世界华人消化杂志®
wcjd@wjgnet.com
世界华人消化杂志 2012年11月8日; 20(31): 2978-2985
ISSN 1009-3079 (print) ISSN 2219-2859 (online)

述评 EDITORIAL

原发性硬化性胆管炎的研究进展

黄颖秋

■背景资料
原发性硬化性胆管炎(PSC)是一种不明原因的自身免疫性肝病, 以慢性阻塞性黄疸、肝内外胆管弥漫性炎症、纤维化及狭窄变形为主要特征, 最终导致胆管阻塞、胆汁性肝硬化和肝衰竭. 尽管PSC少见, 但因其临床及影像学特征与另一种自身免疫性疾病IgG4相关硬化性胆管炎(IgG4-SC)十分相似, 近年来已引起国内外学者的关注, PSC的相关研究也取得很多进展.

黄颖秋, 中国医科大学第五临床学院, 本溪钢铁(集团)总医院消化内科 辽宁省本溪市 117000
黄颖秋, 主任医师, 教授, 研究生导师, 主要从事胃肠动力疾病、消化系肿瘤及肝硬化的基础与临床研究.
作者贡献分布: 文献检索、论文撰写与论文审校均由黄颖秋完成.
通讯作者: 黄颖秋, 教授, 117000, 辽宁省本溪市平山区人民路29号, 中国医科大学第五临床学院, 本溪钢铁(集团)总医院消化内科. huangyingqiu_bx@126.com
电话: 0414-2215137
收稿日期: 2012-06-26 修回日期: 2012-08-16
接受日期: 2012-09-04 在线出版日期: 2012-11-08

Advances in research of primary sclerosing cholangitis

Ying-Qiu Huang

Ying-Qiu Huang, Department of Gastroenterology, General Hospital of Benxi Steel & Iron (Group); the Fifth Clinical College of China Medical University, Benxi 117000, Liaoning Province, China
Correspondence to: Ying-Qiu Huang, Professor, Department of Gastroenterology, General Hospital of Benxi Steel & Iron (Group); the Fifth Clinical College of China Medical University, 29 Renmin Road, Pingshan District, Benxi 117000, Liaoning Province, China. huangyingqiu_bx@126.com
Received: 2012-06-26 Revised: 2012-08-16
Accepted: 2012-09-04 Published online: 2012-11-08

Abstract
Primary sclerosing cholangitis (PSC) is a chronic cholestatic autoimmune liver disease characterized by diffuse inflammation, concentric fibrosis, focal or segmental stricture of intrahepatic and/or extrahepatic bile ducts, which can eventually lead to cirrhosis or hepatic function failure. The pathogenesis of PSC may involve genetic susceptibility, innate or adaptive immunity, and Epstein-Barr virus infection. Diagnostic imaging modalities include endoscopic retrograde cholangiography, magnetic resonance cholangiopancreatography, and high-resolution three-dimensional SPGR. Proteomic analysis of bile and urine may become a new tool for early diagnosis of cholangiocarcinoma in PSC patients. Ursodeoxycholic acid (UDCA), endoscopic therapy and liver transplantation are major treatments for PSC.

Key Words: Primary sclerosing cholangitis; Pathogenesis; Diagnosis; Therapy

Huang YQ. Advances in research of primary sclerosing cholangitis. Shijie Huaren Xiaohua Zazhi 2012; 20(31): 2978-2985

■同行评议者
王刚, 副研究员, 哈尔滨医科大学附属第一医院胰胆外科(普外二科)

摘要
原发性硬化性胆管炎(primary sclerosing cholangitis, PSC)是一种慢性胆汁淤积性自身免疫性肝病(autoimmune liver disease, AILD), 以肝内胆管和/或肝外胆管的弥漫性炎症、同心性纤维化、局灶性或节段性狭窄为主要特征, 最终发展至肝硬化或肝衰竭. PSC的发病机制可能涉及遗传易感性、先天性免疫、获得性免疫及EB病毒感染等. 内镜逆行胆管造影、磁共振胰胆管成像、高分辨三维扰相梯度回波序列等技术已用于PSC的影像诊断. 此外, 胆汁和尿液的蛋白质组学分析可能有助于PSC并发胆管癌的早期诊断. 熊去氧胆酸(ursodeoxycholic acid, UDCA)、内镜以及肝移植是治疗PSC的方法. 上述最新进展为PSC的诊断和治疗提供了新的思路.

关键词: 原发性硬化性胆管炎; 发病机制; 诊断; 治疗

黄颖秋. 原发性硬化性胆管炎的研究进展. 世界华人消化杂志 2012; 20(31): 2978-2985
http://www.wjgnet.com/1009-3079/20/2978.asp

0 引言
原发性硬化性胆管炎(primary sclerosing cholangitis, PSC)是自身免疫性肝病(autoimmune liver disease, AILD)的一种类型, 以慢性胆汁淤积、胆管弥漫性炎性浸润、纤维化、节段性狭窄为主要特征[1-3], 其临床表现和影像特征与IgG4相关硬化性胆管炎(immunoglobulin G4-related sclerosing cholangitis, IgG4-SC)或胆管癌(cholangiocarcinoma, CC)相似[4]. PSC的发病机制可能涉及自身免疫反应[1], 但因对免疫抑制剂缺乏有效应答, 因此还不能称其为典型的自身免疫性疾病[5]. AILD包括自身免疫性肝炎(autoimmune hepatitis, AIH)、原发性胆汁性肝硬化(primary biliary cirrhosis, PBC)和PSC[6]. 部分AIH可同时具有PSC的临床和病理特征, 称为重叠综合征

(overlap syndrome, OLS)[7]. PSC在临床少见, 年发病率约为0-1.3/100 000[8], 常并发炎症性肠病(inflammatory bowel disease, IBD)[1,5]. 此外, 主胆管狭窄的PSC发生CC的风险高达26%[9]. 除肝移植外, 迄今尚无有效治疗终末期PSC的方法[10]. 本文就PSC的最新研究进展概述如下.

