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·文献综述·

腹主动脉瘤腔内治疗的合理化手术阈值探讨

张昊，陆清声

（中国人民解放军海军军医大学附属长海医院 血管外科，上海 200433）

摘　要　腹主动脉瘤（AAA）是血管外科的常见疾病，一旦发生破裂，病死率极高，对患者生命构成严重威胁。其主要治疗方式包括腹主动脉瘤腔内修复术（EVAR）和开放修复术（OR）。随着手术器械和技术的不断进步，EVAR 已逐渐成为首选治疗方法。然而，EVAR 与 OR 在手术原理及并发症方面存在显著差异，目前 EVAR 仍沿用为 OR 制定的手术指征，但这在一定程度上限制了 EVAR 的优势发挥。随着越来越多的临床研究证据表明，将 AAA 破裂风险和手术风险进行赋分量化后再比较，显然有助于更合理地制定个体化治疗方案。

关键词　主动脉瘤，腹；动脉瘤，破裂；血管内操作；手术指征；综述
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Discussion on the rationalization of surgical thresholds for endovascular treatment of abdominal aortic aneurysm

ZHANG Hao, LU Qingsheng

(Department of Vascular Surgery, Changhai Hospital, Naval Medical University, Shanghai 200433, China)

Abstract　Abdominal aortic aneurysm (AAA) is a prevalent condition encountered in vascular surgery, characterized by a high mortality rate upon rupture, posing a serious threat to patients' lives. The primary treatment options include endovascular aneurysm repair (EVAR) and conventional open repair (OR). With advancements in surgical instruments and techniques, EVAR has gradually become the preferred method. However, EVAR and OR differ significantly in surgical principles and associated complications. EVAR continues to follow surgical indications originally developed for OR, limiting its full realization of its advantages. As clinical evidence continues accumulating, it has become increasingly clear that quantifying and comparing AAA rupture risk and surgical risk through scoring systems significantly aids in developing more rational and individualized treatment strategies.

Key words　Aortic Aneurysm, Abdominal; Aneurysm, Ruptured; Endovascular Procedures; Surgical Indications; Review
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作者简介：张昊，中国人民解放军海军军医大学附属长海医院硕士研究生，主要从事腹主动脉瘤腔内治疗相关方面的研究。
通信作者：陆清声，Email: luqs@newvascular.cn

支架移植物最早是在1987年由苏联外科医生Nicholas Volodos发明[1]，直到1991年Parodi等[2]报道了真正应用于临床的腹主动脉瘤腔内修复术（endovascular abdominal aortic repair，EVAR）才逐渐被世界所熟知。早先受限于技术水平及器具，EVAR适用范围有限。目前，随着腔内治疗技术及器具的发展，EVAR已取得明显进步，EVAR适用范围也逐渐放宽[3-4]。EVAR较开放手术（open repair，OR）具有手术创伤小、恢复快等围术期优势[5-6]。目前，国内EVAR成功率高达99.8%[7]。现EVAR仍基本沿用OR手术指征，腹主动脉瘤（abdominal aortic aneurysm，AAA）直径仍被公认为是决定手术的首要因素[8]。AAA最大风险是破裂，破裂性AAA病死率高达90%[7]，其围手术期病死率高于30%[9]，故预测其破裂风险，提前手术治疗高危AAA，防止破裂势在必行。本文主要就目前手术指征、影响AAA转归的因素及手术指征的局限等方面进行阐述。

1 现行手术指征

1.1 发展历史

在Parodi等[2]报道EVAR之前，人工移植物置换术（prosthetic graft replacement）是AAA首选的治疗方式，但合并严重并发症的老年患者手术死亡发生率超过了60%。自1991年EVAR出现后，其已逐渐成为一种新的选择，尤其适用于合并严重并发症的老年患者，弥补了OR高危患者死亡发生率高的不足。但EVAR的适用条件较高、远期并发症较多，且未显著降低手术风险，因此EVAR仍沿用OR手术指征，并建议注重个体化，而不是制定统一的修复阈值[10-12]。

基于20世纪90年代的荷兰ADAM研究、英国UKSAT研究两项大型随机对照研究，证实早期手术并未获益，AAA直径>55 mm时进行手术干预是合理的，同时发现女性在较小直径容易破裂，女性的修复阈值改为50 mm，但EVAR仍沿用OR手术指征[13]。

