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在线投稿: http://www.baishideng.com/wcjd/ch/index.aspx
帮助平台: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.11569/wcjd.v24.i25.3641

世界华人消化杂志 2016年9月8日; 24(25): 3641-3646
ISSN 1009-3079 (print) ISSN 2219-2859 (online)

述评 EDITORIAL

超声内镜在胃癌TNM分期中的作用

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基金项目: 国家自然科学基金资助项目, No. 81470039.

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收稿日期: 2016-04-25
修回日期: 2016-05-16
接受日期: 2016-05-23
在线出版日期: 2016-09-08

Role of endoscopic ultrasonography in TNM staging of gastric cancer

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Supported by: National Natural Science Foundation of China, No. 81470039.

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Received: 2016-04-25
Revised: 2016-05-16
Accepted: 2016-05-23
Published online: 2016-09-08

Abstract

Gastric cancer is a common malignancy that has a poor prognosis and high mortality. Cancer staging is the optimal method for evaluating prognosis. Endoscopic ultrasonography (EUS) has been considered the first-choice imaging modality for regional staging of gastric cancer because different structural layers of the gastric wall show remarkable differences in their echogenic appearance. However, the results of recent studies about the accuracy of EUS for staging of gastric cancer are contradictory. The aim of this article is to review the role of EUS in preoperative TNM staging of gastric cancer.

Key Words: Endoscopic ultrasonography; Gastric cancer; TNM staging

Tang XL, Lin R, Han CQ, Ding Z. Role of endoscopic ultrasonography in TNM staging of gastric cancer. Shijie Huaren Xiaohua Zazhi 2016; 24(25): 3641-3646 URL: http://www.wjgnet.com/1009-3079/full/v24/i25/3641.htm DOI: http://dx.doi.org/10.11569/wcjd.v24.i25.3641

摘要

胃癌是常见的恶性肿瘤之一, 其预后差, 死亡率高. 判断胃癌的预后主要依赖于胃癌的分期. 由于超声内镜(endoscopic ultrasonography, EUS)能够区分胃壁的各层结构, 所以他被认为是术前判断胃癌原位浸润深度的首选方法. 然而, 近年来越来越多的研究认为EUS对胃癌TNM分期准确性和敏感性存在争议. 本文将对EUS在胃癌TNM分期中

背景资料
胃癌是常见的恶性肿瘤之一, 其预后差, 死亡率高, 判断胃癌的预后主要依赖于胃癌的分期. 由于超声内镜(endoscopic ultrasonography, EUS)能够区分胃壁的各层结构, 所以他被认为是术前判断胃癌原位浸润深度的首选方法. 然而, 近年来越来越多的研究认为EUS对胃癌TNM分期准确性和敏感性存在争议, 尤其是对胃癌T分期的作用争议较多.

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研发前沿
EUS在消化系肿瘤中的应用价值、早期胃癌筛查、规范化的消化系早癌内镜下的治疗、胃癌的治疗手段等是该领域研究热点, 早期胃癌的筛查、规范化的消化系早癌内镜下的治疗是亟待研究的问题.

的作用作一综述.

关键词: 超声内镜; 胃癌; TNM分期

核心提要: 超声内镜(endoscopic ultrasonography, EUS)对T1期和T4判断的正确率较高, 对T2期和T3期及早期胃癌浸润深度判断欠佳, 但EUS仍是胃癌术前T分期重要的检查项目, 具有较高的临床应用价值, 但他对术前N和M分期, 特别是M分期存在一定的局限性.

唐雪莲, 蔺蓉, 韩超群, 丁震. 超声内镜在胃癌TNM分期中的作用. 世界华人消化杂志 2016; 24(25): 3641-3646 URL: http://www.wjgnet.com/1009-3079/full/v24/i25/3641.htm DOI: http://dx.doi.org/10.11569/wcjd.v24.i25.3641

0 引言

胃癌是最常见的消化系恶性肿瘤之一, 在世界范围内, 其发病率位居癌症第2位, 其预后差、病死率高, 严重威胁着人类的健康[1,2]. 其预后的主要因素依赖于癌肿原位浸润深度(T分期), 淋巴结转移情况(N分期)以及远处转移(M分期), 5年生存率5%-95%, 所以准确的胃癌术前分期非常重要[1-4]. 并且, 过去外科手术治疗是胃癌最主要、最根本的手段, 然而随着新的治疗方法, 如早期胃癌仅限于黏膜层, 可行内镜下黏膜剥离切除术(endoscopic mucosal resection, EMR)或内镜黏膜下层剥离术(endoscopic submucosal dissection, ESD), 进展期胃癌可以结合新辅助化疗等, 所以, 精确的胃癌术前分期显得更为重要, 合理的胃癌分期对临床治疗决策的制定和判断患者的预后具有重要的意义[5-9].

