

·述评·

# 侵犯动脉的胰腺癌外科治疗新选择:动脉鞘剥除技术

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**【摘要】**根治性切除是改善胰腺癌患者预后的关键,合并动脉侵犯是局部进展期胰腺癌不可切除的主要原因。对于累及动脉的胰腺癌进行更精准的可切除性评估,选择适宜的外科技术,有赖于对肿瘤侵犯动脉解剖学、组织学以及肿瘤生物学的进一步深入理解。传统基于累及动脉周径的肿瘤影像学评估不等于真实意义上的病理学侵犯。在可切除性评估中,动脉被侵犯的深度比受累及的周径更重要。对动脉结构的形态学观察发现:动脉外弹力层是否受侵犯决定动脉鞘剥除的可行性与联合动脉切除的必要性。动脉鞘剥除技术为合并动脉侵犯的胰腺癌患者提供根治性切除机会,同时可避免动脉切除重建的高死亡率与并发症发生率。对肿瘤侵犯深度和生物学行为更精准地评估将为侵犯动脉局部进展期胰腺癌的外科决策提供更可靠的依据。

**【关键词】**胰腺肿瘤; 局部进展期; 可切除性评估; 动脉鞘剥除技术; 联合动脉切除

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## A novel surgical option for artery-involving pancreatic cancer: sub-adventitial divestment technique

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**【Abstract】** Radical resection remains as the key treatment to improve the prognosis of pancreatic cancer, and arterial invasion hinders radical resection for locally advanced lesions. More accurate assessment of resectability and selection of appropriate surgical techniques depend on better understanding of the anatomy, histology, and tumor biology of pancreatic cancer invasion to the artery. Traditional radiology assessment for artery involvement, based on the circumference of involved arteries, is not equivalent to pathological artery invasion. The depth of arterial invasion is more important than the circumference in evaluating resectability. Results of morphological observation on arterial structure shows that both the feasibility of sub-adventitial divestment technique (SDT) and the necessity of arterial resection depend on whether the external elastic lamina of artery is invaded. The SDT can provide an opportunity for radical resection for pancreatic cancer with arterial invasion, while avoiding the high mortality and incidence of complications caused by arterial resection. A more precise assessment of tumor invasion depth and biological behavior will provide a more reliable basis for surgical decision for the treatment of locally advanced pancreatic cancer with

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arterial invasion.

**【Key words】** Pancreatic neoplasms; Locally advanced; Resectability evaluation; Sub-adventitial divestment; Combined artery resection

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胰腺癌是预后最差的恶性肿瘤之一,5 年总生存率仅为 10%,而根治性手术仍是胰腺癌患者改善预后的关键和获得长期生存的必要条件<sup>[1]</sup>。然而>50%的胰腺癌患者确诊时已发生远处转移,失去根治性手术机会,仅有 10%~20%的患者初诊时肿瘤局限于胰腺内,目前,根治性手术联合辅助化疗可为 30%~50%的患者提供>5 年的生存时间<sup>[2-5]</sup>。有>30%的胰腺癌患者初诊时虽然未发生肿瘤远处转移,但由于肿瘤局部进展、累及胰腺周围重要血管而无法行根治术,其中累及胰腺周围动脉是导致肿瘤在技术上无法切除的最重要原因<sup>[6-7]</sup>。长久以来,联合动脉切除是累及动脉胰腺癌(artery-involving pancreatic cancer, ai-PC)最主要的手术方式,但由于手术难度大、围手术期风险高,该手术方式一直仅推荐由高手术量胰腺外科中心在高度选择性的患者中施行<sup>[8-10]</sup>。2016 年,基于长期外科实践和既往文献报道,笔者团队率先在国际上提出“动脉外膜下剥除技术”治疗累及动脉的局部进展期胰腺癌,并逐渐获得国内外同道认可,成为胰腺外科医师治疗 ai-PC 的一种新选择<sup>[11-13]</sup>。

一、ai-PC 的可切除性评估:肿瘤侵犯动脉的深度比周径更重要

肿瘤的可切除性评估分为技术性和生物学性两个维度。技术性不可切除见于病变本身导致的手术技术障碍,主要为肿瘤侵犯动脉,其他还包括手术条件、术者能力及意愿、患者的手术耐受性以及社会因素。生物学性不可切除见于手术本身不能给患者带来生存获益,包括肿瘤生物学行为不佳、发生远处转移或肿瘤残留,而无论是否存在切除的技术性障碍<sup>[14]</sup>。因此,精准客观地评估肿瘤的可切除性至关重要,错误判断将导致患者失去根治性手术机会或接受不能获益的无效手术,也会误导研究者对新辅助治疗等伴随性治疗效果的客观评价<sup>[14]</sup>。

追溯 ai-PC 可切除性评估体系的发展历程,笔者发现早在 1997 年,美国加州大学医学院 Lu 等<sup>[15]</sup>报

道采用患者增强 CT 检查横断面图像中肿瘤累及血管周径>180°作为预测手术可切除性的诊断阈值,灵敏度和特异度分别为 84%和 98%。此后,基于动脉受累周径的影像学评估体系被美国得克萨斯大学安德森癌症中心、美国肝胆胰协会、美国国立综合癌症网络等学术机构和组织所接受并在临床上沿用至今<sup>[16-19]</sup>。

