肾脏功能评价与替代: 历史、进展与挑战

乐偲, 陈丽萌*

中国医学科学院&北京协和医学院, 北京协和医院肾内科, 疑难重症及罕见病国家重点实验室, 北京 100730

* 联系人, E-mail: chenlimeng@pumch.cn

收稿日期: 2021-06-03; 接受日期: 2021-07-21; 网络版发表日期: 2021-08-16

摘要 肾脏是机体排泄代谢废物和毒素, 产生促红细胞生成素、1,25二羟维生素D和肾素, 维持机体水、盐代谢和酸碱平衡的重要器官。各种原发或继发性肾脏病均可导致肾实质性改变, 若未经充分及时的治疗则可进展至不可逆病变, 表现为肾单位逐渐减少, 机体排出代谢废物和维持内环境稳定的功能障碍, 致体内代谢产物潴留, 水、电解质、酸碱平衡紊乱, 肾脏内分泌功能异常甚至进展到肾功能不可逆衰退的终末期肾病(end stage kidney disease, ESKD)。完整的肾脏功能评价包括肾小球功能、肾小管功能和内分泌功能, 可用于早期识别肾脏疾病, 完成定位和定性诊断, 确定肾功能分期, 并可监测肾脏对治疗的反应。肾脏替代治疗则是挽救ESKD患者生命、提高生活质量的重要手段。本文将对肾功能评价及替代治疗的历史及现状进行简要综述及展望。

关键词 肾功能, 肾脏替代, 慢性肾脏病

肾脏是机体排泄代谢废物和毒素, 产生促红细胞生成素、1,25二羟维生素D和肾素, 维持机体水、盐代谢和酸碱平衡的重要器官。各种原发或继发性肾脏病均可导致肾实质性改变, 若未经充分及时的治疗则可进展至不可逆病变, 表现为肾单位逐渐减少, 机体排出代谢废物和维持内环境稳定的功能障碍, 致体内代谢产物潴留, 水、电解质、酸碱平衡紊乱, 肾脏内分泌功能异常甚至进展到肾功能不可逆衰退的终末期肾病(end stage kidney disease, ESKD)^[1-3]。完整的肾脏功能评价包括肾小球功能、肾小管功能和内分泌功能, 可用于早期识别肾脏疾病, 完成定位和定性诊断, 确定肾功能分期, 并可监测肾脏对治疗的反应^[4]。肾脏替代治疗则是挽救ESKD患者生命、提高生活质量的重要手段^[5]。本文将对肾功能评价及替代治疗的历史及现

状进行简要综述及展望。

1 肾脏功能的评估

肾脏通过排泄代谢废物维持内环境稳定。水和溶质排泄的精准、个体化调节, 依赖肾小球滤过功能及肾小管重吸收、分泌功能。肾脏分泌的激素则参与调节全身及肾脏的血流动力学、红细胞生成及矿物质和骨代谢。

1.1 肾脏的小球滤过功能

肾小球滤过是指血液流过肾小球毛细血管时产生超滤液的生理过程, 肾小球滤过率(glomerular filtration rate, GFR)代表有功能的肾单位滤过率总和, 是慢性

引用格式: 乐偲, 陈丽萌. 肾脏功能评价与替代: 历史、进展与挑战. 中国科学: 生命科学, 2021, 51: 927-937

Yue C, Chen L M. Evaluation and replacement of renal function: history, advancement, and challenges (in Chinese). Sci Sin Vitae, 2021, 51: 927-937, doi: 10.1360/SSV-2021-0182

肾脏病分期的重要依据, 及预测预后的独立危险因素^[6]。

评价GFR的理想标志物应为无毒, 在肾小球自由滤过, 不被肾小管分泌、重吸收或代谢的内源性或外源性溶质, 尿液排泄率等于肾小球滤过率。经典金标准为菊粉清除率, 因操作复杂而临床应用受限^[7]。肌酐(creatinine, Cr)是最常用的内源性标记物, 但其生成具个体差异, 受肌肉容量影响且有一定比例的肾小管分泌, 故采用肌酐清除率间接反映GFR有其局限性^[8]。另一常用内源性标记物是胱抑素C(cystatin C, Cys-C), 有研究显示血Cys-C浓度与GFR的联系可能比血Cr与GFR的联系更为密切, 不过Cys-C的生成亦有个体差异, 且在肾小管代谢, 其清除率无法直接测量^[9]。GFR估算公式通过整合影响血Cr浓度的已知人口统计学及临床变量, 改善GFR估算, 并可联合其他内源性标记物应用, 临床使用便捷准确^[10]。目前常用的GFR估算公式包括CKD-EPI公式、MDRD公式及Cockcroft-Gault公式等^[10]。国内左力及北京协和医院等多单位先后在中国成年人中对上述公式进行验证。纳入血Cr和Cys-C的CKD-EPI公式对于中国成年人的GFR估算最为准确^[11,12]。

双血浆法是通过注射外源性溶质如碘酞酸盐、碘海醇、二乙基三胺五乙酸(DTPA)或EDTA, 通过检测不同时点的血浓度来计算GFR, 与菊粉清除率同为GFR评估的金标准^[6]。2009年北京协和医院肾内科与儿科、核医学科合作, 首次建立了儿童GFR检测的双血浆法, 改良的碘海醇法通过邮寄干血样滤纸片即可实现, 解决了微量血远程检测GFR的临床难题^[13,14]。

肾脏储备功能最早于1983年提出, 定义为应激状态下GFR由基础值增加到最高限度的能力^[15]。血肌酐正常状态时, 肾脏储备功能减退与肾脏长期不良预后相关^[16]。蛋白质负荷前后的GFR变化是评价肾脏储备功能的可靠方法^[17]。北京协和医院在国内率先成功建立了利用蛋白负荷试验评估肾脏储备功能的标准流程及正常值, 可用于肾脏疾病的早期诊断、疗效评估和预后判断^[18]。

随着CKD进展, 肾脏病理表现为肾小球硬化、肾小管萎缩和间质纤维化、肾组织弹性降低、硬度增加。新兴的肾脏功能影像有助于通过无创方法将肾功能和结构联系起来。2012年, 北京协和医院探索了声触诊组织定量(virtual touch tissue quantification, VTQ)

超声技术在CKD及IgA肾病中的应用, 发现VTQ技术测定的肾皮质剪切波速度(shear wave velocity, SWV)与多项临床/病理指标相关^[19,20]。2017年, 北京协和医院率先将先进的MRI技术-扩散峰度成像(diffusion kurtosis imaging, DKI)应用于IgA肾病, 发现其特征性参数K及ADC与IgA肾病患者肾功能及肾脏病理显著相关; 同时, 在CKD患者中应用基于MRI成像数据的纹理分析, 发现其与肾功能亦存在显著相关性; 随访资料则表明, 功能性MRI数据与CKD患者肾脏预后亦存在相关性^[21,22]。

