

幽门螺杆菌感染与胃癌发病关系的文献计量学分析

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收稿日期: 2006-08-14 接受日期: 2006-09-12

Bibliometric analysis of literatures on relationship between *Helicobacter pylori* infection and gastric carcinogenesis

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Received: 2006-08-14 Accepted: 2006-09-12

Abstract

AIM: To present the research progress on the correlations between *Helicobacter pylori* infection and the risks of gastric cancer, and conclude the hot topics.

METHODS: The international papers, published from 2001 to 2006 on this topic, were analyzed by the method of citation analysis, and then the highly-cited references were clustered by SPSS soft package. Based on the contents of the papers in each cluster, the hot-topic researches were concluded.

RESULTS: Research literatures about the topic mainly come from the comprehensive journals that were well-known in the world, and the core journals of oncology and gastroenterology took the second place. There were 1547 related papers covered in Science Citation Index (SCI) from 2001 to 2006, of which 42 were cited more than 60 times, and then they were clustered into five parts according to their co-cited frequencies.

CONCLUSION: The hot topics are classified as: *H pylori* infection and epidemiology of gastric cancer; *H pylori* infection and animal model of gastric cancer; eradication of *H pylori* and gastric cancer; *H pylori* infection, cytokine polymorphisms and gastric cancer; genes related to *H pylori*-associated diseases.

Key Words: *Helicobacter pylori*; Gastric cancer; Bibliometrics analysis

Wang XN, Cui L. Bibliometric analysis of literatures on relationship between *Helicobacter pylori* infection and gastric carcinogenesis. Shijie Huaren Xiaohua Zazhi 2006;14(29):2883-2888

摘要

目的: 了解*H pylori*感染与胃癌关系研究现状, 总结研究热点, 提供参考信息。

方法: 采用引文分析方法对国外2001-2006有关该主题的重要文献进行调查分析, 并用SPSS对高频被引文献进行聚类分析, 根据各分类中的文献内容分析当前研究的热点。

结果: *H pylori*感染与胃癌关系研究的重要文献多数发表于世界著名的综合性刊物上, 肿瘤学与胃肠病学核心期刊次之。检得SCI数据库中相关文献1547篇, 其参考文献出现频次高于60次论文42篇。高被引论文聚类分析树图分5类。

结论: *H pylori*感染与胃癌流行病学、胃癌动物模型, *H pylori*感染的根除与胃癌的关系, *H pylori*感染、宿主细胞因子多态性与胃癌易感性, 以及*H pylori*致病相关基因的为研究热点。

关键词: 幽门螺杆菌; 胃癌; 文献计量学

王孝宁, 崔雷. 幽门螺杆菌感染与胃癌发病关系文献计量学分析. 世界华人消化杂志 2006;14(29):2883-2888

<http://www.wjgnet.com/1009-3079/14/2883.asp>

0 引言

胃癌是世界范围内癌症导致死亡的第二大原

■背景资料

胃癌是发病率很高的肿瘤之一, 其发病涉及多因素。最近研究显示, 幽门螺杆菌(*H pylori*)感染是诱发胃癌的一个重要危险因素, 但*H pylori*感染诱发胃癌发生的具体机制目前尚不清楚。

■研发前沿

胃癌的发病是多因素多步骤的过程,大量的流行病学和病理组织学资料表明,*H pylori*感染是诱发胃癌最重要的单一危险因素。但是,关于*H pylori*与胃癌的关系仍存在一些无法解释的现象,现代分子生物学技术的发展有望为这些问题的解决开辟一条新的途径。

因,每年大约导致65万人死亡。胃癌的发病是多因素多步骤的过程,研究显示,幽门螺杆菌(*Helicobacter pylori*, *H pylori*)感染是诱发胃癌的一个重要危险因素,世界卫生组织下属的国际癌症研究机构(IARC)已将其定为人胃癌的I类致癌原^[1]。*H pylori*感染与胃癌的关系近年来引起了广泛的关注,是医学界的热点问题。

本文采用文献计量学中的引文分析方法^[2]对国外近年来有关该主题的重要文献进行调查分析,总结出该领域的研究热点,为广大专业人员深入开展*H pylori*感染与胃癌关系的研究提供参考信息。

