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：张涛

专业学位类别：临床医学

专业学位领域：外科学

工作单位：保定市第二医院

2025 年 5 月

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中华人民共和国
居民身份证
签发机关 保定市公安局新市分局
有效期限 2015.05.07-2035.05.07

普通高等学校

毕业证书

中华人民共和国教育部监制

No. 02135629

学生 张涛 性别 男，

一九七七年十二月十一日生，~~于九九七~~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：10093120020500200

硕士学位证书

张涛，男，1977年12月11日生，在华北煤炭医学院公共卫生与预防医学学科（专业）已通过硕士学位的课程考试和论文答辩，成绩合格，根据《中华人民共和国学位条例》的规定，授予医学硕士学位。

院　长　袁聚祥

华北煤炭医学院

学位评定委员会主席

证书编号：T10000320090000284

二〇〇九年　六月　二十日

河北省专业技术职务任职资格证书

姓　　名 Name：张涛

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.：132401197712110314

系　　列 Category：卫生系列-外科

专　　业 Specialism：普通外科

资格名称 Title of Qualification：主任医师（省市级）

批文号 Approval No.：冀人社函〔2024〕236号

授予时间 Date of Conferment：2024年11月11日

工作单位 Place of Work：保定市第二医院

管理号 File No.：2024A116564

颁证机关：河北大学附属医院 职称专用章

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

保科发〔2021〕18号　　签发人：徐春齐

保定市科学技术局
关于下达2021年保定市科技计划自筹经费项目（第二批）的通知

有关县（市、区）科技局，有关单位：

现将2021年保定市科技计划自筹经费项目（第二批）下达给你们，请于12月18日前组织项目承担单位与市科技局签订项目任务书，尽快落实研究任务，并按照《保定市科技计划自筹经费项目管理办法》（保科发〔2020〕15号）的有关规定，加强对项目的组织与管理，确保计划项目的顺利实施。

附件：2021年保定市科技计划自筹经费项目表（第二批）

保定市科学技术局

2021年12月13日

序号	项目编号	项目名称	承担单位	合作单位	起止年月	归口管理部门
13	2141ZF187	食品加工中热伤害指标控制技术的研究及规模化应用	保定蒙牛饮料有限公司	保定蒙牛饮料有限公司	2021.12-2023.11	望都县
14	2141ZF188	超声联合多因素分析下肢静脉血栓应用价值	保定市第二医院	保定市第二医院	2021.11-2023.10	保定市第二医院
15	2141ZF189	COPD合并肺气肿患者MSCT肺容积百分比与常规肺功能的相关性研究	保定市第二医院		2021.11-2023.10	保定市第二医院
16	2141ZF190	光活化消毒配合Vitapex牙胶尖充填根管治疗对牙周牙髓联合病变患者牙周微生态环境	保定市第二医院		2021.11-2023.10	保定市第二医院
17	2141ZF191	排石方联合体外冲击波碎石治疗输尿管壁段结石的临床效果及与预后的相关性研究	保定市第二医院		2021.05-2023.04	保定市第二医院
18	2141ZF192	sSema4D、IGF-1、AT1受体与原发性高血压患者左心室重构的 相关性	保定市第二医院		2021.11-2023.10	保定市第二医院
19	2141ZF193	氯吡格雷代谢相关基因多样性与ACS不良事件、氯吡格雷抵抗相关性分析	保定市第二医院		2021.05-2023.03	保定市第二医院
20	2141ZF194	筛查、宣教和延续性护理为一体的营养护理模式对脑卒中术后患者营养状况和生活质量	保定市第二医院		2021.05-2023.01	保定市第二医院
21	2141ZF195	腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的	保定市第二医院		2021.11-2023.10	保定市第二医院
22	2141ZF196	多模态高场强磁共振成像与高频彩色多普勒超声技术对乳腺癌诊断的对比研究	保定市第二医院		2021.11-2023.10	保定市第二医院
23	2141ZF197	咽鼓管咽口周围酸性环境对咽鼓管功能及中耳疾病影响的临床研究	保定市第二医院	保定市第二医院	2021.12-2023.11	保定市第二医院
24	2141ZF198	加减桂枝龙骨牡蛎方经验方对病毒性心肌炎患儿多种炎性因子的表达情况及预后的相关	保定市第二医院		2021.02-2023.01	保定市第二医院
25	2141ZF199	基于形态学参数自动测定及定量评估对儿童DDH的应用价值研究	保定市第二医院		2021.06-2023.02	保定市第二医院
26	2141ZF200	心脏康复运动配合阻力运动对慢性心衰患者焦虑抑郁情绪、认知功能的影响研究	保定市第二医院		2021.06-2023.03	保定市第二医院
27	2141ZF201	基于活血续筋方熏洗的中医康复护理对胫骨骨折术后康复效果和生活质量的效果研究	保定市第二医院		2021.06-2023.05	保定市第二医院
28	2141ZF202	无创正压机械通气联合注射用甲泼尼龙琥珀酸钠对重症肺炎呼吸衰竭患者临床疗效及动	保定市第二医院		2021.11-2023.07	保定市第二医院
29	2141ZF203	食管癌患者的EC-SMBRS测评量表编制及信、效度检验	保定市第二医院		2021.05-2023.03	保定市第二医院
30	2141ZF204	超声引导下聚桂醇硬化剂注射治疗大隐静脉曲张的疗效观察的临床研究	保定市第二医院		2021.12-2023.11	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：普通外科

项目名称：腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究

项目依托单位：保定市第二医院

参加单位：

项目组长：张涛

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：2021年

项目起止年月：2021.11-2023.10

申报日期：2021-11-16

保定市科学技术局制

项目依托单位概况	名称	腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究				
	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	本课题拟研究腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响。选取我院住院的老年结肠癌患者，随机分为两组，即研究组与对照组。其中研究组患者接受腹腔镜下结肠癌切除+完整结肠系膜切除术，术后给予免疫增强剂治疗，对照组患者接受常规开放结肠癌切除手术+完整结肠系膜切除术。对比分析两组患者的各项手术指标，包括平均手术时长、术中出血总量、术中淋巴结清除数量、术后引流管拔出时间，平均住院时长等指标，以及手术并发症的发生情况如肺部感染、下肢静脉血栓、淋巴漏、肠梗阻、切口愈合不良等。所有患者均随访6~12月，在患者治疗前，术后第2天、治疗后3月抽取静脉血，检测患者T淋巴细胞亚群数量以及凝血功能、肿瘤标记物水平，对比分析两组患者治疗前后上述指标的变化情况，客观评估腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的益处.					

应用行业	医院	创新类型	知识创新
技术领域	医疗卫生技术		
学科分类	普通外科学		
科技活动类型	应用研究		

一、项目的立项背景和意义

结肠癌是全球第二大癌症【1】。结肠癌已经成为威胁人类身体健康的重要问题，目前，对于结肠癌的治疗，临床上仍以手术为主【2】。肠系膜切除术已逐渐成为结肠癌根治术的标准术式，可显著提高结肠癌患者预后，具有术后并发症较低，临床疗效较好，远期存活率较高，死亡率低等优点。目前，腹腔镜在结肠癌手术中已经广泛应用。腹腔镜完整结肠系膜切除术切除范围较传统根治手术更大，然而，消化道恶性肿瘤疾病中，结肠癌主要发病群体是老年人，因其早期不易发觉与诊断，使得患者错过最佳的治疗时间而大大影响治疗效果。老年患者机体免疫力低下，术后恢复慢，手术并发症相对于年轻患者出现的几率多且严重。关于腹腔镜完整结肠系膜切除联合术后免疫治疗对于高龄患者的手术效果和安全性研究较少，因此，本研究主要评价腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响，客观评估腹腔镜完整结肠系膜切除联合免疫治疗对于老年结肠癌患者的有效性、安全性。

参考文献：

1、Wen J, Min X, Shen M, et al. ACLY facilitates colon cancer cell metastasis by CTNNB1. J Exp Clin Cancer Res. 2019 Sep 12;38(1):401.,

2、Mou YP, Yang P, Yan JF, et al. Clinical evaluation of laparoscopic radical resection of colon cancer. Zhonghua Wai Ke Za Zhi. 2006 May 1;44(9):581-3..

