



穿刺活检针道处理方式对钇-90选择性内放射治疗肝癌的影响

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引用本文:

徐振远, 刘学, 申淑群, 等. 穿刺活检针道处理方式对钇-90选择性内放射治疗肝癌的影响[J]. 中国临床医学, 2025, 32(2): 288-294.

XU Z Y, LIU X, SHEN S Q, et al. Effect of different liver biopsy needle track management on Yttrium-90 selective internal radiation therapy on liver cancer[J]. Chin J Clin Med, 2025, 32(2): 288-294.

在线阅读 View online: <https://doi.org/10.12025/j.issn.1008-6358.2025.20250084>

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中国临床医学. 2025, 32(1): 9-14 <https://doi.org/10.12025/j.issn.1008-6358.2025.20241508>

DOI: 10.12025/j.issn.1008-6358.2025.20250084

· 技术与方法 ·

穿刺活检针道处理方式对钇-90 选择性内放射治疗肝癌的影响



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[摘要] **目的** 探讨肝癌患者穿刺活检后不同针道处理方式对钇-90 微球选择性内放射治疗 (Yttrium-90 microsphere selective internal radiation therapy, ^{90}Y -SIRT) 的影响。**方法** 回顾性分析 2023 年 6 月至 2024 年 12 月肝组织穿刺活检后接受 $^{99\text{m}}\text{Tc}$ 标记的大颗粒聚合白蛋白 (Technetium- $^{99\text{m}}$ -macroaggregated albumin, $^{99\text{m}}\text{Tc}$ -MAA) 评估和 ^{90}Y -SIRT 的 21 例肝癌患者的临床资料, 记录针道处理方式、肝动-静脉分流情况及肺分流百分数 (lung shunt fraction, LSF), 分析不同方式处理穿刺针道后肝动静脉瘘 (hepatic arteriovenous fistula, HAVF) 的发生情况, 以及应对措施。**结果** 21 例肝癌患者中, 7 例 (医用胶组) 穿刺活检后即刻使用医用胶 [α -氰基丙烯酸正丁酯 (N-butyl 2-cyanoacrylate, NBCA)] 封堵穿刺针道, $^{99\text{m}}\text{Tc}$ -MAA 评估中未出现明显 HAVF; 14 例 (非医用胶组) 采用延迟拔针法或明胶海绵颗粒封堵法, 其中 7 例患者出现明显 HAVF, 采用医用胶封堵瘘道。医用胶组的 LSF 显著低于非医用胶组 [$(7.06 \pm 2.33) \%$ vs $(12.43 \pm 7.73) \%$, $P=0.037$]。21 例患者均顺利完成 ^{90}Y -SIRT。**结论** 肝组织穿刺活检可能通过形成医源性 HAVF 影响 ^{90}Y -SIRT, 活检取材后即刻以医用胶封堵针道或 $^{99\text{m}}\text{Tc}$ -MAA 评估中使用医用胶封堵瘘道可降低其影响。

[关键词] 肝癌; 选择性内放射治疗; 钇-90; 肝活检; 动静脉瘘

[中图分类号] R 735.7 **[文献标志码]** A

Effect of different liver biopsy needle track management on Yttrium-90 selective internal radiation therapy on liver cancer

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[Abstract] **Objective** To explore the effect of different needle track management on Yttrium-90 microsphere selective internal radiation therapy (^{90}Y -SIRT) on liver cancer after liver biopsy. **Methods** A retrospective analysis was conducted on the clinical data of 21 patients with liver cancer who underwent Technetium- $^{99\text{m}}$ -macroaggregated albumin ($^{99\text{m}}\text{Tc}$ -MAA) evaluation and ^{90}Y -SIRT after liver biopsy from June 2023 to December 2024. The methods of needle track management, hepatic arteriovenous shunting, and lung shunt fraction (LSF) were recorded. The occurrence of hepatic arteriovenous fistula (HAVF), as well as the corresponding countermeasures were analyzed. **Results** Among the 21 liver cancer patients, 7 cases (medical glue group) underwent embolization of the needle tract with medical glue (N-butyl 2-cyanoacrylate [NBCA]) immediately after biopsy, and no significant HAVF was observed during the $^{99\text{m}}\text{Tc}$ -MAA tests; 14 cases (non-medical glue group) were treated with delayed needle extraction or gelatin sponge particle blocking after biopsy, among which 7 cases developed significant HAVF, and the fistulas were treated with NBCA. The LSF of the medical glue group was significantly lower than that of the non-medical glue group [$(7.06 \pm 2.33) \%$ vs $(12.43 \pm 7.73) \%$, $P=0.037$]. All 21 patients successfully completed ^{90}Y -SIRT. **Conclusions** Liver biopsy may affect ^{90}Y -SIRT by causing iatrogenic HAVF. Immediate NBCA-embolization of the needle tract after biopsy or timely NBCA-embolization of fistulas during $^{99\text{m}}\text{Tc}$ -MAA tests may reduce the impact.