1.2 肾小管功能

肾脏对水、盐、电解质、酸碱平衡的精确调控, 依赖肾小管的浓缩、稀释、分泌和酸化等功能。对肾小管功能的评估, 对疾病的定位、定性诊断、预后判断具有重要临床意义。肾小管功能评价含多个维度, 如尿量、血尿渗透压可反映肾小管浓缩功能; 血尿电解质水平、酸碱水平、尿酸、尿氨基酸、尿糖等指标可反映肾小管的重吸收、分泌及酸化功能。国内最早的研究包括北京协和医学院1919年发表的《骆驼尿液排泄的研究》^[23]。除了可直接检测上述指标, 还可通过肾小管生理功能试验来评估相关转运子功能^[24]。20世纪50年代以来, 北京大学第一医院、北京协和医院、中山医科大学附属第一医院、上海华山医院等多家医院率先在国内开展了自由水清除试验、氯离子清除试验、肾糖阈值测定、磷廓清试验、碳酸氢根排泄分数、氯化铵负荷试验、碳酸氢钠重吸收及负荷试验、吡嗪酰胺抑制试验或苯溴马龙抑制试验等肾小管功能试验。

肾小管性酸中毒(renal tubule acidosis, RTA)是由于各种病因导致肾脏酸化功能障碍而产生的临床综合征, 根据病变部位及病生理机制分为不同类型。20世纪80年代, 北京大学第一医院、北京协和医院先后在国内率先开展了尿可滴定酸检测、尿气分析, 进而开展氯化铵负荷试验、碳酸氢钠重吸收及负荷试验等, 是RTA的定性、定位诊断的有力手段^[25]。

噻嗪类利尿剂和袢利尿剂分别作用于位于远曲小管的NCC转运子和位于髓袢升支粗段的NKCC2转运子, 根据患者对两类利尿剂的反应, 可以确定疾病部位和转运子损害程度, 根据该原理设计的氯离子清除试验不仅可用于鉴别Barter综合征(NKCC2缺陷)和Gitel-

man综合征(NCC缺陷),敏感性和特异性均超过93%,也可用于部分原发或继发性肾小管疾病的定位、定性诊断^[26].2015年,北京协和医院在国内首次建立了简化的氯离子清除试验检测方法,并确立了氯离子清除试验中国人群正常值范围^[27,28].

肾糖阈是尿中出现葡萄糖的最低血糖浓度,代表近端肾小管重吸收葡萄糖的功能.2015年,北京协和医院在国内首次建立肾糖阈的检测方法,通过口服葡萄糖后的尿糖排出量,采用数学模型拟合、数值逼近方法估算肾糖阈,与金标准葡萄糖钳夹法相比,一致性相关系数达0.94,而测定流程大大简化,为临床提供了简便易行的肾糖阈值测定方法^[29].

1.3 肾脏内分泌功能

(i) 促进红细胞生成功能.早在1839年,Christison^[30]便认识到肾功能受损患者中的贫血现象.20世纪50年代,随肾脏分泌促红细胞生成素(erythropoietin, EPO)的功能被揭示, EPO缺乏被证实是导致慢性肾脏病患者贫血的主要原因,称为肾性贫血^[31,32].肾性贫血的发生率随肾脏功能衰退逐渐增高,故测定EPO与血红蛋白水平,可以评估肾脏内分泌功能^[33].需注意EPO检测方法学的局限性及肾脏病患者中EPO相对不足的状态,可能会影响对肾脏的实际内分泌功能的评估^[34].1992年, Semenza和Wang^[35]发现一种在低氧条件下增加EPO基因转录的因子(hypoxia inducible fac-

tor, HIF), 并因上述工作获2019年诺贝尔生理学医学奖, 开启了探索更符合生理的缺氧诱导因子途径治疗肾性贫血研究的序幕^[36].

(ii) 骨矿物质平衡调节功能.1935年,北京协和医院刘士豪等人^[37]率先揭示了活性维生素D与骨软化的关系,于1942在*Science*上首次提出了“肾性骨营养不良”(renal osteodystrophy, ROD)的疾病命名,并沿用至今(图1).2005年, KDIGO建议用慢性肾脏病骨矿物质异常(chronic kidney disease CKD-mineral and bone disorder, CKD-MBD)来定义与CKD相关矿物质紊乱、骨骼病变和/或血管及软组织钙化这组临床症候群^[38,39].在CKD中,肾实质丢失、GFR下降导致血磷升高,直接或间接致1,25-羟维生素D合成减少、低钙血症,通过位于甲状旁腺的维生素D受体(vitamine D receptor, VDR)和钙感受受体(calcium-sensing receptor, CaSR),促进甲状旁腺素(parathyroid hormone, PTH)分泌及甲状旁腺增生,进一步加重高磷血症,促进FGF23的分泌,进而导致骨病、心脏瓣膜和重要血管钙化、心肌肥厚等多系统损伤,是预测CKD患者预后的独立危险因素.对肾脏骨矿物质平衡调节功能的评估,除血钙、磷、碱性磷酸酶、PTH、1,25-羟维生素D和FGF23等,还需要评价骨病和心血管钙化^[40].

1.4 肾素调节血压和肾小球滤过率

肾素-血管紧张素系统(renin angiotensin system,

图1 刘士豪教授及早期关于肾性骨矿物质异常的研究.左:刘士豪教授;右:刘士豪教授等人在国际上首次提出了“肾性骨营养不良”的疾病命名,于1942年撰文发表于*Science*

Figure 1 Shihao Liu and his work on mineral bone disorder in chronic kidney disease. Left: Shihao Liu. Right: Shihao Liu and coworkers' early work on renal osteodystrophy. Published on *Science*, 1942

RAS)是机体控制细胞外容量, 维持血压的重要激素, 其限速酶肾素95%由肾脏球旁器颗粒细胞分泌, 并在肾小管和肾小球之间近距离管球反馈中发挥重要作用. 在美国NIH Schnermann教授指导下, 北京协和医院在亚洲首次建立了原代培养球旁器颗粒细胞的方法^[41-43]. 同时, 利用多种基因敲除小鼠, 在体内外试验中确定了血管紧张素II(angiotensin II, Ang II)与肾素之间的近距离反馈环, 证实了临床中多种高肾素疾病的病理生理基础是肾素产生细胞的再募集; 肾素与腺苷协同导致的管球反馈失衡在多种代谢因素导致的高血压和GFR降低、急性肾损伤(acute kidney injury, AKI)发病中发挥关键作用^[44-46]. 2020年, 浙江大学赖恩茵团队^[47]首次利用显微灌注技术证实了AKI时Ang II收缩脑血管也与近端小管分泌的成纤维细胞生长因子及其受体相关.