1 发病机制

1.1 PSC的遗传易感性

1.1.1 HLA与PSC: Bergquist等[11]对678例PSC患者研究发现, 其子女、兄妹及父母的PSC风险较正常对照组显著升高, 其风险比率分别为11.5、11.1和2.3, 提示遗传易感因素在PSC的发病机制中起重要作用. 人类白细胞抗原(human leukocyte antigen, HLA)已被证实与PSC的易感性密切相关[12]. HLAⅠ类分子在全部有核细胞表达, 形成CD8+淋巴细胞的内源性抗原, 在自然杀伤(natural killer, NK)细胞及γδT-淋巴细胞(γδT-lymphocytes)充当抑制杀伤细胞免疫球蛋白样受体(killer immunoglobulin-like receptors, KIRs)的配体[1]. HLAⅡ类分子表达于呈递细胞(presenting cells), 形成CD4+淋巴细胞的外源性抗原[1]. HLA-DR3(DRB1*0301)和HLA-B8(HLA-B*0801)单体型(haplotype)被认为是PSC易感性的重要标志物[1]. 此外, HLA-A1、HLA-C7等位基因也与PSC的易感性密切相关[1]. HLAⅡ类单体型编码的易感性等位基因为HLA-DRB1*0301(DR3)和-DRB1*13(DR6)[1]. PSC与某些HLAⅡ类单体型呈正相关, 包括HLA-DRB1*03、-DQA1*0501、-DQB1*02、-DRB1*15、-DQA1*0102、-DQB1*0602、-DRB1*13、-DQA1*0103及-DQB1*0603, 而与HLA-DRB1*04、-DQA1*03及-DQB1*0302等单体型呈负相关[1]. PSC相对易感性最高的基因为HLA-DRB1*03、-DQA1*0501及-DQB1*02纯合子基因型[1].

1.1.2 非HLA与PSC: Karlsen等[13]研究发现, KIRs和/或HLAⅠ类配体失衡致使抑制减少或激活增加在PSC的发病机制中至关重要. MICA5.1、MICB24、CCR5、MDR1等非HLA基因被证实与PSC的易感性密切相关[1]. 此外, ICAM-1的基因多态性也被证实与PSC的易感性显著相关[12]. Naess等[14]对PSC患者的全基因组关联分析(genome-wide association analysis, GWA)确认的遗传易感基因位点包括2q13、2q35、3p21、4q27和13q31. Srivastava等[15]对992例PSC患者的3p21(MST1)和10p15(IL2RA)位点的GWA分析首次确认了10p15(IL2RA)基因位点的变异, 表明IL-2/IL2RA通路在PSC发病中起重要作用, 并进一步确认了MST1基因的易感性. Folseraas等[16]对1 221例PSC患者的GWA扩展分析发现, 位于lp36的MMEL1和TNFRSF14基因有强烈的潜在致病风险; 位于19q13的FUT2基因对病原体易感性存在变异; 位于19q13染色体rs601338位点的分泌型FUT2基因显著影响PSC患者胆汁微生物菌落的成分. Karlsen等[17]研究显示, 非HLA的变异型与PSC的胆汁体内平衡及炎症通路的调节密切相关, 若根据炎症、胆管上皮细胞功能、纤维化及致癌作用4个方面的遗传易感性将PSC分为相应的亚型对以后的基础和临床研究或许更有价值. Melum等[18]应用GWA对715例PSC患者的单核苷酸多态性(single nucleotide polymorphisms, SNPs)研究进一步证实了非HLA与PSC的相关性, 且至少存在2个额外的非HLA易感基因位点涉及T细胞激活和免疫耐受, 一个辨识成分可能参与PSC的发病机制.

1.2 免疫因素与PSC

1.2.1 体液免疫与PSC: 业已证实, PSC患者血清中含有多种自身免疫性抗体[19], 包括抗-胆管上皮细胞抗体(Anti-BEC)、抗-中性粒细胞胞浆抗体(ANCA)、抗-核抗体(ANA)、抗-平滑肌抗体(SMA)、抗-酿酒酵母菌抗体(ASCA)、抗-线粒体抗体(AMA)、抗-肝肾微粒体抗体(Anti-LKM)、抗-可溶性肝抗原/肝胰抗原抗体(Anti-SLA/LP)、抗-内皮细胞抗体(AECA)、抗-甲状腺过氧化物酶抗体(Anti-TPO)、抗-肾小球基底膜抗体(Anti-GBM)及抗-谷胱甘肽S-转移酶θ1抗体(Anti-GSTT1)等, 但大多数抗体的特异性较低[19]. ANCA对PSC的特异性相对较高, 包括胞浆型(c-ANCA)和核周型(p-ANCA), 后者又进一步被分为典型p-ANCA和不典型p-ANCA[20]. 逾80%的PSC患者含有不典型p-ANCA, 似乎更具特异性, 主要为IgG抗体[1]. 不典型p-ANCA能识别人中性粒细胞微管蛋白β5同工型(tubulin beta isoform 5, TBB-5)和细菌细胞分裂蛋白(bacterial cell division protein)FtsZ, 这一发现重新引起了人们对微生物在PSC潜在致病机制的兴趣和探讨[20,21]. Terjung等[22]研究发现, p-ANCA直接与TBB-5、FtsZ的交叉反应可能反映了易感人群对肠微生物的异常免疫应答, 提示p-ANCA可能参与PSC的发病机制. Ardesjö等[23]研究证实, Anti-GSTT1对PSC既无特异性, 也非敏感性, 但其在自身免疫性疾病患者的发生频率却显著高

■研发前沿
全基因组关联分析(GWA)已确认了许多基因位点的遗传易感性, 随着研究的不断深入, 更多的易感基因将被发现, 这对于探讨PSC的发病机制有十分重要的意义.

■相关报道
Lankisch等采用蛋白质组学分析技术准确鉴别PSC和CC, 为胆道恶性肿瘤的早期诊断提供了新的思路.

于对照组. 此外, 少数PSC患者血清IgG4升高, 且与疾病严重程度相关[24-27]. Navaneethan等[26]发现, 50例PSC患者中10例血清IgG4升高, 且术后生存率显著低于IgG4正常的PSC患者. 此外, 血清IgG4升高的PSC患者可合并系统性淀粉样变性, 而IgG4-SC则无[27]. IgE在PSC发病机制中的作用尚存争议. Hirano等[28]发现, 血清IgE增高的PSC患者其发病年龄高于IgE正常者, 且并发CC的风险降低. 而Navaneethan等[29]研究显示, 19例PSC患者中8例(42.1%)IgE增高, 且发病年龄低于IgE正常者, 但并发CC的风险增高.

