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# Renal replacement therapy may be initiated in patients with hepatorenal syndrome who are not transplant candidates

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**ABSTRACT** A clinical decision report using:

Allegretti AS, Parada XV, Eneanya ND, et al. Prognosis of Patients with Cirrhosis and AKI Who Initiate RRT. *Clin J Am Soc Nephrol.* 2018;13(1):16-25. <https://doi.org/10.2215/CJN.03610417>

for a patient being considered for RRT who was not yet a candidate for liver transplant.

**Keywords:** *hepatorenal syndrome, renal replacement therapy, liver transplant, alcoholic cirrhosis*

## Clinical-Social Context

Jennifer Smith (pseudonym) is a 41-year-old white female who was transferred to our tertiary care center after a lengthy stay at an outside hospital for acute decompensated alcoholic liver cirrhosis. Her course was complicated by spontaneous bacterial peritonitis, ascites, and hepatorenal syndrome (HRS) type 1. Prior to her admission she worked as a real estate agent and enjoyed spending time with her husband and 7-year-old daughter.

Mrs. Smith admitted to drinking a pint of liquor a day. About five years ago, her primary care provider had advised her to stop drinking after her liver enzymes came back elevated. She had a remote history of two DUIs for which she successfully completed court mandated rehabilitation. However, after the death of her mother two years prior to her presentation, she had a relapse in her drinking. She had attempted to quit on her own for short periods of time, but “life got stressful” according to Mrs. Smith. Her last drink was the day she presented to the outside hospital.

Despite all of this, Mrs. Smith was “shocked” to find herself in this position. She had been healthy, active and had no prior medical conditions, giving her no reason to think that her drinking was life threatening. When she arrived at our center, Mrs. Smith’s liver was failing, and she had a MELD score of 36. Liver transplant policy at our institution mandated six months sobriety before consideration, however her concurrent HRS diagnosis meant this was time Mrs. Smith didn’t have.<sup>1</sup> She did not respond to maximum doses of recommended midodrine, albumin, and octreotide and she felt hopeless as she is not yet a transplant candidate. For patients with HRS, renal replacement therapy (RRT) is usually considered as a bridge to transplant for people who have already been listed. Intermittent hemodialysis (iHD) comes with increased risk in this population due to hemodynamic instability.<sup>2</sup> Because Mrs. Smith is young and was in prior good health, should she be offered iHD even though she is not a

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transplant candidate? With her young daughter at home, Mrs. Smith was desperate to increase her chances of survival, but could dialysis cause quicker decompensation? With these questions in mind, a literature review and critical appraisal was performed to better educate Mrs. Smith and her family on her options.

## Clinical Question

Should renal replacement therapy be initiated in patients with hepatorenal syndrome who are not yet liver transplant candidates to improve chances of survival?

## Research Article

Allegretti AS, Parada XV, Eneanya ND, et al. Prognosis of Patients with Cirrhosis and AKI Who Initiate RRT. *Clin J Am Soc Nephrol.* 2018;13(1):16-25. <https://doi.org/10.2215/CJN.03610417><sup>3</sup>

## Description of Related Literature

A search of PubMed using the terms “hemodialysis” and “hepatorenal syndrome” yielded 78 results. No further filters were used. Abstracts were reviewed specifically for studies that included patients that were not listed for transplant at the time of the study. Citations and “related articles” were also reviewed for relevance. Ultimately, 5 papers were identified including 1 case series, 4 retrospective studies and 1 prospective study. All other articles discussed unrelated topics.

Capling et al. performed a case series of four patients who received over 3 weeks of dialysis in an attempt to bridge to transplant. Mean survival time was 236 days, with only 1 patient receiving transplant.<sup>4</sup> Due to small sample size and lack of control, this paper was not selected for appraisal.

Witzke et al. conducted a prospective study of 30 patients with liver cirrhosis and HRS to assess 30 day and overall survival on HD therapy.<sup>5</sup> Half the patients received continuous venovascular hemodialysis (CVVH), and not the intermittent HD that Mrs. Smith would be offered. Of the 15 remaining patients who received HD, only 3 survived more than 1 year, all with successful transplant. Due to the small sample size, this article was not selected.

Keller et al. performed a retrospective study of 107 patients with acute decompensated liver disease and acute renal failure, 82 of which were initiated on dialysis; however the original article was not in English and ultimately did not answer the clinical question.<sup>6</sup>

Olivera et al performed a retrospective study of 68 patients with cirrhosis and type 1 HRS syndrome who were not candidates for transplant who were treated with combinations of vasopressors, albumin and dialysis<sup>6</sup>. Median survival for the entire group was 13 days, and the authors found the use of dialysis did not change outcomes significantly.<sup>7</sup> Although this is the population of interest, this study was not recent and included patients from 1996 to 2008. It may not account for advancement in care of patients with cirrhosis and it was not selected for appraisal.