超声内镜(endoscopic ultrasonography, EUS)由于其能清晰地显示消化道管壁结构及其周围邻近脏器的关系, 目前已普遍应用于癌肿浸润深度的判断、周围淋巴结的转移以及邻近脏器的侵犯情况, 被认为是术前估计病情、选择合理手术方式及评价预后的有效手段[10]. 然而近几年来, 越来越多的研究认为EUS在胃癌分期中存在分期不足或过度分期的现象, 其对胃癌TNM分期准确性和敏感性存在争议. 本文旨在探讨EUS在胃癌TMN分期中的临床诊断价值.

1 EUS在胃癌T分期中的作用

EUS能够清晰地显示与组织学相对应的胃壁的5个层次结构, 即第1层为高回声带, 代表黏膜界面回声及浅表黏膜; 第2层为低回声带, 相当于其余的黏膜层; 第3层为高回声带, 相当于黏膜下层; 第4层为低回声带, 相当于固有肌层; 第5层为高回声带, 相当于浆膜层及浆膜下层.

在EUS图像中, 黏膜癌(T1a期)累及黏膜肌层, 表现为第1-2层结构模糊、增厚、欠规则、变薄或缺损, 第3层结构完整; 黏膜下癌(T1b期)表现为第1-3层结构模糊、增厚、内部回声不均匀, 边界欠清, 第4层结构完整无增厚; T2期, 表现为第1-4层胃壁结构病变, 表现为从第4层起的不规则突向腔内的低回声肿块, 或呈大面积局限性管壁增厚伴中央凹陷, 伴1-3层结构消失; T3期, 表现5层胃壁结构的破坏、回声带分层不清; T4期, 表现为低回声肿块突破第5层高回声带侵入外周组织等明显向邻近脏器浸润的征象[11].

以往报道[12]认为EUS对胃癌T分期诊断具有很高的准确性, 平均准确率在80%以上, 并在各期都保持了较高的敏感性和特异性. 随着对EUS的研究越来越深入, 有关其在胃癌T分期中的作用出现了不同的观点. EUS对胃癌T分期的作用在各个国家的报道中不尽相同. 一项包含116例德国患者的前瞻性研究显示, EUS对胃癌T分期的总准确率为78%, 对T1期、T2期、T3期、T4期胃癌的诊断准确率分别为: 80%、63%、95%、83%[13], 在各期中, 以T2期准确性最低; 在韩国的一项前瞻性研究中, EUS对胃癌T分期的总准确率为87.5%, 对T1期、T2期、T3期、T4期胃癌的诊断准确率分别: 87.1%、50.0%、92.2%、100%[14]; Ang等[15]认为在新加坡EUS对胃癌T分期的总准确率为77.2%, 对T1期、T2期、T3期、T4期胃癌的诊断准确率分别为: 82.9%、57.0%、57.1%、81.8%, 同样认为EUS对T2期的准确性欠佳; 而在日本EUS对胃癌T分期的总准确率最低, 只有71%[16]. Meta分析结果显示EUS对胃癌T分期的总准确率为65.0%-92.1%, 并且在判断浆膜层侵犯时其灵敏度和特异度分别为77.8%-100%、67.9%-100%[17]. 最新一项美国胃癌协会的多中心研究[18]显示EUS与术后病理结果对比, 其对T分期总的准确性非常低, 仅

有46.2%; 但是当按时间进行亚组分析时发现, EUS对T1期胃癌的诊断敏感性在过去20年里提升明显(1986-1994年为56.3%, 1995-1999年为82.2%, 2000-2006年为84.8%)[19].

