉留管化疗——CTC检测等相关指标——对数据进行处理、分析、得出结果——撰写论文——实验研究结束

创新点：

1、肝动脉留管化疗对结直肠癌肝转移患者治疗优势：改变化疗给药的模式及肝脏局部药物浓度高。

2、通过与肿瘤标记物、影像学检测对比，显示CTC评估结直肠癌肝转移患者肝动脉留管化疗的化疗疗效及预后的优势。

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）

此项研究成果在医院的推广应用，首先对于结直肠癌肝转移患者通过肝动脉留管化疗改变化疗给药的模式及肝脏局部药物浓度高以延长患者生存期、提高生活质量；其次通过检测CTC更早预测结直肠癌肝转移患者肝动脉留管化疗的化疗疗效及预后，使结肠癌肝转移患者受益，预期发表论文3篇。

三、进度、安排和阶段目标

本项目起止时间为2019.01-2020.07

项目实施进度具体安排如下：

2019.1-2019.5 阅读相关文献，进行实验设计

2019.5-2020.5 收集病例资料

2020.5-2020.7 数据统计分析、结题并参加评奖

四、项目承担单位、合作单位任务分工、知识产权归属

保定市第二医院作为项目承担单位，始建于1920年，是一所集医疗、教学、科研、预防、保健和康复功能为一体的三级甲等综合性医院。我院肿瘤内科是保定市市属医院最早成立的肿瘤临床科室之一，历经十余年的发展，现已成为集医疗、教学、科研于一体，能够开展肿瘤个体化治疗、靶向治疗、肿瘤微创介入治疗；并在保定市有一定知名度的肿瘤学科，现为保定市重点学科，目前承担着河北大学、华北理工大学、承德医学院等多所院校的理论和实践教学任务。本学科目前能开展恶性肿瘤的化疗、靶向、微创等多种治疗手段，部分治疗达手段达到市内先进水平。

知识产权归属明确。

五、参加人员及分工

序号	姓名	性别	年龄	证件号码	职称	学历	学位	现从事专业	单位名称	分工
1	冯承保	男	39	13080219791010101X	副主任医师	本科	学士	肿瘤治疗学	保定市第二医院	项目负责人
2	刘锦燕	女	50	130604196903180626	主任医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集、CTC检测
3	王晶晶	女	37	130604198202160621	其他中级	本科	无	基础护理学	保定市第二医院	资料收集
4	杨雪	女	37	130603198112180622	其他中级	本科	无	基础护理学	保定市儿童医院	资料收集
5	臧雪芳	女	44	130603197408011241	其他中级	本科	无	基础护理学	保定市第二医院	资料收集
6	周海坤	女	36	13068119830412582X	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集
7	张二营	女	30	130628198805024224	医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、CTC检测、数据分析
8	李海飞	女	34	130882198406131625	副主任药师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析
9	刘博	男	37	130631198204150215	主治医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集
10	陈振敏	女	52	130602196701020349	主任药师	本科	无	药剂学	保定市第二医院	资料收集
11	王丽	男	41	130603197801130925	副主任医师	本科	硕士	肿瘤治疗学	保定市第二医院	资料收集
12	王鹏	男	40	130602197811070616	副主任医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析

六、经费概算

单位：万元（保留两位小数）

序号	预算科目名称	合计	专项经费	自筹经费	配套经费
1	一、经费来源	0	0	0	0
2	二、经费支出	0	0	0	0
3	（一）直接经费	0	0	0	0
4	1、设备费	0	0	0	0
5	（1）购置设备费	0	0	0	0
6	（2）试制设备费	0	0	0	0
7	（3）设备改造与租赁费	0	0	0	0
8	2、材料费	0	0	0	0
9	3、测试化验加工费	0	0	0	0
10	4、燃料动力费	0	0	0	0
11	5、会议/差旅/国际合作与交流费	0	0	0	0
12	6、出版/文献/信息传播/知识产权事务费	0	0	0	0
13	7、劳务费	0	0	0	0
14	8、专家咨询费	0	0	0	0
15	9、其他支出	0	0	0	0
16	（二）间接经费	0	0	0	0
17	其中：绩效支出	0	0	0	0

七、承担单位、合作单位经费预算明细表

序号	单位名称	单位类型	任务分工	研究任务负责人	合计	专项经费		自筹经费	配套经费
						小计	其中:间接费用		
1	保定市第二医院	承担单位	项目负责	冯承保	0.0	0.0	0.0	0.0	0.0

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。

丙方：

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：

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、 按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

（计划专用章）

主管业务处处长：　　日期：

主管局长：　　日期：

乙方（承担单位）：保定市第二医院

（公章）

项目负责人：冯承保　　日期：

所在单位负责人：陈建婕　　日期：

合作单位：

（公章）

日期：

丙方（归口管理单位）：保定市第二医院　　（科研计划专用章）

负　责　人：陈建婕　　日期：

经　办　人：　　日期：

附件目录：		
序号	附件名称	附件说明

保定市科技计划项目验收证书

保科验字〔2021〕03-233 号

项 目 编 号：1941ZF003

项 目 名 称：结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究

承 担 单 位：保定市第二医院

合 作 单 位：

验收主持部门：河北大学附属医院

验 收 方 式：函审验收

验 收 日 期：2022-05-26

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。

2. 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日期。

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

<table>
<tr><td>项目名称</td><td colspan="8">结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究</td></tr>
<tr><td>第一承担单位名称</td><td colspan="3">保定市第二医院</td><td colspan="2">单位性质</td><td colspan="3">医院</td></tr>
<tr><td rowspan="2">项目负责人</td><td>姓名</td><td>冯承保</td><td>联系电话</td><td>+8631230599635</td><td>电子邮箱</td><td colspan="3">in ovingw ing@ sina.com</td></tr>
<tr><td>学 历</td><td>本科</td><td>学位</td><td>学士</td><td>职称</td><td colspan="3">副主任医师</td></tr>
<tr><td rowspan="3">参研人员情况</td><td rowspan="2">总人数（人）</td><td colspan="4">按专业技术职务分布</td><td colspan="4">按学位分布</td></tr>
<tr><td>高级职称</td><td>中级职称</td><td>初级职称</td><td>其它人员</td><td>博士</td><td>硕士</td><td>学士</td><td>其它</td></tr>
<tr><td>13</td><td>4</td><td>8</td><td>1</td><td>0</td><td>0</td><td>4</td><td>9</td><td>0</td></tr>
<tr><td colspan="5">累计投入项目研究的工作量（人月）</td><td>26</td><td colspan="2">吸引省外人才（人）</td><td>0</td></tr>
<tr><td>所属领域</td><td colspan="8">医疗卫生技术</td></tr>
<tr><td rowspan="2">产学研联合</td><td>主要合作单位名称</td><td colspan="3"></td><td>合作单位性质</td><td colspan="3"></td></tr>
<tr><td>合作形式</td><td colspan="7"></td></tr>
<tr><td rowspan="2">累计经费筹集情况（万元）</td><td rowspan="2">总投入</td><td>省科技厅拨款</td><td>市科技局拨款</td><td>市县匹配资金</td><td>单位自筹</td><td>银行贷款</td><td colspan="2">其他</td></tr>
<tr><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td colspan="2">0</td></tr>
<tr><td rowspan="2">累计实现的直接经济效益</td><td colspan="2">新增产值（万元）</td><td>0</td><td colspan="3">出口创汇（万美元）</td><td colspan="2">0</td></tr>
<tr><td colspan="2">上缴税金（万元）</td><td>0</td><td colspan="3">净利润额（万元）</td><td colspan="2">0</td></tr>
</table>

<table>
<tr><td rowspan="11">累计实现的直接社会效益</td><td>成果转让数（项）</td><td>0</td><td>成果转让获得收入（万元）</td><td>0</td><td>获省部级以上奖励（项）</td><td>0</td></tr>
<tr><td>新产品、新材料（种）</td><td>0</td><td>新工艺、新装置（项）</td><td>0</td><td>出版科技著作（万字）</td><td>0</td></tr>
<tr><td>科技论文、报告（篇）</td><td>4</td><td>其中：发表科技论文（篇）</td><td>4</td><td>其中：被EI、SCI、ISTP、ISR收录（篇）</td><td>1</td></tr>
<tr><td colspan="2">动植物新品种开发个数（个）</td><td>0</td><td colspan="2">动植物新品种推广面积或扩繁数量（亩或头）</td><td>0</td></tr>
<tr><td colspan="2">累计建立试验示范区（基地）数（个）</td><td>0</td><td colspan="2">累计建立试验示范区规模（亩或头）</td><td>0</td></tr>
<tr><td colspan="3">专利申请数（项）</td><td colspan="3">专利授权数（项）</td></tr>
<tr><td>发明</td><td>实用新型</td><td>外观设计</td><td>发明</td><td>实用新型</td><td>外观设计</td></tr>
<tr><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td colspan="2">制定技术标准（项）</td><td colspan="2">企业标准</td><td colspan="2">地方标准</td><td>行业标准</td><td>国家标准</td><td>国际标准</td></tr>
<tr><td colspan="2">0</td><td colspan="2">0</td><td colspan="2">0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td colspan="2">培养人才数（人）</td><td colspan="3">获博士学位人数</td><td colspan="2">获硕士学位人数</td><td colspan="2">培训专业技术人员（人次）</td></tr>
<tr><td colspan="2">0</td><td colspan="3">0</td><td colspan="2">0</td><td colspan="2">0</td></tr>
<tr><td rowspan="2">累计环保节能效益</td><td>节煤（万吨）</td><td>0</td><td>节电（万度）</td><td>0</td><td>节水（万吨）</td><td>0</td></tr>
<tr><td>减排废气（万立方米）</td><td>0</td><td>减排废水（万吨）</td><td>0</td><td>减排废物（万吨）</td><td>0</td></tr>
</table>

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

项目共纳入了十六例结直肠癌肝转移患者，所有研究对象均严格按照入组标准，排除标准进行筛选，术前采集外周血进行循环肿瘤细胞（Circulating tumor cell，CTC）检测，完善术前各项检查及准备后，家属签署知情同意书，行肝动脉留管化疗术，通过介入技术，将微导管留置于肝固有动脉或肝左、右动脉分支内（靶病灶所在区域），给予肝动脉留管化疗。常选用方案为：奥沙利铂（伊立替康、洛铂）、亚叶酸钙、氟尿嘧啶（雷替曲塞）土贝伐珠单抗/西妥昔单抗，同时予以保肝、止吐、保护胃肠膜等治疗，肝动脉化疗结束后拔除导管和导管鞘，压迫穿刺部位止血，包扎伤口。3-4周后进行下一周期的肝动脉留管化疗，并监测肿瘤标记物、全血尿脚计数、血生化、凝血试验、循环肿瘤细胞等检测。每六到八周进行肿瘤影像学评估，大部分患者进行四到六周期的肝动脉留管化疗，之后定期随访观察。通过数据统计分析，应用肝动脉留观化疗后肝转移灶局部客观反应率提高，有统计学意义，无进展生存时间（PFS）延长，且无严重不良事件和不良反应，外周血循环肿瘤细胞检测能显示动脉化疗疗效，且能够及早预测肿瘤的复发。

创新性简介

1、循环肿瘤细胞检测在肝动脉留管化疗中的意义

2、循环肿瘤细胞与肿瘤标记物、影像学检测在HAIC治疗中的一致性或相关性

3、肝动脉留管化疗对结直肠癌肝转移患者有治疗优势，其能改变化疗给药的模式及有、提高肝脏局部药物浓度高。

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

在结直肠癌肝转移患者肝动脉留管化疗过程中，外周血循环肿瘤细胞计数可以用于评估化疗疗效，可作为判断预后的指标，与肿瘤标记物、影像学检查可共同作为判断肿瘤复发、转移及治疗疗效的指标。此结论具有显著社会效益，对于临床中此类患者采用本研究，可以提高患者的PFS、OS，值得在临床大力推广。