Lenhart et al. conducted a retrospective chart review of patients hospitalized with decompensated alcoholic cirrhosis and hepatorenal syndrome or acute tubular necrosis to determine the outcomes of renal replacement therapy in patients with less than 6 months of sobriety.<sup>8</sup> Over 20% of patients survived 6 months to be evaluated for transplant with 12.8% recovering renal function.<sup>8</sup> This article was heavily considered for appraisal as the population matched Mrs. Smith well. However, because there was no comparison to a non-dialysis or listed cohort it was not selected for appraisal.

Allegretti et al. conducted a retrospective cohort study of patients with cirrhosis and acute kidney injury (AKI) who were initiated on RRT that was stratified by transplant listing status. The study also included a reference group of patients with severe AKI and cirrhosis who did not receive RRT (n=157). Of not listed patients, 135 had cirrhosis secondary to alcohol use, and 24 of these had concurrent HRS similar to Mrs. Smith.<sup>3</sup> The primary outcome was six-month survival. This article was selected for appraisal because of its applicability to our patient, use of a reference group, large sample size and recent publication. Using SORT criteria this study



qualifies as Level 2 evidence as it assesses prognosis using a retrospective cohort design.<sup>9</sup> The overall body of evidence on this topic is limited-quality patient-oriented evidence with some inconsistency and thus has a SORT level B9.<sup>9</sup>

## Critical Appraisal

Allegretti et al. performed a retrospective cohort study involving all inpatients with cirrhosis and AKI secondary to HRS or acute tubular necrosis (ATN) requiring RRT from 2005 to 2015 at a network of five hospitals.<sup>3</sup> These patients were stratified into two groups based on being listed (n = 131) or not listed for liver transplant (n = 341). These were compared with a reference group of patients with cirrhosis and severe AKI who did not receive RRT based on provider decision (n = 159). One author confirmed the diagnosis of ATN versus HRS via chart review, assigning ATN if there was a mixed picture. In the event of disagreement between the author and treating clinician, a second author provided the final say.<sup>8</sup>

Demographics such as age, gender, and race were similar across groups. The authors also did not specify what treatment, if any, the control group received. Average blood urea nitrogen (BUN) was the same for listed and not listed groups and average creatinine was similar (4.1 and 4.3, respectively). With the only reported exclusion criteria being if a patient was lost to follow-up (n = 3), our patient could have been included in this study. Unlike our patient, the majority of the population studied did not have HRS as their etiology of AKI. 84% of not listed patients (285 of 341) were diagnosed with ATN. For patients who were not listed, those with HRS did have higher MELD and CLIF-C ACLF scores at the initiation of dialysis. However, when controlling for MELD score, age, and RRT modality survival was similar between HRS and ATN subgroups regardless of listing status.

Mortality was high regardless of transplant listing status, with only 24% (114/472) of all subjects alive at six months. Overall, those alive were more likely to be white, have lower CLIF-C ACLF scores, and be initiated on iHD compared to CVVH. For not listed patients receiving RRT, 15% were alive at six months (51 of 341). For those alive at 6 months, 78% (40 of 51) recovered renal function and came off dialysis. Among the listed subjects initiated on RRT, about half (63 of 131) received a transplant. Of those listed who did not receive a transplant, 38% recovered renal function (3 of 8). Reference group patients compared to not listed patients had a shorter median hospital stay and shorter median survival.<sup>8</sup> For all subjects, those who were younger, had no preadmission history of CKD, had no prior history of ascites and/or had alcoholic cirrhosis were more likely to experience renal recovery. Factors of renal recovery in all subjects also included diagnosis of ATN versus HRS, sepsis, leukocytosis, mechanical ventilation requirement and CVVH.

Like all retrospective studies, this paper is prone to information bias. The reliance on the documentation of others permits room for error in diagnosis. The authors had to use the record of what others had written to determine ATN or HRS. HRS is a diagnosis of exclusion, so it may have been misdiagnosed if all other apparent causes of kidney injury were not worked up. If critical information was not included in a chart or there was incorrect documentation, this could also lead to error. The patients in this study span five hospitals and ten years. There was likely variability in the way they were treated based on institutional protocols and evolution of care over time. As there are not strict guidelines in place as to when to offer dialysis for HRS patients, individual clinicians have different thresholds at which they may do so. There is likely some indication bias at play as clinicians may be more apt to offer RRT to patients who are less sick and have a better chance of survival. In fact, the authors did find that patients who were not listed were less likely to be initiated on RRT for HRS (relative risk, 0.59; 95% CI, 0.48 to 0.72; P <0.001).

## Clinical Application

Our team met with Mrs. Smith, her husband, sister, and a double board-certified nephrologist and palliative medicine physician. We explained there is very limited research on the use of dialysis in HRS patients. The data we do have, such as Allegretti et al, shows a poor prognosis, but there is poor prognosis without dialysis as well. We also explained that dialysis might cause quicker decompensation. They were understandably overwhelmed and Mr. Smith wanted to know what the nephrologist would do if he were in their position. He responded that he "almost never answers that question". However, in the case of the Smiths, if he had a 7-year-old at home, he "would opt for dialysis". We made it clear that we could support whatever choice she made. As the treatment team, we felt comfortable that Mrs. Smith understood the implications of her decision.

