LIVER DISEASE
in Palliative Care: An Update

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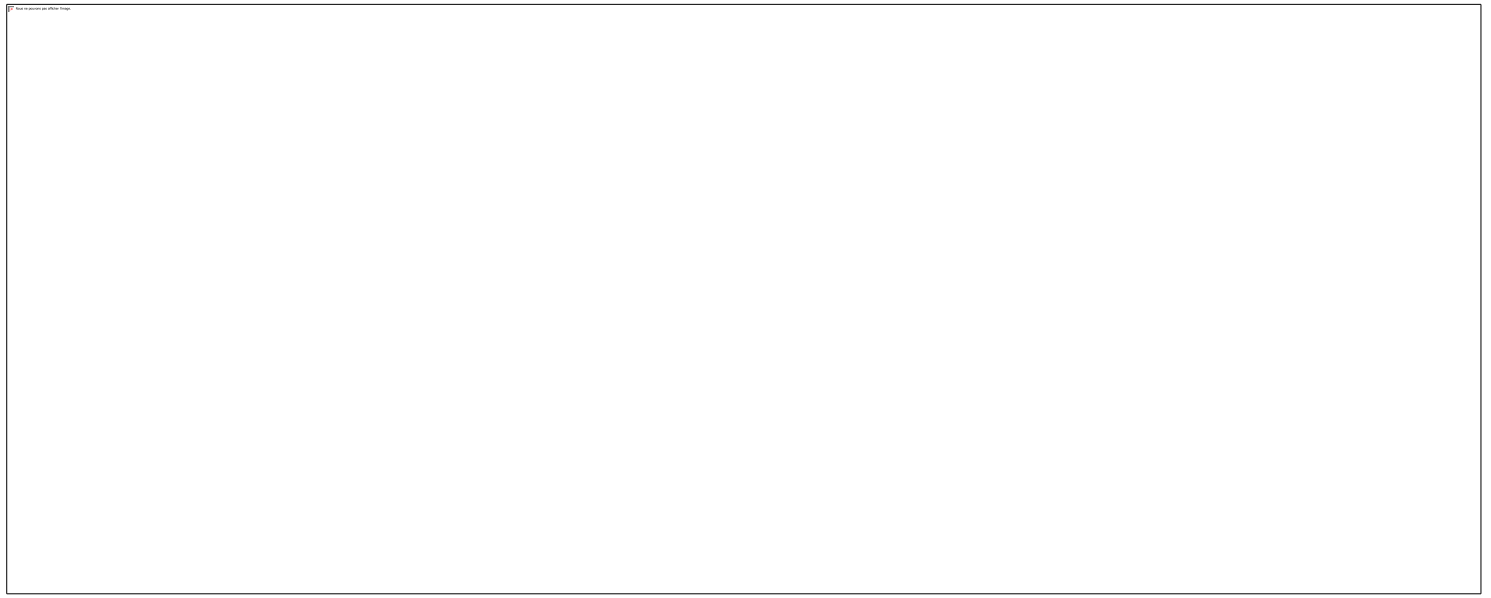
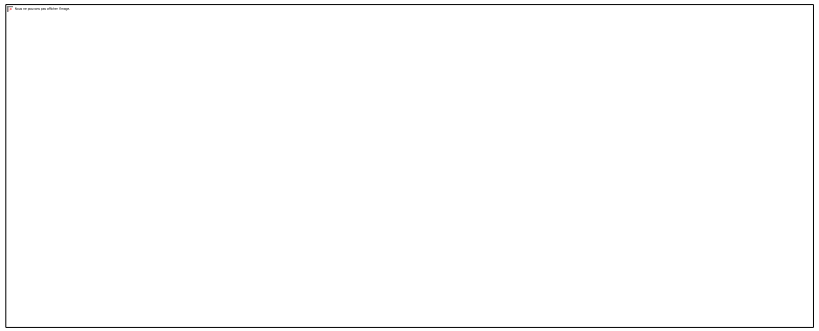
CONFLICTS OF INTEREST DECLARATION

No Conflicts of Interest



LEARNING OBJECTIVES



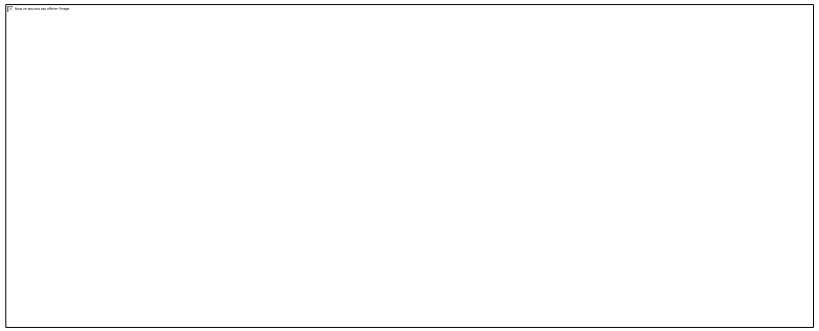
At the conclusion of this presentation, participants will be able to:

Apply	Master	Incorporate	Recognize
Apply cirrhosis progression to prognostication in end-stage liver disease (ESLD)	Master several clinical pearls for symptom management, and explore: cirrhosiscare.ca	Incorporate new evidence for treatment of: • Ascites • Variceal Hemorrhage • Encephalopathy	Recognize anti-cancer treatment issues (hepatocellular carcinoma)

CanMEDS COMPETENCY FRAMEWORK

- Collaborator
- Leader
- Professional
- Health Advocate
- Communicator
- Scholar
- Medical Expert

Attention to Survival Data



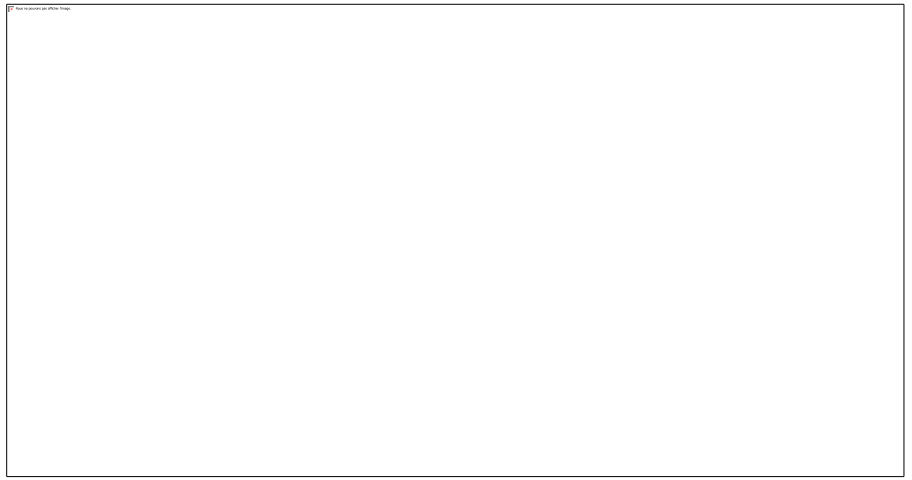
As high-level practitioners providing care to our patients, they need to be involved in discussions about survival and what that means to their care.

Brisebois, A et. al. Advance Care Planning for specialists managing cirrhosis: a focus on patient-centered care. Hepatology. May 2018; 67 (5); p2025-2040

Prospective ACP/GCD readiness research:
Surveys of 100 patients with cirrhosis, mean age 62, 59% male, mean MELD 11.5 2018

Preferred timing of first ACP discussion. When the disease has progressed or when more stable?

Components of ACP



Brisebois, A. et. al. Hepatology 2018

Cirrhosis is considered the “end stage” of chronic liver disease of any etiology and results from progressive fibrogenesis

