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· 文献综述 ·

残胃癌的诊治研究进展

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摘要

残胃癌(GSC)是指胃良性疾病行胃切除术后5年以上或胃癌行胃切除术后10年以上,残胃出现的新发癌。由于早期GSC患者临床表现不典型,就诊时多数已进展,加之本病的特殊性,导致其预后较差。GSC的发生率呈逐年上升的趋势,为探讨近年来GSC诊治的若干问题,笔者复习国内外相关文献,就其的病因、临床表现、治疗手段、预后及预防等研究进展作一综述,并提出首次胃切除手术后的随访尤为重要,早期发现、诊断及早期治疗是提高患者的生存率、改善生活质量关键。

关键词

胃肿瘤/诊断;胃肿瘤/治疗;胃残端;综述文献
中图分类号:R735.2

Research progress in diagnosis and treatment of gastric stump cancer

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Abstract

Gastric stump cancer (GSC) refers to a primary carcinoma arising from the gastric remnant more than 5 years after surgery for benign ulcer disease or more than 10 years after surgery for gastric cancer. Because of the atypical clinical presentations of the GSC patients at the early stage, most of them are found in advanced stage when seeking for treatment, which plus the particularity of this condition, result in a poor prognosis. The incidence of GSC has shown an increasing tendency over the years. For discussion of several issues concerning the diagnosis and treatment of GSC in recent years, the authors based on review of the relevant literature at home and abroad, address its pathogenesis, clinical manifestations, treatment methods, prognosis and prevention, and also propose that the postoperative follow-up after the first gastrectomy is particularly important, and early detection, early diagnosis and early treatment are essential for improving the survival rates and the quality of life of the patients.

Key words

Stomach Neoplasms/diag; Stomach Neoplasms/ther; Gastric Stump; Review
CLC number: R735.2

残胃癌(gastric stump cancer, GSC)作为一种特殊类型的胃肿瘤,是指胃良性疾病行胃切除术后5年以上或胃癌行胃切除术后10年以上,残

胃出现的新发癌^[1]。随着目前胃肠外科的日益发展,行胃切除术患者的不断增多,GSC的发生率呈逐年上升的趋势^[2],由于早期GSC患者临床表现不

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典型,就诊时多数已进展,加之本病的特殊性,导致其预后较差,5年存活率仅为7%~20%^[3]。因此,GSC的早期诊断、治疗尤为重要,现就GSC近年来的诊治研究进展做一综述。旨在使广大临床医生更深入地了解本病,为日后临床工作提供指导依据。

1 病因

目前认为GSC的发病原因有以下几个方面:

(1) 残胃是胃癌发生的“母巢”,前次手术后碱性反流液损害胃黏膜上皮细胞及胃黏膜屏障减弱是GSC发生的重要因素^[4]; (2) 胃切除术后胃酸分泌减少,胃内pH升高,厌氧菌繁殖生长,内源性亚硝酸盐增多,加剧GSC癌前病变; (3) 前次手术长期未愈合的吻合口或缝线溃疡,作为应激性刺激的重要因素; (4) GSC的发生发展与EB病毒感染关系密切^[5]; (5) GSC的发生亦与前次手术方式有关:据报道^[6-8]胃大部切除术后,Billroth II式手术GSC发生率较高,因其有较高的反流率。而Roux-en-Y式吻合可相对减少吻合口反流,减少残胃炎的发生,降低了GSC的发生率^[9-11]; (6) 幽门螺杆菌(Hp)感染是原发胃癌的主要致病因素,虽然对GSC的发生影响作用尚不明了^[3],但Giuliani等^[12]研究发现,胃术后残胃出现慢性活动性胃炎与Hp感染有关,抗Hp治疗可以减轻活动性胃炎的程度,这有可能会降低GSC的发病率; (7) 行远端胃切除术时迷走神经被切断也是致癌的一个原因,神经切断后,胃的防御因子减少,胃黏膜的血液循环、分泌和再生受到影响,导致其在增生过程中发生细胞DNA的突变,从而致癌^[4]; (8) 另外,GSC的发生与年龄、遗传、性别等因素相关,研究^[13]表明在诊断GSC的患者中,中位年龄在67~71岁之间,男性患者发展为GSC的风险是女性的4~9倍。

2 临床表现

GSC早期临床表现无特异性,发现时多为中晚期,易导致患者的忽视和临床医师的误诊,常见的症状包括:恶心呕吐、食欲不振、腹痛、黑便、贫血、消化道梗阻等。对初次行胃大部切除术的患者,如果术后长期出现上述的消化道症状,则视为GSC的高危患者^[14],故胃部分切除术后,尤其是行Billroth II式患者,除定期检查外,

