DOI: 10.13241/j.cnki.pmb.2014.04.039

胃癌前哨淋巴结检测的临床研究

王路兵 张超峰 陈明干 龚庆豪 黄 侠△

(上海交通大学医学院附属新华医院崇明分院普外科 上海 202150)

摘要 目的:探讨胃癌术中前哨淋巴结(sentinel lymph node,SLN)定位检测的可行性及其临床意义。**方法:**使用亚甲蓝对40例胃癌患者行前哨淋巴结术中标识活检，随后行D2或D2以上手术。**结果:**40例胃癌患者中,38例找到前哨淋巴结，检出率为38/40(95%),有32例存在SLN转移,8例SLN为唯一转移部位,且均为T1、T2期。由SLN的病理学状态来预测胃周围淋巴结转移情况的敏感性为32/34(94.12%),特异性为4/4(100%),假阴性率为2/34(5.88%),准确率为34/38(89.47%),其中假阴性的2例,肿瘤都处于T4期。**结论:**胃癌SLN定位及活检技术能较准确反映早期胃癌的淋巴结转移状况,但对进展期胃癌而言假阴性率较高,对胃癌整个区域淋巴结状态预测的可靠性和可行性尚需进一步验证。

关键词:胃癌;前哨淋巴结检测;淋巴结转移

中图分类号:R735.2 **文献标识码:**A **文章编号:**1673-6273(2014)04-759-02

Clinical Research on the Sentinel Lymph Node Biopsy in Gastric Cancer

WANG Lu-bing, ZHANG Chao-feng, CHEN Ming-gan, GONG Qing-hao, HUANG Xia△

(Department of General Surgery, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, 202150, China)

ABSTRACT Objective: To identify the feasibility and clinical significance of sentinel lymph node (SLN) in gastric cancer. **Methods:** Methylene blue was used to map lymphatic and SLNB forty patients with gastric cancer intraoperatively, then they were underwent D2 or >D2 surgery. **Results:** Among 40 cases included, the SLN was identified successfully in 38 cases. The detection rate was 95%(38/40). 32 patients were found to have lymph node metastasis in SLNs, 8 in SLNs alone all in T1 and T2 group, The sensitivity of SLN status in the diagnosis of the lymph node metastasis status of the patients was 94.12%, false nagetive rate was 5.88%, Specificity was 100% and accuracy was 89.47%, 2 patients were found to have false nagetive lymph node metastasis in SLN, all in T4 group. **Conclusion:** The study confirmed that the procedure of lymphatic mapping and sentinel lymph node biopsy in the patients with gastric cancer was feasible. For the early gastic cancer, the histologic of the SLN accurately predict the status of the patients. For high false negative rate of SLN detection in advanced gastric cancer. Further verifying the reliability and feasibility of SLN was required on the area of gastric cancer lymph node status prediction.

Key words: Gastric cancer; Sentinel lymph node biopsy; Lymph node metastasis

Chinese Library Classification(CLC): R735.2 Document code: A

Article ID: 1673-6273(2014)04-759-02

前哨淋巴结(sentinel lymphnode,SLN)是指首先引流肿瘤部位淋巴液并最先发生转移的淋巴结,其定位及活检技术是近些年发展起来的一项新兴的技术[1]。研究表明,当前哨淋巴结阴性时,区域淋巴结往往无转移,这在乳腺癌和黑色素瘤中已得到证实[2,3],但关于此技术在胃癌中的应用,目前尚有争论[4]。本研究采用亚甲蓝检测了40例胃癌患者术中前哨淋巴结定位和活检的情况,探讨胃癌前哨淋巴结检测(SLNB)的临床应用价值,并以免疫组化方法检测前哨淋巴结CEA、CA199水平预测局域淋巴结的转移的准确率,为术中确定临床分期,指导胃癌的手术方式以及术后辅助治疗提供理论依据。

1 对象与方法

1.1 对象

选择我院2010年7月至2011年7月间40例胃癌患者为研究对象,均行胃癌根治术,术前无化疗或放疗史,且无腹部手术史。其中男性患者22例，女性患者18例，平均年龄52岁(35~80岁);肿瘤部位:胃窦22例,胃体11例,胃底7例。

1.2 前哨淋巴结定位及活检方法

常规进腹及探查后，暴露肿瘤部位。用5 mL注射器抽取1%亚甲蓝注射液4.0 mL,距病灶边缘1.0 cm处,于周围选取四点浆膜下各注射0.8~1.0 mL,退出针头,用电凝快速闭合各穿刺点,避免亚甲蓝外逸干扰SLN的识别。5~10分钟后可见到1条至数条蓝染的淋巴管从肿瘤的部位向周围延伸,沿着蓝染的淋巴管找到的第一个蓝染的淋巴结即为前哨淋巴结,等蓝染的淋巴结(即SLN)出现后,予活检另送,送冰冻病理检查,同时记录其所属的组别、站数。对患者行标准胃癌根治术,同时逐个收集术中清扫的非蓝染淋巴结(n-SLN),并详细记录其所属的组别和站数。