二、国内外现状及发展趋势

结肠癌临床发病率和死亡率均较高，以老年男性多见，发病原因与生活水平、饮食习惯和饮食结构改变、人口老龄化等有关【6】。结肠癌的治疗目的主要是提升患者的术后生活质量，延长患者的生存时间。外科手术是治疗结肠癌的主要临床手段【7】，传统的结肠癌根治术主要是切除癌体为主，肿瘤组织在术中分离切除过程中极易受到挤压，造成扩散，患者具有较大的术后复发风险。同时，手术过程中患者具有较重的损伤，手术之后患者具有较多的术后出血量。此外，患者的术后吻合口瘘及感染发生率会在也较高，远期存活状况较差。完整结肠系膜切除术作为新型治疗方式，其临床疗效显著，简单易操作，术后恢复时间缩短，降低了患者的死亡率，为有效治疗结肠癌患者提供更多可能【8】。近些年来，随着腹腔镜技术的发展以及手术器械的不断完善，腹腔镜结肠癌根治术得到广泛开展【9】，腹腔镜可以在清晰视野下进行操作，对机体损伤小，具有术中出血少、住院时间短和并发症低等优点。

研究认为【10】结肠癌手术过程中所清扫淋巴结的数目是影响结肠癌临床预后的独立因素，淋巴结数目检出较少可导致病理分期不明确、术后转移的风险增加，腹腔镜具有视野放大作用，能够更加清晰的显示局部解剖视野，更有利于辨认血管，游离血管根部并清扫淋巴结，保护周围临近组织结构，减少手术副损伤。腔镜器械较长且精细，因此可以全面探查腹腔。

结肠癌的发病群体多数为老年人【11】，早期缺乏特异性的临床症状，因此早期诊断具有一定的难度，相当数量的患者发现时临床分期较晚，老年患者机体免疫力低下，因此相对于年轻患者术后恢复慢，并发症相对多，增强免疫及机体抵抗力对于老年患者术后康复非常重要【12】。乌苯美司为新一代免疫增强剂可增强免疫功能，用于抗癌化疗、放疗的辅助治疗，老年性免疫功能缺陷等。可配合或联合应用于多种实体瘤患者的治疗【13】。并且具有一定的直接抗癌作用。研究认为，氨肽酶N（APN）属于氨基肽酶家族，广泛分布于整个动物和植物界。APN被认为是癌症治疗的一个非常重要的目标，因为它与癌症的进展和转移有关【14】。乌苯美司可以作为APN抑制剂来抑制肿瘤发生过程中细胞外基质的降解。另外乌苯美司还可诱导自噬细胞死亡和凋亡。因此，对于老年患者术后的辅助治疗具有一定的优势。

【参考文献】

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14、Jiang YK, Shen DD, He P, et al. Chemically synthesized LYRM03 could inhibit the metastasis of human breast cancer MDA-MB-231 cells in vitro and in vivo. Bioorg Med Chem Lett. 2019 Jul 15;29(14):1719-1726.

三、项目依托单位、参加单位现有工作基础、特色及优势

课题依托单位保定市第二医院是综合性三级甲等医院，是一所学科齐全、设备先进、技术雄厚、环境优雅、基础设施良好的集医疗教学、科研、预防保健和康复为一体的现代化综合医院。医院现有职工1507人，专业技术人员1268人，中高级专业技术人员500人，设医疗专业40个，现有床位1250张。普通外科、烧伤科是医院成立较早、规模较大的科室。全科医师均为大学本科及以上学历，人员梯队结构合理，大部分从北京协和医院、解放军301医院、中科院肿瘤医院、北大人民医院进修学习过。我科拥有多种先进的医疗设备，如：日本大型介入治疗仪、美国放疗设备、日本奥林巴斯电子胃镜、结肠镜、德国一流Storz腹腔镜系列设备和胆道镜、十二指肠镜、结肠灌注治疗机、胃石碎石器以及多台多功能监护仪，可开展左右半肝规则或不规则切除术、胰十二指肠切除术、门脉高压症断流术或分流术、肝胆盆式肝肠内引流术、复杂胆道成形术、胃癌全胃切除术、次全切除、多脏器联合根治切除术，大肠癌根治切除术、甲状腺癌根治切除术、甲亢甲状腺次全切除术、乳腺癌标准及改良根治术、保留乳头乳晕乳腺癌根治术、肛式先天性巨结肠切除术、小儿复杂肠道畸形等高难度手术，开展了晚期消化道肿瘤的化疗泵置入与肿瘤的综合治疗，开展腹腔镜胆囊切除术、甲状腺切除术、疝修补术、阑尾切除术、剖腹探查术等各类微创手术，在全国开展了首例经脐单孔免气腹腹腔镜阑尾切除术，术后无任何切口瘢痕，深受患者喜爱，得以大力推广。目前我院普外科主任医师3名，副主任医师5名，主治医师4名，住院医师2名，近年来本科研团队参与完成省市级科研课题十四项，获保定市科技进步奖九项，其中一等奖二项、二等奖五项，三等奖二项。我院病理科目前有主任医师2名，副主任医师2名，主治医师1名，主管技师2名，技师1名，先后赴北京协和医院病理科、首都医科大学附属医院病理科、北京大学第一医院病理科及上海复旦大学附属中山医院病理科进修学习，业务范围由原来的普通石蜡切片诊断和HE细胞学涂片诊断，增加了术中快速冰冻切片诊断、尸检病理诊断、免疫组化、液基细胞学诊断以及分子病理的诊断等项目，大大提高了病理科的社会知名度。科室拥有彩色病理图文分析系统、英国丽硕全自动脱水机、全自动染色机、烤箱片机、石蜡切片机及冰冻切片机等大型设备，德国蔡司多人共览显微镜一台、日本奥林巴斯显微镜5台、德国徕卡显微镜2台，我科最新引进英国罗氏免疫组化仪1台，大大提高了早期肿瘤的检出率，为临床早期肿瘤的诊断及科研提供可靠依据。

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）

1、实施内容：入选标准：①年龄65~78岁；②相关资料齐全；③符合结肠癌诊断标准并具有手术指征；④所有患者均经结肠镜检查并经病理学检查确诊；⑤患者家属同意纳入研究并签署知情同意书；⑥无明显精神神经系统症状，能够配合完成研究；⑦愿意接受随访。

排除标准：①存在严重精神障碍，无法配合完成研究；②存在其他严重基础疾病无法纠正，不耐受手术者；③存在严重感染性疾病者；④合并严重肝肾功能障碍，不能耐受手术患者；④合并其他恶性肿瘤者；⑤预计生存时间<6个月者；⑥既往存在腹部手术史患者；⑦存在肿瘤远处转移患者。

拟选取于我院住院的老年结肠癌患者患者80例，随机分为两组，研究组采用腹腔镜结肠癌切除+完整结肠系膜切除联合乌苯美司治疗，对照组采用常规开放结肠癌根治术，对比分析两组患者的各项手术指标，包括平均手术时长、术中出血总量、术中淋巴结清除数量、术后引流管拔出时间，平均住院时长等指标，以及手术并发症的发生情况如肺部感染、下肢静脉血栓、淋巴漏、肠梗阻、切口愈合不良等。所有患者均随访6~12月，在患者治疗前，术后第2天、治疗后3月抽取静脉血，检测患者T淋巴细胞亚群数量以及凝血功能、肿瘤标记物水平，对比分析两组患者治疗前后上述指标的变化情况。

2、创新点：目前对于结肠癌患者患者，多采用结肠癌根治术，腹腔镜完整结肠系膜切除为近年新的治疗方案，相关报道较少，对于结肠癌的免疫治疗。目前国内外常用的治疗方案是树突状细胞免疫治疗。该治疗方法为有创治疗，操作复杂，要求条件较高。乌苯美司是近年来新型的免疫增强剂同时具有抗癌作用，应用方便，不良反应少。目前腹腔镜完整结肠系膜切除联合乌苯美司对老年患者的效果，国内外国内外文献报道极少。

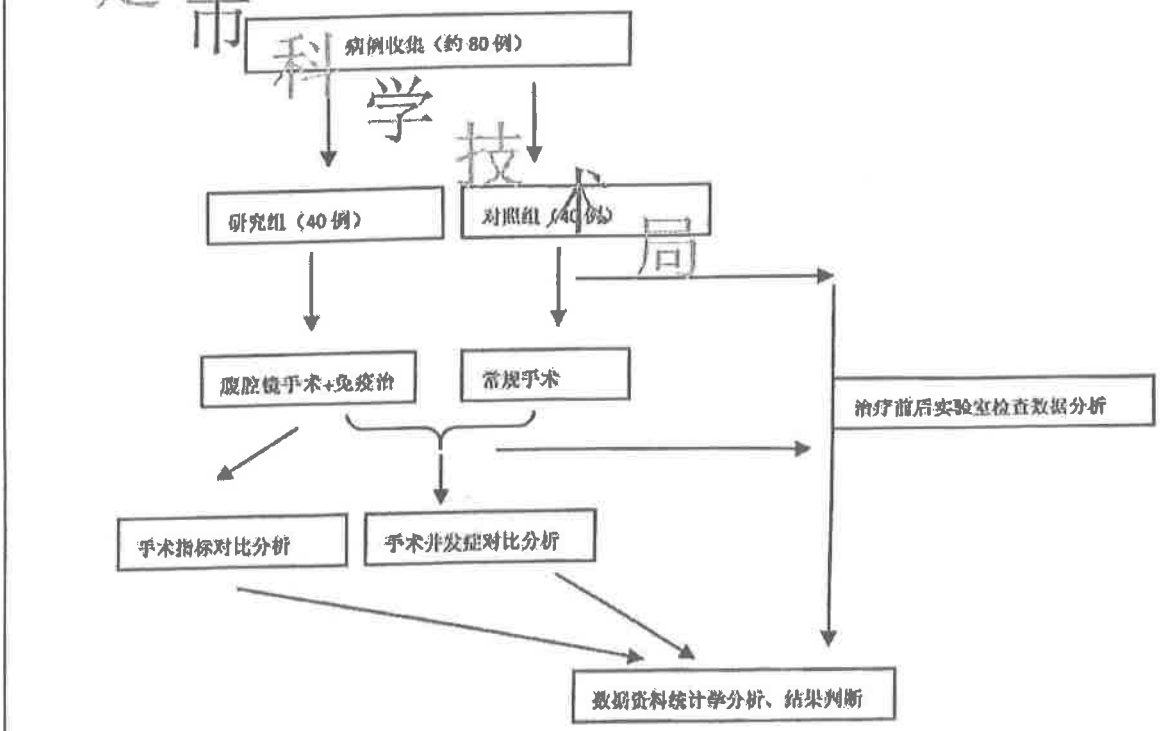
3、技术路线及技术关键：临床资料搜集→分组→治疗→对比分析各项手术指标、术后并发症分析→两组分别抽取静脉血，检测实验室相关指标→分别收集数据→数据统计→撰写论文

