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# 心脏核磁共振评估缺血性心脏病的应用价值

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**【摘要】**中国心血管疾病发病人数呈逐渐上升趋势,冠心病已成为中国有较高的病死率、复发率及致残率的疾病之一。冠心病诊断及评估对患者的治疗与预后有重要作用。心脏磁共振时间分辨率及空间分辨率近年来随着软、硬件技术的发展明显提高,具备多参数、多序列和任意方向断层成像的技术优势,在一次检查中心脏磁共振便可准确提供整体心功能、节段性室壁运动及心肌血流灌注、活性心肌等信息,并且避免电离辐射、放射性同位素及碘造影剂等对人体的不良影响。现讨论心脏磁共振成像技术及其在冠心病的应用价值。

**【关键词】**冠心病;磁共振成像;心肌灌注;负荷试验
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# Value of Cardiac Magnetic Resonance Assessment of Ischemic Heart Disease

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【**Abstract**】The incidence of cardiovascular diseases is increasing in China, and ischemic heart diseases have a high mortality, recurrence rate and disability rate. As such, the diagnosis and evaluation of coronary heart disease are important. Cardiac magnetic resonance (CMR) time and spatial resolution has improved with the development of software and hardware technology. Additionally CMR has the advantages of multi-parameter, multi-sequence and arbitrary orientation. CMR can provide information of the overall cardiac function, regional ventricular function, myocardial perfusion and myocardial viability in one single examination. The article will discuss the CMR imaging technology and the value in the ischemic cardiac disease.

【**Key words**】Coronary heart disease; Magnectic resonance imaging; Myocardial perfusion; Stress test

## 1 心脏成像技术

### 1.1 亮血成像

亮血技术是心脏磁共振(cardiac magnetic resonance, CMR)的主要技术之一,因为有较高的空间分辨率、血池和心肌的良好对比及全心覆盖等优点,已成为评价心功能的"金标准"[1]。其序列主要包括扰相梯度回波和稳态自由进动序列。扰相梯度回波序列采集图像时间较长,且受血液流动影响较明显,血流缓慢区域心肌和血池对比度明显降低,故心功能减弱的患者成像图像质量较差,并不能广泛应用于临床。随后引入的稳态自由进动序列是扰相梯度回波的有效代替。稳态自由进动序列的图像信噪比较梯度回波明显提高,具备约 1.5 mm × 1.8 mm 的空间分辨率及 50 ms 的时间分辨率。其成像可准确提供血液流动及心功能等信息。亮血成像主要应用于评估整体及局部心功能,测量心室容积,显示血液流动及冠状动脉大体解剖。有学者认为,稳态自由进动序列电影成像可有效代替传统超声评估心功能[2-3]。

### 1.2 黑血成像

该技术由于在扫描成像中使快速流动的血液表现为低信号,称为黑血成像技术。其成像图像血液与心腔、血管壁及心瓣膜能够形成良好的对比度,在临床上主要应用于描绘心室及血管壁的结构异常。黑血图像常用序列为快速自旋回波序列。快速自旋回波序列结合双倍反转恢复、三倍反转恢复及短时间反转恢复等技术,使成像速度明显加快,最小化呼吸及心脏运动的伪影,且较梯度回波序列受磁场不均匀影响较小,对有心脏支架植入的患者仍可有较好的心血管成像图像。有文献表明[4] $T_2$ 结合三倍反转恢复及短时间反转恢复技术的图像可反映急性心肌梗死的缺血危险区,在图像上表现为高信号。

