History of KDIGO

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ture evidence base by identifying the key research agenda.

By 2009 KDIGO had become a global leader in nephrology guidelines designed to inform clinical decisions.

The economic downturn in 2009 and 2010 caused the NKF to rethink its priorities. One area to be cut back was global guidelines. This came at a time when KDIGO's reputation was growing. Two landmark Controversies Conferences were held during this time: Definition, Classification, and Prognosis in CKD, and Cardiovascular Disease in CKD.

KDIGO's Mineral and Bone Disorder guideline created CKD-MBD as a near-universal term and had major global impact, and work began on other new guidelines. In 2011 John Davis left the NKF but retained the title of Chief Executive Officer of KDIGO. A meeting was held in the Netherlands with Bert Kasiske, Kai-Uwe Eckardt, David Wheeler, and John to discuss KDIGO's future. The decision was made to go at it alone. Negotiations began to terminate KDIGO's management contract with the NKF, and plans were made for moving forward. John continued to manage KDIGO and recruited Danielle Green to join him. With great help from Dr. Yusuke Tsukamoto in Tokyo, some money was raised to bridge this critical period of transition.

KDIGO officially became an independent Belgian corporation on October 1, 2012. It had €19,000 in the bank. Bert and David were the co-chairs, with John and Danielle as the staff. A small but excellent executive committee was recruited to provide governance and guidance. KDIGO then began a steady building process that was directed at sustaining its place in global nephrology.

To reassert the organization's standing in the nephrology community, KDIGO published four original guidelines in 2012. Two more guidelines came in 2013, along with two Controversies Conferences. Michael Cheung and Tanya Green were subsequently recruited to the staff, and efforts were made to bring all of KDIGO's operations into full compliance with Belgian regulations and standard nonprofit practices.

KDIGO's goal in those early years was simply to get better every day and to strengthen its independent status. Being self-governed, self-managed, and self-funded were important elements of KDIGO's growth. The guideline on the Evaluation and Care of Living Kidney Donors was the first to be wholly developed under its independence, as was the Controversies Conference on CKD–MBD: Back to the Future, and KDIGO has been remarkably active since then (Table 1).

KDIGO began an emphasis on implementation programs and developed a presence in major congresses, both globally and locally. New volunteers were brought in, and previous volunteers were recognized as members of the KDIGO global network. A reception in Philadelphia in 2015 attracted over 200 people. KDIGO is continuing to be innovative and transparent while experimenting with new technologies like electronic guideline publishing. Naturally, KDIGO also pays more attention to updating its existing guidelines and is increasingly focusing on a more robust and streamlined guideline development process and methodology.

Corporate support has always sustained KDIGO's growth. While KDIGO does not solicit or accept funding for the development of guidelines or its updates, KDIGO has attracted several major sustaining partners which provide the resources needed to conduct all of its programs. KDIGO especially appreciates the long-term commitments of companies like Fresenius, Boehringer-Ingelheim, and AstraZeneca. KDIGO takes pride in our transparency and full disclosure policy while striving to enhance its conflict of interest safeguards.

KDIGO now has three guidelines in development at all times and holds four or five Controversies Conferences each year. Implementation presentations and tools, along with an improved website and app, are part of a concerted effort to make the work more accessible to clinicians everywhere. KDIGO's vision focuses on its core programs while seeking appropriate collaborations and strengthening its volunteer base.

Although still relatively young, KDIGO has come a long way. It has taken a few risks but remains dedicated to its only mission: to improve outcomes for patients. It is with this optimism and commitment that KDIGO builds on the past and looks toward the future with enthusiasm. ■

John Davis is Chief Executive Officer of Kidney Disease: Improving Global Outcomes.

New Guideline Update: Hepatitis C in Patients with Chronic Kidney Disease

By Michel Jadoul

The 2008 KDIGO guideline on the prevention, diagnosis, evaluation, and treatment of hepatitis C virus (HCV) infection in patients with chronic kidney disease (CKD) was the very first guideline produced by KDIGO. Since then, there have been dramatic changes in the field of antiviral treatments, which prompted a timely reassessment and publication of this guideline update in 2018 (1). The purpose of this short review is to summarize the key recommendations from this important guidance document.