1 材料和方法

1.1 材料 本研究采用美国科学情报研究所出版的大型综合性数据库《科学引文索引》(science citation index, SCI)为样本来源,以“*Helicobacter pylori* AND gastric cancer”为检索策略,检索到2001/2006-07的相关文献1547篇。将全部相关文献的引文(即参考文献,共65457条)套录下来,统计每一篇参考文献的出现频次,并由高到低进行排序,截取其中出现频次高于60次的论文作为高频被引文献,共42篇。这些高频被引文献是目前本专业领域的研究人员在进行*H pylori*感染与胃癌关系这一主题研究的时候最为关注的论文,也是该主题的核心文献。因此,对这些核心文献的分析可以反映出当前研究的热点。

1.2 方法 为了反映这些核心文献之间的内在联系,本文采用了同被引分析方法:2篇文献如果同时被后来的某一篇文章或者多篇文章引用,则称这2篇文献为同被引。如果同被引次数越多,说明他们在引用者看来具有共同的特点。因此,根据论文的同被引次数可以分析出他们之间的亲疏关系(距离),运用统计分析软件SPSS对这些高频被引文献进行聚类分析。由此形成这些高频被引论文的聚类树图,根据各个类中的文献内容分析当前*H pylori*感染与胃癌关系研究的热点。

2 结果

2.1 高频被引论文及被引频次 高频被引论文大多数发表在世界著名的综合性刊物上,如Nature, Science, New England Journal of Medicine等,共20篇(47%),发表于肿瘤学核心期刊9篇(21%),如Cancer Research等,发表于胃肠病学核心期刊9篇(21%),如Gastroenterology, Gut, 其余4篇(1%)(表1)。

2.2 高频被引论文的同被引聚类分析 聚类树图见图1。纵轴的文字是这些论文的作者姓名和文献发表年代等内容,其后面数字代表表1中的文献序号;横轴的数字代表2个高频被引论文之间的距离,如果2篇文献在越短的距离内聚集到一起,说明他们关系密切。可以看到,文献15和文献30首先聚在一起,说明这2篇文献之间的距离是所有文献中最小的,因此他们的关系也是最近的,从文献题目中也可以看出他们都是有关*H pylori*全基因组序列测定的研究。

3 讨论

根据上面聚类分析的结果,我们可以把这42篇论文分为5个类别,分别是:(1)*H pylori*感染与胃癌流行病学研究:包括文献2, 6, 9, 10, 1, 4, 7, 14, 5, 21和33。流行病学调查最先证实了*H pylori*感染与胃癌的发生相关,特别是3例前瞻性病例对照研究(Parsonnet *et al*, Nomura *et al*和Forman *et al*)相继一致发现,感染*H pylori*的人群发生胃癌的危险性增加(*OR*值分别为3.6, 6.0和2.77)。Uemura *et al*前瞻性研究了1246例感染者,平均随访7.8 a,结果2.9%罹患胃癌。胃癌发生于*H pylori*阳性胃病患者,如胃溃疡、胃增生性息肉和非溃疡性消化不良等;尽管十二指肠球部溃疡患者*H pylori*阳性,但无一例发生胃癌;所有*H pylori*阴性患者均无胃癌发生。这项研究充分说明,感染*H pylori*有可能发展为胃癌。国际性机构EUROGAST的大规模流行病学调查显示,*H pylori*感染人群发生胃癌的风险是非感染人群的6倍。Huang *et al*采用Meta分析方法评价二者的关系,结果显示*H pylori*感染是胃癌发生的危险因素,并指出现有研究结果不一致的原因是由于对照组的选择、患者的年龄、胃癌发生的部位及分期差异等多种混杂因素的影响。(2)*H pylori*感染与胃癌动物模型的研究:包括文献8, 24和42。来自动物实验的依据证实,长期单独感染*H pylori*可诱发胃癌。例如Watanabe *et al*用*H pylori*感染50只♂蒙古沙鼠,于感染后连续观察胃黏膜的形态变化,发现第6周动物胃黏膜出现严重的急、慢性炎症和上皮增生,第26周出现胃溃疡和肠上皮化生等病变,到第62周时,59%发生了胃溃疡,85%出现了肠上皮化生,37%发生了胃腺癌。此研究表明,*H pylori*感染可直接诱发蒙古沙鼠胃癌,以高分化的腺癌为主,从而在动物实验中直接证实了*H pylori*与胃癌发生有关。(3)*H pylori*感染的根除与胃癌关系的研究:

Dendrogram using Average Linkage (Within Group)

