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·综述·

牙髓活力状态的影响因素及评估方法研究进展

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【摘要】 健康牙髓是保留天然牙并维持其正常功能的关键。活髓保存治疗因其能够最大限度地保留全部或部分牙髓，提高患牙的远期保存率，在临床应用中越来越广泛。牙髓活力状态是活髓保存治疗方案选择以及疗效评估的关键因素。然而，如何准确评估牙髓活力状态，在临床实际操作中依然具有一定的挑战性。牙髓活力状态受多种因素的影响，包括牙髓暴露类型、龋损状态、牙周炎、外伤、治疗因素、年龄及宿主个体差异等。评估牙髓活力状态，不仅需要医生综合考虑病史和临床表征，还需结合牙髓感觉测试、牙髓血流测试、影像学检查以及分子诊断技术等多种辅助手段。未来，评估牙髓活力状态的技术应当朝着椅旁化、可视化和精准化的方向发展，以期达到临床诊断与组织学诊断的高度一致性，从而为患者提供更为准确和有效的治疗方案。

【关键词】 活髓保存治疗；　牙髓活力状态；　牙髓暴露类型；　龋损状态；　宿主个体差异；　牙髓感觉测试；　牙髓血流检测；　分子诊断技术
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Research progress on influencing factors and assessment methods of pulp vitality

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【Abstract】 Healthy dental pulp is essential for preserving teeth and maintaining their normal function. Vital pulp therapy (VPT) is widely used in clinical applications because it aims to preserve vital pulp and enhance the long-term survival of teeth. An accurate diagnosis of pulp vitality is a prerequisite for successful VPT. However, accurately assessing pulp viability remains challenging in clinical practice. Pulp viability is influenced by various factors, including the type of pulp exposure, caries status, periodontitis, trauma, treatment factors, patient age, and individual differences. Assessing pulp viability requires a comprehensive consideration of medical history and clinical manifestations, along with a combination of various auxiliary methods, such as pulp sensibility tests, pulp blood flow tests, imaging techniques and molecular diagnostics. In the future, the technology for assessing pulp vitality should evolve toward chairside, visualization, and precision techniques, to achieve consistency between clinical and histological diagnoses, thereby providing patients with the most effective treatment.

【Key words】 vital pulp therapy;　pulp vitality;　type of pulp exposure;　caries status;　individual differences;　pulp sensibility tests;　pulp blood flow tests;　molecular diagnostics

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活髓保存治疗(vital pulp therapy,VPT)通过将生物活性材料直接或间接覆盖于牙髓断面,利用牙髓-牙本质复合体固有防御及修复潜能来维持牙髓活性[1]。以往,VPT适应证局限于龋源性、机械性或创伤性微小露髓患牙。但近年临床证据突破了这一认知框架,VPT在不可复性牙髓炎甚至根尖周炎病例中亦能获得成功治疗[2]。影响VPT疗效的三个关键要素包括精准的牙髓活力评估、彻底的感染清除及盖髓材料的合理选择[3]。然而,如何准确评估牙髓活力状态,在临床实际操作中依然具有一定的挑战性。临床诊断与组织学表现的不一致导致部分病例出现治疗决策偏差,这种困境源于传统评估体系技术上的制约,以及新兴检测技术临床应用转化的滞后[4]。因此,本文系统综述牙髓活力状态的影响因素与评估方法,为临床决策中治疗方案选择及预后判断提供参考,以期提高VPT成功率。

1　牙髓活力状态的影响因素

牙髓活力状态受局部及全身多种因素影响,局部因素涵盖牙髓暴露类型、龋损状态、牙周炎、外伤、治疗因素等;全身因素则与年龄、宿主的个体差异性等相关。了解这些因素对临床实践中准确评估牙髓活力状态至关重要。

1.1　牙髓暴露类型

牙髓暴露类型包括外伤或医源性损伤等引起的机械性暴露和龋源性暴露。龋源性暴露因微生物持续侵袭,导致促炎因子如白细胞介素-6(interleukin-6,IL-6)和白细胞介素-8(interleukin-8,IL-8)表达水平较机械性暴露升高[5],显著抑制牙髓修复潜能。临床队列研究证实,机械性暴露行直接盖髓术后12个月成功率(92.1%)显著高于龋源性暴露(33.4%)[6],提示暴露类型是治疗预后评估的关键参数。