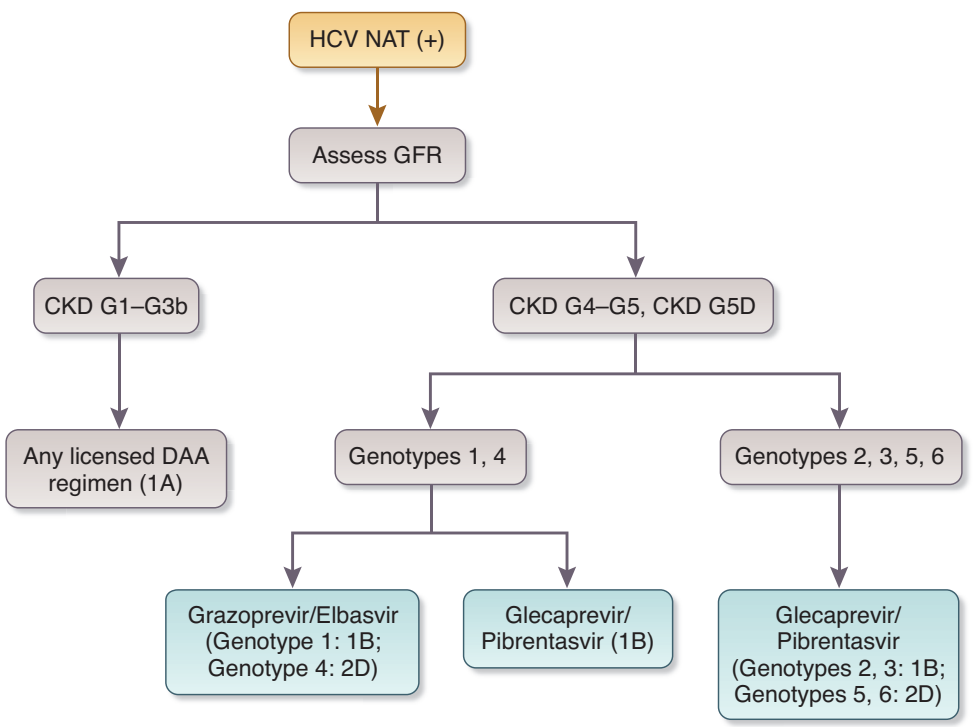
As in the previous guideline edition, Chapter 1 addresses the detection and evaluation of HCV in CKD. It should be stressed that the guideline now recommends that all patients be screened once for HCV at the time of initial CKD evaluation. This new recommendation is based on multiple large observational studies that have consistently identified HCV positivity as a risk factor for adverse clinical outcomes, independently of classic CKD and cardiovascular risk factors. These adverse outcomes include CKD onset, rapid CKD progression, and development of ESKD and cardiovascular complications.

Recent evidence further shows that in patients with various causes of CKD, including diabetic nephropathy or nephrosclerosis, and thus not just HCV-associated membranoproliferative glomerulonephritis, HCV treatment is associated with delayed onset of CKD (2) and cardiovascular complications. The cost of a single immunoassay for HCV thus appears small in comparison with the potential clinical benefit(s). A second key change in this chapter is the recommendation to start investigating HCV-positive patients via non-invasive means such as transient elastography (e.g., FibroScan) and/or biochemical indexes. These have indeed been shown, even in late CKD patients including candidates for kidney transplantation, to accurately quantify noninvasively the extent of liver fibrosis. Thus, a liver biopsy is now required only if there is a high suspicion of another cause of liver disease than HCV, and/or if noninvasive results are discordant (1).

Chapter 2 addresses HCV antiviral treatments, also known as direct-acting antiviral agents (DAAs), which can effectively cure HCV infections in more than 95% of cases over a course of 12 weeks. DAA treatments thus now become the rule rather than the exception in CKD patients as well, if life expectancy is reasonable (no uniform minimum threshold can be proposed, although a life expectancy of at least 12 months appears reasonable). As highlighted in Figure 1, certain DAA regimens can be used even in patients with an eGFR <30 mL/min per 1.73 m^2. Similarly, prevalent kidney transplant recipients can also be treated effectively and safely with DAA regimens (Figure 2), with careful attention to the level of immunosuppressive agents during DAA treatment so as to minimize the risk of drug–drug interactions.

Chapter 3 deals with the prevention of nosocomial HCV

Figure 1. Algorithm showing treatment scheme for chronic kidney disease (CKD) G1 to G5D



Recommendation grades (1–2) and strength of evidence (A–D) are provided for each recommended treatment regimen and hepatitis C virus (HCV) genotype. Pangenotypic sofosbuvir/velpatasvir-based regimens are not listed because they were not formally reviewed by the Evidence Review Team at the time of guideline publication. However, FDA has recently indicated that no dose adjustments are required for these regimens in CKD patients including those on dialysis. These regimens may be considered pending their availability in various jurisdictions. Abbreviations: CKD G, chronic kidney disease GFR category; FDA, Food and Drug Administration; DAA, direct-acting antiviral agent; GFR, glomerular filtration rate; NAT, nucleic acid testing. Reproduced with permission from reference 1.

transmission within hemodialysis units. This risk remains significant, as shown by a very recent Dialysis Outcomes and Practice Patterns Study report (3). Thus, the guideline still recommends meticulous attention to hygienic precautions and regular auditing of infection control procedures. Also, in line with the 2008 KDIGO guideline and the recommendations by the United States Centers for Disease Control and Prevention, the guideline still does not advocate the use of dedicated dialysis machines for HCV-positive patients or the isolation of HCV-positive patients in a specific ward. These are indeed unnecessary and may tend to reduce the attention devoted to proper infection control practices.