三、主要技术文件目录及来源

验收大纲——保定市科学技术局

工作报告——保定市第二医院

技术报告——保定市第二医院

论文：

（1）抗KRAS免疫脂质磁球修饰的结直肠癌循环肿瘤细胞构建及鉴定，《癌症调查与研究》 2020;12 10057 - 10075，作者：冯承保 王晶晶 杨雪 臧雪芳 周海坤 张二营 李海飞 刘博 陈淑敏 王颖 王鹏 刘锦燕

（2）卡培他滨结合介入疗法在结直肠癌术后肝转移患者的疗效与安全性，《中国保健营养》 2021年3月上第7期 第31卷 作者：冯承保 刘锦燕 王晶晶 杨雪 臧雪芳 周海坤 张二营 李海飞 刘博 陈淑敏 王颖 王鹏

（3）结直肠癌肝转移应用雷替曲塞行介入治疗疗效的临床探析，《母婴世界》 2021年1月 第2期 作者：冯承保 刘锦燕 王晶晶 杨雪 臧雪芳 周海坤 张二营 李海飞 刘博 陈淑敏 王颖 王鹏

（4）奥沙利铂联合方案经动脉介入治疗结直肠癌肝转移的临床研究，《母婴世界》 2021年2月 第6期 作者：冯承保 刘锦燕 王晶晶 杨雪 臧雪芳 周海坤 张二营 李海飞 刘博 陈淑敏 王颖 王鹏

四、主要研制人员名单

序号	姓名	性别	年龄	职称	学历	学位	现从事专业	单位名称	分工	本人签名
1	冯承保	男	39	副主任医师	本科	学士	肿瘤治疗学	保定市第二医院	项目负责人	
2	刘丽丽	女	50	主任医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集、CTC 检测	
3	王晶晶	女	37	其他中级	本科	无	基础护理学	保定市第二医院	资料收集	
4	杨雪	女	37	其他中级	本科	无	基础护理学	保定市儿童医院	资料收集	
5	臧雪芳	女	44	其他中级	本科	无	基础护理学	保定市第二医院	资料收集	
6	周海坤	女	36	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集	
7	张二营	女	30	医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、CTC 检测、数据分析	
8	李海飞	女	34	副主任药师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析	
9	刘博	男	37	主治医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集	
10	陈淑敏	女	52	主任药师	本科	无	药剂学	保定市第二医院	资料收集	
11	王颖	男	41	副主任医师	本科	硕士	肿瘤治疗学	保定市第二医院	资料收集	
12	王鹏	男	40	副主任医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析	

三、主要研制人员名单 （项目承担单位盖章、管理部门盖章）

序号	姓 名	性别	年龄	职称	学历	学位	现从事专业	单位名称	分工	本人签名
1	冯承保	男	39	副主任医师	本科	学士	肿瘤治疗学	保定市第二医院	项目负责人	
2	刘锦燕	女	50	主任医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集、CTC 检测	
3	王晶晶	女	37	主管护师	本科	无	基础护理学	保定市第二医院	资料收集	
4	杨雪	女	37	主管护师	本科	无	基础护理学	保定市儿童医院	资料收集	
5	臧雪芳	女	44	主管护师	本科	无	基础护理学	保定市第二医院	资料收集	
6	周海坤	女	36	主管护师	本科	学士	基础护理学	保定市第二医院	资料收集	
7	张二雷	女	30	医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、CTC 检测、数据分析	
8	李海飞	女	34	主治医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析	
9	刘博	男	37	主治医师	本科	学士	肿瘤治疗学	保定市第二医院	资料收集	
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11	王颖	女	41	副主任医师	本科	硕士	肿瘤治疗学	保定市第二医院	资料收集	
12	王鹏	男	41	副主任医师	研究生	硕士	肿瘤治疗学	保定市第二医院	资料收集、数据分析	

注：本表由承担单位如实填写。

五、验收专家名单

序号	姓名	工作单位	所学专业	现从事专业	职务	职称	本人签名
1	李润涌	保定市第二中心医院	肿瘤治疗学	肿瘤治疗学	科主任	主任医师	
2	张惠卿	保定市第一中心医院	普通外科学	普通外科学	科副主任	主任医师	
3	张金卓	保定市第一中心医院	胃肠病学	胃肠病学	科副主任	主任医师	
4	刘向东	河北医科大学第三医院	临床放射学	肿瘤治疗学	科副主任	主任医师	
5	鲁惹彩	河北大学附属医院	胃肠病学	胃肠病学	科主任	主任医师	

四、验收专家名单

序号	姓　名	工 作 单 位	所学专业	现从事学科	职务/职称	本人签名
1	鲁素彩	河北大学附属医院	消化内科	消化内科	科主任/主任医师	
2	刘向东	河北医科大学第三医院	临床医学	介入放射学	科副主任/主任医师	
3	张惠卿	保定市第一中心医院	外科学	普通外科	科副主任/主任医师	
4	张金卓	保定市第一中心医院	消化内科	消化内科	科副主任/主任医师	
5	李润浦	保定市第一中心医院	临床医学	肿瘤内科	科主任/主任医师	

六、验收意见

由保定市第二医院承担研究的2019年保定市科学技术研究与发展指导计划项目《结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究》，项目编号为1941ZF003，已按项目申报书和任务书完成，经审查，提供的技术资料完整、规范，符合验收要求。综合其他验收委员意见，形成验收意见如下：

1，该课题立题准确，数据详实，符合验收要求。

2，本研究通过检测结直肠癌肝转移患者肝动脉持续留管化疗前后循环肿瘤细胞计数，来评价结直肠癌肝转移患者肝动脉化疗疗效。肝动脉持续留管化疗后CTC数目较化疗前减少，且化疗后CTC阳性率逐渐下降，在结直肠癌肝转移患者肝动脉留管化疗过程中，外周血循环肿瘤细胞计数可以用于评估化疗疗效，可作为判断预后的指标，与肿瘤标记物、影像学检查可共同作为判断肿瘤复发、转移及治疗疗效的指标。

3，该课题理论与临床实际结合，着眼于解决实际问题，研究过程完整，科学合理，针对性强，可为临床解决紧要问题，有很大推广使用价值。

综上所述，承担单位按规定完成了科研的研究，得出可靠结论，此结论具有显著社会效益，值得在临床大力推广。目前已发表论文4篇。验收组一致同意通过完成验收。

建议增加样本数量，并开展多中心研究，增加副作用指标观察，增加开发症观察时间等。这样证据会更多，加快该项目的推行应用。

五、验收意见

由保定市第二医院承担研究的 2019 年保定市科学技术研究与发展指导计划项目《结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究》，项目编号为 19ZF003，已按项目申报书和任务书完成，经审查，提供的技术资料完整、规范，符合验收要求。综合其他验收委员意见，形成验收意见如下：

1、该课题立题准确，数据详实，符合验收要求。

2、本研究通过检测结直肠癌肝转移患者肝动脉持续留管化疗前后循环肿瘤细胞计数，来评价结直肠癌肝转移患者肝动脉化疗疗效。肝动脉持续留管化疗后 CTC 数目较化疗前减少，且化疗后 CTC 阳性率逐渐下降，在结直肠癌肝转移患者肝动脉留管化疗过程中，外周血循环肿瘤细胞计数可以用于评估化疗疗效，可作为判断预后的指标，与肿瘤标记物、影像学检查可共同作为判断肿瘤复发、转移及治疗疗效的指标。

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建议增加样本数量，并开展多中心研究，增加副作用指标观察，增加并发症观察时间等。这样证据会更多，加快该项目的推行应用。

验收委员会主任：

_____年_____月_____日

七、项目管理部门意见

项目承担单位意见

负责人签字：

（公章）

年 月 日

项目归口管理部门意见

负责人签字：

（科研管理章）

年 月 日

市科技局意见

项目主管处室负责人签字：

（科技项目验收专用章）

年 月 日

验收文件和资料目录		
序号	附件名称	附件说明
1	专家签字的函审表扫描件	河北医科大学第二医院对商东签字的函审表扫描件
2	专家签字的函审表扫描件	保定市第二中心医院李国强签字的函审表扫描件
3	专家签字的函审表扫描件	保定市第一中心医院张惠卿签字的函审表扫描件
4	专家签字的函审表扫描件	保定市第一中心医院张金生签字的函审表扫描件
5	专家签字的函审表扫描件	河北大学附属医院曾素彩签字的函审表扫描件
6	验收意见页扫描件	验收意见页扫描件
7	完成人签字扫描件	完成人签字扫描件
8	函审专家签字扫描件	函审专家签字扫描件

河北省科学技术成果

证书

河北省科学技术厅

成果名称：结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究

完 成 人：冯承保（第壹完成人）

所在单位：保定市第二医院

第一完成单位：保定市第二医院

省级登记号：20230002

二〇二三年十月

河北省科学技术厅 科技成果登记专用章

证书

为表彰荣获河北医学科技奖的优秀医学科技工作者，特发此证，以资鼓励。

编　　号：223904-1

成果名称：结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究

完成单位：保定市第二医院

完 成 人：冯承保　刘锦燕　王晶晶　杨雪　臧雪芳

奖励等级：叁等奖

河北省医学会

2023年5月

附表 1

应用证明

项目名称	结直肠癌肝转移患者肝动脉留管化疗前后循环肿瘤细胞检测的临床研究
应用单位	保定市第二医院
单位注册地址	保定市东风西路 338 号
应用起止时间	2019.1-2021.5

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：本课题已在保定市第二医院临床工作中投入应用，在临床工作中通过对结直肠癌肝转移患者肝动脉留管化疗过程中，外周血循环肿瘤细胞计数可以用于评估化疗疗效，可作为判断预后的指标，与肿瘤标记物、影像学检查可共同作为判断肿瘤复发、转移及治疗疗效的指标。此结论具有显著社会效益，对于临床中此类患者采用本研究，可以提高患者的 PFS、OS。

应用单位法定代表人签名： 年　月　日	应用单位公章 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

报告编号：2025a04606

收录检索报告

委托内容：冯承保发表的论文

委托机构：保定市第二医院

委托日期：2025 年 4 月 25 日

检索机构（盖章）：河北省科学技术情报研究院

（国家一级科技查新咨询单位）

检索完成日期：2025 年 4 月 25 日

一、检索要求：

1、被检作者：冯承保

2、委托机构：保定市第二医院

二、检索范围：

Science Citation Index Expanded （SCI-EXPANDED）.....2009-present

三、检索结果：

提供的待检论文中有 1 篇被 SCI 收录：

Accession Number：WOS:001217275200001

Clinical value of circulating tumour cells in evaluating the efficacy of continuous hepatic arterial infusion among colorectal cancer patients

By: 冯承保（Feng, Chengbao；通讯作者）

JOURNAL OF CHEMOTHERAPY Volume: 37 Issue: 1 Published: JAN 2 2025

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检索人：王雪冯

河北省科学技术情报研究院

2025 年 4 月 25 日

SCI 收录：

Clinical value of circulating tumour cells in evaluating the efficacy of continuous hepatic arterial infusion among colorectal cancer patients

By: Zhang, Erying; Li, Haifei; Liu, Caiyun; Zhou, Haikun; Liu, Bo; Feng, Chengbao

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Volume: 37 Issue: 1 Pages: 76-84
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Abstract: Few studies have been conducted to evaluate the efficacy of HAIC using circulating tumour cells (CTCs). In this study, a total of 100 patients who received HAIC treatment and CTC detection were selected. The results showed that after HAIC treatment, the levels of CTC, carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) decreased. Postoperative progression-free survival (PFS) rates between patients with positive and negative preoperative CTC results, and for CA19-9, CEA were significantly different. The positive rate of CTCs was 61% before chemotherapy and 23% after chemotherapy, and the correlation coefficient between the two was 0.385. Those whose CTC values increased after chemotherapy had shorter PFS rates. CTCs are an independent predictor of recurrence. Patients with CTC-positive results are more susceptible to recurrence. The CTC count in peripheral blood has a close bearing on the postoperative chemotherapy efficacy of patients with CRC and affects patients' PFS.