1.2　龋损的深度、部位和活动状态

当龋损与牙髓之间的距离超过1.1 mm时,牙髓的炎症反应可忽略不计;若该距离小于0.5 mm,牙髓的炎症程度会显著增加;而当修复性牙本质受微生物或其代谢产物等刺激因素侵害时,牙髓炎症程度剧烈[7]。Kassa等[8]指出,当牙齿近中面的龋损深度超过牙本质厚度的50%时,相较于咬合面具有相似深度的龋损,其炎症性变化更为广泛。

Bjørndal等[9]将龋损病变活动性分为三类:①活跃龋损,呈浅黄色或黄色,质地潮湿柔软;②缓慢进展龋损,呈浅棕色,质地干燥坚硬;③静止龋损,呈深棕色或黑色。进一步对龋损表面状态与组织学关联研究发现,活跃和缓慢进展的龋坏牙本质的颜色、稠度和表面环境(即湿或干)可能反映牙本质内生物活性分子梯度,进而提示其牙髓炎症状态差异。

1.3　牙周炎

慢性牙周炎对牙髓组织具有持续性刺激效应,牙髓组织可呈现纤维化、矿化和炎症浸润等变化,且糖尿病会加重这种病理变化[10]。牙槽骨吸收超过根长1/2时,牙髓变性概率随吸收水平增加而增高[11];牙髓组织中白细胞介素-17(interleukin-17,IL-17)和白细胞介素-1(interleukin-1,IL-1)水平升高,活性氧和凋亡水平也高于正常[12]。

尽管牙周致病微生物所产生的毒性物质可通过交通途径进入牙体组织内,有可能导致牙髓活力改变,但对于牙周炎发展到何种程度会引起牙髓病变至今没有统一的标准。

1.4　外伤

牙外伤致冠折累及深层牙本质时,细菌及温度刺激可经牙本质小管引发牙髓慢性炎症。露髓时间直接影响炎症进展:1.5 h内可出现浅表炎症;超过24 h将导致冠部牙髓广泛感染;72 h后则可能引发牙髓完全坏死[13]。牙齿移位会损害髓腔和根管内血供,若未及时处理,牙髓将坏死。研究显示,患者年龄每增加1岁,外伤的年轻恒牙牙髓坏死率增加1.2倍,且牙周支持组织损伤程度与牙髓坏死发生率呈正相关[14]。

1.5　治疗因素

正畸力可引起牙髓血管生成、细胞代谢和血流量的改变,同时增加细胞损伤和调亡的可能性。

组织学研究显示，正畸力可使牙髓组织的呼吸作用减弱、循环受阻、玻璃样变性甚至坏死[15]；还可引起牙髓组织中IL-8及肿瘤坏死因子α（tumor necrosis factor-α，TNF-α）活性升高[16]。在治疗初1个月内，正畸力就会提高牙齿对感觉测试的阈值，使牙髓活力变迟钝[17]。

此外，牙体缺损治疗过程中，备洞的深度、牙体预备和抛光过程中所产生的机械摩擦、高速手机的负压冷水刺激及充填材料等均可能引起牙髓损伤。但若无细菌的侵入，随着时间的推移，牙髓可逐渐恢复健康。

1.6　年龄

随着年龄增长，牙髓腔因继发性牙本质的不断形成而逐渐缩小，牙髓细胞数量也显著减少[18]。有研究发现，每相隔10岁牙髓细胞数量存在显著的年龄梯度差异，40岁末期的细胞数量约为20岁的一半，60岁时仅为20岁时的14.3%[19]。牙髓基质渐进性退变表现为神经纤维减少、钙盐异常沉积及根尖孔缩窄影响血供和神经支配。

牙髓组织的增龄性变化比身体其他组织更显著，可能与其所处的特殊环境有关：血供单一加之根尖孔不断缩小，极易导致循环障碍从而使牙髓组织发生退变[20]，但其根本机制仍有待进一步阐明。