近10年，更多的大型队列研究证实，EVAR的中远期生存率与OR无明显差异，但再干预率升高，因此，现指南[14]仍推荐EVAR沿用OR手术指征，此时期手术阈值无变化。

1.2 制定依据

手术指征是在患者的总体预期寿命范围内，基于AAA破裂的风险与手术的风险制定的[15]。现手术指征的争议点主要在手术阈值，包括：保守治疗无法阻止AAA进展[16]；随着AAA增大，部分患者失去EVAR机会[17]；小腹主动脉瘤（small abdominal aortic aneurysm，sAAA）行EVAR手术效果及安全性更高等方面[18]，因此有研究者提出，降低手术阈值，发病早期尽早治疗。

1.3 目前手术指征

目前国内专家共识[8]推荐：(1) 男性AAA直径>5.0 cm，女性>4.5 cm。(2) 瘤体直径增长>10 mm/年。(3) 出现因动脉瘤引起的疼痛，不能除外破裂可能者。(4) 因瘤腔血栓脱落引起栓塞者。与国内指南[8]相比，国外最新指南[14]区别主要在于手术直径阈值，目前国外推荐男性>55 mm、女性>50 mm作为手术修复阈值。

2 影响AAA转归的因素

2.1 瘤体、瘤颈、流出道解剖条件

2.1.1 瘤体解剖条件 (1) 瘤体直径直接影响AAA的转归。研究[19]表明，瘤体直径<5 cm年破裂率在1%以下，瘤体直径5~5.9 cm年破裂率约为3%~15%。瘤体直径6~6.9 cm年破裂率约为10%~20%，瘤体直径>7 cm年破裂率达25%以上。尽管sAAA破裂率较低，但是由于主动脉解剖结构更加适配，sAAA的EVAR的手术难度更低、支架置入数量更少、费用及术后内漏等并发症发生率更低，并且直径每增加1 cm，EVAR的解剖学适用性降低5倍，当AAA直径的增加达到5.5 cm时，解剖结构可能不再适用于EVAR，从而不得不选择风险较大的OR[20-21]。同时，瘤体直径影响EVAR术后的安全性，直径越大，患者术后远期病死率、并发症发生率及再干预率越高[22]。(2) 瘤体附壁血栓（intraluminal thrombus，ILT）影响AAA管壁强度。高达80%的AAA瘤腔存在ILT[23]。Haller等[24]研究提示，高ILT负荷可能是主动脉壁强度降低的替代标志物，也是高风险sAAA的特征。Ma等[25]建议sAAA的ILT负荷的快速增加应作为早期手术修复的新金标准。研究表明，ILT与动脉壁缺氧、细胞炎症和细胞外基质凋亡相关，并可促进动脉瘤生长并最终导致动脉瘤破裂[26]，同时可能导致AAA

管壁缺氧、炎症增加和管壁弱化，这可能与sAAA破裂相关，因此被认为是评估AAA管壁强度的参数之一[27]。ILT影响EVAR术后转归，单中心研究[28]表明，EVAR后更高的ILT与死亡、内漏、动脉瘤破裂、移植物移位和再干预等严重不良事件独立相关。另外有一项前瞻性研究[29]发现，ILT可降低EVAR术后Ⅱ型内漏的发生率，ILT的厚度、覆盖率与Ⅱ型内漏呈负相关。Whaley等[30]研究进一步揭示了不同ILT类型对EVAR术后转归影响，瘤壁后外侧和环周ILT相比其他位置，术后内漏发生率较低。因此，ILT是评估AAA管壁强度的可靠目标，但对EVAR术后的转归仍存争议，需进一步研究。(3) 瘤壁钙化率。Buijs等[31]表明，有先兆破裂或破裂AAA患者的钙化程度有增加的趋势。O'Leary等[32]通过对行OR的患者中采集AAA壁前部区域的组织进行研究，进一步表明钙化是AAA破裂风险的关键因素。然而，另有一项研究[33]表明，血管钙化稳定主动脉瘤壁，从而防止AAA的进行性扩张，起到一定保护作用。此外，瘤体钙化率越高，瘤囊皱缩越小，这可能与钙化增加瘤壁内张力有关，但还需进一步证实[34-35]。因此，瘤壁钙化率增加可能与AAA破裂相关，应列为破裂风险因素，但其机制有待进一步研究。