2 肾功能的替代

2.1 血液净化治疗

ESKD的重要病理生理后果为尿毒素因排泄困难在血液中的聚集以及水电解质酸碱平衡紊乱. 血液净化治疗可以有效清除尿毒素, 维持机体内平衡. 随透析技术成功用于临床, ESKD患者可以长期生存, 且生存质量逐步提高^[5].

1854年, Thomas Graham首次提出“透析(dialysis)”的概念, 1912年, Johns Abel等人首次对活体动物进行透析^[48]. 1926年, 北京协和医学院林可胜(Robert Kho-Seng Lim)和Necheles^[49-51]以牛肠制膜, 利用扁透析管, 对犬进行活体透析, 并在透析中首次使用肝素抗凝, 为中国乃至世界血液净化的先驱(图2). 1945年, Willem Kolff首次成功对人进行透析, 1960年, Quinton, Dillard和Sinbner等人首次利用动静脉外分流的方式, 建立透析通路, 成功对ESKD进行维持性透析, 标志慢性肾衰竭维持行血液透析的实现^[52]. 20世纪50~60年代, 国内各大医院便开始探索血液透析(hemodialysis, HD)和腹膜透析(peritoneal dialysis, PD)治疗急性肾衰患者. 1972年, 血液透析正式用于ESKD的维持性治疗^[53]. 20世纪70年代末、80年代初以来, 随着透析膜材料和水处理装置的进步, 我国血液净化技术快速发展^[53]. 截至2018年底, 全国有血液净化病历信息登记系统已登记在透血液透析患者超过57万例, 腹膜透析患者超过

3292

Demonstration of a Gastric Secretory Excitant in Circulating Blood by Vivi-Dialysis.

R. K. S. LIM AND H. NECHELES.

From the Department of Physiology, Peking Union Medical College, Peking, China.

Since it has been proved that the transplanted stomach will secrete after a meal (Ivy and Farrel,¹ Lim, Loo and Liu²), it has become necessary to obtain the exciting substance or substances from the blood, as the first step towards identification. We have, therefore, attempted to obtain the excitant (or excitants) by dialysing the circulating blood of dogs during digestion.

The animals were either narcotised with amytal, or given no anesthetic at all. The vessels were exposed (under novocaine in the latter case), and connected with a set of dialysing membranes (Necheles³) immersed in warm Locke's solution. The blood was rendered incoagulable by recurring injections of heparin (Howell) or hirudin, or both. Circulation through the membranes was permitted for periods up to 5 hours, usually 2 hours, with the animal fed, 200 gr. meat and 100-200 cc. water, before or sometimes during the observation. The dialysate, concentrated or unconcentrated, was injected, subcutaneously, intravenously or intraperitoneally, into gastric pouch of dogs, whose secretory ability was determined by meal or histamine stimulation.

图2 林可胜和Heinrich Necheles早期关于活体透析的研究, 1926年发表于*Proc Exp Biol Med*

Figure 2 Robert Kho-Seng Lim and Heinrich Necheles' work on vivi-dialysis, published in *Proc Exp Biol Med*, 1926

9.4万例^[54].

目前, 主流的血液净化方式包括HD和PD. HD的基本原理是通过体外循环的透析器, 让血液与透析液借助透析膜完成水和溶质的交换, 进而清除水、电解质和尿毒症毒素. 而PD则是以腹膜为半透膜, 腹膜毛细血管内血液与腹腔内透析液进行水和溶质交换. 相较于PD, HD效率更高, 医患交流更多, 而PD不需体外循环血流动力学更稳定, 不需要频繁往返医院, 适合高龄、衰弱及行动不便的患者, 两种透析模式互为补充, 综合生存益处及卫生经济学没有显著性差异^[55].

2020年以来, 新型冠状病毒肺炎(novel coronavirus disease 2019, COVID-19)全球大流行期间, HD患者COVID-19感染率是PD患者的3倍, 我国肾脏病医疗质量控制中心推荐腹透作为首选的透析方式^[56,57]. 针对新冠相关的AKI, 武汉的肾科同行和来自全国的医务人员, 积极利用CRRT等血液净化手段对重症患者生命支持, 并针对细胞因子风暴探索吸附滤过、全血吸附等治疗方法, 改善病情, 第一时间向世界分享了中国经验^[58-61].

自动化腹膜透析(automated peritoneal dialysis,

APD)在发达国家居家透析患者中比例超过50%, 中国约为0.3%, 北京协和医院比例为13%^[62]. 相较于传统的持续非卧床腹膜透析(continuous ambulatory peritoneal dialysis, CAPD), APD效率更高, 对透析时间和人力需求更低, 北京协和医院报告中国APD患者生存、技术生存和无腹膜炎生存与CAPD无差异, 甚至中位生存期优于CAPD者, 与国际最新研究结论相似^[63,64]. 除ESKD患者, APD也适用于AKI和危重症患者等未能建立长期透析通路患者而需要紧急透析患者^[65-67]. APD可以实现睡眠中短时间多次交换, 克服腹膜液留腹体积小及患者持续卧床的不利情况, 并可有效避免术后腹膜液渗漏. 北京协和医院近10年来紧急腹透患者与常规腹膜透析患者生存总体生存无差异, 而APD与非紧急腹膜透析患者相比, 无论在透析效果、并发症、技术生存和生存方面均无差异^[68,69]. 随着我国经济发展和医疗水平的提高, 患者对生活质量和回归社会的更高要求, 医保对腹透耗材的支持力度增加, 可以预见在不远的未来, APD会有更广泛的应用前景^[62].

同种异体肾移植是完全的肾脏功能替代, 1960年, 吴阶平在国内首次开展, 已广泛用于临床. 大量新型免疫抑制剂均是首先在抗移植排异中使用, 而后用于其他免疫相关的疾病. 肾移植是最完全的肾脏替代治疗方式, 条件允许, 应作为首选的肾脏替代方式, 但因为肾脏来源的限制, 尚远不能满足临床的需求, 未来随着脑死亡被更多的公众所接受, 我国ESKD肾移植比例有望达到发达国家水平.

2.2 并发症控制

肾衰竭并发症直接关系患者的生活质量及预后, 肾脏替代治疗不仅需要通过透析不完全替代维持内环境平衡, 还需要替代肾脏的内分泌功能, 控制各种并发症.

(i) 肾性贫血. 在发现EPO之前, 肾性贫血的治疗主要依赖输血来维持血红蛋白水平60~90 g/L. 20世纪70年代以来, 重组人EPO及相关的红细胞刺激因子(erythropoiesis stimulating agents, ESAs)的问世, 为肾性贫血治疗带来里程碑式的突破, ESA也曾作为外交礼物, 由美国卡特总统赠予中国, 首先在北京协和医院试用^[70]. 1998年, 我国国产EPO的临床疗效和安全性首次被证实, 价廉物美, 通过间断皮下或静脉注射可有效维持患者血红蛋白达到KDIGO国际指南标准

110~120 g/L^[71,72]. 北京协和医院参与了中国首批国产促红素的研发和临床试验, 获得国家科技进步二等奖^[73,74]. 但是EPO治疗剂量高于生理剂量, 也带来了高血压、血栓栓塞事件、肿瘤进展等风险, 且在10%~20%的患者中, 存在ESAs抵抗, 促使新的肾性贫血药物的探寻^[34].