还应动态分析和鉴别术后的不适症状是消化道功能障碍,还是发生了GSC。

3 诊断

GSC的诊断主要依靠胃镜检查及胃黏膜活检^[15-16],但在GSC早期,其镜下表现与吻合口溃疡、残胃炎等极为相似,易误诊;此外,行活检时取材不佳也易漏诊。检查时应注意观察残胃的黏膜,若发现色泽苍白、糜烂、隆起,则有早期癌的可能,应行常规活检。如临床考虑早期GSC,内镜下尽管外观未见明显异常,仍须在GSC的好发部位行多处取材,且要有足够的取材深度,同时应注意术后胃原有结构的变化带来的干扰,提高阳性诊断率;内镜检查及黏膜活检对GSC的诊断至关重要,针对因良性疾病行胃大切的患者,术后尤其10年以上者,不论症状有无,均应常规检查,而胃恶性肿瘤术后的患者应每年行内镜检查^[15],对可疑黏膜分化者,应及时活检,争取早期诊断。GSC的CT和MRI影像与胃癌基本相同,可提示周围组织浸润情况和有无远处转移,是TNM分期的重要手段,目前认为GSC的分期标准以第7版UICC为可靠依据^[17]。GSC的CT影像一般表现在胃充盈状态下,胃壁可有不规则的增厚,厚度达4~5 mm,若胃壁呈环周性增厚,可致胃腔不规则狭窄变形、胃壁韧性丧失、僵硬。若癌肿局限性突向胃腔内或腔内外同时生长,则可观察到表面凹凸不平的不规则软组织肿块影。当残胃形态不清、癌肿处的浆膜面粗糙、与周围组织器官间的脂肪间隙消失或间隙内出现索条影或相连续而接触面凹凸不平时,常提示肿瘤突破浆膜,侵犯周围组织和器官。近年来随着多层螺旋CT技术的不断升级,能够清晰的观察残胃胃腔外、肠系膜及腹腔的情况,效果令人满意,术前三维重建技术进一步提高了评估的准确率^[18]。因此,临床上行多层螺旋CT用于胃术后患者的复查,对于可疑病例,结合胃镜检查进行充分评估,使患者得到最合理的治疗。EUS既可以观察到病变浸润的深度,亦可显示胃周淋巴结受累情况,其与CT结合可进一步提高T、N分期的准确性,吴齐等^[19]报道应用EUS对GSC术前TN分期的诊断率T可达81%,N可达76%,可对癌肿的浸润和转移情况进一步了解。另外,钡餐检查亦可应用于患者术后随访,但推荐“低张”气钡双对比造影,其可观察到病变处充盈缺

损、吻合口狭窄、残胃狭窄段胃壁僵硬,有时可见龛影,其优点是对病变处黏膜面较敏感,缺点是无法评估残胃胃壁及胃腔外的变化,故需结合其它检查方法明确诊断。为早期诊断GSC,应做到:(1)加强胃术后患者的随访,认识到GSC的发生与术后经过时间关系呈正比,做到早期发现。(2)正确分析胃切除术后患者临床表现的动态变化:对于胃大部分切除术后的患者,重新出现了消化道症状,均应行临床检查。(3)选择正确的检查手段,争取做到及时确诊。

4 治疗

GSC一经诊断,治疗原则应以手术切除为主的综合治疗^[20-21]。应遵循“安全、根治、功能”的原则行规范化清扫手术;无法根治者做姑息性切除或转流手术,再结合辅助放、化疗。GSC的手术治疗包含切除病灶、重建消化道及淋巴结根治性清扫,具体手术方式可根据患者术前TNM分期及全身情况来定。GSC如伴肝、肺、腹膜等远处转移则视为手术禁忌证。

4.1 手术治疗

4.1.1 病灶切除 目前的观点是扩大切除范围,应包括残胃、胃肠吻合口及其侵犯的组织器官。因残胃多伴不典型增生且弥散分布的癌灶,St-Louis等^[22]认为无论早期或晚期与否,均应行残胃全切,确保切缘阴性,即手术切缘至肿瘤边缘的距离至少要 ≥ 5 cm。GSC患者约31%~53%有浸润胃空肠吻合口情况,是肿瘤进展、远处转移的主要形式之一,因此必须一并切除原吻合口及空肠系膜,既可提高患者预后,又可准确的了解实际病理分期。Chowdappa等^[23]通过对90例GSC患者的分析研究表明GSC发生于胃空肠吻合口与非吻合口的患者3年生存率分别为10.5%、36.4%。因胃大部分切除术改变了正常的解剖结构,若合并其他脏器侵犯,应一并切除^[24]。Corcione等^[25]报告对于晚期GSC患者来说,行姑息性手术及非手术治疗,生存率均不到1年,因此,对于术前确诊为晚期的GSC患者行手术治疗应慎重考虑。