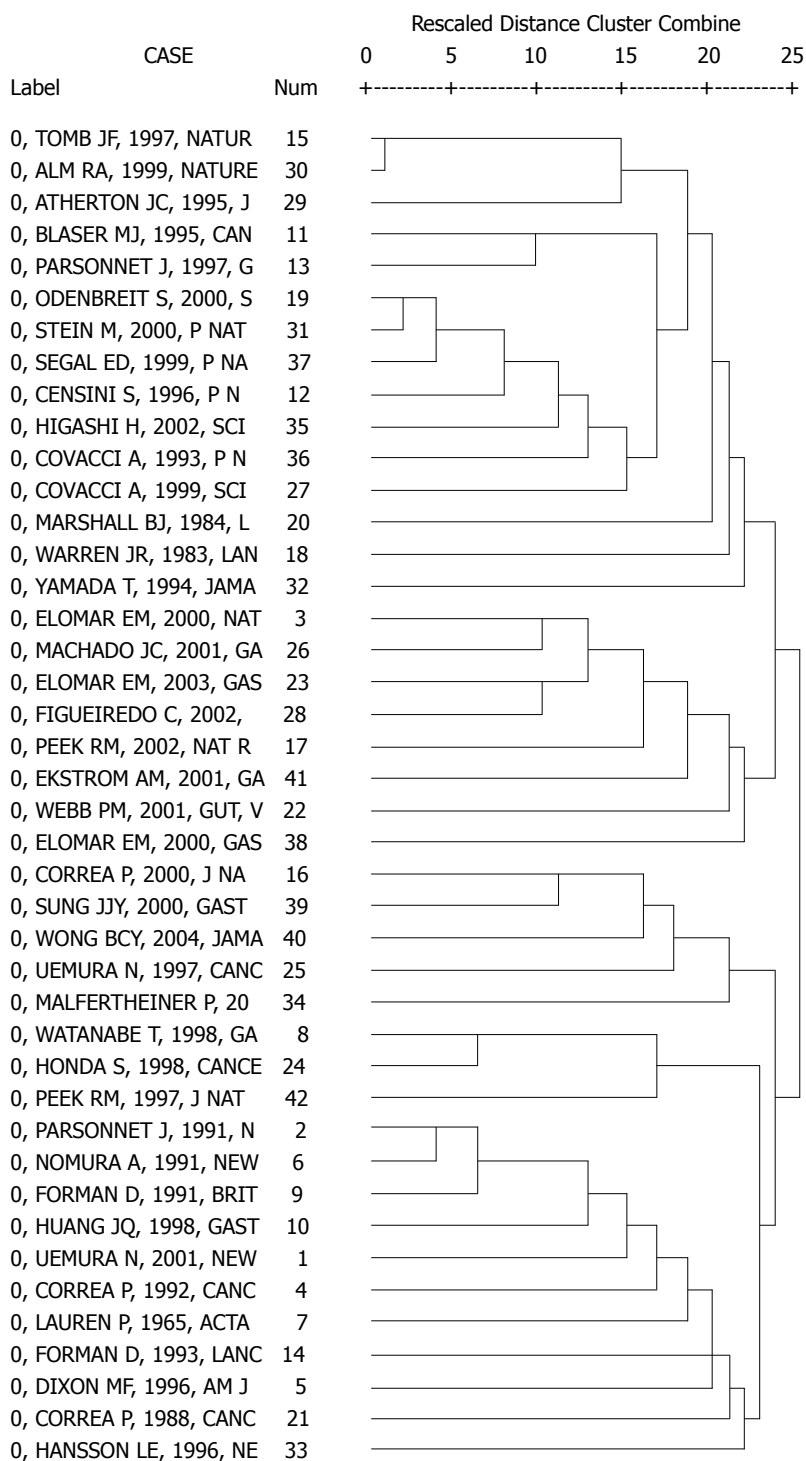


图 1 42篇高频被引论文的聚类分析图.

■ 相关报道

此前曾有报道运用引文分析方法分析SCI数据库收录胃癌前病变专题文献的参考文献,以确定胃癌前病变研究的核心作者和核心期刊,探索胃癌前病变专题文献的外部特征及核心信息来源.