[Key Words] liver cancer; selective internal radiation therapy; Yttrium-90; liver biopsy; arteriovenous fistula

肝细胞癌 (hepatocellular carcinoma, HCC) 是中国癌症相关死亡的第二大常见原因。中国约 85% 的 HCC 患者在确诊时已是中晚期, 无外科手

术机会, 只能接受局部或全身治疗降低肿瘤负荷、延长生存期^[1]。钇-90 微球选择性内放射治疗 (Yttrium-90 microsphere selective internal radiation

[收稿日期] 2025-01-23 **[接受日期]** 2025-03-03

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therapy, ^{90}Y -SIRT) 作为肝癌的局部微创治疗手段, 在国外已有近 20 年的临床使用经验, 其安全性和有效性得以验证。近年来, ^{90}Y -SIRT 在我国逐步推广, 成为治疗肝癌的重要手段之一^[2-4]。与经导管肝动脉化疗栓塞术 (transcatheter arterial chemoembolization, TACE) 相比, ^{90}Y -SIRT 操作更加复杂、治疗更加精准, 术前须进行特殊的影像学评估, 包括锝-99m 标记的大颗粒聚合白蛋白 (Technetium-99m-macroaggregated albumin, $^{99\text{m}}\text{Tc}$ -MAA) 灌注以及单光子发射计算机断层成像/计算机断层成像 (single-photon emission computed tomography/computed tomography, SPECT/CT) 检测, 以模拟 ^{90}Y 微球在肝内的分布以及肺部、胃肠道的分流情况^[5-6]。 $^{99\text{m}}\text{Tc}$ -MAA 评估中, 明显的肝动-静脉分流可导致 $^{99\text{m}}\text{Tc}$ -MAA 异位分布, 增加肺分流百分数 (lung shunt fraction, LSF), 从而增加 ^{90}Y -SIRT 难度及风险。肝动-静脉分流即肝动静脉瘘 (hepatic arteriovenous fistula, HAVF), 是指肝动脉与门静脉或肝静脉之间形成异常吻合支, 可分为肝动脉-门静脉瘘 (hepatic artery-portal venous fistula, HAPVF)、肝动脉-肝静脉瘘 (hepatic artery-hepatic venous fistula, HAHVF)、混合型 3 种, 其中 HAPVF 发生率较高^[7]。

肝穿刺活检是肝癌的常规诊断手段, 可以明确病灶性质及分子分型, 从而指导后续治疗、判断患者预后^[8]。Dutta 等^[9]和 Pupilim 等^[10] 研究报道, 肝穿刺活检后可能因瘘道形成医源性 HAVF。因此, 本研究对单中心接受肝穿刺活检后 ^{90}Y -SIRT 的肝癌患者的临床资料进行分析, 探讨不同穿刺针道处理方式对 ^{90}Y -SIRT 的影响。

1 资料与方法

1.1 研究对象 回顾性分析 2023 年 6 月至 2024 年 12 月海军军医大学第三附属医院穿刺活检后接受 $^{99\text{m}}\text{Tc}$ -MAA 评估的 21 例肝癌患者的临床资料。所有患者完成术前影像学评估, 且于穿刺活检后 10 d 内行 $^{99\text{m}}\text{Tc}$ -MAA, 并最终完成 ^{90}Y -SIRT。本中心根据《钇-90 微球选择性内放射治疗肝脏恶性肿瘤规范化操作专家共识 (2024 版)》^[5], 排