Keywords
Author Keywords: colorectal cancer; liver metastasis; hepatic arterial infusion chemotherapy; circulating tumour cells
KeyWords Plus: LIVER METASTASES; SYSTEMIC CHEMOTHERAPY; PERIPHERAL-BLOOD; PROGRESSION; SURVIVAL; OUTCOMES; SURGERY

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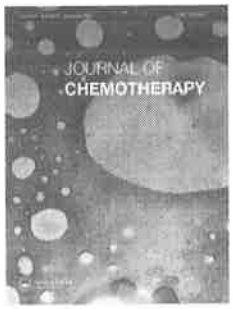

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Clinical value of circulating tumour cells in evaluating the efficacy of continuous hepatic arterial infusion among colorectal cancer patients

Erying Zhang, Haifei Li, Caiyun Liu, Haikun Zhou, Bo Liu & Chengbao Feng

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ANTICANCER ORIGINAL RESEARCH PAPER

Clinical value of circulating tumour cells in evaluating the efficacy of continuous hepatic arterial infusion among colorectal cancer patients

Erying Zhang[a], Haifei Li[a], Caiyun Liu[a], Haikun Zhou[b], Bo Liu[a] and Chengbao Feng[a]

[a]Department of Medical Oncology, No. 2 Hospital of Baoding, Baoding City, People's Republic of China; [b]Department of Surgery Oncology, No. 2 Hospital of Baoding, Baoding City, People's Republic of China

ABSTRACT

Few studies have been conducted to evaluate the efficacy of HAIC using circulating tumour cells (CTCs). In this study, a total of 100 patients who received HAIC treatment and CTC detection were selected. The results showed that after HAIC treatment, the levels of CTC, carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) decreased. Postoperative progression-free survival (PFS) rates between patients with positive and negative preoperative CTC results, and for CA19-9, CEA were significantly different. The positive rate of CTCs was 61% before chemotherapy and 23% after chemotherapy, and the correlation coefficient between the two was 0.385. Those whose CTC values increased after chemotherapy had shorter PFS rates. CTCs are an independent predictor of recurrence. Patients with CTC-positive results are more susceptible to recurrence. The CTC count in peripheral blood has a close bearing on the postoperative chemotherapy efficacy of patients with CRC and affects patients' PFS.

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Received 20 October 2023
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KEYWORDS
colorectal cancer; liver metastasis; hepatic arterial infusion chemotherapy; circulating tumour cells

Introduction

According to the latest cancer data statistics, colorectal cancer (CRC) is the third most common malignant tumour in the world, ranking second among malignant tumours in terms of mortality [1]. Approximately 30% of patients with CRC will develop liver metastasis over the course of their disease, resulting in death in more than two-third of the patients [2, 3]. This demonstrates the importance of the treatment of liver metastases for the long-term survival of patients. Surgical resection is the preferred treatment for the radical cure of CRC liver metastases (CRCLM). However, only 15%–20% of patients with CRCLM meet the criteria for surgical resection when initially diagnosed. Furthermore, almost half of the patients who have undergone surgery will still experience a relapse after surgery [4, 5]. With the innovation of anti-tumour drugs and the rapid development of treatment techniques, the non-surgical resection treatment strategies for CRCLM have gradually diversified. As one of the representative methods of non-surgical resection, local minimally invasive treatment has gradually attracted attention due to its advantages of reproducibility, minimal invasion, and a high local control rate [6]. Minimally invasive interventional therapy includes transvascular minimally invasive interventional therapy (e.g. hepatic arterial infusion chemotherapy [HAIC], transarterial embolisation [TACE]), and non-vascular minimally invasive interventional therapy (e.g. microwave ablation, radiofrequency ablation) [7].

The topical treatment of CRCLM can significantly delay the progression of liver lesions and thus prolong survival time [8]. The most commonly used topical treatments include HAIC, TACE, and ablation, with HAIC involving a direct infusion of chemotherapeutic drugs into the hepatic artery. The blood supply of liver metastases mainly derives from the hepatic artery, whereas that of normal liver tissue is supplied by the portal vein [9]. Moreover, some chemotherapy drugs will be metabolised after passing through the liver due to the 'first-pass effect' of the liver. Therefore, HAIC can increase the drug concentration in tumour cells and reduce systemic toxicity compared with intravenous chemotherapy [10]. To date, no standard regimen for HAIC medication has been established. In clinical practice, it has been found that, even for patients who have progressed after previous systemic chemotherapy regimens based on oxaliplatin and 5-fluorouracil (FU), HAIC treatment

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combined with oxaliplatin and 5-FU remains effective. When liver metastases are effectively controlled, this combination therapy can significantly prolong the survival time of patients. Therefore, it is of great importance to monitor the efficacy of HAIC treatment [11]. However, the current commonly used efficacy evaluation methods, such as alpha-fetoprotein, abnormal prothrombin, computed tomography, and magnetic resonance, are unable to reflect long-term efficacy due to their poor prognostic prediction ability, low positive rate, and long intervals between imaging examinations.

Liquid biopsy, a concept introduced by Lianidou ES et al. [12], has been a popular topic of research in recent years. As one of the pivotal markers of liquid biopsy, circulating tumour cells (CTCs) are tumour cells that are shed from primary lesions or metastases and then enter the circulation system to reach various target organs or tissue types in the body [13]. The half-life of CTCs in the blood circulation is only 1–2.4 h [14]. The vast majority of CTCs are cleared by the body's immune system after surgery [15]. For this reason, the persistence or reappearance of CTCs after the removal of the primary tumour may reflect the likelihood that the tumour is in an active metastatic state. Jiangmin Zhou performed CTC detection on 137 patients with hepatocellular carcinoma at different time periods (e.g. preoperative, intraoperative, postoperative) and concluded that postoperative CTCs remained at a high level (CTCs $\geq$5), indicating a risk of early recurrence [16]. Furthermore, CTCs can also be used to predict disease progression and prognosis in patients with metastatic cancer. Circulating tumour cells can be detected when hepatocellular carcinoma metastasises to distant organs, but solid tumour foci cannot be observed with radiographic imaging [17, 18]. A meta-analysis of 1,191 patients with hepatocellular carcinoma revealed that patients with CTC-positive results had a significantly worse prognosis than those with negative CTC results [19]. A growing body of research has demonstrated the potential of CTCs in predicting tumour prognosis and tumour progression. Carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) are common markers of CRCs, and the detection of their content is helpful for the diagnosis of colon cancer [20, 21].

In summary, CTCs can be used as an alternative to traditional methods for HAIC efficacy evaluation to further monitor early recurrence and predict prognosis [22]. However, few studies have been conducted to evaluate the efficacy of HAIC using CTCs, and the efficacy of CTCs for HAIC evaluation, as well as the prognosis of CTCs after HAIC treatment, are worthy of further exploration. In this study, patients with CRC were selected as the participants to investigate the value of CTCs in evaluating the efficacy of HAIC.

Methods and materials

Participants

One hundred patients who underwent CTC detection and received HAIC treatment in the oncology department of our hospital between January 2019 and May 2021 were selected using the convenience sampling method. The sample size was tested by power analysis (a sample size of 36 is required when power is greater than 0.8) and met the requirements for experimental conduct. The inclusion criteria were as follows: (1) patients aged >18 years; (2) those without a history of other malignant tumours; (3) those without a history of blood diseases; (4) those who have progressed on systemic chemotherapy or could not tolerate systemic chemotherapy, or who have refused systemic chemotherapy; (5) those who met the RECIST 1.0 criteria (i.e. one measurable lesion in the liver with a length of 1.5 cm and a diameter of 20 cm); and (6) those with an Eastern Cooperative Oncology Group Performance Status score of 0–2. The exclusion criteria were as follows: (1) patients with an infection; (2) those with fever exceeding 38 °C; (3) those with a history of other malignant tumours; (4) those who had previously received treatment for CRC, including chemotherapy or radiation; and (5) those with serious underlying diseases who could not tolerate relevant treatment options. This study was approved by the hospital's ethics committee. All patients were informed and signed an informed consent form for inclusion in the research.

Study methods

Circulating tumour cell detection

(1) Sample collection: 5–10 ml of peripheral venous blood was taken from each patient before and after a chemotherapy cycle. (2) In this study, Leica DM4B and Leica DM6B life science research systems were used for CTC detection. (3) The CTC determination criteria were CD45 negative, tumour-specific nuclear antigen DAPI, and cytoplasmic antigen CK-FITC positive cells. The definition of patients with a CTC-positive result was CTCs >5; for patients with a CTC-negative result, this was CTCs <5.

Hepatic arterial infusion chemotherapy surgical methods and drug administration regimen

The patient was placed in a supine position on the operating table, and the femoral artery was punctured using the Seldinger technique after administering local anaesthesia. Subsequently, angiography of the common hepatic artery and superior mesenteric artery on the abdominal aorta was performed to clarify the number of tumours, blood supply, anatomic location, and nutrient artery, and to better understand the anatomical variations among blood vessels. A treatment plan was created according to the distribution of blood vessels and the condition of the portal system in the portal venous phase. The catheter was inserted into the left or right hepatic artery according to the location of the tumour, and a coaxial microcatheter (Renegade™ Hi-Flo™ Boston Scientific, United States/Stride ASAHI INTECC, Japan) was utilised to superselect the tumour-supplying artery as far as possible. In cases where superselected tumour nutrient vessels failed, or the tumour was large and supplied by multiple arteries, the catheter was placed in the right or left hepatic artery for chemotherapy. After each drug (5-FU) infusion cycle, the catheter and arterial sheath were pulled out, and the femoral artery was bandaged with a compressor or bandage. Nine hours later, the patient could perform off-bed activities. Hepatic arterial infusion chemotherapy was performed every 3–4 weeks or terminated for the following reasons: (1) the efficacy was evaluated as complete remission; (2) the efficacy was evaluated based on progressive disease; or (3) the liver function had changed to Child–Pugh grade C or a grade that the patient could not tolerate. Abdominal ultrasound or computed tomography should be performed every 6 weeks after 2 cycles of HAIC.

Data collection

Patients' general clinical data, including gender, age, tumour location, tumour diameter, tumour marker (CEA, CA19-9), TNM tumour stage, histological type, and depth of invasion, were collected.

All 100 recruited patients were followed up *via* outpatient visits, telephone calls, or WeChat, from the date of blood collection until disease progression, to determine the PFS rate. The PFS rate was defined as the time from blood sampling for CTC detection to disease progression during or after chemotherapy. The data cut-off date was December 2022.

Statistical analysis

Data were statistically analysed using the SPSS 26.00 software. Measurement data were expressed as $x \pm s$, and an independent samples *t*-test was used for intergroup comparisons. The sample size was tested by power analysis. The count data were represented by frequency (n) or rate (%), the chi-square [χ^2] test was used for group design comparison, and Pearson's correlation coefficient was used for correlation analysis. Moreover, the Wilcoxon rank-sum test was used to analyse the rank data. The Kaplan–Meier method was used to draw the survival curve, and the log-rank test was used to compare the survival rates between groups, with the test level $\alpha = 0.05$. A *P*-value of <0.05 was considered statistically significant.

Results

Correlation between the positive rate of circulating tumour cells, and clinicopathological features before treatment

A total of 100 patients with CRC were recruited in this study, of which 39 had negative CTC results, including 23 men and 16 women. Sixty-one cases had positive CTC results, including 34 men and 27 women; 53.85% of patients with negative CTC results had TNM stage III + IV, whereas 73.77% of patients with positive CTC results had TNM stage III + IV, with a statistically significant difference ($\chi^2 = 8.002$, $p = .018$). The infiltration depth of T_3 in patients with negative CTC results was 48.72% and that of patients with positive CTC results was 95.08%, with a statistically significant difference ($\chi^2 = 31.482$, $p < .001$). No statistically significant differences were observed between the two groups in terms of gender, age, tumour location, CEA, CA19-9, histological type, and tumour size ($p > .05$). See Table 1 for details.

