

乳腺癌细胞增殖核抗原 Ki-67 表达与肿瘤浸润淋巴细胞相关性的系统评价与 Meta 分析



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【摘要】目的 系统评价乳腺癌中细胞增殖核抗原 Ki-67 表达水平与肿瘤浸润淋巴细胞 (TILs) 水平的相关性。**方法** 计算机检索 PubMed、Embase 和 Web of Science 数据库, 搜集关于乳腺癌 Ki-67 表达水平与 TILs 水平的相关性研究, 检索时限均从建库至 2025 年 11 月 30 日。由 2 位研究者独立筛选文献、提取资料并评价纳入研究的偏倚风险后, 采用 RevMan 5.4 和 Stata 17.0 软件进行 Meta 分析。**结果** 共纳入 31 项研究, 包括 13 633 例乳腺癌患者。Meta 分析结果显示, Ki-67 高表达组的高 TILs 水平患者比例显著高于 Ki-67 低表达组 [RR=2.02, 95%CI (1.73, 2.36), $P < 0.001$]。亚组分析结果显示, 在不同类型 TILs、不同人群、不同样本量的亚组中, Ki-67 表达水平与 TILs 水平的相关性均与总 Meta 分析结果一致。敏感性分析显示总 Meta 分析结果稳健。**结论** 乳腺癌中 Ki-67 表达水平与 TILs 水平显著相关, 乳腺癌细胞增殖活跃程度可能与肿瘤微环境中免疫激活密切相关, 但上述结论尚需更多高质量研究予以验证。

【关键词】 乳腺癌; 肿瘤浸润淋巴细胞; 细胞增殖抗原 Ki-67; 系统评价; Meta 分析

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Correlation between the expression of cell proliferation nuclear antigen Ki-67 and tumor-infiltrating lymphocytes in breast cancer: a systematic review and Meta-analysis

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【Abstract】Objective To systematically review the correlation between cell proliferation nuclear antigen Ki-67 expression and tumor-infiltrating lymphocytes (TILs) level in breast cancer. **Methods** PubMed, Embase and Web of Science databases were systematically searched to collect studies on the correlation between Ki-67 expression level and TILs level in breast cancer from inception to November 30, 2025. Two researchers independently screened literature, extracted data and assessed the risk of bias of included studies. Meta-analysis was performed using RevMan 5.4

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software and Stata 17.0 software. **Results** A total of 31 studies involving 13,633 patients with breast cancer were included. Meta-analysis results showed that the proportion of patients with high levels of TILs in the Ki-67 high-expression group was significantly higher than that in the Ki-67 low-expression group [RR=2.02, 95%CI (1.73, 2.36), $P < 0.001$]. Subgroup analysis showed that the positive correlation between Ki-67 expression level and TILs level remained consistent with the overall Meta-analysis results across different subgroups, including different TILs subtypes, study populations, and sample sizes. Sensitivity analysis indicates that the results of the overall findings of the Meta-analysis was robust. **Conclusion** Current evidence shows that the TILs level is significantly positively correlated with Ki-67 expression level in breast cancer. This finding suggests that the proliferation activity of breast cancer cells may be closely associated with immune activation in the tumor microenvironment, but the above conclusion needs to be verified by more high-quality studies.

【Keywords】 Breast cancer; Tumor-infiltrating lymphocytes; Cell proliferation nuclear antigen Ki-67; Systematic review; Meta-analysis

据全球癌症统计数据报告, 2022年全球女性乳腺癌新发病例数达229.6万, 位居恶性肿瘤发病例数第2位, 同时在女性恶性肿瘤中, 其发病例数居首位、死亡例数居第2位^[1]。2026年美国癌症统计数据显示, 乳腺癌新发病例达32.19万例, 死亡病例4.21万例, 分别位居美国女性恶性肿瘤发病和死亡的第1位和第2位^[2]; 据中国国家癌症中心数据显示, 2022年乳腺癌新发病例35.72万人, 死亡病例7.5万人, 分别位于女性恶性肿瘤发病和死亡的第2位和第5位^[3]。综合全球和两大经济体癌症统计数据可见, 尽管乳腺癌患者的生存率不断提升, 但该病在癌症死亡病例中的占比仍位居前5名。因此, 持续探索乳腺癌的生物学行为和相关机制, 可为乳腺癌患者的诊断、治疗和预后提供依据。