1.2.2 细胞免疫与PSC: PSC的发生可能由透过肠黏膜进入门脉循环的细菌或病原体相关分子模式(pathogen-associated molecular patterns, PAMPs)等外源性因素触发[1]. 巨噬细胞、树突状细胞(dentritic cells, DCs)及NK细胞被激活后释放细胞因子, 并使DCs不断持续炎症反应[12]. 此外, 胆管上皮细胞(biliary epithelial cells, BECs)可获得一种粘附分子过度表达的反应性表型, 致使炎性细胞因子、趋化细胞因子及生长因子进一步促进炎症过程[1]. BECs作为胆道系统防御腔内微生物的第一道防线, 通过表达各种病原体识别受体(pathogen recognition receptors), 并使若干细胞内通路激活开启防御过程, 包括产生抗微生物肽、细胞因子、趋化因子及粘附分子[30]. 此外, BECs还能分泌免疫球蛋白A, 通过粘附分子和免疫介质的表达和释放与其他细胞相互作用[30]. PSC患者汇管区可见密集的T细胞浸润, 但T细胞的构成比(CD4/CD8比例)在不同的研究中却迥然不同, 这或许反映了肝内T细胞亚型的分布, CD4细胞更常见于汇管区, 而CD8细胞则在小叶性肝炎区域占优势[1]. CD8+T细胞缺陷在PSC的发病机制中可能起重要作用[31]. CD8+T细胞缺陷可导致其控制的EB病毒(epstein-barr virus, EBV)感染辨识性B细胞(autoreactive B cells), 后者积聚于靶器官产生致病性自身抗体, 并将共刺激残余信号提供给辨识性T细胞, 否则将通过激活诱导凋亡死于靶器官[31].

1.3 感染因素与PSC 自身免疫性疾病的某些易感基因可能影响病原体的外显率, 使诱发自身免疫的病毒或细菌反复引发感染[32]. EBV感染已被证实与经常并发AILD的几种自身免疫性疾病有关[32]. EBV感染的作用过去常归因于EBV与自身抗原间的免疫交叉反应, 但近年来提出的EBV感染辨识性B细胞假说被认为是人类自身免疫性疾病的基础[31]. 尽管尚无直接证据表明EBV参与PSC的发病机制, 但已确认EBV与并发或不并发PSC的UC有关[32]. EBV是否介导PSC的发病还有待于进一步研究.

1.4 其他因素与PSC 异生物质(xenobiotic)可诱导出胆管炎动物模型, 但常因炎症反应的转瞬即逝而使人们低估和忽视其在PSC发病机制中的作用. 然而, 这种胆管炎症最终可发展至胆管消失综合征(vanishing bile duct syndrome)、胆管纤维化及肝硬化[33]. 因此, 异生物质在PSC发病机制中的作用应引起足够重视.

2 PSC的临床特征

PSC的典型临床表现为慢性胆汁淤积和皮肤瘙痒[1-3], 主胆管狭窄者并发CC的风险明显增加[9]. 最近, Ngu等[34]完成了一项基于人群的AILD发病率、死亡率及恶性肿瘤发生率的相关研究. 结果显示, PSC队列的风险率为613人/年, 在95%可信区间内, PSC的全因标准化死亡率(standardized mortality ratios, SMRs)为4.1, 肝胆管病因SMRs为116.9, 所有肿瘤标准化发病率(standard incidence ratios, SIRs)为5.2, 肝外肿瘤SIRs为3.0. PSC患者罹患肝癌及其他恶性肿瘤的风险显著增加, 此外, 肝脏相关死亡率也显著增加, 表明当前的治疗措施仍不尽如人意. 约2/3的PSC患者常合并IBD, 尤其是溃疡性结肠炎(ulcerative colitis, UC). Halliday等[35]研究发现, 240例PSC患者中有129例合并UC, 32例合并克隆恩病(Crohn's disease, CD). Ngu等[36]研究发现, 伴发IBD的PSC患者其年龄低于不伴发IBD者, 前者更易并发恶性肿瘤、更需要肝移植、更易死亡, 提示IBD影响PSC患者预后, 但Navaneethan等[37]对167例合并UC和55例未合并UC的PSC患者研究显示, 前者的发病年龄确实明显低于后者(38岁 *vs* 47岁, $P<0.001$), 但UC并未影响PSC患者的长期预后. Jørgensen等[38]研究证实, 84%的PSC患者合并IBD, 多数为UC, 少数为CD. 此外, PSC还可合并肝细胞腺瘤(hepatocellular adenomas, HCA)[39]、系统性淀粉样变性[27]、消化道大出血[40]、重症肌无力(myastheniagravis)[41]、直肠非Hodgkin's淋巴瘤(non-Hodgkin's lymphoma)[42]、黄色肉芽肿性胆囊炎(xanthogranulomatouscholecystitis, XGC)[43]、干燥综合征(Sjogren's syndrome, SS)[44]、胆囊黏液腺癌(mucin-producing carcinoma of the gallbladder)[45]、胆囊淋巴瘤(gallbladder lymphoma)[46]以及AIH[7,47]或PBC[48], 即所谓的OLS[49,50]. 上述特征无疑使PSC的临床表现更为

复杂. 在某些国家, PSC不仅已跻身于肝移植的最常见人群, 而且也被认为是肝胆恶性肿瘤, 尤其是胆管癌的癌前状态, 合并IBD者并发结肠癌的风险也显著增加[51].

