The cirrhotic patient with ascites presents unique challenges to the renal caregiver. This patient population has relative contraindications both to hemodialysis (HD) and to peritoneal dialysis (PD). Challenging hemodynamics and the bleeding risk from acquired coagulopathy make HD problematic. In PD, tense ascites can increase the risk of early catheter leak and complicate the initial instillation of dialysate. These patients are at increased risk of spontaneous bacterial peritonitis and would be suspected to have peritonitis rates different from those in non-cirrhotic patients. Ongoing protein losses in the dialysate may aggravate underlying malnutrition. Despite these concerns, available clinical reports suggest that patients with cirrhosis can be successfully managed on PD.

The present review focuses on the application of PD therapy in the cirrhotic patient with ascites. Technical aspects of initiating PD are reviewed, and clinical reports, peritonitis risk, and infection control strategies are discussed. Dialysate increases intra-abdominal pressure and may oppose the formation of ascites; the impact of these mechanics on dialysate protein losses and portal hemodynamics are reviewed.

Keywords
Cirrhosis, liver disease, ascites

Introduction
Patients with cirrhosis and ascites present unique challenges when the initiation of dialysis therapy is being considered. This population has relative contraindications to both hemodialysis (HD) and peritoneal dialysis (PD) (1).

Cirrhotic patients often have an acquired coagulopathy, increasing the risk of bleeding during cannulation for HD access. The abrupt hemodynamic challenges during traditional HD are often poorly tolerated in a population with hepatorenal physiology, systemic vasodilation, increased cardiac output, and relative hypotension (2). Patients with cirrhosis are prone to changes in mental status from hepatic encephalopathy and cerebral edema, the latter of which can be exacerbated by the rapid drop in plasma osmolality that occurs during HD treatment (3).

Potential disadvantages of PD therapy are the possibilities of increased peritonitis risk, worsened malnutrition from dialysate protein losses, and intra-abdominal bleeding from catheter trauma. Hypokalemia occurring during chronic PD can worsen hepatic encephalopathy because it increases proximal tubule ammonia generation in patients with residual kidney function (4).

On the other hand, PD therapy may offer some unique advantages to the cirrhotic patient. In this population, PD provides the possibility of a more stable hemodynamic profile and removal of endotoxins suspended in the ascites; the dialysate also serves as a source of calories in the patient with malnutrition and poor appetite (5).

Some reports raise the interesting speculation that increased intra-abdominal hydrostatic pressure during PD therapy may slow the appearance of protein-rich ascites, leading to improved nutrition. These, and other issues, are addressed in this review.

Discussion
Technical aspects of initiating PD
Many reports describe using the newly placed PD catheter for an initial large-volume paracentesis, giving symptomatic relief, permitting the catheter site to heal, and reducing the chance of early leak. Ascites drain volumes of more than 5 L have been described, and paracentesis is often combined with intravenous albumin infusions to provide hemodynamic stability (6).

If the catheter is used within days or a week, PD therapy should be instituted using a low-volume supine regimen, with no ambulatory dialysis, to reduce the chance of leak. The initial PD regimen is described as a “controlled paracentesis.” In this approach, low
dextrose concentrations are used, because ultrafiltration is not initially required. The drainage volume is adequate because it is composed of a mixture of dialysate and ascites. To allow for the safe and slow decompression of the abdomen, a 2-L dialysate infusion is followed, after the dwell, by a drain restricted to 2300 – 2400 mL (6,7). This pattern of drainage-restricted exchanges allows for the eventual slow removal of ascites.

**Clinical experiences**

Smaller case series are the main source for the clinical data presented here, because no large registry contains data detailing outcomes in cirrhotic PD patients.

De Vecchi and colleagues compared 21 cirrhotic PD patients with 41 PD patients without liver disease (8). Surprisingly, 5-year technique and patient survival were similar in the two groups. Hospitalization rates were similar. No cirrhotic patients were reported to develop hypertension, but they trended toward lower erythropoietin and intravenous iron use and had higher rates of ongoing malnutrition. Eleven cirrhotic patients were on PD for more than a year, and 8 were followed for more than 2 years.