1.3 标本病理检查方法

作者简介:王路兵(1977-),男,大学,主治医师,主要研究方向:肝胆外科,E-mail:350054634@qq.com

△通讯作者:黄侠,E-mail:xiahuang@citiz.net

(收稿日期:2013-04-27 接受日期:2013-05-21)

术后对摘取的前哨淋巴结及其它淋巴结（即非前哨淋巴结）常规行 HE 染色病理检查和 CEA、CA199 免疫组化染色，判断有无肿瘤转移；切除的胃组织标本常规病理检查判断肿瘤浸润深度及范围。

2 结果

术后病理证实 40 例手术标本中，T1 期 2 例，T2 期 13 例，T3 期 18 例，T4 期 7 例。40 例胃癌患者中，38 例找到前哨淋巴结，检出率为 38/40(95%)，其中 32 例存在前哨淋巴结转移，24 例同时伴有非前哨淋巴结转移，有 8 例前哨淋巴结为唯一转移的淋巴结，6 例前哨淋巴结无转移，而其中有 2 例存在非前哨淋巴结转移。

检出的 83 枚 SLN，用常规 HE 染色的方法发现有 53 个前哨淋巴结转移，而用 CEA、CA199 免疫组化染色的方法发现有 59 个前哨淋巴结转移。用常规 HE 染色检测为转移的前哨淋巴结，在用 CEA、CA199 免疫组化染色检测的时候都发现为肿瘤转移。余下的 6 个前哨淋巴结判断为微转移，其中 4 个为 T3 期和，2 个为 T4 期。由前哨淋巴结的病理学状态来预测胃周围淋巴结转移情况的敏感性为 32/34（94.12%），特异性为 4/4（100%），假阴性率为 2/34(5.88%)，准确率为 34/38(89.47%)，其中假阴性的 2 例，肿瘤都处于 T4 期。

3 讨论

肿瘤的前哨淋巴结定位及活检技术是近些年发展起来的一项新的技术，在阴茎癌、皮肤黑色素瘤和早期乳腺癌的应用中已逐渐成熟。前哨淋巴结是指首先引流肿瘤部位淋巴液并最先发生转移的淋巴结，其组织病理学状态基本上能代表整个区域淋巴结的病理状态，如果前哨淋巴结没有发现肿瘤转移，理论上能够推测整个区域淋巴结未发生转移，如果前哨淋巴结发现有肿瘤转移，那么有可能受累[5]。

本研究发现，SLN 多出现于肿瘤区域淋巴引流的第一站，这种现象与胃癌淋巴结转移的一般规律相符合[1]。一般先转移到第 1 站淋巴结，然后转移到第 2、3 站淋巴结，最后才转移到腹主动脉旁的淋巴结[6]，表明 SLN 为各组中最易受累的淋巴结。在本研究中，有 2 例 SLN 同时在第 1、2 站淋巴结出现，还有 1 例仅在第 2 站淋巴结出现，并且是唯一有转移的淋巴结，除此之外其他淋巴结均为阴性，即所谓的胃癌的“跳跃转移”[1]。国外一些研究者发现 SLN 的跳跃式转移是显著的[7-9]。本研究中有 5 例 SLN 阴性，其中有 2 例出现非前哨淋巴结癌转移，也就是假阴性。出现假阴性的机率随着肿瘤浸润深度的加深而明显升高，分析其原因可能为以下两种情况：(1)引流原发肿瘤的淋巴管已经发生肿瘤转移，造成淋巴管的阻塞，改变了原先的引流路径，以至于亚甲蓝染料不能到达前哨淋巴结；(2)术者对 SLN 定位活检技术的操作熟练程度不够或者具体方法不恰当，导致蓝染的淋巴结并非真正引流的肿瘤的前哨淋巴结[10]。

如果临床评估为早期胃癌，SLN 是可以推广使用的，其准确率和敏感度均较高，可以减少肿瘤的清扫范围，减轻手术创伤[11,12]。但是，由于胃癌淋巴引流具有多向性和跳跃转移的特点，使得进展期胃癌 SLN 检测假阴性率较高[13,14]。此外，根据文献报道，相对于乳腺癌和恶性黑素瘤，胃癌的 SLN 检测敏感性较低[15]，现在国内外学者统一致认为 D2 手术对于进展期胃癌患者的淋巴结清扫是有益处的[16-19]。