1.7　宿主的个体差异性

Duncan等[21]指出，尽管细菌及其代谢产物的侵入在龋病和牙髓炎症发生中的关键作用已被广泛认可，但宿主牙髓组织对病原刺激的反应存在个体差异。

既往研究尝试由龋损表征推断牙髓的病理状态，但临床观察发现龋病表征与牙髓实际病变程度缺乏明确对应关系：部分广泛龋损仅呈现为修复性牙本质形成，牙髓组织未见明显炎性反应；而某些仅有轻微的牙本质龋损，却引发牙髓组织显著的牙髓炎症反应[22]。这可能是由于龋损相关的微生物毒力因子和宿主自身的免疫防御能力存在个体差异性。

2　牙髓活力状态的评估方法

2.1　牙髓感觉测试法

2.1.1　牙髓温度测试和电活力测试　牙髓温度测试和电活力测试通过对牙齿表面施加低温、高温、电流等外源性的刺激以检测牙髓内感觉神经的功能状态。其原理为通过施加温度或电流刺激激活Aδ神经纤维（瞬时锐痛）及C神经纤维（持续钝痛），患者根据自身的主观感受对测试做出反应[23]。

临床常用的冷测试、热测试和电测试具有操作简便[平均耗时（2.1±0.3）min]、无创等优势，但也存在一定局限性，表现为：①主观依赖性强，易致假阳性、假阴性率高[24]；②无法量化血流动力学参数及炎症介质浓度梯度；③与组织病理学诊断符合率仅63.2%[25-26]。新型带有透照器的牙髓敏感性测试仪通过标准化刺激强度（冷：5℃±0.5℃；热：45℃±0.5℃）与透照成像联动，已使诊断准确率提升至78.9%[27]。

2.1.2　诊断性局部麻醉　适用于症状来源不明的急性疼痛，通过对可疑患牙周围注射局部麻醉剂后，逐步排除牙齿区域，直到患者的不适感消失即可确定来源，但无法评估牙髓炎进展阶段[28]。

2.1.3　试验性备洞　试验性备洞主要根据备洞时对牙本质刺激所产生的酸软样牙本质过敏症状来判断牙髓活力状态，但其侵入性致患者难以接受。

2.2　牙髓血流测试

牙髓血流测试通过检测患牙牙髓血流量或血流强度等客观指标获得能反映血氧饱和度、血细胞移动速率的信号波形，以此来反映牙髓活力状态变化。因其不依赖于患者的反应，因此可提供更客观、准确的临床评估结果[29]。目前研究较多的是脉搏血氧测定法（pulse oximetry，PO）和激光多普勒血流（laser doppler flowmetry，LDF）测试。

2.2.1　脉搏血氧测定法　脉搏血氧测定法以光学原理为设计基础，基于氧合/脱氧血红蛋白对不同频率光吸收比例不同从而对牙髓血氧饱和度（peripheral oxygen saturation，SpO_2）进行测定，通过量化牙髓SpO_2反映牙髓血管健康和代谢状态[30]。国外学者对大量健康乳恒前牙和一些根管治疗后的患牙进行SpO_2检测，发现牙髓坏死及已行根管治疗的牙齿其SpO_2检测值为0，而健康牙髓的SpO_2在一定的范围内（65%～98%）[31]。

脉搏血氧测定法其非侵入性技术的测定结果客观可靠，但探头设计的精密程度、周围来源的信号参入、外周组织血液灌注不良等均会影响测试结果[32]。

2.2.2　激光多普勒血流测试　激光多普勒血流测试发射激光至牙髓组织，通过检测循环血细胞反向散射光的多普勒频移信号，经傅里叶变换处理后以灌注单位（perfusion units，PU）量化血流状

态[33]。目前，激光多普勒血流测试在牙髓活力评估、创伤牙管理、外科术后监测及再植牙血供重建中均展现出重要临床价值[34]。Mainkar等[35]的Meta分析显示，冷、热、电活力测试的诊断准确率分别为0.840、0.723、0.817；而激光多普勒血流测试与脉搏血氧测定法的准确率分别达0.971和0.974，几乎无异质性，是牙髓活力测试中最接近金标准的方法。