3 PSC的影像学特征

内镜逆行胆管造影(endoscopic retrograde cholangiography, ERC)一直被认为是诊断PSC的金标准[52]. 其影像学特征主要表现为肝内外胆管的多灶性狭窄, 胆管壁僵硬缺乏弹性, 似铅管状, 狭窄上端的胆管可扩张, 呈串珠样表现[52]. ERC不仅用于PSC的诊断, 还可以对完全或不完全闭塞的大胆管行内镜球囊扩张和/或置放支架治疗[53]. 然而, ERC仍有其固有风险, 如急性胰腺炎、胆管炎及十二指肠穿孔[52]. 此外, PSC患者的慢性胆道病变致Oddi氏括约肌屏障缺失, ERC可能导致严重的并发症和慢性复发性胆管炎、肝脓肿及肝功能减退等问题[52]. PSC与IgG4-SC或CC的影像学特征酷似, 及时而准确的鉴别十分重要. Kalaitzakis等[4]研究发现, 尽管ERC诊断PSC的特异性很好, 但敏感性很差, 仅靠ERC尚不能准确与IgG4-SC或CC鉴别. 磁共振成像(magnetic resonance imaging, MRI)及磁共振胰胆管成像(magnetic resonance cholangiopancreatography, MRCP)也是诊断PSC的良好选择[52]. MRI的典型特征为肝脏各叶形态改变及胆管扩张, MRCP则显示胆管狭窄、扩张、呈串珠样或剪枝样改变[52]. 其诊断PSC的敏感性与ERC相似, 但因非侵入性及并发症很低使其更具诊断优势[52]. 最近, Nagle等[54]研究发现, 高分辨三维扰相梯度回波序列(three-dimensional-SPGR)MRI肝胆管成像可用于PSC诊断, 尽管SPGR在某些患者可致肝功能减退, 但对PSC患者极佳的影像质量及胆汁分泌的可视化扫描, 常能提供传统MRCP无法得到的诊断信息. Frydrychowicz等[55]研究显示, 钆塞酸(gadoxetic acid)增强T1加权MRI胆管造影(T1-weighted MRI cholangiography, T1w-MRC)与T2w-MRCP对PSC的诊断相辅相成, 不可替代. T1w-MRC有助于T2w-MRCP的形态学评估并为之提供额外的诊断信息. Kubota等[56]研究显示, 胆管内超声(intraductal ultrasonography, IDUS)有助于PSC与IgG4-SC或CC鉴别. 此外, Alkhawaldeh等[57]研究发现, 以SUV_{max}>3.9作为恶性肿瘤标准, F-18氟脱氧葡萄糖正电子发射计算机断层扫描(F-18 FDG PET)的半定量分析可提高PSC与CC鉴别诊断的准确性.

4 PSC的组织病理学特征

PSC的典型组织病理学特征为同心性“洋葱皮”样纤维化, 但因肝穿刺活检组织的阳性率不足10%, 这种典型的组织学改变很难看到, 通常的活检组织仅表现为零星的炎细胞浸润、小叶间胆管扭曲、胆管上皮空泡化、灶性淋巴细胞浸润, 细胞核呈角状或出现不规则空隙. 前已述及, PSC的临床及影像学特征酷似IgG4-SC, 且有20%的PSC患者血清IgG4升高[26], 但二者的组织病理学特征迥然不同. IgG4-SC的汇管区周围组织内可见由成纤维细胞、浆细胞、淋巴细胞和嗜酸性粒细胞组成的特异性纤维炎症结节以及大量IgG4阳性的淋巴细胞、浆细胞浸润, 而PSC则无此特征, 以此可对二者鉴别[58]. 此外, 小胆管PSC(small duct PSC)是PSC的一种特殊类型, 具有典型的胆汁淤积和PSC组织学改变, 但胆管影像正常[59].

5 蛋白质组学分析对PSC的诊断价值

PSC合并CC的早期诊断十分困难. Lankisch等[60]研究发现, 胆汁的蛋白质组学分析(proteomic analysis)能准确区别PSC和CC, 这不仅为诊断胆道恶性肿瘤提供了新的思路, 也可能成为未来的一种诊断工具. Reinhard等[61]应用蛋白质组学技术对45例PSC患者研究发现, PSC患者的胆汁S100A9表达比对照组高95倍(P<0.005). 提示, 胆汁S100A9水平是PSC活性的有效标志物. 但此方法的弊端在于胆汁的采集需要侵入性的ERC检查. 因此, Metzger等[62]评估了CC、PSC和良性胆道疾病(benign biliary disorder, BBD)患者的尿蛋白质组学分析. 结果显示, 其敏感性为83%, 特异性为79%. 提示, 尿蛋白质组学分析可准确区别CC、PSC及其他BBD, 并可作为PSC和CC新的非侵入性诊断工具.

6 PSC的治疗

6.1 *药物治疗* 熊去氧胆酸(ursodeoxycholic acid, UDCA)是治疗早期或中期PSC的常用药物, 可降低肝功转氨酶、缓解乏力和皮肤瘙痒, 其可能的作用机制包括[63,64]: (1)通过下调MHCI基因表达而抑制炎症反应; (2)通过替代或清除内源性胆酸而保护胆管上皮细胞; (3)通过调节免疫活性细胞重新构建胆汁分泌功能; (4)通过刺激胆管碳酸氢盐分泌拮抗胆汁淤积. 肝细胞摄入UDCA是后续代谢及有效治疗的先决条件[65]. UDCA是否位于肝细胞基底膜的转运蛋白OATP1B1、OATP1B3、OATP2B1及钠牛磺酸盐共转运多

■创新盘点
本文详尽阐述了PSC的发病机制、诊断及治疗取得的最新进展, 提供了大量有价值的信息.

■应用要点
本文全面系统阐述了遗传易感性、体液免疫及细胞免疫在PSC发病机制中的作用, 详尽阐述了PSC的临床、影像、组织病理学以及治疗方面的最新研究进展, 提供了大量有价值的信息, 对PSC的基础与临床研究有重要的指导意义.

肽(Na^+-taurocholate co-transporting polypeptide, NTCP)尚不清楚[65]. 为此, König等[65]研究发现, OATP1B1、OATP1B3、OATP2B1、NTCP与人类肝细胞对UDCA的摄取及作用无关. 换言之, UDCA并非位于肝细胞基底膜的转运蛋白. 目前, UDCA治疗PSC的常规剂量尚无定论, 通常采用10-30 mg/(kg•d). 但近年来推荐高剂量UDCA. Imam等[66]应用28-30 mg/(kg•d)对PSC患者治疗发现, 高剂量UDCA导致的不良风险增加仅出现于组织学早期改变或总胆红素正常的患者. Lindström等[67]研究显示, 高剂量UDCA长期治疗并不能阻止合并IBD的PSC患者罹患结直肠癌或异型增生的风险. 此外, 其他药物或许对PSC也有一定治疗作用. Martin等[68]研究发现, 二十二碳六烯酸(docosahexaenoic acid, DHA)致血清DHA增加可使PSC患者碱性磷酸酶显著降低, 提示DHA对PSC有一定辅助治疗作用. Karaahmet等[69]研究认为, 西罗莫司(rapamycin)可减缓PSC的进展. 除此之外, 大量的临床试验尚未证实免疫抑制剂、抗纤维化制剂、抗生素等药物对PSC治疗有效[70].