除 ^{90}Y -SIRT 绝对禁忌证和相对禁忌证。

1.2 材料与仪器 采用美国 Argon 公司的活检穿刺枪 (BioPince™ Ultra 全芯活检针) 进行肝脏穿刺活检, 荷兰 Philips 公司的彩色超声诊断仪 (ClearVue 580) 进行超声检查, 美国 GE 公司的数字血管造影成像系统 (INNOVA 3100-IQ) 进行动脉造影。明胶海绵颗粒购自杭州艾力康医药科技有限公司。

1.3 超声引导下肝癌穿刺活检 21 例患者均使用 16G BioPince™ Ultra 全芯活检针。穿刺点常规消毒、铺巾, 局部浸润麻醉, 超声引导下使用 16G 同轴穿刺针穿刺至预定位置, 使用全芯活检枪取材, 取 1~2 条长约 2 cm 的组织条, 退出活检枪。7 例患者即刻使用医用胶封堵穿刺针道, 3 例患者使用明胶海绵颗粒封堵法, 11 例采用延迟拔针法。根据活检针道处理方式将患者分为医用胶组和非医用胶组 (明胶海绵颗粒封堵法和延迟拔针法)。(1) 医用胶配置: 以 5 mL 注射器先后抽取 1 mL 医用胶 [α -氰基丙烯酸正丁酯 (N-butyl 2-cyanoacrylate, NBCA) 及 1 mL 碘油, 混匀后备用。(2) 明胶海绵颗粒配置: 以 10 mL 注射器抽取 3~5 mL 生理盐水, 与明胶海绵颗粒 (710~1 000 μm) 混匀后备用。(3) 延迟拔针法: 活检取材后将针芯放入穿刺针, 超声引导下拔出穿刺针至肝包膜下 1~2 cm, 静置 3~5 min 后拔出针芯, 无活动性出血即可全部拔除。

1.4 $^{99\text{m}}\text{Tc}$ -MAA 及 ^{90}Y -SIRT 使用 Seldinger 法经股动脉穿刺置管, 进行选择性动脉造影, 包括但不局限于腹腔干、肝总动脉、肝固有动脉及肝内动脉分支。使用锥形束 CT (cone beam computed tomography, CBCT) 检查, 结合术前影像仔细识别肿瘤供血动脉及异常解剖, 记录与穿刺针道相关的 HAVF。对可能导致 ^{90}Y 微球异位分布的解剖异常血管行预防性栓塞。对于明显 HAVF, 进一步行分支动脉造影以确定责任动脉, 注入医用胶与碘油混悬液 (比例 1:3) 予以栓塞; 对于造影后责任动脉不明的 HAVF, 行门静脉造影, 使用医用胶与碘油混悬液 (比例 1:3) 予以栓塞。结合血流动力学参数、肿瘤血供特点确定靶血管及

^{99m}Tc -MAA 输注剂量。2 h 内完成 SPECT/CT 显像, 分析 ^{90}Y 微球肝内分布以及肺部、消化道分流情况, 计算处方剂量。2 周内完成 ^{90}Y -SIRT。

1.5 统计学处理 采用 SPSS 26.0 软件进行统计学分析。计量资料以 $\bar{x} \pm s$ 表示, 采用 t 检验; 计数资料以 $n(\%)$ 表示, 采用 Fisher 确切概率法。检验水准 (α) 为 0.05。

2 结果

2.1 肝癌患者基线资料 21 例肝癌患者中, 医用胶组 7 例、非医用胶组 14 例。活检与 ^{99m}Tc -MAA 评估间隔时间 (3.4 ± 2.4) d, LSF (11.64 ± 7.30)%。结果 (表 1) 显示: 医用胶组和非医用胶组患者的年龄、性别、肿瘤最大径、活检与 ^{99m}Tc -MAA 评估间隔时间和病理分型差异均无统计学意义。