肿瘤免疫在乳腺癌的发生发展中扮演着重要角色, 已成为乳腺癌领域的研究热点^[4-5]。肿瘤浸润淋巴细胞 (tumor-infiltrating lymphocytes, TILs) 作为肿瘤免疫微环境中重要的免疫细胞, 可通过调控肿瘤细胞的生物学行为影响乳腺癌的侵袭与转移^[6-7]。研究发现, 乳腺癌中TILs的水平与新辅助治疗反应^[8-9]和患者预后^[10-11]密切相关。研究结果显示, 肿瘤直径越大、组织学分级越高的乳腺癌, 其TILs水平也越高, 表明乳腺癌患者高TILs水平可能与肿瘤细胞的高增殖特性相关^[12-13]。肿瘤细胞增殖核抗原Ki-67的表达水平与乳腺癌细胞的高增殖相关, 且会影响抗肿瘤药物的治疗反应^[14-16]和乳腺癌的复发转移及患者预后^[17-19]。因此, Ki-67表达水平与TILs水平之间是否存在相关性, 以及这种相关性在预测乳腺

癌治疗反应及预后中的价值值得深入探讨。目前, 已有多项研究分析了乳腺癌中Ki-67表达水平与TILs水平的相关性^[20-25], 其中部分研究发现乳腺癌中Ki-67高表达与高TILs水平相关^[24-25], 但这一相关性仍缺乏系统的证据支持。

本研究对已发表的乳腺癌Ki-67表达水平与TILs水平相关性文献进行系统评价与Meta分析, 并对乳腺癌中Ki-67表达水平与不同分子标记TILs水平的相关性进行分析, 旨在为阐明二者相关性在预测乳腺癌治疗反应和预后中的意义奠定研究基础, 为乳腺癌肿瘤免疫评估提供新策略。

1 资料与方法

本研究根据PRISMA作为规范标准进行报告^[26]。

1.1 纳入与排除标准

纳入标准: ①研究类型: 队列研究和病例对照研究; ②研究对象: 明确研究对象或者研究队列为经病理诊断证实为乳腺癌患者; ③暴露因素: Ki-67表达水平 [通过免疫组织化学 (immunohistochemistry, IHC) 对Ki-67表达水平进行评估, 并按其表达水平分组]; ④结局指标: TILs水平 [通过苏木素-伊红 (hematoxylin-eosin, HE) 染色或IHC对TILs水平进行评估, 并按其水平分组]。

排除标准: ①会议论文、仅为摘要发表或无法获得全文的文献; ②无完整的乳腺癌标本HE染色和IHC结果的文献; ③数据信息不全、无法提取研究所需数据的文献; ④重复发表的文献。

1.2 文献检索策略

计算机检索PubMed、Embase和Web of Science

数据库, 搜集关于乳腺癌患者Ki-67表达水平与TILs水平的相关性研究, 检索时限均从建库至2025年11月30日。此外, 采取手工检索文献和参考文献回溯法寻找相关文献。检索采取主题词和自由词相结合的方式。检索词包括Breast cancer、Breast carcinoma、Mammary cancer、Mammary carcinoma、Ki-67、MKI67、MIB-1、Tumor-infiltrating lymphocytes、TILs、Lymphocytes、Tumor-Infiltrating、T-Lymphocytes等。以PubMed为例, 检索策略见附件框1。

