P.O.Box 2345 Beijing 100023, China
Fax: +86-10-85381893
Email: wcjd@wjgnet.com www.wjgnet.com

World Chin J Digestol 2003 May;11(5):613-618
世界华人消化杂志 ISSN 1009-3079 CN 14-1260/R

• 文献综述 REVIEW •

胆道系统运动调节及功能性胆道运动异常的诊治

陈仕珠

陈仕珠,中国人民解放军解放军第 451 医院 陕西省西安市 710054
项目负责人:陈仕珠,710054,陕西省西安市友谊东路 269 号,中国人民解放军解放军第 451 医院内科. chen sz@pub.xaonline.com
电话:029-2257105
收稿日期:2002-03-29 接受日期:2002-11-18

摘要

胆道系统运动调节十分复杂，其功能紊乱的诊治难度亦大. 正常胆管的结构及压力梯度是胆汁流动的动力. 胆系运动受多种神经和激素的调节,大多数胃肠激素不同程度地参与胆系运动的调节. 胆囊(GB)容量、胆汁排出量(GEF)受年龄、性别、体重、饮食量及其成分、吸烟、血糖、血氨基酸和胆盐等影响. 试餐超声检查及核素闪烁照相、ERCP 对本病有一定诊断价值；胆道压力测定结果为诊断本病的金标准，但广泛应用受限制. 功能性胆道运动不良(含 GB 切除术后胆道动力障碍)分III型，舒张 Oddi 括约肌(SO)的药物对 II 和III型有较好疗效.内镜SO切开术有效率达 90 % 以上.

陈仕珠. 胆道系统运动调节及功能性胆道运动异常的诊治. 世界华人消化杂志 2003;11(5):613-618

http://www.wjgnet.com/1009-3079/11/613.htm

0 引言

功能性胆道疾病临床上十分常见，发生率约占消化系疾病门诊数的 20 %[1]. 由于其中 60 % 以上的患者症状不明显或因同时存在胃肠功能紊乱等而被其他症状所掩盖，加上检查和治疗手段的限制，仅约 10-20 % 的患者得到诊断[1,2]. 为了提高对本病的认识，本文对近年来有关功能性胆道疾病的研究进展作一介绍.

1 胆管动力与调节

1.1 胆管结构及动力学 肝内胆管均无平滑肌细胞，肝外胆管平滑肌细胞发现率分别为肝总管 24 %，胆总管十二指肠上段 53 %，胰腺段 87 %；胆总管上段仅有少量环行或纵行平滑肌束，在壶腹部形成胆总管括约肌[3]. 胆汁流动主要依靠胆内压力梯度[4,5]. 正常时肝内静水压(肝内胆汁分泌压)为 2.64-2.94 kPa，肝外胆管内压为 0.98-1.3 kPa，而 SO 压为 1.07-1.4 kPa. 胆囊(GB)排空后，其内压力下降至 0.98 kPa 以下(最低至 0.49 kPa)时，胆液便流入 GB，GB 充盈，压力升高可达 1.77-2.16 kPa. 胆管括约肌和 SO 松弛时胆液很快排入胆管，进而排入十二指肠. 如 SO 功能障碍致胆汁排出障碍，使胆管压力超过 2.94 kPa(直径≥ 9 mm)时，则考虑胆管有扩张[3].

1.2 胆管运动调节 胆管壁内有较多的神经细胞，但未形成界限明显的壁内神经丛. 胆总管有主动伸长或缩短运动功能，有助于转送胆汁[4]. 自主神经使胆道张力维持正常状态. 胆汁流动的原动力是肝胆汁的正常分泌压在 GB 排空过程中，胆管系统主要起输送管道及顺应性收缩或扩张的作用.而起动力或控制作用的是 GB 和 SO[6,7].

2 SO 和 GB 运动调节

2.1 SO 结构功能 SO 由胆总管括约肌、胰管括约肌、壶腹括约肌、中间纤维组成. 胆总管括约肌和中间纤维可见于所有人，只有 1/3 和 1/6 的人有胰管和壶腹括约肌. 正常人胆总管压力约 0.66 kPa，胰管压 1.26 kPa，SO 基础压 1.33 kPa. 胆总管压升高时，SO 即松弛，胆汁排出，压力降低，故胆汁一般不会流入胰管[3]. 调节SO运动的因素多而复杂，涉及神经和激素(以肽类激素为主)[8,9].

2.2 GB 容量及 GB 排空 GB 分为底、体、颈和 GB 管. GB 管长约 3-4 cm；直径 2-3 mm. GB 管近 GB 管颈有螺旋黏膜皱襞称海斯特瓣，由平滑肌构成，可防止 GB 管的过度扩张和塌陷[3,9]. GB 有纵行肌、斜行肌和少许松散排列的环形肌组成的平滑肌层，GB 平滑肌收缩可排出胆汁，是 GB 胆汁排空的原动力，GB 管内螺旋状黏膜皱襞有 GB 泵作用，有助于 GB 充盈[1-3].