2.2 HAVF 发生情况及处理 21 例肝癌患者活检后均无出血等并发症。医用胶组的 7 例患者在 ^{99m}Tc -MAA 评估中均未出现明显 HAVF (图 1)。非医用胶组的 14 例患者中, 7 例 (50.0%) 出现穿刺相关 HAVF, 其中 3 例为 HAPVF, 使用医用胶配合弹簧圈行选择性门静脉栓塞术 (portal vein embolization, PVE; 图 2); 4 例为混合型 HAVF, 其中 3 例患者使用医用胶行相应责任肝动脉栓塞术 (transarterial embolization, TAE; 图 3), 1 例患者使用医用胶进行 TAE 联合 PVE。

2.3 两组患者 HAVF 和 LSF 比较 医用胶组的 HAVF 发生率显著低于非医用胶组 (0 vs 50%, $P=0.047$)。医用胶组的 LSF 显著低于非医用胶组 [$(7.06 \pm 2.33)\%$ vs $(12.43 \pm 7.73)\%$, $t=21.000$, $P=0.037$]。21 例肝癌患者均顺利通过 ^{99m}Tc -MAA 评估, 并最终完成 ^{90}Y -SIRT。

表 1 两组患者一般资料比较

Table 1 Comparison of general data between the two groups

Characteristic	Total ($N=21$)	Medical glue group ($n=7$)	Non-medical glue group ($n=14$)	Statistical value	P
Age/year	57.2 ± 11.3	52.1 ± 14.0	59.7 ± 9.3	1.485	0.154
Sex $n(\%)$				2.670	0.521
Male	18(85.7)	7(100.0)	11(78.6)		
Female	3(14.3)	0	3(21.4)		
Maximum tumor diameter/cm	8.9 ± 4.0	8.0 ± 2.6	9.4 ± 4.5	0.735	0.471
Interval between biopsy and ^{99m}Tc -MAA $n(\%)$				0.329	0.573
0-3 d	10(47.6)	4(57.1)	7(50.0)		
4-9 d	11(52.4)	3(42.9)	7(50.0)		
Pathology $n(\%)$				4.804	0.095
HCC	16(76.2)	7(100.0)	9(64.3)		
ICC	2(9.5)	0	2(14.3)		
mCRC	3(14.3)	0	3(21.4)		

^{99m}Tc -MAA: Technetium-99m-macroaggregated albumin; HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; mCRC: metastatic colorectal cancer.

3 讨论

HCC 是最常见的原发性肝癌, 全球有数百万人受其影响。由于 HCC 缺乏系统性的放射治疗手段, 自 20 世纪 60 年代以来, 研究人员一直在探索通过 ^{90}Y 微球实现局部区域肿瘤控制的可能性。随着 ^{90}Y 玻璃微球和树脂微球的发展, ^{90}Y -SIRT 显

示出相比 TACE 和靶向治疗等替代疗法更高的局部控制率和更久的疗效。此外, ^{90}Y -SIRT 还具有较好的肿瘤反应性和耐受性。目前, ^{90}Y -SIRT 已逐渐应用于不同分期 HCC^[11]、肝内胆管癌 (intrahepatic cholangiocarcinoma, ICC) 及转移性结直肠癌 (metastatic colorectal cancer, mCRC) 的治疗^[12-13]。

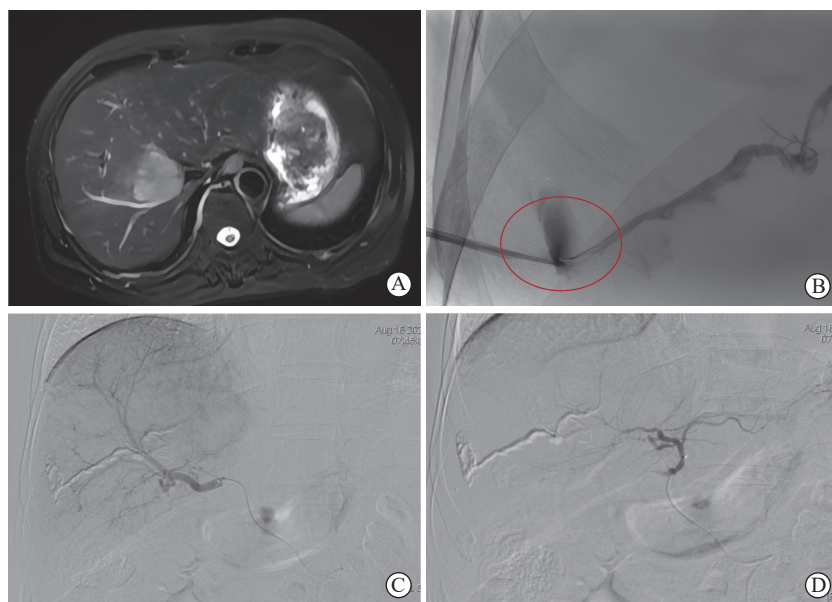


图1 医用胶封堵穿刺针道患者进行^{99m}Tc-MAA 评估

Figure 1 ^{99m}Tc-MAA test was performed on the patient with puncture needle track sealed by medical glue