### 1.3 动态首过灌注成像

心肌首过灌注是采用钆喷酸葡合剂作为造影剂,在其注射后立刻开始扫描,进行连续采集 $T_1$ 加权图像,动态跟踪造影剂在心肌分布扩散过程。造影剂缩短心肌 $T_1$ 时间,从而使信号增高。现灌注序列常采用快速小角度激发序列(turbo fast low-angle short, turbo FLASH)及平面回波序列(echoplanar imaging, EPI)。turbo FLASH 序列其覆盖层面有限,多为 1 ~ 3 层,空间、时间分辨率及信噪比较低。EPI 可在一次射频脉冲激励下获取多条 K 空间线,采集图像数据的时间较 turbo FLASH 明显缩短,覆盖层面提高至 3 ~ 4 层[5]。该技术相对于 turbo FLASH 序列时间及空间分辨率有所提高,但成像图像质量及覆盖范围限制了其在临床的广泛应用。滑动窗共轭梯度高限性反向投射重建(sliding window and conjugate-gradient highly constrained back-projection reconstruction, SW-CG-HYPR)是一种新的序列方式,这种技术基于增加局部梯度场强及相位阵列线圈,降低 K 空间采样密度来提高信噪比。扫描范围可以覆盖整个左心室,空间分辨率、时间分辨率及信噪比较 turbo FLASH 及 EPI 均明显提高,SW-CG-HYPR 的空间分辨率可达 1.2 mm × 1.2 mm, Ge 等[6-7]的动物实验研究表明,SW-CG-HYPR 图像峰值信噪比较 turbo FLASH 及 EPI 所得图像信噪比更高,且 SW-CG-HYPR 序列所得图像有效减少了运动伪影。

### 1.4 延迟增强成像

延迟增强扫描(late gadolinium enhancement, LGE)一般在静脉注射造影剂后 10 ~ 15 min 进行图像的采集,成像序列多采用反转恢复快速梯度回波或平衡稳态自由进动序列。在临床上该技术用于识别梗死心肌区域。活性心肌细胞间质成分较少且具有完整的细胞膜,细胞膜将对比剂限制在细胞外组织间隙中,使之不能进入细胞内,随着增强扫描时间的延长,组织间隙的造影剂被洗脱,并不会造成延时强化。急性心肌梗死后,梗死心肌细胞膜破裂,对比剂进入细胞内,对比剂洗脱延时,造成 $T_1$ 值明显缩短,在图像上显示高信号;而陈旧性心肌梗死的患者坏死心肌区被瘢痕组织取代,细胞外间隙较正常心肌的细胞外间隙明显增大,造影剂沉积在细胞外间质中,造成洗脱时间延长,延时增强。延时增强过程中应用了反转恢复脉冲,旨在消除正常心肌的信号,反转时间是 LGE 主要的成像控制参数,直接影响成像的质量。反转时间主要受给药后时间的影响,为了清晰显示梗死心肌的范围,在进行核磁共振成像(MRI)扫描前需要调整反转

时间[8-9]。LGE 对急性心肌梗死及瘢痕的检出率非常高。Ibrahim 等[10]研究显示，LGE 诊断急性心肌梗死的敏感性与单光子发射计算机断层扫描（SPECT）相比分别为 99% 和 94%。Schelbert 等[11]研究显示 LGE 较小剂量多巴胺负荷对未发现陈旧性心肌梗死灶检出率更高。

## 2　CMR 在冠心病的应用

### 2.1　CMR 在慢性缺血性冠心病的应用

#### 2.1.1　静息-负荷灌注试验

心肌低灌注是冠心病发展病程中最早可被检测的生理异常状态。对于冠状动脉狭窄 <75% 的患者，在静息状态下，由于侧支循环的代偿性扩张能力，可使心肌灌注血流量维持在正常水平，MRI 首过灌注图像未见异常表现。在注入血管扩张药（如腺苷或潘生丁）后，冠状小动脉失去再扩张能力，狭窄冠状动脉供血区血流灌注量相对减少，而表现为灌注图像低信号。心肌首过灌注减低主要表现为灌注缺损和灌注延迟，国外常用半定量心肌灌注指标，如最大信号强度、达高峰时间、时间信号曲线下面积、最大斜率及心肌灌注储备指数等来评估缺血心肌。

MRI 比 SPECT 有更高的空间分辨率和时间分辨率，能提供更好的组织特性信息。静息-负荷灌注对于冠心病有较高的诊断价值，Michèle 等[12]发布的一项纳入 55 项研究的 meta 分析表明，CMR 负荷灌注诊断冠心病有较高的敏感性和特异性，分别为 89% 和 86%。Greenwood 等[13]发表的随机对照试验结果与之相仿，CMR 静息-负荷灌注比 SPECT 有更高的敏感性和阴性预测值，以及相同的特异性和阳性预测值。另外有研究报道，与冠状动脉造影下检测的心肌血流储备分数相比，负荷灌注评估冠状动脉狭窄（心肌血流储备分数 <0.75）的敏感性、特异性及准确性分别达 91%、90% 和 91%[14]。