近年来，国内外对胃癌前哨淋巴结的研究还处于单中心的初步研究探索阶段，还没有多中心大样本的前瞻性研究结果报道。本研究结果表明，SLN 检测对胃癌的分期和手术方式的选择及预后评估可能具有一定的参考意义，但其对胃癌整个区域淋巴结状态预测的可靠性和可行性尚需进一步验证。只有通过多中心大样本的临床随机对照试验和循证医学的验证，才能使胃癌前哨淋巴结检测的临床应用价值得到进一步的证实。

参考文献(References)

[1] 徐慧绵, 徐岩. 胃癌转移规律研究新进展 [J]. 中国实用外科杂志, 2011, (8): 666-669
Li Hui-mian, Xu Yan. The new research progress of laws of gastric cancer metastasis[J]. Chinese Journal of Practical Surgery, 2011, (8): 666-669

[2] Nagao T, Hojo T, Kurihara H, et al. Sentinel lymph node biopsy in breast cancer patients with previous breast augmentation surgery[J]. Breast Cancer, 2011 Jun 14 [Epub ahead of print]

[3] Nathanson SD, Mahan M. Sentinel lymph node pressure in breast cancer[J]. Ann Surg Oncol, 2011, 18(13): 3791-3796

[4] Orsenigo E, Kusamura S, Staudacher C. Sentinel lymph node and prognostic factors in gastric cancer[J]. Surg Endosc, 2011, 25(11): 3715-3716

[5] 刘建明,马利林. 前哨淋巴结技术在胃癌手术中的应用[J]. 中华胃肠外科杂志, 2003, 6(6): 345-346
Liu Jian-min, Ma Li-lin. The use of tinel lymph node technique in gastric surgery[J]. Chinese Journal of Gastrointestinal Surgery, 2003, 6(6): 345-346

[6] Namieno T, KoitoK, Higashi T, et al. General pattern of lymph node metastasis in gastric carcinoma[J]. World J Surg, 1996, 20(9):996-1000

[7] Liu CG, Lu P, Lu Y, et al. Distribution of solitary lymph nodes in primary gastric cancer: a retrospective study and clinical implications[J]. World J Gastroenterol, 2007, 13(35): 4776-4780

[8] Li C, Kim S, Lai JF, et al. Solitary lymph node metastasis in gastric cancer[J]. J Gastrointest Surg, 2008, 12(3): 550-554

[9] Lee JH, Ryu KW, Kook MC, et al. Feasibility of laparoscopic sentinel basin dissection for limited resection in early gastric cancer [J]. J Surg Oncol, 2008, 98(5): 331-335

[10] 许啸声, 郑民华. 前哨淋巴结活检在早期胃癌淋巴结转移评估中的应用[J]. 外科理论与实践, 2010, (2): 194-196
Xu Xiao-sheng, Zheng Min-hua. The utilization of Sentinel lymph node biopsy in early gastric cancer of lymph node metastasis assessment[J]. Journal of Surgery Concepts & Practice, 2010, (2): 194-196

[11] 王琦三, 王海江, 尹东, 等. 前哨淋巴结活检在胃癌外科中临床意义的研究[J]. 新疆医科大学学报, 2010, (2): 180-182
Wang Qi-san, Wang Hai-jiang, Yin Dong, et al. The clinical significance of sentinel lymph node biopsy in gastric cancer surgery[J]. Journal of Xinjiang Medical University, 2010, (2): 180-182

[12] Lee SE, Lee JH, Ryu KW, et al. Sentinel node mapping and skip metastases in patients with early gastric cancer [J]. Ann Surg Oncol, 2009, 16(3): 603-608

[13] 尤建权, 马利林, 朱建伟, 等.胃癌前哨淋巴结定位活检技术的临床应用及意义[J]. 实用癌症杂志, 2008, 5: 503-506

（下转第 730 页）

on techniques[J]. Radiology, 2010, 257: 373-383

[11] Pontana F, Pagniez J, Flohr T, et al. Chest computed tomography using iterative reconstruction vs filtered back projection (Part 1): evaluation of image noise reduction in 32 patients [J]. Eur Radiol, 2011, 21: 627-635

[12] Moscariello A, Takx RA, Schoepf UJ, et al. Coronary CT angiography: image quality, diagnostic accuracy, and potential for radiation dose reduction using a novel iterative image reconstruction technique-comparison with traditional filtered back projection[J]. Eur Radiol, 2011, 21: 2130-2138

[13] Winklehner A, Karlo C, Puippe G, et al. Raw data-based iterative reconstruction in body CTA: evaluation of radiation dose saving potential[J]. Eur Radiol, 2011, 21: 2521-2526