Increasing liver fibrosis

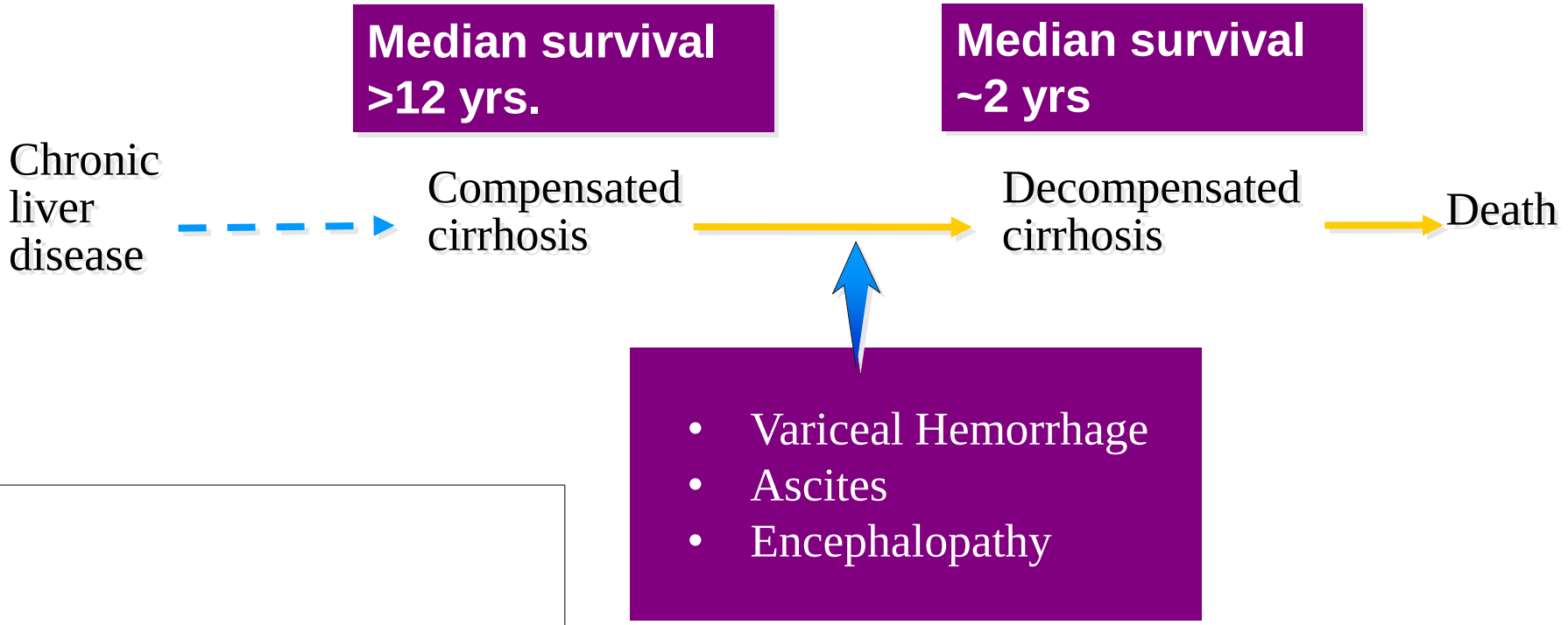
Chronic liver disease

- Alcohol
- Hepatitis C/B
- NASH
- Cholestatic
- Autoimmune

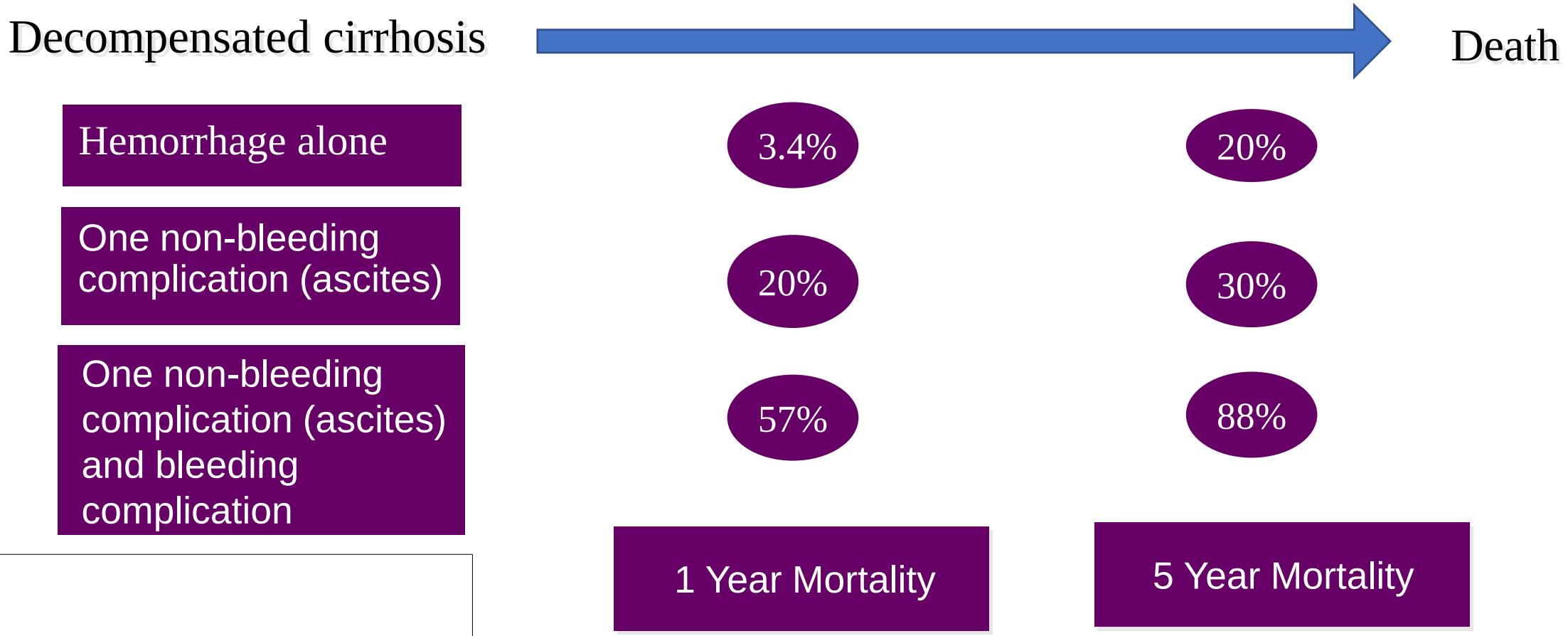
Cirrhosis

Slide courtesy of Dr. Tandon Hepatology University of Alberta Hospital

Based on these complications, cirrhosis can be divided into two distinct prognostic stages



Sub-staging of patients with decompensated cirrhosis is not as well defined as that of compensated patients



D'Amico et al. Aliment Pharmacol Ther 2014; 39: 1180-93

There is a stage of “further” decompensation

Worsening vasodilatation

Compensated cirrhosis → **Decompensated cirrhosis** → **Further decompensation** → **Death**

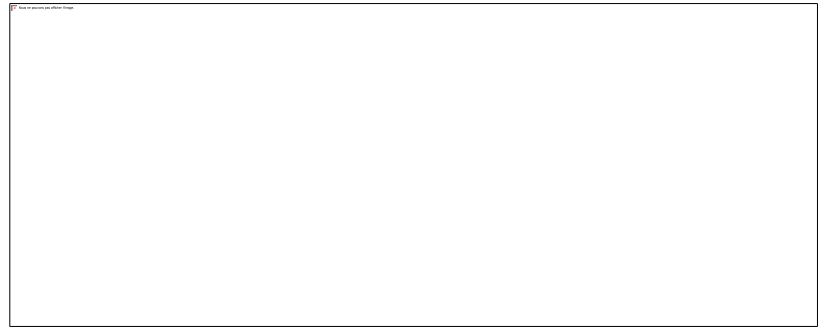
- VH
- Ascites
- HE

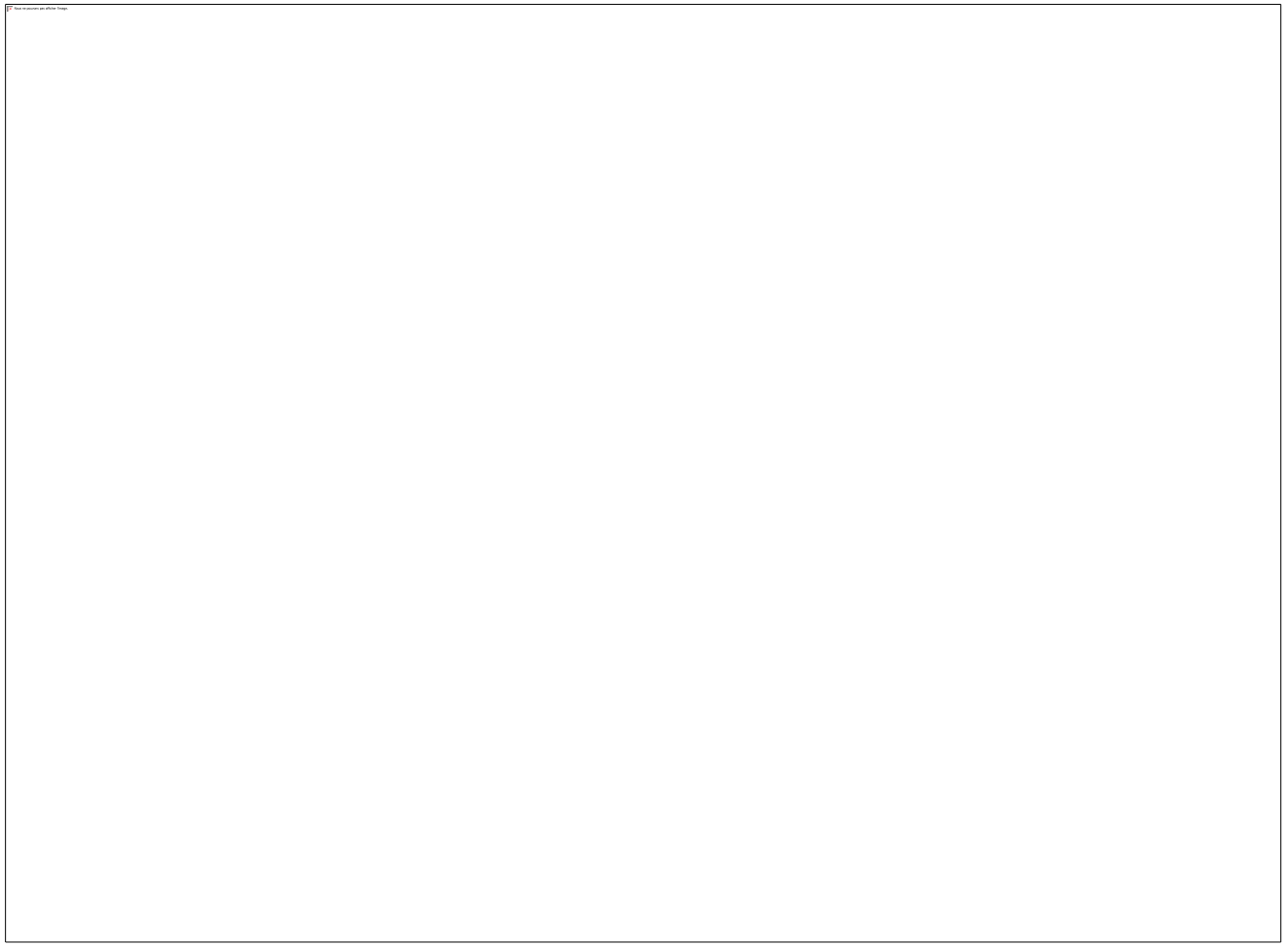
- Recurrent VH/HE
- Refractory Ascites
- Hyponatremia
- Renal Failure (HRS)
- Coagulopathy
- Thrombocytopenia
- Jaundice

VH = Variceal haemorrhage HE = Hepatic encephalopathy HRS = hepatorenal syndrome

PROGNOSTICATION in CIRRHOSIS

- Child-Turcotte-Pugh, MELD, MELD Na, CLIF – SOFA, CLIF-C ACLF
- PALLIATIVE PROGNOSTIC SCORES
- Co-morbidities are not taken into consideration with prognosticating tools for non-cancer illnesses.
- NACSELD-ACLF (APP) Survival at 30 days in hospitalized patients





Child-Pugh Classification of Severity of Liver Disease

Measure	1 Point	2 Points	3 Points
Bilirubin, uM/L	< 34	34 - 50	> 50
Albumin, g/L	> 35	28 - 35	< 28
Prothrombin time INR	< 1.7	1.7 – 2.2	> 2.2
Ascites	None	Slight	Moderate

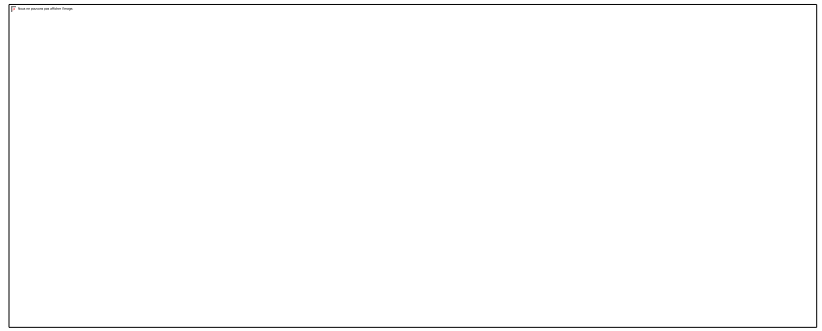
Grade	Total Points	Surgical Risk	2-Yr Survival, %
A (well-compensated disease)	1-6	Good	85
B (significant functional compromise)	7-9	Moderate	60
C (decompensated disease)	10-15	Poor	35

Pugh RN, et al. Br J Surg. 1973;60:646-649. Lucey MR, et al. Liver Transpl Surg. 1997;3:628-637.

MELD & MELD-Na

MELD (model for end-stage liver disease)

Identify patients whose predicted survival post-procedure would be three months or less.