Selgas *et al.* described 8 cirrhotic patients on PD therapy (6). At the time of publication, 3 of the 8 patients had died at 8, 14, and 16 months from causes that were felt to be unrelated to PD. The report noted that all patients had stable hemodynamics, with no hypotension. The authors concluded that “PD represents the best current treatment for cirrhotic patients with ascites that require dialysis.”

Marcus and colleagues described 9 cirrhotic PD patients: 7 patients were on continuous ambulatory PD, and 2 were on intermittent PD (9). During the observation period, 4 of the 9 patients died, with 3 deaths being attributed to liver failure and 1 to an empyema in the 8th year of PD therapy. One patient developed encapsulating peritoneal sclerosis after 8 years on PD, and one eventually switched to HD after being unable to continue self-care. At 18 – 24 months of observation, 3 other patients were alive. The authors concluded that “PD can be successfully used to treat end-stage renal disease in patients with chronic liver disease and ascites.”

These reports suggest that outcomes in patients with cirrhosis can be comparable to those in the non-cirrhotic PD population and that long-term survival on PD is possible.

**Peritonitis risk**

Patients with cirrhosis are at increased risk of infection because of a reduction in leukocytic phagocytosis and recruitment, complement activity, function of the reticuloendothelial system, and humoral opsonic activity in ascitic fluid (10). These abnormalities contribute to the development of spontaneous bacterial peritonitis (SBP), suspected to be the result of hematogenous spread of enteric organisms to the peritoneum or direct transmural migration across the bowel mucosa. Concern may therefore arise that cirrhotic patients on PD are at increased risk of peritonitis because of an inherent risk of SBP added to the catheter and the technique-related peritonitis risks.

The largest report to date of peritonitis risk comes from Chow and colleagues, who compared 25 patients who had hepatitis B cirrhosis with 36 hepatitis B patients who did not have cirrhosis (11). Surprisingly, the peritonitis rate was not different between the two groups. The cirrhotic group had a median peritonitis-free survival of 40 months as compared with 37 months in the non-cirrhotic group. The patients with cirrhosis experienced 1 episode of peritonitis every 19.2 patient–months, and those without experienced 1 episode every 20.5 patient–months. The time to first peritonitis episode did not differ between the two groups, and the overall response to antibiotic treatment was similar, as were the outcomes. The presence or absence of ascites was not detailed, but no cirrhotic patient was taking SBP prophylaxis.

In the description by De Vecchi *et al.*, the peritonitis rate was significantly less in the cirrhotic group (8). An overall peritonitis rate of 1 episode in 39 months was noted in the cirrhotic group as compared with a rate of 1 in 22 months in the control group. In the smaller study by Selgas *et al.*, the peritonitis rate was higher in the cirrhotic cohort (6). It is unclear whether the patients were taking SBP prophylaxis in the foregoing studies.

In the Chow *et al.* report from Hong Kong, organisms identified in cirrhotic PD patients did not differ from those identified in the non-cirrhotic PD population. The rates of *Staphylococcus aureus* and coagulase-negative *Staphylococcus* peritonitis were relatively low. This low incidence of staphylococcal infections may be a result of the exit-site protocols and care plans practiced in these Hong Kong centers, which report some of the lowest rates of infectious complications in the world.
Patients with cirrhosis are at increased risk of streptococcal infections, and *Streptococcus pneumoniae* peritonitis has been described (12). The reports from Chow *et al.* and others confirm the increased rate of streptococcal peritonitis in this population (6,11). It is unclear whether vaccination for *Streptococcus* reduces the risk of subsequent peritonitis, but it seems prudent to immunize as early in the clinical course as possible.

Bacterial organisms implicated in non-dialysis SBP tend to be the coliform species such as *Escherichia coli*, *Klebsiella*, the Enterobacteriaceae, and *Streptococcus* species such as *bovis* and *pneumoniae*. Empiric peritonitis treatment protocols should therefore be broad and should cover streptococci and other gram-positive and gram-negative coliform organisms (13). Based on renal and hepatic clearance, clinicians must carefully dose-adjust the medications administered, and they must be cognizant of potential hepatotoxicity from antibiotics (14).