但脉搏血氧测定法和激光多普勒血流测试也存在以下局限性：①牙周及黏膜组织血流干扰（需保留≥3 mm临床牙冠以隔绝软组织信号干扰）；②检测结果易受探头位置及环境温度影响；③存在潜在牙体损伤风险[36]；④受试者需排除全身性疾病及药物干扰因素；⑤设备成本较高且缺乏标准化的灌注参考值。上述因素制约了其临床推广，亟待技术优化与标准建立。

2.2.3　其他牙髓血流测试方法　激光散斑衬比成像（laser speckle contrast imaging，LSCI）通过量化激光照射生物组织产生的散斑图案时空衬比度以解析微循环血流速率。该技术已成功应用于视网膜、脑皮质及皮肤血流监测[37]。透射式LSCI可无创评估血流，具有数据采集快且不需要使用夹板的优势[38]。最新研究表明，垂直偏振光LSCI凭借更优的衬比度动态范围，能覆盖更广流速谱，显著提升牙髓血流检测灵敏度[39]。双波长分光光度法（dual wavelength spectrophotometry，DWS）通过同步检测760 nm与850 nm波长光束的吸收度差异（与血红蛋白浓度呈正相关）以解析牙髓腔血氧饱和度变化。Nissan等[40]通过离体牙模型证实，DWS可有效区分牙髓摘除、固定及氧合血灌注等不同状态。上述两种方法（LSCI、DWS）目前仍多局限于体外模型验证，缺乏大规模临床对照数据。

2.3　影像学检查

2.3.1　通过X线检查评估牙髓炎症进展程度　组织学研究表明，不同龋损深度的细菌渗透程度与牙髓炎症呈显著相关性，由此可以将不同深度龋损之间的放射学阈值作为治疗前牙齿中细菌渗透水平和牙髓反应严重程度的指标[41]。然而，此种方法仍处于理论阶段，目前尚未说明龋病在放射学上穿透到何种程度会引起牙髓病变，对应什么样的牙髓活力状态。值得注意的是，即使根尖有阴影的患牙根管内仍可残留炎性活髓组织，保存这些组织可促进患牙牙根生理性发育[2]。

最新研究显示，人工智能（artificial intelligence，AI）具有比人眼更强的灰度辨别能力，使用人工智能进行X线图像分析训练，可更精准地评估乳牙牙髓活力状态[42]。

2.3.2　颌面部磁共振成像（magnetic resonance imaging，MRI）　磁共振成像（MRI）相较于X线、锥形束CT，凭借四维软组织成像优势，可通过血流灌注参数定量反映牙髓生理病理状态，其特异性信号特征已在牙髓血流检测、髓腔解剖评估、根尖周病变分析等领域[43-44]中得到应用。但现阶段磁共振成像牙髓状态评估仍受限于：①高成本设备与复杂操作流程导致普及率低[45]；②心脏起搏器、金属修复体等引发的禁忌证与图像伪影干扰[46]，亟待技术迭代与临床方案优化。

2.4　分子诊断学

牙髓炎症是一个由细胞和分子介导的过程，表现为炎性细胞的分化、增殖、趋化、迁移以及分子水平上一系列基因和蛋白的表达改变[47]。由于分子信号的改变要早于细胞水平以及组织学水平的改变，更显著早于牙髓疾病相关的临床症状的出现[48]，因而通过采集牙齿样本，应用蛋白质印迹技术、实时荧光定量PCR、酶联免疫吸附测定等技术对相关蛋白或基因表达量进行定性或定量分析比较，可直接反映牙髓的生理或病理状态，以此来识别牙髓状态或预测治疗预后[49]。