缺氧诱导因子脯氨酰羟化酶抑制剂(hypoxia inducible factor-prolyl hydroxylase inhibitor, HIF-PHI)应运而生, 2020年首个HIF-PHI罗沙司他(roxadustat)全球首先在中国完成临床研究上市, 并被纳入医保报销范围. 北京协和医院牵头或参与了从一期到四期的临床试验, 2019年, HIF-PHI治疗透析和非透析肾性贫血患者的两项三期临床试验结果同步发表于*New England Medical Journal*^[75,76]. 在透析和非透析的慢性肾脏病患者中, HIF-PHI可以促进红细胞生成, 提高铁的生物利用度, 降低铁调素水平, 对于肾性贫血的疗效不劣于ESA, 且疗效不受炎症状态的影响^[75-78].

(ii) 肾性骨矿物质异常. CKD-MBD的治疗包括, 应用饮食控制及口服磷结合剂将血磷控制在正常范围; 利用维生素D及其类似物就诊维生素D缺乏, 从而控制血PTH在合理水平. 近年来, 采用作用于CaR的拟钙剂, 可以有效控制继发于CKD的甲状旁腺功能亢进及相伴的骨矿物质紊乱. 对于甲状旁腺呈腺瘤样增生的患者, 药物治疗效果不佳, 需手术切除甲状旁腺腺瘤^[79]. 20世纪50年代, 北京协和医院率先在全国开始甲状旁腺切除手术, 对于术前超声定位困难的甲状旁腺瘤, 在国内率先通过经股静脉插管检测甲状旁腺激素进行定位; 使用⁹⁹Tc^m-MIBI显像、¹¹C-胆碱PET/CT显像等技术对传统的超声定位进行有力补充; 颈丛麻醉小切口微创术式则可减少ESKD患者中全身麻醉的诸多风险, 是积极的尝试^[80-83]. 随着KDIGO和中国CKD-MBD中国指南的相继问世, 多学科合作治疗为全国多数医院接受和采纳, 北京协和医院的甲旁亢协作组, 不仅在国内较早制定了CKD-MBD诊治协和规范, 还开展全国甲状旁腺手术术式调查, 牵头编写了《慢性肾脏病继发性甲状旁腺功能亢进症临床实践》, 并通过全国巡讲和基于智能手机CKD-MBD现患率调查, 推动了CKD-MBD的多科协作诊治模式和规范化诊疗^[84].

(iii) 心、脑血管并发症. 慢性肾脏病与高血压互为因果, 心、脑血管事件不仅是CKD患者的主要死亡

原因,也是CKD进展的独立危险因素。其中血管病变、容量负荷、神经体液因素、电解质水平和EPO,均参与其中^[85],特别是透析患者控制更加困难。北京协和医院证实血透患者的透析前血压存在季节变异,其中个体血压的变异率是透析患者死亡的独立危险因素,加强透析患者的自我管理,包括水盐管理及控制透析间期的体重增长能有效降低患者的血压^[86,87]。

对于ESKD患者心血管疾病的一级预防措施,包括控制血压、调脂、戒烟等一级预防。对于已经存在心血管疾病表现的患者,传统的治疗包括抗血小板、缓解心绞痛、心率控制、RAS抑制剂等二级预防措施,以及适时的血运重建。北京协和医院作为中国区PI与国际同行共同证实了对于稳定性心绞痛的CKD患者,血运重建并不能使患者获益,为CKD患者冠心病防治提供了循证依据^[88]。尿毒症患者还存在毒素潴留、贫血、炎症状态、骨矿物质异常等非传统的危险因素,其中尿素导致的白蛋白氨甲酰化在透析患者中的预测预后和可干预性为学者们所关注,北京协和医院与其国际肾脏病学会的姊妹医院哈佛大学麻省总医院一起进行了积极的探索^[89]。

CKD中的脑血管疾病包括传统的急性脑病、周围神经系统和自主神经系统疾病等,但最为常见的认知障碍因为随GFR下降而逐渐发生而最易被忽略^[90]。2018年ASN年会上,JASN杂志将血液透析对脑灌注的直接影响研究评为年度最佳论文,为透析患者的认知障碍机制提供了有力的证据^[91]。北京协和医院在国内率先开展多中心认知功能研究,采用MoCA评分系统,PD患者中认知障碍的发病率高达86.8%^[92]。认知障碍的病因与血管损伤、尿毒素、甲状旁腺功能亢进、贫血、营养状态、微炎症状态等均相关,颈动脉内膜-中膜厚度是认知障碍的独立危险因素^[90,92,93]。利用MRI评价维持性HD患者的脑改变,发现高达47%的患者存在微出血,39%的患者存在腔隙性脑梗,可能是其病理基础^[94]。这些探索为透析患者认知障碍的多学科共同干预提供了新的思路。

3 展望

肾脏替代治疗发展的长远趋势,是促使ESKD患者达到更高质量的长期生存。因此,基于便携设备、简便操作、自我管理、家庭进行的肾脏替代模式,是

肾脏替代治疗发展的方向。如与自动化腹膜透析相对应的家庭血液透析(home hemodialysis, HHD)目前在发达国家较为成熟,在国内尚鲜有开展^[95]。可穿戴式人工肾(wearable artificial kidneys, WAKs)和可植入式人工肾(implantable artificial kidneys, IAKs)旨在使用便携的设备提供持续性的肾脏替代治疗,首先需克服物理尺寸、动力来源以及透析用水的重量和体积三大难题^[96]。2005年,首次在动物实验中获得成功以来,目前在研的便携式肾脏替代设备包括WAK(wearable artificial kidney)和AWAK(automated wearable artificial kidney),采用电池供能及纳米材料的透析液再生技术开展HD和PD,重量小于5 kg,已进入临床试验阶段^[97-99]。而可植入式人工肾是将高选择性的透析膜的血液透析装置植入人体内髂动静脉间,模拟肾小球持续滤过功能,植入于生物骨架上的小管细胞完成肾小管的功能,利用心脏搏动提供透析所需的血流速度,无需电池,可轻至0.5 kg。虽然尚在动物实验阶段^[96],但随着材料科学的进展,便携式透析设备有望实现突破。