Chapter 4 addresses the management of HCV before and after kidney transplantation. The key point here is that as a result of the ongoing opioid epidemic, there is currently a significant number of HCV-positive organs available for transplantation, whose acceptance by HCV positive recipients may markedly shorten their waiting time for a graft. This calls for a collaboration with transplantation centers in decisions about the timing of HCV treatment in potential candidates for a kidney transplant.

The decision to treat HCV before versus after kidney transplantation will therefore be dependent on the severity of liver disease (which may prompt a simultaneous kidney-liver transplantation in cases of decompensated cirrhosis) but will also be markedly influenced by the expected waiting time for a kidney graft, as detailed in Figure 3. Interestingly, recent evidence shows that HCV-negative recipients who are willing to accept HCV-positive organs may also undergo transplantation much more rapidly than otherwise and have good outcomes. However, given the unknown long-term safety of this approach, the KDIGO Work Group thought that this practice should remain strictly investigational pending further studies.

Chapter 5 discusses the management and treatment of HCV-associated glomerulonephritis. In patients with rapidly progressive glomerulonephritis, severe cryoglobulinemia or nephrotic syndrome, the guideline now recommends immunosuppressive treatment with rituximab in addition to DAA treatment. This recommendation is based on two randomized controlled trials, admittedly relatively small, demonstrating the efficacy and superiority of rituximab over alternative regimens (5).

Over the past decade, remarkable progress has been achieved in the management of HCV. The shift from weaker guideline statements a decade ago to the present strong recommendations on HCV treatment can be attributed to the arrival of these highly effective and well-tolerated DAA regimens. As such, this is the right time for nephrologists to greatly reduce the burden of HCV in CKD patients in line with the World Health Organization's commitment to eliminate viral hepatitis as a significant public health problem by 2030 (6). ■

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References

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2. Park H, et al. Chronic hepatitis C virus (HCV) increases the risk of chronic kidney disease (CKD) while effective HCV treatment decreases the incidence of CKD. *Hepatology* 2018; 67:492–504.
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5. De Vita S, et al. A randomized controlled trial of rituximab for the treatment of severe cryoglobulinemic vasculitis. *Arthritis Rheum* 2012; 64:843–853.
6. Towards elimination of viral hepatitis by 2030. *Lancet* 2016; 388:308.

Figure 2. Algorithm showing treatment scheme for kidney transplant recipients (KTRs)

