mg of dry liver is ~7 g of mobilized excess iron (Figure 1, dashed line), whereas 21 μmol/100 mg dry liver is ~14 g (Figure 1, solid lines). If we solve using the regression equation of Brissot *et al.*[2] (LIC = (1.3 × mobilized excess iron) + 3.5), then the TBI is 7.3 g and 13.6 g, respectively, for these 2 examples. Based on Rottembourg's expected hemodialysis annual blood losses,[3] (1.68 g/yr), patients with severe iron overload by MRI-LIC would take at least 8.0 years to normalize their LIC, and yet Rostoker's group[4] reports that they did this in 10 to 12 months.

Additionally, Figure 2 of Brissot *et al*. demonstrates that semiquantitative histologic estimates of LIC, as Rostoker used in another publication, frequently overestimate the actual LIC.[2,6] At least one-half of the grade 2 LIC estimates had normal actual LIC, whereas ~15% of grade 3 LIC estimates had normal LIC, and many others should have been categorized as grade 2.[2]

In summary, these data indicate that MRI-LIC measurement in dialysis patients overestimates TBI by a factor of 10 when applying Brissot's equation, whereas I conservatively estimated that they were off by a factor of 3 to 6.[2,7] Brissot also demonstrates that histologic assessments of LIC are inferior to actual determinations.[2] I could not have made my points any better.

1. Rottembourg J. Other estimation of blood losses in hemodialysis and formula for translating liver iron concentration from iron balance calculation based on iron removal by phlebotomy. *Kidney Int Rep*. 2018;3:220.
2. Brissot P, Bourel M, Herry D, et al. Assessment of liver iron content in 271 patients: a reevaluation of direct and indirect methods. *Gastroenterology*. 1981;80:557–565.
3. Rottembourg J, Rostoker G. [Use of intravenous iron supplementation in chronic kidney disease: Interests, limits, and recommendations for a better practice]. *Nephrol Ther*. 2015;11:531–542.
4. Rostoker G, Griuncelli M, Loridon C, et al. Hemodialysis-associated hemosiderosis in the era of erythropoiesis-stimulating agents: a MRI study. *Am J Med*. 2012;125:991–999.e1.
5. Issad B, Ghali N, Beaudreuil S, et al. Hepatic iron load at magnetic resonance imaging is normal in most patients receiving peritoneal dialysis. *Kidney Int Rep*. 2017;2:1219–1222.
6. Rostoker G, Laroudie M, Blanc R, et al. Signal-intensity-ratio MRI accurately estimates hepatic iron load in hemodialysis patients. *Heliyon*. 2017;3:e00226.
7. Coyne DW. Iron overload in dialysis patients: rust or bust? *Kidney Int Rep*. 2017;2:995–997.

Daniel W. Coyne[1]

[1]Division of Nephrology, Washington University, St. Louis, Missouri, USA

Correspondence: Daniel W. Coyne, Division of Nephrology, Washington University, St. Louis, Missouri 63110-1093, USA. E-mail: dcoyne@wustl.edu

Received 21 November 2017; accepted 21 November 2017; published online 1 December 2017

Kidney Int Rep (2018) **3,** 220–222; https://doi.org/10.1016/j.ekir.2017.11.011

American Geriatrics Society Beers Criteria and Anticoagulant Use in Older Adults With Renal Impairment

To the Editor: We are writing you regarding the 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[1] Specifically, this letter is in reference to the use of oral anticoagulants based on creatinine clearance (CrCl) thresholds in this population.

The 2015 criteria provide, for the first time, recommendations on the use of the newer oral anticoagulants (e.g., rivaroxaban, apixaban, edoxaban, dabigatran). The recommendations are provided in Table 6 of the criteria and ultimately direct physicians to either "Avoid" or use a "Reduced dose" for these therapies based on the patient's CrCl. Although most of the recommendations made in these criteria are based on evidence from literature searches, the CrCl thresholds listed for these newer oral anticoagulants are based on the respective Phase 3 clinical trial exclusion criteria, which may not match the actual prescribing direction provided in the labels.