狭义的生物人工肾(bioartificial kidney, BAK)的雏形是在透析膜上植入肾脏自有细胞,最大程度地模拟自体肾脏功能。如尝试将肾上皮细胞植入半透膜的中空纤维中,获得滤过屏障功能及活跃的转运功能;用猪肾小管上皮细胞植入传统的血液滤器,可以显著改善急性肾损伤的死亡率。生物人工肾的安全性及有效性,尚待后续进一步验证^[100]。

无论血液净化还是药物治疗,都无法做到对肾脏功能的充分替代。肾移植是完全肾脏替代的最佳手段,但是由于肾源的获取受限,限制了其临床应用。近年来,采用诱导性多能干细胞(induced pluripotent stem cells, iPSCs)技术已可构建初具形态及功能的肾单位(organoids),为人造肾脏的进一步研发奠定了基础^[101]。

4 总结

肾功能评价和替代,是诊治肾脏病的关键。理想的方法应包括肾小球功能、肾小管功能、内分泌功能的综合评估和完全的替代,除血液净化手段,还包括并发症管理在内的综合管理。在未来,多学科协作、跨学科医工合作及新技术的应用,将为肾功能评价和替代带来新的机会,甚至改变未来肾脏病学的治疗模式。

致谢 感谢秦岩、张磊、刘岩、夏鹏、赵冰彬在成文过程中提供文献及数据支持. 感谢李雪梅教授对文章的最终修订和建议.

参考文献

- 1 Meyer T W, Hostetter T H. The pathophysiology of uremia. In: Skorecki K, Taal M W, Chertow G M, et al., eds. *Brenner and Rector's The Kidney*. Amsterdam: Elsevier, 2015
- 2 Webster A C, Nagler E V, Morton R L, et al. Chronic kidney disease. *Lancet*, 2017, 389: 1238–1252
- 3 Meyer T W, Hostetter T H. Uremia. *N Engl J Med*, 2007, 357: 1316–1325
- 4 Chmielewski C. Renal physiology series: part 1 of 8. Renal anatomy and overview of nephron function. *ANNA J*, 1992, 19: 34–38
- 5 Pastan S, Bailey J. Dialysis therapy. *N Engl J Med*, 1998, 338: 1428–1437
- 6 Levey A S, Inker L A, Coresh J. GFR estimation: from physiology to public health. *Am J Kidney Dis*, 2014, 63: 820–834
- 7 Rahn K H, Heidenreich S, Brückner D. How to assess glomerular function and damage in humans. *J Hypertension*, 1999, 17: 309–317
- 8 Shemesh O, Golbetz H, Kriss J P, et al. Limitations of creatinine as a filtration marker in glomerulopathic patients. *Kidney Int*, 1985, 28: 830–838
- 9 Dharnidharka V R, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. *Am J Kidney Dis*, 2002, 40: 221–226
- 10 Qin Y, Li X M. The characteristics and clinical application of various GFR detection methods (in Chinese). *Beijing Med J*, 2010, 32: 249–250 [秦岩, 李雪梅. GFR各种检测方法的特点与临床应用. *北京医学*, 2010, 32: 249–250]
- 11 Guo X, Qin Y, Zheng K, et al. Improved glomerular filtration rate estimation using new equations combined with standardized cystatin C and creatinine in Chinese adult chronic kidney disease patients. *Clin Biochem*, 2014, 47: 1220–1226
- 12 Kong X, Ma Y, Chen J, et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating glomerular filtration rate in the Chinese population. *Nephrol Dial Transplant*, 2013, 28: 641–651
- 13 Wang B B, Wu Y, Fu Q, et al. Establishment and application of a method for determination of serum iothexol concentration by high performance liquid chromatography (in Chinese). *Basic Med Sci Clin*, 2015, 35: 963–967 [王宝宝, 武元, 付强, 等. 高效液相色谱法测定血清碘海醇浓度方法的建立和应用. *基础医学与临床*, 2015, 35: 963–967]
- 14 Wang B B, Wu Y, Qin Y, et al. Application of iothexol clearance rate in the evaluation of renal function in children with chronic kidney disease (in Chinese). *J Chin Aca Med Sci*, 2015, 37: 171–178 [王宝宝, 武元, 秦岩, 等. 碘海醇清除率在慢性肾脏病儿童肾功能评价方面的应用. *中国医学科学院学报*, 2015, 37: 171–178]
- 15 Bosch J P, Saccaggi A, Lauer A, et al. Renal functional reserve in humans. *Am J Med*, 1983, 75: 943–950
- 16 Spinelli A, Sharma A, Villa G, et al. Rationale for the evaluation of renal functional reserve in living kidney donors and recipients: a pilot study. *Nephron*, 2017, 135: 268–276
- 17 Fliser D, Zeier M, Nowack R, et al. Renal functional reserve in healthy elderly subjects. *JASN*, 1993, 3: 1371–1377
- 18 Zhao B B. Clinical characteristics and risk factors of secondary renal proximal tubule injury (in Chinese). Dissertation for Doctoral Degree. Beijing: Peking Union Medical College, 2020 [赵冰彬. 继发性肾脏近端小管损伤的临床特点及危险因素研究. 博士学位论文. 北京: 北京协和医学院, 2020]
- 19 Wang L, Xia P, Lv K, et al. Assessment of renal tissue elasticity by acoustic radiation force impulse quantification with histopathological correlation: preliminary experience in chronic kidney disease. *Eur Radiol*, 2014, 24: 1694–1699
- 20 Wang L, Lu K, Chen L M, et al. Application of acoustic palpation tissue quantification technology in IgA nephropathy (in Chinese). *Med J PUMC*, 2014, 5: 50–53 [王亮, 吕珂, 陈丽萌, 等. 声触诊组织定量技术在IgA肾病的应用. *协和医学杂志*, 2014, 5: 50–53]
- 21 Liu Y, Zhang G M Y, Peng X, et al. Diffusional kurtosis imaging in assessing renal function and pathology of IgA nephropathy: a preliminary clinical study. *Clin Radiol*, 2018, 73: 818–826
- 22 Zhang G, Liu Y, Sun H, et al. Texture analysis based on quantitative magnetic resonance imaging to assess kidney function: a preliminary study. *Quant Imag Med Surg*, 2021, 11: 1256–1270