3.1研究组手术方法：研究组患者行腹腔镜完整结肠系膜切除，采用气管插管、全麻、仰卧位方式，中间入路，4孔操作法。根据血管解剖标志分离，中央血管高位结扎，从血管根部离断回结肠血管、胃结肠静脉干及结肠中动脉右支血管，清扫肠系膜淋巴组织。沿结肠系膜周围脏、壁层筋膜间无血管区域锐性分离，完整剥离切除肿瘤、血管及淋巴结周围的脏层筋膜。右半结肠癌采取Kocher入路，锐性分离覆盖胰腺及系膜的脏层筋膜及覆盖腹膜后组织的壁层筋膜，至肠系膜上血管；左半结肠癌锐性分离覆盖降结肠、乙状结肠的脏层筋膜与覆盖肾周脂肪、输尿管等的壁层筋膜。整块切除肠管和系膜组织，体外行吻合器消化道重建。术后可进食后给予乌苯美司30mg 3/日。

3.2对照组手术：对照组采用开放手术方式，切除范围及操作同研究组。手术操作由同一医生担任，由同一医生负责挑拣组织标本内淋巴结。

3.3实验组检查方法：分别于术前以及术后第2天、治疗后3月，采集受试者晨起空腹血液3mL，以3000r/min的速度进行离心处理，离心分组，提取上层血浆，对肿瘤标志物行酶联免疫吸附法进行检测，采用流式细胞术检测研究对象外周血T淋巴细胞各亚群的数量及百分比。上述指标的检测均同一名实验员严格按照说明书操作。

技术路线图



<table>
<tr><td rowspan="2">知识产权情况</td><td>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>是否运用现有专利技术进一步开发研究</td><td>是</td></tr>
<tr><td>项目完成后技术所有权是否是自主知识产权</td><td>是</td><td>项目完成后，是否申请国家专利</td><td>是</td><td>拟申请何种专利</td><td>实用新型专利</td></tr>
<tr><td rowspan="6">预计成果水平及效益</td><td>预期成果形式</td><td colspan="2">论文论著</td><td colspan="2">预计技术成果水平</td><td>国内领先</td></tr>
<tr><td rowspan="2">经济效益</td><td>工业</td><td>年产量
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>农业</td><td>试验（或推广应用）面积（公顷）</td><td>年产值（万元）</td><td>年人均产值（万元）</td><td>年亩产（Kg）</td><td>年纯收入（万元）</td><td>年人均纯收入（万元）</td></tr>
<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="5">通过本研究，客观分析腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的应用优势，采用实验室检查方法对两组患者的免疫功能、肿瘤标志物、凝血功能等进行客观的了解。为进一步评估该治疗方案对患者的益处提供依据。本研究所涉及到的各种评估方法操作简单，均为临床上常用的诊治技术手段，无额外投入。在现有技术条件及硬件建设下，能够直接开展，老年结肠癌发病率高。通过本研究，为提高治疗效果，增加快速康复，改善预后及生活质量提供客观理论依据。通过本研究，可发表相关科技核心论文1篇，培养相关技术骨干1名。</td></tr>
<tr><td>项目实施进度安排</td><td colspan="6">本项目起止时间为:2021.11-2023.10
项目实施进度具体安排如下：
本项目起止时间为：2021.11-2023.10
项目实施进度具体安排如下：
2021年11月～2022年6月 文献检索、立题、完成试验设计；
2022年3月～2023年6月 选择病例，整理病例资料，进行统计学分析；
2022年6月～2023年10月 整理、汇总试验数据，撰写论文并发表，进行科技成果鉴定。</td></tr>
</table>

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	3.5	0	3.5	0
2	二、经费支出	3.5	0	3.5	0
3	（一）直接经费	3.5	0	3.5	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	2	0	2	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	1	0	1	0
15	9、劳务费	0	0	0	0
16	10、专家咨询费	0.3	0	0.3	0
17	11、其他支出	0.2	0	0.2	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	主要协助	张婷	3.5	0.0	0.0	3.5	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	张涛	男	44	132801197712110314	副主任医师	研究生	硕士	普通外科学	普通外科学	保定市第二医院	项目负责人	24
2	刘志	男	39	130184198202151033	副主任医师	研究生	硕士	普通外科学	普通外科学	保定市第二医院	资料收集分析	24
3	杨华	女	39	130624198211014525	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	资料收集分析	20
4	张文丽	女	36	130622198507263026	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	资料收集分析	20
5	朱冬琴	女	36	130635198505294824	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	资料收集分析	20
6	林倩	女	39	130622198212218025	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	资料收集分析	20
7	董晨	女	36	130623198510050060	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	资料收集分析	20

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
1	发表论文	被SCI/核心期刊数据库收录论文1-3篇	发表论文被SCI/核心期刊数据库收录数量	3	2	1	0

项目承担单位基本情况简介	上年度(2020)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。医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、德国西门子VB30E 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。

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
张涛	男	1977.12	研究生	副主任医师	普通外科学	普通外科学
所在单位	保定市第二医院					
联系电话	0312-3099752		手机	13932250222	E-Mail	ztoaaa@163.com
通讯地址	东风西路338号				邮政编码	071000

个人经历与业绩：

本人，男，42岁，2002年承德医学院临床医学专业本科毕业，2009年华北煤炭医学院在职研究生毕业，2010年北京大学人民医院国内访问学者学习1年，2018年河北医科大学第二医院进修学习，本科毕业后保定市第二医院普外科从事临床工作至今，2013年晋升为副主任医师，具备了丰富的普通外科专业理论知识及实践经验，能独立解决本专业复杂疑难的技术问题，完成较复杂的会诊和抢救工作，能熟练掌握普通外科专业领域中各种常见病、多发病的外科治疗的适应症、禁忌症、操作技术规范；多发病的常见误诊、误治原因，能够正确判断并制定正确的治疗方案；熟练掌握了普通外科危重患者的临床特点、诊断、鉴别诊断、紧急救治和综合治疗的原则，熟练掌握了多器官功能障碍综合征的诊断与处置。熟练掌握了普外科领域中各种少见病、疑难病的特点、病因、病理特征及发病机制。熟悉现代普通外科常用的诊疗技术的基本原理、应用范围、适应症、禁忌症、操作要领、结果判定、及其常见病发症的诊断和治疗；掌握了普外专业领域中腹腔镜手术的应用指征、禁忌症和操作规范；了解普通外科领域中内镜外科的基本原理、应用范围、治疗措施和操作原则；了解普通外科领域中常用药物的药理及药代动力学，能独立完成普通外科常见手术及完成中大复杂手术，重视科研工作，于核心期刊发表学术论文多篇，并多次负责及参与多项科研工作。通过这些年的学习进修，在胃肠癌诊治方面取得了极大进步，尤其在腹腔镜胃肠癌根治手术方面提升显著，同时还注重总结实践经验，使之理论化，形成学术论文。这些文章有《胃癌手术患者生活质量影响因素分析》，山东医药，2011.1.14，第51卷第2期，《完全腹腔镜下D2淋巴结清扫胃癌根治术的安全性与可行性研究》，陕西医学，2013.6.第42卷，《腹腔镜手术治疗胃肠肿瘤的临床效果探讨》，医药卫生，2019.1，《腹腔镜结肠癌根治术与开腹结肠癌根治术的近远期疗效对比分析》，医药卫生，2019.6.同时积极开展科研工作，主要参与的科研项目《两种经脐单孔微创阑尾切除术的安全性比较》获保定市2011年科学进步三等奖，《血清SCD105与VEGF联合监测复发转移乳腺癌的意义》获保定市2012年科学技术进步二等奖，《VEGF、MVD、Ki-67联合检测与大肠癌临床病理特征及预后相关性的研究》获保定市2017年科学技术进步二等奖。

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：

日期：

保定市科技计划项目任务书

项目名称：腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究

项目编号：2141ZF195

签订年度：2021 年

项目起止年月：2021.11-2023.10

承担单位（乙方）：保定市第二医院

合作单位：

项目负责人：张涛 联系电话：15630839222

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）

1、本课题拟研究腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响。选取我院（保定市第二医院）住院的老年结肠癌患者，随机分为两组，即研究组与对照组。其中研究组患者接受腹腔镜下结肠癌切除+完整结肠系膜切除术，术后给予免疫增强剂治疗，对照组患者接受常规开放结肠癌切除手术+完整结肠系膜切除术。对比分析两组患者的各项手术指标，包括平均手术时长、术中出血总量、术中淋巴结清除数量、术后引流管拔出时间，平均住院时长等指标，以及手术并发症的发生情况如肺部感染、下肢静脉血栓、淋巴漏、肠梗阻、切口愈合不良等。所有患者均随访6~12月，在患者治疗前，术后第2天、治疗后3月抽取静脉血，检测患者T淋巴细胞亚群数量以及凝血功能、肿瘤标志物水平，对比分析两组患者治疗前后上述指标的变化情况，客观评估腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的益处。

2、技术路线及技术关键：临床资料收集→分组→治疗→对比分析各项手术指标、术后并发症分析→两组分别抽取静脉血，检测实验室相关指标→分别收集数据→数据统计→撰写论文。

3、创新点：目前对于结肠癌患者患者，多采用结肠癌根治术，腹腔镜完整结肠系膜切除为近年新的治疗方案，相关报道较少，对于结肠癌的免疫治疗，目前国内外常用的治疗方案是树突状细胞免疫治疗，该治疗方法为有创治疗，操作复杂，要求条件较高。乌苯美司是近年来新型的免疫增强剂同时具有抗癌作用，应用方便，不良反应少。目前腹腔镜完整结肠系膜切除联合乌苯美司对老年患者的效果，国内外国内外文献报道较少。