A: T₂ phase of MRI indicated a lesion in liver segment 5/8; B: Medical glue was injected under DSA fluoroscopy to seal the puncture needle track after liver biopsy; C: No obvious HAVF was found on right hepatic arteriography; D: No obvious HAVF was found on left hepatic arteriography. ^{99m}Tc-MAA: Technetium-99m-macroaggregated albumin; MRI: magnetic resonance imaging; DSA: digital subtraction angiography; HAVF: hepatic arteriovenous fistula.

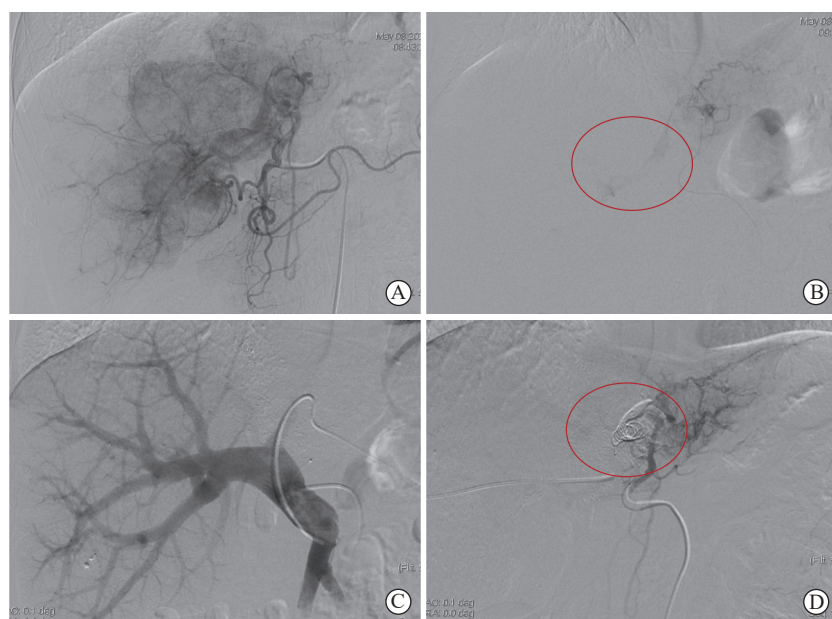


图2 采用医用胶配合弹簧圈进行选择性PVE以封堵HAPVF

Figure 2 Medical glue combined with spring coil were used for selective PVE of HAPVF

A: Hepatic arteriography showed HAPVF during ^{99m}Tc-MAA test; B: Left hepatic arteriography showed HAPVF, and TAE was inappropriate because the responsible artery provided more blood supply to the tumor; C: Percutaneous hepatic puncture portal venography; D: Left hepatic arteriography showed that HAPVF had disappeared after selective PVE with medical glue and spring coil. HAPVF: hepatic artery-portal venous fistula; ^{99m}Tc-MAA: Technetium-99m-macroaggregated albumin; PVE: portal vein embolization; TAE: transarterial embolization.