包括文献16, 39, 40, 25和34. 根除*H pylori*能否降低发生胃癌的风险是一个很重要的问题,目前已有的一些关于根除*H pylori*能否改善胃黏膜组织形态学的研究结果. 例如Wong *et al*在中国胃癌高发的福建长乐地区的7.5 a随访研究结果显示,胃内无癌前疾病(如萎缩性胃炎)和癌前病变(如肠化生、异型增生)者, *H pylori*根除后无胃癌发生,对于已有癌前疾病和病变者,根除*H pylori*还

不能防止胃癌的发生. Uemura *et al*对*H pylori*阳性早期胃癌在内镜切除癌肿病变后接受*H pylori*根除治疗, 3 a的内镜随访研究显示,根除*H pylori*可改善胃黏膜嗜中性粒细胞渗透和肠化生,抑制新发癌灶的产生. (4)*H pylori*感染、宿主细胞因子多态性与胃癌易感性研究: 包括文献3, 26, 23, 28, 17, 41, 22和38. *H pylori*感染关键的病理生理效应是启动了炎症反应,其主要介质是细

■应用要点

本文采用文献计量学中的引文分析方法对国外近年来有关该主题的重要文献进行调查分析,总结该领域的研究热点,以期对*H pylori*感染与胃癌关系的研究提供参考信息。

表 1 2001–2006年有关*H pylori*感染与胃癌关系研究的高频被引论文

序号	文献出处	被引频次
1	Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. <i>Helicobacter pylori</i> infection and the development of gastric cancer. <i>N Engl J Med</i> 2001; 345: 784–789	275
2	Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelmann JH, Orentreich N, Sibley RK. <i>Helicobacter pylori</i> infection and the risk of gastric carcinoma. <i>N Engl J Med</i> 1991; 325: 1127–1131	261
3	El-Omar EM, Carrington M, Chow WH, McColl KE, Bream JH, Young HA, Herrera J, Lissowska J, Yuan CC, Rothman N, Lanyon G, Martin M, Fraumeni JF Jr, Rabkin CS. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. <i>Nature</i> 2000; 404: 398–402	248
4	Correa P. Human gastric carcinogenesis: a multistep and multifactorial process—First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. <i>Cancer Res</i> 1992; 52: 6735–6740	202
5	Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. <i>Am J Surg Pathol</i> 1996; 20: 1161–1181	198
6	Nomura A, Stemmermann GN, Chyou PH, Kato I, Perez-Perez GI, Blaser MJ. <i>Helicobacter pylori</i> infection and gastric carcinoma among Japanese Americans in Hawaii. <i>N Engl J Med</i> 1991; 325: 1132–1136	165
7	Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification. <i>Acta Pathol Microbiol Scand</i> 1965; 64: 31–49	159
8	Watanabe T, Tada M, Nagai H, Sasaki S, Nakao M. <i>Helicobacter pylori</i> infection induces gastric cancer in mongolian gerbils. <i>Gastroenterology</i> 1998; 115: 642–648	152
9	Forman D, Newell DG, Fullerton F, Yarnell JW, Stacey AR, Wald N, Sitas F. Association between infection with <i>Helicobacter pylori</i> and risk of gastric cancer: evidence from a prospective investigation. <i>BMJ</i> 1991; 302: 1302–1305	138
10	Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between <i>Helicobacter pylori</i> seropositivity and gastric cancer. <i>Gastroenterology</i> 1998; 114: 1169–1179	135
11	Blaser MJ, Perez-Perez GI, Kleanthous H, Cover TL, Peek RM, Chyou PH, Stemmermann GN, Nomura A. Infection with <i>Helicobacter pylori</i> strains possessing cagA is associated with an increased risk of developing adenocarcinoma of the stomach. <i>Cancer Res</i> 1995; 55: 2111–2115	132
12	Censini S, Lange C, Xiang Z, Crabtree JE, Ghiara P, Borodovsky M, Rappuoli R, Covacci A. cag, a pathogenicity island of <i>Helicobacter pylori</i> , encodes type I-specific and disease-associated virulence factors. <i>Proc Natl Acad Sci USA</i> 1996; 93: 14648–14653	116
13	Parsonnet J, Friedman GD, Orentreich N, Vogelmann H. Risk for gastric cancer in people with CagA positive or CagA negative <i>Helicobacter pylori</i> infection. <i>Gut</i> 1997; 40: 297–301	103
14	An international association between <i>Helicobacter pylori</i> infection and gastric cancer. The EUROGAIST Study Group. <i>Lancet</i> 1993; 341: 1359–1362	100
15	Tomb JF, White O, Kerlavage AR, Clayton RA, Sutton GG, Fleischmann RD, Ketchum KA, Klenk HP, Gill S, Dougherty BA, Nelson K, Quackenbush J, Zhou L, Kirkness EF, Peterson S, Loftus B, Richardson D, Dodson R, Khalak HG, Glodek A, McKenney K, Fitzgerald LM, Lee N, Adams MD, Hickey EK, Berg DE, Gocayne JD, Utterback TR, Peterson JD, Kelley JM, Cotton MD, Weidman JM, Fujii C, Bowman C, Watthey L, Wallin E, Hayes WS, Borodovsky M, Karp PD, Smith HO, Fraser CM, Venter JC. The complete genome sequence of the gastric pathogen <i>Helicobacter pylori</i> . <i>Nature</i> 1997; 388: 539–547	95
16	Correa P, Fontham ET, Bravo JC, Bravo LE, Ruiz B, Zarama G, Realpe JL, Malcom GT, Li D, Johnson WD, Mera R. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti- <i>helicobacter pylori</i> therapy. <i>J Natl Cancer Inst</i> 2000; 92: 1881–1888	92
17	Peek RM Jr, Blaser MJ. <i>Helicobacter pylori</i> and gastrointestinal tract adenocarcinomas. <i>Nat Rev Cancer</i> 2002; 2: 28–37	87
18	Unidentified curved bacilli on gastric epithelium in active chronic gastritis. <i>Lancet</i> 1983; 1:	87

