

老年活体供肾风险及移植肾疗效综述

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摘要: 老年活体供肾移植是治疗尿毒症的方法之一, 但肾功能随供者年龄增长而下降, 因此老年活体供肾者及受者术后并发症风险高, 疗效仍有争议。本文对老年活体供肾移植的相关研究进行综述。

关键词: 老年供者; 肾移植; 活体供者

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Risks and outcomes of kidney transplantation from older living donors

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Abstract: Kidney transplantation from older living donor is an important option to treat uremia. But living kidney donation from older donor remains controversial due to higher incidence of comorbidity and greater risk of postoperative complications in both donors and recipients because of decreasing renal function with aging. The outcome of kidney transplantation from older living donor is reviewed in this article.

Keywords: senile donor; kidney transplantation; living donor

肾移植作为终末期肾病的治疗方法可有效提高患者的生活质量和生存率^[1]。但肾源短缺限制了肾移植的发展和运用。活体供肾肾移植的开展有助于缓解肾源短缺, 其应用比例逐年上升^[2]。活体供肾组织相容性高、缺血时间短, 避免了供者脑死亡带来的肾损伤, 有排斥率低、器官存活时间长等优点^[3-5]; 而且受者透析时间短, 术前有充分的治疗时间, 纠正水电解质紊乱, 改善贫血等全身状况^[6]; 因此活体供肾效果优于尸体供肾^[7]。我国活体供者为受者亲属, 以父母为主^[8-9]。但父母作为供者, 年龄对供受者预后均是重要的影响因素。老年活体供肾切取手术期及远期并发症风险较高^[10]; 而受者出现移植肾功能延迟恢复(delayed graft function, DGF)、急性排斥反应(acute rejection, AR)等并发症风险也较高^[11-12]。因此老年活体供肾的疗效仍有争议。本文就老年活体供肾移植的疗效进行综述。

1 老年供者的选择

肾功能随年龄增长而逐渐下降, 30岁以上的健康个体每年GFR下降大概1 ml/min^[13], 这同老年人肾小球硬化、功能肾单位减少及肾间质纤维化等微观结构改变有关^[14]; 肾动脉硬化及心脏输出量的降低减少了肾血流量, 也促进肾衰老^[15-16]。除GFR下降外, 肾小管重吸收及转运功能均同年龄呈负相关^[17]。老年人易并发糖尿病、高血压、血脂

异常等多种以肾为靶器官的全身疾病, 加速肾功能衰退^[18]。另外, 肾的免疫原性随年龄而增强, 可吸引更多的炎细胞聚集^[19-21], 老年器官移植早期免疫反应更强烈^[22], 导致了老年肾抗损伤能力差, 修复损伤能力弱, 肾储备能力减少^[23]。

目前国内外指南未规定活体供者的年龄上限^[24-26], 单纯的高龄并非肾捐献的绝对禁忌^[25, 27]。但应对>65岁的供者充分告知相关风险, 完善包括肾功能、糖尿病、心血管系统等术前的评估^[24]。尽管年龄并非影响移植肾预后的独立危险因素, 但与年龄相关的长期高血压及GFR降低却对移植肾预后显著影响^[28]。因此对老年供者的筛选应更关注其肾功能及合并症情况而非供者年龄^[29]。

目前多以GFR的测定评估肾功能。我国肾移植指南推荐活体供者GFR>80 ml/(min·1.73 m²)^[24]。虽然供者GFR对移植肾功能有重要影响^[30-32], 但只要符合供肾要求, 较低的术前GFR并不会对受者中远期肾功能有不利影响^[33]。评估供者肾功能需考虑到年龄对GFR的影响, 老年供者的低代谢水平会影响我们对老年肾代偿能力的计算^[34]。英国移植协会依据供者年龄分别制定了GFR的要求标准, 例如对于80岁的供者, GFR仅需>50 ml/(min·1.73 m²)即可^[25]。因此, 术前肾功能评估应以GFR为主, 综合血肌酐、肌酐清除率、静脉尿路造影等检查综合判断, 单一指标异常不应轻易否认供者资格^[35-36]。肾功能正常的老年供者对肾移植预后并无显著影响^[37]。目前对60岁以上的供者尚无合适可推荐的GFR截断值^[38]。

高血压会导致肾慢性损伤。我国一项流行病学调查发现, 高血压发病率为29.6%, 而>60岁的个体高血压发病率为58.2%, 其中仅有52.1%的患者知道自己患有高血压,