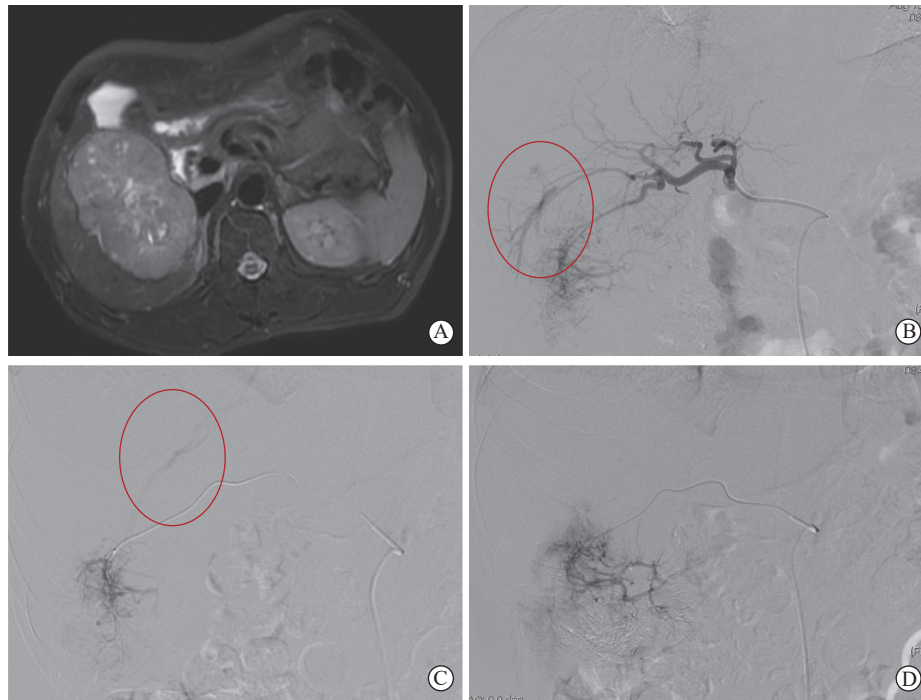


图3 采用医用胶进行TAE以封堵混合型HAVF

Figure 3 Medical glue was used for TAE of mixed HAVF

A: T₂ phase of MRI indicated a lesion in liver segment 5/6; B: Hepatic arteriography showed puncture related HAPVF during ^{99m}Tc-MAA test; C: HAHVF was observed by superselective angiography of the responsible artery; D: Imaging after TAE with medical glue indicated that HAVF had disappeared. TAE: transarterial embolization; HAVF: hepatic arteriovenous fistula; MRI: magnetic resonance imaging; ^{99m}Tc-MAA: Technetium-99m-macroaggregated albumin; HAPVF: hepatic artery-portal venous fistula; HAHVF: hepatic artery-hepatic venous fistula.

肝组织活检是诊断肝脏占位的金标准^[8]。目前,常用的肝组织活检方式有经皮肝活检(包括夹式针、吸式针、切割式针等)、经颈静脉肝活检、手术肝活检(包括开腹手术、腹腔镜手术)^[14]。超声引导下经皮肝穿刺活检是目前较常用的肝活检方式,其中的切割式肝穿刺活检法由于操作简单、可调节穿刺肝组织长度、成功率高、肝组织不易破碎等优点,近年来得到广泛应用^[15]。肝组织穿刺活检具有一定创伤性,活检取材后需使用血凝酶等止血药物。采用不同方式封堵穿刺针道,均可降低出血发生率。近年来,本中心采用延迟拔针法处理穿刺针道,出血发生率较低^[16]。封堵针道法也较为常用,封堵材料包括自体血凝块、异体水凝胶、异体纤维蛋白胶等。明胶海绵颗粒因其成本低、易吸收降解,临床应用最多^[17]。医用胶是以NBCA为主要成分的液体栓塞剂,可

在血液或组织液作用下发生阴离子聚合而迅速固化形成胶体,发挥栓塞止血的作用,其黏合作用强、速度快、组织相容性好,可用于封堵活检穿刺针道^[18]。本研究结果显示,医用胶组的LSF显著低于非医用胶组,提示在肝癌⁹⁰Y-SIRT中,使用医用胶封堵肝组织活检穿刺针道或许可以避免潜在的LSF,从而使患者获益。

根据本研究经验,医用胶在肝活检后的穿刺针道内可迅速聚合、固化,形成胶体,性状稳定,不易吸收降解,或可避免穿刺相关HAVF。医用胶组的7例患者在^{99m}Tc-MAA评估时均未发现明显HAVF。活检后采用延迟拔针法或明胶海绵颗粒封堵穿刺针道,穿刺针道内血凝块或明胶海绵颗粒容易吸收降解,仍有可能发生穿刺相关HAVF,导致^{99m}Tc-MAA异位分布,从而影响⁹⁰Y-SIRT。非医用胶组14例患者中,7例出现穿刺相关

