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•临床经验•

胃癌前哨淋巴结体外检测的临床意义

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Clinical significance of *ex vivo* detection of sentinel lymph node in gastric cancer

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Abstract

AIM: To investigate the feasibility of *ex vivo* sentinel lymph node (SLN) mapping and its clinical significance in improving the staging of gastric cancer.

METHODS: Nineteen patients received curative resection of primary gastric cancer with extended lymph node dissection were included in this study. Gastric specimens were submucosally or subserosally injected with 10 g/L Patent Blue. The blue-stained SLNs were excised for routine pathological examination (hematoxylin and eosin staining). The SLNs, which were negative after HE staining, were further examined by cytokeratin immunohistochemistry.

RESULTS: The SLNs were identified in 89.5%(17/19) cases, with a mean number of 1.4 (1-3) for each case. After HE staining, the accuracy of the SLNs in diagnosis of the regional lymph node metastasis was 70.5% (12/17), and the false-negative rate was 38.4%. However, one case (25%) was upstaged by cytokeratin immunohistochemistry. Thus, the diagnostic accuracy increased to 88.2% and the false-negative rate decreased to 14.2%.

CONCLUSION: *Ex vivo* SLN mapping in gastric cancer

is technically feasible and may upstage some of the gastric cancer.

Key Words: Gastric cancer; Sentinel lymph node; Mapping

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摘要

目的：探讨胃癌前哨淋巴结(sentinel lymph node，SLN)体外测图技术的可行性及其对提高胃癌淋巴结病理分期准确性的临床意义.

方法：整块切除的新鲜胃癌标本19例病灶周围浆膜或粘膜下注入10 g/L专利蓝，将标本内蓝染淋巴结视为SLN，予以切除行常规病理检查，对阴性结果者进一步行细胞角蛋白免疫组化(immunohistochemistry，IHC)染色.

结果：SLN检测阳性率89.5%(17/19)，获取SLN 1-3个/例，平均1.4个/例.常规HE染色时，SLN诊断胃癌淋巴结转移的准确性为70.5%(12/17)，假阴性率为38.4%(5/13)；IHC染色后使25.0%(1/4)胃癌病例的淋巴结病理分期得到上调，诊断准确性提高至88.2%(15/17)，假阴性率降低至14.2%(2/14).

结论：胃癌SLN体外检测可作为辅助手段使部分胃癌病例的病理分期得到上调.

关键词：胃癌；前哨淋巴结；测图

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0 引言

胃癌术中体内前哨淋巴结活检(sentinel lymph node biopsy，SLNB)已有成功经验[1,2]，但关于胃癌术后体外SLN检测迄今尚无报道.我们用专利蓝对外科切除的新鲜胃癌标本进行淋巴显像(lymphatic mapping，LM)，在体外定位和识别胃癌SLN，并对其进行重点病理检查，以研究胃癌体外SLN检测的可行性及其对提高胃癌淋巴结病理分期准确性的临床意义.

1 材料和方法

1.1 材料 术前胃镜确诊、影像学和超声内镜检查未发现明显邻近器官浸润和区域淋巴结转移的胃癌患者19例，男13例，女6例，年龄32-76岁.上1/3(U)、中1/3(M)和下1/3(L)胃癌分别为2，1和16例；Borrmann 1-4型胃癌各3，5，9和2例；乳头状腺癌、管状腺癌、印戒细胞癌和粘液腺癌分别为4，9，3和3例；T1-T4期胃癌分别为2，12，5和0例；行远端胃大部分切除16例，行全胃切除3例.行D2和D3淋巴结清扫的分别为12和7例.专利蓝(Sigma)配制成10 g/L溶液，灭菌后分装备用.鼠抗细胞角蛋白(cytokeratin，CK)广谱mAb AE1/AE3，S-100蛋白和CD68 mAb，及免疫组化二步法Elivision试剂盒均为Maxim Bio公司产品.剖腹后常规探查腹腔，行D2-D3胃癌根治.手术遵循整块切除的原则，尽量将胃区域淋巴结一并包涵在整块切除的标本内，并保持相应淋巴通道的完整.胃癌淋巴结的分组分站参照日本胃癌处理规约第13版[3].No 9-11和No 13-16淋巴结分别予以单独切除.

