·综述·

腹主动脉瘤流行病学研究进展

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【关键词】 腹主动脉瘤；流行病学

A review on the advancement of epidemiology on abdominal aortic aneurysm *WEI Ying-qi*[1], *ZUO Shang-wei*[2], *HU Yong-hua*[1]. 1 *Department of Epidemiology and Biostatistics School of Public Health, Peking University Health Science Center, Beijing* 100191, China; 2 *Vascular Surgery, Chinese PLA General Hospital*

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腹主动脉瘤为腹主动脉壁发生永久性、局限性扩张，与临近的正常腹主动脉相比直径扩大50%以上或腹主动脉直径>3 cm，是受遗传与环境因素共同影响的复杂性疾病[1]。腹主动脉瘤的进程隐匿，并且一旦破裂具有极高死亡率，严重威胁中老年人的生命健康。随着影像和外科技术的提高，可通过超声检查筛检腹主动脉瘤患者，并及早进行干预和治疗，能够有效预防腹主动脉瘤破裂，降低相关疾病的病死率。

一、临床分类

腹主动脉直接延续于发自左心室的主动脉、胸主动脉之下，位于横隔与髂总动脉分支之间。以肾动脉分支水平为基准，根据腹主动脉瘤生长位置，分为肾上和肾下腹主动脉瘤，其中90%的患者为肾下腹主动脉瘤；呈纺锤状或囊状，极少数位于横隔与肾动脉分叉之间。腹主动脉瘤按照扩张直径大小通常分为两类：管腔直径<55 mm，称为小腹主动脉瘤，约占腹主动脉瘤患者人数的93%；管腔直径≥55 mm，称为大腹主动脉瘤，虽然人数较少，但其破裂率明显升高，在2年内约有45%发生腹主动脉瘤破裂[2-4]。

二、临床特征

1. 隐匿性强，早诊率较低：腹主动脉瘤的发生发展具有隐匿性，仅在破裂前较短时间内或发生破裂后才出现症状[5]。英国经过15年随访的大样本临床随机对照试验（RCT）发现，接受手术治疗的腹主动脉瘤患者中超过50%因瘤体破裂而被诊断[6]；香港大型筛检研究发现，腹主动脉瘤破裂前择期手术施行率仅为8%，而破裂后急诊手术施行率高达56%[7]，提示有较大比例的腹主动脉瘤患者直到破裂才接受治疗。

低诊断率将造成漏诊患者腹主动脉瘤持续扩张，带来极大危害。Vega等[8]随访小腹主动脉瘤患者发现直径<40 mm的腹主动脉瘤年扩张率仅为1.6～2.8 mm/年，破裂风险仅为0.9/100人年；直径为40～50 mm的腹主动脉瘤年扩张率上升至3.0～6.9 mm/年，2年内有2/3的腹主动脉瘤直径超过50 mm；直径>55 mm的腹主动脉瘤破裂风险上升至28/100人年。

2. 致死率高：腹主动脉瘤具有较高病死率，是西方发达国家重要的致死原因。在美国55岁以上男性人群中腹主动脉瘤的死因顺位为第10位，全人群中死因顺位为第13位[9]。2006年统计美国每年约9000人确定死于腹主动脉瘤破裂，据估计每年全人群原因不明的突发性死亡约20万例，其中有4%～5%归因于腹主动脉瘤破裂[10-12]。腹主动脉瘤一旦破裂，病情凶险，只有50%的患者有机会进入医院接受急诊治疗，但是急诊手术后30 d病死率高达30%～70%，综合估计腹主动脉瘤破裂病死率高达80%。在英格兰和威尔士每年65岁以上男性和女性分别有1.36%、0.45%死于腹主动脉瘤破裂[13-15]。2004年在澳大利亚年龄为65～83岁的男性人群中进行RCT研究，干预组给予超声筛查，并对腹主动脉瘤患者进行手术治疗或随访干预，对照组不作任何干预措施，平均随访43个月，接受干预组、对照组年龄标化后与腹主动脉瘤有关的死亡率分别为7.48/10万人年、18.91/10万人年，差异具有统计学意义，死亡主要由腹主动脉瘤破裂和手术造成[4]。