6.2 内镜治疗 Chapman等[9]研究发现, PSC患者主胆管狭窄的平均生存期显著低于无主胆管狭窄者(13.7岁 *vs* 23.0岁), 且生存期的明显差异与前者26%的罹患CC风险密切相关. 因此, 如何延缓或减轻PSC患者的主胆管狭窄是临床医生面临的重要课题. 研究显示, 内镜球囊扩张或置放支架可减轻PSC患者的胆管狭窄、缓解临床症状、改善胆汁淤积引起的酶学改变, 但仅限于胆道梗阻的进展期PSC患者[70].

6.3 肝移植治疗 肝移植(liver transplantation, LTX)是目前终末期PSC患者的唯一有效治疗手段[10]. 在某些国家, PSC已成为LTX的首要适应症[51]. LTX术后的5年生存率接近80%, 但复发问题已越发明显, 大约1/5的PSC患者LTX术后复发(recurrent primary sclerosing cholangitis, rPSC), 还有相当比例的LTX患者因供肝失活而影响其长期生存率[10]. rPSC的发病机制仍不清楚, 但被认为与PSC相似[10]. 排斥和复发或许显示了LTX术后PSC患者供肝所发生的连续免疫反应[10]. 减少rPSC的最可信机制似乎与合并IBD以及LTX术前PSC患者未行结肠切除术而起的保护作用有关[10]. 因此, PSC患者LTX术前不必行结肠切除术似乎非常重要[10].

7 结论

PSC是一种发病机制尚未十分清楚的AILD, 常合并IBD, 最终至肝硬化或肝衰竭. GWA的应用使PSC更多的易感基因被发现, 对其发病机制的认识有十分重要的意义. 蛋白质组学技术的飞速发展使PSC并发CC的早期诊断似乎成为可能. PSC新的易感基因和特异性诊断标志物的寻找应是目前研究的重点, 而如何减少LTX的术后复发率应是未来努力的方向.

8 参考文献

1 Pollheimer MJ, Halilbasic E, Fickert P, Trauner M. Pathogenesis of primary sclerosing cholangitis. *Best Pract Res Clin Gastroenterol* 2011; 25: 727-739
2 Chandok N, Hirschfield GM. Management of primary sclerosing cholangitis: conventions and controversies. *Can J Gastroenterol* 2012; 26: 261-268
3 Milkiewicz P, Wunsch E. Primary sclerosing cholangitis. *Recent Results Cancer Res* 2011; 185: 117-133
4 Kalaitzakis E, Levy M, Kamisawa T, Johnson GJ, Baron TH, Topazian MD, Takahashi N, Kanno A, Okazaki K, Egawa N, Uchida K, Sheikh K, Amin Z, Shimosegawa T, Sandanayake NS, Church NI, Chapman MH, Pereira SP, Chari S, Webster GJ. Endoscopic retrograde cholangiography does not reliably distinguish IgG4-associated cholangitis from primary sclerosing cholangitis or cholangiocarcinoma. *Clin Gastroenterol Hepatol* 2011; 9: 800-803. e2
5 Chapman R, Cullen S. Etiopathogenesis of primary sclerosing cholangitis. *World J Gastroenterol* 2008; 14: 3350-3359
6 Fallatah HI, Akbar HO. Autoimmune liver disease - are there spectra that we do not know? *Comp Hepatol* 2011; 10: 9
7 Hunter M, Loughrey MB, Gray M, Ellis P, McDougall N, Callender M. Evaluating distinctive features for early diagnosis of primary sclerosing cholangitis overlap syndrome in adults with autoimmune hepatitis. *Ulster Med J* 2011; 80: 15-18
8 Boonstra K, Beuers U, Ponsioen CY. Epidemiology of primary sclerosing cholangitis and primary biliary cirrhosis: a systematic review. *J Hepatol* 2012; 56: 1181-1188
9 Chapman MH, Webster GJ, Bannoo S, Johnson GJ, Wittmann J, Pereira SP. Cholangiocarcinoma and dominant strictures in patients with primary sclerosing cholangitis: a 25-year single-centre experience. *Eur J Gastroenterol Hepatol* 2012; 24: 1051-1058
10 Fosby B, Karlsen TH, Melum E. Recurrence and rejection in liver transplantation for primary sclerosing cholangitis. *World J Gastroenterol* 2012; 18: 1-15
11 Bergquist A, Montgomery SM, Bahmanyar S, Olsson R, Danielsson A, Lindgren S, Prytz H, Hultcrantz R, Lööf LA, Sandberg-Gertzén H, Almer S, Askling J, Ehlin A, Ekbom A. Increased risk of primary sclerosing cholangitis and ulcerative colitis in first-degree relatives of patients with primary sclerosing cholangitis. *Clin Gastroenterol Hepatol* 2008; 6: 939-943
12 Aron JH, Bowlus CL. The immunobiology of primary sclerosing cholangitis. *Semin Immunopathol* 2009; 31: 383-397
13 Karlsen TH, Boberg KM, Olsson M, Sun JY, Senitzer D, Bergquist A, Schrumpf E, Thorsby E, Lie BA. Particular genetic variants of ligands for natural killer cell receptors may contribute to the HLA as-

