Novel techniques and innovation in blood purification: a clinical update from Kidney Disease: Improving Global Outcomes

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Mortality in patients with end-stage renal disease (ESRD) remains unacceptably high. Emerging techniques and advances in dialysis technology have the potential to improve clinical outcomes in the ESRD population. This report summarizes the deliberations and recommendations of a conference sponsored by Kidney Disease: Improving Global Outcomes to address the following questions: (1) what is the appropriate frequency and duration of hemodialysis; (2) how should we optimize water quality and dialysate composition; and (3) what technical innovations in blood purification and bioengineering can result in better clinical outcomes? The conference report will augment our current understanding of clinical practice in blood purification and will pose several high-priority research questions.

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Kidney Disease: Improving Global Outcomes convened a Controversies Conference in Paris from 14 to 15 October 2011, titled 'Novel techniques and innovation in blood purification: How can we improve clinical outcomes in hemodialysis?' The conference, attended by 50 international experts, was designed to establish consensus and directions for optimal modes of blood purification. The plenary session presentations were followed by breakout group discussions to address three specific topic areas: (1) dialysis technique—frequency and duration; (2) dialysate composition and toxins; and (3) technical advances in dialysis. The breakout group deliberations were reported to the entire group, and a consensus-building process led to the clinical practice and research recommendations from the conference attendees, which are the substance of this report. The report was reviewed by all breakout group leaders, cochairs, and representatives of the Kidney Disease: Improving Global Outcomes Board of Directors. The conference agenda, selected presentations, and abstracts of the meeting are available on the Kidney Disease: Improving Global Outcomes website (http://www.kdigo.org/meetings_events/novel_tech.php).

The recent interest in novel techniques and innovation in blood purification was born out of the impasse in an effort to improve survival and quality of life of patients with end-stage renal disease (ESRD). Although there have been medical and technical advances, mortality rate of patients with ESRD remains unacceptably high at about 10–20% per year. To date, most medical interventions have failed to change the survival of ESRD patients.[1,2] It was suggested that the high mortality rate in ESRD was related to poor clearance of uremic toxins within the three-times-a-week paradigm. This hypothesis was tested in the Hemodialysis Study, a randomized controlled study that did not demonstrate a positive effect on patient

survival when dialysis dose was increased from a pretreatment Kt/V of 1.32 to 1.71.[3] Of equal importance is that the Hemodialysis Study did not demonstrate any overall benefit related to the use of high-flux versus low-flux dialyzers.[3] Recently, another randomized trial in Europe, the Membrane Permeability Outcome Study, was unable to show improved survival in all patients treated with high-flux membranes.[4] Although the provision of more intensive conventional hemodialysis has not reduced mortality, more frequent hemodialysis has demonstrated improvements in several clinical surrogate outcomes. Indeed, the Frequent Hemodialysis Network (FHN) Daily Dialysis and the Alberta Kidney Disease Network (AKDN) Trials have reported regression of left ventricular (LV) hypertrophy, improved blood pressure control, and better quality of life.[5–7] Other observational studies have suggested better survival (compared with conventional hemodialysis) with more frequent hemodialysis.[8,9] At the same time, use of convective techniques, such as hemodiafiltration (HDF), has increased and is now common in Europe and in other parts of the world. Survival advantage,[10] hemodynamic stability,[11] and enhanced clearance of small and middle molecules[12] have been reported with the use of HDF, but reports of larger controlled trials in Turkey and the Netherlands have not shown an overall survival advantage.[13,14]

With the increase in the worldwide chronic dialysis population and the growth of renal replacement therapy programs in large countries such as China and India, it has become evident that advances in technology and process are required to facilitate the widespread clinical application of renal replacement therapy. At present, most dialysis machines are not engineered to be used easily by patients. Improved flexibility of a dialysis platform for users with different levels of training and skills will likely transform the clinical landscape of ESRD care. Other novel technical advances in blood purification include application of nanotechnology,[15,16] the use of sorbents to remove uremic toxins and regenerate water for dialysis,[17] 'wearable kidneys,'[18,19] and the incorporation of renal cells as part of a bioartificial kidney.[15,20,21] The clinical applications of novel biomaterials[22] and therapeutic use of endothelial[23] or endothelial progenitor cells[24] may provide much needed innovation in vascular access devices (Figure 1).

HEMODIALYSIS TECHNIQUES: DURATION AND FREQUENCY

Nomenclature

More frequent dialysis than the standard three-times-a-week has been performed since the 1960s;[25–30] however, there is no uniform nomenclature to describe the different types of more frequent hemodialysis. Our group proposes that all hemodialysis prescriptions should be described by indicating both duration of the individual dialysis session and the frequency per week (Table 1).

Other frequencies can also be derived from this nomenclature, such as conventional indicates three times per week,

Table 1 | Descriptive nomenclature for hemodialysis frequency and duration

Conventional hemodialysis	3–5 h per session, three times per week
Short daily hemodialysis	Less than 3 h per session, six times per week
Standard daily hemodialysis	3–5 h per session, six times per week
Long daily hemodialysis	More than 5 h per session, six times per week

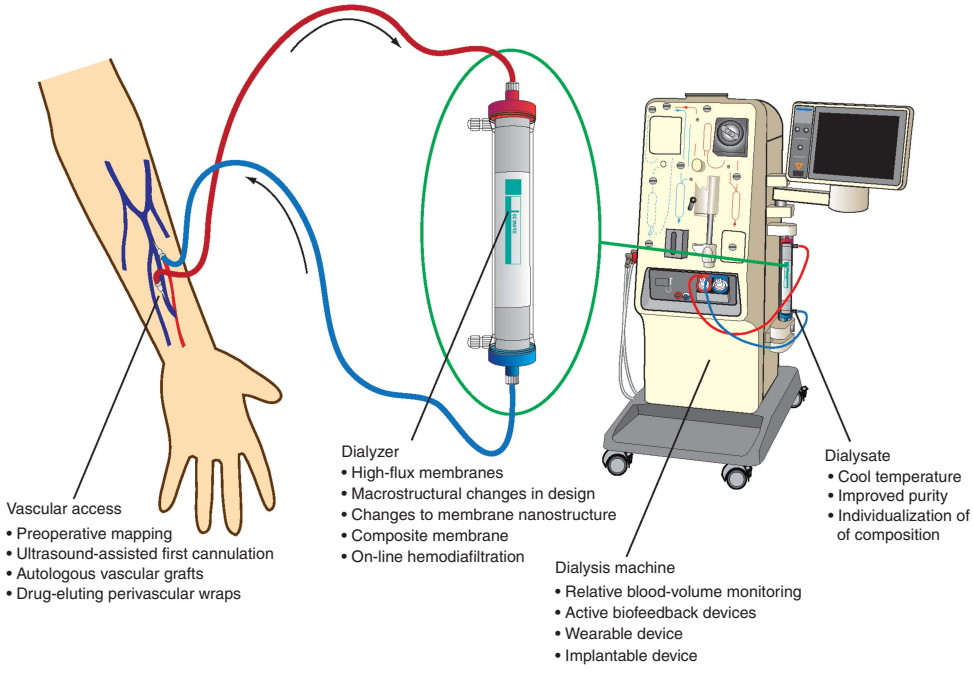

Figure 1 | Innovations in hemodialysis technology.