Changes in the levels of circulating tumour cells, carbohydrate antigen 19-9, and carcinoembryonic antigen after treatment

In this study, the levels of CTC, CA19-9, and CEA of patients within 6 cycles were counted. The results showed that the levels of CTC, CA19-9, and CEA decreased gradually with the progression of treatment. The CTC level before HAIC was selected as the predictor. The CTC level of patients decreased by an average of 2.59 during 2 cycles of treatment, by an average of 2.72 during 4 cycles of treatment, and by an average of 1.25 during 6 cycles of treatment. The

Table 1. Correlation between the positive rate of CTC and clinicopathological features.

Item		CTC		χ^2/Z value	P value
		Negative (n = 39)	Positive (n = 61)		
Gender	Male	23	34	0.102	.750
	Female	16	27		
Age (year)	≥60	23	32	0.408	.523
	<60	16	29		
Tumor location	Rectum	12	21	0.144	.704
	Colon	27	40		
CEA	Positive	21	35	0.120	.729
	Negative	18	26		
CA19-9	Positive	27	46	0.461	.497
	Negative	12	15		
Histological type	Well differentiated	4	10	−0.474	.636
	Intermediate differentiation	26	37		
	Poorly differentiated	9	14		
Tumor size	<5 cm	23	35	0.014	.907
	≥5cm	16	26		
TNM staging	I	9	3	8.002	.018
	II	9	13		
	III + IV	21	45		
Depth of infiltration	T_1+ T_2	20	3	31.482	<.001
	T_3	19	58		

Note: CTC: circulating tumor cells; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9.

CA19-9 level of patients was reduced by an average of 81.40 u/ml during 2 cycles of treatment, by an average of 81.71 u/ml during 4 cycles of treatment, and by an average of 27.36 u/ml during 6 cycles of treatment. The CEA levels of patients were reduced by an average of 15.34 ng/ml during 2 cycles of treatment, by an average of 7.69 ng/ml during 4 cycles of treatment, and by an average of 9.22 ng/ml during 6 cycles of treatment. See Table 2 for details.

Table 2. Changes in the levels of CTC, CA19-9 and CEA after treatment.

Time	CTC (pcs)	CA19-9 (u/ml)	CEA (ng/ml)
Baseline	6.81 ± 5.23	233.99 ± 327.688	38.12 ± 36.91
2 cycles of treatment	4.22 ± 4.75	152.59 ± 214.756	22.78 ± 18.19
t value	2.439	2.214	2.445
p value	.028	.043	.027
2 cycles of treatment	4.22 ± 4.75	152.59 ± 214.76	22.78 ± 18.19
4 cycles of treatment	1.50 ± 2.39	70.88 ± 79.81	15.09 ± 16.53
t value	2.15	2.141	2.364
p value	.048	.049	.032
4 cycles of treatment	1.50 ± 2.39	70.88 ± 79.81	15.09 ± 16.53
6 cycles of treatment	0.25 ± 045	43.52 ± 62.02	5.87 ± 4.17
t value	2.207	2.197	2.137
p value	.043	.044	.049

Note: CTC: circulating tumor cells; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9.

Relationship between circulating tumour cells, carbohydrate antigen 19-9, carcinoembryonic antigen, and progression-free survival of patients

A total of 100 patients were followed up and no cases were lost to the follow-up. The follow-up lasted from 5 to 27 months, with a median time of 15.0 ± 5.5 months. Taking recurrence as the outcome, the Kaplan–Meier method was used to draw the survival curve, and the log-rank test was used to analyse the difference in recurrence rates in different indicator categories. There were 60 cases of recurrence in the CTC-positive group and eight cases in the CTC-negative group, with a statistically significant difference in the PFS rate between the two groups (100.00% vs 20.51%, $p = .008$) (Figure 1(A)). There were 58 cases of recurrence in the CA19-9 positive group and 10 cases in the CA19-9 negative group, with a statistically significant difference in PFS rate between the two groups (79.45% vs 40.74%, $\chi^2 = 13.809$, $p < .001$) (Figure 1(B)). There were 44 cases of recurrence in the CEA-positive group and 14 cases in the CEA-negative group, with a statistically significant difference in PFS rate between the two groups (78.57% vs 31.82%, $\chi^2 = 22.110$, $p < .001$) (Figure 1(C)).

Value of circulating tumour cells, carbohydrate antigen 19-9, and carcinoembryonic antigen in predicting postoperative recurrence

Here, CTC, CEA, and CA19-9 all exhibited a degree of predictive value for the PFS of patients with CRCLM receiving HAIC treatment ($p < .05$). Among them, CTC predicted the area under the curve (AUC) of PFS as 0.786 (95% confidence interval [CI]: 0.710, 0.840) for patients with CRCLM receiving HAIC treatment; CEA predicted the AUC of PFS as 0.708 (95% CI: 0.684, 0.744) for the same patients, and CA19-9 predicted the AUC of PFS as 0.724 (95% CI: 0.675, 0.831) for such patients. See Table 3 for details.

The combined prediction effect of the 3 indicators was better than that of a single indicator. Specifically,

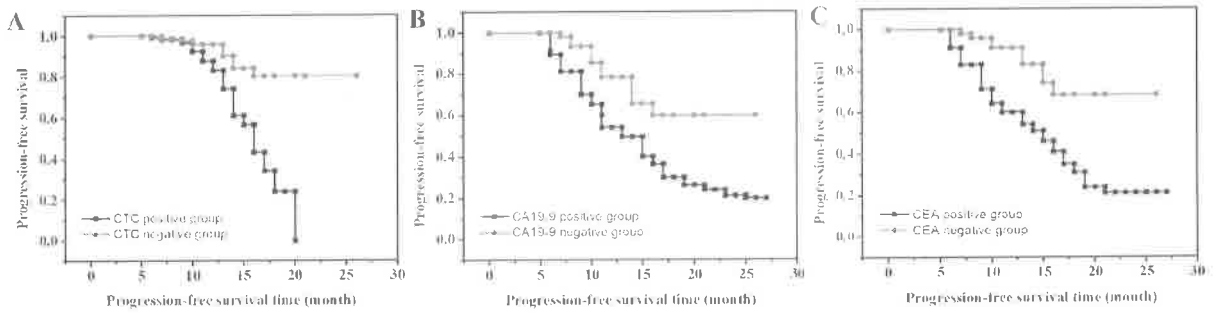

Figure 1. (A) Progression-free survival curve of patients grouped with CTC; (B) progression-free survival curve of patients grouped with CA19-9; (C) progression-free survival curve of patients grouped with CEA.

Table 3. Value of CTC, CEA and CA19-9 in predicting postoperative recurrence.

Variable	AUC	95%CI	Cutoff value	Sensitivity (%)	Specificity (%)
CTC	0.786	(0.710, 0.840)	0.5	71.89	70.35
CEA	0.708	(0.684, 0.744)	0.5	68.12	60.30
CA19-9	0.724	(0.675, 0.831)	0.5	64.24	61.48
CTC + CEA	0.832	(0.804, 0.854)	–	74.38	69.31
CTC + CA19-9	0.817	(0.802, 0.843)	–	74.56	76.65
CTC + CEA + CA19-9	0.887	(0.831, 0.924)	–	85.34	83.61

Note: CTC: circulating tumor cells; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9.

CTC + CEA predicted the AUC of PFS as 0.832 (95% CI: 0.804, 0.854) for patients with CRCLM receiving HAIC treatment; CTC + CA19-9 predicted the AUC of PFS as 0.817 (95% CI: 0.802, 0.843) for the same patients, and the 3 indicators combined predicted the AUC of PFS as 0.887 (95% CI: 0.831, 0.924) for such patients. See Table 3 for details.

Correlation between circulating tumour cells, chemotherapy efficacy, and progression-free survival

The correlation between CTC and chemotherapy was analysed. The results indicated a positive CTC rate of 61% before chemotherapy and 23% after chemotherapy; the correlation coefficient between the two was 0.385, with a statistically significant difference ($p < .001$) (Table 4). For patients whose CTC values increased after chemotherapy, shorter PFS rates were observed compared with those who had unchanged or even decreased CTC values, and the difference was statistically significant ($p < .001$) (Table 5).

Table 4. Correlation Between CTC and chemotherapy efficacy.

Indicator	Number of CTC-positive cases	Number of negative CTC cases	*r* value	*P* value
Before chemotherapy	61	39	0.385	<.001
After chemotherapy	23	77		

Table 5. Correlation Between CTC and PFS.

	CTC content after chemotherapy			
Indicator	Not elevated ($n = 72$)	Elevated ($n = 28$)	*t* value	*P* value
PFS	16.6 ± 6.5	12.1 ± 2.5	4.577	<.001

Discussion

The past few decades have witnessed an increase in the incidence of CRC worldwide [23–27]. The HAIC method is widely used in patients with CRCLM because of its reproducibility, minimal invasion, and high local control rate [28]. In recent years, studies have highlighted the CTC count as a robust and independent prognostic/predictive biomarker for effective chemotherapy in patients with breast cancer, prostate cancer, and CRC [29]. Studies have shown that CTCs were detected 1 month after the first cycle of chemotherapy in patients with CRC [30, 31]. In summary, as a non-invasive liquid biopsy technique, measuring CTCs has been widely considered for clinical application due to its great potential in the prognosis and treatment of patients with CRC. This conclusion was confirmed in the current study, for which a total of 100 patients with CRC were recruited, 61 of whom had positive CTC results; additionally, patients with positive CTC results reflected a more severe tumour stage and infiltration depth of T_3.

A study revealed that the positive CTC rate in patients with CRC dropped from 59% before chemotherapy to 31% after 3 months of chemotherapy using a standardised regimen [32]. It can be inferred that CTCs serve as indicators of patient sensitivity to

chemotherapy. Yen et al. [33] found the *KRAS* of peripheral blood CTC to be of great significance for evaluating the efficacy of cetuximab targeted therapy. Yalcin et al. [34] detected CTCs in patients with CRC before and after chemotherapy and found that the probability of progression in patients with decreased CTCs after treatment was lower than in patients with increased CTCs. A study by Abdallah et al. [35] monitored the CTCs in the peripheral blood of patients with advanced CRC who received 5-FU monotherapy. The results suggest that CTC detection can help provide a basis for the accurate treatment of patients.

In the present study, patients with positive CTC results had a more severe TNM stage and depth of invasion. It was shown that the positive CTC rate dropped from 61% to 23% after treatment, while the level of CTCs in patients with positive results also gradually decreased with treatment. Additionally, patients with positive CTC results before treatment and elevated CTC levels after treatment had lower PFS rates, which conforms to existing results.

Multiple studies have shown that CTCs can indicate clinical characteristics, such as tumour invasion and lymph node metastasis, in patients with CRC. Circulating tumour cells adhere to the vascular endothelium through cell adhesion molecules and serve as the basis of various biological mechanisms of cancer metastasis [36]. This was confirmed by preclinical studies involving mouse models [37]. Circulating tumour cells contain genetic information on both primary and metastatic lesions [38]. In patients without recurrence or metastasis, CTCs detected preoperatively can serve as effective prognostic factors for cancer progression and survival [39, 40]. For those treated with surgery, CTCs indicate a high risk of postoperative metastasis [41], and their persistence after surgery is associated with a poor prognosis and PFS rate [42]. In metastatic pancreatic ductal adenocarcinoma, changes in CEA and CA19-9 were also good predictors of PFS rate [43]. In this study, 60 patients relapsed in the CTC-positive group and 8 patients relapsed in the CTC-negative group, and there was a statistically significant difference in the PFS rate between the two groups. Concurrently, the proportion of recurrence in the CA19-9-positive and CEA-positive groups was also higher than in their corresponding negative groups. This study also showed that CTC alone, as well as CTC combined with CEA and CA19-9, have a degree of predictive value for postoperative recurrence of CRC. In addition, the combined prediction effect of the 3 indicators showed better efficacy compared with a single indicator.