sociated risk of primary sclerosing cholangitis. *J Hepatol* 2007; 46: 899-906
14 Næss S, Shiryaev A, Hov JR, Franke A, Karlsen TH. Genetics in primary sclerosing cholangitis. *Clin Res Hepatol Gastroenterol* 2012; 36: 325-333
15 Srivastava B, Mells GF, Cordell HJ, Muriithi A, Brown M, Ellinghaus E, Franke A, Consortium UP, Karlsen TH, Sandford RN, Alexander GJ, Chapman RW, Rushbrook SM, Melum E. Fine mapping and replication of genetic risk loci in primary sclerosing cholangitis. *Scand J Gastroenterol* 2012; 47: 820-826
16 Folseraas T, Melum E, Rausch P, Juran BD, Ellinghaus E, Shiryaev A, Laerdahl JK, Ellinghaus D, Schramm C, Weismüller TJ, Gotthardt DN, Hov JR, Clausen OP, Weersma RK, Janse M, Boberg KM, Björnsson E, Marschall HU, Cleynen I, Rosenstiel P, Holm K, Teufel A, Rust C, Gieger C, Wichmann HE, Bergquist A, Ryu E, Ponsioen CY, Runz H, Sterneck M, Vermeire S, Beuers U, Wijmenga C, Schrumpf E, Manns MP, Lazaridis KN, Schreiber S, Baines JF, Franke A, Karlsen TH. Extended analysis of a genome-wide association study in primary sclerosing cholangitis detects multiple novel risk loci. *J Hepatol* 2012; 57: 366-375
17 Karlsen TH, Franke A, Melum E, Kaser A, Hov JR, Balschun T, Lie BA, Bergquist A, Schramm C, Weismüller TJ, Gotthardt D, Rust C, Philipp EE, Fritz T, Henckaerts L, Weersma RK, Stokkers P, Ponsioen CY, Wijmenga C, Sterneck M, Nothnagel M, Hampe J, Teufel A, Runz H, Rosenstiel P, Stiehl A, Vermeire S, Beuers U, Manns MP, Schrumpf E, Boberg KM, Schreiber S. Genome-wide association analysis in primary sclerosing cholangitis. *Gastroenterology* 2010; 138: 1102-1111
18 Melum E, Franke A, Schramm C, Weismüller TJ, Gotthardt DN, Offner FA, Juran BD, Laerdahl JK, Labi V, Björnsson E, Weersma RK, Henckaerts L, Teufel A, Rust C, Ellinghaus E, Balschun T, Boberg KM, Ellinghaus D, Bergquist A, Sauer P, Ryu E, Hov JR, Wedemeyer J, Lindkvist B, Wittig M, Porte RJ, Holm K, Gieger C, Wichmann HE, Stokkers P, Ponsioen CY, Runz H, Stiehl A, Wijmenga C, Sterneck M, Vermeire S, Beuers U, Villunger A, Schrumpf E, Lazaridis KN, Manns MP, Schreiber S, Karlsen TH. Genome-wide association analysis in primary sclerosing cholangitis identifies two non-HLA susceptibility loci. *Nat Genet* 2011; 43: 17-19
19 Hov JR, Boberg KM, Karlsen TH. Autoantibodies in primary sclerosing cholangitis. *World J Gastroenterol* 2008; 14: 3781-3791
20 Terjung B, Spengler U. Atypical p-ANCA in PSC and AIH: a hint toward a "leaky gut"? *Clin Rev Allergy Immunol* 2009; 36: 40-51
21 Op De Beéck K, Van den Bergh K, Vermeire S, Decock S, Derua R, Waelkens E, Rutgeerts P, Nevens F, Bossuyt X. Immune reactivity to β-tubulin isotype 5 and vesicular integral-membrane protein 36 in patients with autoimmune gastrointestinal disorders. *Gut* 2011; 60: 1601-1602
22 Terjung B, Söhne J, Lechtenberg B, Gottwein J, Muennich M, Herzog V, Mähler M, Sauerbruch T, Spengler U. p-ANCAs in autoimmune liver disorders recognise human beta-tubulin isotype 5 and cross-react with microbial protein FtsZ. *Gut* 2010; 59: 808-816
23 Ardesjö B, Hansson CM, Bruder CE, Rorsman F, Betterle C, Dumanski JP, Kämpe O, Ekwall O. Autoantibodies to glutathione S-transferase theta 1 in patients with primary sclerosing cholangitis and other autoimmune diseases. *J Autoimmun* 2008; 30: 273-282
24 Webster GJ, Pereira SP, Chapman RW. Autoimmune pancreatitis/IgG4-associated cholangitis and primary sclerosing cholangitis--overlapping or separate diseases? *J Hepatol* 2009; 51: 398-402
25 Björnsson E, Chari S, Silveira M, Gossard A, Takahashi N, Smyrk T, Lindor K. Primary sclerosing cholangitis associated with elevated immunoglobulin G4: clinical characteristics and response to therapy. *Am J Ther* 2011; 18: 198-205
26 Navaneethan U, Gk Venkatesh P, Choudhary M, Shen B, Kiran RP. Elevated immunoglobulin G4 level is associated with reduced colectomy-free survival in patients with primary sclerosing cholangitis and ulcerative colitis. *J Crohns Colitis* 2012 May 1. *[Epub ahead of print]*
27 Kato T, Komori A, Bae SK, Migita K, Ito M, Motoyoshi Y, Abiru S, Ishibashi H. Concurrent systemic AA amyloidosis can discriminate primary sclerosing cholangitis from IgG4-associated cholangitis. *World J Gastroenterol* 2012; 18: 192-196
28 Hirano K, Tada M, Mizuno S, Isayama H, Takahara N, Nagano R, Hamada T, Miyabayashi K, Ito Y, Mohri D, Kawakubo K, Sasaki T, Kogure H, Yamamoto N, Sasahira N, Yamashiki N, Sugawara Y, Kokudo N, Toda N, Koike K. Lower incidence of biliary carcinoma in patients with primary sclerosing cholangitis and high serum levels of immunoglobulin E. *Clin Gastroenterol Hepatol* 2012; 10: 79-83
29 Navaneethan U, Venkatesh PG, Kiran RP. Immunoglobulin E level and its significance in patients with primary sclerosing cholangitis. *Clin Gastroenterol Hepatol* 2012; 10: 563; author reply 563-564
30 Kawata K, Kobayashi Y, Gershwin ME, Bowlus CL. The Immunophysiology and Apoptosis of Biliary Epithelial Cells: Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis. *Clin Rev Allergy Immunol* 2012 Jun 12. *[Epub ahead of print]*
31 Pender MP. CD8+ T-Cell Deficiency, Epstein-Barr Virus Infection, Vitamin D Deficiency, and Steps to Autoimmunity: A Unifying Hypothesis. *Autoimmune Dis* 2012; 2012: 189096
32 Rigopoulou EI, Smyk DS, Matthews CE, Billinis C, Burroughs AK, Lenzi M, Bogdanos DP. Epstein-barr virus as a trigger of autoimmune liver diseases. *Adv Virol* 2012; 2012: 987471
33 Österreicher CH, Trauner M. Xenobiotic-induced liver injury and fibrosis. *Expert Opin Drug Metab Toxicol* 2012; 8: 571-580
34 Ngu JH, Gearry RB, Frampton CM, Stedman CA. Mortality and the risk of malignancy in autoimmune liver diseases: a population-based study in Canterbury, New Zealand. *Hepatology* 2012; 55: 522-529
35 Halliday JS, Djordjevic J, Lust M, Culver EL, Braden B, Travis SP, Chapman RW. A unique clinical phenotype of primary sclerosing cholangitis associated with Crohn's disease. *J Crohns Colitis* 2012; 6: 174-181
36 Ngu JH, Gearry RB, Wright AJ, Stedman CA. Inflammatory bowel disease is associated with poor outcomes of patients with primary sclerosing cholangitis. *Clin Gastroenterol Hepatol* 2011; 9: 1092-1107; quiz e135

■名词解释
胆管消失综合征(VBDS): 指多种原因导致的胆管树破坏而使肝内胆管局灶性或弥漫性消失, 组织学检查无胆管正常结构存在, 临床表现以胆汁淤积为特征.