3. 预防与干预：随着影像学和外科学技术的提高，及早筛查、诊断、治疗能够大幅度降低腹主动脉瘤的病死率。由于腹主动脉瘤进程隐匿，大规模筛查能够有效识别潜在的腹主动脉瘤患者，确诊后进行随访观察或择期手术治疗等干预措施。有研究证实择期手术治疗腹主动脉瘤成功率高，术后30 d死亡率仅为2%～6%，远低于破裂后进行急诊手术的死亡率[16]。超声筛查的灵敏度、特异度分别为100%和98%，现已成为国际范围内腹主动脉瘤筛检的常用方法[17]。丹麦、英国、澳大利亚、美国、意大利等发达国家已开展大规模高危人群超声筛查，Cochrane系统综述发现筛检确实降低了65～79岁男性腹主动脉瘤患者的死亡率[18]，并且2005年美国预防服务工作组（USPSTF）推荐年龄在65～75岁有吸烟史的男性均应进行腹主动脉瘤的筛查，并已在2007年1月开始实施[19]。因此流行病学研究对于识别腹主动脉瘤独立危险因素，开展高危人群干预对降低腹主动脉瘤病死率具有重要意义。

三、流行现状

早在1988年Collin等[20]利用超声技术在65～74岁男性人群中筛查腹主动脉瘤，并且初步探讨腹主动脉瘤与吸烟的关联。目前世界范围内已开展多项大型流行病学研究探讨腹主动脉瘤的流行现状，我国香港地区也曾开展大规模的筛检研究，但大陆地区尚缺乏多中心、大样本流行病学研究成果。

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1. 地区分布：腹主动脉瘤的患病率在不同地区存在巨大差异，欧美人群患病率较亚非人群高。2010年丹麦公布筛检研究结果腹主动脉瘤患病率约为4.0%；同年美国310万人大型筛检研究估计腹主动脉瘤患病率约为1.4%；澳大利亚相隔9年的两次大型筛检研究结果分别为4.0%、7.2%，差异较大。亚洲国家中，韩国2009年启动以医院为基础的筛检研究结果腹主动脉瘤患病率仅为0.43%，明显低于白种人群，与日本在2000年开展的筛检项目所得结果相近[21-24]。中国香港全人群筛检结果腹主动脉瘤患病率为0.14%（表1）。表1所显示的各项研究结果存在差异，其原因可能在于选取的筛检对象在性别、年龄、种族、应答率等方面的可比性较低，从而造成研究结果具有一定的差异，但是对比各大洲间的研究结果可发现，亚洲腹主动脉瘤患病率明显低于美洲、欧洲及澳洲。

表1 部分流行病学研究腹主动脉瘤地区分布

第一作者	国家/地区	发表时间（年）	研究类型	样本人数	研究人群	患病率（%）
美洲						
Kent[22]	美国	2010	筛检	3 100 000	<84岁	1.4
Puech-Leao[25]	巴西	2004	筛检	2 756	>50岁	2.3
欧洲						
Grondal[26]	丹麦	2010	筛检	50 000	65～74岁[a]	4.0
Ashton[27]	英国	2002	筛检	27 147	65～74岁[a]	4.9
澳洲						
Scott[23]	澳大利亚	1995	筛检	15 775	65～80岁	4.0
Norman[4]	澳大利亚	2004	筛检	12 203	65～83岁	7.2
亚洲						
Oh[24]	韩国	2010	筛检	6 267	12～98岁	0.43
Adachi[28]	日本	2000	筛检	10 057	>60岁[a]	0.30
Cheng[7]	中国香港	2003	筛检	100 000	全人群	0.14

注：[a] 男性

2. 人群分布：

（1）年龄：随着年龄增长，腹主动脉瘤患病率显著升高，并且破裂将导致更高的死亡率。欧美发达国家腹主动脉瘤患者的平均年龄在70岁左右，<50岁罕见；而腹主动脉瘤破裂在<65岁患者中极为罕见[22]。Forsdahl等[29]在挪威人群中建立队列平均随访7年，发现>75岁人群发生腹主动脉瘤的风险是65～69岁人群风险的8倍；澳大利亚的筛检研究也发现80～83岁男性腹主动脉瘤患病率高达10.8%，远远高于65～69岁人群[4]。在美国的310万人群筛检研究发现，<60岁腹主动脉瘤患者仅占筛检所得患者人数的6.7%，70～79岁年龄段腹主动脉瘤患者最多，占筛检腹主动脉瘤患者的43.62%[13]。

（2）性别：腹主动脉瘤患病率具有明显的性别差异，经多个研究证实腹主动脉瘤在男性人群中发病率高。美国全人群男性腹主动脉瘤患病率从1.3%～8.9%不等，而女性只有1.0%～2.2%，另外女性腹主动脉瘤患者的平均年龄较男性晚10年[30,31]。但是值得注意的是，虽然女性腹主动脉瘤患者数量仅为男性患者的1/5，但是所有腹主动脉瘤破裂患者中有1/3为女性，并且死亡人数与男性相当[32]。