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）

通过本研究，客观分析腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的应用优势，采用实验室检查方法对两组患者的免疫功能、肿瘤标志物、凝血功能等进行客观的了解。为进一步评估该治疗方案对患者的益处提供依据。本研究所涉及到的各种评估方法操作简单，均为临床上常用的诊治技术手段，无额外投入。在现有技术条件及硬件建设下，能够直接开展，老年结肠癌发病率高。通过本研究，为提高治疗效果，增加快速康复，改善预后及生活质量提供客观理论依据。通过本研究，通过本研究，至少发表相关核心论文1篇

三、进度、安排和阶段目标

本项目起止时间为:2021.12-2023.10

项目实施进度具体安排如下：

本项目起止时间为：2021.12-2023.11

项目实施进度具体安排如下：

2021年12月～2022年6月 文献检索、立题、完成试验设计；

2022年3月~-2023年6月 选择病例，整理病例资料，进行统计学分析；

2022年6月~-2023年11月 整理、汇总试验数据，撰写论文并发表，进行科技成果验收结题。

四、项目承担单位、合作单位任务分工、知识产权归属

项目承担单位：保定市第二医院

合作单位分工：无

知识产权归属：保定市第二医院

保 市 学 术 局

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	张涛	男	44	132401197712110314	副主任医师	研究生	硕士	普通外科学	保定市第二医院	项目负责人
2	刘志	男	39	130184197[illegible]751033	副主任医师	研究生	硕士	普通外科学	保定市第二医院	资料收集分析
3	杨华	女	39	130624198211014525	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析
4	张文丽	女	36	130622198507263026	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析
5	朱冬琴	女	36	130635198505294824	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析
6	林倩	女	39	130622198212218025	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析
7	董晨	女	36	130623198510050060	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析

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	3.5	0	3.5	0
2	二、经费支出	3.5	0	3.5	0
3	（一）直接经费	3.5	0	3.5	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	2	0	2	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	1	0	1	0
13	7、劳务费	0	0	0	0
14	8、专家咨询费	0.3	0	0.3	0
15	9、其他支出	0.2	0	0.2	0
16	（二）间接经费	0	0	0	0
17	其中：绩效支出	0	0	0	0

保定市科技计划项目验收证书

保科验字（2023）03-253 号

项 目 编 号：2141ZF195

项 目 名 称：腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究

承 担 单 位：保定市第二医院

合 作 单 位：

验收主持部门：市科技局

验 收 方 式：函审验收

验 收 日 期：2023-08-16

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="7">腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究</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>单位性质</td><td colspan="3">[illegible]</td></tr>
<tr><td rowspan="2">项目负责人</td><td>姓名</td><td>张涛</td><td>联系电话</td><td>15630839222</td><td>电子邮箱</td><td colspan="2">zhotao@163.com</td></tr>
<tr><td>学历</td><td>研究生</td><td>学位</td><td>硕士</td><td>职称</td><td colspan="2">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>7</td><td>2</td><td>5</td><td>0</td><td>0</td><td>0</td><td>2</td><td>5</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>24</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="2"></td><td>合作单位性质</td><td colspan="4"></td></tr>
<tr><td>合作形式</td><td colspan="6"></td></tr>
<tr><td rowspan="2">累计经费筹集情况（万元）</td><td>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>3.5</td><td>0</td><td>0</td><td>0</td><td>3.5</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>

29

<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>3</td><td>其中：发表科技论文（篇）</td><td>3</td><td>其中：被EI、SCI、ISTP、ISR收录（篇）</td><td>2</td></tr>
<tr><td colspan="2">动植物新品种开发个数（个）</td><td colspan="2">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 colspan="2">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>专利申请数（项）</td><td>发明</td><td>实用新型</td><td>外观设计</td><td>专利授权数（项）</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>制定技术标准（项）</td><td>企业标准</td><td>地方标准</td><td>行业标准</td><td>国家标准</td><td colspan="2">国际标准</td></tr>
<tr><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td colspan="2">0</td></tr>
<tr><td>培养人才数（人）</td><td colspan="2">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>0</td><td colspan="2">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

本课题的主要研究内容：1.收集80例老年结肠癌患者的临床资料，探讨腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响，为临床上结肠癌的治疗提供参考。2.检测两组不同治疗方式的80例老年结肠癌患者治疗前后免疫分子CD3+、CD4+、CD8+、CD4+/CD8+及肿瘤标记物CCSA-2、PTN、SIL2等水平，探讨腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者免疫功能及肿瘤标志物水平的影响。通过研究，得出腹腔镜完整结肠系膜切除联合免疫治疗效果显著优于传统开腹手术，淋巴结清扫更彻底，减少了手术风险，有利于术后恢复。同时能够改善患者细胞免疫功能，降低肿瘤标记物水平及术后并发症发生率，具有一定的治疗效果这一结论，为临床上老年结肠癌患者的治疗提供参考。

创新性简介

本研究的创新性主要体现在：通过对手术相关指标、术中淋巴结清除数量、术后并发症发生情况、治疗前与治疗后CD3+、CD4+、CD8+、CD4+/CD8+等免疫分子及CCSA-2、PTN、SIL2等肿瘤标记物情况的对比分析，客观评价腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响，为临床上结肠癌的治疗提供参考。

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

随着腹腔镜技术的发展以及手术器械的不断完善，腹腔镜结肠癌根治术得到广泛开展。腹腔镜可以在清晰视野下进行操作，对机体损伤小，具有术中出血少、住院时间短和并发症低等优点。本研究将腹腔镜完整结肠系膜切除与免疫治疗联合，对比分析发现腹腔镜完整结肠系膜切除联合免疫治疗效果显著优于传统开腹手术，减少手术风险，淋巴结清扫更加彻底，有利于术后恢复。同时能够改善患者细胞免疫功能，降低肿瘤标记物水平及术后并发症发生率，为临床医生结肠癌的治疗提供参考，具有良好的经济效益及社会效益。

三、主要技术文件目录及来源

1.工作报告——保定市第二医院

2.技术报告——保定市第二医院

3.验收大纲——保定市科技局

4.刊发论文:

[1]Zhang T, Liu Z, Lin Q. Clinical effect and safety of targeted therapy combined with chemotherapy in the treatment of patients with advanced colon cancer. Pak J Med Sci. 2023;39(4):1074-1079. doi: https://doi.org/10.12669/pjms.39.4.7105

[2]Zhang T, Lin Q, Liu Z, Yang H. Effect of laparoscopic complete mesocolic excision combined with immunotherapy and its impact on immune function and tumor markers in elderly patients with colon cancer. Pak J Med Sci. 2023;39(5):---------. doi: https://doi.org/10.12669/pjms.39.5.7090

[3]张涛,刘志,杨华,张文丽,朱冬琴,林倩,张晨.腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究[J].智慧医学,2023,03(06):14-16.

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	张涛	男	44	副主任医师	研究生	硕士	普通外科学	保定市第二医院	项目负责人	
2	刘志	男	39	副主任医师	研究生	硕士	普通外科学	保定市第二医院	资料收集分析	
3	杨华	女	39	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析	
4	张文丽	女	36	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析	
5	朱冬琴	女	35	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析	
6	林倩	女	39	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析	
7	董晨	女	36	其他中级	本科	学士	专科护理学	保定市第二医院	资料收集分析	

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	李日恒	河北大学附属医院	外科学其他学科	外科学其他学科	主任	主任医师	
2	靳小石	河北大学附属医院	普通外科学	普通外科学	主任	主任医师	
3	刘进忠	保定市第一医院	普通外科学	普通外科学	主任	主任医师	
4	姜战武	保定市第一中心医院	普通外科学	普通外科学	主任	主任医师	
5	刘欣	保定市第一中心医院	实验诊断学	实验诊断学	副主任	其他高级	

六、验收意见

由保定市第二医院承担的2021年保定市科学技术研究与发展指导计划项目“腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究”（编号：21417F195），已按项目任务书完成，经审查，提供的技术资料完整、规范，符合验收要求。综合其他委员意见，形成验收意见如下：

该技术设计合理，研究方法得当，技术资料完整、规范，结论明确，组织管理有序。通过将80例老年结肠癌患者，随机分为两组，每组40例，研究组采用腹腔镜完整结肠系膜切除联合免疫治疗，对照组采用常规手术。运用手术相关指标、术中淋巴结清除数量、手术并发症发生情况及治疗前与治疗后免疫因子和肿瘤标志物水平，评价腹腔镜完整结肠系膜切除联合免疫治疗对老年结肠癌患者的疗效及免疫功能、肿瘤标志物的影响，为临床治疗结肠癌的治疗提供参考，具有一定的临床指导意义。

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

建议：本研究样本量较少，缺乏随访且为单中心研究，建议后续进行多中心、大样本的研究并完善随访内容。

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

36

验收文件和资料目录		
序号	附件名称	附件说明
1	李日恒函审意见	李日恒函审意见
2	靳小石函审意见	靳小石函审意见
3	刘进忠函审意见	刘进忠函审意见
4	拳战武函审意见	拳战武函审意见
5	刘欣函审意见	刘欣函审意见
6	验收意见	验收意见
7	验收专家组成员签字	验收专家组成员签字
8	项目组成员签字	项目组成员签字

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。

附表 1

应用证明

项目名称	腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究	
应用单位	容城县人民医院	
单位注册地址	容城县金台路 78	
应用起止时间	2021.01—2023.06	
经济效益（万元）		
自然年	新增销售额	新增利润
2019 年		
2020 年		
2021 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：