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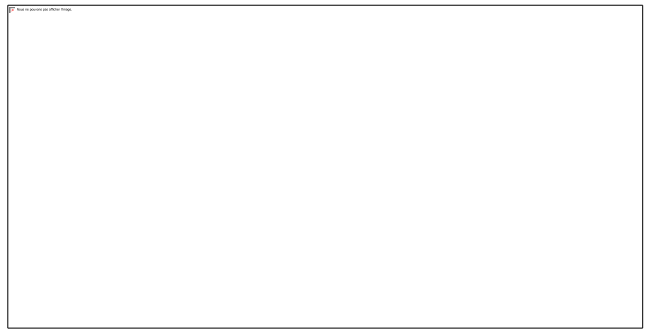
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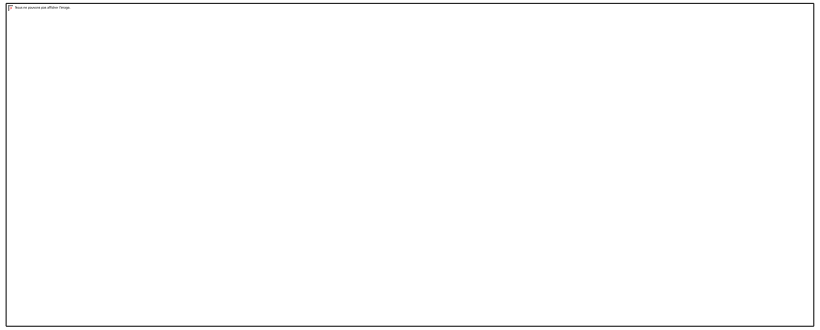
Performance Status	Functional Capacity	Mortality at 3 months
Low	Unable to care for self	23%
Intermediate	Able to care for most personal needs but needs some assistance	11%
High	No special care needs	5%

PALLIATIVE PERFORMANCE STATUS: Hospitalized Patients with Cirrhosis



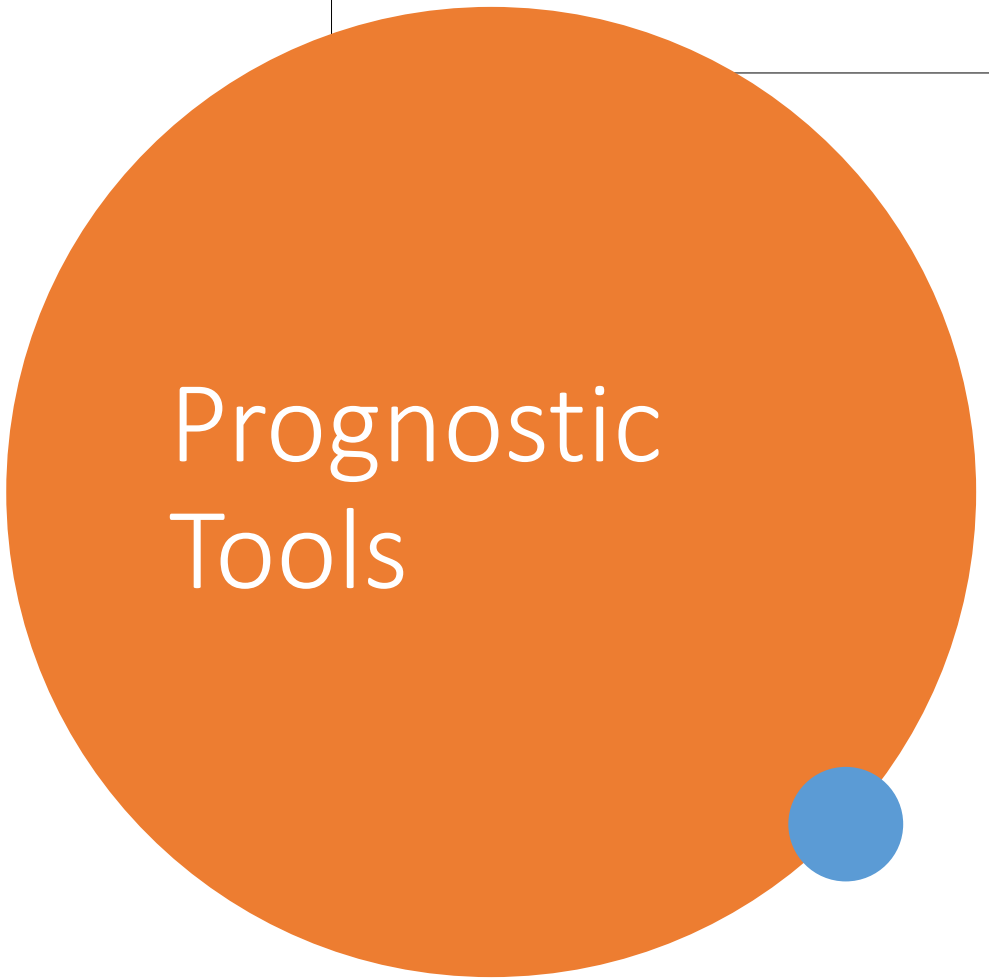
Tandon et. al 2016. Performance Status predicts death in hospitalized patients

APACHE III (acute physiology and chronic health evaluation system)

- Risk of dying in the hospital
- 129 variables from initial 24 hours of intensive care unit admission

SAPS 3 (Simplified Acute Physiology Score)

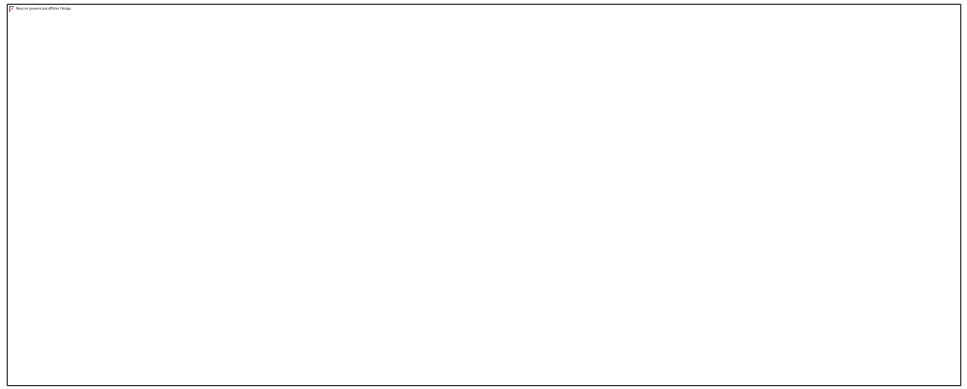
- Only uses 25 variables

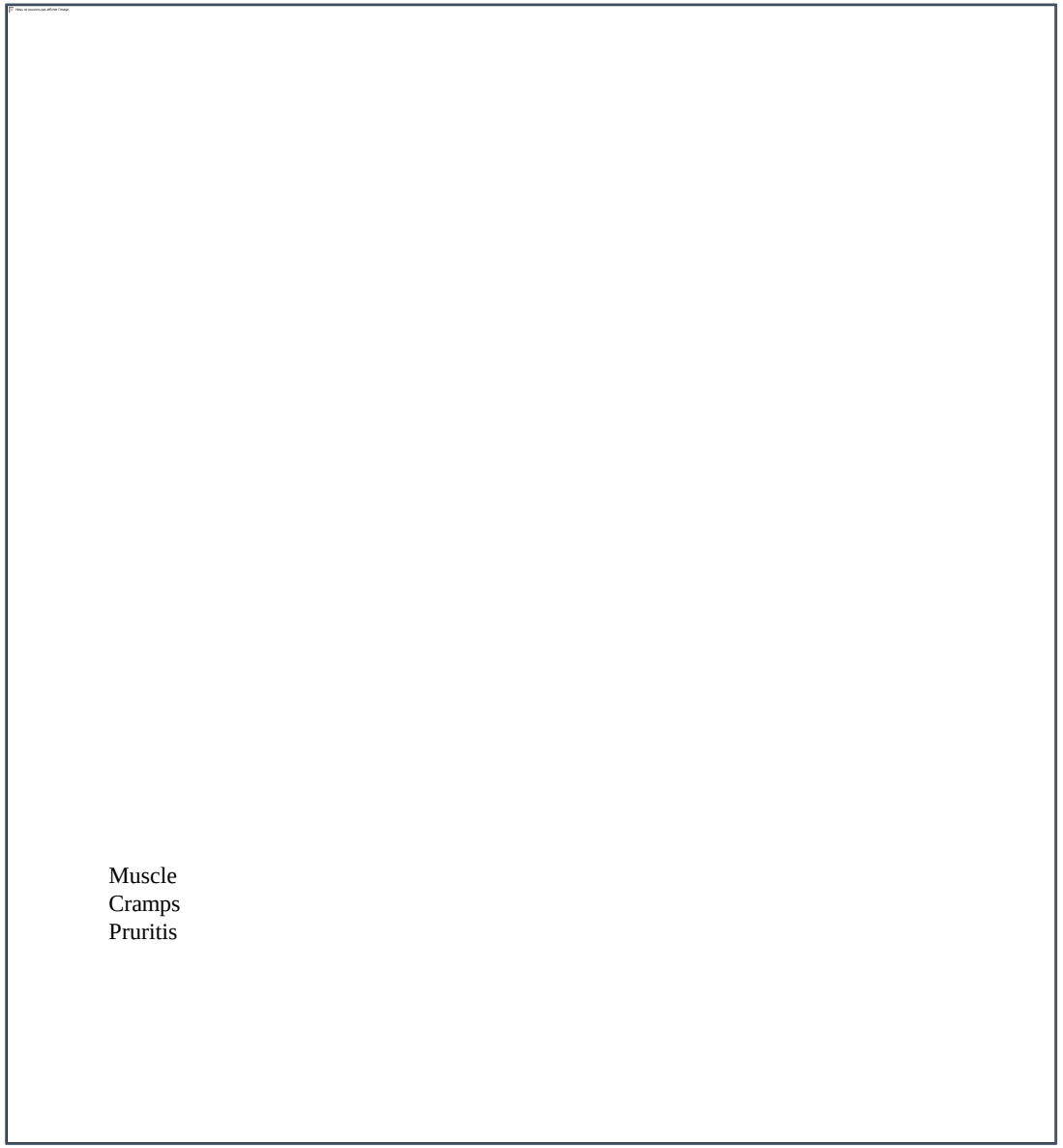


SYMPTOMS IN CIRRHOSIS CARE

SYMPTOMS IN CIRRHOSIS

CIRRHOSISCARE.CA

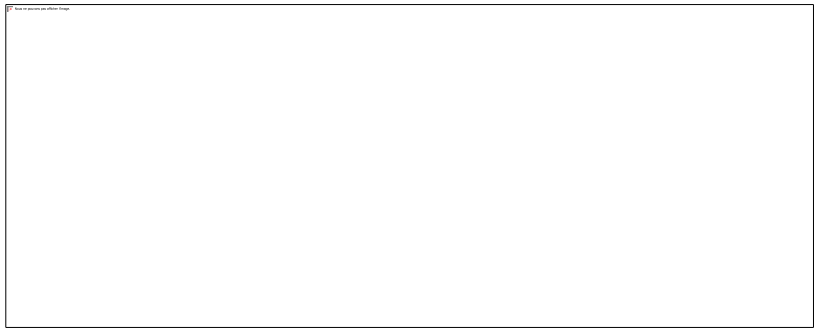




Muscle
Cramps
Pruritis

The burden of symptoms in cirrhosis

(n=400 outpatients)



