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NLR和THR及二者联合在预测冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效中的应用价值

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摘 要

目的：探讨中性粒细胞比淋巴细胞比值(NLR)和总胆固醇比高密度脂蛋白胆固醇比值(THR)及二者联合对冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床预后的预测价值。方法：纳入2020年6月至2024年6月成功行冠状动脉旋磨术并植入药物洗脱支架的270例冠状动脉严重钙化患者，对其术后进行为期1年的随访，排除失访及资料缺失患者，最终纳入241例患者。观察终点是1年随访期间发生包括心源性死亡、再发心肌梗死、靶血管血运重建(TVR)和急性心力衰竭在内的主要不良心血管事件(MACE)。运用Logistic回归模型分析预后相关因素，并结合受试者工作特征(ROC)曲线下面积(AUC)评价NLR、THR及二者联合对冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效的预测价值。结果：左心射血分数、植入支架数量、NLR和THR与冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效相关(均$p < 0.05$)。ROC曲线下面积表明，NLR，THR及二者联合对预测MACE发生有较好的区分度，AUC分别为0.691 (95% CI: 0.628~0.748)，0.703 (95% CI: 0.641~0.760)和0.764 (95% CI: 0.705~0.816)，灵敏度分别为71.5%、65.38%、80.77%，特异度分别为59.26%、71.43%、67.72%，且二者联合预测的曲线下面积大于NLR和THR，具有统计学意义(均$p < 0.05$)。结论：NLR和THR是预测冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效的有效指标，且二者联合的预测价值更高。

关键词

冠状动脉，血管钙化，旋磨术，中性粒细胞比淋巴细胞比值，总胆固醇比高密度脂蛋白胆固醇比值，心血管不良事件

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Application Value of Neutrophil to Lymphocyte Ratio, Total/HDL Cholesterol Ratio, and Their Combination in Predicting the Clinical Efficacy of Rotational Atherectomy and Drug-Eluting Stent Implantation in Patients with Severe Coronary Artery Calcification

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Abstract

Objective: To investigate the predictive value of neutrophil to lymphocyte ratio (NLR), total/HDL cholesterol ratio (THR) and their combination in predicting the clinical prognosis of rotational atherectomy and drug-eluting stent implantation in patients with severe coronary artery calcification. Methods: 270 patients with severe coronary artery calcification who successfully underwent rotational atherectomy and drug-eluting stent implantation from June 2020 to June 2024 were followed up for one year. Finally, to exclude the patients with loss of follow-up and missing data, 241 patients were included. The end point of observation was major adverse cardiovascular events (MACE) including cardiogenic death, acute myocardial infarction, target vessel revascularization (TVR) and acute heart failure during 1-year follow-up. Logistic regression model was used to analyze the prognostic factors, and combined with the receiver operating characteristic (ROC) curve to evaluate the predictive value of NLR, THR and their combination in the clinical efficacy of drug-eluting stent implantation in patients with severe coronary artery calcification after rotational atherectomy. Results: Left ventricular ejection fraction, number of stents, NLR and THR were related to the clinical efficacy of drug-eluting stent implantation in patients with severe coronary artery calcification after rotational atherectomy ($p < 0.05$). The area under the ROC curve shows that NLR, THR and the combination of the two have a good discrimination degree for predicting the occurrence of MACE. The area under the curve is 0.691 (95% CI: 0.628~0.748), 0.703 (95% CI: 0.641~0.760) and 0.764 (95% CI: 0.705~0.816), the sensitivity is 71.5%, 65.38% and 80.77%, and the specificity is 59.26%, 71.43% and 67.72%, respectively. The combined indicators had a larger area under the curve than NLR or THR ($p < 0.05$). Conclusion: NLR and THR are effective indexes to predict the clinical efficacy of drug-eluting stent implantation in patients with severe coronary artery calcification after rotational atherectomy, and their combination has a higher predictive value.