HAVF, 其中3例为HAPVF, 超选择动脉造影后见责任动脉的肿瘤供血较多, 为避免封堵⁹⁰Y微球输注路径, 采用医用胶配合弹簧圈进行选择性的PVE, 再次肝动脉造影见HAPVF消失; 4例为混合型HAVF, 采用医用胶行TAE或TAE联合PVE, 再次肝动脉造影见HAVF消失。7例发生HAVF的患者经封堵分流道后均通过^{99m}Tc-MAA评估, 并完成⁹⁰Y-SIRT。然而, SPECT/CT显示, 使用医用胶栓塞HAVF患者的^{99m}Tc-MAA在术区的分布欠佳, 与术前影像评估所示肿瘤范围略有不符。可见, 医用胶栓塞分流道虽然可能避免LSF增高, 但也可能通过减少^{99m}Tc-MAA灌注区域, 进而影响⁹⁰Y微球剂量测算及分布。

医用胶在血液中聚合作用强、固化迅速, 发生异位栓塞后致并发症的风险较高。不同的配比浓度可影响其在肝内及血管内的分布。本研究中, 肝穿刺活检后封堵穿刺针道时医用胶与碘油以1:1比例混合, 目的在于医用胶注入穿刺针道后可迅速形成胶体, 避免异位栓塞; ^{99m}Tc-MAA评估中栓塞动脉或门静脉时医用胶与碘油以1:3比例混合, 目的在于延迟聚合, 使医用胶充分分布于远端瘘口, 以封堵分流道。

与肝组织活检相比, HCC合并血管侵犯是形成HAVF的更常见原因^[19]。中国晚期HCC患者合并门静脉瘤栓(portal vein tumoral thrombus, PVTT)的比例很高, 为44%~62.2%, 27%~63.2%的晚期HCC病例报告了HAPVF^[20]。ICC、mCRC瘤体缺少血供, 合并PVTT的报道较少。本研究4例HAVF患者的影像学评估显示无血管侵犯, 在^{99m}Tc-MAA评估中见HAVF形成, 且与穿刺针道的位置相吻合, 因此, 考虑动静脉瘘是由肝穿刺活检引起的医源性HAVF。3例HAPVF患者影像学评估显示合并PVTT, 肝动脉造影见广泛HAPVF形成, 局部亦可见与穿刺针道位置相吻合的分流道影, 因此, 考虑为PVTT相关HAPVF合并医源性HAVF。

综上所述, 肝穿刺活检可能通过形成医源性HAVF而影响^{99m}Tc-MAA评估, 继而影响⁹⁰Y-SIRT治疗策略。活检后即刻以医用胶封堵针道或^{99m}Tc-MAA评估中使用医用胶栓塞分流道或可降

低其影响。医用胶栓塞分流道也可能通过减少^{99m}Tc-MAA灌注区域进而影响⁹⁰Y微球分布及剂量测算, 本研究未能进一步分析论证。由于样本量较少, 缺乏自身对照研究和横向对比, 本文旨在总结经验, 以期临床提供借鉴。

伦理声明 本研究通过海军军医大学第三附属医院伦理委员会审核, 免除患者的知情同意。本研究的设计和实施方案符合《赫尔辛基宣言》的伦理原则及相关法律法规的要求。

利益冲突 所有作者声明不存在利益冲突。

作者贡献 徐振远、刘学、申淑群、徐志嘉、李长凯、杨业发: 数据分析, 文章撰写和修改, 最终版本核查。

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[本文编辑] 殷悦

引用本文

徐振远, 刘学, 申淑群, 等. 穿刺活检针道处理方式对钇-90 选择性内放射治疗肝癌的影响[J]. *中国临床医学*, 2025, 32(2): 288-294.

XU Z Y, LIU X, SHEN S Q, et al. Effect of different liver biopsy needle track management on Yttrium-90 selective internal radiation therapy on liver cancer[J]. *Chin J Clin Med*, 2025, 32(2): 288-294. DOI: [10.12025/j.issn.1008-6358.2025.20250084](https://doi.org/10.12025/j.issn.1008-6358.2025.20250084)