- 75% pain
- 50% anxiety or depression
- 65% mobility issues
- Mean Quality of Life Score 59/100
- Psychological stress, family worries, social stigma, financial distress, transplant list concerns
- Burden high despite Child-Pugh status

Clinical Liver Disease. Vol 6, Issue 1. pages 19-21, 28 JUL 2015. http://onlinelibrary.wiley.com

Symptom complexity: “total pain” application to all symptoms – extremely important in cirrhosis care

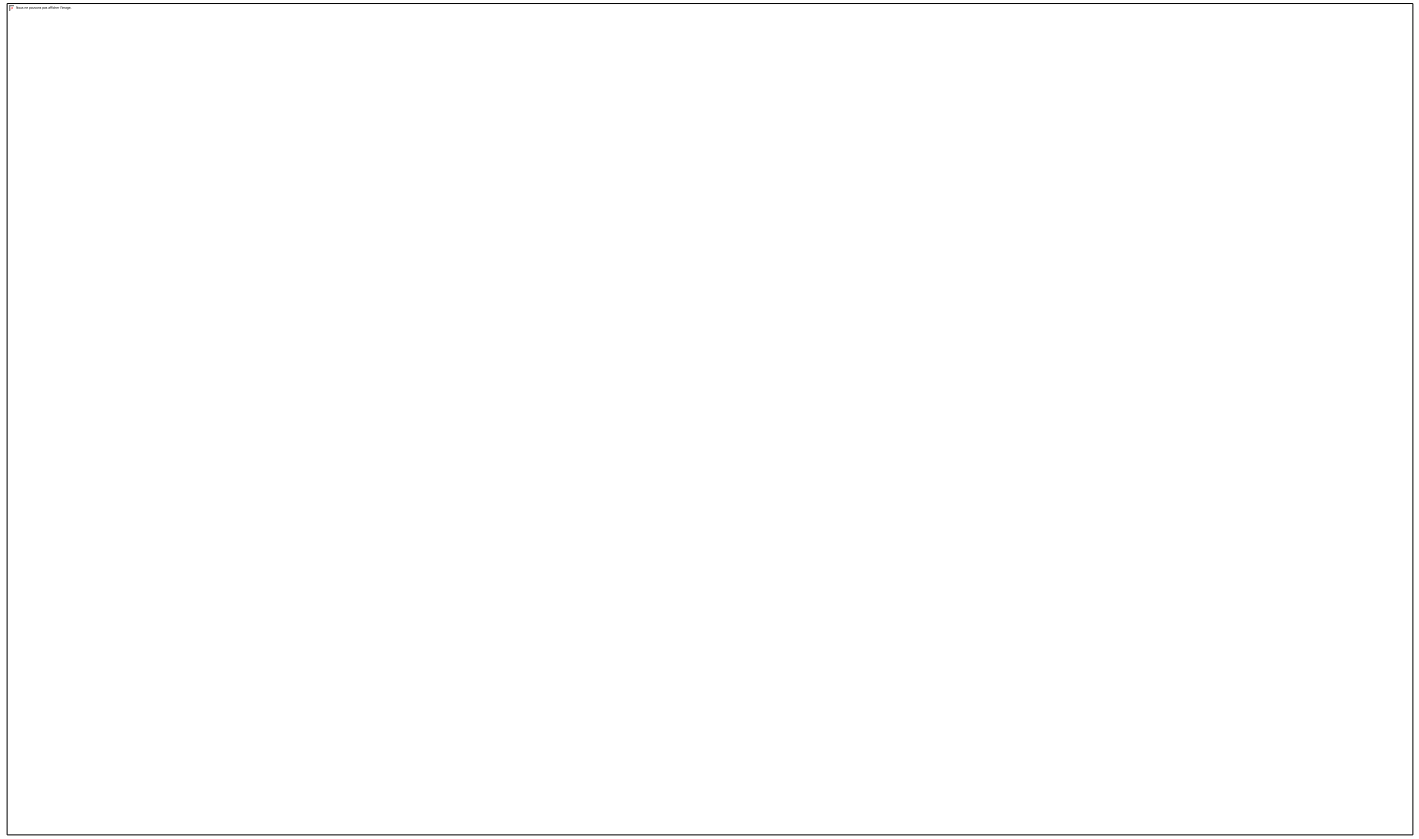


Image from Pallium.ca

APPROACH TO SYMPTOMS

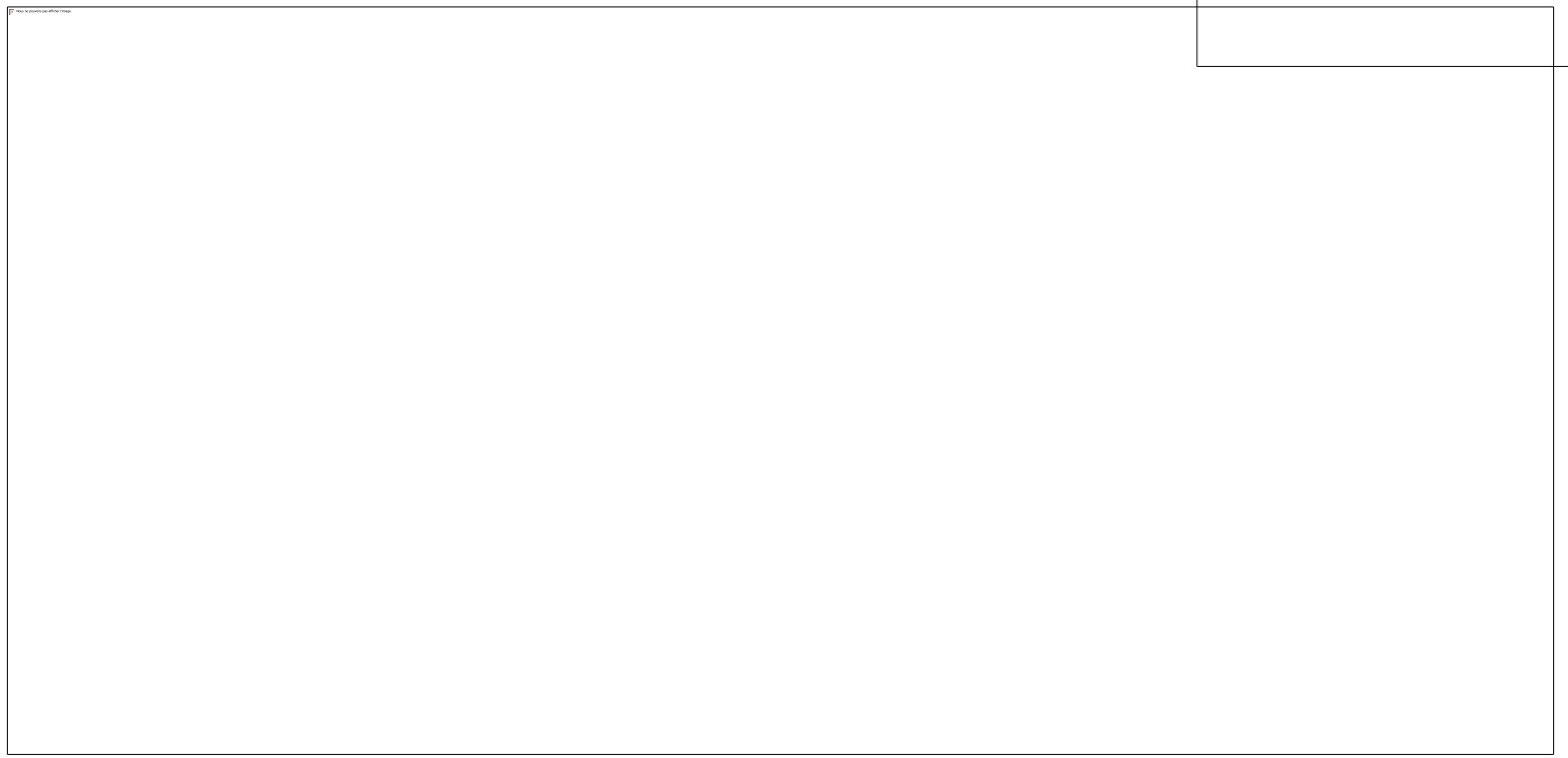
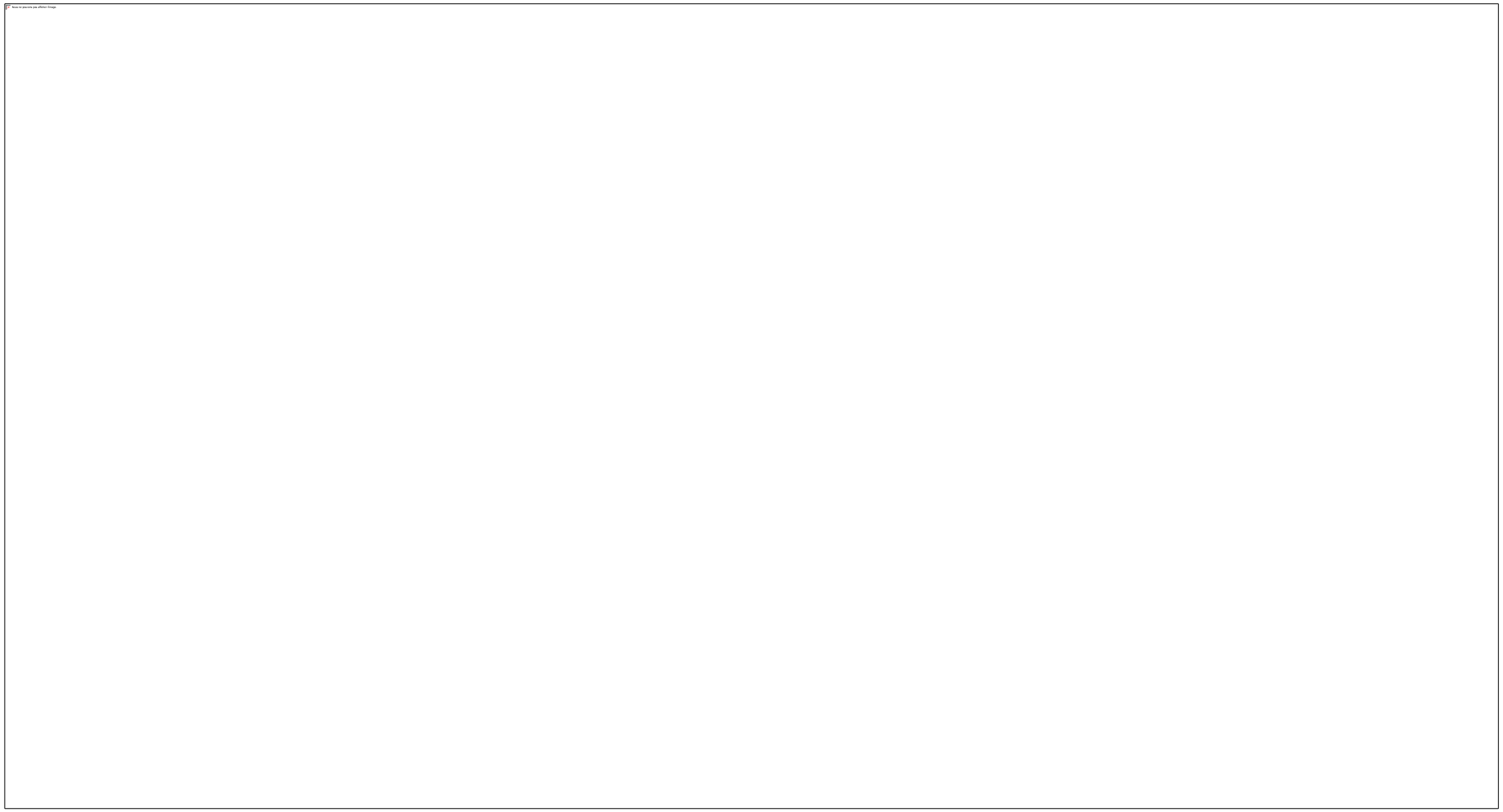