我院自 2021 年应用腹腔镜完整结肠系膜切除联合乌苯美司免疫治疗老年结肠癌患者 [illegible] 例，疗效显著。该方法具有临床效果好，手术风险小，淋巴结清扫更加彻底，术后并发症少等优点，术后可进食后给予乌苯美司，能够改善患者细胞免疫功能，该方法能够降低肿瘤标记物水平及术后并发症发生率，具有良好的社会效益、经济效益及广阔的应用前景。

应用单位法定代表人签名：

年 月 日

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

附表 1

应用证明

项目名称	腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究	
应用单位		
单位注册地址		
应用起止时间	2021.01—2023.06	
经济效益（万元）		
自然年	新增销售额	新增利润
2019 年		
2020 年		
2021 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：

我院自 2021 年应用腹腔镜完整结肠系膜切除联合乌苯美司免疫治疗老年结肠癌患者 50 余例，疗效显著。该方法具有临床效果好，手术风险小，淋巴结清扫更加彻底，术后并发症少等优点。术后可进食后给予乌苯美司，能够改善患者细胞免疫功能。该方法能够降低肿瘤标记物水平及术后并发症发生率，具有良好的社会效益、经济效益及广阔的应用前景。

应用单位法定代表人签名：	
年　月　日	应用单位财务章 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

河北省科学技术成果

证书

河北省科学技术厅

成果名称：腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究

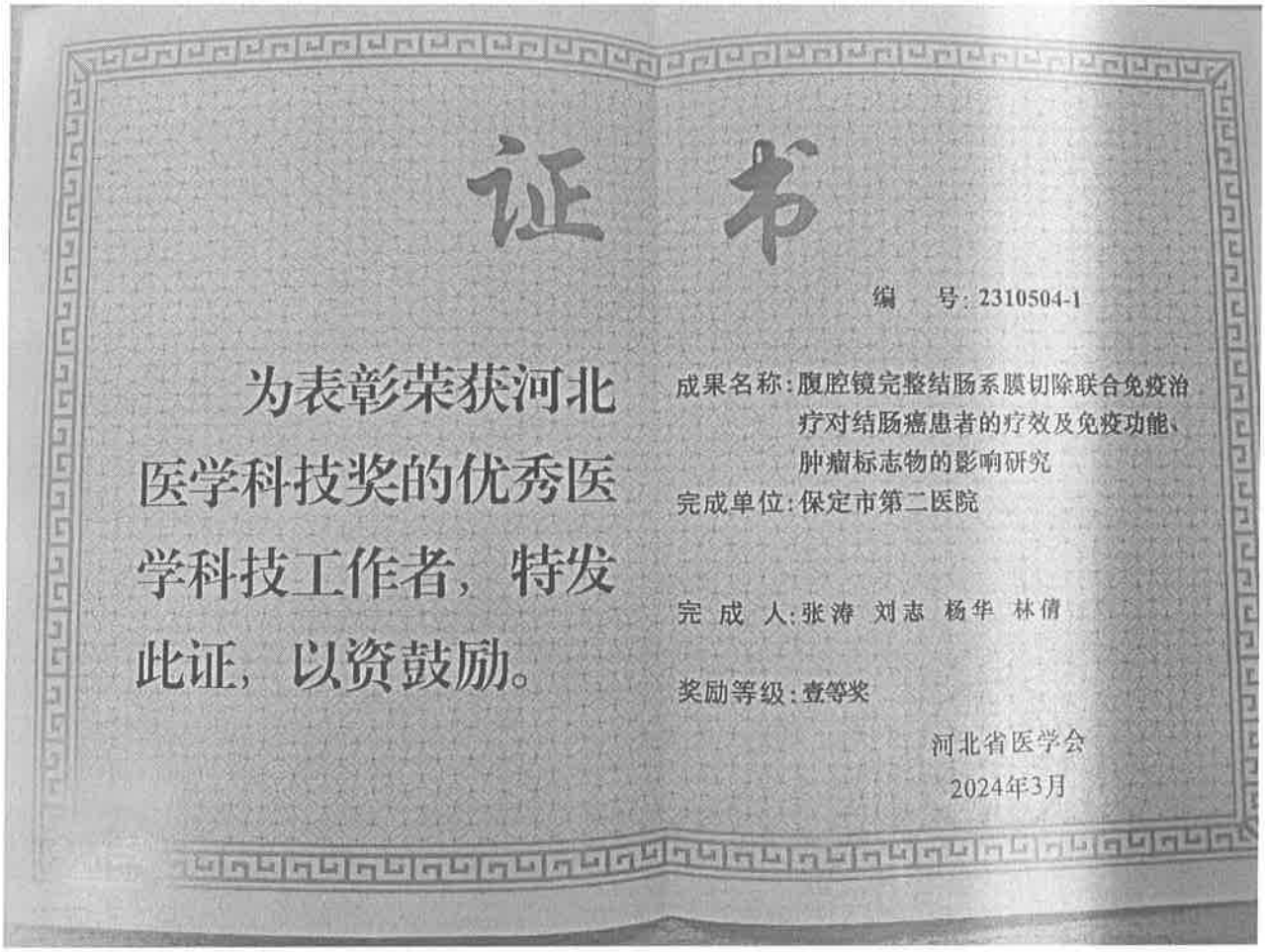
完成单位：保定市第二医院

完成人：张涛 刘志 杨华 张文丽 朱冬琴 林倩 董晨

省级登记号：20232535

二〇二三年八月二十九日

河北省科学技术厅 科技成果登记专用章



证书

编　号：2310504-1

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。

成果名称：腹腔镜完整结肠系膜切除联合免疫治疗对结肠癌患者的疗效及免疫功能、肿瘤标志物的影响研究

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Original Article

Clinical effect and safety of targeted therapy combined with chemotherapy in the treatment of patients with advanced colon cancer

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ABSTRACT

Objective: To evaluate the clinical effect and safety of immunotherapy combined with chemotherapy in patients with advanced colon cancer.

Methods: This is a retrospective study. The subjects of this study were 120 patients with advanced colon cancer who were admitted to The No.2 Hospital of Baoding from November 30, 2019 to November 30, 2021. The enrolled patients were randomly divided into two groups, with 60 cases in each group. Patients in the control group were given FOLFOX4 regimen, while those in the study group were provided with Bevacizumab therapy on the basis of the method in the control group. All patients were evaluated after two cycles of treatment. The comparison of outcome measures included the curative effects, adverse drug reactions, improvement of quality-of-life scores and changes in tumor markers between the two groups.

Results: The total effective rate of the study group was significantly better than that of the control group. There was no significant difference in the incidence of adverse drug reactions between the two groups. After treatment, the study group had a significantly higher rate of improved quality of life score, while the obviously lower rate of the aggravated score than those in the control group. The levels of CEA, CA19-9 and CA125 in the study group were significantly lower than those in the control group after treatment.

Conclusion: Targeted therapy combined with chemotherapy is a safe and effective therapeutic option that has a definite curative effect in the treatment of patients with advanced colon cancer.

KEYWORDS: Targeted therapy, Chemotherapy, Advanced colon cancer, Prognosis.

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INTRODUCTION

Colon cancer is a common digestive tract malignant tumor with a high incidence clinically, ranking fifth among malignant tumor diseases.[1] It has no significant symptoms in the early stage, only including fecal occult blood, dyspepsia, etc. However, in case of progressing to the advanced stage, patients will show obvious symptoms such as abdominal distension, bloody stool, low fever, anemia and other adverse symptoms, which will threaten the safety-of-life of patients in serious cases.[2] In clinical practice, surgery is considered to be the primary therapeutic option for the treatment of colon cancer.[3] Nevertheless, due to the lack of specificity of symptoms in the early stage, some patients are often diagnosed at an advanced stage and already lost the opportunity of surgery. The main measures for the treatment of advanced colon cancer include chemotherapy, neoadjuvant therapy, radiotherapy and chemoradiotherapy. Significantly, the formulation of an effective chemotherapy regimen is of great importance in treating these patients.[4]

A prior randomized trial has documented that the FOLFIRI regimen can realize an excellent progression-free survival for patients with advanced colon cancer, which is better than 5-FU or other chemotherapeutics alone.[3] While the serious side effects of chemotherapy are also a common problem that cannot be ignored since patients may show poorer tolerance to the therapy, and some patients even give up the treatment. Consequently, there may be poor curative effects and poor tolerance in patients, leading to poor improvement of patients' symptoms. Significantly, molecular targeted drugs and chemotherapy drugs have been reported to have synergistic effects in the treatment of advanced tumors.[6,7] At the same time, with the continuous improvement of symptoms, the tolerance of patients is higher. Bevacizumab is one of the molecular targeted agents that is commonly used clinically. Its mechanism of action is competitive binding with vascular endothelial growth factor (VEGF) receptor, inhibiting the migration and proliferation of endothelial cells, blocking angiogenesis and inhibiting tumor proliferation.[8] At present, some reports show that bevacizumab combined with chemotherapy has certain benefits in the treatment of colon cancer.[9,10] However, there is still a lack of high therapeutic research on the efficacy of bevacizumab combined with FOLFOX4 regimen in the treatment of advanced colon cancer. With respect to the above, the present study was performed to discuss the clinical effect and safety of targeted therapy combined with FOLFOX4 regimen in patients with advanced colon cancer.

METHODS

In this retrospective study, clinical effect and safety of immunotherapy combined with chemotherapy in patients with advanced colon cancer. A total of 120 patients with advanced colon cancer who were admitted to The No.2 Hospital of Baoding from November 30, 2019 to November 30, 2021.The enrolled patients were randomly divided into two groups, with 60 cases in each group. This study has been approved by the medical ethics committee of The No.2 Hospital of Baoding (No.:HX2021040; date: November 30,2021), and written informed consent was obtained from all participants.