正常人空腹 GB 容量(fasting gallbladder volume，FGV)与性别、年龄[10,11]、饮食习惯、胃十二指肠功能状态等有关[12-15]. 女性 FGV 通常较男性为少[11]. 肥胖者 FGV 通常较多. 瘦男性和胖女性随年龄增加 FGV 也增加. 低脂低蛋白饮食可使FGV增加[2]. 长期饮酒者饮入较多酒后可使 SO 等的运动发生变化而影响 GB 排空[16,17]. 肠易激综合征及胆汁返流性胃炎患者FGV增加[12-15]. 正常人进脂肪餐后，GB 可排出其中 80 % 以上的容量，于 1 h 内 GB 排出量(gallbladder ejection fraction，GEF)即可达最大[1,18]，尔后 GB 开始充盈(充盈多于排出). 禁食状态下，GB 呈周期性收缩并排出少量胆汁入十二指肠，随胃十二指肠移动蠕动复合波(interdigestive motor complex，IMC)向下推移[1,12,19]. 空腹和餐后 GB 排空是交替进行的，在 IMC 的 I 相和III相时，SO 以 6-8 次 /min 规则地正向蠕动，使胆汁以脉冲式挤入十二指肠，结果使充盈大于排空，II 相时 GB 开始收缩，同时 SO 松弛，胆汁以 1 mL/min 流向十二指肠[5,19-23]，总体排空多于充盈. 如进食大量脂肪饮食 GB 可加倍收缩，以 3 mL/min 将胆汁排入十二指肠，此种排空多于餐后 1 h 内达高峰[20-22] 这样，使来自肝脏新

的稀薄的胆汁不断进入GB，同时GB胆汁陆续被排出而不致过分浓缩. 进一步研究发现，餐后90 min GB排出的胆汁量为基础量的6倍[22]，即约5倍多的胆汁是肝脏新分泌出来的. GB排空速度与量除与食物成分有关外，与食物到达十二指肠的速度及十二指肠产生的GB收缩素(cholecystokinin，CCK)等的含量、GB和SO上CCK等受体密度和敏感性等关系密切[21,22].

2.3 GB和SO运动的神经调节 已知GB和SO运动受胆碱能及肾上腺素能神经控制和调节. GB壁内存在黏膜层和肌层神经丛及较多神经细胞，但未形成界限清楚的壁内神经丛. GB壁和SO上存在α、胆碱能及β受体，前二者介导收缩，后者介导舒张，正常情况下GB收缩和SO舒张是同时发生的. 此外，GB和SO上还分布有生长抑素(somatostatin，SS)等多种肽能神经及其受体，参与GB排空的调节. 切除迷走神经可显著延缓GB排空并减少GEF，改变GB排空方式，表现为连续排空及再充盈[23,24]. 刺激迷走神经使GB内压增加，SO松弛，GB排空增快、增多[25]. 除肾上腺素能和胆碱能神经外，免疫组化研究表明，SO上存在密集的含神经肽的肌间神经[26,27]，豚鼠GB壁分布有组胺受体，并通过激活H_1和H_2受体调节GB收缩[28]. 表明肽能神经、组胺能神经等均参与GB排空的调节.此外，GB排空亦存在头相，可能是感官-胃液分泌-十二指肠酸化-CCK-胆碱能神经-GB和SO的结果，而胃相-肠相及回肠结肠相则与食物所达部位继发的神经和体液调节所致[29].

2.4 GB和SO运动的体液调节 已知许多胃肠激素(gastrointestinal homone，GH)参与GB和SO运动的调节[2,3,29-31]. 脂肪餐进入十二指肠后引起CCK释放，CCK与GB及SO上的CCK受体结合或经胆碱能神经作用产生排空效应. 静注CCK-8可使胆总管压明显升高，SO活动增强，压力减低[23]. 但GB及SO对含肽数量不同的CCK反应有异，GB对同样剂量的CCK-3(10-80 nmol/kg)和CCK-2(10-160 nmol/kg)无反应，而SO则可完全松弛. 用于阻滞CCK对SO作用的药物剂量要比对GB的剂量大得多. 除循环CCK调节GB排空外，将CCK-8、CCK-5和胃泌素置于GB腔内，可引起由神经介导的GB收缩，并呈剂量相关，其机制可能是通过CCK-B型受体，经内脏神经介导的[2]. 血管活性肠肽(vasoactive intestinal peptide，VIP)与CCK联用时，可拮抗CCK-8对SO的作用，但单独输注VIP则对SO活动无明显影响[23,31]. 静注P物质、阿片肽对SO的作用与CCK-8相似，使SO收缩，减少胆汁流出，但作用稍弱[1,32]. 内源性前列腺素(PG)系统对正常人空腹及餐后GB排空均无明显影响[1]，可参与CCK引起的GB收缩的调节. 但PGE通过刺激GB黏液分泌，抑制GB排空，使GB张力增加，其拮抗剂消炎痛可消除此作用，防止胆固醇核的形成，促进GB排空. 有研究发现，心房利钠肽使餐后GB收缩，而空腹则否，可能是GB胆汁对GB的作用不同[33]. 蛙皮素刺激的GB收缩可被阿托品和SS所抑制，提示蛙皮素对GB的作用是经胆碱能神经实现的，而SS抑制GB排空可能是通过抑制蛙皮素刺激的CCK释放[34,35]. 胃动素调节胃肠运动，亦调节GB排空. 胃动素拟似剂红霉素可促进GB排空异常的人的GB排空，提示胃动素可能刺激其GB收缩及SO舒张[34]. 胃泌素释放肽直接刺激豚鼠GB收缩[1,2]. SS通过抑制几乎所有刺激GB收缩和/或SO松弛的激素的作用而抑制GB排空. 静注SS可完全消除由进固体、液体食物及胆碱能和CCK等引起的GB排空，抑制静息状态时SO运动[30,34-36]，而奥曲肽抑制空腹和进餐引起的SO运动，增加SO基础压和收缩波[31,34-37]. Weber et al [37]研究发现，皮下注射100 ug奥曲肽显著增加SO收缩频率和基础压，抑制GB收缩，该作用持续超过1 h(而循环SS半衰期仅约3 min). 进一步证实奥曲肽可引起SO功能不良及减少GB排空，但在SOD患者则可使SO松弛，利于GB排空[38,39]. 由于长期应用奥曲肽使GB排空缓慢而引起的GB结石者高达20 %[1,2,40]. 神经减压素10-40 ng/(kg·h)使餐后GB排空明显减少，而用2-5 pmol/(kg·min)者则否. 表明神经减压素抑制GB排空的作用与剂量有关[41]. McKirdy et al [42-44]研究发现，一氧化碳可能为GB平滑肌收缩的抑制性递质，参与GB运动的调节. 进一步研究表明，刺激狗SO非胆碱能非肾上腺素能(non-adren-ergic non-cholinergic，NANC)神经引起的SO松弛可被河豚毒及氧合血红蛋白消除，但不受阿托品、心得安、酚妥拉明、消炎痛、CCK及VIP的影响，推测可能是电刺激使NANC释放一氧化氮，进而使SO松弛[45]. 内源性雌激素可延长胃排空，使食物到达十二指肠的速度减慢，进而经CCK使GB排空延缓[46]，可部分解释女性GB结石发生率高的原因. 此外，甲状腺素、神经肽Y可直接或间接抑制SO收缩，调节胆囊排空[46,47].