Image from Chronic Pain Scotland: Alternative Pain Management Techniques
http://chronicpainscotland.org/alternative-pain-management-techniques/

LIVER METABOLISM

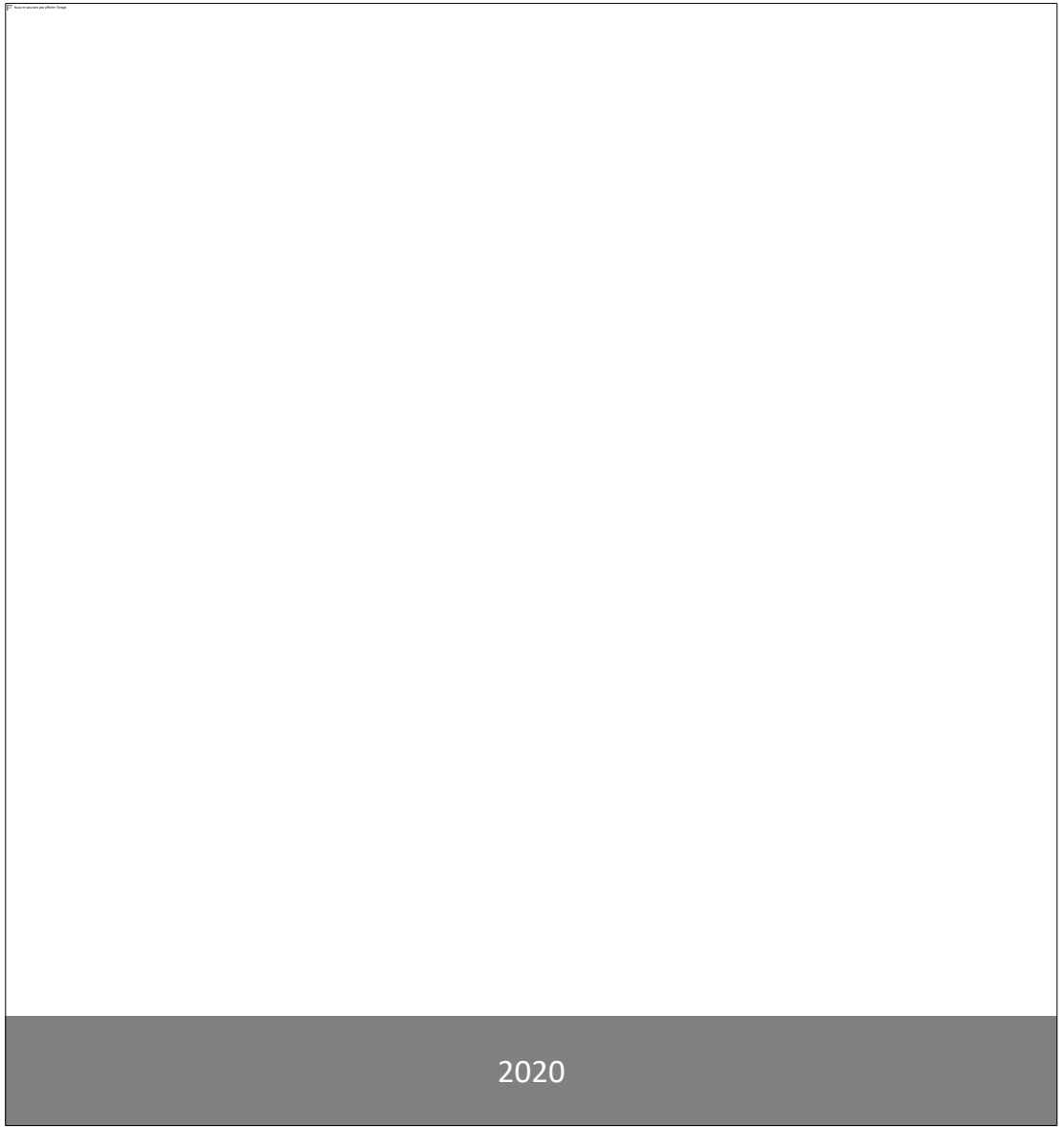
https://livertox.nlm.nih.gov

LIVER PHARMACODYNAMICS



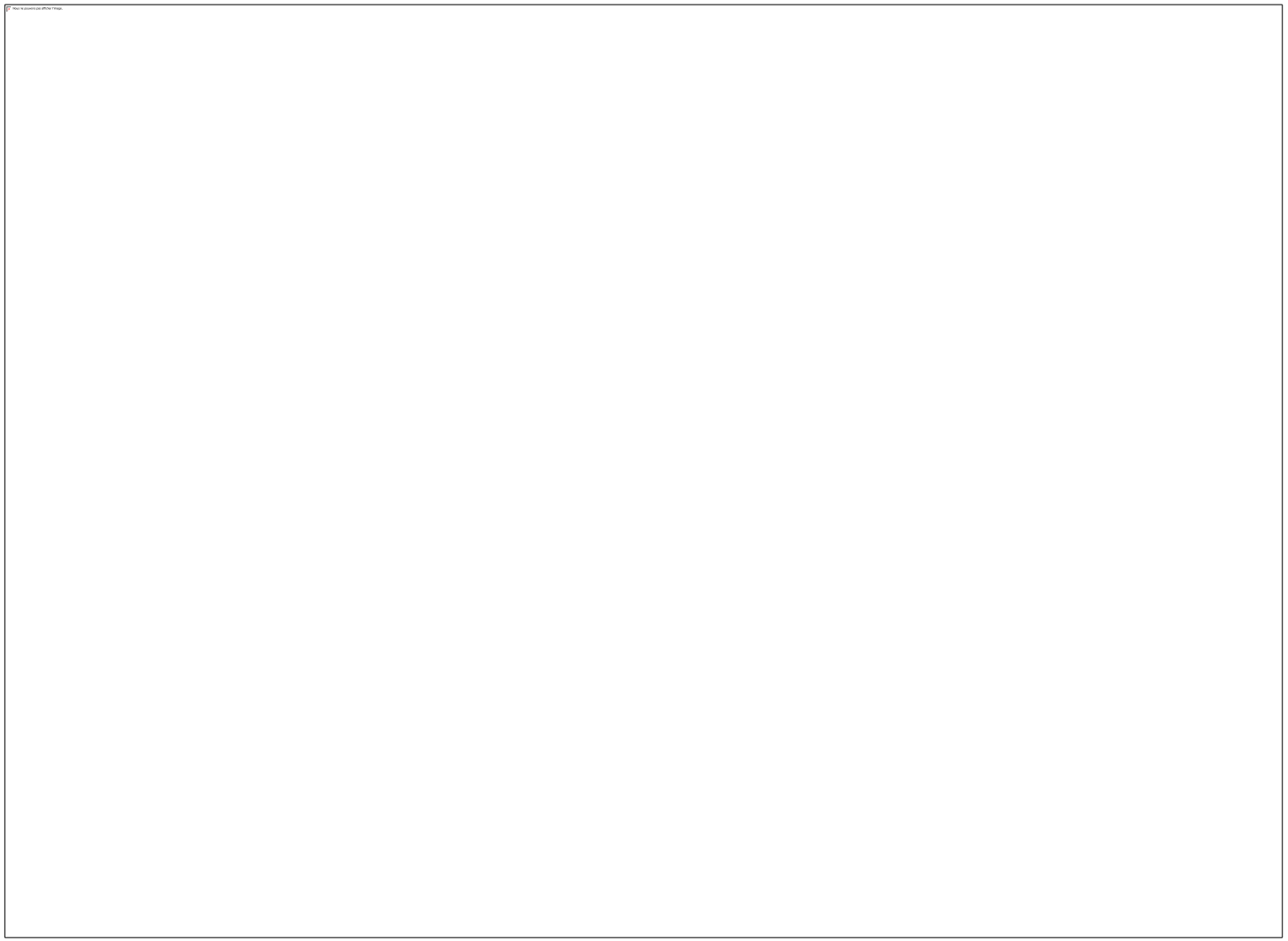
https://livertox.nlm.nih.gov

Critically Ill Patients with Cirrhosis



Data in this presentation from this book (unless otherwise stated)

ASCITES



ASCITES

No survival
Advantage of large volume paracentesis (LVP) over diuretic therapy

No more than 4-liter removal per week (unless comfort care only)

Diuretic Resistance: no response to diuretics and Na restriction, occurs in 10% of patients with ascites

REFRACTORY ASCITES

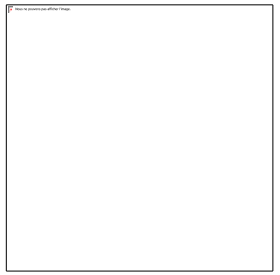
Diuretic resistance

- spironolactone 400mg/day + furosemide 160mg/day for at least 1 week, mean weight loss < 0.8kg over 4 days

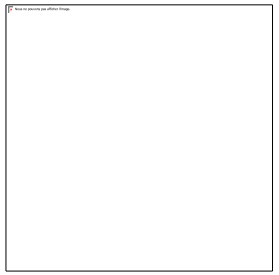
Diuretic intractable

- Complications – creatinine >177umol/L, Sodium <125mmol/L, potassium <3 or >6 despits appropriate measures, diuretic induced encephalopathy (no other precipitants for encephalopathy)

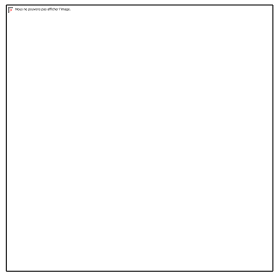
Refractory ascites: Who gets a paracentesis?