■同行评价
本文较详尽地阐述了近年来PSC发病机制、诊断及治疗等方面所取得的最新进展，对指导PSC的基础研究与临床治疗具有重要意义.

37 Navaneethan U, Venkatesh PG, Lashner BA, Shen B, Kiran RP. The Impact of ulcerative colitis on the long-term outcome of patients with primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2012 Mar 19. *[Epub ahead of print]*

38 Jørgensen KK, Grzyb K, Lundin KE, Clausen OP, Aamodt G, Schrumpf E, Vatn MH, Boberg KM. Inflammatory bowel disease in patients with primary sclerosing cholangitis: clinical characterization in liver transplanted and nontransplanted patients. *Inflamm Bowel Dis* 2012; 18: 536-545

39 Maylee H, Harada K, Igarashi S, Tohda G, Yamamoto M, Ren XS, Osawa T, Hasegawa Y, Takahashi N, Nakanuma Y. Case of telangiectatic/inflammatory hepatocellular adenoma arising in a patient with primary sclerosing cholangitis. *Hepatol Res* 2012; 42: 611-618

40 Srirajaskanthan R, Agarwal K, Karanyi J. Massive gastrointestinal bleed in a patient with primary sclerosing cholangitis. *Gastroenterology* 2011; 140: e7-e8

41 Lorenzoni PJ, Scola RH, Kay CS, Muzzillo DA, Werneck LC. Coexistence of primary sclerosing cholangitis in a patient with myasthenia gravis. *Ann Indian Acad Neurol* 2011; 14: 316-318

42 Van Hauwaert V, Meers S, Verhoef G, Tousseyn T, Sagaert X, Vermeire S, Rutgeerts P, Van Assche G. Rectal non-Hodgkin's lymphoma in an infliximab treated patient with ulcerative colitis and primary sclerosing cholangitis. *J Crohns Colitis* 2010; 4: 683-686

43 Mori A, Doi R, Yonenaga Y, Nakabo S, Yazumi S, Nakaya J, Kono F, Manabe T, Uemoto S. Xanthogranulomatous cholecystitis complicated with primary sclerosing cholangitis: report of a case. *Surg Today* 2010; 40: 777-782

44 Katsanos KH, Saougos V, Kosmidou M, Doukas M, Kamina S, Asproudis I, Tsianos EV. Sjogren's syndrome in a patient with ulcerative colitis and primary sclerosing cholangitis: Case report and review of the literature. *J Crohns Colitis* 2009; 3: 200-203

45 Noda H, Chiba F, Toyama N, Konishi F. Mucin-producing carcinoma of the gallbladder associated with primary sclerosing cholangitis and ulcerative colitis. *J Hepatobiliary Pancreat Surg* 2009; 16: 83-85

46 Willingham DL, Menke DM, Satyanarayana R. Gallbladder lymphoma in primary sclerosing cholangitis. *Clin Gastroenterol Hepatol* 2009; 7: A26

47 Thakker A, Karande S. Overlap syndrome: autoimmune sclerosing cholangitis. *Indian Pediatr* 2010; 47: 1063-1065

48 Jeevagan A. Overlap of primary biliary cirrhosis and primary sclerosing cholangitis - a rare coincidence or a new syndrome. *Int J Gen Med* 2010; 3: 143-146

49 Trivedi PJ, Chapman RW. PSC, AIH and overlap syndrome in inflammatory bowel disease. *Clin Res Hepatol Gastroenterol* 2012 Feb 2. *[Epub ahead of print]*

50 Boberg KM, Chapman RW, Hirschfield GM, Lohse AW, Manns MP, Schrumpf E. Overlap syndromes: the International Autoimmune Hepatitis Group (IAIHG) position statement on a controversial issue. *J Hepatol* 2011; 54: 374-385

51 Ponsioen CY. Recent insights in primary sclerosing cholangitis. *J Dig Dis* 2012; 13: 337-341

52 Andraus W, Haddad L, Nacif LS, Silva FD, Blasbalg R, D'Albuquerque LA. The best approach for diagnosing primary sclerosing cholangitis. *Clinics* (Sao Paulo) 2011; 66: 1987-1989

53 Gotthardt D, Stiehl A. Endoscopic retrograde cholangiopancreatography in diagnosis and treatment of primary sclerosing cholangitis. *Clin Liver Dis* 2010; 14: 349-358

54 Nagle SK, Busse RF, Brau AC, Brittain JH, Frydrychowicz A, Iwadate Y, Reeder SB. High resolution navigated three-dimensional T(1) -weighted hepatobiliary MRI using gadoxetic acid optimized for 1.5 tesla. *J Magn Reson Imaging* 2012; 36: 890-899

55 Frydrychowicz A, Jedynak AR, Kelcz F, Nagle SK, Reeder SB. Gadoxetic acid-enhanced T1-weighted MR cholangiography in primary sclerosing cholangitis. *J Magn Reson Imaging* 2012; 36: 632-640

56 Kubota K, Kato S, Uchiyama T, Watanabe S, Nozaki Y, Fujita K, Yoneda M, Inamori M, Shimamura T, Abe Y, Kirikoshi H, Kobayashi N, Saito S, Nakajima A. Discrimination between sclerosing cholangitis-associated autoimmune pancreatitis and primary sclerosing cholangitis, cancer using intraductal ultrasonography. *Dig Endosc* 2011; 23: 10-16

57 Alkhawaldeh K, Faltten S, Biersack HJ, Ezziddin S. The value of F-18 FDG PET in patients with primary sclerosing cholangitis and cholangiocarcinoma using visual and semiquantitative analysis. *Clin Nucl Med* 2011; 36: 879-883

58 Deshpande V, Sainani NI, Chung RT, Pratt DS, Mentha G, Rubbia-Brandt L, Lauwers GY. IgG4-associated cholangitis: a comparative histological and immunophenotypic study with primary sclerosing cholangitis on liver biopsy material. *Mod Pathol* 2009; 22: 1287-1295

59 Krones E, Graziadei I, Trauner M, Fickert P. Evolving concepts in primary sclerosing cholangitis. *Liver Int* 2012; 32: 352-369