2.5 影响GB排空的其他因素 在体外，生理剂量胆盐抑制GB收缩；在体内，GB内胆盐亦抑制GB收缩[48,49]. 高血糖时GB收缩减少[50]. 静注氨基酸显著引起正常人的GB收缩[51-53]，而高血糖者则无此反应[1,2]. Garg et al通过静注氨基酸刺激胆汁排泄来从十二指肠收集胆汁亦证实氨基酸有促进GB排空作用[52-54]. 进脂肪餐时吸烟不影响GB收缩，但进餐后20-40 min吸烟则引起GB排空延缓[55]. GB开始收缩反应由胆碱能神经胞体或轴突上尼古丁受体介导，而GB松弛则可能为释放尼古丁的神经末端上的尼古丁受体被激活所致[56]. 肠外营养和低脂低蛋白饮食使FGV增加，GEF减少，胆汁潴留，为GB结石形成的危险因素之一[56,57]. 快速减肥期间GB容量增加，胆汁成分发生有利于成石的变化[58]，其GB收缩减少，胆固醇饱和度增加，胆结石形成增多[59,64] ，而胆汁胆固醇增加抑制GB肌收缩，促进结石形成[57]. 应用熊脱氧胆酸[65,66]及熊胆醇(ursodid)或ibuprofen[67]对防止减肥诱发的胆结石有一定作用.

3 功能性胆道运动不良的临床表现、诊断和治疗

3.1功能性胆道运动不良的临床意义 功能性胆道运动功能不良的直接结果是GB排空不良，而GB排空不良为GB结石形成和胰腺炎的重要原因. 动物研究表明，GB排空不良常是GB结石形成的原因而非结果. 肥胖及限食、体重快速减轻时，由于GB排空减少，胆固醇饱和指数增加，易形成结石[56-65];如限食至2.092 kg/d(500 cal/d)，则GB结石发生率明显增加，≥3.765 kg/d(900 cal/d)则很少发生GB结石[59]. 肢端肥大症患者由于长期应用对GB排空有抑制作用的奥曲肽，使GB结石发生率明显增加[34-37]. SO功能不良(sphincter of oddi dysfunction，SOD)可引起胆汁潴留、胰腺炎及上腹痛综合征[68-71].

3.2 功能性GB排空不良的临床表现及诊断 一般而言，SO痉挛者症状多较明显[69,70]，而GB收缩无力者则甚少出现明显症状. 约20 %有症状者亦因发生机制不同而表现不一[49]. 主要症状有右上腹不适、隐痛、胀痛或绞痛，部分患者可酷似胆绞痛表现：疼痛较剧烈，向肩背部放射，并可出现黄疸，谷丙转氨酶(ALT)、胰淀粉酶升高等肝胰损害表现[69-71]. 急性特发性胰腺炎患者中79 %为SOD所致[72]. 由于有SOD患者常伴胃肠运动功能紊乱[66,67]，故需与Vater壶腹/十二指肠痉挛所致之上腹痛相区别，后者可通过闪烁照像或十二指肠压力测定鉴别[68]. 在部分SOD患者，其胆管括约肌和胰管括约肌为两个独立部分[71,73]，对CCK反应亦异，临床表现及治疗方法亦有不同[72-74]. 试餐超声及核素闪烁照相检查患者FGV明显增多，餐后GEF明显减少，最大GB排空速度明显减慢，GB残留胆汁增多，GB排空时间延长[75-77]. SO痉挛或失弛缓者可见胆总管扩张(≥12 mm)[70,71]. 有胆总管综合征者胆总管内径可≥15 mm[76]. 造影及药物试验 内镜逆行胰胆管造影(ERCP)可见造影剂排空缓慢[1,78]. 对GB收缩无力所致排空不良者应用拟胆碱能药物或胃动素激动剂[32]或多巴胺拮抗剂[79]和作用于壁内神经药物如西沙必利(cisapride)[80,81]等可使GB排空明显改善. 对II、III型SOD患者，应用钙通道阻滞剂等可迅速缓解症状，增加GEF，加快排空速度[71,82-84]. 胆道压力测定常表现为[85,86]: (1) SO基础压升高(≥5.3 kPa，40 mmHg); (2) SO收缩频率、幅度增加；(3)收缩传导顺行减少而逆行增加；(4)SO对CCK等反应异常；(5)胆管、胰管压力升高. 35 %的患者Vater乳头压力增加(>10.7 kPa，80 mmHg)[68,71,74]. 有研究表明，SO压力测定结果与患者的临床表现大多一致[87]，不明原因急性胰腺炎患者31 %有SOD[88]. ERCP可引起严重并发症，而胆道压力测定并发胰腺炎的发生率较ERCP更高. 但Chan et al [89]认为，如技术上可行则测SO压对诊断还是必要的.行压力测定等操作时应用镇静剂对测定结果无明显影响[90-92]. SOD诊断标准为：(1)有胆绞痛史；(2)血清胆红素升高，碱性磷酸酶(ALP)为正常上限的1.5倍；(3) ERCP发现胆总管扩张(≥12 mm)；(4)ERCP仰卧位45 min胆道仍有造影剂潴留[78]. 根据该标准将SOD分为三型[74]. I型:上述4条标准均有；II型：有胆绞痛史加其他任1-2条标准；III型：仅有胆绞痛. 进一步研究发现，在诊断为SOD的患者中，除I型外，II型、III型分别有61 %和50 %的患者有SO压力异常. 关于胆总管扩张的标准，亦曾有人提出>15 mm作为扩张的指标[69,70,74]，达此数者通常示扩张显著，应排除器质性病变所致. 胆道压力测定虽是诊断SOD的金指标，但因增加患者痛苦和受条件限制，故对反复发作，症状典型，经超声、CT等检查符合SOD并排除原发器质性病及经药物试治有效者亦可诊断. Sugawa et al [92]认为，对I型SOD，行内镜括约肌切开术(EST)前不必行SO压力测定. 定量肝胆闪烁照相对SOD的诊断价值与SO压力测定接近，故可以前者代替后者[93].