但是以 ai-PC 累及动脉周径评估其可切除性只是从影像学角度观察得到的一种评估标准,并不一定与事实上的外科切除结果或是病理学侵犯一致。2013 年,美国哈佛大学麻省总医院 Fong 等<sup>[20]</sup>的研究结果显示:按上述影像学标准评估为胰腺周围血管受侵犯的患者中,97%的患者可以在不联合血管切除的情况下完成肿瘤根治性切除,与此同时,患者胰腺钩突切缘阳性率与影像学评估为没有胰腺周围血管侵犯的患者比较并无显著升高,因此,该研究认为增强 CT 检查评估的血管侵犯并不能排除根治性手术的可能。此外,2011 年,法国斯特拉斯堡大学医院的 Bachellier 等<sup>[21]</sup>报道因动脉血管受累及而行联合血管切除的胰腺癌患者中,仅有 15.4%的患者被切除动脉存在肿瘤的病理学侵犯,作为参照,高达 70.7%的被切除静脉存在肿瘤的病理学侵犯。2012 年, Watanabe 等<sup>[22]</sup>进一步的研究结果显示:即使胰腺癌侵犯动脉,90.9%的患者侵犯深度仅局限于动脉外膜,只有极少数患者肿瘤侵犯至动脉外弹力层<sup>[22]</sup>。

动脉外弹力层位于外膜下,包裹血管平滑肌层,是腹腔干、肠系膜上动脉等胰腺周围肌性动脉维持物理强度和弹性的组织结构<sup>[23]</sup>。见图 1。笔者在临床实践中发现:在动脉外膜与外弹力层之间存在一个相对疏松的间隙,是良好的外科分离界面;多数 ai-PC 患者从外表看似动脉被肿瘤包绕如铜墙铁壁,但是一旦进入上述分离界面,沿着外弹力层表面可以将被侵犯的动脉外膜剥除。这一分离界面的存在可能基于两种原因:(1)动脉搏动的机械作用。(2)外弹力层富含弹力纤维等致密胶原

的组织学特征。类似于被称作“神圣平面”,位于骶前筋膜和直肠系膜间的Toldt's间隙,在外弹力层表面实施肿瘤与动脉的钝性和(或)锐性分离通常比较顺利,途经的滋养血管可以利用热电外科设备进行安全凝切,而动脉分支也可经由结扎等外科技术安全离断<sup>[11]</sup>。此时,决定ai-PC技术可切除性更本质的因素方才显现,即胰腺癌侵犯动脉的深度是否超过外弹力层。如果外弹力层没有被侵犯,即使是360°包绕动脉的肿瘤,亦可能经由在外弹力层表面的外科解剖与动脉成功分离;但如果外弹力层受侵犯,完整的肿瘤切除将导致外弹力层连续性丧失,从而出现术中即时或术后迟发的假性动脉瘤;而姑息性解剖亦将导致肿瘤的肉眼残留而无法达到根治性手术要求<sup>[11,24-25]</sup>。因此,笔者认为:在ai-PC的技术性可切除评估中,影像学检查累及不等于病理学侵犯,肿瘤侵犯深度比肿瘤包绕周径更重要。

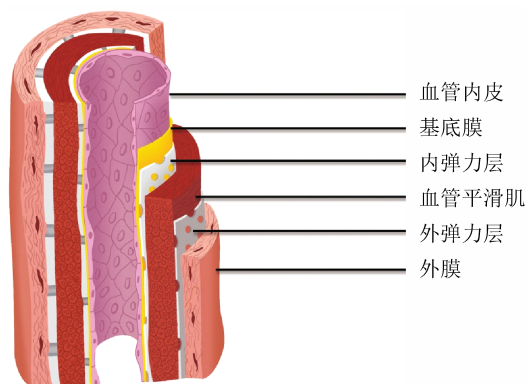


图1 动脉血管壁结构示意图

Figure 1 Schematic diagram of arterial wall

## 二、ai-PC根治性切除的新选择:动脉鞘剥除技术

联合动脉切除重建的胰腺切除术已经逐渐成为一种治疗ai-PC的前沿时尚<sup>[26-27]</sup>。而更加激进的胰腺切除手术如胰腺切除联合自体小肠移植等多脏器、多血管切除重建也有部分病例报道<sup>[28-29]</sup>。近年来较大样本量的队列研究中,联合动脉切除重建的胰腺切除手术仍有高达5.0%~18.5%的围手术期病死率<sup>[10,30-31]</sup>。有研究团队报道:即使度过学习曲线波动期,联合动脉切除重建患者术后90 d的病死率仍仅从29%下降至9%<sup>[10]</sup>。一项国际多中心回顾性队列分析结果显示:对于仅需行动脉切除而不要重建的联合腹腔干切除远端胰腺切除术,在胰腺外科手术量不足的医院开展甚至有高达18%的病死率<sup>[30]</sup>。德国海德堡大学医院2021年发表的纳入3 953例胰十二指肠切除术全世界最大单中心回顾