4.1.2 消化道重建 为防止反流,在残胃切除术后一般选择经典Roux-en-Y术式^[26-27],该优点是可避免发生反流性食管炎,在以往的GSC根治术中,行食管-空肠Roux-en-Y吻合时,常做管状吻合,术后部分患者出现吻合口梗阻、狭窄等

情况,Etoh等^[20]报告狭窄率约为2.8%,近年来,食管-空肠三角吻合得到广大医师的认可,因其增大了吻合口的面积,术后发生梗阻、狭窄等并发症的几率明显下降^[28],但其缺陷是无贮存功能,故在其基础上增加空肠贮袋则必然是较理想的手术方式。目前刘宏斌等^[29]提出空肠R型代胃食管-空肠三角吻合技术,其优点主要体现在以下几个方面:(1)“R”型空肠起到“贮袋”作用,增加了食物停留的时间,降低了倾倒综合征的发生率;(2)食糜通过吻合口后可在“R”环中顺蠕动循环,使营养得以充分吸收;(3)此术式吻合口更高,不易发生食管反流,同时降低了十二指肠腔内压力,避免发生十二指肠残端瘘等优点。但此手术方式在临床上未广泛推广,还需大样本分析。

4.1.3 GSC的淋巴结清扫 胃大切术后常发生局部淋巴管的漏、阻塞、重建及新生。GSC较易发生淋巴转移,Iguchi等^[30-31]报告脾动脉旁及脾门淋巴结的转移率较高,GSC淋巴结转移途径不同于原发性胃癌,应更加彻底的行淋巴结清扫,以达根治目的。考虑到残胃淋巴管可与邻近脏器的淋巴管粘连相通,故GSC手术要将其粘连的脏器及淋巴组织一并切除。文献^[32-33]指出,目前残胃的淋巴通过以下路径引流:(1)逆向路径,前次手术胃左动脉被切断,沿胃左动脉的淋巴转向贲门右动脉走行,再流向腹腔动脉周围;(2)胃短血管路径,切断了胃左动脉,淋巴液流向腹腔动脉旁淋巴结被阻断,而通过胃短血管周围淋巴结向脾动脉及脾门周围淋巴结的引流未受影响;(3)新生淋巴路径,胃十二指肠或空肠吻合及其系膜方向新产生的淋巴通路引流;(4)其它路径,肿瘤侵及食管引起纵隔内的淋巴引流。因此,GSC手术中必须认识到上述异常淋巴引流路径,以便清扫淋巴结的范围更合理,淋巴结清扫应包括No.1~13组淋巴结^[3]。如胃大切术后Billroth I式吻合,亦应清扫胰前淋巴结(No.17),如Billroth II式吻合,应清扫肠系膜上血管旁淋巴结(No.14),如癌肿侵犯食管则应对贲门区附近的淋巴结进行清扫,包括膈下、食管裂孔、下段食管旁、膈上淋巴结(No.19~20、No.110~111)。另外,Kunisaki等^[34]根据淋巴流向及淋巴结转移特点,认为进展期GSC均应清扫腹主动脉旁淋巴结。

4.1.4 腹腔镜行GSC根治术 近年,由于腹腔镜技术的不断成熟、其较传统手术具有不少优点,激发了我国学者对腹腔镜GSC根治术的探索,但由

于GSC局部解剖关系的改变,腹腔器官粘连严重,增加了手术操作的难度,在国内目前无多中心的病例报道。与开腹手术相比较,腹腔镜GSC根治术有着术中出血少,淋巴结检出率高,术后排气快,并发症少等优点,而比较腹腔镜组和开腹组的5年生存率方面两者差异无统计学意义^[35-37],表明腹腔镜GSC根治术治疗GSC的近期临床疗效肯定,值得临床推广。Yamamoto等^[38-39]认为随着操作技术的不断规范,理念的不断完善,严格把握手术适应证,会更突显腹腔镜在GSC根治术中的优势,定能达到甚至超越开腹手术的远期效果。而近年来马凯等^[40]通过对8例GSC患者行达芬奇机器人辅助下GSC根治术的分析表明,达芬奇机器人应用于GSC根治术中是安全、有效、可行的,且手术更加微创、并发症少。机器人手术系统代表了微创外科的发展方向,相信日后其能在GSC治疗中起到重要作用。