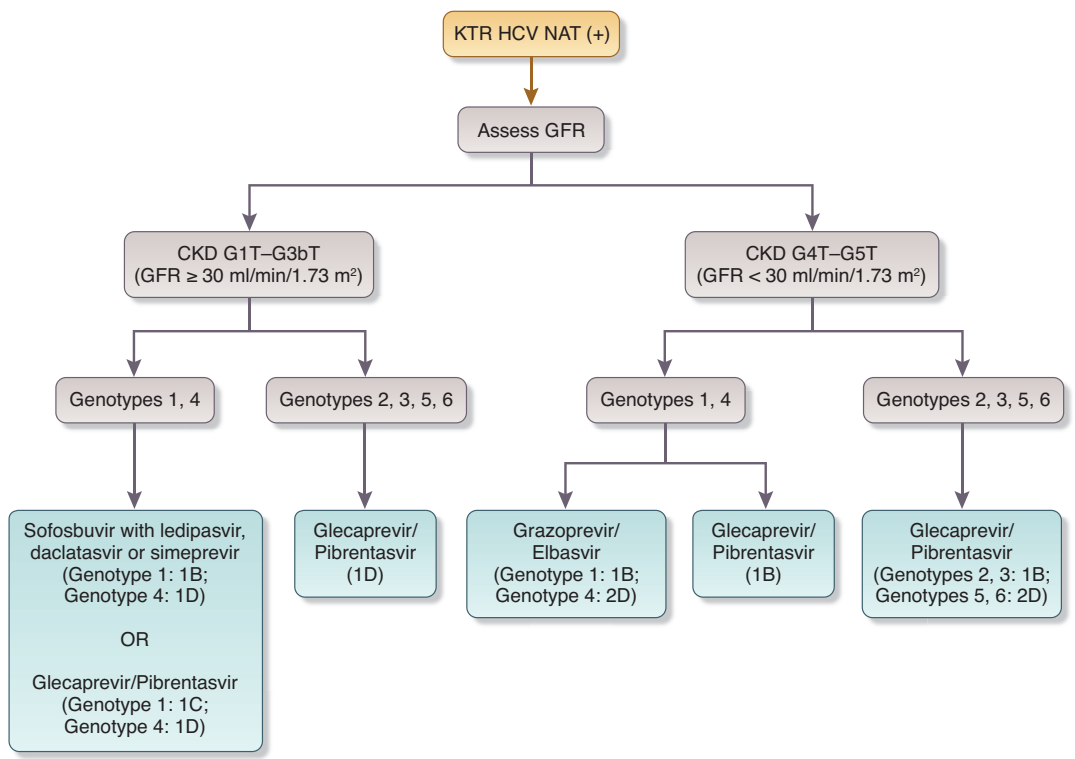

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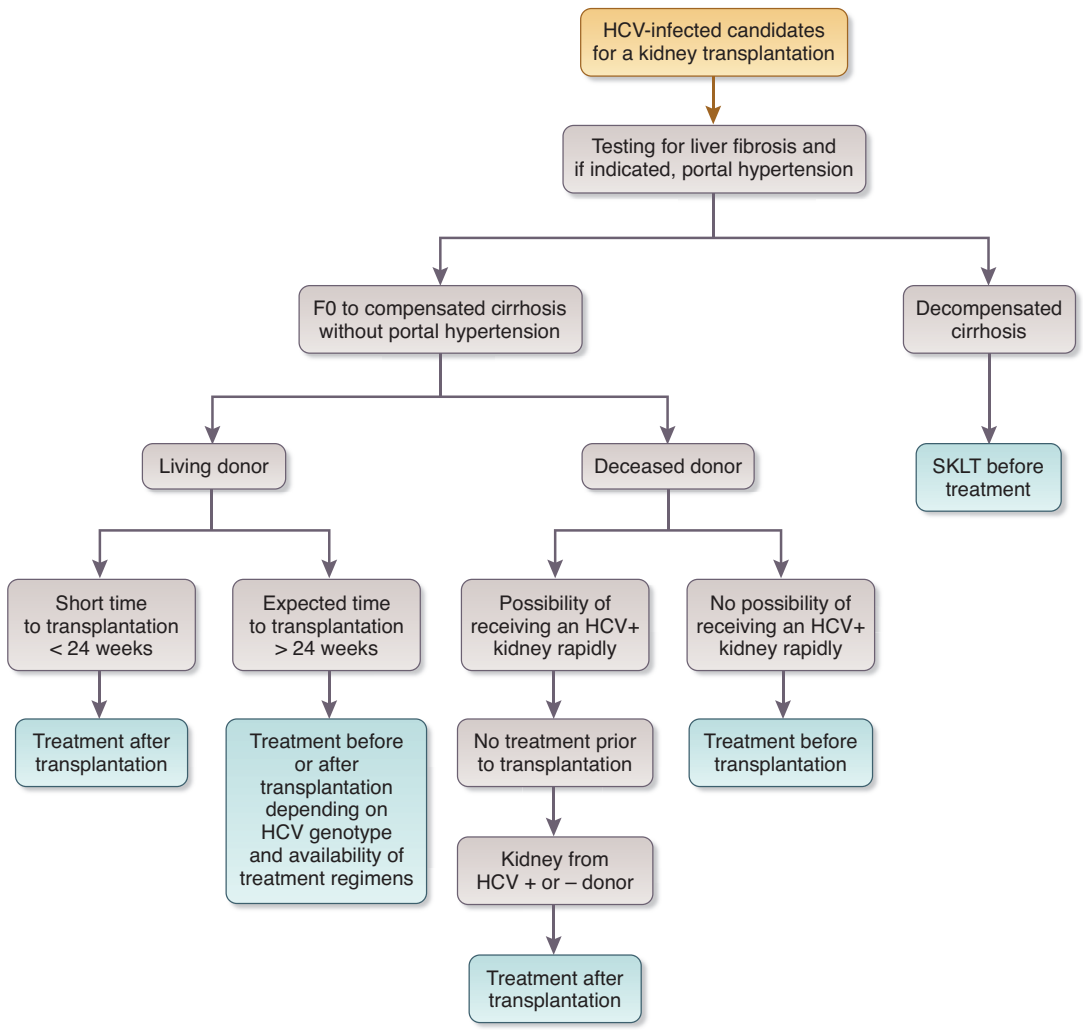
Figure 3. Algorithm showing proposed strategy in a kidney transplantation candidate infected with hepatitis C virus (HCV)



Abbreviation: SKLT, simultaneous kidney-liver transplantation. Reproduced with permission from reference 1.