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11.7%的患者得到了有效的控制^[39]。因此,老年供者术前筛查高血压十分必要。但得到控制的轻中度高血压只是肾捐献的相对禁忌^[24]。

2 老年供者供肾切取术后并发症

老年供肾切取术由Hsu等^[40]于2002年首次报道并取得了较好的疗效。文献报道供肾切除术后供者90天死亡率约为0.031%,老年供者略高(0.066%),但并无显著差异^[41]。罗用文等^[42]报道了44例后腹腔镜老年活体供肾切取术,术后并发症发生率及术后6个月血肌酐与同期中青年供者组相比差异不显著,与其他学者报道相近^[43-46]。符合供肾条件的供者围手术期死亡率并不会因为年龄而改变。

供肾切取术后,余肾血流量及GFR迅速升高,可恢复至术前总GFR的70%^[46],同时由于肾单位过度肥大使肾体积增大30%^[47]。供者肾功能代偿率与年龄有显著关系^[48]。有研究显示<50岁和>50岁的供者术后1个月肾功能代偿率分别为12.14%和26.82%,但血肌酐水平相近^[49]。郭丰富等^[50]对比了45例>50岁供者的活体供肾移植与同期<50岁供者的术后1年肾功能无显著差异。Dols等^[51]统计了569名活体供者术后肾功能,尽管老年供者术后eGFR低于年轻供者,但两组eGFR下降比例均接近35%。然后老年供者术后易出现蛋白尿^[56]。文献报道了573名平均年龄为61.5岁的活体供者14年后出现微量蛋白尿的比率约为21%^[52]。GFR的下降及蛋白尿的出现使老年供者终末期肾病的发病率依然稍高于健康人群^[53-54]。尽管如此,年轻供者预期寿命长,若术后并发糖尿病等相关疾病,有足够的时间最终进展为终末期肾病,风险高于老年供者^[55]。但老年供者预期寿命较短,即使术前因为糖耐量异常等原因肾受损,也常因为其他原因死亡而未进展到终末期肾病^[38]。

肾功能下降会增加心血管疾病的发病风险,而老年供者术前合并糖耐量异常及高血压可能性大,因此术后出现心血管并发症的风险也高于年轻供者^[36,56]。供肾切取后,供者平均动脉压升高约5 mmHg/年^[57]。但由于术前的严格筛查,肾移植供者身体往往较平均人群健康,预期寿命也接近甚至高于平均人群^[3,41,58]。因此对符合供肾标准的供者,肾捐献并不会增加心血管疾病的发生风险,甚至有数据显示,肾移植供者的心血管疾病风险低于平均人群(2.8% vs 4.1%)^[41,59]。而一项对55岁以上活体供者的健康调查也没有发现捐肾与心血管疾病发生率有关^[60]。Toyoda等^[61]对活体供者进行了7年的随访发现老年供者及年轻供者间的心血管发病风险无显著区别。

3 老年供肾移植肾疗效

老年供肾移植肾预后良好,并不较年轻供者差^[9,12,42,62-67]。郭丰富等^[50]报道的老年供肾术后1、3年移植肾存活率分别为97.8%和77.8%,血肌酐为148.40 μmol/L,与年轻供者对比均无显著差异。李金锋等^[68]对比了66例边缘供者与标准供者移植术后短期与长期疗效,两组受者术后1年血肌酐、DGF、AR、并发症发生率及人/肾存活率均无统计学差异,供者年龄并非肾移植预后的独立影响因素。Gill等^[69]研究表明,接受>55岁供肾后3、5年存活率分别为85%和

76%,而接受<55岁供者分别为89%和82%,两组差异无统计学意义。一篇对31篇文献的系统回顾显示,老年供肾移植肾5年生存率低于年轻供者(70% vs 87%, $P=0.21$),但差异并不显著^[70]。印度一项活体肾移植分析显示,尽管老年供肾移植肾功能较年轻供肾差,但急性排异反应风险无统计学差异^[71]。贾保祥等^[8]报道父母为供者时,父母供肾移植肾功能劣于子女供肾,但供者年龄并不影响术后移植肾功能及移植肾DGF或AR发生率。方佳丽等^[72]发现老龄供肾在青年受者体内6个月后病理学结构改善,间质纤维化速度缓解,为老年供肾应用的安全性提供了病理学的支持。