3.3 GB切除术后胆道动力障碍(PCBD) 约30 %的慢性GB炎、胆结石术后患者仍有上腹不适或疼痛等症状，其中50 %主要由PCBD引起[94]，以女性多见，男：女为1：4. 这些患者SO基础受缩频率及幅度增高，逆向受缩比例增多.其中1型SOD患者中90 %，II型患者中31.8 %，III型患者中6.7 % SO压力异常；约3-4 %的严重者有胆管扩张. 进一步研究发现[95]，PCBD患者血胃泌素水平明显高于对照组. 认为GB切除后GB与SO协调作用被破坏，SO缺乏GB收缩反射性引起SO松弛的调节而经常处于受缩或痉挛状态. 此外，部分患者在其GB切除前可能就已有SOD，只是其症状被误认为胆石症所致未被诊断而已. PCBD的诊断: 即在上述SOD诊断标准的基础上排除消化系溃疡，胆管结石，肿瘤，特发性胰腺炎的无诱因间歇性右上腹痛.

3.4 功能性GB排空不良的治疗 (1)一般治疗:调节饮食，适当减少可诱发SOD的食物的摄入；调节情绪和胃肠功能，可减少SOD的发作频率. (2)内镜SO切开术(EST): 对反复发作，有明显症状并引起肝、胰损害，经压力测定等检查确诊为SOD和PCBD的患者，行内镜下SO切开术，可显著改善GB运动和GB排空[92,95-99]，消除症状，其近、远期效果较好(有效率达91.7 %)，但其术后再狭窄率达12 %[100]. 对I型SOD因效果不佳而不主张用EST. (3)气囊扩张:不能使SOD完全缓解[101]，对不能行EST的患者可考虑用气囊扩张[102]. (4)经十二指肠括约肌切开术:效果不佳者达7-35 %，可能与手术适应证较难掌握有关[103-105]. (5)药物治疗:已知有胃肠运动功能紊乱患者常同时存在GB或SO运动功能不良或二者运动不协调. 应用调节胃肠运动的药物治疗常可使GB排空功能改善[1,79,83]. 对伴胃肠运动缓慢者，应用多潘立酮、西沙必利和左舒必利(Levsoulpiride)(75 mg/d)可促进胃排空，同时显著增加GB排空[79-81,83,84]. 对正常人，多潘立酮和西沙必利均抑制GB排空，其机制可能是使SO收缩加强所致[79]; 对其长期应用是否增加患者GB结石的发生率尚未定论. 红霉素为胃动素拟似药，通过增强GB收缩，减少SO压力及收缩幅度而显著增加GB排空，使剩余胆汁减少[32,106]. 硝苯吡啶抑制正常人GB收

缩，减少GB排空[107]，但不增加胆结石的发生率；对SOD引起的胆绞痛，特别是对II型和III型SOD有显著疗效[71]. 硝酸盐类制剂如消心痛等亦具硝苯吡啶样作用，松弛SO. PGE拮抗剂消炎痛可促进餐后GB排空，显著减少GB残余量[95,108]. 阿司匹林350 mg/d治疗2 wk对正常人GB排空无影响，但可明显促进GB结石患者GB排空，减少溶石后GB结石的复发，增加剂量至1.4 g/d，疗效并不增加[109]. 长期应用阿司匹林等非甾醇类抗炎药可减少GB黏液分泌，改变胆汁脂质含量从而阻碍结石的形成[106]，对预防GB结石的发生可能有一定作用，但此类药物不能逆转收缩减弱的GB的收缩功能[109,110].