2.4.1　分子诊断学用于牙髓疾病诊断　目前研究中，基因水平测定使用的样本均为牙髓组织，其中大多数研究集中于比较健康和不可逆性牙髓炎患牙在mRNA水平上的分子差异。蛋白水平测定所使用的样本则包含牙髓组织、牙髓血液、龈沟液和牙本质液，其中与牙髓组织相关的研究最多。蛋白水平测定的分子种类已有约77种，其中对白细胞介素-1β（interleukin-1，IL-1β）、IL-8、基质金属蛋白酶-9（matrix metalloproteinase-9，MMP-9）、TNF-α、IL-6、白细胞介素-2（interleukin-2，IL-2）、降钙素基因相关肽（calcitonin gene related peptide，CGRP）以及P物质（substance P）的研究较为广泛。本文将不同牙髓炎症状态下所涉及的基因水平和蛋白水平的表达差异分子总结于表1。

Karrar等[49]的Meta分析显示，IL-6与IL-8对不可逆性牙髓炎具有突出的诊断效能（灵敏度：0.95/0.91；特异性：0.97/0.90），可作为高价值诊断标志物。中性粒细胞相关标志物（如MMP-9、IL-8）因在健康牙髓中近乎缺失，且其蛋白水解活性直接介导组织破坏，显示出重要病理指示意义[67]。

表1　不同牙髓炎症状态下所涉及的基因水平和蛋白水平的表达差异分子

Table 1　Differentially expressed genes and protein involved in various states of pulpal inflammation

	Sample	IRP *vs.* Normal	IRP *vs.* RP	RP *vs.* Normal
Change reported in gene expression studies	Pulp tissue	IL-1β↑, IL-8↑, TNF-α↑, MMP-9↑, IL-1α↑, IL-6↑, CXCR4↑, eNOS↑, iNOS↑, etc.[50-55]	IL-1β↑, TNF-α↑, NLRP3↑, eNOS↑, iNOS↑, Caspase-1↑[53, 55-56]	TNF-α↑, NLRP3↑, eNOS↑, iNOS↑[53, 55-56]
Change reported in protein expression studies	Pulp tissue	IL-8↑, IL-6↑, MMP-9↑, TNF-α↑, IL-1β↑, IL-2↑, IL-1α↑, FGF↑, VEGF↑, etc.[57-62]	IL-8↑, IL-6↑, MMP-9↑, TNF-α↑, IL-1β↑, IL-2↑, IL-1α↑, FGF↑, VEGF↑, etc.[60-61]	IL-1β↑, IL-8↑, TNF-α↑, IL-6↑, IL-1α↑, FGF↑, VEGF↑, etc.[60-61]
	Pulp blood	IL-1α↑, IL-1β↑, IL-8↑, MMP-9↑, TNF-α↑, IL-2↑, etc.[61-62]	IL-8↑, MMP-9↑, TIMP-1↑[61, 63]	IL-8↑[63]
	GCF	IL-8↑, MMP-8↑, CGRP↑, Substance P↑[64-65]	Lack of relevant studies	Lack of relevant studies
	Dentinal fluid	Lack of relevant studies	IL-6↑, TIMP-1↑, IL-1α↑, FGF-acid↑[66]	Lack of relevant studies

RP: reversible pulpitis; IRP: irreversible pulpitis; CXCR4: chemokine receptor 4; eNOS: endothelial nitric oxide synthase; iNOS: inducible nitric oxide synthase; NLRP3: NOD-like receptor thermal protein domain associated protein 3; Caspase-1: cysteine-requiring aspartate protease 1; FGF: fibroblast growth factor; VEGF: vascular endothelial growth factor; TIMP-1: tissue inhibitor of metalloproteinase-1; GCF: gingival crevicular fluid; CGRP: calcitonin gene related peptide; MMP: matrix metalloproteinase; ↑: arrow indicates upregulation

当前研究在最佳样本及采样工具上仍存困境：侵入性样本（牙本质液、牙髓血液）虽能精准反映炎症状态，但存在获取困难、样本量不足等局限[68]；非侵入性样本（龈沟液）易获取但研究证据基础薄弱[69]；样本采集工具尚未标准化（如滤纸条吸附会导致蛋白定量偏差），微量样本检测技术瓶颈，均制约临床应用。进一步开发便携式检测手段[70]（如生物传感器[71]、微流控芯片[68]）实现椅旁快速分析，是突破当前困境的关键。

