·综 述·

高龄终末期肾脏病患者肾脏替代治疗时机和治疗方式的选择

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【摘 要】 高龄（≥80岁）终末期肾脏病（ESRD）患者人数不断增加，年龄是透析患者生存率的独立危险因素，有关高龄ESRD患者治疗时机与治疗方式选择的报道较少。本文从保守治疗与肾脏替代治疗对高龄患者生存率的差异、透析时机对患者生活质量及预后的影响、肾脏替代治疗方式的选择、血液透析和腹膜透析治疗效果和并发症的差异等方面总结了国内外的相关文献报道，以期为高龄ESRD患者的治疗决策提供参考。

【关键词】 老年人，80以上；肾透析；终末期肾脏病；肾脏替代治疗；腹膜透析
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Choice of treatment timing and approaches for renal replacement therapy in elderly patients with end-stage renal disease

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【Abstract】 Patients over 80 years old with end-stage renal disease (ESRD) are increasing in recent years. Age is an independent risk factor for the survival of ESRD patients. However, studies on the choice of time and treatment approach for renal replacement therapy in these patients are limited. In this paper, we compared the effects of conservative and replacement therapy on survival rate and dialysis timing on life quality and prognosis, reviewed the options of different renal replacement approaches and the differences of therapeutic efficacies and complications between hemodialysis and peritoneal dialysis, in order to provide clinical evidence on the treatment decision-making for ESRD patients aged over 80 years.

【Key words】 aged, 80 and over; renal dialysis; end-stage renal disease; renal replacement therapy; peritoneal dialysis
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截至2016年底，全国血液透析患者信息登记系统显示，我国血液透析人数超过50万，其中高龄（≥80岁）终末期肾脏病（end-stage renal disease，ESRD）患者的比例不断增长。有研究认为，与年龄<80岁的患者相比，高龄透析患者肾脏替代治疗的并发症并没有增加，可以有令人满意的生活质量[1]。因此，对于高龄透析患者，更多需要考虑的是患者的生理、心理和家庭等社会问题，透析可能会造成相当大的家庭负担。进行肾脏替代治疗选择时，部分高龄ESRD患者更愿意放弃一定的预期寿命，从而避免过长的住院时间及肾脏替代治疗带来的并发症和家属负担[2]。

1 保守治疗和肾脏替代治疗选择

迄今为止最大的回顾性观察研究结果显示[3]，对于年龄大于80岁的ESRD患者，肾脏替代治疗与保守治疗的生存优势无明显差别。也有研究发现，高龄患者肾脏替代治疗的生存优势不再存在，透析治疗对存在器官功能障碍或慢性营养不良的高龄ESRD患者，并无生存优势或功能状态和生活质量的改善[4]。台湾10 759例年龄大于75岁的血液透析患者的队列研究显示，老年患者的住院时间和住院总费用增加，年龄为老年血液透析患者生存率的预测因子，建议高并发症和低生存率的75岁以上的

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ESRD患者考虑保守治疗[5]。对于高龄ESRD患者,保守治疗成为一个合理的选择。临床医师为高龄患者选择肾脏替代治疗时,应关注影响其生存率的因素,如是否有影响预期寿命的疾病(如肿瘤)、营养状况、是否可用动静脉内瘘作为血液透析通路、透析前的治疗方案等[6]。长期的透析前随访对高龄患者透析是否成功最为重要[7]。

2 透析时机的选择

既往有研究认为,早期开始透析能改善尿毒症症状及患者的营养状况。改善全球肾脏病预后组织(Kidney Disease: Improving Global Outcomes, KDIGO)建议当出现下列1个或多个症状时开始透析治疗[8]:出现与肾脏衰竭有关的症状(如浆膜炎、酸碱平衡失调、电解质紊乱和皮肤瘙痒等);无法控制的高容量负荷与高血压;营养状况恶化、饮食干预无效;认知损害。这些症状出现时,估算肾小球滤过率(estimated glomerular filtration rate, eGFR)并不总在5~10 ml/(min·1.73 m^2)之间。将eGFR值为10~14 ml/(min·1.73 m^2)作为早期透析时机,eGFR值为5~7 ml/(min·1.73 m^2)作为晚期透析时机,两者进行对比,以全因死亡率作为主要评估结果,发现早期透析与晚期透析相比并没有显示出有益的效果[9-11],生存率、心血管事件和感染等并发症的发生率也并未明显改变[12]。对于年龄大于70岁的患者,早期透析组的死亡率高于晚透析组($HR=3.29$;$P=0.048$)[13]。超声心动图检查显示,早期透析治疗并没有改变患者的心脏结构和功能[14]。还有研究认为,早期透析可能增加额外风险,如血液透析通路感染和腹膜感染、加剧炎症反应、蛋白质或血色素流失、加速肾功能丧失,因而反对过早进行透析治疗[9]。临床医师不能仅根据eGFR值来确定透析开始的时间,稳定无症状患者的透析应推迟到有更多透析治疗指征出现,启动透析的决定不能仅仅依赖肾功能eGFR值,而应根据患者的临床症状综合评估,透析开始的时机应因人而异,目前没有证据表明无明显症状、单纯低eGFR就开始透析有优势[9],某些情况下晚期透析与降低患者的死亡风险相关,尤其是对于高龄患者[13]。