4 参考文献

1 陈仕珠.胆囊排空调节及功能性胆囊排空异常.新消化病学杂志 1997;5(特刊6):19
2 Toouli J. Biliary dyskinesia. *Curr Treat Options Gastroenterol* 2002;5:285-291
3 吴培俊. 胆道系统运动功能及障碍. 世界华人消化杂志 1999;7:603-604
4 Hanyu N,Dodds WJ,Layman RD,Hogan WJ,Chey WY, Takahashi I. Mechanism of cholecystokinin-induced contraction of the opossum gallbladder. *Gastroenterology* 1990;98:1299-1306
5 Ura K,Sarna SK,Condon RE. Antral control of gallbladder cyclic motor activity in the fasting state. *Gastroenterology* 1992;102:295-302
6 Lonovics J, Madacsy L, Szepes A, Szilvassy Z, Velosy B, Varro V. Humoral mechanisms and clinical aspects of biliary tract motility. *Scand J Gastroenterol Suppl* 1998;228:73-89
7 Radberg G,Asztely M ,Moonen M,Svanvik J.Contration and evacuation of the gallbladder studied simultaneously by ultrasonography and 99m Tc-labeled diethyl-iminodiacetic acid scintigraphy. *Scand J Gastroenterol* 1993;28:709-713
8 Grace PA,Poston GJ,Williamson RC.Biliary motility. *Gut* 1990;31:571-582
9 陈仕珠,冯少华,邢保华,郭志刚. 急性病毒性肝炎患者胆囊排空功能研究. 华人消化杂志 1998;6:204-206
10 Keane P,Colwell D,Baer HP,Clanachan AS,Scott GW. Effects of age, gender and female sex hormones upon contractility of the human gallbladder in vitro. *Surg Gynecol Obstet* 1986;163:555-560
11 Palasciano G,Serio G,Portincasa P,Palmieri V,Fanelli M,Velardi A,Calo'Gabrieli B, Vinciguerra V. Gallbladder volume in adults, and relationship to age,sex,body mass index, and gallstones:A sonographic population study. *Am J Gastroenterol* 1992;87:493-497
12 陈仕珠,张路,陈旭春,白兰. 肠易激综合征患者胆囊排空功能的研究. 解放军医学杂志 1995;20:362
13 陈仕珠,赵红,吴春燕,付卫红,陈旭春. 胆汁返流性胃炎患者胆囊排空功能研究. 华人消化杂志 1998;6:427-429
14 Sood GK,Baijal SS,Lahoti D,Broor SL.Abnormal gallbladder function in patients with irritable bowel syndrome. *Am J Gastroenterol* 1993;88:1387-1390
15 Mearin F,De Ribot X,Balboa A,Antolin M,Varas MJ, Malagelada JR. Duodenogastric bile reflux and gastrointestinal motility in pathogenesis of functional dyspepsia:Role of cholecystectomy. *Dig Dis Sci* 1995; 40: 1703-1709
16 杨春敏,毛高平,张秀荣,张映辉,间一平. 乙醇对清醒兔Oddi括约肌运动功能的影响.世界华人消化杂志 2000;8(特刊8):87
17 Goff JS.The effect of ethanol on the pancreaticduct sphincter of Oddi. *Am J Gastroenterol* 1993;88:656-661
18 Stolk MF, van Erpecum KJ, Smout AJ, Akkermans LM, Jansen JB, Lamers CB, Peeters TL, vanBerge-Henegouwen GP. Motor cycles with phase III in antrum are associated with high motilin levels and prolonged gallbladder emptying. *Am J Physiol* 1993;264(4 Pt 1):G596-600
19 陈仕珠,张忠兵,荆文科,许东谱,周焕章,张洪博,胡家露,王振雄. 胆汁返流性胃炎患者胃、十二指肠黏膜胃肠激素含量及其意义研究. 新消化病学杂志 1993;1:208-210
20 Abiru H,Sarna SK,Condon RE.Contractile mechanisms of gallbladder filling and emptying in dogs. *Gastroenterology* 1994;106:1652-1661
21 Nilsson BI,Svenberg T,Tollstrom T, Hellstrom PM,Samuelson K,Schnell PO. Relationship between interdigestivegallbledder emptying,plasma motilin and migrating motor complex in man. *Acta Physiol Scand* 1990;139:55-61
22 Jazrawi RP, Pazzi P, Petroni ML, Prandini N, Paul C, Adam JA, Gullini S, Northfield TC. Postprandial gallbladder motor function: refilling and turnover of bile in health and in cholelithiasis. *Gastroenterology* 1995;109:582-591
23 Behar J,Biancani P. Pharmacologic characterization of excitatory and inhitory cholecystokinin receptors of the cat gallbladder and sphincter of Oddi. *Gastroenterology* 1987;92:764-770
24 Nabae T, Yokohata K, Otsuka T, Inoue K,Yamaguchi K, Chijiiwa K, Tanaka M. Effect of truncal vagotomy on sphincter of oddi cyclic motility in conscious dogs. *Ann Surg* 2002;236:98-104
25 Patankar R,Ozmen MM,Sanderson A,Johnson CD. Effect of cisapride on gallbladder emptying and plasma CCK in normal and vagotomized human subjects. *Dig Dis Sci* 1996;41:543-548
26 Deng ZL, Nabae T, Konomi H, Takahata S, Yokohata K, Ogawa Y, Chijiiwa K, Tanaka M. Effects of proximal duodenal transection and anastomosis on interdigestive sphincter of Oddi cyclic motility in conscious dogs. *World J Surg* 2000;24:863-869
27 Sand J,Tainio H,Nordback I.Peptidergic innervation of human sphincter of Oddi. *Dig Dis Sci* 1994;39:293-300
28 Jennings LJ, Salido GM, Pozo MJ, Davison JS, Sharkey KA, Lea RW, Singh J. The source and action of histamine in the isolated guinea-pig gallbladder.*Inflamm Res* 1995;44:447-453
29 Shaffer EA. Review article: control of gall-bladder motor function. *Aliment Pharmacol Ther* 2000;14(Suppl 2):2-8
30 Bandyopadhyay A, Chakder S, Lynn RB, Rattan S.Vasoactive intestinal polypeptide gene expression is characteristically higher in opossum gastrointestinal sphincters.*Gastroenterology* 1994;106:1467-1476
31 Binmoeller KF, Dumas R, Harris AG, Delmont JP. Effect of somatostatin analog octreotide on human sphincter of Oddi. *Dig Dis Sci* 1992;37:773-777
32 Cox MR, Padbury RT, Harvey JR, Baker RA, Toouli J,Saccone GT. Substance P stimulates sphincter of Oddi motility and inhibits trans-sphincteric flow in the Australian brush-tailed possum. *Neurogastroenterol Motil* 1998;10:165-173
33 Oh SH, Cho KW, Kim SH, Jeong GB, Kang CW, Hwang YH, Seul KH, Cho BH. Identification of immunoreactive atrial natriuretic peptide in the gallbladder and bile juice of rabbit, pig and human. *Regul Pept* 1994;49:217-223
34 Fiorucci S,Santucci L,Morelli A. 5-Hydroxytryptamine 3-receptor antagonist modulates gallbladder emptying and motilin release induced by erythromcycin. *Dig Dis Sci* 1993;38:2236-2240
35 Mitsukawa T, Takemura J, Nishizono F, Nakatsuru K, Ohgo S, Matsukura S. Effects of atropine, proglumide, and somatostatin analogue (SMS 201-995) on bombesin-induced gallbladder contraction and CCK secretion in humans. *Am J Gastroenterol* 1989;84:1371-1374
36 Kiedrowski RV,Huijghebaert S,Raedsch R. Mechanisms of cisapride affecting gallbladder motility. *Dig Dis Sci* 2001;46:939-944
37 Weber FH Jr, Sears RJ, Kendall B, Pruett TL, Shaffer HA Jr, Yeaton P. Effect of octreotide on human sphincter of Oddi motility following liver transplantation. *Dig Dis Sci* 1997;42:1168-1175
38 Redfern JS, Fortuner WJ. Octreotide-associated biliary tract dysfunction and gallstone formation: pathophysiology and management. *Am J Gastroenterol* 1995;90:1042-1052
39 Fazel A, Li SC, Burton FR. Octreotide relaxes the hypertensive sphincter of Oddi: pathophysiological and therapeutic implications. *Am J Gastroenterol* 2002; 97:612-616
40 Grosman I, Simon D. Potential gastrointestinal uses of somatostatin and its synthetic analogue octreotide. *Am J Gastroenterol* 1990;85: 1061-1072
41 Gullo L, Ancona D, Pezzilli R, Fusconi F, Bolondi L. Study of the effect of neurotensin on meal- and cerulein-induced gallbladder contraction. *Digestion* 1992;53:67-71