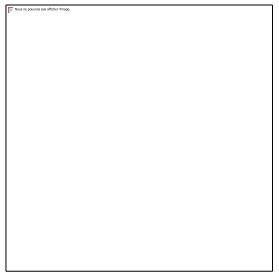
Clinical Deterioration



Lab suggestion of possible bacterial peritonitis



GI Bleeding (high risk for infection)



Symptom management

REFRACTORY ASCITES: Survival

Refractory ascites – 6-month survival 50%, 1 year survival 25%

Poor survival - low protein in ascitic fluid, higher Child-Pugh score, previous SBP, and history of heavy alcohol consumption.

Paracentesis of small volumes has less effect on hemodynamic changes

No BENEFIT OF ALBUMIN INFLUSIONS TO INCREASE SERUM ALBUMIN

China et. al. NEJM 2021

ALBUMIN REPLACEMENT: Large Volume Paracentesis (>5L)

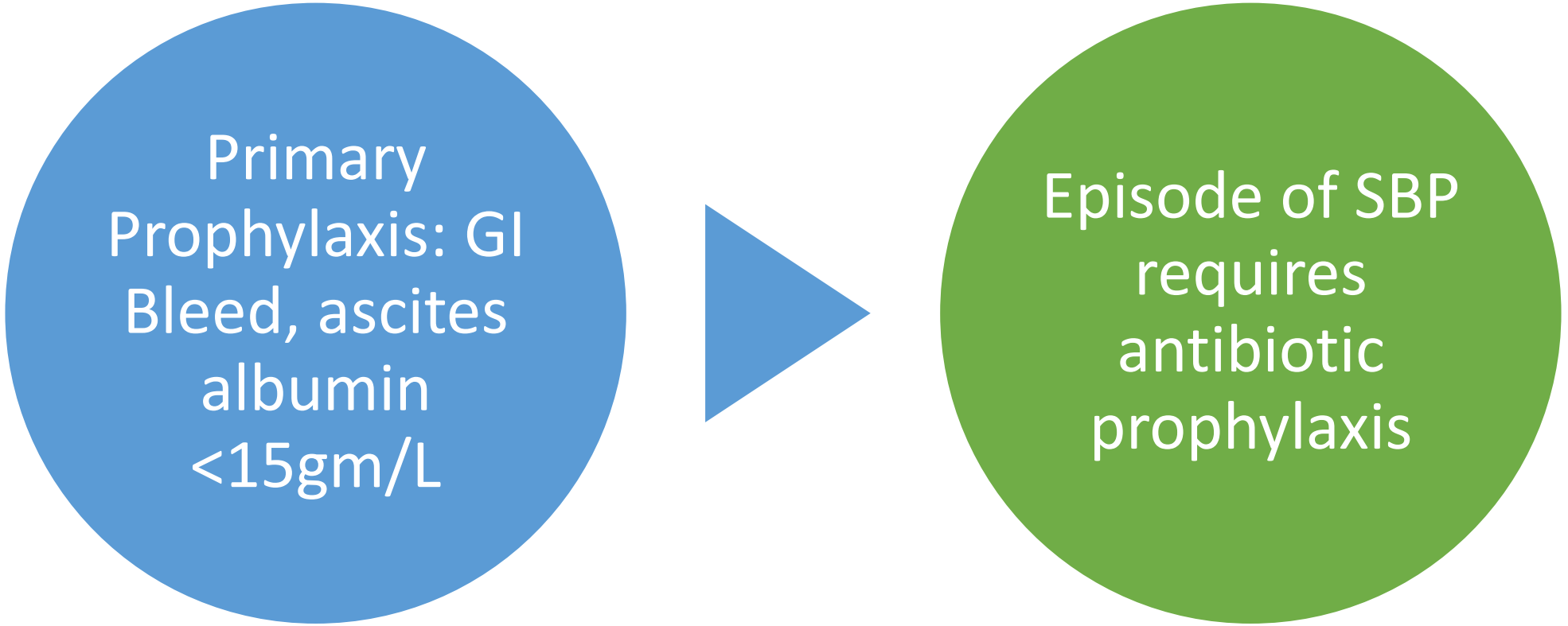
Albumin replacement is standard treatment in both ascites sensitive to diuretics and refractory ascites

Ascites and Diffuse Intra-abdominal Carcinoma

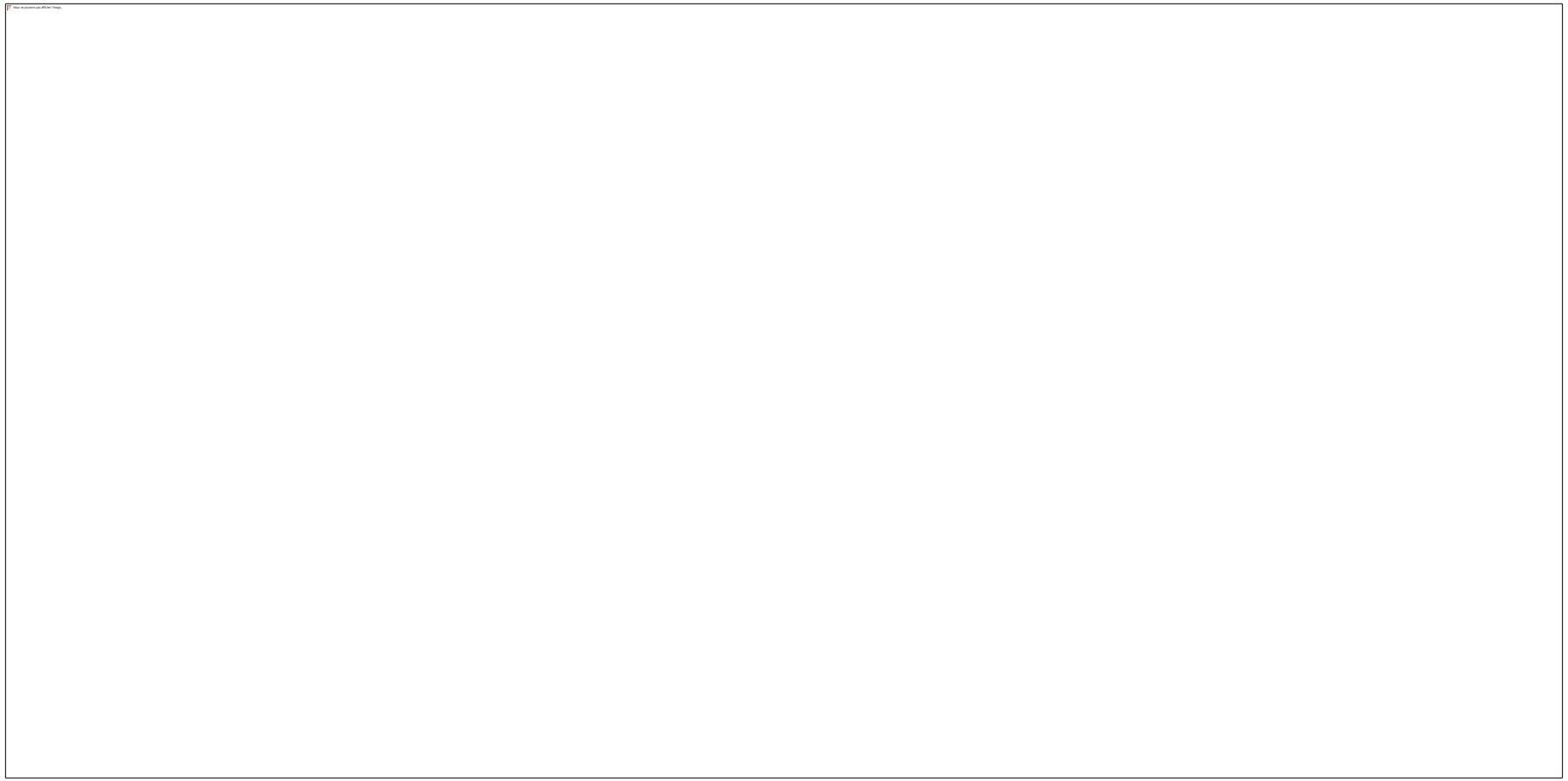
- Large volumes removed without fear of hemodynamic sequelae.
- Trials of albumin infusion have not been performed.
- Clinical experience suggests that intravenous albumin infusion is generally **not** necessary
- Giving albumin increases the time undergoing paracentesis, and likely will need to be in an infusion center to receive it.
- No trials on furosemide efficacy, tend not to use, but could try if peritoneal catheter not an option