Keywords

Coronary, Vascular Calcification, Rotational Atherectomy, Neutrophil to Lymphocyte Ratio, Total Cholesterol to High Density Lipoprotein Cholesterol, Adverse Cardiovascular Events

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1. 背景

冠状动脉严重钙化明显增加了冠状动脉介入治疗的风险，且与术中并发症及远期主要不良心血管事件的发生密切相关[1]，因此一直是冠状动脉介入治疗的重大难题之一。目前，冠状动脉旋磨术及术后植入药物洗脱支架是治疗冠状动脉钙化的有效手段[2] [3]，但其预后仍较非钙化冠状动脉病变患者差。因此，寻找一种简单，有效的指标来预测冠状动脉严重钙化患者旋磨术后植入药物洗脱支架的临床疗效是非常有意义的。研究表明，动脉钙化常发生在动脉粥样硬化处，炎症和血脂与动脉粥样硬化及动脉钙化密切相关[4]-[6]。而 NLR 和 THR 作为新型炎症和血脂指标，与冠状动脉性疾病关系密切[7]-[10]，但目前关于两者及两者联合来预测冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效的研究尚少，预测价值不明确。本研究探讨冠状动脉严重钙化患者旋磨术后植入药物洗脱支架 NLR 和 THR 水平及二者联合对其临床疗效预测的可行性。

2. 对象与方法

2.1. 研究对象

纳入安徽医科大学第三附属医院(合肥市第一人民医院) 2020 年 6 月至 2024 年 6 月成功行冠状动脉旋磨术并植入药物洗脱支架的 270 例冠状动脉严重钙化患者，所有患者在出院前常规进行血常规、血脂等指标复查(由我院检验中心完成)并对其进行术后为期 1 年的随访。排除失访及资料缺失患者，最终纳入 241 例患者。根据 1 年随访期间是否发生不良心血管事件分为 MACE 组(52 例)，非 MACE 组(189 例)。

2.2. 纳入及排除标准

纳入标准：临床诊断为冠心病，同时冠状动脉造影或血管内超声证实存在严重钙化病变，且需行冠状动脉旋磨术。

排除标准：(1) 心源性休克；(2) 存在明确的感染病变；(3) 严重肝肾功能不全；(4) 家族性高胆固醇血症；(5) 自发性冠脉夹层及冠状动脉桥血管病变。

2.3. 冠状动脉严重钙化及冠脉旋磨术

本研究主要根据冠状动脉造影来判断冠状动脉钙化严重程度。依据造影结果可将钙化病变分为[11]：(1) 无钙化；(2) 轻度钙化，只有心脏搏动时可见钙化高密度模糊阴影，不搏动时完全不见高密度阴影；(3) 中度钙化，心脏搏动时可见较清楚的高密度钙化阴影；(4) 重度钙化，心脏搏动和不搏动时钙化阴影均清晰可见。部分患者通过 IVUS 进行钙化程度判断，将范围大于 270 度的沿冠脉血管分布的强回声团伴声影定义为严重钙化。

冠脉旋磨术：手术首选桡动脉入路，旋磨仪、旋磨导丝和旋磨头均由 Boston Scientific 公司提供。选用 6F 导管(1.25 mm 磨头、1.5 mm 磨头)或 7F 导管(1.75 磨头)，旋磨头直径与血管直径的比值控制在 0.5~0.6 之间，旋磨转速为 130,000~180,000 r/min，术者根据造影及病变具体情况决定是否球囊扩张，最后植入第二代药物洗脱支架，使狭窄 < 30%，术后无穿孔、夹层等冠脉并发症。

2.4. 旋磨术前及术后药物治疗

所有患者术前给予阿司匹林 300 mg 和氯吡格雷 300 mg (或替格瑞洛 180 mg)进行双抗治疗。手术结束后根据体重给予补充普通肝素 100 U/Kg，连续 3 天皮下注射低分子肝素 8000 u/d，出院后均口服阿司匹林及氯吡格雷(或替格瑞洛)双联抗血小板聚集至少 1 年。根据病情给予他汀类降脂药及 β 受体阻断剂等进行冠心病二级预防治疗。

2.5. 随访及血清学指标检测

所有患者在旋磨术后 1 年内通过门诊或电话进行随访，部分患者通过冠状动脉造影进行随访。观察终点为 1 年内是否发生主要不良心血管事件(MACE)，包括：心源性死亡、再发心肌梗死、TVR 和急性心力衰竭。