4.2 内镜治疗

内镜手术包含内镜下黏膜切除术(EMR)及黏膜下层剥离术(ESD)。尽管GSC的标准术式是切除残胃+淋巴结清扫。Fukui等^[41-44]的资料报道,部分GSC患者并没有发生淋巴结转移,提示内镜手术可用于早期GSC的治疗,从而减少创伤及相关并发症的发生。Lee等^[45]报道,ESD治疗早期GSC,完整切除率与上1/3部胃癌没有明显差别,癌灶整块切除率达97%,完整切除率为74%。GSC的ESD治疗手术适应证与原发胃癌相同。(1)非溃疡型黏膜内癌:组织分化好、不论肿瘤大小;(2)溃疡型黏膜内癌:组织分化好、肿瘤直径<3cm(组织分化好:乳头状或高中分化型肿瘤);如癌灶侵及黏膜下层,则非ESD的手术适应证,因其可能伴有淋巴转移。GSC的内镜治疗,操作难点在于残胃腔小,腔内有大量的缝钉且附近严重纤维化,传统的ESD很难整块切除严重纤维化的区域,缝钉妨碍吻合口病灶的切除,故完整切除率不高。国外学者^[46]提出使用绝缘透热刀(insulation tipped diathermic knife, ITESD),可提高完整切除率,从40%升至82%,有望解决该操作难点。为了避免并发症的发生,推荐有经验的术者行内镜治疗GSC,特别是位于吻合口处的癌灶,操作平面在吻合口,要克服因残腔空间小、缝钉及大片纤维化带来的困难。

4.3 辅助治疗

GSC的辅助治疗包括辅助及新辅助放、化

疗。但由于本病发病率低,且病例难以集中,相关的研究报道较少,针对原发性胃癌的辅助治疗方案对GSC仍然有效。

5 预后及预防

国外文献^[47]报告I、II期GSC的5年生存率分别为90%~100%及40%~80%,而进展期预后差,5年生存率仅有14%,提示GSC早期预后良好;Schaefer等^[48]报告如伴空肠浸润,无病生存>5年,中位生存期仅6.6个月。GSC被看成为残余胃的二次原发性癌,因其位置与胃上1/3的胃上部原发癌(primary upper third gastric cancer, PTUGC)相似,因此,常比较其与PTUGC的预后差异以明确两者的异同。而PTUGC与GSC的预后是否相同,目前仍存在争议。近年来部分研究认为,GSC的总体预后要差于PTUGC^[8]。若进一步按照分期进行比较,对于I、II期患者而言,GSC的预后好于PTUGC;对于III、IV期患者而言,GSC的预后要差于PTUGC,就目前总体研究结果而言,当相同分期时,GSC的预后应与原发胃癌无异,但由于相关研究样本量均较小,仍待进一步验证^[49-50]。影响GSC预后的主要因素:(1)癌肿的组织学类型及浸润深度;(2)胃周淋巴结转移情况;(3)可否根治性切除肿瘤。其中,能否行根治切除手术是最重要的独立预后因素^[51]。研究^[52-53]表明GSC的预后与淋巴结转移密切相关,淋巴结转移越多的患者预后多较差。故GSC的早期发现、早期诊断尤为重要,一经确诊,应积极做好手术准备,限期行根治性手术。术中要严格遵循根治原则,争取达到R₀切除,并加强术后的随访,发现异常及时取材活检,做到对GSC患者的早期诊断和根治性的手术治疗,从而改善GSC患者的预后,延长生存期^[54]。针对GSC的病因,对因胃部疾患需行手术或术后的患者,预防措施应包括:(1)手术适应证的严格掌握;(2)术中消化道的吻合方式多采用Roux-en-Y式;(3)注重幽门功能的保留,高选迷走神经切断代替胃大切治疗胃十二指肠溃疡,该手术方式保留了胃、幽门,从而避免了十二指肠液的反流;(4)术后应用吗丁啉等胃肠动力药;(5)根除Hp;(6)戒烟、酒。另外,对行胃大切的患者加强随访,定期复查胃镜,尤其是术后5年以上伴有相关症状者,力争做到早诊断、早治疗,以提高GSC患者的整体生存率。

6 结 论

总之, GSC是一易漏诊和难治的恶性肿瘤, 其有着组织分化差、恶性程度高的特点, 需引起医患对该病的认识。对胃切除术后5年以上的患者, 尤其是前次手术采用Billroth II式术式或已出现胃部不适者, 需做好随诊, 定期复查胃镜。一旦发现异常, 及时取材活检, 做到早发现、早诊断及早治疗, 以改善患者的预后。

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