UptoDate 2022 Accessed On Line

Antibiotics for SBP and Prevention



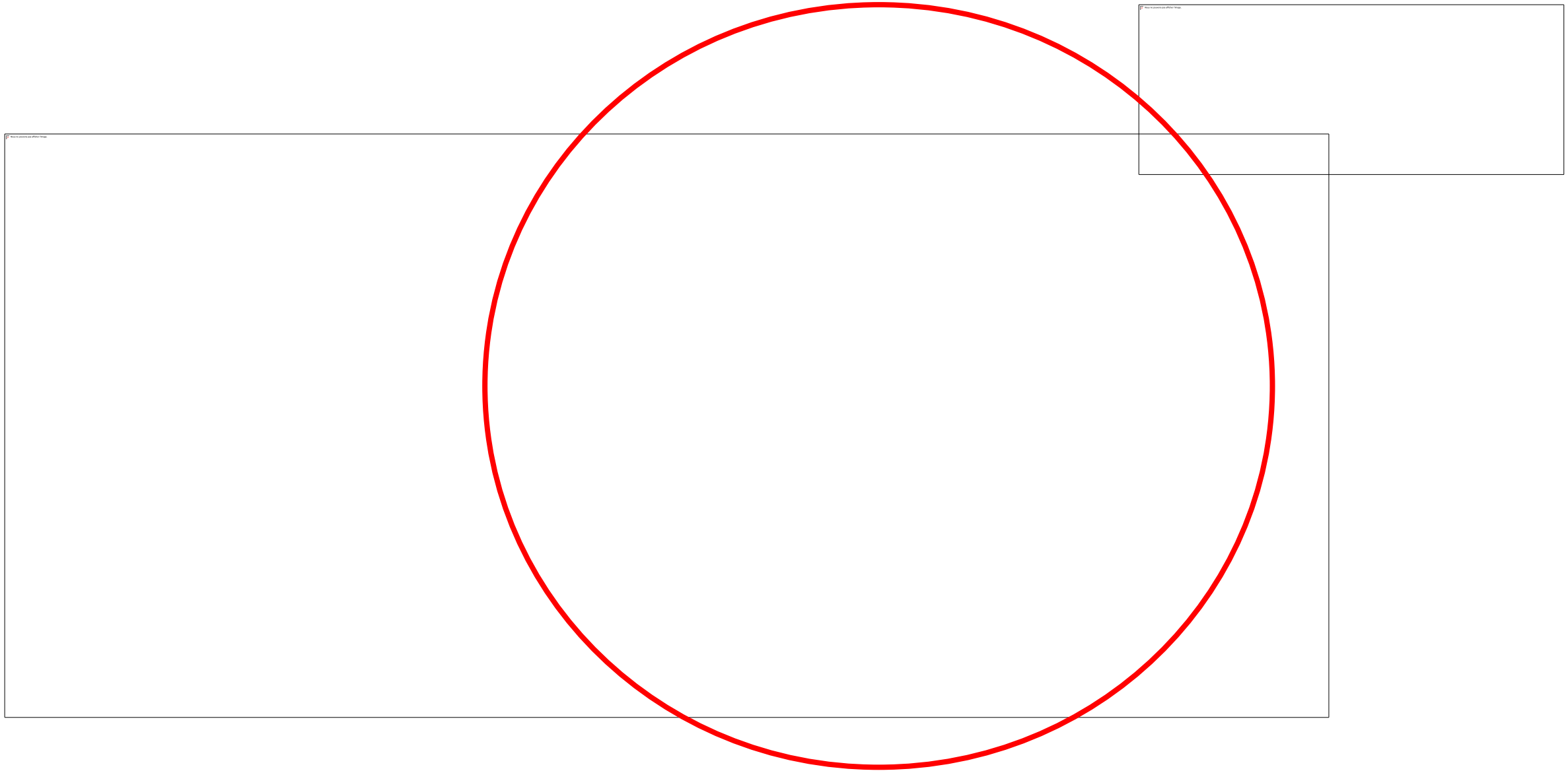
Indwelling catheters vs. LVP for cirrhosis related ascites



Tunnelled Uncuffed Catheters: Tunneled Uncuffed Pigtail Drainage Catheter Placement in Patients with Refractory Ascites or Pleural Effusion: A Single-Center Experience **Source:** *CardioVascular and Interventional Radiology* [0174-1551] yr:2022 pg:1-7

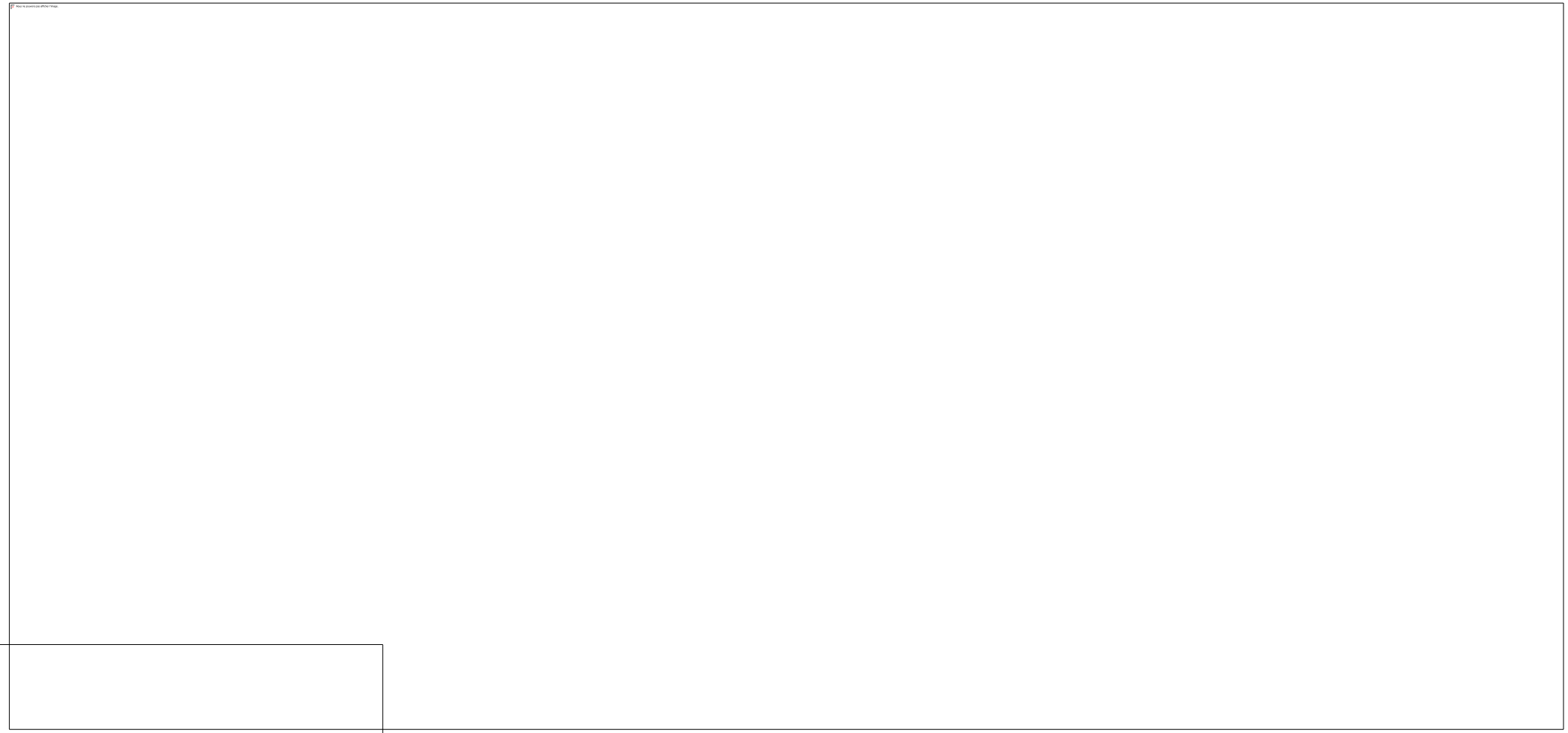
Alpha
Pump

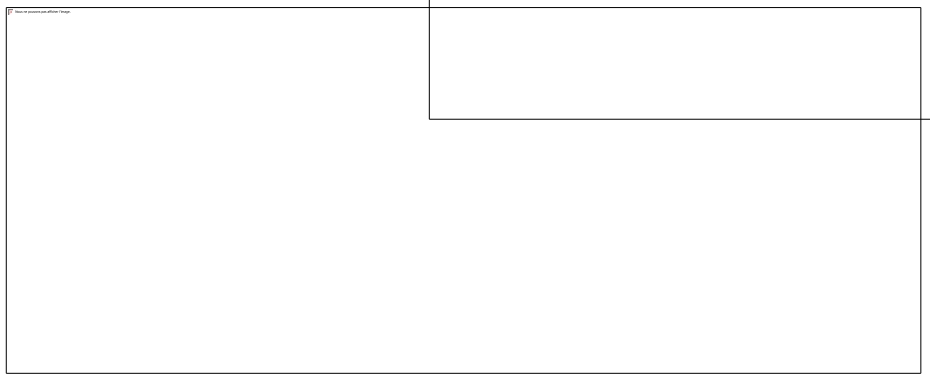
30% of patients develop acute kidney injury (AKI) and infections are quite frequent



Will V, Rodrigues SG, Berzigotti A. Current treatment options of refractory ascites in liver cirrhosis-A systematic review and meta-analysis. *DIGESTIVE AND LIVER DISEASE*. 2022;54(8):1007-1014.

ASCITES: HYPONATREMIA, HYPOTENSION





IPC = Indwelling Peritoneal Catheter

The proportion of patients with hyponatremia increased to 84.8% after IPC placement.

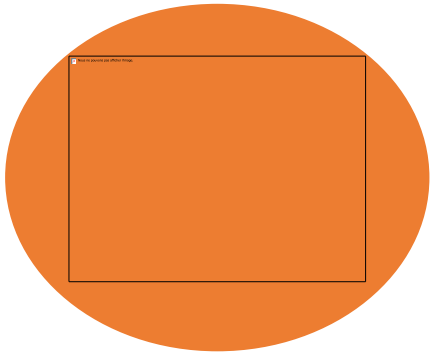
Risks: Lower Serum Na level before IPC placement, lower BMI, and underlying hepatopancreatobiliary malignant neoplasms

Removing 2 L of ascites per day amounts to a total body loss of 250 to 280 mEq of sodium = more than the sodium content of a typical American diet

This accounts for 5% of the total body sodium and approximately 10% of extracellular fluid sodium.

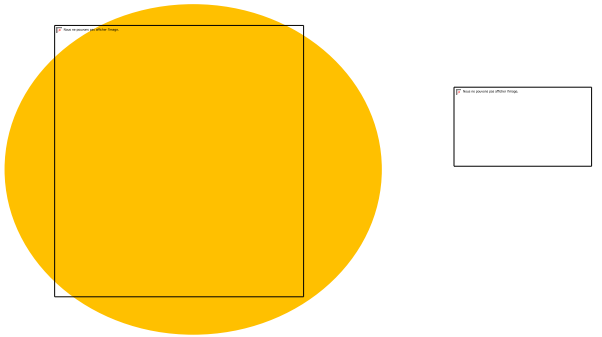
There is also a high prevalence of hyponatremia among patients with hepatocellular carcinoma and pancreatic malignant neoplasms

MANAGEMENT OF HYPONATRAEMIA: TIPS



MALIGNANT ASCITIC DRAINAGE

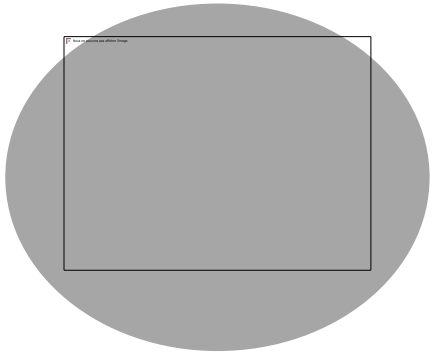
REPLACE WITH ISOTONIC IVF AND/OR ALBUMIN (154 MEQ OF SODIUM IN 1 L OF 25% ALBUMIN)



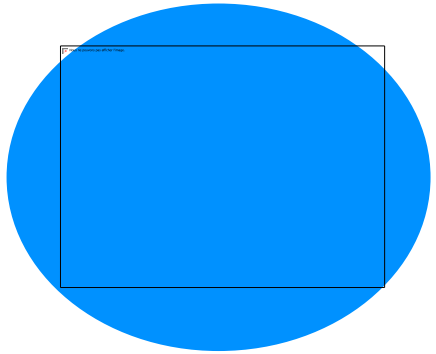
MALIGNANT ASCITES ACCUMULATES INDEPENDENT OF VOLUME STATUS.

ADMINISTRATION OF CRYSTALLOID DOES NOT WORSEN ASCITES.