[14] Brenner DJ, Hall EJ. Computed tomography – an increasing source of radiation exposure[J]. N Engl J Med, 2007, 357: 2277-2284

[15] Gervaise A, Osemont B, Lecocq S, et al. CT image quality improvement using Adaptative Iterative Dose Reduction with wide-volume acquisition on 320-detector CT[J]. Eur Radiol, 2012, 22: 295-301

[16] Dougeni E, Faulkner K, Panayiotakis G. A review of patient dose and optimisation methods in adult and paediatric CT scanning [J]. Eur J Radiol, 2012, 81: e665-683

[17] Hu XH, Ding XF, Wu RZ, et al. Radiation dose of non-enhanced chest CT can be reduced 40 % by using iterative reconstruction in image space[J]. Clin Radiol, 2011, 66: 1023-1029

[18] Leipsic J, Nguyen G, Brown J, et al. A prospective evaluation of dose reduction and image quality in chest CT using adaptive statistical iterative reconstruction[J]. AJR Am J Roentgenol, 2011, 195: 1095-1099

[19] Pontana F, Pagniez J, Flohr T, et al. Chest computed tomography using iterative reconstruction vs filtered back projection (Part 1): Evaluation of image noise reduction in 32 patients [J]. Eur Radiol, 2011, 21: 627-635

[20] Yanagawa M, Honda O, Kikuyama A, et al. Pulmonary nodules: Effect of adaptive statistical iterative reconstruction (ASIR) technique on performance of a computer-aided detection (CAD) system-Comparison of performance between different-dose CT scans [J]. Eur J Radiol, 2012, 81: 2877-2886

[21] Min JK, Swaminathan RV, Vass M, et al. High-definition multidetector computed tomography for evaluation of coronary artery stents: comparison to standarddefinition 64-detector row computed tomography[J]. J Cardiovasc Comput Tomogr, 2009, 3: 246-251

[22] Mayo JR, Aldrich J, Muller NL, et al. Radiation exposure at chest CT: a statement of the Fleischner Society [J]. Radiology, 2013, 228: 15-21

[23] Yanagawa M, Honda O, Yoshida S, et al. Adaptive statistical iterative reconstruction technique for pulmonary CT: image quality of the cadaveric lung on standard- and reduced-dose CT [J]. Acad Radiol, 2010, 17: 1259-1266

[24] Singh S, Kalra MK, Hsieh J, et al. Abdominal CT: comparison of adaptive statistical iterative and filtered back projection reconstruction techniques[J]. Radiology, 2010, 257: 373-383

[25] Martinsen AC, Saether HK, Hol PK, et al. Iterative reconstruction reduces abdominal CT dose[J]. Eur J Radiol, 2012, 81: 1483-1487

[26] Matsuda I, Hanaoka S, Akahane M, et al. Adaptive statistical iterative reconstruction for volume-rendered computed tomography portovenography: improvement of image quality[J]. Jpn J Radiol, 2010, 28:700-706

（上接第 760 页）

You Jian-quan, Ma Li-lin, Zhu Jian-wei, et al. Clinical application and significance of sentinel lymph node biopsy technology in gastric [J]. Cancer, 2008, 5: 503-506

[14] LiC, Kim S, Lai JF, et al. Solitary lymph nodemetastasis in gastric cancer[J]. J GastrointestSurg, 2008, 12(3): 550-554

[15] 尤建权, 马利林. 胃癌前哨淋巴结活检技术及其微转移检测应用研究[J]. 中国实用外科杂志, 2009, (4): 333-336
You Jian-quan, Ma Li-lin. Applied research of sentinel lymph node biopsy technique and micrometastasis detection in gastric cancer[J]. Chinese Journal of Practical Surgery, 2009, (4): 333-336

[16] 日本胃癌学会.胃癌取扱い规约[M].第 14 版.东京:金原出版株式会社, 2010: 2-18
The Japanese gastric cancer society. Gastric cancer Xi statute [M]. Fourteenth edition. Tokyo: the original Publishing Corporation, 2010: 2-18

[17] Yang SH, Zhang YC. Commentary for an evidence-based medicine review of lymphadenectomy extent for gastric cancer [J]. Am J Surg, 2010, 197(2): 246-251

[18] Chen XZ, Hu JK, Zhou ZG, et al. Meta-analysis of effectiveness and safety of D2 plus para-aortic lymphadenectomy for resectable gastric cancer[J]. J Am Coll Surg, 2010, 210(1): 100-105

[19] Mcculloch P, Niita ME, Kazi H, et al. Gastrectomy with extended lymphadenectomy for primary treatment of gastric cancer [J]. Br J Surg, 2005, 92(1): 5-13