- 23 Read B E. The secretion of urine in the camel. *Chin Medial J*, 1920, 34: 18
- 24 Gowda S, Desai P B, Kulkarni S S, et al. Markers of renal function tests. *N Am J Med Sci*, 2010, 2: 170–3
- 25 Zheng F L. Prevent missed diagnosis and misdiagnosis of renal tubular acidosis (in Chinese). *Clin Misdiagn Misther*, 1987: 48–49 [郑法雷. 防止肾小管酸中毒漏诊、误诊. 临床误诊误治, 1987: 48–49]
- 26 Shi X, Chen Z, Wang J, et al. Primary Sjögren's syndrome with renal Fanconi syndrome: good responses to treatment with glucocorticoids. *Semin Arthritis Rheumatism*, 2020, 50: 1326–1332
- 27 Peng X, Zhao B, Zhang L, et al. Hydrochlorothiazide test as a tool in the diagnosis of gitelman syndrome in Chinese patients. *Front Endocrinol*, 2018, 9: 559
- 28 Peng X Y, Jiang L P, Yuan T, et al. Application of chloride ion scavenging test in the differential diagnosis of Gitelman syndrome (in Chinese). *J Chin Acad Med Sci*, 2016, 38: 275–782 [彭晓艳, 蒋兰萍, 袁涛, 等. 氯离子清除试验在Gitelman综合征鉴别诊断中的应用. 中国医学科学院学报, 2016, 38: 275–782]
- 29 Xu L B. Genetic diagnosis and clinical characterization of familial renal glucosuria (in Chinese). Dissertation for Doctoral Degree. Beijing: Peking Union Medical College, 2017 [徐鲁斌. 家族性肾性糖尿基因与功能诊断方法建立及临床应用. 博士学位论文. 北京: 北京协和医学院, 2017]
- 30 Christison R. On Granular Degeneration of the Kidnies and Its connexions With Dropsy Inflammations and Other Diseases. Edinburgh: Black, 1839
- 31 Erslev A. Humoral regulation of red cell production. *Blood*, 1953, 8: 349–357
- 32 Jacobson L O, Goldwasser E, Fried W, et al. Role of the kidney in erythropoiesis. *Nature*, 1957, 179: 633–634
- 33 Hanna R M, Streja E, Kalantar-Zadeh K. Burden of anemia in chronic kidney disease: beyond erythropoietin. *Adv Ther*, 2021, 38: 52–75
- 34 Babitt J L, Lin H Y. Mechanisms of anemia in CKD. *JASN*, 2012, 23: 1631–1634
- 35 Semenza G L, Wang G L. A nuclear factor induced by hypoxia *via de novo* protein synthesis binds to the human erythropoietin gene enhancer at a site required for transcriptional activation. *Mol Cell Biol*, 1992, 12: 5447–5454
- 36 2021 NMA. The Nobel Prize in Physiology or Medicine 2019
- 37 Liu S H, Chu H I. Treatment of renal osteodystrophy with dihydrotachysterol (A.T.10) and Iron. *Science*, 1942, 95: 388–389
- 38 Summary of Chinese guidelines for the diagnosis and treatment of mineral and bone disorders in chronic kidney disease (in Chinese). *J Nephrol Dial Kid Transpl*, 2019, 28: 52–57 [中国慢性肾脏病矿物质和骨异常诊治指南概要. 肾脏病与透析肾移植杂志, 2019, 28: 52–57]
- 39 Moe S, Drüeke T, Cunningham J, et al. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*, 2006, 69: 1945–1953
- 40 Covic A, Vervloet M, Massy Z A, et al. Bone and mineral disorders in chronic kidney disease: implications for cardiovascular health and ageing in the general population. *Lancet Diabetes Endocrinol*, 2018, 6: 319–331
- 41 Chen L M, Huang Y N, Schnermann J. The effect of $\beta 1/\beta 2$ adrenergic receptor gene deletion on the secretion of renin in the granular cells of the renal paraglobular apparatus (in Chinese). *Chin J Nephrol*, 2007, 23: 722–727 [陈丽萌, 黄宇宁, Schnermann J. $\beta 1/\beta 2$ 肾上腺素能受体基因缺失对肾脏球旁器颗粒细胞肾素分泌的影响. 中华肾脏病杂志, 2007, 23: 722–727]
- 42 Chen L M, Huang Y N, Qin Y, et al. The role of prostaglandin E2 in regulating the secretion of renin in the paraglomerular organs (in Chinese). *Chin J Nephrol*, 2009, 23: 217 [陈丽萌, 黄宇宁, 秦岩, 等. 前列腺素 E2 在肾脏球旁器调节肾素分泌中的作用. 中华肾脏病杂志, 2009, 23: 217]
- 43 Chen L M, Huang Y N, Qin Y. Study on the mechanism of angiotensin II regulating the synthesis of renin by granular cells of the renal paraglobular apparatus (in Chinese). *Chin J Nephrol*, 2010, 26: 28–33 [陈丽萌, 黄宇宁, 秦岩. 血管紧张素 II 调节肾脏球旁器颗粒细胞合成肾素的机制研究. 中华肾脏病杂志, 2010, 26: 28–33]
- 44 Chen L, Kim S M, Eisner C, et al. Stimulation of renin secretion by angiotensin II blockade is Gs- α -dependent. *JASN*, 2010, 21: 986–992
- 45 Chen L, Faulhaber-Walter R, Wen Y, et al. Renal failure in mice with Gs- α deletion in Juxtaglomerular cells. *Am J Nephrol*, 2010, 32: 83–94
- 46 Tian D, Shi X, Zhao Y, et al. The effect of A1 adenosine receptor in diabetic megalin loss with caspase-1/IL18 signaling. *DMSO*, 2019, 12: 1583–1596
- 47 Zhao L, Cao X, Li L, et al. Acute kidney injury sensitizes the brain vasculature to ang II (angiotensin II) constriction *via* FGFBP1 (fibroblast growth factor binding protein 1). *Hypertension*, 2020, 76: 1924–1934