尽管研究显示EUS对T1期胃癌诊断的敏感性有提升, 但目前EUS对早期胃癌浸润深度的判断准确率尚存在很多争议. 在早期胃癌的治疗中, ESD是安全、有效的治疗手段之一, 能够通过ESD手术移除的病变一般要求是黏膜下浸润不深, 无淋巴及血行浸润、转移的病灶[9,12,20]. 目前, 早期胃癌ESD的适应证: 肿瘤直径≤20 mm, 无合并溃疡的未分化型黏膜内癌; 无论病灶大小, 无合并溃疡的分化良好的黏膜内癌(M); 直径≤30 mm, 伴有溃疡的分化良好的黏膜内癌(M); 直径≤30 mm, 无合并溃疡的分化良好的黏膜下SM1癌[21]. 所以, 对早期胃癌浸润深度的准确判断很大程度上决定了患者是否可以内镜下微创治疗. 传统观点认为EUS是消化系肿瘤T分级的重要手段, 包括早癌的判断, 但现在有不同观点, 很多学者提出了相反的意见[12,22-24]. 有研究[25,26]认为EUS对早癌诊断的准确性低, 仅有70%; Mocellin等[27]的荟萃分析结果显示EUS对T1-4期的胃癌的检测的准确性高, 尤其是区分T1-2期胃癌和T3-4期胃癌, 敏感度为86%, 特异度为91%, 但是其在早期胃癌黏膜及黏膜下浸润深度的检测中效果不佳, 难以区分T1a和T1b期肿瘤; 甚至有研究[24,25]提出EUS对早癌的分期并不比普通内镜有优势. 近期有一项Meta分析同样认为EUS对胃早癌浸润深度的判断的准确率较低: EUS对早期胃癌黏膜层(M)病变诊断的敏感度和特异度分别为76%和72%, 对黏膜下层病变(SM)诊断的准确性和特异度分别为62%和78%, 而对M/SM1诊断的敏感度和特异度分别为90%和67%[25]. 而且, EUS对不同类型的早期胃癌判断能力有所不同, 对隆起型和平坦型早期胃癌浸润深度判断准确率为100%, 对凹陷型的准确率仅为58.6%; 对分化和未分化的早期胃癌浸润深度判断准确率分别为71.4%和57.9%; 对早期胃癌浸润深度判断的准确率随肿瘤直径的增大而降低, 直径<10 mm为100%, 10-20 mm为80.0%, >20 mm仅为41.2%[28]. 除EUS外, 多层螺旋CT(multislice spiral computed tomography, MSCT)也是胃癌术前分期常用的技术. 他用来判断胃癌分期的准确性也一直被用来与EUS相比较[14,29-31], 近期有研究显示: EUS和MSCT对胃癌术前T分期总的准确性分别为76.7%和78.2%, 差别无统计学意义; 但进行分层分析时发现, EUS对T1、T2期胃癌判断的准确性明显高于MSCT, 而对T3、T4期胃癌判断准确性不如MSCT[32]. 对于早期胃癌, 窄带成像结合放大内镜(magnifying endoscopy with narrow-band imaging, ME-NBI)判断其浸润深度准确率较EUS高[33-35], 研究[36]显示ME-NBI对早期胃癌诊断的准确性可达97.8%, 敏感度和特异度分别为87.2%、98.6%.

EUS对胃癌的T分期确实存在一些不足, 尤其是在早期胃癌浸润深度方面的判断. 对T1期和T4判断的正确率较高, 考虑可能因为EUS下黏膜下层与固有肌层分界较清晰, 容易判断, 浆膜外结构紊乱或腹水的形成也易于判断; 对T2期和T3期胃癌诊断正确率较低, 可能是因为浆膜层薄, 且受周边结构和脏器的影响, 其病变深度难以判断; 对早期胃癌浸润深度的判断准确率也较差, 可能是因为黏膜层和黏膜下层内病变较难通过EUS区分病变层次, 且受炎症水肿等多方面因素的影响. EUS判断T分期过浅可能与肿瘤的局部微小浸润或EUS扫描角度不全有关; 而癌旁组织炎性细胞浸润和纤维化可能是导致分期过深的主要原因; 超声探头的不同也会影响判断的准确性. 总的来说, 他仍然是目前现有的评估胃癌浸润深度较为准确的方法, 我们可以将EUS和CT、ME-NBI等其他检查相结合以提高术前胃癌T分期的准确性.

创新盘点

本文系统阐述了EUS在胃癌TNM分期中的作用, 并综合大量研究针对近几年争议较多的EUS在胃癌T分期中的作用进行了较为系统的概述.

2 EUS在胃癌N分期中的作用

癌周淋巴结转移多表现为直径>1 cm的圆形、界限清楚的低回声结节影[11]. EUS可根据淋巴结回声类型、界限及大小判断转移情况. 关于EUS在判断胃癌淋巴结转移方面, Puli等[19]研究显示EUS对胃癌N分期的诊断准确率欠佳, 对N1期胃癌诊断的灵敏度和特异度分别为58.2%和87.2%, N2期分别为64.9%和92.4%, 美国胃癌协会的一项研究中认为EUS对N分期的准确率为66.7%, 敏感度和特异度分别为48.6%、83.8%[37]. 新近的Meta分析认为EUS判断的准确率仅为64%[38].