Hypokalemia should be avoided in this patient population. Cirrhotic patients often have intestinal bacterial overgrowth and motility disorders that may be worsened by hypokalemia (15,16). Hypokalemia may also increase ammonia production and act as a risk factor for hepatic encephalopathy (4).

With the risks of peritonitis from SBP and the PD technique, it is surprising that the largest reports do not demonstrate increased peritonitis rates and severity. Could peritonitis risk in cirrhotic patients be reduced by the procedure itself? Could PD therapy improve peritoneal immune function in these patients? In patients with cirrhosis, ascitic fluid has been demonstrated to contain high levels of endotoxin, a component of the bacterial cell wall of gram-negative bacilli (17). This endotoxin alters the normal peritoneal milieu by stimulating macrophages and release of inflammatory cytokines such as tumor necrosis factor and interleukin 6 (18). By removing these inflammatory mediators, the dialysis process may return the peritoneal cavity to a less inflamed baseline. Removal of endotoxins and ascitic NO may also reduce portal pressure and the related hepatic venous pressure gradient, the main determinants of the development of, and bleeding from, esophageal and gastric varices (19,20). It is interesting to speculate that PD removal of endotoxins and NO could improve immune function, reduce the risk of subsequent variceal bleeding, and prevent renal deterioration during SBP (21).

Many patients with cirrhosis are treated with chronic lactulose therapy to reduce the manifestations of hepatic encephalopathy. Recently, lactulose therapy was associated with a reduction in peritonitis rates (22). Lactulose is a disaccharide that is not absorbed across the intestinal wall, creating an osmotic cathartic effect. Lactulose is metabolized by colonic bacteria into pyruvate and lactate, which acidify the stool and reduce the bacterial colony count (23,24). In the reports mentioned earlier, it is unclear whether the patients were being treated with chronic lactulose therapy, but it is interesting to speculate that cirrhotic peritonitis rates were lower because of lactulose administration.

Are there other unique approaches to the treatment of peritonitis in this population? Perhaps so. Patients with cirrhosis are often given intravenous albumin for volume expansion and to prevent deterioration in renal function during SBP. A recent study demonstrated that during SBP in cirrhotic patients, antibiotics administered with intravenous albumin reduced cytokine and NO production more than did antibiotics administered alone (25). In another study, antibiotics plus albumin lowered the mortality rate and prevented subsequent deterioration in renal function (26). Albumin not only provides colloidosmotic pressure, but also acts as a carrier protein capable of binding to a variety of deleterious cytokines produced during peritonitis (27). It is interesting to speculate that therapy with antibiotics plus albumin for PD-related peritonitis in cirrhotic patients could reduce peritonitis morbidity and better protect residual kidney function by maintaining renal perfusion and reducing NO levels (28).

**Nutritional aspects**

Patients with advanced liver disease marked by cirrhosis and ascites are often malnourished. The causes of the malnutrition are multifocal, including abnormalities in appetite and gastric emptying, marked abdominal distention, and inflammation (29). Proponents of PD therapy suggest that the dialysate can serve as a needed source of calories—a component of “food.” Nevertheless, the cirrhotic patient initiated on PD must be carefully monitored by subjective global assessment, serum albumin, and other parameters of nutrition. Protein losses in the dialysate may worsen hypoalbuminemia, and excessive protein supplements may risk worsening hepatic encephalopathy.
Whether PD therapy worsens or ameliorates protein wasting in the ascites has been evaluated in small studies. Bajo et al. followed serum albumin levels and peritoneal protein losses in a cirrhotic population and, surprisingly, noted that serum albumin significantly improved in many patients and that peritoneal protein losses diminished over time (7). The increase in serum albumin could possibly be attributed to an improvement in the uremic state leading to improved appetite and intake of needed protein and calories. Other studies have documented a decline in total peritoneal protein losses in cirrhotic patients, and those authors have speculated that the increased intra-abdominal pressure during PD therapy may serve as hydrostatic pressure to oppose the portal and splanchnic hypertension that leads to ascites formation. By opposing the hydrostatic forces that generate ascites, dialysate could possibly reduce the protein losses that normally occur in ascites (30). If this mechanism and others are occurring, PD therapy would be considered the desired dialysis option for these patients—a strategy to reduce ascites formation and albumin losses into the peritoneum (31). More investigation in this line of research is clearly needed.