- 48 Cameron J S. The prehistory of haemodialysis as a treatment for uraemia. *G Ital Nefrol*, 2016, 33: 33.S66.2
- 49 Lim R K S, Necheles H. Demonstration of a gastric secretory excitant in circulating blood by vivi-dialysis. *Exp Biol Med*, 1926, 24: 197–198
- 50 Necheles H. A method of vivi-dialysis. *Chin J Physiol*, 1927, 1: 69–80
- 51 Lim R K S, Necheles H. Recovery of a pancreatic secretory excitant by vivi-dialysis of the circulating blood. *J Physiol*, 1927, 64: 28–9
- 52 Gottschalk C W, Fellner S K. History of the science of dialysis. *Am J Nephrol*, 1997, 17: 289–298
- 53 Wang Z G. The development history and current status of blood purification therapy (in Chinese). In: *Blood Purification*, 4th ed. Beijing: Beijing Science and Technology Publishing Co. Ltd., 2016. 1–3 [王质刚. 血液净化疗法的发展历史和现状. 见: 血液净化学(第四版). 北京: 北京科学技术出版社, 2016. 1–3]
- 54 Cai G Y. Current status and challenges of patients with end-stage renal disease in China (in Chinese). In: Chen J H, Liu B C, eds. *Advances in Nephrology*. Beijing: Chinese Medical Multimedia Press, 2020. 20–25 [蔡广研. 中国终末期肾病患者登记现状与挑战. 见: 陈江华, 刘必成, 编. 肾脏病学进展. 北京: 中华医学电子音像出版社, 2020. 20–25]
- 55 Trinh E, Chan C T, Perl J. Dialysis modality and survival: done to death. *Semin Dial*, 2018, 31: 315–324
- 56 Brown E A, Perl J. Increasing peritoneal dialysis use in response to the COVID-19 pandemic: will it go viral? *JASN*, 2020, 31: 1928–1930
- 57 National Kidney Disease Medical Quality Control Center. Expert advice for the prevention and control of new coronavirus pneumonia in the hemodialysis center (in Chinese). <http://www.cnrd.net/>, 2020 [国家肾脏病医疗质量控制中心. 血液透析室(中心)防控新型冠状病毒肺炎疫情的专家建议. <http://www.cnrd.net/>, 2020]
- 58 Xia P, Wen Y, Duan Y, et al. Clinicopathological features and outcomes of acute kidney injury in critically ill COVID-19 with prolonged disease course: a retrospective cohort. *JASN*, 2020, 31: 2205–2221
- 59 Chen G, Zhou Y, Zhang L, et al. Core principles for infection prevention in hemodialysis centers during the COVID-19 pandemic. *Infect Control Hosp Epidemiol*, 2020, 41: 865–866
- 60 Chen G, Hu R, Wang Y, et al. Recommendation from Peking Union Medical College Hospital for urgent hemodialysis during the COVID-19 pandemic. *Int Urol Nephrol*, 2020, 52: 1809–1810
- 61 Ma J, Xia P, Zhou Y, et al. Potential effect of blood purification therapy in reducing cytokine storm as a late complication of critically ill COVID-19. *Clin Immunol*, 2020, 214: 108408
- 62 Wang Y, Chen L M. History and application status of automated peritoneal dialysis (in Chinese). *J Clin Nephrol*, 2017, 17: 580–584 [王颖, 陈丽萌. 自动化腹膜透析的历史与应用现状. 临床肾脏病杂志, 2017, 17: 580–584]
- 63 Wang Y, Wang H Y, Xia P, et al. Prognostic analysis of assisted peritoneal dialysis (in Chinese). *J Clinical Nephrol*, 2020, 20: 357–363 [王颖, 王海云, 夏鹏, 等. 辅助腹膜透析的预后分析. 临床肾脏病杂志, 2020, 20: 357–363]
- 64 Xia P, Wang H Y, Li Y, et al. Long-term prognosis analysis of patients with end-stage diabetic nephropathy treated by automated peritoneal dialysis (in Chinese). *Chin Blood Purif*, 2019, 18: 160–165 [夏鹏, 王海云, 黎颖, 等. 自动化腹膜透析治疗终末期糖尿病肾病患者长期预后分析. 中国血液净化, 2019, 18: 160–165]
- 65 Gabriel D P, Caramori J T, Martim L C, et al. High volume peritoneal dialysis vs daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. *Kidney Int*, 2008, 73: S87–S93
- 66 Ponce D, Berbel M N, Abrão J M G, et al. A randomized clinical trial of high volume peritoneal dialysis versus extended daily hemodialysis for acute kidney injury patients. *Int Urol Nephrol*, 2013, 45: 869–878
- 67 El Shamy O, Patel N, Abdelbaset M H, et al. Acute start peritoneal dialysis during the COVID-19 pandemic: outcomes and experiences. *JASN*, 2020, 31: 1680–1682
- 68 Wang Y, Wang H Y, Li Y, et al. Application of automated peritoneal dialysis in emergency dialysis (in Chinese). *Chin Blood Purif*, 2019, 18: 83–89 [王颖, 王海云, 李阳, 李斌, 刘炳岩, 周紫鹏, 等. 自动化腹膜透析在紧急透析中的应用. 中国血液净化, 2019, 18: 83–89]
- 69 Wang Y, Li Y, Wang H, et al. Early-start and conventional-start peritoneal dialysis: a Chinese cohort study on outcome. *Renal Failure*, 2020, 42: 305–313
- 70 Winearls C G, Pippard M J, Downing M R, et al. Effect of human erythropoietin derived from recombinant DNA on the anaemia of patients maintained by chronic haemodialysis. *Lancet*, 1986, 328: 1175–1178
- 71 Zheng F L, Li M X, Shan Y D, et al. The therapeutic effect of domestic recombinant human erythropoietin injection in the treatment of renal anemia (in Chinese). *Chin J Pract Intern Med*, 1998, 18: 726–728 [郑法雷, 李明喜, 单渊东, 等. 国产重组人红细胞生成素注射液治疗肾性贫血的疗效观察. 中国实用内科杂志, 1998, 18: 726–728]