血清学指标检测：所有患者在出院前 1 日清晨采集空腹 12 h 静脉血，常规完成血常规、血脂、心功能等指标复查。

2.6. 统计学方法

应用 SPSS 26.0 软件进行分析，计量资料采用 $\bar{x} \pm s$ 表示，正态分布资料组间差异比较采用 t 检验；非参数秩和检验用于非正态分布资料组间差异比较。计数资料以例数(百分比)进行表示，组间比较采用 χ^2 检验或 Fisher 确切概率法检验，Logistic 回归模型用于影响预后相关因素分析。运用 MedCalc 软件绘制 ROC 曲线并分析 NLR，THR 及二者联合因素对冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效的预测效果，同时对曲线下面积进行两两比较。均采用双侧检验，$p < 0.05$ 为差异有统计学意义。

3. 结果

3.1. 基线资料比较及影响预后的危险因素分析

纳入符合标准患者 241 例，术后随访 1 年，根据是否发生主要不良心血管事件分为 MACE 组(52 例)，非 MACE 组(189 例)，与非 MACE 组相比，MACE 组患者心功能($p = 0.005$)及肾功能($p = 0.004$)更差，高脂血症比例更高(88.5% vs 70.9%, $p = 0.010$)。两组基线资料在冠心病危险因素包括性别、年龄、高血压和糖尿病病史等方面基本相似，无统计学意义(均 $p > 0.05$)。介入治疗基线资料方面，MACE 组植入支架数更多($p = 0.002$)，左主干病变相对较多，两组在旋磨冠脉，多支病变等方面无统计学差异(均 $p > 0.05$)。将性别、年龄、高血压病史、糖尿病病史及基线资料比较中 $p < 0.05$ 的指标进行二元 Logistic 回归分析，结果显示左心射血分数降低、植入支架数量增加、NLR 及 THR 升高均与冠状动脉严重钙化患者旋磨术后临床预后不良相关(均 $p < 0.05$)，见表 1、表 2、表 3。

Table 1. Clinical baseline data
表 1. 临床基线资料

基线资料	MACE 组(52 例)	非 MACE 组(189 例)	Z/t/χ^2	p 值
男性[例，%]	28 (53.8%)	113 (59.8%)	0.593	0.441
年龄[$\bar{x} \pm s$，岁]	69.1 ± 1.3	71.2 ± 0.6	1.526	0.128
高血压[例，%]	34 (65.4%)	120 (63.5%)	0.063	0.801
糖尿病[例，%]	20 (38.5%)	62 (32.8%)	0.581	0.446
吸烟[例，%]	10 (19.2%)	34 (18.0%)	0.042	0.837
既往介入史[例，%]	21 (40.4%)	50 (26.5%)	3.808	0.051

续表

高血脂症[例，%]	46 (88.5%)	134 (70.9%)	6.653	0.010
NLR [N (Min, Max)]	3.8 (1.24, 14.78)	2.6 (0.76, 13.33)	4.206	<0.001
THR [N (Min, Max)]	4.5 (2.85, 8.17)	3.80 (2.11, 8.76)	4.500	<0.001
LVEF [$\bar{x} \pm s$, %]	51.4 ± 1.7	57.5 ± 0.8	3.079	0.002
肌酐[$\bar{x} \pm s$, μmol/L]	111 ± 13.0	88 ± 5.4	2.914	0.004
ACS [例，%]	18 (34.6%)	59 (31.2%)	0.217	0.642

注：NLR：中性粒细胞比淋巴细胞比值；THR：总胆固醇比高密度脂蛋白胆固醇比值；LVEF：左心射血分数；ACS：急性冠脉综合征。

Table 2. Baseline data related to interventional therapy
表 2. 介入治疗相关基线资料

基线资料	MACE 组(52 例)	非 MACE 组(189 例)	Z/t/χ^2	p 值
旋磨冠脉：左冠[例，%]	37 (71.2%)	127 (67.2%)	0.294	0.588
左主干病变[例，%]	6 (11.5%)	17 (9.0%)	-	0.596
多支病变[例，%]	46 (88.5%)	162 (85.7%)	0.26	0.610
支架数[N (Min, Max)]	3 (1, 5)	3 (1, 6)	3.114	0.002
球囊扩张[例，%]	45 (86.5%)	152 (80.4%)	1.022	0.312
磨头大小[N (Min, Max)]	1.5 (1.25, 2.5)	1.5 (1.25, 1.75)	0.938	0.348