Relevant studies have shown that the serum CEA and CA19-9 concentrations of patients increase significantly when malignant tumours are detected in the digestive system [44], while the serum CEA values of patients with positive CTC results are higher than those with negative results. Shinkins et al. [45] suggested that the sensitivity and specificity of CEA detection for recurrence were only 50.0% (95% CI: 40.1%–59.9%) and 93.3% (95% CI: 90.6%–95.3%). Peng Jiang et al. [46] showed that the sensitivity and specificity of CEA in the prognostic diagnosis of CRC were 75.7% and 70%. The sensitivity and specificity of CA19-9 were 62.9% and 68.1%. In the present study, both CEA and CA19-9 exhibited a certain value in terms of predicting the PFS rate of patients with CRCLM receiving HAIC treatment, and the predictive value of CA19-9 was slightly higher than that of CEA. In some cases, the levels of CEA, CA19-9, and other tumour markers are not measurable, whereas CTCs enable superior disease monitoring [31]. In short, CTCs are crucial in predicting tumourigenesis. This study provides a basis for the prediction of disease recurrence in clinical practice in patients with CRC using CTCs as an independent predictor and is thus worthy of attention.

This study has some limitations. First, the research was a single-centre study with a relatively small sample size, and the statistical impact of clinical variables on survival may not be significant. When performing stratified analyses, larger samples should be included to improve and provide more accurate information for evidence-based treatment. Second, the study lacked dynamic monitoring of CTCs. Dynamic CTC counts can better reflect the aggressiveness and prognosis of the disease than CTC counting alone. Finally, several patient physical indicators (e.g. the side effects caused by chemotherapy, body weight) were not observed in this study. In subsequent studies, more indicators should be included to comprehensively reflect patients' physical condition.

In summary, CTCs can serve as an independent predictor of recurrence, and patients with CTC-positive results are more susceptible to recurrence than those with negative results. Additionally, the CTC count in peripheral blood has a close bearing on the postoperative chemotherapy efficacy of patients with CRC and affects their PFS rate.

Ethics approval and consent to participate

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval

from the Ethics Committee of No. 2 Hospital of Baoding. Written informed consent was obtained from all participants.

Author contributions

(I) Conception and design: Zhang EY
(II) Administrative support: Li HF and Liu CY
(III) Provision of study materials or patients: Zhou HK and Liu B
(IV) Collection and assembly of data: Feng CB and Zhang EY
(V) Data analysis and interpretation: Li HF and Zhou HK
(VI) Manuscript writing: All authors
(VII) Final approval of manuscript: All authors

Consent for publication

The manuscript is not submitted for publication or consideration elsewhere.

Disclosure statement

The authors declare that they have no competing interests.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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The mechanisms of tumor necrosis factor α in regulating Krüpple-like factor 4 expression in SK-BR-3 breast cancer cells

By: 冯承保（Feng, Chengbao；并列第一作者）

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The mechanisms of tumor necrosis factor α in regulating Krüpple-like factor 4 expression in SK-BR-3 breast cancer cells

By: Liu, Caiyun; Feng, Chengbao; Li, Haifei; Zhang, Erying; Liu, Bo; Wang, Ying; Wang, Peng

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Abstract: Objective To explore the expression and functional role of Krupple-like factor 4 (KLF4) protein stimulated by tumor necrosis factor alpha (TNF-alpha) in SK-BR-3 breast cancer cells.Methods SK-BR-3 cells were stimulated with various concentrations of TNF-alpha at 0, 1, 5, 10, and 20 ng/mL. Expression levels of KLF4 protein were detected by Western blotting. In the detection of apoptosis, flow cytometry, and DAPI staining were used for detecting the level of apoptosis.Results KLF4 expression was markedly elevated following stimulation of SK-BR-3 with TNF-alpha. At the same time, the expression of KLF4 protein increased gradually with the increase of TNF-alpha stimulation concentration. TNF-alpha stimulation of SK-BR-3 cells increased apoptosis as measured by apoptosis levels. By overexpressing KLF4 protein in SK-BR-3 cells, it similarly increased apoptosis and promoted cell death of SK-BR-3 cells.Conclusion TNF-alpha promotes KLF4 expression, while TNF-alpha promotes apoptosis in SK-BR-3 cells, a process that may be due to elevated KLF4 protein expression.

Keywords
Author Keywords: apoptosis; KLF4; SK-BR-3 cells; TNF-alpha
KeyWords Plus: KLF4

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ORIGINAL ARTICLE

The mechanisms of tumor necrosis factor α in regulating Krüpple-like factor 4 expression in SK-BR-3 breast cancer cells

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Abstract

Objective: To explore the expression and functional role of Krüpple-like factor 4 (KLF4) protein stimulated by tumor necrosis factor α (TNF-α) in SK-BR-3 breast cancer cells.

Methods: SK-BR-3 cells were stimulated with various concentrations of TNF-α at 0, 1, 5, 10, and 20 ng/mL. Expression levels of KLF4 protein were detected by Western blotting. In the detection of apoptosis, flow cytometry, and DAPI staining were used for detecting the level of apoptosis.

Results: KLF4 expression was markedly elevated following stimulation of SK-BR-3 with TNF-α. At the same time, the expression of KLF4 protein increased gradually with the increase of TNF-α stimulation concentration. TNF-α stimulation of SK-BR-3 cells increased apoptosis as measured by apoptosis levels. By overexpressing KLF4 protein in SK-BR-3 cells, it similarly increased apoptosis and promoted cell death of SK-BR-3 cells.

Conclusion: TNF-α promotes KLF4 expression, while TNF-α promotes apoptosis in SK-BR-3 cells, a process that may be due to elevated KLF4 protein expression.

KEYWORDS
apoptosis, KLF4, SK-BR-3 cells, TNF-α

1 | INTRODUCTION

Breast cancer (BC) is a malignant tumor with a serious threat to women's health. Because the breast tissue is rich in lymphatic vessel network and blood, hematogenous metastasis, and lymphatic metastasis can occur in the early stage of breast cancer, which brings great disadvantages to the diagnosis and treatment of BC.[1,2] Finding target molecules in the treatment of BC so as to better inhibit the growth of breast cancer leading to the death of BC cells is still an important problem to be solved. Kruppel-like factor 4 (KLF4) belongs to the KLF family of proteins and is related to a variety of tumors. It is reported that KLF4 is involved in tumorigenesis, development, invasion, and metastasis process.[3,4] KLF4 not only regulates cell proliferation, differentiation, and inflammatory gene expression but also is one of the four transcription factors essential for reprogramming somatic cells into induced Pluripotent Stem (iPS) cells.[5] Reduced KLF4 expression has been found in colorectal cancer, cancer of the esophagus, and gastric cancer.[3,6–8] Tumor necrosis factor α (TNF-α) is a proinflammatory factor produced by monocyte macrophages, involved in the body's inflammation and immune response process.[9,10] However, in recent years, whether TNF-α can regulate cell proliferation through KLF4 in breast cancer remains unknown. SK-BR-3 cell line is one of the malignant BC cell lines. The specific molecular mechanism of KLF4 action in BC is currently unknown. In this study, we aimed to investigate whether TNF-α can regulate the proliferation of SK-BR-3 breast cancer cells through KLF4.

Caiyun Liu and Chengbao Feng contributed equally to this study.

2 | MATERIALS AND METHODS

2.1 | Cell culture

SK-BR-3 cells were obtained from the Cell Resource Center. SK-BR-3 cells were cultured in RPMI 1640 medium with 10% fetal bovine serum (FBS) and 100 U/mL penicillin and streptomycin in an incubator of 37°C, 5%CO_2, and 90% relative humidity. Cells were periodically replaced and passed. Cells were digested at passage with trypsin at 37°C for 3 min. Passages were performed every 3 days using a 1:3 split ratio. Log growth stage cells were taken for experiments.

2.2 | Main reagents

RPMI 1640 medium was purchased from Gibico (Catalogue number: 61870-036). FBS was purchased from Biological, Inc. (Catalogue number: 04-121-1A). Trypsin digestion solution was purchased from Sigma Corporation (Catalogue number: T9253). TNF-α was purchased from Pepro Tech, Inc. (Catalogue number: AF-300-01A). The human KLF4 antibody was purchased from ABGENT, Inc. (Catalogue number: AP2725f). The β-actin antibody was purchased from Santa Cruz Inc (Catalogue number: sc-47778). A secondary antibody was purchased from Abcam (Catalogue number: ab205718). Enhanced Chemiluminescence Reagent (Millipore Company, Catalogue number: 43513). 4′,6-diamidino-2-phenylindole (DAPI, Catalogue number: MBD0015) and PI dyes (Catalogue number: P4170) were purchased from Sigma Corporation. M-MLV was purchased from Promega Corporation (Catalogue number: M1701). The SYBR qPCR kit was purchased from Invitrogen (Catalogue number: ABI 11736).

2.3 | Construction of the adenovirus expression vectors

The GFP-KLF4 and GFP cDNA sequences were amplified with the pGFP-KLF4 plasmid containing human KLF4 as template and reconstituted to the adenoviral vector pAD/CMV/V5-DEST (Invitrogen) to construct the GFP-KLF4 and GFP adenoviral plasmids. The specific primers used in the construction of KLF4 plasmid were as follows: Forward: 5′- GGCAGTTTCCCGACCAGAGAGA –3′; Reverse: 5′- TTCAGATAAAATATTATAGG –3′. The above plasmids were transfected into A293 cells for viral packaging with liposome Lipofectamine 2000 (Invitrogen) according to the kit instructions. Supernatant from A293 cells was used to infect SK-BR-3 cells.

2.4 | Western blot analysis

Cells from each group were collected and subsequently lysed using lysate buffer in an ice bath for 30 min for sufficient cell lysis. The protein was quantified by modified Lowry assay.[11] Sodium dodecyl sulfate-polyacrylamide gel electrophoresis for protein separation and transmembrane was conducted and the protein was blocked by skim milk powder and reacted with KLF4 antibody (ABGENT) and β-actin antibody (Santa Cruz) and the corresponding secondary antibody, and detected by ECL chemiluminescence reagent. The signal intensities were analyzed by relative quantification with the Bio 1D image analysis software.

2.5 | Cell cycle and apoptosis detection

Cells were stimulated with TNF-α for 24 h. Cells and supernatant were used for assays. By cell counting, the number of cells per group was adjusted to 1 × 106 cells and subsequently, cells were fixed using pre-chilled 70% ethanol for 12 h at 4°C. And cells were supplemented with 500 L of working solution and incubated for 15 min before detection by flow cytometry. Repeat for 3 times.

2.6 | DAPI fluorescent staining

SK-BR-3 cells growing on the glass slide were incubated for 24 h with TNF-α stimulation, fixed in 4% paraformaldehyde for 15 min, and 10 μg/mL DAPI was used for staining for 5 min. The excess dye solution was washed and sealed by a fluorescent tablet and observed under an Olympus BX53 fluorescent microscope.

2.7 | Statistical analysis

SPSS16.0 statistical software was used for data analysis. The mean ± standard deviation ($\bar{x} \pm$ S.D.) was used for data expression. One-way analysis of variance (for three or more groups) or two-tailed unpaired student's t-test (for two groups) was performed for statistical analysis, and $p < 0.05$ was a statistically significant difference.

3 | RESULTS

3.1 | TNF induces KLF4 expression in SK-BR-3 cells

SK-BR-3 cells were stimulated with TNF-α (0, 1, 5, 10, and 20 ng/mL). It was found that KLF4 expression was also gradually increased with increasing TNF-α concentration (Figure 1).