#### 2.1.2　大剂量多巴酚丁胺负荷试验

大剂量多巴酚丁胺[40 μg/(kg · min)]可短期增加心肌收缩力和心率血压乘积，使心肌耗氧量增加，诱发心肌缺血，正常的冠状动脉有良好的储备功能，心肌供氧-耗氧平衡，狭窄的冠状动脉储备功能低下，未能及时给心肌供养，导致相应节段心肌室壁的运动异常。CMR 清晰显示各节段心肌的收缩、舒张室壁运动变化而达到评估缺血心肌的目的。大剂量多巴胺负荷超声及大剂量多巴胺负荷 MRI 均是诊断心肌缺血的可靠检查，近年来多项研究表示大剂量多巴胺负荷 MRI 比大剂量多巴胺负荷超声对诊断缺血性心脏病更有价值。Nagel 等[15]单项研究表示大剂量多巴胺负荷 MRI 与大剂量多巴胺负荷超声敏感性、特异性分别为 86.2%、74.3% 和 85.7%、69.8%，这种结果可能由于 CMR 空间分辨率较高，能够清晰显示心肌边界及在肥胖及肺气肿患者检查亦有较好的图像质量所致。另外，文献报道大剂量多巴胺负荷 MRI 与其他使用多巴酚丁胺负荷的检查安全性及不良反应相仿[16]。

#### 2.1.3　小剂量多巴胺负荷试验

静息状态下存活心肌及梗死心肌均可表现为运动功能障碍，但前者具有收缩功能储备，给予正性肌力药物下可恢复收缩功能。在小剂量多巴胺负荷下[10 μg/(kg · min)]，存活心肌运动增强，室壁增厚，而死亡心肌无反应。一般来说，表现为运动减弱或不运动的心肌节段在低剂量多巴胺负荷后，室壁增厚至少 2 mm 才被考虑为存活心肌，反之为死亡心肌。小剂量多巴胺负荷试验鉴别心肌梗死后存活心肌，是预测心功能恢复可靠、安全的检查[17-18]。区分心肌梗死后不可逆性受损心肌和可挽救活性心肌对临床的治疗具有重要价值。有研究表明慢性闭塞性冠心病患者中，小剂量多巴胺负荷试验识别出活性心肌的患者再灌注术后心功能恢复明显[19]。

### 2.2　CMR 在急性心肌梗死中的应用

CMR 对 ST 段抬高型及非 ST 段抬高型心肌梗死均有较高的诊断价值，CMR 可识别急性心肌梗死，准确评估危险心肌的区域，发现微血管梗阻及心肌缺血等急性心肌梗死后遗症。另外，CMR 能够预测冠状动脉再通后心功能恢复的可能性。这些独特的性能较传统左室容积、射血分数等对冠心病的评价更有意义。

#### 2.2.1　心肌水肿

急性心肌梗死及再灌注术后，心肌内自由水含量增加，$T_2$ 横向弛豫延长，MRI $T_2$ 表现为高信号。心肌水肿持续 2 ~ 3 周再缓慢消退，是鉴别陈旧性及急性心肌梗死的重要手段。发生在急性心肌梗死后的心肌水肿区，又称缺血危险区，包括梗死区域（LGE 高信号区）及可挽救区（缺血危险区除去梗死区域部分）。有研究表明，存在心肌水肿的患者在半年内不良心脏事件（包括再次心肌梗死、心力衰竭、死亡）的发生率高于不存在心肌水肿的患者[20]。Eitel 等[21-22]对急性心肌梗死患者再灌注治疗后的可挽救心肌进行量化，发现心肌挽救指数（可挽救区/危险区域）大于组内中位数的患者在短、长期的死亡发生率明显减低。另外，有学者发现，急性心肌梗死早期，甚至在心肌酶指标异常之前，呈现为心肌水肿状态，在 MRI 上表现为 $T_2$ 高信号，因此记录心肌水肿存在及追踪其区域相关冠状动脉显得尤为重要[23]。