Table 3. Logistic multivariate regression analysis
表 3. Logistic 多因素回归分析

影响因素	β 值	SE 值	Wald χ^2 值	OR 值(95% CI)	p 值
LVEF	−0.031	0.015	4.017	0.970 (0.941, 0.999)	0.045
支架数量	0.396	0.201	3.896	1.486 (1.003, 2.202)	0.048
NLR	0.240	0.083	8.391	1.271 (1.081, 1.494)	0.004
THR	0.386	0.161	5.708	1.471 (1.072, 2.018)	0.017

3.2. NLR 和 THR 及二者联合与患者预后的相关性分析

以冠状动脉严重钙化患者旋磨术后植入药物洗脱支架是否发生 MACE 为变量，将可能影响患者临床预后的指标作为自变量进行 *Spearman* 相关性分析，结果表明支架数量(r = 0.185, p = 0.004)、NLR (r = 0.272, p < 0.001)、THR (r = 0.276, p < 0.001)及二者联合预测(r = 0.351, p < 0.001)与冠状动脉严重钙化患者旋磨术后是否发生 MACE 呈正相关，LVEF (r = −0.216, p = 0.001)与其呈负相关，见表 4。

Table 4. Correlation analysis between prognosis and clinically relevant indicators
表 4. 预后与临床相关指标的相关性分析

影响因素	r	p 值
LVEF	−0.216	0.001
支架数量	0.185	0.004
NLR	0.272	<0.001

续表

THR	0.276	<0.001
NLR 联合 THR	0.351	<0.001

3.3. NLR 和 THR 及二者联合对患者术后 MACE 发生的预测价值

运用 SPSS 26.0 软件通过 Logistic 模型算出 NLR 和 THR 联合因素的变量。运用 MedCalc 软件绘制 NLR 和 THR 及二者联合因素 ROC 曲线，结果显示，三者 ROC 曲线下面积分别为 0.691、0.703 和 0.764，灵敏度分别为 71.5%、65.38%、80.77%，特异度分别为 59.26%、71.43%、67.72%。NLR 和 THR 联合因素的 AUC 大于 NLR、THR (p = 0.047; p = 0.003)具有统计学意义(均 p < 0.05)，而 NLR 与 THR 之间的 AUC 差异无统计学意义(p = 0.820)。同时，Hosmer-Lemeshow 检验提示 NLR 和 THR 及二者联合校准度较好，见表 5、图 1。

Table 5. Area under the ROC curve and Hosmer-Lemeshow test for NLR, THR, and their combination
表 5. NLR、THR 及二者联合的 ROC 曲线下面积和 Hosmer-Lemeshow 检验

影响因素	AUC	95% CI	灵敏度	特异度	p 值			Hosmer-Lemeshow
					NLR	THR	二者联合	p 值
NLR	0.691	0.628~0.748	71.15%	59.26%	-	0.820	0.047	9.811 (0.279)
THR	0.703	0.641~0.760	65.38%	71.43%	0.820	-	0.030	6.142 (0.631)
二者联合	0.764	0.705~0.816	80.77%	67.72%	0.047	0.030	-	13.278 (0.103)