3 有关肾脏替代治疗方式的选择

在大多数国家血液透析是主要的透析方式,但目前仍缺乏对高龄患者最佳透析方式的共识。我国对216例透析患者的队列研究显示[15],3年生存率分别为血液透析:98.7%、93.2%和85.5%,腹膜透析:90.9%、81.5%和73.8%,校正年龄、体质量等因素后,2组之间没有明显的区别。Seyed等[16]对伊朗239例透析患者的研究显示,3年生存率分别为血液透析:63%、53%和38%,腹膜透析:67%,46%和29%,差异无统计学意义。两个研究都对血液透析和腹膜透析的生存率进行了分析,认为透析模式本身对ESRD患者生存率无影响。按不同年龄分层的老年患者生存获益存在争议,分析患者透析两年的生存率:一些研究倾向于腹膜透析比血液透析的死亡率低(33% *vs* 44%)[17],认为腹膜透析与血液透析相比有生存优势($r=0.87$, 95% *CI* 0.76~0.99)[18];一些研究相反,倾向于腹膜透析患者的死亡率高于血液透析患者($r=1.20$, 95% *CI* 1.13~1.28)[19];也有研究认为腹膜透析和血液透析的死亡率无差别[20-22]。

血液透析和腹膜透析各有利弊。血液透析可提供系统的医疗随访,有认为血液透析对高龄ESRD患者比腹膜透析更安全[23],但由于动脉静脉内瘘的成熟需要较长时间,且血管通路在老年人中成功率较低,中央静脉导管使用率高,这些又都与高死亡率相关[24]。与年轻患者相比,高龄患者更易出现血液透析相关并发症[25],如低血压、营养不良、感染和消化道出血,因心血管疾病和自主神经功能障碍,老年人对液体变化特别敏感,难以耐受较高的超滤量。且血液透析患者由于血管通路损伤,若同时合并动脉粥样硬化则可增加远端缺血的风险[23]。血液透析中血流动力学压力的变化会导致周期性的节段性缺血性损伤,连续性心脏核磁共振评估结果显示血液透析中所有收缩期功能指标均下降,透析后部分恢复,且所有患者均有一定程度的节段性左室功能障碍,严重程度与超滤率和血压降低有关[26]。血液透析期间使用肝素抗凝剂会增加出血风险,出血性并发症发病率更高,如血液透析患者硬膜下血肿的危险大于腹膜透析(29.1% *vs* 25.3%, $HR=1.30$, 95% *CI* 0.70~2.41)[27]。血液透析患者消化系统出血[23]和出血性卒中[28]的风险高于腹膜透析患者。对631 421例老年患者的回顾性分析显示,腹膜透析患者的死亡率明显高于血液透析患者[29],与血液透析相比腹膜透析的长期生存率较低($HR=1.20$, 95% *CI* 1.13~1.28, $P<0.001$)。大多数ESRD患者重视与健康相关的生活质量(health-related quality of life, HRQoL),并希望了解不同透析方式的影响。有研究以HRQoL作为评价指标,随机安排332例已进入规律透析的患者接受频繁血液透析(6次/周)或常规血液透析(3次/周),与常规血液透析对比,

进行频繁血液透析的患者有更高的总体健康评分和较短的恢复时间[30]。

腹膜透析患者不需要血管通路,为24 h缓慢持续超滤,心血管稳定性好[23]。腹膜透析对血流动力学影响小,更能保护患者的残余肾功能。作为一种居家治疗方法,腹膜透析减少了对患者日常生活的干扰,给高龄患者提供了更高的独立自主性[31]。研究表明,对有机会接受肾移植的患者,腹膜透析者的生存率比血液透析者高5年($HR = 0.86$, 95% CI 0.79~0.95, $P < 0.05$),提示腹膜透析比血液透析是更好的透析模式[32]。腹膜透析与血液透析患者相比,死亡率较低且身体和精神上都有更好的生活质量[33]。对46个国家进行腹膜透析与血液透析的成本分析发现,大多数发达国家腹膜透析医保费用比血液透析低,发展中国家情况相对复杂,但多数情况下与发达国家相似[34]。感染是影响透析患者死亡率的主要原因,有研究认为,透析模式与免疫系统之间有一定联系,透析模式的某些特征如液体超载、尿毒素积累及氧化应激的持续暴露等会影响免疫系统[35]。腹膜透析患者透析相关感染的住院风险高于血液透析患者,而非透析相关的感染风险在血液透析患者中更高[36]。透析方式对ESRD患者睡眠质量的调查结果显示,腹膜透析患者不宁腿综合征的发病率更高[37]。这些差异也可能与实践模式、种族、非随机化潜在选择偏差等有关。

研究透析方式选择对生存率影响的唯一的随机对照试验宣告失败,因为大多数ESRD患者坚持自己选择透析方式而不接受随机分配,ESRD患者更看重个人选择权和透析模式的益处[38]。20余年来的研究结果汇总均显示,腹膜透析患者和血液透析患者存活率相似或仅对特定的亚组有差异。因比较透析方式的方法有限,有研究者认为肾脏病学界不应再资助、执行或发表关于透析方式选择的研究[39]。在临床实践中,透析模式的选择应个体化,以最大限度地提高生活质量并达到以患者为中心的目标。老年人eGFR评估受肌肉水平及饮食等影响,可能存在一些偏差[40]。对高龄血液透析人群,生活质量比生存时间更重要。医师应致力于促进ESRD患者的生活质量最优化,加强患者对于战胜疾病的信念。

4 小结

目前评估高龄ESRD患者是否进行肾脏替代治疗的原则是要综合考察患者的基础疾病、预期寿命、合并症、患者及家属愿望,不建议用牺牲生存质量、增加并发症来延长无质量的存活时间。选择透析时机时,更倾向于综合评判患者的临床症状,而非单纯依赖肾功能eGFR值,保守治疗或晚透析治疗并不一定缩短生存时间。高龄患者血液透析与腹膜透析相比,近期生存率并无差异。但相关研究有限,存在一定局限性,具体还需要结合患者自身状况、家庭及社会因素综合评估。

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