1.2 方法 前16例为单独行体外LM，后3例先在术中行体内LM，并将染色淋巴结用缝线标记，整块切除后在体外对标本再进行LM.标本切除离体后30 min内，用5 mL注射器接4号半针头于胃癌病灶周围4点浆膜下分别注入1 mL 10 g/L的专利蓝溶液,揉按注射部位约2-5 min，10-15 min后可见胃壁表面和网膜内的蓝色淋巴管，并循蓝色淋巴管追踪至蓝染淋巴结(图1)，将其视为SLN，逐一解剖获取标本内的SLN和其他淋巴结，标本固定包埋后，每间隔200 μm取4张厚度为4 μm的石蜡切片，其中1张作为常规HE染色用，另3张分别用于CK、S-100蛋白和CD68免疫组化染色.非SLN仅行常规病理检查；SLN经HE染色诊断为转移阴性或可疑阳性，则以AE1/AE3为探针，采用二步法Eli Vision对其行IHC染色.用已知AE1/AE3阳性的结肠腺癌标本切片作阳性对照，用磷酸缓冲盐液(PBS)代替特异性抗体(一抗)为阴性对照.当淋巴结边缘窦内的上皮样细胞浆内或细胞膜上仅表达AE1/AE3，只要镜下见有染色的细胞团或散在的染色细胞即视为淋巴结微转移(lymph node micrometastasis，LNMM)阳性.通过SLN的病理状态预测胃癌周围淋巴结转移情况的各项诊断指标(诊断敏感率、诊断准确率、阴性预测率和假阴性率)按Veronesi *et al*[4]报道的方法计算.

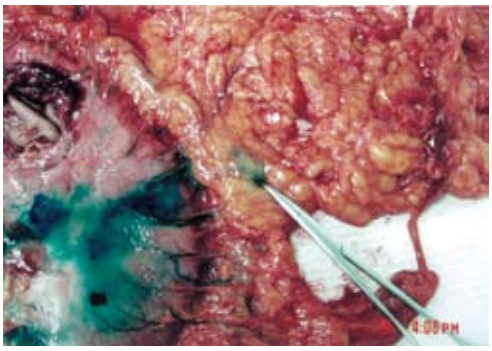

图1 新鲜胃癌手切除标本内大弯侧蓝染淋巴结（SLN）.

2 结果

2.1 HE染色结果 在19例中至少获得1个或1个以上染色淋巴结的有17例，成功率89.5%(17/19).检测失败的2例中有1例染色组织经镜下检查证实为非淋巴结，还有1例

未发现染色组织.SLN检出为1-3个/例，平均1.4个/例.3例先行体内后体外LM的病例中，先前缝线标记的蓝染淋巴结染色进一步加深，未发现新的蓝染淋巴结.19例共获取非染色淋巴结295个，平均每例15.5个.SLN检测成功的17例胃癌中有13例发生了淋巴结转移,其中SLN转移阳性者占8例，SLN阴性而其他淋巴结阳性(假阴性)5例，SLN和非SLN皆阴性者4例.这样SLN诊断胃癌淋巴结转移状况的敏感性为61.5%(8/13)，准确率为70.5%(12/17)，阴性预测值为44.4%(4/9)，假阴性率为38.4%(5/13).

2.2 IHC染色结果 假阴性SLN 5例中发现3例IHC染色阳性(图2)，SLN和非SLN皆阴性4例中发现1例SLN有微转移灶，这样就使25%(1/4)胃癌病例的淋巴结病理分期得到上调(upstaged)，SLN诊断胃癌淋巴结转移状况的敏感性、准确率和阴性预测值分别提高到85.6%(12/14)，88.2%(15/17)和60%(3/5)，假阴性率降至14.2%(2/14).

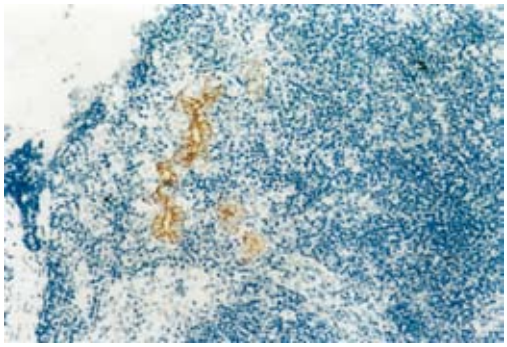

图2 胃癌SLN微转移灶 (CK-IHC，×100).

