MANAGEMENT OF THE CIRRHOTIC PATIENT: CARE GAPS AND OPPORTUNITIES FOR IMPROVEMENT

ERIN KELLY, MD MSC FRCPC
DIVISION OF GASTROENTEROLOGY
THE OTTAWA HOSPITAL

CANADIAN SOCIETY OF INTERNAL MEDICINE
NOVEMBER 4, 2017
The following presentation represents the views of the speaker at the time of the presentation. This information is meant for educational purposes, and should not replace other sources of information or your medical judgment.

Speaker: Title - date
## Conflict Disclosures

“I have the following conflicts to declare

<table>
<thead>
<tr>
<th>Conflict Type</th>
<th>Company/Organization</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advisory Board or equivalent</td>
<td>Intercept</td>
<td></td>
</tr>
<tr>
<td>Speakers bureau member</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Payment from a commercial organization. (including gifts or other consideration or ‘in kind’ compensation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant(s) or an honorarium</td>
<td>Lupin, Gilead</td>
<td></td>
</tr>
<tr>
<td>Patent for a product referred to or marketed by a commercial organization.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investments in a pharmaceutical organization, medical devices company or communications firm.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participating or participated in a clinical trial</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Some of the drugs, devices, or treatment modalities mentioned in this presentation are:

- Diuretics (spironolactone, furosemide)
- Antibiotics (norfloxacin, trimethoprim-sulfamethoxazole)
- Lactulose, rifaximin
OBJECTIVES

Overview
Brief overview of cirrhosis and complications

Costs
Examine Canadian data on burden of disease and cost in ESLD

Guidelines
Review newest guidelines for patients with cirrhosis

Care Gaps
Identify gaps in health care delivery in patients with advanced liver disease

Strategize
Explore strategies to improve health care delivery and clinical outcomes in patients with end stage liver disease
LIVER DISEASE- CANADIAN PERSPECTIVE

- An estimated 25% of Canadians have NAFLD
- Over 900,000 Canadians have Hepatitis C
- Deaths from Chronic liver disease rising in Canada
- Rates of HCC and deaths from HCC rising
- An estimated 400 liver transplants are performed annually in Canada, even though number of deaths from chronic liver disease estimated to be ~5000 per year
COST OF END STAGE LIVER DISEASE IN LAST YEAR OF LIFE

Kelly et al, in press
COSTS IN ESLD AT END OF LIFE

At 90 days ESLD associated with:

- Higher chance of dying in an institution (p<0.0001)
- Greater days spent in acute care (p<0.0001)
- Greater cost
Drivers of Costs in ESLD

- Hospital readmissions cost the Canadian healthcare system as much as $1.8 billion dollars per year
- 30 day readmission rates overall: 8.5%
- 30 day readmission rates in ESLD: 30%
  - >50% of return within 3 months
  - Many have multiple admissions

Decompensated liver disease is costly

Patients are predominantly accessing acute care resources for their health care needs
SO WHAT CAN WE DO

1) Try to practice evidenced based to prevent complications and initial hospitalization

2) Develop strategies to minimize rehospitalization
COMPLICATIONS OF CIRRHOSIS

Cirrhosis

- Portal Hypertension
- Liver Insufficiency

Variceal Hemorrhage

- Ascites
- Encephalopathy
- Jaundice

Spontaneous bacterial peritonitis
Hepatorenal syndrome
PATIENTS WITH CIRRHOSIS DECOMPENSATION SHORTENS SURVIVAL

**ASCITES AND COMPLICATIONS**

- Cirrhosis is the most common cause of ascites
- Patients with new onset ascites are frequently admitted to hospitals for assessment
- Effective care of these patients can reduce the frequency of readmissions
- Complications of ascites:
  - Electrolyte imbalances and impaired renal function
  - Diuretic resistant ascites
  - Hepatorenal syndrome
  - Spontaneous bacterial peritonitis
A FEW CASE EXAMPLES- CASE 1:

63M, married, 2 children, retired
PMH: pulmonary sarcoidosis based on imaging, discovered incidentally.
Social: Heavy drinking in his youth, “social” in the past few years but now cut down to minimal amounts
HPI: Went to ER with increasing shortness of breath, sudden increased abdominal girth, peripheral edema. Imaging showing signs of cirrhosis and large volume ascites. Medicine consult for further evaluation.
2L paracentesis performed, no SBP. Started on furosemide 20 mg daily and spironolactone 50 mg and sent home
Presents to ER 2 weeks later for weakness. Creatinine found to have risen from 80 to 500
What is the most likely cause for his renal injury?
- Failure to give albumin during paracentesis
- Diuretics
- Sarcoidosis
- Infection

What further investigations would you perform?
Diagnostic paracentesis if clinically apparent new-onset ascites and send for analysis. (class I, Level C)