Management strategies in cirrhotic patients on PD therapy

From the literature described here, and from other reports, a management strategy can be established for the PD patient with cirrhosis and ascites. Table I sets out this overall strategy. Management in this population would be aided by further research to address the many outstanding clinical concerns (Table II).

Summary

Cirrhotic patients with ascites who require dialysis for end-stage renal disease represent a unique population with multi-organ failure that requires a tailored management strategy. Peritoneal dialysis may offer special benefits to this population, and it is probably the dialysis option of first choice. The traditional cardiovascular risk factors contributing to death do not...

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### Table I Management strategies for the peritoneal dialysis (PD) patient with cirrhosis and ascites

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<td>1</td>
<td>Apply large-volume paracentesis at the time of initial catheter placement to lessen the chance of an early leak and to allow for tissue ingrowth.</td>
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<td>2</td>
<td>Consider intravenous albumin support during the initial large-volume paracentesis.</td>
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<td>3</td>
<td>Start with recumbent, drainage-controlled PD therapy to allow for subsequent complete drainage of ascites.</td>
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<td>4</td>
<td>While patient is not recumbent, consider dry days to lessen chance of early leak.</td>
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<td>5</td>
<td>Consider, initially, continuation of prophylaxis for spontaneous bacterial peritonitis.</td>
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<td>6</td>
<td>Use topical antibiotics for exit-site care.</td>
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<td>7</td>
<td>Maintain a normal serum potassium level.</td>
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<td>8</td>
<td>Consider lactulose therapy.</td>
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<td>9</td>
<td>Regularly monitor parameters of nutrition.</td>
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<td>10</td>
<td>Provide aggressive nutritional support if indicated, but be cautious with the use of high-protein supplements if there is a risk of encephalopathy.</td>
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<td>11</td>
<td>Vaccinate for <em>Pneumococcus</em>.</td>
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### Table II Areas for further research

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<tr>
<td>1</td>
<td>Investigate the effects of prophylaxis for spontaneous bacterial peritonitis, if used, on subsequent peritonitis rates.</td>
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<td>2</td>
<td>Using a randomized controlled trial design, investigate whether chronic lactulose therapy reduces risk of peritonitis.</td>
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<tr>
<td>3</td>
<td>Determine whether vaccination for <em>Pneumococcus</em> lowers the occurrence of streptococcal peritonitis.</td>
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<td>4</td>
<td>Conduct protein-balance studies to better determine whether the increased intra-abdominal pressure from dialysate reduces ascites formation and peritoneal protein losses.</td>
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<td>5</td>
<td>Determine whether ascitic endotoxin removal by peritoneal dialysis therapy reduces the portal and hepatic venous pressure gradient and lessens the risk of variceal bleeding.</td>
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<td>6</td>
<td>Determine the effects of endotoxin removal on systemic hemodynamics and on residual kidney function.</td>
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<tr>
<td>7</td>
<td>Determine whether, compared with hemodialysis, peritoneal dialysis therapy normalizes the renin–angiotensin system and thus allows for safer use of angiotensin II inhibition.</td>
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<tr>
<td>8</td>
<td>Investigate the role of intestinal decontamination in reducing subsequent peritonitis rates.</td>
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not seem to be as prevalent in this population, and so survival can best be affected by PD technique success and management of nutritional and infectious complications. Whether endotoxin and NO removal with PD lowers portal hypertension and subsequent risk of upper gastrointestinal bleeding requires further study. Further investigation is also needed to clarify whether the intra-abdominal hydrostatic pressure exerted by dialysate slows ongoing ascites formation and peritoneal protein losses. Finally, the roles of SBP prophylaxis, peritoneal endotoxin removal, and intestinal decontamination in altering the hemodynamic profile of cirrhosis—and consequently, of peritonitis rates—need further clarification. Hopefully, these issues will be addressed in the coming years.

References


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