Inclusion criteria:

- Patients with colon cancer diagnosed as stage III B ~ IV by pathological and imaging examination.[11-13]
- Patients with Karnofsky Performance Score (KPS) ≥80 points and estimated survival of >three months.
- Patients aged ≤75 years old.
- Patients with written informed consent, and patients with good treatment compliance and whose families were willing and able to cooperate to complete the study.

Exclusion criteria:

- Patients with severe infectious diseases, immune diseases and serious dysfunction of important organs.
- Patients with malignant tumors of other systems.
- Patients with severe organic diseases or congenital diseases (such as valvular heart disease, severe pancreatitis, congenital heart disease, etc.).
- Patients with mental disorders or cognitive abnormalities who could not cooperate to complete the study.
- Patients who took relevant drugs (e.g., immunosuppressants, hormones, etc.) that might affect the study in the near future.
- Patients without contraindications to the drugs used in this study.

Before treatment, patients in both groups were given basic tests such as blood cell analysis, liver function and renal function, with the corresponding improvement of the abnormal indicators. Following pre-chemotherapy hydration one day before chemotherapy, patients in the control group were provided with an FOLFOX4 regimen, including Oxaliplatin (80mg/m^2) in 5% glucose solution (250ml) for two hours of intravenous drip on Day one; formyltetrahydrofolate (200mg/m^2) in 5% glucose solution (250ml) for two hours of intravenous drip on Day 1~2; and Fluorouracil Injection (400mg/m^2) for 22 hours of intravenous injection through micro-pump continuously.[14] The above therapeutic regimen was performed once every two weeks, and four weeks was a cycle. Patients were given antiemetic's and drugs for increasing white cells during treatment. Simultaneously, patients in the study group were treated with an intravenous drip of Bevacizumab (5mg/kg) dissolved in 500ml normal saline on the basis of the treatment in the control group. Patients in this group were treated with two cycles (14 d/cycle).

Outcome measures: (1) *Evaluation of curative effect:* The curative effect was evaluated after two cycles of treatment,[15] which was classified into the following types: complete remission (CR): Disappearance of the focus and normal recovery of the level of tumor markers for >four weeks; partial remission (PR): Decrease in the sum of length and diameter of the lesion by >30% and reduction in the level of tumor markers for >four weeks; no change (NC): No narrowing of the target focus, but with an increase in the sum of length and diameter within 20%, and no significant change in the level of tumor markers; and progressive disease (PD): Increase in the sum of baseline length and diameter of the lesion by >20%, and increase in the level of tumor markers. Overall response rate (RR) was calculated based on the formula of RR=CR+PR/CR+PR+NC+PD×100%. (2) Evaluation of adverse drug reactions.

The adverse reactions of the two groups of patients within one month after medication were recorded, including proteinuria, leucopenia, erythropenia, thrombocytopenia, gastrointestinal symptoms, etc. (3) *Quality of life score:* Eastern Cooperative Oncology Group (ECOG) score[16] was used to observe the improvement of quality of life in the studied patients before and after treatment, including improved (score decrease ≥1 point's), stable (no change in the score)

Table-I: Comparison of general data of the study group and the control group [($\bar{X}\pm S$). (n, %)]

Indexes	*Study group*	*Control group*	t/χ^2	*P*
n	60	60		
Age (years)	68.27±5.38	67.73±6.52	0.49	0.62
Male (n %)	37 (62%)	35 (58%)	0.14	0.71
Pathological type				
Adenocarcinoma	33 (55%)	37 (62%)	0.55	0.46
Mucinous adenocarcinoma	19 (32%)	16 (27%)	0.36	0.55
Others	8 (13%)	7 (11%)	0.07	0.78
Tumor site			0.85	0.36
Left	32 (53%)	37 (62%)		
Right	28 (47%)	23 (38%)		
Clinical stage			0.20	0.66
IIIB	48 (80%)	46 (77%)		
IV	12 (20%)	14 (23%)		
Degree of differentiation				
High	22 (37%)	25 (42%)	0.31	0.58
Moderate	30 (50%)	29 (48%)	0.03	0.86
Low	8 (13%)	6 (10%)	0.32	0.57

P>0.05.

and aggravated (score increase ≥1 point's) quality of life scores. (4) Comparative analysis of tumor markers: Fasting blood was taken from each patient before and after treatment to detect carcinoembryonic antigen (CEA) (normal range < 5.0ng/ml), CA19-9 (normal range < 37U/ml) and CA125 (normal range < 35U/ml). The differences in these markers were further compared and analyzed between the two groups.

Statistical analysis: This study adopted SPSS 20.0 software for statistical analysis of all data. The measurement data were expressed in ($\bar{X}\pm S$). Inter-group comparison used two independent samples t-test, and intra-group analysis was realized using paired t-test. In addition, Chi-square (c^2) test was used to compare the rates between groups. The difference was statistically significant when $p<0.05$.

RESULTS

There were 37 males and 23 females in the study group, with an average of (68.27±5.38) years (63~73 years old); and the control group included 35 males and 25 females, with an average age of (67.73±6.52) years (61~75 years old). There was no significant difference in the general data between the study group and the control group, indicating the comparability between the groups (Table-I).

Shows the results of the comparison of curative effects between the two groups. The overall RR was 85% in the study group and 70% in the control group, which was significantly better in the former group than that in the latter group, with a statistically significant difference (p=0.03, Table-II).The incidence of adverse

Table-II: Comparison of the curative effect of the two groups of patients (n, %)

Groups	*CR*	*PR*	*NC*	*PD*	*RR*
Study group (n=60)	17	34	6	3	51 (85%)
Control group (n=60)	11	31	12	6	42 (70%)
c^2	-	-	-	-	4.66
p	-	-	-	-	0.03

P<0.05.

Notes: CR, remission; PR, partial remission; NC, no change; PD, progressive disease; RR,overall response rate.

Table-III: Comparison of adverse drug reactions between the two groups of patients (n, %)

Groups	Rash	Bone marrow suppression	Allergy	Fever	Abnormal liver function	Gastrointestinal reaction	Incidence
Study group (n=60)	2	5	3	2	3	3	18 (30%)
Control group (n=60)	0	4	3	1	1	4	13 (22%)
c^2	-	-	-	-	-	-	1.09
p	-	-	-	-	-	-	0.30

p>0.05.

Table-IV: Comparison of quality of life scores (determined by ECOG) between the two groups before and after treatment.

Groups	Improved*	Stable	Aggravated*
Study group (n=60)	48	9	3
Control group (n=60)	37	11	12
c^2	4.88	0.24	7.21
p	0.03	0.62	0.00

Notes: *p<0.05.

reactions was 30% in the study group and 22% in the control group. There was no significant difference in the incidence of adverse reactions between the two groups (p=0.30, Table-III).

After treatment, the study group had a significantly higher rate of improved quality of life score (p=0.03), while the obviously lower rate of the aggravated score (p=0.00) than those in the control group. Results in (Table-IV) suggested that the study group had obvious advantages in the improved quality of life score. Before treatment, no significant difference was detected in CEA, CA19-9 and CA125 levels between the two groups (p>0.05). While the levels of these indicators in the study group were significantly lower than those in the control group after treatment, with a statistically significant difference (p=0.00, Table-V).

DISCUSSION

In our study, patients with combination therapy in the study group had a higher RR rate and obviously improved quality of life scores after treatment. It can be speculated that for the treatment of advanced colon cancer, by making up for the deficiency of chemotherapy alone, Bevacizumab combined with chemotherapy can play a synergistic role and improve the anti-tumor effect. Colon cancer has been accepted to be a common digestive tract malignant tumor with a high incidence in middle-aged and elderly patients. Its pathological types mainly include adenocarcinoma, mucinous adenocarcinoma and undifferentiated carcinoma, with adenocarcinoma as the most common type.[17] It is generally characterized by the lack of specific clinical symptoms in the early stage. Hence, some patients have developed into the advanced stage upon diagnosis, which means the loss of the surgery opportunity to achieve an effective therapeutic role.[18] Medical treatment is the primary therapeutic option for patients with advanced colon cancer. Commonly, the use of chemotherapy can play a significant therapeutic effect, reduce the tumor size and further alleviate the clinical symptoms of patients.[19] In addition,

Table-V: Comparison of tumor markers levels between the two groups before and after treatment ($\bar{x}\pm s$)

Indicators	Time of observation	Study group	Control group	t	p
CEA (ng/ml)	Before treatment	7.48±2.32	7.43±2.07	1.24	0.91
	After treatment*	3.27±0.93	5.92±1.07	14.48	0.00
CA19-9 (U/ml)	Before treatment	14.73±2.03	14.58±2.32	0.38	0.71
	After treatment*	4.32±1.06	7.88±2.01	12.14	0.00
CA125 (U/ml)	Before treatment	4.87±0.36	4.79±0.41	1.14	0.26
	After treatment*	1.86±0.07	3.05±0.23	13.84	0.00

Notes: *p <0.05.

immunotherapy for colon cancer is also being carried out gradually.[20]

However, and notably, traditional chemotherapeutics are not favored by clinicians gradually owing to their poor therapeutic effect according to previous research.[21] In recent decades, combined chemotherapy involving Oxaliplatin is extensively applied in clinical treatment, with the achievement of obvious therapeutic results.[22] Oxaliplatin is a novel platinum derivative, which has significantly less toxicity to kidney and bone marrow than carboplatin and cisplatin and can effectively inhibit tumor growth. In combination therapy, besides improving the effect of other chemotherapeutics, it can also alleviate the adverse reactions caused by chemotherapy. It has been reported to have established anti-tumor activity in advanced or metastatic malignant tumor diseases.[23]

Furthermore, five-fluorouracil has higher activity and higher accuracy for tumor cells. Besides, it has less toxicity and will not cause adverse effects on the human body at a normal dose. Therefore, the combination of Oxaliplatin and five-fluorouracil may exhibit some advantage in treatment.[24] However, additional researchers also considered a relatively unsatisfactory effect of chemotherapy alone.[25] In terms of the major causes, tumor cells may spread widely in patients with advanced colon cancer, leading to a higher risk of complications, poor overall resistance of the body and compromised immunity in these patients. Consequently, these patients can't bear the adverse reactions caused by chemotherapy.