All patients with ascites admitted to the hospital should undergo abdominal paracentesis. Paracentesis should be repeated if signs of infection (in/outpatient) (Class I, Level B)

The initial laboratory investigation of ascitic fluid should include an ascitic fluid cell count and differential, ascitic fluid total protein, and serum-ascites albumin gradient. (Class I, Level B)

FFP before paracentesis not recommended (Class III, Level C)
Consider serial therapeutic paracenteses if refractory ascites (Class I Level C)

Post-paracentesis albumin infusion may not be necessary for a single paracentesis of less than 4 to 5 L. (Class I, Level C)

For large-volume paracenteses, an albumin infusion of 6-8 g per liter of fluid removed appears to improve survival and is recommended. (Class IIa, Level A)

TIPS should be considered for select patients (Class I, Level A)
Recall: 2L paracentesis performed, no SBP. Started on furosemide 20 mg daily and spironolactone 50 mg and sent home. Presents to ER 2 weeks later for weakness. Creatinine found to have risen from 80 to 500

Your paracentesis shows no SBP and a further infectious work up is negative

Can you confidently make a diagnosis of hepatorenal syndrome at this time?
HEPATOrenal SYNDROME- CRITERIA

- Diagnostic criteria:
  - Cirrhosis with ascites
  - Serum creatinine greater than 133 umol/L
  - No improvement of serum creatinine after at least two days with diuretic withdrawal and volume expansion with albumin
  - Absence of shock
  - No current or recent treatment with nephrotoxic drugs
  - Absence of parenchymal kidney disease
Albumin infusion plus administration of vasoactive drugs such as octreotide and midodrine should be considered in the treatment of type I hepatorenal syndrome. (Class IIa, Level B)

Albumin infusion plus administration of norepinephrine should also be considered in the treatment of type I hepatorenal syndrome, when the patient is in the intensive care unit. (Class IIa, Level A)

Patients with cirrhosis, ascites, and hepatorenal syndrome should have an expedited referral for liver transplantation. (Class I, Level B)
CASE 2

- 38M, history of polysubstance abuse including alcohol (“as much as I can get my hands on”) and cocaine IV
- Presents to ER with new onset ascites, jaundice, abdominal pain
- In ER: looks unwell, unkempt, poor dentition. Bulging flanks and tender abdomen, peripheral edema
- Labs: Creatinine 80, WBC 14, bilirubin 32, INR 1.4 platelets 110
- Ultrasound: cirrhosis and moderate volume ascites, no portal vein thrombosis
CASE 2: COURSE IN HOSPITAL

- Diagnostic paracentesis: Total WBC 400, 80% PMN
  - Started on ceftriaxone empirically
  - Cultures grow pan-sensitive e. Coli

- Patient improves in hospital and ready for discharge by PAD#5
How would you complete the management of his SBP?

- Switch to ciprofloxacin x2 days to complete a 7 day course of antibiotics
- Start trimethoprim-sulfamethoxazole and continue indefinitely
- Discontinue antibiotics as patient has improved clinically
- Monitor for signs of recurrence and if develops second episode of SBP then needs suppressive antibiotic therapy to prevent additional episodes
Present in about 12% of patients at the time of admission to hospital

Mortality from SBP has remained unchanged:
- In hospital: 33%
- Among survivors: 1-month 33%, 6-month 50% and 1-year 58% mortality rates

Patients with ascitic fluid PMN counts >=250 cells/ml should receive empiric antibiotic therapy, e.g., IV third-generation cephalosporin (Class I, Level A)

Patients with ascitic fluid PMN <250 cells/mm³ but signs/symptoms of infection (febrile or abdo pain) should receive empiric antibiotics while waiting for cultures. (Class I, Level B)

If nosocomial SBP or atypical clinical response to treatment, follow-up paracentesis after 48 hrs of treatment to assess the response in PMN count and culture. (Class IIa, Level C)
Patients who have survived an episode of SBP should receive long-term prophylaxis with daily norfloxacin or trimethoprim/sulfamethoxazole. (Class I, Level A)

In patients with cirrhosis and ascites, long-term norfloxacin or septra can be justified if the ascitic fluid protein <15g/L and impaired renal function (creatinine ≥106, BUN ≥25 or serum Na ≤130) OR liver failure (Child score ≥9 and bilirubin ≥51). (Class I, Level A)
CASE 2

- The patient represents 2 months later with confusion and is diagnosed with hepatic encephalopathy.
- A thorough work up including repeat paracentesis does not reveal secondary causes.
- The patient is started on lactulose in hospital and improves.
Should you have discharged him on lactulose to prevent hepatic encephalopathy?

How would your management change if he continues to have episodes of encephalopathy despite adherence to lactulose?
Overt HE will occur in up to 40% of those with cirrhosis.