2.4.2　分子诊断学用于治疗结果的预测　乳牙牙髓血中前列腺素E2[72]、牙髓组织中IL-1α、IL-6、IL-8[73]的高表达与活髓切断术失败率正相关；恒牙牙本质液[67]及牙髓血中MMP-9[74-75]的高水平表达分别与直接盖髓术及牙髓切断术治疗的成功率呈负相关。尽管分子诊断可预判牙髓活力变化趋势，目前临床应用仍受限于：侵入性取样；检测灵敏度与时效性难以满足临床需求；缺乏标准化的生物阈值体系。未来研究方向应聚焦于开发单分子阈值检测系统，通过便携设备实现炎症程度分级与预后风险即时评估。

3　小结与展望

在临床实践中，对牙髓活力状态的评估不仅需要医生综合考虑病史和临床表征，还需依靠影像学检查、牙髓感觉测试和血流检测等多种辅助手段。随着牙髓活力状态评估技术的不断进步与完善，牙髓疾病诊断的准确率得到了显著提升，同时活髓保存治疗的适应证也得到了拓展。然而，当前技术手段尚存在相应的局限性（表2），例如，临床表征主要依赖于患者的主观反应；牙髓血流测试会受到周围组织的灌注状况的影响；MRI技术的高昂成本和较长的检查时间也限制了其应用。因此，准确评估牙髓活力状态的技术仍需进一步的完善与开发。

随着检测技术与牙髓病理状态之间关联性的深入研究，分子诊断学有望在未来成为临床上精准评估牙髓活力状态的新技术。

目前，该领域仍需进一步的探索，主要包括以下几个方面：①寻找具有“黄金标准”的生物分子标志物，即该标志物能在其浓度超过特定阈值时能准确指示疾病及其严重程度并具有较高的特异性和灵敏度；②研发方便椅旁操作且非侵入性的分子检测手段，能够迅速提供客观数据；③探索适宜的采样工具，具有便携性、可操作性以及最小体积的样本量需求性。未来，评估牙髓活力状态的技术应当朝着椅旁化、可视化和精准化的方向发展，以期达到临床诊断与组织学诊断的高度一致性，从而为患者提供更为准确和有效的治疗方案。

表2　不同牙髓活力状态评估方法

Table 2　Different methods of pulp vitality assessment

Classification	Method of detection	Dental trauma	Clinical application	Basis for assessment	Advantages	Disadvantages
Pulp sensibility test	Cold pulp test, heat pulp test, electric pulp test	Noninvasive	Wide application	Subjective feelings of patients	The technique has low sensitivity and simple operation. It consumes less time than other methods and is readily accepted by patients	The accuracy is low. Depending on the subjective response, false positives and false negatives often occur
	Diagnostic local anesthesia	Noninvasive			Further, the technique does not damage the integrity of the tooth	Only used to locate the affected tooth and does not reflect the degree of pulpal inflammation
	Test hole preparation	Invasive			The last resort for clinically determining the status of dental pulp	Destroys the integrity of teeth, and some teeth are not suitable for patients
Pulp blood flow test	Pulse oximetry	Noninvasive	Not yet widespread	Objective data and waveform analysis	Accurate, non-invasive, easy to perform and objective	Peripheral tissue signal interference, lack of detection pr obes, poor perfusion of peripheral blood, lack of normal reference values, and high cost
	Laser Doppler flowmetry test	Noninvasive				
Imaging-assisted techniques	X-ray	Noninvasive	Preliminary Application	Objective imaging data analysis	Painless, noninvasive, simple operation, and the results are objective and visible	The equipment is expensive, the examination process is complicated, there are cont raindications and image artifacts
	MRI	Noninvasive				
Molecular Diagnostics	Quantification of genes	Invasive: pulp tissue, pulp blood, dentinal fluid	Theoretical research stage	Objective quantitative data analysis	Results and visualization are objective, and the dynamic change and outcome of pulp vitality can be predicted	Lack of reference threshold, difficulty in sampling, invasive to teeth, and long detection time
	Quantification of protein	Noninvasive: GCF				

MRI: magnetic resonance imaging; GCF: gingival crevicular fluid

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