❖述评

Progresses in clinical application of contrast-enhanced ultrasound

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[**Abstract**] Contrast-enhanced ultrasound (CEUS) is an imaging technique that can be used to *in vivo* assess microvascular perfusion and quantify microvascular blood volume, which has developed into a highly specialized area of medical diagnostics. The unique feature of CEUS is real-time representation of the inflow and outflow behavior of the contrast medium in the tissue, accordingly allowing the characterization of microvascular perfusion to be visualized and quantified and increasing the sensitivity and specificity in assessment of lesions. Over the years, universal guidelines regarding the application of CEUS in clinical settings had been developed. In addition to perfusion imaging, CEUS will be applied in clinical practice for molecular imaging and as therapeutic agent to realize site-specific drug delivery.

[**Keywords**] microvascular; perfusion; ultrasonography; contrast media

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超声造影临床应用进展

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[**摘 要**] 超声造影(CEUS)是可用于在体评估微血管灌注并量化微血管血容量的成像技术,现已发展成为高度专业化的医学诊断领域,其独特之处在于可实时显示造影剂在组织中的灌注与廓清过程,显示并量化病灶微血管灌注特征,提高诊断敏感性和特异性。近年 CEUS 相关临床应用指南也在不断推出及更新。除灌注成像外,未来 CEUS 还将用于临床分子成像,并实现携带药物的精准治疗。

[**关键词**] 微血管; 灌注; 超声检查; 造影剂

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微血管可反映往往先于疾病临床表现的局部组织和细胞氧化代谢情况,观察微血管变化有利于早期诊断疾病。超声造影(contrast-enhanced ultrasound, CEUS)评估微细血管及血流现已广泛用于评价肿瘤内新生血管、不同组织器官的微血流灌注及斑块新生血管等。动态 CEUS 定量分析可同时无创评估新生血管密度及其分化程度,为评价肿瘤生物学行为提供了新思路[1]。相比实体瘤疗效评价标准(respond evaluation criteria in solid tumors, RECIST),CEUS 可在肿瘤体积改变前评估抗肿瘤药物或放射治疗所致微循环改变,早期评估疗效、指导临床决策[2]。通过与微血管内皮细胞上的特异性标志物结合,靶向微泡、纳

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米泡可提高 CEUS 检查的特异性,使精准评估及治疗疾病成为可能。

1 用于心脏、大血管

心脏 CEUS 由 Joyner 于 1966 年提出,随后 Gramiak 将之用于临床;现已成为比较成熟的无创检查技术,可定位解剖结构。右心声学造影对诊断及治疗房间隔缺损、肺动静脉瘘等先天性心脏病具有独特优势;左心声学造影能清晰显示心内膜边界,有助于诊断心肌病、尤其心尖肥厚型心肌病,可重复性强[3],评估左心功能更为精确;而心肌超声造影(myocardial contrast echocardiography, MCE)可评估冠状动脉病变程度及冠状动脉血流储备,用于胸痛患者危险分层、判定心肌存活比例、评估侧支循环、监测心肌再灌注情况等。全自动准确分割 MCE 心肌区域新技术可检测心肌缺血[4]。

CEUS 可通过评估颈动脉斑块内新生血管及溃疡等鉴别斑块易损性,为预测脑卒中风险和术前评估提供参考[5-7];评估腹主动脉瘤腔内修复术(endovascular aneurysm repair, EVAR)后内漏并进行分型,成为 EVAR 术后随访的有效手段[5,8];亦可用于诊断腹主动脉夹层、假性动脉瘤及动静脉瘘等[8-9],并有助于评估血管炎症性疾病病情、判断疗效及随访监测[6],根据造影剂增强程度及灌注方式鉴别癌栓与血栓[10-12]。

2 用于消化系统

CEUS 极大地提高了超声对肝脏局灶性病变的检出及诊断准确性[13-14],不仅可鉴别病灶性质,还可提示原发性肝癌的分化程度,甚至可通过 CEUS 表现预测其治疗反应,有助于选择适宜的治疗方式。CEUS 还可用于鉴别门静脉血栓和癌栓。CEUS 肝脏影像报告和数据系统(liver imaging reporting and data system, LI-RADS)适用于肝细胞肝癌高危人群的病灶诊断。术中 CEUS 可提高肿瘤的检出,可发现并准确评估术前未发现的肝脏局灶性病变,有助于确定手术方式。

CEUS 可提供胰腺局灶性病变及周边胰腺实质的血流灌注信息,提高超声对胰腺病的诊断能力,尤其是对胰腺癌的发现和诊断,且对于预后也有一定的预测价值[15-16]。CEUS 对胰腺囊性病变的恶性风险可进行评估[17](如胰腺黏液性囊性肿瘤、导管内乳头状黏液性肿瘤、实性假乳头状肿瘤),指导临床处理方式的选择。