（3）种族：腹主动脉瘤在白种人群中患病率较高。美国1994—2006年的大规模筛检研究发现，土著美国人和白人腹主动脉瘤患病率为8.1%，而西班牙裔和亚洲裔人群患病率则低于3.0%，可见种族是影响其发病的重要因素[33]。Fleming等[3]综述了四项大型RCT研究发现，黑人相对于白人腹主动脉瘤患病风险仅为0.53（95%*CI*：0.40～0.96），另外2010年在肯尼亚进行的一项研究发现黑种人首诊年龄较白人早10～15年[34]。

3. 长期趋势：二十多年来，腹主动脉瘤发病率不断上升，这与各国相继开展大规模流行病学筛检和队列随访研究密不可分。Wainess等[35]研究发现，自1988—2000年美国成年人腹主动脉瘤发病率由54.6/10万人年上升至74.4/10万人年。Acosta等[36]报道，与1986年相比，瑞典男性人群2004年腹主动脉瘤发病率在各年龄组都存在显著上升，60～69岁男性发病率由16/10万人年上升至56/10万人年，而70～79岁男性发病率更上升至117/10万人年。

四、危险因素

腹主动脉瘤是受环境和遗传因素共同作用的复杂性疾病，普遍认为腹主动脉瘤的形成是一个相当复杂的过程，涉及到生物化学、炎性反应、环境、血流动力学等因素共同影响。识别腹主动脉瘤的危险因素对于筛选高危人群进行一级预防具有重要意义。以下将从行为因素、既往病史、遗传因素三方面对腹主动脉瘤危险因素的研究进展进行介绍。

1. 行为因素：

（1）吸烟：吸烟是腹主动脉瘤较为明确的危险因素，与腹主动脉瘤的发生、发展都存在关联。美国一项大型筛检人群组成的回顾性队列研究发现，80.22%的腹主动脉瘤患者有吸烟史，吸烟35年以上患病风险是吸烟10年以下者的8倍[13]。Cornuz和Sidotipinto[37]对2004年以前发表的文章系统综述发现，吸烟能使患腹主动脉瘤的风险上升2.89倍。Forsdahl等[29]在2009年依据7年的前瞻性队列研究得出的结论认为，挪威人群中吸烟者患腹主动脉瘤的风险是非吸烟者的13.7倍。Brady等[38]发现吸烟使腹主动脉瘤加速生长，较非吸烟患者年扩张多达4 mm。

（2）饮酒：饮酒可能是腹主动脉瘤的危险因素，目前尚未获得统一结论。2007年Wong等[39]在近4万名美国男性人群中进行了18年的队列研究，发现平均每天摄入酒精30 g以上患腹主动脉瘤的风险是普通人群的1.65倍，他认为，Tornwall等[40]的研究之所以未发现饮酒是腹主动脉瘤的危险因素，可能是由于饮酒对动脉壁的作用呈现"J"形曲线，而数据分析过程中对酒精摄入的不正确分层，可能模糊了饮酒与腹主动脉瘤的关联，导致阴性结果的出现。

2. 既往病史：动脉粥样硬化（AS）、心血管疾病（CVD）、慢性阻塞性肺疾病（COPD）等病史均与腹主动脉瘤的发生有关联。2004年Cornuz和Sidotipinto[37]的系统综述发现，由严重AS导致的外周血管闭塞性疾病（PVD）患者发生腹主动脉瘤的风险是一般人群的2.5倍；而具有心衰史的人群患腹主

动脉瘤的风险是一般人群的2.5倍。Fleming等[3]研究还发现，腹主动脉瘤患者中COPD的发生率较一般人群高；另有以社区为基础研究认为，腹主动脉瘤与COPD患病有关，COPD人群同患腹主动脉瘤风险较高的原因可能与COPD接受激素等药物治疗有关，而病因通路方面两种疾病并不一定存在因果关联[41]。

3. 遗传因素：

(1)家族史：是一个较为综合的指标，它不仅可以反映共同的生活环境、生活习惯，还可以反映一定的遗传因素。自1977年有文献报道腹主动脉瘤存在家族聚集性，研究者进行了多项家系研究证明腹主动脉瘤存在着明显的遗传倾向。研究发现高达20%的新西兰腹主动脉瘤手术患者家族中至少有一个直系亲属同样患有该病，先证者的一代直系血亲患病风险是一般人群的2～5倍[42-44]。2005年Ogata等[45]分别对腹主动脉瘤患者和其配偶的同胞进行筛查，发现患者的同胞患病风险是其配偶同胞的8倍。2010年瑞典双生子研究发现同卵双生子中若有一人患有腹主动脉瘤，其同胞有24%的患病风险，远高于异卵双生子，遗传度高达70%[46]。根据同胞对和家庭聚集性的研究，发现家族史是腹主动脉瘤的独立危险因素，而且提出该因素是一个重要的、有效的疾病预测因子。