1.3 文献筛选与资料提取

由2名研究者独立筛选文献、提取资料并交叉核对。如有分歧, 则请研究设计者复核或与研究组成员讨论解决。借助文献管理软件(医学文献王)管理文献题录、摘要信息、全文等。文献筛选时首先独立阅读候选文献的标题和摘要, 剔除不符合/与主题无关的候选文献; 然后, 阅读候选文献全文, 以确定最终是否纳入。资料提取内容包括: 第一作者, 研究人群地区, 发表年份, 研究设计, 年龄中位数及范围, 分子分型 [Luminal型、三阴性乳腺癌(triple-negative breast cancer, TNBC)、人类表皮生长因子受体2 (human epidermal growth factor receptor 2, HER2) 过表达型], 组织学分级, TNM (tumor node metastasis) 分期, 高Ki-67表达的数量、截断值和相关抗体, TIL类型及其高水平的数量、截值和方法, 主要的TILs分子标记 [包括分化簇3 (cluster of differentiation 3, CD3)、CD4、CD8、CD45和叉头框蛋白P3 (forkhead box protein P3, FOXP3)] 等。

1.4 纳入研究的偏倚风险评价

2名研究者采用纽卡斯尔-渥太华量表(Newcastle-Ottawa Scale, NOS)^[27]评价纳入研究的偏倚风险并交叉核对, 如有分歧, 与研究设计者讨论解决。评估包括8个方面, 9个条目; 根据得分分为低、中和高质量3个等级 (<5分, 5~<8分, 8~9分)。

1.5 统计学分析

采用RevMan 5.4和Stata 17.0软件进行Meta分析。所有病例数据按Ki-67表达高或低分组, 作为队列标记, 统计Ki-67高或低表达队列中高TILs水平的例数。二分类变量采用相对危险度(relative risk, RR)为效应分析统计量, 并提供其95%置信区间(confidence interval, CI)。纳入研究结果间的异质性采用 χ^2 检验进行分析, 同时

结合 I^2 值定量判断异质性大小。若各研究结果间无统计学异质性($I^2 \leq 50\%$ 或 $P > 0.10$), 则采用固定效应模型进行Meta分析; 反之, 则使用随机效应模型进行Meta分析。通过亚组分析探讨合并结果可能的影响因素; 采用逐一排除法或省略小样本量研究等方法进行敏感性分析, 以探讨异质性来源及对结果稳定性的影响。使用漏斗图、Begg's检验和Egger's检验探索纳入研究的发表偏倚^[28]。所有检验均采用双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 文献筛选流程及结果