Bevacizumab is a targeted drug that can be applicable for the treatment of various tumors. It can play a role by targeting and inhibiting the biological activity of VEGF. The use of Bevacizumab can reduce tumor angiogenesis and inhibit the progress of metastasis, which has been approved for the treatment of metastatic colorectal cancer, non-small cell lung cancer, etc.[26] Concerning its mechanism of action, Bevacizumab can bind to VEGF released by tumor, prevent VEGF from binding to specific sites on vascular endothelial cells (VEGF receptors) to inhibit tumor angiogenesis, so as to disrupt the supply of nutrients to tumor cells and achieve the purpose of inhibiting tumor growth.[27] The application of Bevacizumab can induce rapid tumor regression, restore the structure of surviving tumor vasculature simultaneously, and reduce intratumoral pressure, thereby facilitating the delivery of chemotherapeutics to exert anti-tumor effect.[28]

It may be related to the fact that Bevacizumab can reverse the immunosuppression caused by chemotherapy and enhance the resistance of the body,[29] resulting in reduced adverse reactions to some extent. Sakaguchi et al.[30] pointed out that oxaliplatin-based chemotherapy plus bevacizumab and laparoscopic resection could be very effective for locally advanced colon cancer. On the basis of surgical treatment, Yonemitsu et al.[31] used bevacizumab combined with chemotherapy to effectively treat a case of juvenile colon cancer with peritoneal dissemination. According to Mikami et al.,[32] chemotherapy with bevacizumab/FOLFOX4 plays a role in the management of advanced/unresectable colon cancer.

Furthermore, there was no significant difference in adverse drug reactions between the study group and the control group after treatment. It is suggested that targeted therapy of Bevacizumab combined with chemotherapy exhibit certain safety without aggravation in adverse reactions, which is basically consistent with the report of Kanieri et al.[33] In addition, the level of tumor markers in the study group was significantly lower than that in the control group after treatment. Accordingly, Bevacizumab combined with oxaliplatin and fluorouracil can play a synergistic effect by compensating for the deficiency of chemotherapy alone and enhance the anti-tumor effect in the treatment of advanced colon cancer. Our results provide a reference for the application of bevacizumab combined with chemotherapy in the treatment of advanced colon cancer.

Limitation of the study: However, the present study still has some limitations that deserve to be emphasized, such as the small sample size and short follow-up period. Our future research will be continued based on the expanded sample size and prolonged duration of follow-up. Through expanded investigation, it is expected to further elaborate on the impact of different treatment schemes on the long-term effect and survival of patients, so as to evaluate the benefits of the proposed therapeutic schedule to patients more comprehensively.

CONCLUSION

In conclusion, findings in our study suggest that targeted therapy combined with chemotherapy is a safe and effective treatment with obvious curative effects in the treatment of patients with advanced colon cancer. It can contribute to the significant improvement of quality of life and reduced levels of tumor markers, without an obvious increase in adverse reactions.

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Authors' Contributions:

TZ, ZL and QL: Carried out the studies, participated in collecting data, and drafted the manuscript, and are responsible and accountable for the accuracy or integrity of the work.
TZ and QL: Performed the statistical analysis and participated in its design.
All authors read and approved the final manuscript.

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检索工具	SCI Expanded Web	查证机构	
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Original Article

Effect of laparoscopic complete mesocolic excision combined with immunotherapy and its impact on immune function and tumor markers in elderly patients with colon cancer

Tao Zhang[1], Qian Lin[2], Zhi Liu[3], Hua Yang[4]

ABSTRACT

Objective: To determine the effect of laparoscopic complete mesocolic excision combined with immunotherapy and its impact on immune function and tumor markers in elderly patients with colon cancer.

Methods: This is a clinical comparative study. Eighty elderly patients with colon cancer hospitalized in the No.2 Hospital of Baoding from May 2020 to May 2022 were randomly divided into two groups, with 40 cases in each group. Patients in the study group received laparoscopic complete mesocolic resection combined with ubenimex orally. While patients in the control group received routine open surgery. The surgical indexes, surgical complications, and the changes of immune molecules and tumor markers before and after treatment were compared between the two groups.

Results: The amount of intraoperative bleeding, retention time of drainage tube and postoperative length of stay in the hospital in the study group were significantly better than those in the control group ($p=0.000$). The incision length of the study group was significantly shorter than that of the control group, the number of lymph nodes removed during the operation was significantly higher than that of the control group, and the incidence of surgical complications was significantly lower than that of the control group ($p<0.05$). After treatment, the levels of immune molecules in the study group were remarkably higher than those in the control group ($p<0.05$), while the levels of tumor markers were much lower than those in the latter group ($p=0.000$).

Conclusion: Laparoscopic complete mesocolic excision combined with immunotherapy exhibits a superior therapeutic effect to traditional open surgery in elderly patients with colon cancer, and is worthy of clinical promotion.

KEYWORDS: Laparoscopic complete mesocolic excision, Immunotherapy, Colon cancer in the elderly, Immune function, Tumor markers.

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INTRODUCTION

With the changes in living and dietary habits of the public, colon cancer has become the second most common cancer in the world, with a gradual increase in its incidence.[1,2] Surgery is still the primary approach for the treatment of colon cancer.[3] Mesocolic excision has gradually become the standard radical operation for colon cancer, which can significantly improve the prognosis of colon cancer patients.[4] At present, laparoscopic-assisted surgery has been widely adopted for colon cancer.[5] Laparoscopic complete mesocolic excision has a larger surgical margin than that of traditional radical surgery.

Besides, due to its high difficulty of detection and diagnosis in the early stage, these patients may lose the best opportunity for surgery and experience significantly compromised therapeutic effects. Meanwhile, elderly patients have low immunity, slow postoperative recovery, and high risk of serious surgical complications

than young patients.[6] At the same time, there are few studies on the effect and safety of laparoscopic complete mesocolic excision combined with postoperative immunotherapy in elderly patients. Accordingly, the present study was performed to evaluate the effect of laparoscopic complete mesocolic excision combined with immunotherapy and its impact on immune function and tumor markers in elderly patients with colon cancer.

METHODS

This is a clinical comparative study. Eighty elderly patients with colon cancer hospitalized in the No.2 Hospital of Baoding from May 2020 to May 2022 were randomly divided into two groups, with 40 cases in each group. They're existed comparability between the two groups as there was no significant difference in the comparison of general data between groups (Table-I). This study has been approved by the medical ethics committee of Ethical Approval: The No.2 Hospital of Baoding (No.:2041ZF014; date: March 20, 2021), and written informed consent was obtained from all participants.

Inclusion criteria:

- Patients aged 65-75 years old.
- Patients who met the diagnostic criteria of colon cancer and had surgical indications.[7]
- Patients with complete relevant data.
- Patients who agreed to be included in the study and provided the written informed consent and those agreed by family members.
- Patients who agreed to be followed up.

Exclusion criteria:

- Patients with severe mental disorders who cannot cooperate to complete the study.
- Patients with other serious underlying diseases that cannot be corrected and cannot tolerate surgery.
- Patients with severe infectious diseases.
- Patients with other malignant tumors.
- Patients with an estimated survival time of <six months.
- Patients with previous abdominal surgery.
- Patients with distant metastasis of tumor.

Patients in the study group received laparoscopic complete mesocolic excision combined with immunotherapy. Via tracheal intubation under general anesthesia, the operation was started through a medial approach by using the four-hole method. After that, the ileocolic blood vessels, the gastrocolonic venous trunk and the branches of the middle colonic artery were severed from the root of the blood vessels, after which the mesenteric lymph nodes were dissected. Further sharp dissection was made along the visceral layer of fascia around the mesocolon and the avascular area between spaces to completely remove the tumor, blood vessels and visceral fascia around lymph nodes.

For left colon cancer, a sharp dissection was carried out for the visceral fascia covering the descending colon and sigmoid colon as well as the parietal fascia covering perirenal fat, ureter, etc. After the recovery of food intake after operation, patients were provided with oral ubenimex (30 mg, once a day). Meanwhile, patients in the control group were given open surgery, with the same surgical margin and operation as those in the study group. Postoperative routine treatment in this group included nutritional supplements, correction of water and electrolyte, supplementation of albumin, etc.

Observation indicators: **(1)** Surgical indicators were compared and analyzed between the two groups, including average operation time, total amount of intraoperative bleeding, extraction time of drainage tube, postoperative length of stay in the hospital. **(2)** The number of dissected lymph nodes intraoperatively was compared and analyzed between the two groups. **(3)** Occurrence of surgical complications was also compared between the study group and the control group. **(4)** As

Table-I: Comparison of general data between the two groups ($\bar{x}\pm s$) n=40.