3 讨论

既往多认为恶性肿瘤的SLN检测应在体内生理状态下进行，在体外对手术切除胃癌标本进行胃癌的SLN检测方法难被认同，主要原因在于:(1)失去了活体中生理性的淋巴流动和手术对淋巴管网的解剖性破坏;(2)胃癌的SLN虽然多数在临近病灶处(N1)，但也可以是远离病灶的N2或N3淋巴结，而即便是整块切除的胃癌手术标本也不可能将N1-N3的所有淋巴结都包括在内，这是本研究的主要不足之处，也可能是研究结果不尽满意、假阴性率偏高的原因所在.但本研究的立论依据和临床意义在于:(1)体内SLNB可能对患者产生不利影响：为促进染料播散而对注射部位进行的揉按和为了显示隐蔽染色淋巴结而进行的解剖显露，可能增加肿瘤扩散的机会和破坏整块切除的肿瘤手术原则；人体内注入染料示踪剂可能出现过敏反应并增加污染机会和手术时间等[5-7].而体外SLN检测无此弊端;(2)体外检测SLN在胃癌中虽无报道，但在结直肠癌中已有成功经验[5,6,8]，其机理也得到了说明，提示胃肠道肿瘤SLN体外检测的可行性;(3)Kitagawa *et al*[9]指出：SLNB的本意是对较早期肿瘤病例的SLN进行重点病理检查，以提高判断肿瘤淋巴结转移情况的准确性.本研究显示体外SLN检测已基本能达此目的.目前在胃癌术中进行的体内SLNB，终极目标是能据其结果指导胃癌的淋巴结清扫，但实际上术中体内SLNB可能带来的缩小淋巴结清扫范围在胃癌外科中的意义目前并不明确[10];(4)毕竟胃癌的SLN多数还是在病灶周围，尤其是在较早期胃癌，整块切除的手术标本应能包括多数的SLN(除外少数“跳跃性”转移的远处淋巴结)[11].本研究IHC染色结果显示：体外SLN检测在判断胃癌区域淋巴结转移情况的准确性高达88.2%，此数据与体内SLNB结果相比虽有差距，但已能说明该技术的可行性和有效性.因此具有简便和成本效益优势的体外技术，特别是在体内LM失败的情况下，可作为一种补充手段，结合目前的常规病理检查方法，可能有助提高胃癌病理分期的准确性;(5)区域淋巴结的转移状态是指导胃癌临床病理分期、评估胃癌预后及制定术后辅助治疗方案的最重要依据.但目前对其诊断的方法存在着不全面和不彻底的缺陷.现行的胃癌广泛性淋巴结清扫主要目的之一在于获得尽可能多的淋巴结，以准确判定胃癌的临床病理分期，但仍不能保证胃癌周围所有可能转移的淋巴结都得到了检查，也无法用繁琐的连续切片、IHC染色或逆转录聚合酶链反应(RT-PCR)等方法，对胃癌D2根治所获得的数十个甚至上百个淋巴结都进行彻底的病理检查，导致约有9-31%的LNMM不能被检出[12].临床上胃癌清扫淋巴结病理检查皆阴性而术后复发的情况并不少见，原因可能就在于此[13].而体外标本中检出的胃癌SLN不但可代表其它淋巴结的病理状态，又使病理医师可集中精力和物力对1至数个转移风险最大的SLN进行彻底病理检查.本研究上调了25%(1/4)胃癌病例的淋巴结病理分期，将为胃癌患者的预后评估和制定术后辅助治疗方案提供更可靠的依据.

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•临床经验•

气囊扩张术联合肉毒素注射序惯治疗贲门失弛缓症的近期及远期疗效

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Short-term and long-term effect of pneumatic dilation and botulinum toxin injection in treatment of cardiac achalasia

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Abstract

AIM: To evaluate the short-term and long-term effect of the pneumatic dilation and botulinum toxin A (BTXA) injection for the cardiac achalasia.

METHODS: From July 2000 to May 2004, 35 patients with cardiac achalasia received pneumatic dilation and BTXA injection in our hospital. The improvement of the dysphagia was observed 1 and 12 mo after the treatment.

RESULTS: Of the 35 patients, their conditions of dysphagia were significantly improved. The efficacy rates were 100% and 93.9% in the following up (1 and 12 mo, respectively). Two patients were lost to follow up while dysphagia relapsed in three patients during the following up.

CONCLUSION: The pneumatic dilation and BTXA injection for cardiac achalasia is safe, stable and effective in the treatment of cardiac achalasia.

Key Words: Pneumatic dilation; Botulinum toxin A; Achalasia

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