初检共获得相关文献1 286篇, 经逐层筛选后, 最终纳入31项研究^[20-25, 29-53], 包括13 633例乳腺癌患者, 文献筛选流程及结果见图1。

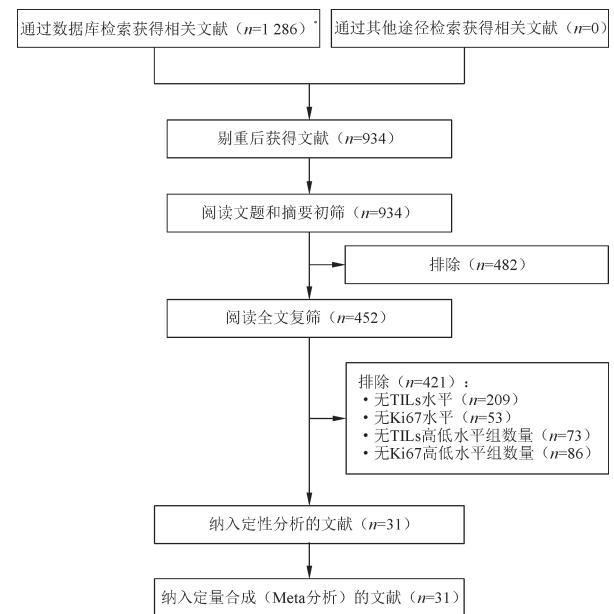


图1 文献筛选流程

Figure 1. Flow chart of literature screening

注: *检索的数据库及检出文献数具体为PubMed (n=224)、Web of Science (n=694)、Embase (n=368)。

2.2 纳入研究基本特征与偏倚风险评价

纳入研究的基本特征和偏倚风险评价结果见附件表1。31项研究中, 队列研究16项^[21-25, 29, 31, 35, 38-43, 51, 53], 病例对照研究1项^[34], 未描述研究类型呈现队列研究14项^[20, 30, 32-33, 36-37, 44-50, 52]。22项研究^[20-21, 23-24, 31-32, 34, 36, 38-41, 43-47, 49-53]根据国际TILs工作组2014年提出的标准化方法^[54]判断TIL水平。最常报告的TILs截值为10%, 共17项研究^[20-21, 24, 32-33, 35-37, 40-41, 43-45, 47, 50-51, 53]。按照不同截

值, 18项研究^[21, 23, 25, 34-36, 38-39, 41-43, 45-47, 49-50, 52-53]根据TILs的百分比分为TILs高水平组和低水平组, 9项研究^[20, 24, 32-33, 37, 40, 44, 48, 51]则分成TILs高、中、低水平3组。为便于分析, 本研究将以11%为截值的研究归为TIL 10%截值组, 以49%为截值的研究归为TIL 50%截值组, 中等水平组归入TILs高水平组进行分析。对于Ki-67水平判断, 10项研究^[20-21, 25, 30, 32, 34, 39, 45, 48, 51]报告的Ki-67水平截值为20%。按照以上截值, 26项研究^[21-23, 25, 29-37, 39-42, 45-53]根据Ki-67的百分比分为Ki-67高、低表达组2组; 3项研究^[20, 24, 44]分成Ki-67高、中、低表达3组; 2项研究^[38, 43]分成Ki-67高、较高、中和低表达4组。为便于分析, 本研究将中等表达组或较高表达组归入Ki-67高表达组进行分析。纳入研究的NOS质量评分为5~9分。

2.3 Meta分析结果

2.3.1 Ki-67表达水平与TILs水平的相关性

共纳入31项研究。研究间有统计学异质性($I^2=82\%$, $P < 0.001$), 采用随机效应模型进行Meta分析。结果显示, Ki-67高表达组的高TILs水平患者比例高于Ki-67低表达组, 差异有统计

学意义[RR=2.02, 95%CI (1.73, 2.36), $P < 0.001$], 说明Ki-67表达水平与TILs水平具有相关性, 见附件图1。

2.3.2 亚组分析

根据不同样本量和研究人群的地区进行亚组分析, 结果显示, 各亚组中Ki-67表达水平与TILs水平的相关性均有统计学意义($P < 0.05$), 且2个样本量亚组间($P=0.13$)、3个地区亚组间($P=0.70$)均无统计学异质性。按不同的TILs截值进行亚组分析, 结果显示, 除TILs 15%和50%截值的亚组中Ki-67表达水平与TILs水平无明显相关性($P > 0.05$)外, 5%、10%、20%、30%和60%截值亚组中Ki-67表达水平与TILs水平的相关性均有统计学意义($P < 0.05$), 且7个亚组间无统计学异质性($P=0.33$)。按不同的Ki-67截值分组进行亚组分析, 结果显示, 除10%和38%的亚组中Ki-67表达水平与TILs水平无明显相关性($P > 0.05$)外, 14%、15%、20%、22.5%、25%、30%和35%的亚组中Ki-67表达水平与TILs水平的相关性均有统计学意义($P < 0.05$), 但9个亚组间存在统计学异质性($P=0.05$), 见表1。

表1 以TILs截值、Ki-67截值、样本量、研究人群地区为分组变量的亚组分析

Table 1. Subgroup analysis based on TILs cutoff, Ki-67 cutoff, sample size, and study population location as grouping variants