Ultimately, Mrs. Smith did elect to try dialysis and agreed to participate in a rehabilitation program on discharge. Her husband had removed all alcohol from the house and was supportive of her recovery with the hope that she

could be ready for transplant evaluation in the coming six months. Luckily over the next few days, her condition improved slightly and it was determined that Mrs. Smith's condition no longer required emergent dialysis. She was discharged and continued to follow with outpatient nephrology who would initiate RRT if needed.

## New Knowledge Related to Clinical Decision Science

"What would you do if you were me?" Is it okay for a physician to answer this question? We feel comfortable recommending treatments when there is clear evidence supporting them but tend to shy away when the situation is more ambiguous. However, just because we are hesitant to express it, does not always mean we do know what we would choose.

In the case of Mrs. Smith, the question of whether to initiate RRT had no medical answer. Her options had been unbiasedly explained and understood by both the patient and her family. Still, they wanted to know what the physician would do. Before we answer this question, we should note what is contributing to our answer. Is it clinical experience or gestalt? Based on the findings of Allegreti et al., Mrs. Smith did have some factor associated with kidney recovery including younger age, no preadmission CKD, leukocytosis and alcoholic cirrhosis. Yet, the basis is not always scientific. Perhaps we feel a connection to the patient that sways our clinical judgement. There could be a murkier motive such as our own beliefs on addiction, or guilt we feel over not being able to do more. If these factors are not in alignment with the patient's values, it may not be appropriate to give one's opinion.

Nevertheless, in the case of Mrs. Smith it seems that the nephrologist's well-intentioned recommendation was the best thing we could do for her. The family had been dealing with the poor prognosis for weeks. Mrs. Smith was utterly overwhelmed, and Mr. Smith was hesitant to voice his opinion out of fear of forcing his wife into the "wrong" decision. When the nephrologist spoke, there was an immediate sense of relief in the room that helped alleviate some of the agony the patient and her family were having with this decision.

Patient autonomy and informed decision making are essential to the integrity of our profession. However, in the appropriate situation perhaps they can be maintained even while a physician offers their opinion. In the case of Mrs. Smith, we were unable to offer her a satisfactory treatment option; however, we were able to take the burden of an impossible decision off the patient, relieving some of her suffering.

## Conflict Of Interest Statement

The author declares no conflicts of interest.

## References

1. Alessandria C, Ozdogan O, Guevara M, Restuccia T, Jiménez W, Arroyo V, Rodés J, Ginès P. MELD score and clinical type predict prognosis in hepatorenal syndrome: relevance to liver transplantation. *Hepatology*. 2005 Jun;41(6):1282-9. <https://doi.org/10.1002/hep.20687>
2. Wilkinson SP, Weston MJ, Parsons V, Williams R. Dialysis in the treatment of renal failure in patients with liver disease. *Clin Nephrol*. 1977 Jul;8(1):287-92.
3. Allegretti AS, Parada XV, Eneanya ND, et al. Prognosis of Patients with Cirrhosis and AKI Who Initiate RRT. *Clin J Am Soc Nephrol*. 2018;13(1):16-25. <https://doi.org/10.2215/CJN.03610417>
4. Capling RK and Bastani B. The clinical course of patients with type 1 hepatorenal syndrome maintained on hemodialysis. *Ren Fail*. 2004;26(5):563-568. <https://doi.org/10.1081/jdi-200035988>
5. Witzke O, Baumann M, Patschan D, et al. Which patients benefit from hemodialysis therapy in hepatorenal syndrome?. *J Gastroenterol Hepatol*. 2004;19(12):1369-1373. <https://doi.org/10.1111/j.1440-1746.2004.03471.x>
6. Keller F, Heinze H, Jochimsen F, Passfall J, Schuppan D, Büttner P. Risk factors and outcome of 107 patients with decompensated liver disease and acute renal failure (including 26 patients with hepatorenal syndrome): the role of hemodialysis. *Ren Fail*. 1995;17(2):135-146. <https://doi.org/10.3109/08860229509026250>
7. Olivera-Martinez M, Sayles H, Vivekanandan R, D' Souza S, Florescu MC. Hepatorenal syndrome: are we missing some prognostic factors? *Dig Dis Sci*. 2012;57(1):210-214. <https://doi.org/10.1007/s10620-011-1861-1>



DONOHUE L. Renal replacement therapy may be initiated in patients with hepatorenal syndrome who are not transplant candidates. *Clin. Res. Prac.* Apr 28 2022;8(1):eP2602.  
<https://doi.org/10.22237/crp/1640995380>

8. Lenhart A, Hussain S, Salgia R. Chances of Renal Recovery or Liver Transplantation After Hospitalization for Alcoholic Liver Disease Requiring Dialysis. *Dig Dis Sci.* 2018 Oct;63(10):2800-2809. <https://doi.org/10.1007/s10620-018-5170-9>
9. Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): A Patient-Centered Approach to Grading Evidence in the Medical Literature. *J Am Board Fam Pract.* 2004;17(1):59-67. <https://doi.org/10.3122/jabfm.17.1.59>