但相关报道不全支持类似结论。有研究显示,使用>60岁供者供肾会加重DGF风险(6.8% vs 2.5%)^[73]。陈国栋等^[74]报道,老年供肾组术后移植肾血肌酐水平高于年轻供肾组,而且受者发生急慢性排斥反应的几率较高,但DGF发生率相近。Galeano等^[75]分别调查了供者年龄<50岁、50~70岁及>70岁的移植肾5年生存率(81%、74%、70%),尽管老年活体供者可获得良好的移植肾存活率,但术后肌酐水平显著高于年轻供者。研究显示供者年龄>50岁患者2、6周排斥反应发生率分别为13.0%和19.5%,显著高于<50岁供者组(2.8%和8.5%)^[64]。AR后肾功能的降低程度与AR前的肾功能相关,这取决于供者的年龄及供肾之前肾受到的损伤^[76]。因此老年供肾对AR的承受能力弱于年轻供肾,AR导致的移植肾丢失率较高^[19]。一项对1063名活体肾移植受者的调查发现,年龄对移植肾存活率有显著影响,尤其是供者年龄>40岁时;>70岁的供者移植肾丢失风险高于50~59岁的供者,但接近50~59岁的尸体供者^[77]。尽管老年活体供肾效果无法媲美年轻供者,但仍优于尸体供肾。Mirgam等^[27]认为60岁活体供者的移植肾存活率同20岁尸体供肾相近。

供者年龄对移植肾慢性排斥反应的作用也存在争议。严群等^[63]的动物实验提示供鼠年龄越大,移植肾中淋巴细胞浸润及间质纤维化越严重。但Schwarz等^[78]对比了70名发生慢性移植肾肾病及120名未发生慢性移植肾肾病的患者,两组患者的供者年龄无明显差异。近年来,对慢性排斥反应的研究表明,其病理过程与肾衰老相似,或许对移植肾衰老进程有加速作用^[79-80]。

受者年龄对移植肾也有显著影响^[73],而这种影响可能比供者年龄因素影响更大。老年受者机体免疫力差,更容易接受免疫原性较强的老年供肾^[81]。而年轻受者免疫系统较强,更容易发生免疫应答^[82-83]。孝晨等^[34]发现虽然移植肾术后eGFR水平与供者年龄负相关,但移植肾代偿能力仅受术前eGFR水平及受者年龄影响而非供者年龄。王振等^[84]统计了327例活体肾移植受者AR发生情况,老年供者并不增加移植后排斥风险,而供受者年龄组合是AR风险的独立危险因素。Chang等^[85]报道,决定肾移植半衰期(50%肾移植受者出现器官衰竭的时间)的是受者年龄而非供者年龄。Masayuki等^[86]也发现,使用>50岁的供肾,受者年龄是移植肾丢失风险的独立危险因素(15年移植肾存活率75% vs 41%)。Shin等^[87]也报道,对年轻受者而言,老年供

者移植肾10年存活率低于年轻供者(83% vs 62%),但供者年龄对老年受者影响较小(5年移植肾存活率92% vs 90%)。Lee等^[88]以受者年龄相差20岁为分界,发现供者年龄差过大对5年血肌酐水平及AR发生率有显著影响,但移植肾存活率无显著差异。因此,美国及欧洲的医生提出可将老年活体供肾应用于老年受者(old-for-old)^[89]。如果1名年轻尿毒症患者有数名潜在供者,那年轻供者是最好的选择,应用年龄匹配策略有助于获得更好的移植肾预后^[56],但如果患者没有更好的选择,老年活体供肾疗效也非常好^[77]。尤其是对于老年尿毒症患者而言,使用1个老年供者的供肾远优于等待1个标准尸体供者^[90]。老年活体供肾的应用可有效缓解肾源短缺,减少透析时间,而减少尿毒症患者肾移植等待时间已经证实对患者生存和移植肾生存率有非常重要的正面影响^[91]。

4 结语

活体肾移植中,保护供者是首要原则。老年个体容易并发多种疾病,对供者的筛查和选择需要谨慎,尽最大可能避免对供者的额外损伤。但对符合条件的老年活体供者而言,肾捐献一方面并不会显著增加供者的远期风险,另一方面也可以获得良好的肾移植疗效。如果能应用年龄匹配策略,减少供受者之间的年龄差距,则可更好地利用现有肾源,为尿毒症患者提供更好的治疗效果。

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