#### 2.2.2　微血管梗阻及心肌出血

早期再灌注心肌已成为急性心肌梗死的首要治

疗手段。但近年来发现,尽管血管成功再通,仍有约30%的患者出现微血管梗阻(microvascular obstruction,MO)现象而不能够完全恢复血流灌注。此现象可能由于毛细血管坏死、血栓碎片堵塞小动脉、急性炎症、血小板异常聚集及小血管痉挛等导致部分心肌呈现无复流现象[24]。首过灌注、早期增强、LGE 均可用于评估 MO。LGE 精确描绘 MO 范围,表现为高信号的梗死心肌内的低信号灶。MO 的程度独立于梗死面积和射血分数,是左室心肌反向重构及临床不良后果的预测因素[25-26]。另外,MO 在数周内缓慢缩小,较少持续一个月,因此它并不是慢性梗阻的特征。

心肌梗死后由于血管内皮细胞坏死、损伤,细胞间隙扩大,红细胞可穿透血管溢出到心肌内,导致心肌出血。心肌内红细胞还原血红蛋白被氧化为正铁血红蛋白,顺磁性增加,缩短了 $T_2$ 弛豫时间,在 MRI 图像上表示为 $T_2$ 低信号。多个研究已证实了 MRI $T_2$ 图像在检测心肌出血中的应用价值[27-28]。

## 3 心肌梗死后存活心肌的评估

现较多学者认为,LGE 高信号区与真实心肌梗死范围有高度一致性。许多动物实验结果表明,心脏延时强化范围经病理证实为死亡心肌。梗死心肌的透壁程度现已被用于心肌梗死再灌注后心功能恢复的评估;有文献表明当心肌透壁程度 <25% 时,再灌注后心功能恢复的可能性更大(梗死节段心肌舒张末期厚度明显增长),当透壁程度 >75% 时,再灌注对心功能恢复似乎并不起作用[29]。另外,SHAH 等研究表明左室收缩功能异常的慢性冠心病患者,LGE 透壁程度与远期病死率密切相关[11,30]。Roes 等[31]研究证实这一观点,表明 LGE 透壁程度较左室射血分数及左室容积更能预测患者的远期病死率。

总之,CMR 作为一种无创、无辐射的技术,能够提供整体心功能、节段性室壁运动及心肌血流灌注、活性心肌等信息,对急、慢性冠状动脉疾病的诊断、血管再通术后的评价、远期疗效的评估有重要应用价值,有望成为常规的心血管检查之一。

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# 抗凝药比伐卢定临床应用进展

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**【摘要】** 比伐卢定是一种新型直接凝血酶抑制剂,2000 年被美国食品药品监督管理局批准应用于临床。比伐卢定由水蛭素提炼而出,利用其有效控制凝血酶正常机能的特性发挥作用,国际上通过让其他抗凝药物和它做对比实验,发现其能够取代一般肝素以及血小板糖蛋白Ⅱb/Ⅲa 受体阻滞剂治疗药物用于手术过程中的抗凝治疗所起到的效果。现具体介绍该药物对应的药效和它在治疗心血管疾病的临床表现。

**【关键词】** 比伐卢定;抗凝药;直接凝血酶抑制剂;临床应用

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# Advance in Research on Clinical Application of Anticoagulant Drug Bivalirudin

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**【Abstract】** Bivalirdin is a direct thrombin inhibitor approved by US Food and Drug Administration in 2000. It is an analogue of hirudin that can inhibit the active site of thrombus. International studies have compared it with other anticoagulants and shown that bivalirudin can substitute for heparin or glycoprotein Ⅱb/Ⅲa inhibitors in patients undergoing invasive treatment.

**【Key words】** Bivalirudin; Anticoagulants; Direct inhibitor of thrombin; Clinical application

冠心病作为常见心血管疾病之一,当出现冠状动脉内斑块破裂以及血栓等情况时,发病时间较快,这也是人们常说的急性心肌梗死。过去往往是通过抗凝药肝素进行预处理,但肝素存在诱导血小板减少及肝素抵抗的局限性,那么作为一种最新研发的抗凝产品,通过在国际上对大量心脏有关的临床治疗情况进

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