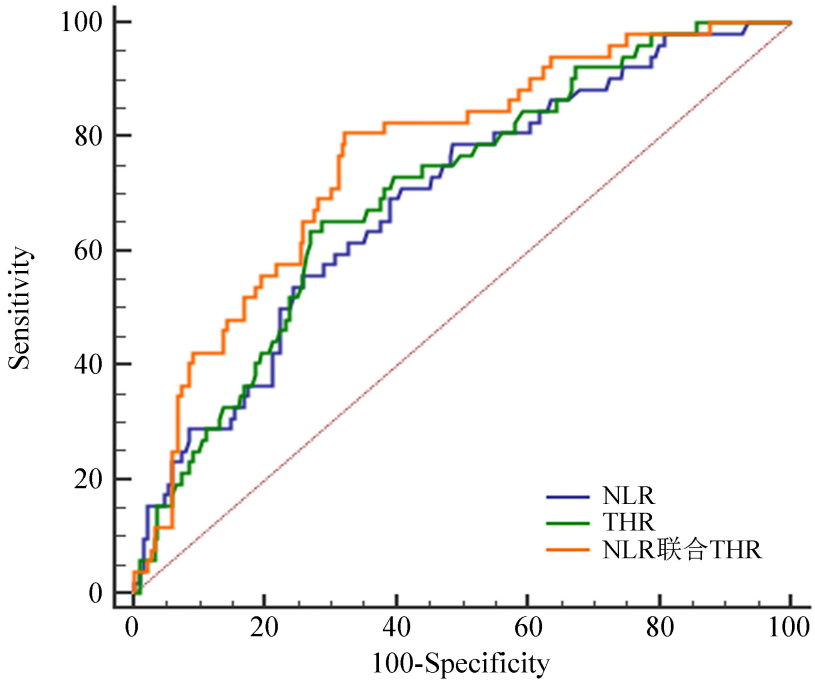

Figure 1. ROC curves of NLR, THR, and their combination in predicting clinical efficacy of drug-eluting stent implantation after rotational atherectomy in patients with severe coronary artery calcification
图 1. NLR、THR 及二者联合预测冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效的 ROC 曲线

4. 讨论

冠状动脉钙化的形成及发病率随着年龄的增加而增加[12] [13]，严重冠状动脉钙化往往伴随着血管成角及扭曲，因此冠脉旋磨术成为这类病变治疗的较好选择[14]。因其病变的复杂性，手术过程中往往容易出现支架膨胀不全、贴壁不良、血管夹层、穿孔及无复流等严重并发症，增加了支架内血栓形成及再狭窄等风险[15]，从而导致远期预后不良。因此，通过相关临床指标判断冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效有益于患者术后病情评估及治疗方案的制定。

NLR 及 THR 作为新的全身炎症指标和血脂指标，目前已证实与心血管疾病的发生发展及预后密切相关[16]-[18]。因两者均为比值指标，有效避免了血容量等因素的影响，较单一指标更稳定。

冠状动脉粥样硬化及钙化形成与炎症密切相关[4] [5]，旋磨术后血管内皮细胞受损及产生的斑块细小颗粒引起炎症反应，大量炎症细胞及炎症介质聚集，易造成支架内血栓及再狭窄形成。在此过程中，中性粒细胞的大量聚集常与炎症反应的发生、发展及严重程度密切相关[19] [20]，而淋巴细胞在机体炎症反应下则大量凋亡，产生大量炎症介质[21]，因此 NLR 可以放大体内炎症反应的效应，更优于原始单一指标。

总胆固醇和高密度脂蛋白分别是促进和抑制动脉粥样硬化的因子，其比值包含了低密度脂蛋白和高密度脂蛋白所表达的 98%的统计信息[22]，同时反映了脂蛋白颗粒大小和浓度信息[23] [24]，可以弥补低密度脂蛋白预测不良心血管事件所出现的残余风险[25] [26]，为患者增加无成本和递增的临床预后信息。

本研究结果表明，在校正相关因素后，NLR 及 THR 均与冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效相关(均 $p < 0.05$)，进一步采用 ROC 曲线分析 NLR、THR 及二者联合对其临床预后疗效的预测能力，AUC 分别为 0.691，0.703 和 0.764，提示三者均对冠状动脉严重钙化患者旋磨术后植入药物洗脱支架临床疗效有一定的预测价值，其中二者联合的 AUC 大于 NLR 和 THR (均 $p < 0.05$)，且表现出良好的灵敏度(80.77%)及特异度(67.72%)，说明二者联合具有更好的预测价值。

总之，NLR、THR 及二者联合对冠状动脉严重钙化患者旋磨术后植入药物洗脱支架的临床疗效具有初步判断价值，可为术后治疗方案的制定提供一定参考。然而，本研究存在以下局限性：第一，研究设计为回顾性分析，样本量有限，且患者年龄偏大，未能控制钙化斑块形态学特征等潜在混杂因素；第二，未将 NLR 与 THR 的预测效能与 SYNTAX 评分、GRACE 评分等成熟的冠心病风险模型进行直接比较，故二者相较于现有评分体系的增量预测能力尚不明确；第三，受数据可及性限制，部分计算上述评分所需的解剖学及临床变量存在缺失。综上，本研究结论需在上述局限性框架内谨慎解读。未来有待通过前瞻性、多中心研究设计，在更全面收集手术细节、术后管理数据及完善风险评分的基础上，进一步验证 NLR 与 THR 联合指标在该人群中的独立预测价值，并明确其在临床风险分层中的实际定位。

声　明

本研究为回顾性病历分析，所用数据均为匿名化处理，不涉及患者隐私及干预措施，故未申请伦理。

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