性队列研究结果显示:与标准胰十二指肠切除术比较,联合动脉切除术后患者总体并发症发生率和病死率都显著升高(并发症发生率:59.0%比41.7%,术后90 d病死率:10.3%比2.9%)<sup>[32]</sup>。如果将标准胰腺癌根治术3%的术后90 d病死率认定为可接受的术后安全性指标,现有报道中的联合动脉切除会使术后死亡风险上升3倍余(约9%),而只有在这样激进的外科操作可使生存获益提高3倍以上的前提下,死亡风险增加才应被认为是合理的,到目前为止,这样显著的治疗效果尚未在任何临床研究中被证实,因此,美国国立综合癌症网络指南也未推荐常规开展联合动脉切除重建的胰腺手术<sup>[33]</sup>。

笔者团队的研究结果显示:联合动脉鞘剥除胰腺癌根治术的术后90 d病死率与标准胰腺癌根治术比较,差异无统计学意义<sup>[11]</sup>。Loos等<sup>[34]</sup>的研究比较195例联合动脉切除与190例动脉鞘剥除的胰腺癌根治术,结果显示:与接受动脉鞘剥除术的患者比较,接受动脉切除术患者的术中出血量显著增加(中位数1 300 mL比900 mL),手术时间显著延长(中位数420 min比366 min),而住院期间死亡风险显著升高;虽未达到统计学显著性,但动脉鞘剥除术似乎较动脉切除可带来更高的R<sub>0</sub>切除率(32.3%比23.8%, $P=0.143$ )以及更好的长期生存获益(中位生存时间21.5个月比17.7个月, $P=0.099$ )。

## 三、动脉鞘剥除技术在ai-PC中的应用前景

目前,国内外相关指南推荐对ai-PC实施新辅助治疗策略<sup>[19,35-36]</sup>。但值得注意的是,术前影像学判断与术中解剖判断的准确性不完全一致。很多患者影像学判断为不可切除,但在之后的手术实际解剖中证实为可切除,这两种评估手段之间的误差通常被误判为伴随治疗措施的效果。如部分新辅助治疗患者,初诊时可能是解剖评估可切除,但被影像学评估为不可切除,转而行新辅助治疗后再手术切除。事实上这类患者一开始可以手术切除,只是没有进入外科程序,新辅助治疗只是一个伴随现象,本质上不具有因果关系。

在更有效的抗胰腺癌药物诞生之前,ai-PC诊断与治疗的发展可能集中于对胰腺癌肿瘤生物学行为预测以及胰腺癌侵犯动脉深度的形态学评估两方面。ai-PC对动脉的累及,不同于神经侵犯、多发的淋巴结转移、分化程度低等不良预后因素,更可能是由于肿瘤本身原发部位毗邻腹腔干、肠系膜上动脉等腹部主要动脉所形成一类显著提高根治



性切除技术难度的胰腺癌亚群<sup>[37-38]</sup>。但这种原发部位的特殊性并不意味着肿瘤生物学行为不佳,患者仍有可能从根治性切除中生存获益。基于各种基因测序手段、类器官模型等当代分子生物学方法和肿瘤生物学模型的肿瘤恶性行为预测,将会为是否行动脉鞘剥除或联合动脉切除等积极的外科治疗手段提供极为重要的参考<sup>[39-42]</sup>。此外,动脉外弹力层的评估在 ai-PC 的外科决策中至关重要。笔者团队未发表的研究数据显示:以动脉外弹力层为基准的胰腺癌动脉侵犯深度病理学分级,可为动脉鞘剥除技术是否可行提供有效参考。包括 CT、MRI、EUS 检查乃至介入放射在内的术前评估手段发展以及影像学-组织学对照研究的开展,有望为临床医师提供动脉壁、肿瘤浸润边界以及动脉-肿瘤交界面的亚解剖甚至组织学图景,为 ai-PC 根治性手术中对动脉鞘剥除还是联合动脉切除的选择提供决策依据<sup>[43-46]</sup>。

#### 四、结语

在形态学观察胰腺癌侵犯动脉的基础上,笔者提出动脉鞘剥除这一新技术,可为部分 ai-PC 患者提供肿瘤根治性切除机会,避免了动脉切除带来的风险。但目前,研究者对胰腺癌分子生物学和细胞生物学层面的认知仍处在相对蒙昧的阶段。全世界每天都有>1 000 例新发胰腺癌患者向临床医师寻求治疗上的帮助。无论是动脉鞘剥除还是联合动脉切除,无论是先行手术还是新辅助治疗,可能都只是最终战胜胰腺癌前为数不多、可供选择的权宜之计而并非终极方案。但无法否认的是,外科医师永远是 ai-PC 能否得到切除的最终评价者和实施者。这要求外科医师在熟练掌握动脉鞘剥除、动脉切除重建等外科技艺之外,应具有更宽阔的临床医学视野,更深刻的肿瘤生物学素养,以便更好地获取、评估和产生循证医学证据,对 ai-PC 患者进行更科学的治疗决策和手术选择,最终使患者生存获益。

**利益冲突** 所有作者均声明不存在利益冲突

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