亚组	纳入研究数	异质性检验		效应模型	Meta分析	
		I ² 值 (%)	P值		RR值 (95%CI)	P值
TILs 截值						
5%	3 ^[25, 38, 48]	91	<0.001	随机	1.67 (1.09, 2.57)	0.020
10%	18 ^[20-21, 24, 32-33, 35-37, 40-41, 43-45, 47, 50-53]	84	<0.001	随机	2.31 (1.86, 2.87)	<0.001
15%	1 ^[31]	-	-	-	1.28 (0.66, 2.48)	0.460
20%	1 ^[23]	-	-	-	1.97 (1.21, 3.22)	0.006
30%	1 ^[34]	-	-	-	2.80 (1.88, 4.15)	<0.001
50%	3 ^[42, 46, 49]	91	<0.001	随机	2.18 (0.22, 21.40)	0.500
60%	1 ^[39]	-	-	-	4.40 (1.10, 17.62)	0.040
Ki-67 截值						
10%	1 ^[44]	-	-	-	1.67 (0.58, 4.75)	0.340
14%	10 ^[36-38, 40-42, 46, 49-50, 52]	67	0.001	随机	2.21 (1.40, 3.49)	<0.001
15%	1 ^[24]	-	-	-	3.16 (2.53, 3.96)	<0.001
20%	10 ^[20-21, 25, 30, 32, 34, 39, 45, 48, 51]	87	<0.001	随机	2.10 (1.58, 2.78)	<0.001
22.5%	1 ^[22]	-	-	-	1.98 (1.33, 2.94)	<0.001
25%	5 ^[29, 33, 43, 47, 53]	89	<0.001	随机	1.81 (1.34, 2.43)	<0.001
30%	1 ^[35]	-	-	-	1.90 (1.20, 3.00)	0.006
35%	1 ^[23]	-	-	-	1.97 (1.21, 3.22)	0.006
38%	1 ^[31]	-	-	-	1.28 (0.66, 2.48)	0.460
样本量 (例)						
≥ 440	9 ^[21, 24-25, 33-34, 38, 43, 47, 53]	92	<0.001	随机	2.33 (1.83, 2.97)	<0.001
< 440	22 ^[20, 22-23, 29-32, 35-37, 39-42, 44-46, 48-52]	64	<0.001	随机	1.82 (1.49, 2.23)	<0.001
地区						
亚洲	23 ^[21, 29-37, 41-53]	82	<0.001	随机	1.95 (1.62, 2.35)	<0.001
欧洲	6 ^[20, 22, 24-25, 38-39]	73	0.002	随机	2.22 (1.70, 2.89)	<0.001
美洲	2 ^[23, 40]	0	0.540	固定	2.15 (1.46, 3.15)	<0.001

根据不同的TILs分子标记进行亚组分析,结果显示,各亚组中Ki-67表达水平与TILs水平的相关性均有统计学意义($P < 0.05$),但5个亚组间存在统计学异质性($P=0.004$)。根据不同的乳腺癌分子分型进行亚组分析,结果显示,除

HER2过表达亚组Ki-67表达水平与TILs水平无明显相关性($P > 0.05$)外,Luminal型和TNBC型亚组中Ki-67表达水平与TILs水平的相关性均有统计学意义($P < 0.05$),且3个亚组间无统计学异质性($P=0.71$),见表2。

表2 不同TILs分子标记和不同乳腺癌分子分型亚组分析

Table 2. Subgroup analysis of different TILs molecular markers and different breast cancer molecular subtypes

亚组	纳入研究数	异质性检验结果		效应模型	Meta分析结果	
		I ² 值 (%)	P值		RR值 (95%CI)	P值
TILs分子标记						
CD3	1 [22]	-	-	-	2.15 (1.45, 3.20)	0.001
CD4	3 [22,30-31]	0	0.540	固定	1.39 (1.17, 1.65)	0.001
CD8	4 [22,30-31,47]	0	0.580	固定	1.70 (1.44, 2.01)	<0.001
CD45	1 [22]	-	-	-	2.36 (1.60, 3.48)	<0.001
FOXP3	3 [22,30,35]	34	0.220	固定	2.20 (1.85, 2.62)	<0.001
分子分型						
Luminal	4 [34,38,44,47]	59	0.060	随机	1.91 (1.39, 2.62)	<0.001
TNBC	3 [23,31,42]	33	0.220	固定	1.95 (1.32, 2.88)	<0.001
HER2过表达	1 [37]	-	-	-	3.81 (0.66, 22.06)	0.140