Overt HE is present at the time of diagnosis of cirrhosis in 10%-14%.

Hospitalizations secondary to HE are on the rise.
First line therapy: lactulose
Second line: Rifaximin plus lactulose to prevent recurrent episodes of HE
Increased blood ammonia alone does not add any diagnostic, staging, or prognostic value for HE in patients with CLD. (GRADE II-3, A, I).

An episode of OHE (whether spontaneous or precipitated) should be actively treated.

Secondary prophylaxis after an episode for overt HE is recommended.

Primary prophylaxis for prevention of episodes of OHE is generally not required.
A four-pronged approach to management of HE is recommended (GRADE II-2,A)

- Initiation of care for patients with altered consciousness
- Alternative causes of altered mental status should be sought and treated
- Identification of precipitating factors and their correction
- Commencement of empirical HE treatment
CASE 3

- Patient with known cirrhosis presenting with hematemesis and melena
- Endoscopy performed in the ER shows large esophageal varices and banded successfully
- Admitted to medicine for ongoing management including octreotide x72h and ceftriaxone
- Started on nadolol 20 mg at the time of discharge
- Outpatient GI scope shows no recurrence of varices.
Patient now stable x 6 months and asking “do I still really need this medication”

What is the optimal management for prevention of GI bleeding in this patient

- OK to discontinue betablocker as patient no longer has evidence of varices
- Continue beta blocker indefinitely and yearly EGD
- Continue beta blocker indefinitely and repeat EGD if signs of GI bleeding
- OK to discontinue beta blocker but monitor with yearly EGD
SELECT EVIDENCED BASED GUIDELINES IN CIRRHOSIS–VARICEAL BLEEDING

Antibiotics (3rd generation cephalosporin) and octreotide for variceal bleeding

Non selective beta blocker at discharge and LIFELONG (unless good reason not to- intolerance, complication)

Banding to obliteration, then frequent relooks as outpatient (q6-12 months)
WE ALL THINK WE FOLLOW ALL/MOST OF THESE GUIDELINES…

But actually we don’t.
PROPORTION OF ESLD PATIENTS RECEIVING RECOMMENDED CARE
QUALITY GAP IN MANAGEMENT OF CIRRHOSIS

- We all know the guidelines
- We know adherence to these guidelines may delay complications, improve QOL and prolong survival
- So why aren’t we applying to all cirrhotic patients?
REASONS FOR QUALITY GAP IN CIRRHOSIS

- Education: provider, patient, and caregiver
- Systems: Location, access, and coordination of care
- "Swiss cheese" model: errors and quality gaps
DO MEASURES FOR IMPROVED QUALITY IMPROVE OUTCOMES IN ESLD?

- Reduced 30 day readmission (41% vs. 13%, P = 0.001) without requiring increasing LOS with education sessions and order sets

- Electronic clinical decision support tools for improving antibiotic prophylaxis and HE treatment resulted in fewer readmissions

- Early paracentesis lowers 30-day readmission rates, and early initiation of diuretic therapy lowers 90-day mortality
DAY HOSPITAL FOR ESLD PATIENTS

- Goal: facilitate outpatient management of ascites and SBP prophylaxis
  - Care management vs usual care
- Reduced 30-day readmissions
  - 42.4% vs. 15.4%, p < 0.01
- Reduced mean #day in hospital/month
  - 6.01 ± 8.38 days vs. 2.92 ± 4.70 days, p<0.01
- Reduced 12-month mortality
  - 45.7% vs. 23.1%, p < 0.025
- Overall cost lower in “care management” group
  - 1479.19 vs 2816.13 (€) per patient month of life

Journal of Hepatology 2013 vol. 59 j 257–264
Demonstrates the important principle that significant improvements in access and adherence to guidelines improves outcomes.

Further work is needed to show that these can be widely sustained in a variety of systems and still impact important outcomes.
IN SUMMARY

Patients with endstage liver disease have frequent complications which often lead to hospitalization.

Although guidelines exist to help guide management in ESLD, in general, adherence is suboptimal.

Improving processes may help reduce hospitalizations, morbidity and mortality for our patients, with minimal to no added overall cost.
HEPATOLOGY GUIDELINES AVAILABLE AT AASLD WEBSITE OR CASL WEBSITE

https://www.aasld.org/publications/practice-guidelines-0
QUESTIONS?
- Diagnosed with cirrhosis, ascites, hepatic hydrothorax and hepatic encephalopathy.
- LVP performed, high SAAG, no SBP
- Started on lactulose, diuretics and condition improved in hospital and eventually discharged home on PAD 6
- Outpatient Hepatology referral

- Over subsequent 4 months, 6 readmissions for complications of liver disease— HE x4, hyponatremia x1, SOB from hydrothorax x1