■名词解释

文献计量学是借助文献的各种特征的数量, 采用数学与统计学方法来描述、评价和预测科学技术的现状与发展趋势的图书情报学分支学科。有助于科研人员分析、追踪热点研究领域、判断科学发展的宏观态势、推测学科发展及确定科研选题等。

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■同行评价

本文采用文献计量学中的引文分析方法对国外近年来有关该主题的重要文献进行调查分析, 以期为 *H pylori* 感染与胃癌关系的研究提供参考信息, 具有一定的指导意义, 课题设计合理, 结论可信, 具有较高的理论水平。

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胞因子。例如El-Omar *et al*报道*IL-1*基因多态性可能表达大量的*IL-1β*蛋白, 与*H pylori*感染导致胃酸分泌减少及胃癌发生相关联。Machado *et al*发现*IL-1B-511T*和*IL-1RN*2*基因型增加肠型胃癌发生的风险(*OR*值为2.7), 进一步证实*IL-1*基因多态性与胃癌发生密切相关, *IL-1B*与*IL-1RN*基因多态性之间存在协同作用。(5)*H pylori*致病相关基因的研究: 包括文献15, 30, 29, 11, 13, 19, 31, 37, 12, 35, 36, 27, 20, 18和32。*H pylori*感染与胃癌发生相关的分子机制研究, 是目前*H pylori*研究的主要方面。Tomb *et al*和Alm *et al*对2株*H pylori* 26695和J99全基因组序列测定工作的完成, 加速了*H pylori*的研究进程。Atherton *et al*报道特异性空泡毒素A(VacA)与体外细胞毒素活力的水平相关, 且与临床表现及进展结果相关。许多研究将注意力集中在CagA上。Parsonnet *et al*报道CagA阳性的*H pylori*感染者发生胃癌的风险是无*H pylori*感染者的5.8倍, 且对肠型和弥漫性癌均如此。Segal *et al*报道*H pylori*与胃上皮细胞共同培养可引起信号传递和145 kDa宿主细胞蛋白的酪氨酸磷酸化。Odenbreit *et al*发现CagA是经由一个复杂的“注射器”样的IV型分

泌系统进入胃上皮细胞的, 此分泌装置由CagA致病岛基因编码。Higashi *et al*发现CagA进入胃上皮细胞后被磷酸化, 磷酸化的CagA结合并激活细胞内的酪氨酸磷酸化酶SHP-2, 使SHP-2锚定于胞膜上, 并进一步活化去磷酸化的信号传导级联反应通路, 导致细胞的形态学改变。

经过对上述有关*H pylori*感染与胃癌关系专题相关文献的引用情况调查分析, 可得如下2个结论: (1)*H pylori*感染与胃癌关系研究的重要文献多数发表于世界著名的综合性刊物上, 肿瘤学与胃肠病学核心期刊次之。(2)目前关于*H pylori*感染与胃癌关系的研究热点包括5个方面: *H pylori*感染与胃癌流行病学研究, *H pylori*感染与胃癌动物模型的研究, *H pylori*感染的根除与胃癌关系的研究, *H pylori*感染、宿主细胞因子多态性与胃癌易感性研究, *H pylori*致病相关基因的研究。

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