2.1.2 瘤颈解剖条件　瘤颈是支架移植物近端的锚定部位，主要影响EVAR术后转归。经典EVAR要求近端瘤颈长度>15 mm，虽然随着支架的进步，对瘤颈要求条件较前降低，但瘤颈条件越差，发生内漏、移植物异位、肾动脉闭塞等并发症发生的概率就越高[4,36-37]。不良瘤颈（hostile neck）目前被定义为近端瘤颈长度<10 mm或近端瘤颈角度<60°[38]。Hovsepian等[39]提示短瘤颈是导致严重并发症的显著风险因素。此外，瘤颈角度也会对AAA进展、破裂产生影响，瘤颈角度过小可能会导致AAA腔内出现大的不规则涡流，且同时会导致近端颈部附近强烈的壁弯曲，从而加重血流模式和升高的壁应力[40]。研究[41]提示，不良瘤颈虽然可能不影响EVAR后瘤腔皱缩，但术后即使囊腔皱缩，也会增加破裂和Ia型内漏等不良事件。此外，在CAESAR研究[17]中，随着AAA进展约1/6患者丧失行EVAR机会，大部分是因不良瘤颈导致。因此，瘤颈的解剖条件对EVAR影响尤为严重。

2.1.3 流出道解剖条件　髂、股动脉作为AAA的远端流出道，是EVAR手术入路，同时是支架远端锚定部位，影响AAA进程及术后转归。Crawford等[42]表明，AAA合并远端流出道闭塞往往在较小直径就发生破裂，可能与增加峰值壁应力有关。不良髂动脉解剖条件定义为至少存在以下特征之一：严重髂动脉呈角（超过90°）；广泛髂动脉壁钙化（>50%）；髂动脉狭窄或梗阻；髂外动脉直径<7 mm；既往髂股动脉手术史。一项前瞻性研究[43]表明，虽然不良的流出道解剖条件对EVAR的早期预后无显著影响，但其在手术技术上要求更高，晚期病死率增加。同时髂动脉迂曲、狭窄或闭塞会限制EVAR手术器具的输送，有研究表明，高达15%的患者由于过度的解剖扭曲而不适合进行EVAR，髂动脉狭窄或闭塞在AAA患者中非常普遍，高达30%的主动脉瘤患者存在相关的髂动脉狭窄[44]。

2.2 患者合并的危险因素

2.2.1 性别　尽管女性AAA患病率低，但AAA生长速度更快，破裂风险高3倍，倾向于在较小直径破裂[45]，以及破裂和择期修复的死亡发生率更高[46]。Skibba等[47]发现，女性患者中1/3的破裂发生在动脉瘤直径<5.5 cm的情况下。Lo等[48]发现了更适合预测女性患者的动脉瘤破裂风险的指标，即主动脉尺寸指数。同时，女性患者EVAR术后预后较差，这可能与年龄更大、AAA解剖条件差有关[49-50]。

2.2.2 吸烟史　吸烟人群AAA患病率高，与从不吸烟者相比，当前和既往吸烟者的患病风险分别增加5倍和2倍，吸烟数量和吸烟年数同样增加患病率[51]。同时，AAA吸烟患者破裂率更高，英国一项研究[52]证实吸烟与较差的生存率和较高的AAA破裂率相关。

2.2.3 家族史　van de Luijtgaarden等[53]对568例AAA患者的家属进行了调查，发现22.5%的患者家属均存在AAA，女性AAA患者亲属罹患AAA风险增加5.5倍，男性则增加2倍。同时，日本一项回顾性研究[54]表明，有家族史的患者AAA进展速度（4.2 mm/年）显著高于其他患者（2.0 mm/年）。

2.2.4 高血压　现已证实，高血压与AAA风险直接相关，高血压使AAA的风险增加66%，舒张压比收缩压的相关性更强[55]。早在1992年Anidjar等[56]通过动物实验证实AAA直径与血压水平呈正相关，肾血管性高血压破裂风险较大。Gadowski等[57]通过动物实验同样证实高血压增加AAA的生长速度。一项回顾性研究[58]表明高血压患者AAA的增

长率（2.3 mm/年）显著高于其他患者（1.7 mm/年）。

2.2.5 慢性阻塞性肺疾病（chronic obstructive pulmonary disease，COPD） COPD增加AAA患病率[59]，COPD与AAA破裂呈正相关[60]。同时合并COPD的AAA患者，住院病死率、肺部并发症和主要术后不良事件显著增加，5年生存率同样显著降低[61]。