42 McKirdy ML, McKirdy HC, Johnson CD. Non-adrenergic non-cholinergic inhibitory innervation shown by electrical field stimulation of isolated strips of human gall bladder muscle. *Gut* 1994;35:412-416

43 Mourelle M, Guarner F, Molero X, Moncada S, Malagelada JR. Regulation of gall bladder motility by the arginine-nitric oxide pathway in guinea pigs. *Gut* 1993;34:911-915

44 Mourelle M, Guarner F, Moncada S, Malagelada JR. The arginine/nitric oxide pathway modulates sphincter of Oddi motor activity in guinea pigs and rabbits. *Gastroenterology* 1993;105: 1299-1305

45 Tanobe Y, Okamura T, Fujimura M, Toda N. Functional role and histological demonstration of nitric-oxide-mediated inhibitory nerves in dog sphincter of Oddi. *Neurogastroenterol Motil* 1995;7:219-227

46 Wedmann B, Schmidt G, Wegener M, Coenen C, Ricken D, Althoff J. Effects of age and gender on fat-induced gallbladder contraction and gastric emptying of a caloric liquid meal: a sonographic study. *Am J Gastroenterol* 1991;86:1765-1770

47 陈宝莹,魏经国,王耀程. Oddi 括约肌解剖生理及其运动功能. 世界华人消化杂志 2002;10:226-229

48 Lin HC, Zhao XT, Kwok GM, Gu YG, Elashoff JD.Bile salt-dependent inhibition of gallbladder emptying. *Am J Physiol* 1995;269:G988-993

49 Xiao ZL, Rho AK, Biancani P, Behar J. Effects of bile acids on the muscle functions of guinea pig gallbladder. *Am J Physiol Gastrointest Liver Physiol* 2002;283:G87-94

50 De Boer SY, Masclee AA, Lam WF, Jansen JB, Lamers CB. Effect of intravenous glucose on intravenous amino acid-induced gallbladder contraction and CCK secretion. *Dig Dis Sci* 1994;39:268-274

51 Nealon WH, Upp JR Jr, Alexander RW, Gomez G, Townsend CM Jr, Thompson JC. Intravenous amino acids stimulate human gallbladder emptying and hormone release. *Am J Physiol* 1990;259(2 Pt 1):G173-178

52 Zoli G, Ballinger A, Healy J, O'Donnell LJ, Clark M, Farthing MJ. Promotion of gallbladder emptying by intravenous aminoacids. *Lancet* 1993;341:1240-1241

53 Mearadji B,Masclee AAM,Onkenhout W,Biemond I,Lamers CBHW. Effect of intraduodenal and intravenous amino acid on proximal gastric motor function in man. *Dig Dis Sci* 2001; 46:38-45

54 Garg PK, Goindi G, Tandon RK. Stimulation of gallbladder by intravenous infusion of amino acid: a new method to obtain duodenal bile for bile analyses. *Dig Dis Sci* 2000;45:904-908

55 Jonderko K,Nowak A,Kasicka-Jonderko A, Blaszczynska M. Effect of cigarette smoking on gallbladder emptying and filling in man. *Am J Gastroenterol* 1994;89:67-71

56 Parkman HP,Pagano AP,Ryan JP.Investigation of endogenous neurotransmitters of guinea pig gallbladder using nicotinic agonist stimulation.*Dig Dis Sci* 1998;43: 2237-2243

57 Fu H, Wu W, Zou S, Huang M, Huang C, Xu Y. Effect of cholesterol in bile on cholecystokinin receptor in the gallbladder. *Zhonghua Waike Zazhi* 2002;40:786-788