3.2 | TNF induces apoptosis of SK-BR-3 cells

SK-BR-3 cells were cultured with TNF-α (0 and 10 ng/mL), and the apoptosis and cycle progression in SK-BR-3 cells were detected by flow cytometry and DAPI staining. The proportion of apoptotic cells in SK-BR-3 breast cancer cells detected by flow cytometry had increased significantly after TNF-α stimulation ($p < .05$) (Figure 2A). After DAPI

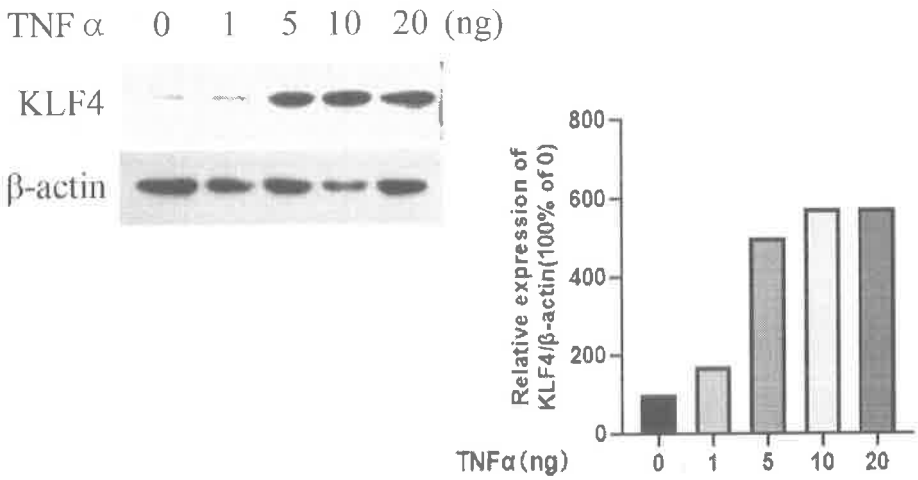

FIGURE 1 Different concentrations of tumor necrosis factor (TNF) induced Krüpple-like factor 4 (KLF4) expression in SK-BR-3 breast cancer cells with Western blot; The representative image of Western blot was shown in the upper panel. The lower panel showed the relative expression chart.

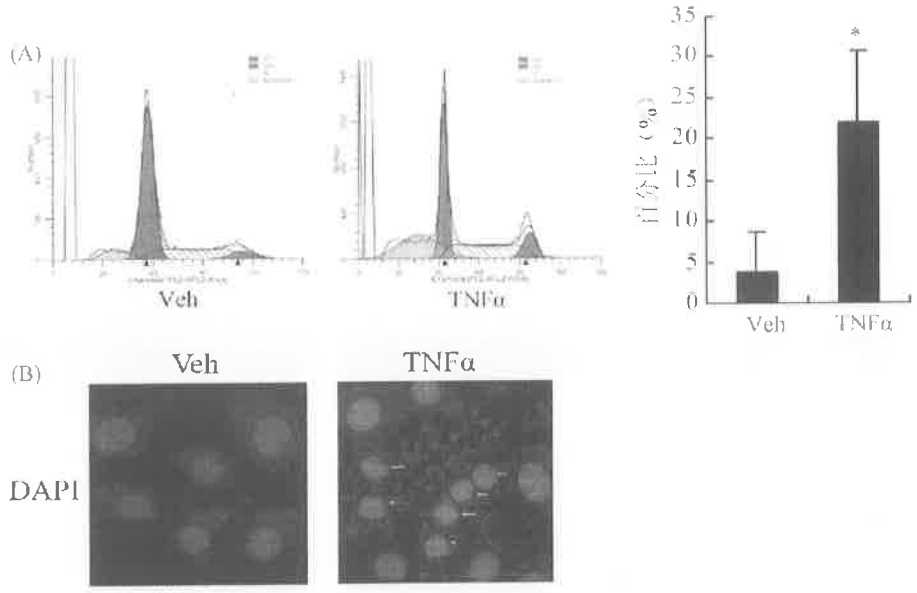

FIGURE 2 Tumor necrosis factor (TNF) induces apoptosis of SK-BR-3 breast cancer cells. (A) The representative images of flow cytometry were shown in the left panel, and the chart for the statistics was shown in the right panel. Error bars mean ± SD. $n = 3$ for each group, by two-tailed unpaired student's t-test analysis. *: $p < .05$. (B) Representative images of DAPI staining were shown.

staining, the results of fluorescence microscopy showed that the SK-BR-3 breast cancer cells showed nuclear was divided into two parts from a completed nuclear after TNF-α stimulation (Figure 2B).

3.3 | Adenoviral vector mediates GFP-KLF4 expression in SK-BR-3 cells

SK-BR-3 cells were infected for 48 h with the GFP and GFP-KLF4 adenovirus and observed by fluorescence microscopy. As shown in Figure 3, the adenoviral vector-mediated the high expression of GFP and GFP-KLF4. As can be seen by fluorescence images, GFP was evenly distributed in the cytoplasm and nucleus, while GFP-KLF4 was mainly in the nucleus, which is consistent with the nature of its transcription factor.

3.4 | KLF4 was involved in TNF-mediated apoptosis in SK-BR-3 cells

Adenovirus was used to infect SK-BR-3 breast for 48 h for KLF4 expression, followed by 10 ng/mL TNF-α for 48 h. Apoptosis and cycle

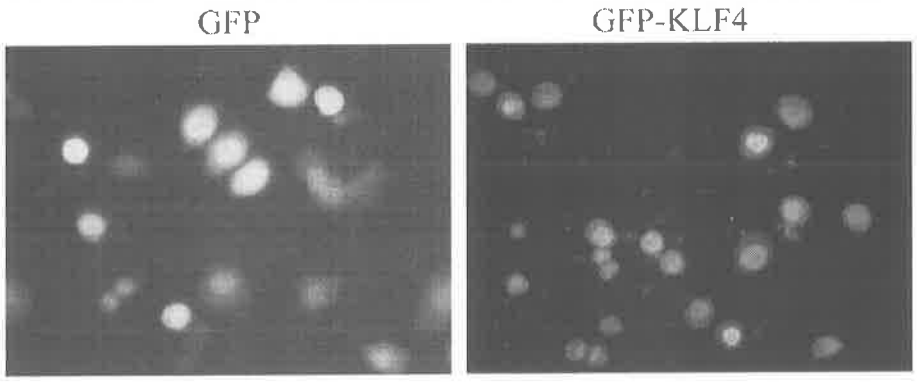

FIGURE 3 GFP and GFP-Krüpple-like factor 4 (KLF4) expression in SK-BR-3 breast cancer cells; Representative images of green fluorescence indicated the GFP and GFP-KLF4 expression.

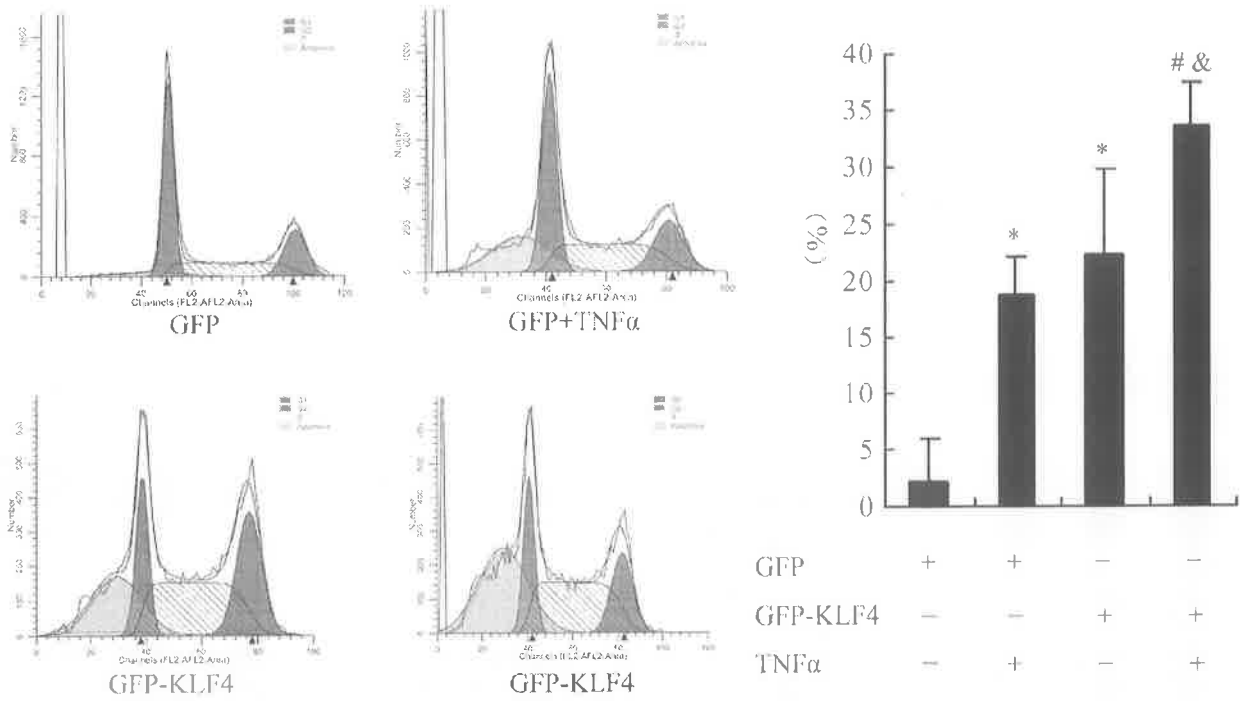

FIGURE 4 Krüpple-like factor 4 (KLF4) was involved in tumor necrosis factor (TNF)-α-mediated apoptosis of SK-BR-3 breast cancer cells. The representative images of flow cytometry analysis for apoptosis were shown in the left panel, and the chart for the statistic was shown in the right panel. Error bars mean ± SD, $n = 3$ for each group, by one-way analysis of variance analysis, *: $p < .05$ (Compared with GFP group), #: $p < .05$ (Compared with GFP-KLF4 group), &: $p < .05$ (Compared with TNF-α group).

progression were analyzed. As shown in Figure 4, KLF4 overexpression could significantly increase apoptotic cells in SK-BR-3 cells ($p < .05$).

4 | DISCUSSION

Breast cancer, a complex disease, is considered the second cancer-related death in women,[1,2] and has become the most common cancer worldwide. The incidence rate grew even faster in China, and the trend of youth is more significant.[3,4]

During the progression of cancer, cells primarily enhance malignancy by activating oncogenes and/or inactivating tumor suppressor genes. It is reported that KLF4 can play a key role in cell transformation and cell proliferation by regulating the cell cycle.[14] KLF4 expression is reduced in various types of advanced tumors, and its loss of expression can lead to epithelial-stromal transformation in cancer cells, strongly stimulating the malignant progression of the tumor.[15] In different tumor tissues, KLF4 can act as both an oncogene and a tumor suppressor gene.[16] KLF4 in breast cancer tissue specimens correlates with the malignancy degree and prognosis of breast cancer, but

how KLF4 affects the specific mechanism of action of breast cancer is not clear and remains to be investigated in further detail. Akaogi et al.[17] demonstrated that KLF4 inhibited estrogen-dependent BC growth by inhibiting the transcriptional activation of estrogen receptors α and achieving its effect as a negative regulatory growth factor in BC. However, it has also been shown that nuclear localization of KLF4 is associated with poor prognosis in breast cancer.[10,18] TNF-αhas multiple biological roles in vivo. TNF-α plays an important role in resisting pathogen infection and anti-tumor and is by far the most potent cytokine against cancer.[19] It was found that TNF-α involved in patient prognosis,[20] and it can regulate MMPs in oral cancer cells.[21] However, whether TNF-α can regulate cell proliferation through KLF4 in breast cancer remains unknown.

In this study, after TNF-α acted on SKBR3 breast cancer cells, it induced KLF4 expression. TNF-α increased the apoptosis in BC cells while inducing KLF4 expression. Is KLF4 expression related to apoptosis induced by TNF-α? To confirm whether KLF4 is involved in the apoptotic progression in breast cancer cells, we constructed a pAd-GFP-KLF4 adenovirus expression vector, with which we could infect SKBR3 breast cancer cells so that the exogenous KLF4 was overexpressed in BC cells. We found that apoptotic cells increased significantly in KLF4-overexpressing breast cancer cells, and after TNF-α stimulation, the KLF-4 overexpression group could further promote the apoptosis of SK-BR-3 and significantly increase the proportion of apoptotic cells. Based on these findings, we conclude that KLF4 is involved in TNF-α-induced apoptosis in SKBR3 cells and may function as a downstream factor of TNF-α action.