(2)易感基因：随着候选基因策略的完善和全基因组关联研究(GWAS)技术的兴起，有关腹主动脉瘤遗传学因素的探讨深入到基因水平。2004和2005年Shibamura等[47]和van Vlijmen-van Keulen等[48]先后利用GWAS技术分析腹主动脉瘤的家系资料，将其致病基因定位于9q13、4q31。2008年Helgadottir等[49]和Bown等[50]先后应用候选基因策略在大人群中发现了位于染色体9p21与腹主动脉瘤发病有关的2个单核苷酸多态性位点(SNP，ID：rs10757278-G；ID：rs1333049-C)。

目前针对腹主动脉瘤易感基因的研究热点主要集中在动脉壁完整性、炎性反应、免疫反应、氧化应激等通路，既往研究已检测出数个与腹主动脉瘤有关的阳性位点，近3年部分大型流行病学研究结果见表2。其中炎性反应通路对腹主动脉瘤的作用被多个研究证实，涉及到的基因包括肿瘤坏死因子-α(TNF-α)、白介素(IL)、干扰素(INF)、基质金属蛋白酶(MMPs)、转化生长因子-β(TGF-β)、血管紧张素转换酶(ACE)等[53,56-58]。2008年Thompson等[59]对既往候选基因策略研究结果进行系统综述，认为与腹主动脉瘤发生有关的基因位点包括ACE I/D、MMP9-1562 C>T、MTHFR +677C>T。

五、我国腹主动脉瘤流行病学研究进展

我国大陆地区腹主动脉瘤的病因研究刚刚起步，研究主要集中在动物实验、体外实验等基础性研究，以人群为基础的流行病学研究的规模、样本量均较小，多数为以医院为基础的单中心、小样本研究，尚未得到全国性、地区性的流行病学数据。然而，流行病学研究正在逐步发展，多所医院和研究所已经开展相关流行病学研究[60-62]。2011年刘媛等[62]回顾性分析70例>50岁中老年腹主动脉瘤患者，研究认为这些患者若合并周围血管病则其发生CAD的风险较一般人群高。赵海光等[61]在2008年运用基因芯片研究5名腹主动脉瘤患者与正常腹主动脉的基因表达谱，筛选出差异表达基因共1962个，功能分析发现炎症反应、免疫反应及某些化学趋化因子有关的基因在腹主动脉瘤组织中表达上调。虽然我国目前的研究规模尚与西方国家存在较大差距，但是填补了中国大陆地区腹主动脉瘤流行病学研究的空白。

腹主动脉瘤发病率逐渐升高，发病隐匿，一旦破裂死亡率高，严重危害中老年男性的生命健康。由于腹主动脉瘤可通过择期手术降低死亡危险，因此对其实行一级和二级预防具有重大意义。该病受人口学因素、行为因素、既往病史、遗传等多种因素共同影响，探究其独立危险因素、识别高危人群、提高早诊率，为降低对老年人群的危害有重要意义。

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表2　腹主动脉瘤相关基因部分阳性位点

第一作者	发表年份	国家	样本量(病例组/对照组)	阳性基因	阳性位点	效应指标 *OR*值(95%*CI*)
Smallwood[51]	2008	澳大利亚	677/656	IL-6	rs1800796	6.00(1.22～29.41)
Jones[52]	2008	新西兰、英国、澳大利亚	1 226/1 723	AGTR1	rs5168	1.60(1.32～1.93)
				ACE I/D	rs4646994	1.33(1.06～1.67)
Helgadottir[49]	2008	冰岛、新西兰等7国	2 836/14 259	CDKN2A	rs10757278	1.31(1.22～1.42)
Korcz[53]*	2009	波兰	133/304	ACE I/D	rs4646994	3.08(1.22～7.79)
Thompson[54]	2009	英国、澳大利亚	741/1 366	CDKN2A	rs10757278	1.38(1.04～1.82)
Gretarsdottir[55]	2010	荷兰、冰岛	1 292/32 503	DAB2IP	rs7025486	1.21(1.11～1.32)
Baas[56]	2010	荷兰	736/1 024	TGFBR1	rs1626340	1.32(1.11～1.56)
				TGFBR2	rs1036095	1.32(1.12～1.54)
					rs4522809	1.28(1.12～1.46)

注：*该研究表型为患有腹主动脉瘤的高血压患者，其他研究的表型均为腹主动脉直径≥3 cm的腹主动脉瘤患者

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