2.4 敏感性分析

采用逐一剔除单个研究后进行敏感性分析,结果显示,剔除单个研究后合并结果未发生明显改变,见附件表2。排除效应量最大的研究^[53]、仅包括大样本量研究($n \geq 440$)^[21, 24-25, 33-34, 38, 43, 47, 53]、仅包括高质量研究(评分 ≥ 7)^[21-25, 29-30, 34, 37-38, 40, 43, 47-49, 53],合并结果也未发生明显改变,见附件表3。提示Meta分析的结果稳健。

2.5 发表偏倚

针对纳入的31项研究绘制漏斗图进行发表偏倚检验,结果显示,各研究点左右分布不对称,提示可能存在发表偏倚,见附件图2。采用Egger's检验($t=0.91, P=0.370$)和Begg's检验($z=0.44, P=0.659$)方法分析,提示纳入研究中存在发表偏倚的可能性较小。

3 讨论

准确识别肿瘤免疫状态对预测乳腺癌的治疗反应与患者预后尤为重要。然而,目前临床仍缺乏能够精准、便捷评估肿瘤免疫状态的预测手段。基于TILs在乳腺癌免疫状态评估和治疗指导中的证据,国际TILs工作组推荐将TILs检测纳入乳腺癌病理检查,用于辅助判断治疗反应、评估患者预后^[54]。近年来,肿瘤细胞增殖能力与肿瘤免疫状态的相关性备受关注。Ki-67作为临床评

估乳腺癌增殖状态的重要分子标志物,其与肿瘤组织TILs水平的相关性已被广泛报道。基于此,本文对现有乳腺癌领域中Ki-67表达水平与TILs水平相关性的研究进行系统评价,结果显示,Ki-67高表达乳腺癌组的高TILs水平患者比例高于Ki-67低表达组,该结果可为综合评估乳腺癌肿瘤免疫状态与肿瘤细胞增殖能力提供相关的循证证据。

肿瘤免疫状态与肿瘤细胞增殖之间存在广泛且复杂的关联。增殖活跃的肿瘤可通过吸引免疫细胞浸润等多种途径使肿瘤免疫微环境更活跃^[55]。Ki-67高表达的肿瘤细胞处于增殖活跃状态,会暴露较多抗原相关成分,进而激活人体免疫系统,吸引较多的淋巴细胞迁移到肿瘤组织,导致抗肿瘤免疫细胞浸润增多^[56];此外,Ki-67高表达的肿瘤细胞因增殖迅速,对营养物质和氧气的需求显著增加,从而诱导肿瘤血管生成,这些新生血管不仅能为肿瘤细胞提供营养支持,还会影响免疫细胞向肿瘤组织的迁移与浸润^[57];同时,Ki-67高表达、增殖能力强的肿瘤细胞还可通过直接释放多种细胞因子和趋化因子,招募免疫细胞浸润至肿瘤组织,发挥相应的抗肿瘤或促肿瘤效应^[58]。上述研究结果表明,反映肿瘤增殖水平的Ki-67表达与反映肿瘤免疫微环境状态的TILs水平存在相关性。此外,肿瘤组织中Ki-67表达还与其他免疫细胞浸润存在关联。一项多组

学和单细胞测序研究发现, Ki-67高表达的TNBC中发挥抗肿瘤作用的M1型巨噬细胞浸润显著增多, 而Ki-67低表达的TNBC中则有更多促肿瘤的M2型巨噬细胞浸润^[59]。证实增殖水平高的肿瘤微环境中肿瘤免疫状态也更为活跃。