	Study group	*Control group*	t/χ^2	*p*
Male (n %)	23 (57.50%)	25 (62.50%)	0.208	0.648
Age (years)	69.83±3.17	69.53±3.42	0.407	0.685
BMI (kg/m^2)	34.32±4.34	34.09±3.54	0.257	0.798
Course of disease (years)	1.78±0.70	1.68±0.73	0.626	0.533
Tumor site			0.474	0.491
Left	14 (35.00%)	17 (42.50%)		
Right	26 (65.00%)	23 (57.50%)		
Tumor stage				
I	8 (20.00%)	9 (22.50%)	0.075	0.785
II	14 (35.00%)	15 (37.50%)	0.054	0.816
III	18 (45.00%)	16 (40.00%)	0.205	0.651
ECOG score	0.3±0.54	0.68±0.66	0.372	0.711

p>0.05.

Table-II: Comparison of surgical indicators between the two groups ($\bar{X}\pm S$) n=40.

Groups	*Operation time (min)*	*Amount of bleeding (ml)**	*Retention time of drainage tube (d)**	*Postoperative length of stay (d)**	*Incision length (cm)**
Study group	161.38±8.51	86.50±5.57	3.65±0.80	7.75±1.26	6.30±0.56
Control group	158.60±5.29	110.85±3.61	4.85±0.77	12.83±1.15	11.15±0.48
t	1.752	23.209	6.827	18.834	41.313
p	0.084	0.000	0.000	0.000	0.000

*p<0.05.

for the comparative analysis of immune molecules and tumor markers, venous blood was collected from each group before operation and three months after operation. Further detection was performed focusing on immune molecules of $CD3^+$, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ and tumor markers of serum colon cancer-specific antigen 2 (CCSA-2), pleiotropic growth factor (pleiotrophin, PTN) and soluble interleukin two (SIL2) to compare and analyze the changes of these indicators before and after treatment. The maximum follow-up time for patients in both groups was three months. And case data collection ceased in May 2022.

Statistical analysis: All data were statistically analyzed using SPSS 20.0 software. The measurement data were presented in the form of ($\bar{X}\pm S$). Two independent samples t-test and paired t-test were respectively used for inter- and intra-group analyses. The comparison of rate adopted c^2 test. P<0.05 was used to indicate the existence of a statistically significant difference.

RESULTS

As shown in Table-II, the study group had significantly less amount of intraoperative bleeding, as well as a shorter retention time of drainage tube and postoperative length of stay in the hospital than those in the control group (p=0.000). The incision length was obviously shorter in the study group than that in the control group (p=0.000).

The comparative analysis of the difference in the number of dissected lymph nodes intraoperatively between the two groups suggests that it was significantly higher in the study group than that in the control group, with consistent results observed based on the subgroup analyses according to different tumor stages and tumor sites (p<0.05, Table-III). According to the comparative analysis, the incidence of surgical complications in the study group was much lower than that in the control group, and the difference was statistically significant (p=0.032; Table-IV). After treatment, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ were obviously higher in the study group than those in the control group (p<0.05, Table-V). After treatment, the levels of CCSA-2, PTN and SIL2 were obviously lower in the study group when compared with those in the control group (p=0.000, Table-VI).

DISCUSSION

In our study, the number of dissected lymph nodes intraoperatively in the study group was significantly higher than that in the control group, regardless of

Table-III: Comparison of the number of dissected lymph nodes intraoperatively between the two groups ($\bar{X}\pm S$) n=40.

Groups	*Stage I**	*Stage II**	*Stage III**	*Left colon**	*Right colon**
Study group	15.88±2.37	16.50±1.84	19.85±2.48	18.48±1.69	22.05±1.34
Control group	14.65±1.99	14.63±1.33	15.75±2.10	16.95±1.72	18.43±2.54
t	2.504	5.219	7.992	3.990	7.983
p	0.014	0.000	0.000	0.000	0.000

*p<0.05.

Table-IV: Comparison of the incidence of surgical complications between the two groups ($\bar{X}\pm S$) n=40.

Groups	*Incision infection*	*Lung infection*	*Venous thrombosis of lower limbs*	*Lymph-orrhagia*	*Intestinal obstruction*	*Poor wound healing*	*Incidence rate (%)**
Study group	0	1	1	1	2	0	5 (12.50%)
Control group	3	0	3	1	4	2	13 (32.50%)
c^2							4.588
p							0.032

*p<0.05.

Table-V: Comparison of T lymphocyte subset level in two groups before and after treatment ($\bar{X}\pm S$) n=40.

Indicators		*Study group*	*Control group*	*t*	*p*
$CD3^+$ (%)	Before treatment	43.03±5.49	42.97±6.22	0.048	0.962
	After treatment*	47.80±6.37	44.13±6.15	2.621	0.011
$CD4^+$ (%)	Before treatment	27.28±4.09	27.01±3.83	0.302	0.764
	After treatment*	35.68±4.64	31.22±4.76	4.243	0.000
$CD8^+$ (%)	Before treatment	21.62±3.70	21.08±3.70	0.653	0.516
	After treatment	22.25±3.73	22.32±3.90	0.082	0.935
$CD4^+/CD8^+$	Before treatment	1.27±0.10	1.29±0.07	1.149	0.254
	After treatment*	1.62±0.16	1.41±0.15	5.992	0.000

*p <0.05.

Table-VI: Comparison of tumor marker levels between the two groups before and after treatment ($\bar{X}\pm S$) n=40.

Indicators		*Study group*	*Control group*	*t*	*p*
CCSA-2 (mg/L)	Before treatment	122.48±7.53	119.89±7.47	1.545	0.126
	After treatment*	62.74±8.14	73.65±7.26	6.323	0.000
PTN (ng/L)	Before treatment	183.65±7.24	180.55±7.44	1.887	0.063
	After treatment*	112.06±5.31	139.81±5.72	22.480	0.000
SIL2 (U/L)	Before treatment	2.27±0.76	2.30±0.42	0.218	0.828
	After treatment*	1.12±0.27	1.59±0.35	6.653	0.000

*p <0.05.

different tumor stages or tumor sites (p=0.00), which may be attributed to the amplification effect of laparoscopy. Meanwhile, the study group was discovered to have a smaller amount of intraoperative bleeding, as well as a shorter retention time of drainage tube, length of stay in the hospital postoperatively and postoperative incision length. In addition, the incidence of complications in the study group was obviously lower than that in the control group.

It has been recognized that there is an intimate association between the levels of postoperative tumor markers and the risk of tumor recurrence.[8] SIL2 can inhibit the immune function of the body; PTN is a pleiotropic growth factor and has a variety of biological functions that can cause tumor cell metastasis and proliferation.[9] CCSA-2 plays an important role in evaluating the prognosis of diseases, which is a colon cancer-specific molecule.[10] In the present study, the levels of CCSA-2, PTN and SIL2 in the study group were lower than those in the control group after treatment. These data further reveal that compared with open radical surgery, laparoscopic surgery can remove tumor tissues more thoroughly, and also has a lower risk of postoperative recurrence.

Colon cancer is featured by relatively higher clinical morbidity and mortality, and high incidence in elderly men.[11] Surgery has been accepted clinically as the major approach to treating colon cancer.[12] Through the resection of the tumor primarily, the traditional radical resection of colon cancer may cause the extrusion and then the spread of tumor tissues during intraoperative separation and resection, leading to a greater risk of postoperative recurrence.[13] Significantly, complete mesocolic excision is a novel therapeutic option surgically, with significant clinical effects.[14] With the assistance of a laparoscope, it may provide a clear field of vision for a surgical operation with minimal damage to the patients, exhibiting advantages of less intraoperative bleeding, short hospital stay, low complications, etc.[15]

Previous research[16] has reported that the number of dissected lymph nodes during colon cancer surgery was an independent factor affecting the clinical prognosis of patients with colon cancer. The use of a laparoscope can magnify the field of vision to display the local anatomical visual field more clearly, which can facilitate the identification of blood vessels to assist in the dissociation of the root of blood vessels and dissection of lymph nodes, eventually protecting the surrounding adjacent tissue structures, and reducing secondary damages of surgery.

Enhancement of immunity and body resistance is of great significance for the postoperative rehabilitation of elderly patients.[17] Ubenimex is a new generation of immunopotentiator that can enhance immune function, which can can be used cooperatively or jointly for the treatment of patients with various solid tumors.[18] Yang et al. suggested that ubenimex also had a certain direct antitumor effect.[19] At the same time, ubenimex, an

inhibitor of CD13, can be used as an immune adjuvant to improve the immune state of patients.[20] Similarly, in our study, after treatment, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ were obviously elevated in the study group than those in the control group ($p<0.05$), which confirmed significant improvement in the cellular immune function of patients after applying immunotherapy jointly.

Limitations: However, the small sample size and the lack of follow-up are two major limitations of our study. Our future research will be continued by including more samples, having follow-ups, and further exploring the impact of the therapeutic scheme on the long-term effect and survival of patients. Through relevant studies, we hope to realize a more comprehensive evaluation of its long-term therapeutic effect so that more patients can benefit from this treatment.

CONCLUSION

Findings in our study supported that laparoscopic complete mesocolic excision combined with immunotherapy has a superior therapeutic effect to traditional open surgery in elderly patients with colon cancer. Simultaneously, this therapeutic schedule also has a certain effect on improving the cellular immune function of patients, reducing the levels of tumor markers and the incidence of postoperative complications.

Conflicts of interest: None.

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Authors' Contributions:

TZ and QL: Carried out the studies, participated in collecting data, and drafted the manuscript, are responsible and accountable for the accuracy and integrity of the work.
ZL: Performed the statistical analysis and participated in its design.
HY: Participated in acquisition, analysis, or interpretation of data and draft the manuscript.
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