5 | LIMITATIONS

First, only the SK-BR-3 cell line was used in this study, and more BC cell lines were needed to verify the rigor of the conclusions. Secondly, the function of KLF4 was only verified in vitro cell lines in this study, and no in vivo experiments were performed, further verification of KLF4 action and function in vivo in animal models is subsequently required. Finally, it remains to be further investigated in this study as to how KLF4 specifically induces apoptosis.

6 | CONCLUSION

In SK-BR-3 breast cancer cells, KLF4 can inhibit tumor cell proliferation and development progression by participating in TNF-α-induced apoptosis, providing new targets for clinical breast cancer treatment, and providing a direction for the development of new effective therapeutic strategies for breast cancer.

AUTHOR CONTRIBUTIONS

Conception and design: Liu CY. *Administrative support*: Feng CB. *Provision of study materials or patients*: Li HF. *Collection and assembly of data*: Zhang EY and Liu B. *Data analysis and interpretation*: Wang Y and Wang P. *Manuscript writing*: All authors. *Final approval of manuscript*: All authors

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The authors declare no conflict of interest.

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All data generated or analyzed during this study are included in this article.

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This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of The No. 2 Hospital of Baoding. Written informed consent was obtained from all participants.

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委托机构：保定市第二医院

委托日期：2025 年 4 月 25 日

检索机构（盖章）：河北省科学技术情报研究院

（国家一级科技查新咨询单位）

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Clinical effect and safety analysis of long-round needle usage in treating cervical spondylotic radiotelegraphy and its effect on pain and functional recovery

By: 冯承保（Feng, Chengbao；并列第一作者）

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检索人：王雪冯

河北省科学技术情报研究院

2025 年 4 月 25 日

SCI 收录：

Clinical effect and safety analysis of long-round needle usage in treating cervical spondylotic radiotelegraphy and its effect on pain and functional recovery

By: Liu, Yingmin; Feng, Chengbao; Li, Yuyuan; Qie, Dandan; Xu, Bin; Wen, Yafei; Ma, Su; Yu, Wanglin; Xie, Zhanqing

JOURNAL OF BACK AND MUSCULOSKELETAL REHABILITATION
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Abstract: BACKGROUND: Long-round needle usage can treat muscular pain, but there is little research on cervical spondylotic radiculopathy (CSR). OBJECTIVE: To explore the efficacy and safety of long-round needle usage in treating CSR. METHODS: Ninety-eight patients with CSR were randomly divided into control and observation groups. They were treated with filiform needles and long-round needles, respectively. The therapeutic effect, safety, inflammatory factors and neck dysfunction index (NDI), McGill pain questionnaire (MPQ) and Generic Quality of Life Inventory-74 (GQOL-74) scores were compared between the two groups. RESULTS: After treatment, the effective rate and safety of the observation group were better than those of the control group. The NDI and MPQ scores in the observation group were significantly lower than those in the control group, and the GQOL-74 score was higher than that in the control group. The level of interleukin-8 in the observation group was significantly lower than that in the control group, and the level of interleukin-10 was significantly higher than that in the control group. CONCLUSIONS: Long-round needle therapy has a good effect on patients with CSR, which can safely improve the quality of life of patients with mild local inflammatory damage.

Keywords
Author Keywords: Treatment outcome; inflammation; quality of life

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Clinical effect and safety analysis of long-round needle usage in treating cervical spondylotic radiotelegraphy and its effect on pain and functional recovery

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Abstract.
BACKGROUND: Long-round needle usage can treat muscular pain, but there is little research on cervical spondylotic radiculopathy (CSR).
OBJECTIVE: To explore the efficacy and safety of long-round needle usage in treating CSR.
METHODS: Ninety-eight patients with CSR were randomly divided into control and observation groups. They were treated with filiform needles and long-round needles, respectively. The therapeutic effect, safety, inflammatory factors and neck dysfunction index (NDI), McGill pain questionnaire (MPQ) and Generic Quality of Life Inventory-74 (GQOL-74) scores were compared between the two groups.
RESULTS: After treatment, the effective rate and safety of the observation group were better than those of the control group. The NDI and MPQ scores in the observation group were significantly lower than those in the control group, and the GQOL-74 score was higher than that in the control group. The level of interleukin-8 in the observation group was significantly lower than that in the control group, and the level of interleukin-10 was significantly higher than that in the control group.
CONCLUSIONS: Long-round needle therapy has a good effect on patients with CSR, which can safely improve the quality of life of patients with mild local inflammatory damage.

Keywords: Treatment outcome, inflammation, quality of life

1. Introduction

Cervical spondylotic radiculopathy (CSR) mainly refers to the degenerative changes of the cervical intervertebral disc and intervertebral joint involving the corresponding segments of the cervical nerve root, resulting in root compression and the stimulation of corresponding symptoms and signs. Patients often have symptoms such as shoulder and back pain, radiation

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pain of upper limbs and fingers, numbness and weakness, which seriously disturb patients' quality of life and threaten their health [1]. According to Traditional Chinese medicine (TCM), CSR belongs to the 'arthralgia syndrome' and 'stiff neck' categories. The condition's primary causes are trauma, feeling cold and damp or pulling muscles, leading to a neck tendon injury. Treatment should be based on the principle of harmonising qi and blood and dredging meridians [2,3]. Currently, acupuncture is commonly used to alleviate and eliminate the influence of diseases, but fine needle therapy focuses on regulating qi and blood. The long-round needle combines the long needle (of the ancient nine needles) with the round needle. One end is sharp, and the other is blunt, which has the combined effect of separating and cutting. This 'sharp and blunt separation and relaxation' is conducive to relieving the compression of transverse collaterals. It is safe and effective in treating patients with lumbar muscle strain, scapulohumeral periarthritis and knee joint stiffness [4,5], but, at present, there are few reports on the clinical efficacy of acupuncture in treating cervical spondylosis, and they are not in-depth. Therefore, this study aims to explore the safety and effectiveness of long-round needle therapy by comparing the curative effect, local inflammatory reaction and quality of life of patients with CSR between the long-round needle and filiform needle treatments, hoping to provide better methods for clinical treatment in the future.

2. Data and methods

2.1. General information

This study was a randomised controlled study. Using convenient sampling, 98 patients with cervical cancer admitted from January 2020 to October 2021 were selected as the research objects. The researchers included all patient case numbers in Excel 2019 and generated random numbers ranging from 0 to 1 for each patient. They were sorted according to their size and divided into two groups. According to the random number, the first 48 cases were included in the observation group and treated with a long-round needle. These were code 1. The other 48 cases were the control group, treated with a filiform needle. These were code 2.

Inclusion criteria: (1) patients who met the efficacy criteria for TCM disease certificate diagnosis in the 'arthralgia syndrome' and 'stiff neck' categories [6]. Primary symptoms: numbness and pain in the shoulder, neck and upper limbs. Secondary symptoms: unfavourable neck movement and a tongue that was hard and reddish and had a heavy head and thin coating; (2) cervical X-ray showed hyperplasia of the vertebral body and (3) the patient or family members were informed and signed consent.

Exclusion criteria: (1) patients who had severe periarthritis of the shoulder and mixed cervical spondylosis; (2) patients who had spinal canal space-occupying lesions and cervical spine tumours; (3) patients who had serious immune system diseases or infectious diseases; (4) patients who had liver and kidney insufficiency; (5) patients who had cardiovascular and cerebrovascular diseases; (6) patients who had mental diseases or medical history and (6) patients who had incomplete clinical data or showed poor compliance.

All participants in this study were informed and agreed to participate. The study passed the examination and was approved by the ethics committee of The No. 2 Hospital of Baoding (ethical approval: number. HX2022009). The study was clinically registered under NCT05587075.

2.2. Methods

Control group (filiform needle treatment): Patients were lying or sitting and kept relaxed. Their Jingjiaji, Fengchi, Jianjing, Tianzhu, Houxi, Hegu and Waiguan points were selected. Preoperative marker points were established. Conventional disinfection for the needle was applied. The disposable sterile acupuncture needle met the application specification of 0.35 mm × 50 mm. Quick needling was applied to the marks subcutaneously, and slow needling was used to search for feelings of acid swelling. The needle was kept in the patients for 30 min. In each course, patients were treated once a day for 5 d. There were a total of four treatment courses.

Observation group (long-round needle therapy): The tendon lesions were marked according to the physical examination results. The patient adopted a proper prone position. Three to five tendon lesion points were selected as acupuncture points. One millimetre of 0.5% lidocaine was injected into the tendon lesion layer by layer. The patient was prepared for needle insertion under local anaesthesia. The long-round needle met the 1.0 mm × (2.5–3.5) cm specification. The needle was used to detect the tendon lesion point in each layer slowly, and it was inserted in them until the patient felt sour, numb and bloated.

To close the normal knot for treatment: The needle was brought straight to the surface of the tendon le-

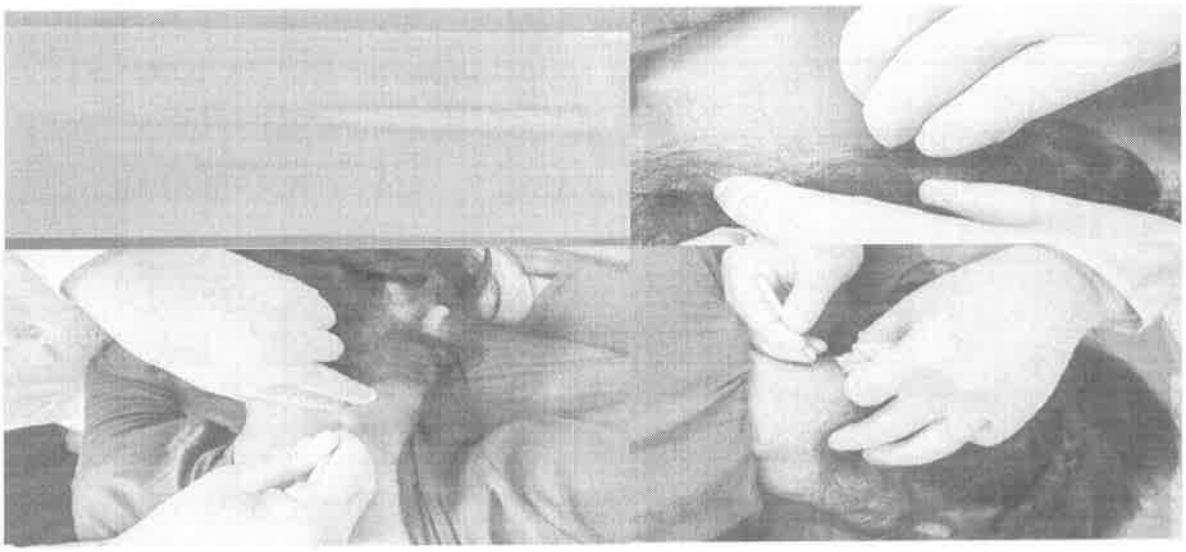

Fig. 1. The shape and operation method of long round needle.

sion point and scraped horizontally from left to right. Acupuncture was performed to relieve the surface adhesion. To relieve pain, the tendon adhesion was picked and cut forwards or backwards along the direction of the needle blade using restoring needling. The doctors were careful not to cross the superficial clavicle and the deep sternocleidomastoid muscle. After the needle puncture, the needle hole was covered with a disposable dressing and bandaged for 2 d. In each course, patients were treated once a week. There was a total of four courses (Fig. 1).

2.3. *Observation indicators*

Patients' treatment effects, safety, inflammatory cytokine levels and neck dysfunction index (NDI), McGill pain questionnaire (MPQ) and Generic Quality of Life Inventory-74 (GQOL-74) scores were compared. Blind researchers conducted data collection. Two doctors with intermediate titles or above led a team to blindly collect the experimental data of the observation and control groups through inspection. They also conducted questionnaire surveys and physical examinations. One deputy chief physician served as the quality controller in the collection process.