EUS对胃癌具体N分期的准确性虽然不高, 但对直径0.5 cm以上的转移淋巴结诊断的准确率仍有较高的准确率, 对直径在0.5-1.0 cm

应用要点
EUS对胃癌T分期仍具有较高的准确性, 对NM分期的价值有限, 因此对胃癌进行术前分期, EUS仍要结合CT、窄带成像结合放大内镜(magnifying endoscopy with narrow-band imaging, ME-NBI)等其他检查综合判断, 以选择最佳的手术方式及治疗方案.

的转移淋巴结判断率为86%, 对1 cm以上的转移淋巴结判断的准确率约为90%, 而对于直径在0.5 cm以下, 尤其是<0.3 cm的小淋巴结不易探及[39].

对于胃癌N分期, MSCT也是常用的检查手段, 各项研究中关于两者在胃癌N分期中的作用也不尽相同[10,12,14,19,31,32,40,41]. 近期有研究显示: 以国际抗癌联盟(Union for International Cancer Control, UICC)第六版胃癌TNM分期为标准, EUS对胃癌术前N分期中N0、N1、N2、N3判断的准确性分别为75.7%、58.6%、27.8%、6.0%、MSCT判断的准确性分别为61.1%、48.5%、38.9%、8.4%, EUS对N0、N1期胃癌判断的准确性高于MSCT, 对N3期胃癌判断的准确性低于MSCT, 对N4期胃癌判断的准确性虽低于MSCT, 但不具有统计学意义[32]. 总体而言, MSCT和EUS对胃癌N分期的诊断准确性不够高, 但各有可取之处, MSCT对淋巴结转移判断的敏感度较高, 而EUS判断的特异度相对较高[14-16,23,41-44].

癌组织的微小浸润不易被EUS发现, 或病灶较大线阵EUS扫描范围较小可能是分期过浅的主要原因. 炎症引起的淋巴结改变和肿瘤转移性淋巴结难以区分、超声无法探测距离病变较远处的转移淋巴结等原因使得EUS在胃癌术前N分期中判断的准确性不太令人满意[12,18,40,43].

3 EUS在胃癌M分期中的作用

Meta分析认为EUS对远处转移的敏感度为73.2%, 特异度88.6%[39]. EUS对M0期胃癌判断的准确性与MSCT相当, 但对M1期胃癌诊断准确性(10.6%)明显低于MSCT的准确性(59.1%)[32]. 正电子发射扫描(positron emission tomography, PET)无法判断肿瘤浸润深度, 对胃癌淋巴结转移诊断的正确率也较低, 但可以用于判断肿瘤远处转移情况[45-49], Seevaratnam等[47]的Meta分析显示, PET-CT与MSCT对胃癌M分期诊断的准确性无明显差异(分别为88.2%和82.2%). 而对于判断腹膜转移, EUS的灵敏度和特异度分别为34%、96%, 与CT(灵敏度和特异度分别为33%和99%)、PET-CT(灵敏度和特异度分别为28%和97%)无明显差别[50]. 但胃癌腹腔转移形成腹水时, 在胃壁周围形成液性暗区, EUS探查腹水的敏感性(87.1%)明显高于传统体表超声和CT结合的敏感性(16.1%), 也高于术中发现腹水的敏感性(40.9%)[51].

EUS虽然可以直接显示邻近脏器的影像, 但由于受到超声穿透性的限制, 不能清晰地探及远处病灶, 故无法对腹膜后及远处脏器是否有转移做出准确的判断, 因此一般认为EUS不能对胃癌进行准确的M分期, 需要结合CT、PET-CT、腹腔镜等其他检查[30].

4 结论

EUS对胃癌T分期仍具有较高的准确性, 对NM分期的价值有限, 因此对胃癌进行术前分期, EUS仍要结合CT、ME-NBI、PET-CT等检查综合准确判断, 以选择最佳的手术方式及治疗方案.

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同行评价
本文选题紧跟临床前沿, 文献收集完整, 层次清晰, 综述全面, 有实用价值.

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编辑: 郭鹏 电编: 胡珊

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton,
CA 94588, USA
Fax: +1-925-223-8242
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ISSN 1009-3079