2.2.6 高同型半胱氨酸血症（hyperhomocysteinaemia，HHcy） Liu等[62]通过对照试验研究证实，HHcy人群AAA的风险是正常人的2.84倍，同型半胱氨酸每增加1 μmol/L，AAA风险增加2%。Halazun等[63]同样证明了同型半胱氨酸水平与AAA生长率之间的正相关性，机制可能是通过增加基质金属蛋白酶2和基质金属蛋白酶9的结合和活化，导致AAA管壁细胞膜中弹性蛋白/纤维性胶原进一步降解。

3 EVAR手术指征局限性及制定依据的探讨

3.1 目前手术指征局限性

EVAR现已成为AAA的主要手术方式，与OR相比，EVAR具有围手术期死亡发生率低、住院周期短、恢复快等优势，同时有独特的并发症，如内漏、支架移位、支架断裂、动脉瘤破裂、支架闭塞等[22,64]。一项大型回顾性研究[65]表明，EVAR术后1年生存率更高，7年后再干预发生率却高于OR组，长期生存同样也无明显优势。因此，EVAR术后短期内优势明显，长期无优势，并且其手术原理、并发症与OR不同，现行手术指征并未体现出其优势及特点。

目前反对修改手术指征、降低手术阈值主要观点在于EVAR远期再干预率和成本费用问题[66]。一项Meta分析[67]得出，随着手术器具及技术的进步，再干预率逐渐降低。一项回顾性研究[35]发现了预测再干预的五个风险因素：手术时间≥3.0 h、动脉瘤直径≥6.0 cm、髂动脉瘤≥2.0 cm、急诊手术和既往主动脉手术史。并且再次干预并不影响EVAR患者的长期生存[68]。

综上，现行EVAR手术指征主要来源于OR，并不完全适用于EVAR，也未体现出其优势、特点。笔者认为应根据EVAR特点制定不同于OR的手术指征，并且可以通过避免再干预的危险因素、发展手术器械及技术水平，进一步降低再次干预风险。

3.2 如何制定新标准及所需临床证据

AAA手术指征的制定主要依照AAA破裂的风险、手术风险，尽管AAA最大直径目前仍然被认为评估破裂风险的金标准，但是，有些AAA破裂时体积却小于手术阈值[69]。过去研究者们致力于寻找能准确预测AAA破裂风险的指标，管壁应力（wall stress）被多项研究证实在预测观察患者破裂风险方面优于AAA直径，但其在临床上难以测量，限制了其实用性[70-71]。近些年Creisher等[72]使用瘤体最大直径、ILT、降压药物种类<2种、未使用降胆固醇药物和主动吸烟综合计算破裂风险，较好地预测了破裂风险。同时研究者们开发出风险评估模型进行评估EVAR的围手术期风险。Grant等[73]评估了Medicare、VGNW和BAR三种风险模型，并证明了这三种风险评分模型能较好地预测EVAR术后的病死率。Steffen等[74]分析了10 404例患者的数据，分别总结了EVAR和OR两种手术围手术期死亡风险因素，从而得出一个可靠的风险评分模型DIGG风险评分，有效预测了术后死亡发生率。综上，笔者认为AAA手术指征的制定应结合AAA破裂风险因素和EVAR的手术风险因素，并结合患者的预期寿命，针对不同患者得出个体化、合理的治疗方案。

4 小结与展望

随着对AAA更深入研究，AAA直径作为个体患者的破裂风险标准可能不可靠，破裂风险显然取决于多种因素的复杂组合。随着EVAR手术器具及手术水平的发展，手术并发症明显降低，如果仍沿用OR手术指征，则存在有些患者达到手术指征却失去EVAR解剖条件，或还未达到手术指征，却发生破裂付出生命代价的可能。笔者认为，EVAR有其独特的优势，应根据患者破裂风险因素及手术风险因素，来决定是否手术治疗。未来研究可以将破裂风险因素和手术风险因素分别赋值加以权重，得出更方便临床应用的评分量表工具，指导临床工作，从而达到更加精准化、个体化治疗的目的，确保患者的利益最大化。

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作者贡献声明：张昊，陆清声负责论文构思；张昊负责文献收集与初稿撰写；陆清声负责论文审阅与修订。

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