58 Shiffman ML, Shamburek RD, Schwartz CC, Sugerman HJ, Kellum JM, Moore EW. Gallbladder mucin, arachidonic acid, and bile lipids in patients who develop gallstones during weight reduction. *Gastroenterology* 1993;105:1200-1208

59 Marks JW, Bonorris GG, Schoenfield LJ. Effects of ursodiol or ibuprofen on contraction of gallbladder and bile among obese patients during weight loss. *Dig Dis Sci* 1996;41:242-249

60 Yang H, Petersen GM, Roth MP, Schoenfield LJ, Marks JW. Risk factors for gallstone formation during rapid loss of weight. *Dig Dis Sci* 1992;37:912-918

61 Zapata R, Severin C, Manriquez M, Valdivieso V. Gallbladder motility and lithogenesis in obese patients during diet-induced weight loss. *Dig Dis Sci* 2000;45:421-428

62 Weinsier RL, Wilson LJ, Lee J. Medically safe rate of weight loss for the treatment of obesity: a guideline based on risk of gallstone formation. *Am J Med* 1995;98:115-117

63 Gebhard RL, Prigge WF, Ansel HJ, Schlasner L, Ketover SR, Sande D, Holtmeier K, Peterson FJ. The role of gallbladder emptying in gallstone formation during diet-induced rapid weight loss. *Hepatology* 1996;24:544-548

64 Vezina WC,Grace DM,Hutton LC,Alfieri MH, Colby PR, Downey DB,Vanderwerf RJ,White NF, Ward RP. Similarity in gallstone formation from 900 kcal/day diets containing 16 g vs 30 g of daily fat : Evidence that fat restriction is not the main culprit of cholelithiasis during rapid weigh reduction. *Dig Dis Sci* 1998;43:554-561

65 Shiffman ML, Kaplan GD, Brinkman-Kaplan V, Vickers FF. Prophylaxis against gallstone formation with ursodeoxycholic acid in patients participating in a very-low-calorie diet program. *Ann Intern Med* 1995;122:899-905

66 Soffer EE, Johlin FC. Intestinal dysmotility in patients with sphincter of Oddi dysfunction. A reason for failed response to sphincterotomy. *Dig Dis Sci* 1994;39:1942-1946

67 Evans PR, Bak YT, Dowsett JF, Smith RC, Kellow JE. Small bowel dysmotility in patients with postcholecystectomy sphincter of Oddi dysfunction. *Dig Dis Sci* 1997;42:1507-1512

68 Koussayer T, Ducker TE, Clench MH, Mathias JR. Ampulla of Vater/duodenal wall spasm diagnosed by antroduodenal manometry. *Dig Dis Sci* 1995;40:1710-1719

69 Fullarton GM, Murray WR. Evaluation of endoscopic sphincterotomy in sphincter of Oddi dysfunction. *Endoscopy* 1992; 24:199-202

70 Meshkinpour H, Mollot M. Sphincter of Oddi dysfunction and unexplained abdominal pain: clinical and manometric study. *Dig Dis Sci* 1992;37:257-261

71 Chen JW, Thomas A, Woods CM, Schloithe AC, Toouli J, Saccone GT. Sphincter of Oddi dysfunction produces acute pancreatitis in the possum. *Gut* 2000;47:539-545

72 Kaw M, Brodmerkel GJ Jr. ERCP, biliary crystal analysis, and sphincter of Oddi manometry in idiopathic recurrent pancreatitis. *Gastrointest Endosc* 2002;55:157-162

73 Evans PR, Dowsett JF, Bak YT, Chan YK, Kellow JE. Abnormal sphincter of Oddi response to cholecystokinin in postcholecystectomy syndrome patients with irritable bowel syndrome. The irritable sphincter. *Dig Dis Sci* 1995;40:1149-1156

74 Devereaux BM, Sherman S, Lehman GA. Sphincter of Oddi (pancreatic) hypertension and recurrent pancreatitis. *Curr Gastroenterol Rep* 2002;4:153-159

75 Toouli J, Craig A. Sphincter of Oddi function and dysfunction. *Can J Gastroenterol* 2000;14:411-419

76 Rosenblatt ML, Catalano MF, Alcocer E, Geenen JE. Comparison of sphincter of Oddi manometry, fatty meal sonography, and hepatobiliary scintigraphy in the diagnosis of sphincter of Oddi dysfunction. *Gastrointest Ends* 2001;54:697-704

77 Madacsy L, Middelfart HV, Matzen P, Hojgaard L, Funch-Jensen P. Quantitative hepatobiliary scintigraphy and endoscopic sphincter of Oddi manometry in patients with suspected sphincter of Oddi dysfunction: assessment of flow-pressure relationship in the biliary tract. *Eur J Gastroenterol Hepatol* 2000; 12:777-786

78 Jung M, Pimentel F, Winter J, Doertenbach J. The common channel syndrome in adults. *Z Gastroenterol* 1993;31:147-150

79 Chen SZ,Chen XC,LiuWX,Yang ZS,Guo XL. Domperidone improves gallbladder emptying function in patients with irritable bowel syndrome.*China Natl J New Gastroenterol* 1995;1:48-51

80 Ziegenhagen DJ, Heitz W, Kruis W, Pohl C, Zehnter E. Cisapride increases gallbladder volume in gallstone patients before and after extracorporeal shock wave lithotripsy. *Aliment Pharmacol Ther* 1993;7:617-622

81 Thorens J, Schnegg JF, Brignoli R, Froehlich F, Jansen JB, Dorta G, Blum AL, Gonvers JJ, Fried M. Effect of cisapride on gallbladder motility after extracorporeal shock-wave lithotripsy. *J Hepatol* 1995;22:333-337