Safety evaluation method: Grade 1: The patient had no adverse reactions. Grade 2: The patient had mild adverse reactions, needed no treatment and could continue treatment. Grade 3: The patient had moderate adverse reactions and could continue treatment. Grade 4: The patient had serious adverse reactions, and the study was suspended [7].

Neck function evaluation method: The NDI was used, and it had 10 items. Each item was given 0–5 points, and the total score was 0–50 points. The score value was inversely related to the patient's cervical spine function [8].

Pain degree scoring method: Before and after treatment, a simplified MPQ score was used to evaluate the pain situation of cervical spondylosis, including the existing pain intensity, visual analogy and emotional score. Each was given 0–6 points, and the total score was 0–30 points. The score was positively correlated with the pain degree of cervical spondylosis [9].

Quality of life scoring criteria: Using the comprehensive assessment questionnaire (GQOL-74) scale, mainly including psychological function, social function, physical function and other items, the score value was positively correlated with the quality of life of patients [10].

Inflammatory factor level detection method: Five millilitres of fasting venous blood was extracted from the two groups before and after treatment and was centrifuged at 3000 r/min and 8 cm for 10 min. The supernatant was selected to detect the interleukin-8 (IL-8) and interleukin-10 (IL-10) levels by enzyme-linked immunosorbent method.

2.4. *Efficacy evaluation criteria*

The treatment's total efficiency judgment criteria: Recovery: After treatment, the patient's shoulder, neck

Table 1
Comparison of baseline data between two groups

	Cases	Gender		Age (years)	Course of disease (years)
		Male	Female		
Observation group	49	27	22	57.00 ± 8.57 (46–86)	4.67 ± 2.57 (1–9)
Control group	49	29	20	56.50 ± 8.56 (45–68)	5.13 ± 1.89 (2–8)
χ^2/t value		$\chi^2 = 0.49$		$t = 1.25$	$t = 1.56$
P value		0.781		0.354	0.671

Table 2
Comparison of treatment effect between two groups

Group	Cases	Recovery (%)	Significant effect (%)	Effective (%)	Ineffectiveness (%)	Total effective efficiency (%)
Control group	49	11 (22.45)	16 (32.65)	13 (26.53)	9 (18.37)	40 (81.63)
Observation group	49	13 (26.53)	18 (36.73)	16 (32.65)	2 (4.08)	47 (95.92)
χ^2 value						5.017
P value						0.025

Table 3
Comparison of safety between two groups

Group	Cases	Level 1 (%)	Level 2 (%)	Level 3 (%)	Level 4 (%)
Control group	49	24 (48.98)	20 (40.82)	4 (8.16)	1 (2.04)
Observation group	49	34 (69.39)	14 (28.57)	1 (2.04)	0 (0.00)
χ^2 value		4.224	1.621	0.843	0.000
P value	0.039	0.202	0.358	1.000	

and upper limb pain and numbness and other clinical symptoms disappeared. Significant effect: After treatment, the patient's numbness and pain in the shoulder, neck and upper limbs were significantly relieved. Effective: After treatment, the clinical symptoms of numbness and pain in the shoulder, neck and upper limbs improved. Ineffective: After treatment, the clinical symptoms, such as numbness and pain in the shoulder, neck and upper limbs, did not improve. Total effective efficiency was the sum of the curative effect, obvious effectiveness and effective efficiency [11].

2.5. Follow-up

All patients were followed for 6 months to monitor recurrence.

2.6. Statistical analysis

SPSS 22.0 software was used for the statistical analysis of data. The measurement data conforming to normal distribution and homogeneity of variance were expressed as mean ± standard deviation. An independent sample t test was used for comparison between the two groups. Qualitative data are expressed as ratios or composition ratios (%). Chi-square analysis was used to compare qualitative data. The test level was $\alpha = 0.05$.

3. Results

3.1. Baseline data comparison

Control group: There were 29 men and 20 women aged 45–68 years (mean: 56.50 ± 8.56), and the disease course was 2–8 years (mean 5.13 ± 1.89); observation group: There were 27 men and 22 women, aged 46–68 years (mean 57.00 ± 8.57), and the disease course was 1–9 years (mean 4.67 ± 2.57); The differences were not statistically significant ($P > 0.05$) (Table 1).

3.1.1. Comparison of the treatment effect between the two groups

The total treatment response rate was 95.92% in the observation group and 81.63% in the control group. The observation group's total treatment response rate was significantly higher than the control group, and the difference was significant ($P = 0.025$) (Table 2). All patients had a recurrence during the follow-up period.

3.2. Safety comparison of the two groups

The safety grade 1 ratio was 69.39% in the observation group and 48.98% in the control group. The observation group's grade 1 ratio was significantly higher than the control group, and the difference between the two groups was statistically significant ($P = 0.039$). The ratios of safety grades 2, 3 and 4 in the observation

Table 4
Comparison of NDI, MPQ and GQOL-74 scores between the two groups

Group	Cases	NDI (score)		MPQ (score)		GQOL-74 (score)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	49	30.52 ± 3.85	18.24 ± 3.02	22.65 ± 3.10	18.87 ± 2.04	26.30 ± 5.32	53.68 ± 6.20
Observation group	49	30.55 ± 4.01	10.98 ± 2.54	22.70 ± 2.96	15.40 ± 1.63	26.54 ± 5.35	62.47 ± 6.30
t value		0.038	12.878	0.082	9.302	0.223	6.961
P value		0.970	0.005	0.935	0.07	0.824	0.013

Table 5
Comparison of inflammatory factor levels between two groups

Group	Cases	IL-8 (pg/mL)		IL-10 (μg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	49	61.23 ± 15.54	48.69 ± 12.32	4.25 ± 1.26	7.45 ± 2.03
Observation group	49	62.04 ± 15.42	34.51 ± 10.25	4.23 ± 1.25	8.55 ± 2.01
t value		0.259	6.194	0.097	2.695
P value		0.796	0.013	0.937	0.028

group were lower than that in the control group, but there was no statistical difference (Table 3).

3.3. Comparison of neck dysfunction index, McGill pain questionnaire and generic quality of life inventory-74 scores between the two groups

Before treatment, the NDI, MPQ and GQOL-74 scores were different between the groups ($P > 0.05$); After treatment, the NDI score was 18.24 ± 3.02 in the control group and 10.98 ± 2.54 in the observation group. The score of the observed group was significantly lower than that of the control group ($t = 12.878$, $P = 0.005$) After the treatment, the MPQ score was 15.40 ± 1.63 in the observation group and 18.87 ± 2.04 in the control group. The score of the observed group was significantly lower than that of the control group ($t = 9.302$, $P = 0.007$). After treatment, the GQOL-74 score observation was 62.47 ± 6.30 and 53.68 ± 6.20 in the control group. The score of the observed group was significantly higher than that of the control group ($t = 6.961$, $P = 0.013$) (Table 4).

3.4. Comparison of inflammatory factor levels in the two groups

Before treatment, the levels of inflammatory factors IL-8 and IL-10 were not significantly different ($P = 0.796$). After treatment, the IL-8 level was 48.69 ± 12.32 pg/mL in the control group and 34.51 ± 10.25 pg/mL in the observation group. The observation group's levels were significantly lower than the control group ($P = 0.13$). After the treatment, the IL-10 level was 8.55 ± 2.01 μg/L in the observation group and 7.45 ± 2.03 μg/L in the control group. The observed group's levels were higher compared with the control group, and the difference between the two groups was statistically significant ($P = 0.028$) (Table 5).

4. Discussion

Cervical spondylotic radiculopathy is a common clinical disease type, and it is dominated by early aseptic inflammation with increased vascular permeability and exudation. With the disease's continuous progress, the soft tissue is often overcompensated due to the repair, causing aseptic inflammation in the early stage. The tissue then develops adhesion, fibrosis, scar formation, etc. This further aggravates the degree of inflammatory exudation stimulation of nerve endings and aggravates the pain [12,13]. Therefore, it is important to seek an effective treatment regimen timely.

Traditional Chinese medicine attributed this disease to 'arthralgia syndrome' and other categories. Tendons and bones strain, and there is an invasion of exogenous pathogens, leading to the body qi imbalance, blood stasis stagnation, meridian obstruction, blood that cannot transport, blood stasis qi stagnation and pain that does not pass [14,15]. Lingshu Hailun said, 'Brain is the sea of marrow, the loss in the cover, under the Fengfu, more than the sea of marrow, light and powerful, from the excessive, if the sea of marrow is insufficient, then the brain turn tinnitus, eyes do not see, lazy reclining' [16,17]. Zhang Jingyue scholars believe that 'No nihility for vertigo should be based on the treatment of nihility'. The prerequisite for treating CSR with acupuncture is to remove the organic factors causing qi and blood obstruction and to take the method of breaking, relieving, dispersing and resolving qi and

blood to make the qi and blood smooth and downward, which is the key premise for adjusting qi, blood, Yin and Yang. Professor Xue Ligong uses the long-round needle to combine the long needle (of the ancient nine needles) with the human needle so that on the flat-blade needle, one end is sharp, and the other is round and blunt. Given the pathological characteristics of CSR, when the long-round needle is taken, the tendon is so, with the thorns, thorns and other methods to remove the compression, loose the blood. The treatment effect is rapid, and the patient's pain relief and function are improved significantly.

The results show that the observation group's total effective treatment rate is significantly higher than that of the control group, suggesting that long-round needle therapy is more beneficial to treating CSR. Further analysis shows that the improvement of cervical dysfunction is more obvious, the quality of life after treatment is also significantly improved, and it has higher safety, which is consistent with the conclusions of Wang Lin [4] and others. The possible reason is that the long-round needle therapy mainly follows the neck and shoulder meridian to find the pathological reaction points of the damaged tendon, such as local tenderness, cord and contracture. By using the 'round needle', the needle is combined with dullness, and the surface of the tendon lesion is adhered and separated so that the tendon point's meridians and the arthralgia can be effectively relieved. In addition, by effectively dredging the tendon tissue around the peeled lesion, the spasticity and muscle tension can be effectively improved, and the dynamic biomechanical balance of the cervical spine can be restored.

Interleukin-8 is a cytokine of acute inflammatory reaction and plays an important role in the progression of CSR. Interleukin-10 is an inflammatory suppressor and has an inhibitory effect on the synthesis of various pro-inflammatory cytokines and colony-stimulating factors [18,19]. The data found that the levels of IL-8 and IL-10 in the observed group improved more significantly, suggesting that the long-round needle treatment method could better inhibit the inflammatory response, mainly because dissecting the corresponding tissue of patients can improve muscle tension and promote blood circulation, thus accelerating the absorption of inflammatory exudates and reducing local inflammatory damage.

Meanwhile, the study has the following limitations: There was no stratified study on CSR TCM syndrome, and there was a small sample size and only a single sample source; there were only 6 months of follow-up and no long-term follow-ups to observe the long-term effect of combination therapy. Subsequently, more sample sizes should be included in large sample and multicentre studies to analyse further the clinical efficacy of long-round needle use in treating CSR.

5. Conclusion

Compared with filiform needle therapy, long-round needle therapy has a higher overall effective rate for patients with CSR. It is also better at relieving pain and restoring the function of diseased parts. At the same time, the local inflammatory damage is lighter, and the overall safety is higher during the treatment, which has the value of further clinical promotion.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The No. 2 Hospital of Baoding (HX2022009).

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Informed consent

Written informed consent was obtained from all participants.

Conflict of interest

None of the authors has any personal, financial, commercial, or academic conflicts of interest to report.

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Not applicable.

Author contributions

Study conception and design: LYM and FCB.
Data collection: LYY, QDD and XB.

Data analysis and interpretation: WYF, MS, YWL and XZQ.
Drafting and critical revision of the article: All authors.
All authors read and approved the final manuscript.

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