3 用于泌尿生殖系统

CEUS 可快速、实时评估肾脏病变微血流灌注情况,诊断效能不低于增强 CT 及增强 MRI[18],其判断肾脏良恶性占位性病变的敏感度甚至超过增强 CT[19],并可用于评估不同亚型肾细胞癌、评价疗效及预后。CEUS 无肾毒性,可用于肾功能不全或肾移植术后患者[20]。

CEUS 可鉴别膀胱、前列腺、睾丸及阴囊良恶性病变,评估动脉栓塞治疗前列腺结核及前列腺增生的效果;其对前列腺结核病灶的检出率高于经直肠超声,还可判断结核病灶所处病理阶段[21]。对于分期、分级诊断膀胱癌及治疗不育症,CEUS 亦具有重要价值[22-23]。

CEUS 中,盆腔恶性肿瘤多呈快进快出型,良性肿瘤呈慢进慢出型。利用三维 CEUS 可鉴别诊断子宫肌层、宫腔内及卵巢良恶性病变:良性病灶周围血管形态规则、分布稀疏,恶性病变则多见血管扭曲[24]。通过评估宫颈上皮内瘤变(cervical intraepithelial neoplasia, CIN)的局部微血管化程度,CEUS 可提示 CIN 术后复发、判断宫内有无妊娠组织残留等[25]。

经腔道(阴道-宫颈管-宫腔)CEUS 的诊断效能与 X 线子宫输卵管碘油造影相近,并可能成为评估输卵管通畅性的首选检查方法[26]。

4 用于浅表器官

CEUS 可在诊断甲状腺结节及乳腺包块中发挥作用。甲状腺恶性肿瘤的主要 CEUS 特征为不均匀增强,大部分癌灶表现为低增强[27],且增强程度与术后复发风险相关[28]。乳腺恶性病变 CEUS 多表现为不均匀高增强,形态不规则,周边可见粗细不均、扭曲或穿入的血管,造影后病灶范围多大于常规超声所示,时间-强度曲线(time-intensity curve, TIC)呈“速升缓降”型;良性病变则多表现为均匀增强,形态规则,TIC 呈“缓升速降”或“速升速降”型。

CEUS 可显示淋巴结血流灌注情况。不均匀、向心性增强是转移性淋巴结的特异性表现,有学者[29]认为高增强及等增强癌灶颈部淋巴结转移率及甲状腺被膜侵犯发生率明显升高,但也有研究[30]结果显示甲状腺癌 CEUS 增强强度与颈部淋巴结转移无关。于乳晕下经皮注射造影剂后,CEUS 可清晰显示淋巴管和前哨淋巴结,判断前哨淋巴结转移与否效果较好[31]。

CEUS 定位原发性和继发性甲状旁腺功能亢进病灶的敏感度优于$^{99}Tc^{m}$-MIBI SPECT/CT 显像[32-33],也可用于初步预测甲状旁腺病变的分泌功能;CEUS 相关参数分析显示,高增强甲状旁腺功能亢进结节的分泌功能高于低增强结节[34]。

5 用于介入诊疗

CEUS 能实时指导活检操作;针对灌注增强区域进行活检可避开坏死或无血管组织,提高经皮肝脏、肾

脏、甲状腺及前列腺等病变穿刺活检的阳性率,可用于对常规超声显示不佳或不能显示病变的活检。由于血管损伤为消融治疗后的最早期变化,CEUS 用于消融治疗不仅能协助制定治疗计划、实时引导治疗,还可即时评估疗效。

CEUS 引导下经皮胆道造影可通过术中或经内镜放置的引流管或 T 形管显示胆道系统,术中三维腔内造影可帮助术者规划切除线。腔内 CEUS 可确定穿刺或插管成功,评估是否与其他结构交通、判断梗阻程度、治疗后情况及有无移位或闭塞,随访期间评估脓肿腔大小及确定或排除引流管移位。

6 展望

分子影像学的发展进一步推动了 CEUS 在精准医疗中的应用。具有靶向亲和作用、可携带治疗药物的第三代声学造影剂是目前 CEUS 相关研究的热点,将使超声技术同时具备诊断与治疗的双重作用。利用靶向超声造影剂联合靶向微泡破坏技术,可将携带药物或基因修饰的超声微泡造影剂定点释放至病变部位,进而靶向诊断及治疗肿瘤;靶向定位释放不仅可减少药物用量,还能提高病灶局部药物浓度而增强疗效,减少不良反应,发展前景广阔。

超声波在远场面临基本的衍射极限,导致常规 CEUS 显示微血管结构细节的能力有限。超分辨率超声血流成像可通过跟踪定位孤立微泡而获得空间分辨率为数十纳米的图像[35],基于此形成的超声定位显微镜技术可解决显示微血管网络细节的难题,成为观察微血流的有力工具,目前广泛用于针对肿瘤、神经及肾脏等领域的临床前研究中。相信随着 3D、4D 成像技术及人工智能的发展,CEUS 将会征服现有挑战,在临床微血管成像领域做出更大贡献。

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