82 Jonderko K, Nowak A, Kasicka-Jonderko A, Sliwinski Z, Kucio C. Effect of nifedipine on interdigestive gallbladder volume and postprandial gallbladder emptying in man. *Dig Dis Sci* 1991;36:1434-1440

83 陈仕珠,步雪,后成才,李莎,陈旭春. 硝苯吡啶改善肠易激综合征患者胆囊排空不良的机制. 华人消化杂志 1998;6:423-426

84 陈仕珠,沙建萍,陈旭春,后成才,付卫红,刘望. 胆汁返流性胃炎患者 Oddi 括约肌松弛不良:硝苯吡啶改善胆囊排空作用研究. 世界华人消化杂志 1999;7:1020-1023

85 Toouli J, Craig A. Sphincter of Oddi function and dysfunction. *Can J Gastroenterol* 2000;14:411-419

86 Thomas PD, Turner JG, Dobbs BR, Burt MJ, Chapman BA.Use of (99m)Tc-DISIDA biliary scanning with morphine provocation for the detection of elevated sphincter of Oddi basal pressure. *Gut* 2000;46:838-841

87 Sherman S, Troiano FP, Hawes RH, O'Connor KW, Lehman GA. Frequency of abnormal sphincter of Oddi manometry compared with the clinical suspicion of sphincter of Oddi dysfunction. *Am J Gastroenterol* 1991;86:586-590

88 Coyle WJ, Pineau BC, Tarnasky PR, Knapple WL, Aabakken L, Hoffman BJ, Cunningham JT, Hawes RH, Cotton PB. Evaluation of unexplained acute and acute recurrent pancreatitis using endoscopic retrograde cholangiopancreatography, sphincter of Oddi manometry and endoscopic ultrasound. *Endoscopy* 2002;34:617-623

89 Chan YK, Evans PR, Dowsett JF, Kellow JE, Badcock CA. Discordance of pressure recordings from biliary and pancreatic duct segments in patients with suspected sphincter of Oddi dysfunction. *Dig Dis Sci* 1997;42:1501-1506

90 Cuer JC, Dapoigny M, Bommelaer G. The effect of midazolam on motility of the sphincter of Oddi in human subjects. *Endoscopy* 1993;25:384-386

91 Fazel A, Burton FR. The effect of midazolam on the normal sphincter of Oddi: a controlled study. *Endoscopy* 2002;34:78-81

92 Sugawa C, Park DH, Lucas CE, Higuchi D, Ukawa K. Endoscopic sphincterotomy for stenosis of the sphincter of Oddi. *Surg Endosc* 2001;15:1004-1007

93 Jagannath S, Kalloo AN. Efficacy of biliary scintigraphy in suspected sphincter of oddi dysfunction. *Curr Gastroenterol Rep* 2001;3:160-165

94 邹多武,许国铭,孙振兴,李兆申,尹宁. Oddi括 约肌测压对胆囊切除术后腹痛患者的诊断价值. 第二军医大学学报 1977;18:117-119

95 王继英,张超,王旺河,马玉春,李国庆,郑万海. 腹腔镜胆囊切除术后胆道动力障碍的研究. 中华肝胆外科杂志 2001;7:400-402

96 Agarwal DK, Sharma BC, Dhiman RK, Baijal SS, Choudhuri G, Saraswat VA. Effect of endoscopic sphincterotomy on gallbladder motility. *Dig Dis Sci* 1997;42:1495-1500

97 Sharma SS. Sphincter of Oddi dysfunction in patients addicted to opium: an unrecognized entity. *Gastrointest Endosc* 2002;55:427-430

98 Chandramouli B, Gupta SM, Cohen GE. Scintigraphic evaluation of bile dynamics before and after endoscopic sphincterotomy. *Clin Nucl Med* 1994;19:800-802

99 Fullarton GM, Murray WR. Evaluation of endoscopic sphincterotomy in sphincter of Oddi dysfunction. *Endoscopy* 1992;24:199-202

100 胡冰,周代云,龚彪,王书智,张风梅,王晓琳. 乳头预切开术在内窥镜逆行胰胆管造影术中的应用.世界华人消化杂志 1999;7:1052-1054

101 Yasuda I, Tomita E, Enya M, Kato T, Moriwaki H. Can endoscopic papillary balloon dilationreally preserve sphincter of Oddi function? *Gut* 2001;49:686-691

102 Carr-Locke DL. Can endoscopic papillary balloon dilation really preserve sphincter of Oddi function? *Gut* 2001;49:608-609

103 李丹. 胆囊切除术胆管损伤的原因及预防方法. 世界华人消化杂志 1999;7:443

104 李兆申. 中国ERCP研究现状. 世界华人消化杂志 2000;8:446-448

105 龚建平,韩本立,周永碧. 良性胆管狭窄568例的分类和外科治疗. 世界华人消化杂志 2000;8:243-244

106 Weber FH Jr, Richards RD, McCallum RW. Erythromycin: a motilin agonist and gastrointestinal prokinetic agent. *Am J Gastroenterol* 1993;88:485-490

107 Craig AG, Toouli J. Slow release nifedipine for patients with sphincter of Oddi dyskinesia:results of a pilot study. *Intern Med J* 2002;32:119-120

108 O'Donnell LJ, Wilson P, Guest P, Catnach SM, McLean A, Wickham JE, Fairclough PD. Indomethacin and postprandial gallbladder emptying. *Lancet* 1992;339:269-271

109 Sterling RK, Shiffman ML, Sugerman HJ, Moore EW.Effect of NSAIDs on gallbladder bile composition. *Dig Dis Sci* 1995;40:2220-2226

110 Li YF, Russell DH, Myers SI, Weisbrodt NW, Moody FG. Gallbladder contractility in aspirin- and cholesterol-fed prairie dogs. *Gastroenterology* 1994;106:1662-1667