Ki-67表达水平可影响TILs水平与乳腺癌预后及治疗反应的相关性。一项纳入717例浸润性乳腺癌患者的研究显示, 尽管所有患者的TILs水平与总生存期和无病生存期(disease free survival, DFS)之间的关联无统计学意义, 但在Ki-67高表达亚组中, 高TILs水平与良好的DFS显著相关; 且多因素分析表明, 高TILs水平是Ki-67高表达组患者获得良好DFS的独立影响因素^[33]。上述研究证实, 乳腺癌中Ki-67高表达可诱导肿瘤微环境中具有抗肿瘤作用的M1型巨噬细胞和TILs呈高水平浸润状态, 继而影响肿瘤细胞的生物学行为及患者预后, 即若肿瘤呈高增殖状态, 但同时有良好的免疫状态, 可改善乳腺癌患者预后。然而, 不同分子标记的TILs具有不同的肿瘤生物学效应^[60]。对新辅助化疗(neoadjuvant chemotherapy, NAC)前乳腺癌样本进行TILs特征分析发现, HER2+且治疗反应良好的肿瘤中CD3⁺CD8⁺FOXP3⁺TILs水平明显高于治疗反应欠佳者; 对NAC前后配对样本的分析则显示, 与其他亚型乳腺癌TILs相比, Luminal型和TNBC残余肿瘤中CD3⁺CD8⁺FOXP3⁺TILs水平更高, 且TNBC残余肿瘤中CD3⁺CD8⁺FOXP3⁺TILs水平也更高^[9]。此外, 在乳腺癌易感基因1(BRCA1)和BRCA2相关乳腺癌中, CD4⁺、CD8⁺或FOXP3⁺TILs高水平与较低的死亡率显著相关, 其中CD8⁺TILs高水平还与更佳的DFS显著相关^[61]。这些结果证实, 不同分子标记的TILs水平对乳腺癌进展及治疗反应的影响较为复杂。本研究结果显示, Ki-67表达水平与CD3、CD4等5种分子标记的TILs水平均具有相关性, 且各亚组内均无统计学异质性, 提示在不同乳腺癌患者群体中, Ki-67表达水平与相同分子标记TILs水平的相关性具有高度一致性, 可为进一步探索两者相关性用于预测疾病进展、评估治疗反应提供系统评价的证据基础。此外, 分子分型亚组分析发现, Luminal型乳腺癌和TNBC中Ki-67表达水平与TILs水平存在显著相关性, 而HER2过表达型乳腺癌(仅纳入1项研究)中二者无相关性。提示Ki-67表达水平与TILs水平的相关性在不同分子分型乳腺癌中的稳定性仍需更多研究进一步探索。

本研究存在一定局限性。首先, TILs水平、Ki-67表达水平的检测均为半定量方式, 纳入研究中对两者的判定标准可能存在差异, 可能会对Ki-67表达水平与TILs水平的真实相关性产生一定影响。其次, 纳入研究中Ki-67和TILs截值存在差异, 可能会干扰对二者相关性的准确评价。再者, 由于纳入研究很少报告TILs分子标记和乳腺癌分子分型, 本项Meta分析仅能对部分研究进行Ki-67表达水平与不同分子标记的TILs水平的相关性分析, 以及Ki-67表达水平与不同分子分型亚组中TILs水平的相关性分析。最后, 本研究仅检索了以英文发表的文献, 可能存在潜在的语言偏倚。基于上述局限性, 建议谨慎解读本研究证据。

综上, 本研究结果表明, 乳腺癌中Ki-67表达水平与TILs水平具有相关性。在临床实践中, 通过评估乳腺癌患者的Ki-67表达水平, 可初步预测其肿瘤微环境的免疫状态。本研究为乳腺癌肿瘤免疫状态与肿瘤细胞增殖能力的相关性提供了临床层面的证据, 可为探索乳腺癌肿瘤免疫评估的新策略提供参考。然而, 在不同分子分型乳腺癌中Ki-67表达水平与TILs水平的相关性, 以及Ki-67表达水平与不同分子标记的TILs水平相关性的临床意义仍需设计更多高质量研究进行解析。

附件见《医学新知》官网附录 (<https://yxzx.whuznhmedj.com/futureApi/storage/appendix/202510138.pdf>)

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