baseline.[8] They reported a higher incidence of acute kidney injury (AKI) with TVR/BOC (N=34/193; 17.6%) than SOF containing regimens (N=26/233; 11.2%). Not surprisingly, univariable logistic regression analyses showed that decompensated cirrhosis, presence of ascites, hypertension, and the use of NSAIDs and diuretics were associated with AKI. The episodes of AKI in general were mild and most resolved (N=51/59; 86.4%) with serum creatinine (SCr) returning to baseline at the end of the follow-up approximately 12 weeks after end of therapy. The majority of the patients in SOF group who experienced AKI (N=17/26; 65%) were cirrhotics and 42% (N=11/26) had decompensated cirrhosis. Three patients in SOF group (1.3%) did not recover their renal function. Two of these patients had impaired renal function at baseline (eGFR 37.9 and 55.1 mL/min) while the other patient had a mild stage 1 AKI with SCr increase of 0.3 mg/dL (26mcg/L) over the baseline.

Despite, its widespread use, sofosbuvir has not been reliably linked to AKI. The study by Manns et al. is important as it examines the incidence of AKI in patients treated with sofosbuvir with normal renal function and it is reassuring that AKI is an infrequent complication. Although mild and mostly reversible, AKI episodes were more frequent in patients with decompensated cirrhosis. It is possible that AKI was a complication of advanced cirrhosis and not necessarily caused by sofosbuvir. Regardless, this study re-enforces that HCV therapy in patients with decompensated cirrhosis require careful monitoring and frequent assessment of renal function.

ACKNOWLEDGEMENTS

Declaration of personal interests: Dr. Hussaini does not have any disclosures. Dr. Yoshida has been an investigator of hepatitis C clinical trials sponsored by Gilead Sciences, Merck Inc, AbbVie Inc and Janssen Inc. He has received honoraria for CME/Ad Board lectures sponsored by Gilead Canada, Merck Canada and AbbVie Canada.

FUNDING INFORMATION

None.

LINKED CONTENT

This article is linked to Maan et al papers. To view these articles visit https://doi.org/10.1111/apt.14117 and https://doi.org/10.1111/apt.14187.

T. Hussaini[1]
E. M. Yoshida[2]
[1]*Department of Pharmacy, Vancouver General Hospital, Vancouver, BC, Canada*
[2]*Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada*
Email: eric.yoshida@vch.ca

REFERENCES

1. Maruyama A, Partovi N, Yoshida EM, Erb SR, Azalgara VM, Hussaini T. A review of direct-acting antivirals for the treatment of hepatitis C in patients with advanced chronic kidney disease. *Nephrol Dial Transplant*. 2017;32:35-41.
2. Hull MW, Yoshida EM, Montaner JS. Update on current evidence for hepatitis C therapeutic options in HCV mono-infected patients. *Curr Infect Dis Rep*. 2016;18:22.
3. Product Monograph. PrSOVALDI® (sofosbuvir) Tablets400 mg sofosbuvir Antiviral Agent. http://www.gilead.ca/pdf/ca/sovaldi_pm_english.pdf Accessed April 25, 2017.
4. Kirby BJ, Symonds WT, Kearney BP, Mathias AA. Pharmacokinetic, pharmacodynamic, and drug-interaction profile of the hepatitis C virus NS5B polymerase inhibitor sofosbuvir. *Clin Pharmacokinet*. 2015;54:677-690.
5. Safety and Efficacy of Sofosbuvir-Containing Regimens in Hepatitis C Infected Patients with Reduced Renal Function: Real-World Experience from HCV-TARGET. http://www.natap.org/2015/EASL/EASL_115.htm Accessed April 30, 2017.
6. Roth D, Nelson DR, Buruchfeld A, et al. Grazoprevir plus elbasvir in treatment-naïve and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4-5 chronic kidney disease (the C-Surfer Study): a combination phase 3 study. *Lancet*. 2015;386:1537-1545.
7. Gane E, Lawitz E, Pugatch D, et al. EXPEDITION IV: safety and efficacy of GLE/PIB in adults with renal impairment and chronic hepatitis C virus genotypes 1-6 infection. *Hepatology*. 2016;64:1118A-1140A.
8. Maan R, Al Marzooqi SH, Klair JS, et al. The frequency of acute kidney injury in patients with chronic hepatitis C virus infection treated with sofosbuvir-based regimens. *Aliment Pharmacol Ther*. 2017;46:46-55.

DOI: 10.1111/apt.14187

Editorial: hepatitis C direct acting antiviral agents and the kidney—authors' reply

We thank Drs. Hussaini and Yoshida for their insightful comments regarding our paper.[1,2] Our research question derived from the clinical observation of patients developing acute kidney injury (AKI) while on direct-acting antiviral (DAA) regimens, followed by reversal of kidney dysfunction when other potentially nephrotoxic drugs were removed (eg diuretics, NSAID's, ACE inhibitors). Although the comparison of sofosbuvir (SOF)-based regimens with antivirals now discontinued from the market (ie boceprevir [BOC] and telaprevir [TPV]) is perhaps not ideal, our intention was to use BOC/TPV as a reference, particularly since these regimens were linked to AKI in postmarketing surveillance publications. Our results showed that SOF-based regimens are less prone to causing AKI than BOC/TPV

despite the fact that we treated sicker patients at high risk of renal injury in the SOF era. We found very few cases of significant and irreversible SOF-induced AKI and as Drs. Hussaini and Yoshida clearly pointed out, when AKI occurred, it was most commonly noted in patients with more advanced liver disease or having other risk factors for nephrotoxicity. Our data suggest that although the overall the risk of AKI with SOF-based therapy is low, kidney function monitoring remains important in patients with higher baseline risk for AKI.

ACKNOWLEDGEMENTS

The authors' declarations of personal and financial interests are unchanged from those in the original article.[2]

LINKED CONTENT

This article is linked to Maan et al, and Hussaini and Yoshida papers. To view these articles visit https://doi.org/10.1111/apt.14117 and https://doi.org/10.1111/apt.14161.

R. Maan[1]
J. J. Feld[2]
A. Duarte-Rojo[3]
[1]*Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands*
[2]*Toronto Centre for Liver Disease, Sandra Rotman Centre for Global Health, University of Toronto, Toronto, Canada*
[3]*Division of Gastroenterology and Hepatology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA*
Email: aduarterojo@uams.edu

REFERENCES

1. Hussaini T, Yoshida E. Editorial: hepatitis C direct acting antiviral agents and the kidney. *Aliment Pharmacol Ther*. 2017;46:378-379.
2. Maan R, Al Marzooqi SH, Klair JS, et al. Frequency of acute kidney injury in patients with chronic hepatitis C virus infection treated with sofosbuvir-based regimens. *Aliment Pharmacol Ther*. 2017;46:46-55.