60 Lankisch TO, Metzger J, Negm AA, Vosskuhl K, Schiffer E, Siwy J, Weismüller TJ, Schneider AS, Thedieck K, Baumeister R, Zürbig P, Weissinger EM, Manns MP, Mischak H, Wedemeyer J. Bile proteomic profiles differentiate cholangiocarcinoma from primary sclerosing cholangitis and choledocholithiasis. *Hepatology* 2011; 53: 875-884

61 Reinhard L, Rupp C, Riedel HD, Ruppert T, Giese T, Flechtenmacher C, Weiss KH, Kloeters-Plachky P, Stremmel W, Schirmacher P, Sauer P, Gotthardt DN. S100A9 is a biliary protein marker of disease activity in primary sclerosing cholangitis. *PLoS One* 2012; 7: e29821

62 Metzger J, Negm AA, Plentz RR, Weismüller TJ, Wedemeyer J, Karlsen TH, Dakna M, Mullen W, Mischak H, Manns MP, Lankisch TO. Urine proteomic analysis differentiates cholangiocarcinoma from primary sclerosing cholangitis and other benign biliary disorders. *Gut* 2012 May 12. *[Epub ahead of print]*

63 Santander C, Moreno-Otero R. Commentary: ursodeoxycholic acid as chemoprevention in inflammatory bowel disease and primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2012; 35: 846; discussion 847

64 Triantos CK, Koukias N, Nikolopoulou V, Burroughs AK. Ursodeoxycholic acid in primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2012; 35: 622-623

65 König J, Klatt S, Dilger K, Fromm MF. Characterization of ursodeoxycholic and norursodeoxycholic acid as substrates of the hepatic uptake transporters

OATP1B1, OATP1B3, OATP2B1 and NTCP. *Basic Clin Pharmacol Toxicol* 2012; 111: 81-86
66 Imam MH, Sinakos E, Gossard AA, Kowdley KV, Luketic VA, Edwyn Harrison M, McCashland T, Befeler AS, Harnois D, Jorgensen R, Petz J, Keach J, DeCook AC, Enders F, Lindor KD. High-dose ursodeoxycholic acid increases risk of adverse outcomes in patients with early stage primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2011; 34: 1185-1192
67 Lindström L, Boberg KM, Wikman O, Friis-Liby I, Hultcrantz R, Prytz H, Sandberg-Gertzén H, Sangfelt P, Rydning A, Folvik G, Gangsøy-Kristiansen M, Danielsson A, Bergquist A. High dose ursodeoxycholic acid in primary sclerosing cholangitis does not prevent colorectal neoplasia. *Aliment Pharmacol Ther* 2012; 35: 451-457
68 Martin CR, Blanco PG, Keach JC, Petz JL, Zaman MM, Bhaskar KR, Cluette-Brown JE, Gautam S, Sheth S, Afdhal NH, Lindor KD, Freedman SD. The safety and efficacy of oral docosahexaenoic acid supplementation for the treatment of primary sclerosing cholangitis - a pilot study. *Aliment Pharmacol Ther* 2012; 35: 255-265
69 Karaahmet F, Kılıncalp S, Altınbas A, Coban S, Yuksel O. Intrabiliary rapamycin may slow progression of primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2012; 35: 490-491
70 Weismüller TJ, Lankisch TO. Medical and endoscopic therapy of primary sclerosing cholangitis. *Best Pract Res Clin Gastroenterol* 2011; 25: 741-752

编辑 李军亮 电编 鲁亚静

ISSN 1009-3079 (print) ISSN 2219-2859 (online) CN 14-1260/R 2012年版权归世界华人消化杂志

• 消息 •

《世界华人消化杂志》正文要求

本刊讯 本刊正文标题层次为 0引言; 1 材料和方法, 1.1 材料, 1.2 方法; 2 结果; 3 讨论; 4 参考文献. 序号一律左顶格写, 后空1格写标题; 2级标题后空1格接正文. 以下逐条陈述: (1)引言 应包括该研究的目的和该研究与其他相关研究的关系. (2)材料和方法 应尽量简短, 但应让其他有经验的研究者能够重复该实验. 对新的方法应该详细描述, 以前发表过的方法引用参考文献即可, 有关文献中或试剂手册中的方法的改进仅描述改进之处即可. (3)结果 实验结果应合理采用图表和文字表示, 在结果中应避免讨论. (4)讨论 要简明, 应集中对所得的结果做出解释而不是重复叙述, 也不应是大量文献的回顾. 图表的数量要精选. 表应有表序和表题, 并有足够具有自明性的信息, 使读者不查阅正文即可理解该表的内容. 表内每一栏均应有表头, 表内非公知通用缩写应在表注中说明, 表格一律使用三线表(不用竖线), 在正文中该出现的地方应注出. 图应有图序、图题和图注, 以使其容易被读者理解, 所有的图应在正文中该出现的地方注出. 同一个主题内容的彩色图、黑白图、线条图, 统一用一个注解分别叙述. 如: 图1 萎缩性胃炎治疗前后病理变化．A: ⋯; B: ⋯; C: ⋯; D: ⋯; E: ⋯; F: ⋯; G: ⋯. 曲线图可按●、○、■、□、▲、△顺序使用标准的符号. 统计学显著性用: $^{a}P<0.05$, $^{b}P<0.01$($P>0.05$不注). 如同一表中另有一套P值, 则$^{c}P<0.05$, $^{d}P<0.01$; 第3套为$^{e}P<0.05$, $^{f}P<0.01$. P值后注明何种检验及其具体数字, 如$P<0.01$, $t = 4.56$ *vs* 对照组等, 注在表的左下方. 表内采用阿拉伯数字, 共同的计量单位符号应注在表的右上方, 表内个位数、小数点、±、-应上下对齐.“空白”表示无此项或未测, “-”代表阴性未发现, 不能用同左、同上等. 表图勿与正文内容重复. 表图的标目尽量用t/min, c/(mol/L), p/kPa, V/mL, t/℃表达. 黑白图请附黑白照片, 并拷入光盘内; 彩色图请提供冲洗的彩色照片, 请不要提供计算机打印的照片. 彩色图片大小7.5 cm×4.5 cm, 必须使用双面胶条粘贴在正文内, 不能使用浆糊粘贴. (5)志谢 后加冒号, 排在讨论后及参考文献前, 左齐.