- 72 Drüeke T B, Parfrey P S. Summary of the KDIGO guideline on anemia and comment: reading between the (guide)line(s). *Kidney Int*, 2012, 82: 952–960
- 73 Zheng F L, Li L, Chen Y P, et al. Multi-center clinical trial report on the treatment of renal anemia with recombinant human erythropoietin injection (Ning Hongxin) (in Chinese). *Chin Blood Purif*, 2002, 1: 5–8 [郑法雷, 李莉, 湛贻璞, 等. 应用重组人红细胞生成素注射液(宁红欣)治疗肾性贫血的多中心临床试验报告. *中国 血液净化*, 2002, 1: 5–8]
- 74 Eschbach J W, Egrie J C, Downing M R, et al. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. *N Engl J Med*, 1987, 316: 73–78
- 75 Chen N, Hao C, Liu B C, et al. Roxadustat treatment for anemia in patients undergoing long-term dialysis. *N Engl J Med*, 2019, 381: 1011–1022
- 76 Chen N, Hao C, Peng X, et al. Roxadustat for anemia in patients with kidney disease not receiving dialysis. *N Engl J Med*, 2019, 381: 1001–1010
- 77 Akizawa T, Iwasaki M, Yamaguchi Y, et al. Phase 3, randomized, double-blind, active-comparator (darbepoetin alfa) study of oral roxadustat in CKD patients with anemia on hemodialysis in Japan. *JASN*, 2020, 31: 1628–1639
- 78 Tsubakihara Y, Akizawa T, Nangaku M, et al. A 24-week anemia correction study of daprodustat in Japanese dialysis patients. *Ther Apher Dial*, 2020, 24: 108–114
- 79 Ketteler M, Block G A, Evenepoel P, et al. Diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder: synopsis of the kidney disease: improving global outcomes 2017 clinical practice guideline update. *Ann Intern Med*, 2018, 168: 422–430
- 80 Meng X W, Liu S Q, Guan H, et al. The value of selective internal jugular vein cannulation and blood sampling for iPTH in localization and diagnosis of pathological parathyroid glands (in Chinese). *Chin J Endocr Metabol*, 1989, 1: 11–13 [孟迅吾, 刘书勤, 管珩, 等. 选择性颈内静脉插管取血测iPTH对病变的甲状旁腺定位诊断的价值. *中华内分泌代谢杂志*, 1989, 1: 11–13]
- 81 Zhou Q, Liu S Z, Li F. Parathyroid imaging localization diagnosis of primary hyperparathyroidism (in Chinese). *Chin J Nuclear Med*, 1994, 14: 5–8 [周前, 刘世贞, 李方. 甲状旁腺显像定位诊断原发性甲状旁腺机能亢进. *中华核医学杂志*, 1994, 14: 5–8]
- 82 Zhou Q, Xu J Y, Liu S Z. ⁹⁹Tc m-MIBI imaging for localization and diagnosis of hyperactive ectopic parathyroid glands (in Chinese). *Chin J Nuclear Med*, 2003, 1: 22–24 [周前, 徐竞英, 刘世贞. ⁹⁹Tc m-MIBI显像定位诊断功能亢进性异位甲状旁腺. *中华核医学杂志*, 2003, 1: 22–24]
- 83 Liu Y M, Dang Y H, Huo L, et al. Application study of carbon-11 choline PET/CT imaging in the preoperative diagnosis of difficult cases of primary hyperparathyroidism (in Chinese). *J Chongqing Med Univ*, 2018, 43: 1647–1651 [刘轶敏, 党永红, 霍力, 等. 碳-11胆碱PET/CT显像在原发性甲状旁腺功能亢进疑难病例术前定位诊断中的应用研究. *重庆医科大学学报*, 2018, 43: 1647–1651]
- 84 Chen L M, Hu Z. Clinical Practice of Chronic Kidney Disease with Secondary Hyperparathyroidism (in Chinese). Beijing: People's Medical Publishing House, 2020 [陈丽萌, 胡昭. 慢性肾脏病继发性甲状旁腺功能亢进症临床实践. 北京: 人民卫生出版社, 2020]
- 85 Lamprea-Montealegre J A, Shlipak M G, Estrella M M. Chronic kidney disease detection, staging and treatment in cardiovascular disease prevention. *Heart*, 2021, 107: 1282–1288
- 86 Wang Y, Qin Y, Fan X, et al. Variability in predialysis systolic blood pressure and long-term outcomes in hemodialysis patients. *Kidney Blood Press Res*, 2018, 43: 115–124
- 87 Huang B, Li Z, Wang Y, et al. Effectiveness of self-management support in maintenance haemodialysis patients with hypertension: a pilot cluster randomized controlled trial. *Nephrology*, 2018, 23: 755–763
- 88 Spertus J A, Jones P G, Maron D J, et al. Health status after invasive or conservative care in coronary and advanced kidney disease. *N Engl J Med*, 2020, 382: 1619–1628
- 89 Li Y. Preliminary observation of carbamylated albumin predicting long-term prognosis of peritoneal dialysis patients (in Chinese). Dissertation for Doctoral Degree. Beijing: Peking Union Medical College, 2017 [李阳. 氨甲酰化白蛋白预测腹膜透析患者长期预后的初步观察. 博士学位论文. 北京: 北京协和医学院, 2017]
- 90 Qian Y J, Zheng K, Li X M. Current status and progress of research on cognitive function in patients with chronic kidney disease (in Chinese). *Chin Blood Purif*, 2019, 18: 495–498 [钱玉珺, 郑可, 李雪梅. 慢性肾脏病患者认知功能研究现状及进展. *中国血液净化*, 2019, 18: 495–498]
- 91 Polinder-Bos H A, García D V, Kuipers J, et al. Hemodialysis induces an acute decline in cerebral blood flow in elderly patients. *JASN*, 2018, 29: 1317–1325

- 92 Zheng K, Wang H, Hou B, et al. Malnutrition-inflammation is a risk factor for cerebral small vessel diseases and cognitive decline in peritoneal dialysis patients: a cross-sectional observational study. *BMC Nephrol*, 2017, 18: 366
- 93 Zheng K, Qian Y, Lin T, et al. Carotid intima-media thickness relative to cognitive impairment in dialysis patients, and their relationship with brain volume and cerebral small vessel disease. *Therapeutic Adv Chronic Dis*, 2020, 11: 204062232095335
- 94 Zheng K, Hou B, You H, et al. Brain damage in maintenance hemodialysis patients (in Chinese). *Chin J Nephrol*, 2015, 31: 277–282 [郑可, 候波, 有慧, 等. 维持性血液透析患者的脑部损害. *中华肾脏病杂志*, 2015, 31: 277–282]
- 95 Gardezi A I, Sequeira A, Narayan R. Going home: access for home modalities. *Adv Chronic Kidney Dis*, 2020, 27: 253–262
- 96 Salani M, Roy S, Fissell Iv W H. Innovations in wearable and implantable artificial kidneys. *Am J Kidney Dis*, 2018, 72: 745–751
- 97 Gura V, Beizai M, Ezon C, et al. Continuous renal replacement therapy for end-stage renal disease. The wearable artificial kidney (WAK). *Contrib Nephrol*, 2005, 149: 325–333
- 98 Davenport A, Gura V, Ronco C, et al. A wearable haemodialysis device for patients with end-stage renal failure: a pilot study. *Lancet*, 2007, 370: 2005–2010
- 99 Lee D B N, Roberts M. A peritoneal-based automated wearable artificial kidney. *Clin Exp Nephrol*, 2008, 12: 171–180
- 100 Basile C, Davenport A, Mitra S, et al. Frontiers in hemodialysis: innovations and technological advances. *Artif Organs*, 2021, 45: 175–182
- 101 Islam M, Nishinakamura R. How to rebuild the kidney: recent advances in kidney organoids. *J Biochem*, 2019, 166: 7–12

Evaluation and replacement of renal function: history, advancement, and challenges

YUE Cai & CHEN LiMeng

Department of Nephrology, Peking Union Medical College Hospital; State Key Laboratory of Complex Severe and Rare Diseases; Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

The kidneys are important for the excretion of metabolic and toxic waste from the body, the production of erythropoietin, 1,25-OH-vitamin D, and renin, and the maintenance of the body's water, salt, and acid-base balance. Various primary or secondary kidney diseases can result in a decreased number of nephrons, resulting in the retention of metabolites in the body, abnormal renal endocrine functions, water, electrolyte, and acid-base balance disorders, and even in the progression to end-stage kidney disease (ESKD) with an irreversible decline in renal function. Complete renal function evaluation includes evaluation of the glomerular function, renal tubular function, and endocrine function, which can be used in the early diagnosis of kidney disease, the determination of the stage of kidney diseases, and monitoring of treatment responses. Renal replacement therapy is essential for maintaining life and improving the quality of life in patients with ESKD. This article will briefly review the history and current status of renal function evaluation and replacement therapy.

renal function, renal replacement, chronic kidney disease

doi: [10.1360/SSV-2021-0182](https://doi.org/10.1360/SSV-2021-0182)