For example, this is evident in the recommendation for rivaroxaban (XARELTO), and patients with atrial fibrillation with a CrCl <30 ml/min. The Beers criteria state that this compound should be avoided in this patient category, whereas the XARELTO package insert, based on clinical trial data, allows for a reduced dose (15 mg) in these patients. It should be noted that the 15-mg dose of rivaroxaban was a dedicated dose for those patients with a CrCl of 30 to 50 ml/min studied in the Phase 3 ROCKET-AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation), a dose paradigm that is unique to XARELTO. Although the 15-mg dose was not studied in those patients with a CrCl of ≤30 ml/min, the pharmacokinetic and pharmacodynamic profile

assessed in clinical pharmacology studies supported the use of this dose strength, as it is expected to result in serum concentrations of XARELTO similar to those observed in the ROCKET trial.[2–4]

The authors point out that the American Geriatrics Society Beers criteria "*are an essential evidence-based tool to use in decision making*"[1]; however, for the renally impaired atrial fibrillation population, the recommendation does not appear to be "evidence based," as it does not consider the wealth of data collected from clinical trials or the real-world evidence collected since these medicines have been made available. The abundance of real-world evidence data continues to support the claims made in the rivaroxaban label.

In this case, the American Geriatrics Society Beers criteria may put patients at greater risk for a serious adverse event (e.g., loss of efficacy) that would have a greater clinical significance than the risk listed as the rationale for why the criteria should be applied. Although the criteria do state that "*they are not meant to override clinical judgement or an individual's preferences, values and needs,*"[1] these criteria are commonly followed by physicians, hospitals, and various national compendia, which again, many times do not reflect the current available data or the label.

Last, when giving the recommendation to reduce the dose, the criteria fail to provide the actual dose that should be given, leaving the practitioner questioning which dose would be appropriate, as the rest of the criteria may not follow the current label. Considering the potential risk for adverse events based on a lack of actual evidence and practitioner confusion, the criteria should be modified to better reflect the wealth of data obtained to date from clinical trial experience, real-world evidence, and the currently approved labels.

DISCLOSURE

KTM and JF are employees of Janssen Pharmaceuticals, Inc.

ACKNOWLEDGMENTS

Financial support was provided by Janssen Pharmaceuticals, Inc.

SUPPLEMENTARY MATERIAL

Table 6. 2015 American Geriatrics Society Beers Criteria for non–anti-infective medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults. Reprinted from the "American Geriatrics Society 2015 Beers Criteria Update Expert Panel": Table 6. 2015. Reproduced with permission from American Geriatrics Society.[1]

Supplementary material is linked to the online version of the paper at www.kireports.org.

1. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2015;63:2227–2246.
2. XARELTO [package insert]. Titusville, NJ: Janssen Pharmaceuticals; revised 03/2017.
3. Kubitza D, Becka M, Mueck W, et al. Effects of renal impairment on the pharmacokinetics, pharmacodynamics and safety of rivaroxaban, an oral, direct factor Xa inhibitor. *Br J Clin Pharmacol*. 2010;70:703–712.
4. Dias C, Moore KT, Murphy J, et al. Pharmacokinetics, pharmacodynamics, and safety of single-dose rivaroxaban in chronic hemodialysis. *Am J Nephrol*. 2016;43:229–236.

JoAnne Foody[1] and Kenneth Todd Moore[1]

[1]Janssen Pharmaceuticals, Inc, Titusville, New Jersey, USA
Correspondence: Kenneth Todd Moore, Janssen Pharmaceuticals, Inc., 1125 Trenton-Harbourton Road, Titusville, New Jersey 08560, USA. E-mail: Tmoore17@its.jnj.com

Received 19 October 2017; revised 6 November 2017; accepted 13 November 2017; published online 4 December 2017

Kidney Int Rep (2018) **3,** 222–223; https://doi.org/10.1016/j.ekir.2017.11.006