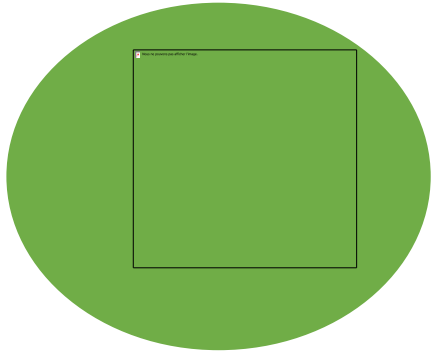
MANAGEMENT OF HYPONATRAEMIA: TIPS



HYPOVOLEMIC HYPONATREMIC: IVF, ALBUMIN, OR BLOOD RESTORES SODIUM LEVEL



REPLACEMENT OF SODIUM LOSSES WITH IVF EQUIVALENT TO ASCITIC FLUID DRAINED



RESTRICT CONSUMPTION OF HYPOTONIC FLUIDS, INCREASE DIETARY SALT

ASCITES CASES

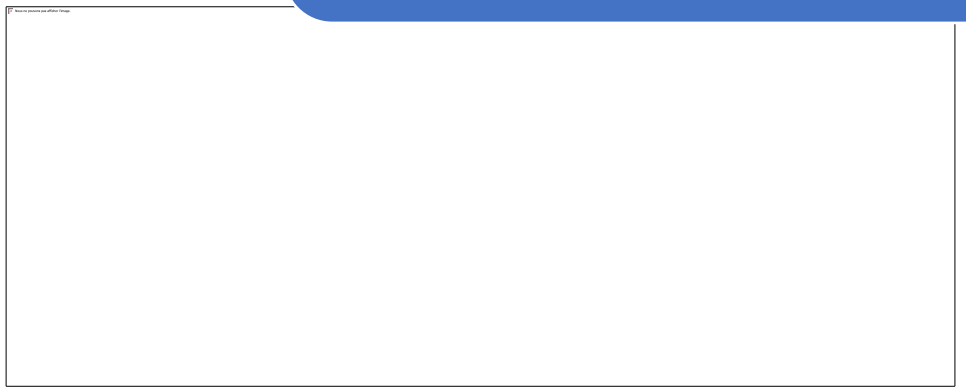
What have you experienced. Let’s TALK!

VARICEAL HEMORRHAGE

6-week mortality rate 10–20% and a 1-year mortality rate 30–60%

Mortality from variceal hemorrhage as the sole decompensating event was 20%

Variceal hemorrhage and a second decompensating event (ascites or encephalopathy), death rate increased to 88%



VARICEAL HEMORRHAGE

- Rebleeding risk is influenced by the treatment of underlying portal hypertension
- 60% of untreated patients experience rebleeding within 1–2 years
- 30% of those given treatments that lower portal pressure experience rebleeding within 1-2 years
- Propranolol should be capped to 160 mg/day and nadolol be capped to 80 mg/day

TRANSFUSIONS

Restrictive hemoglobin (70 mg/dL) transfusion strategy higher probability of survival and fewer adverse events than liberal strategy (90 mg/dL)

VARICEAL HEMORRHAGE

Bacterial infections in > 50% of patients who experience GI bleeding

Antibiotic prophylaxis within 8 hours after endoscopy reduced rebleeding rate (12% and lowered mortality by 25%

Antibiotic prophylaxis was associated with a marked mortality reduction in Child C patients, from 62% to 35%, but less clearly effective in Child A and B patients

Non-selective Beta Blockers

Patients who had to stop B-blockers (BB) for whatever reason: marked rise in mortality, hospitalization, variceal bleeding, bacterial infection, and/or development of hepatorenal syndrome.

Use of BB protects patients against the development of bacterial infections

VARICEAL HAEMORRHAGE CASES

What have you experienced. Let’s TALK!

HEPATIC ENCEPHALOPATHY (HE)

Overt HE will occur in **up to 50%** of those with cirrhosis.

20%-80% have **Minimal /Covert HE**.

Ammonia levels helpful if normal (to rule out as a cause for confusion).

Identify and treat precipitants.

Continue lactulose if tolerated. Evidence for PEG 3350.

HE = hepatic encephalopathy

HEPATIC ENCEPHALOPATHY (HE)

A precipitating cause for HE was found in 92% patients: infection (43%), GI bleeding (16%), medication non-compliance (15%) and electrolyte imbalance (14%)

The most common causes of death were decompensated chronic liver disease (57%) and sepsis (19%).

Survival was 44% and 35% at 12- and 24-months

ENCEPHALOPATHY: Tips

Recent data to suggest that the use of opioids in patients in cirrhosis was associated with altered gut microbiota and increased hospital readmissions

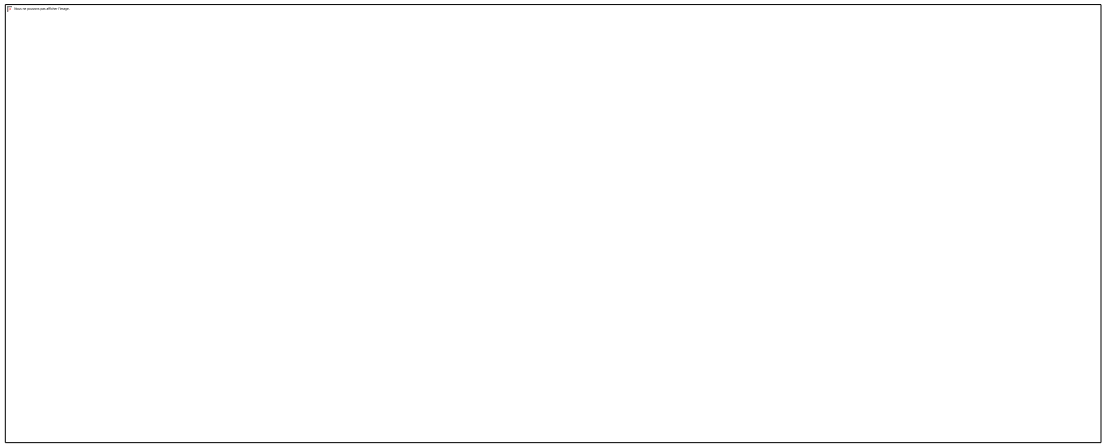
Proton Pump Inhibitors have been associated with an increased risk of hepatic encephalopathy in patients with cirrhosis

Rifaximin in Prevention of Recurrence of Encephalopathy

Bass NM, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362:1071-1081.

ENCEPHALOPATHY CASES

What have you experienced. Let’s TALK!



Hepatocellular Carcinoma

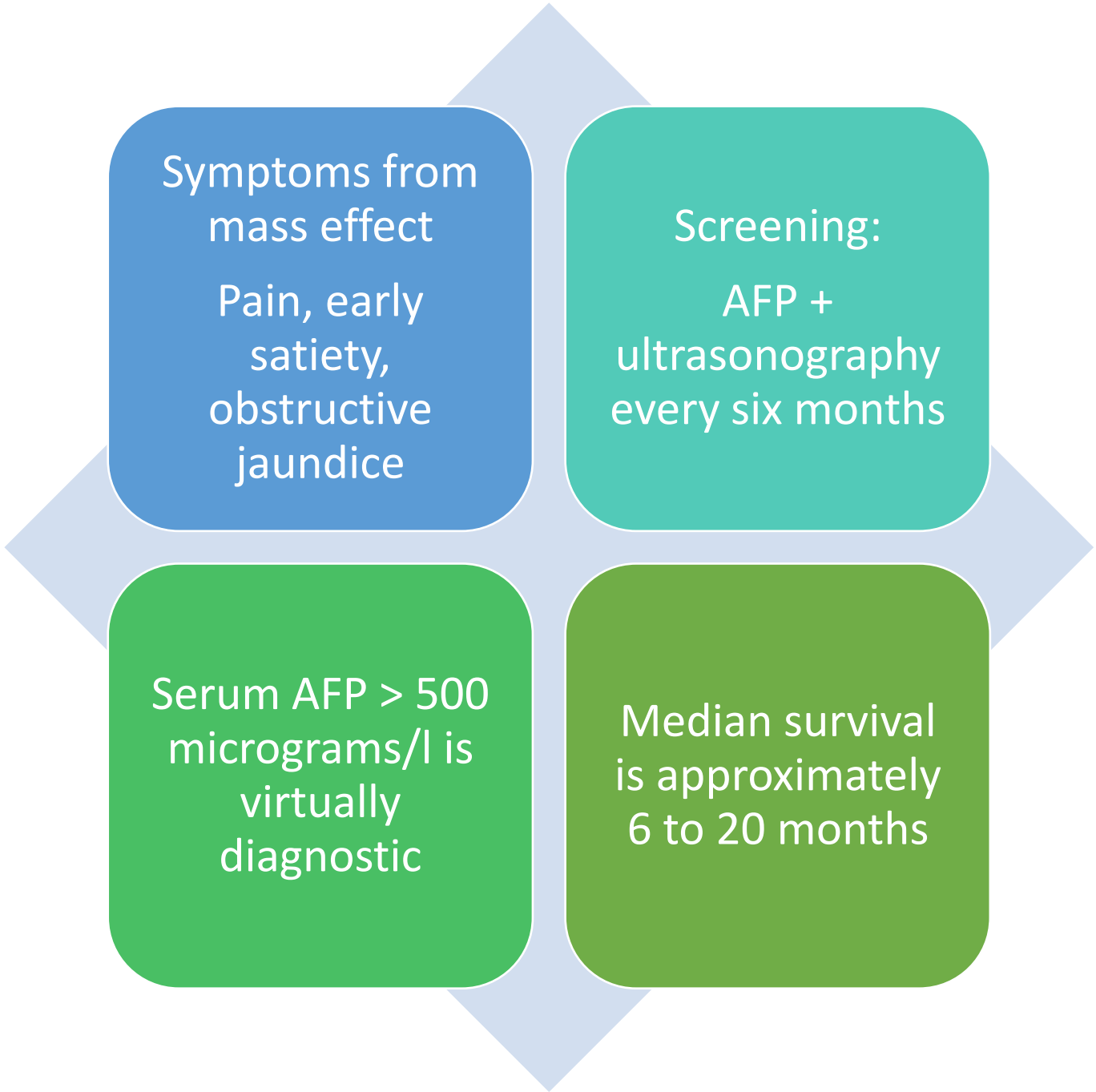
1

Patients with cirrhosis have a markedly increased risk of developing hepatocellular carcinoma.

2

Incidence in well compensated cirrhosis is approximately 3 % per year = 800,000 deaths per year

Hepatocellular Carcinoma



HCC is the sixth most frequent cancer type and the third leading cause of cancer-related death worldwide

https://www.cancer.org/cancer/liver-cancer/detection-diagnosis-staging/survival-rates.html

Hepatol Commun. 2020 Oct; 4(10): 1541–1551. SEER Surveillance, Epidemiology, and End Results

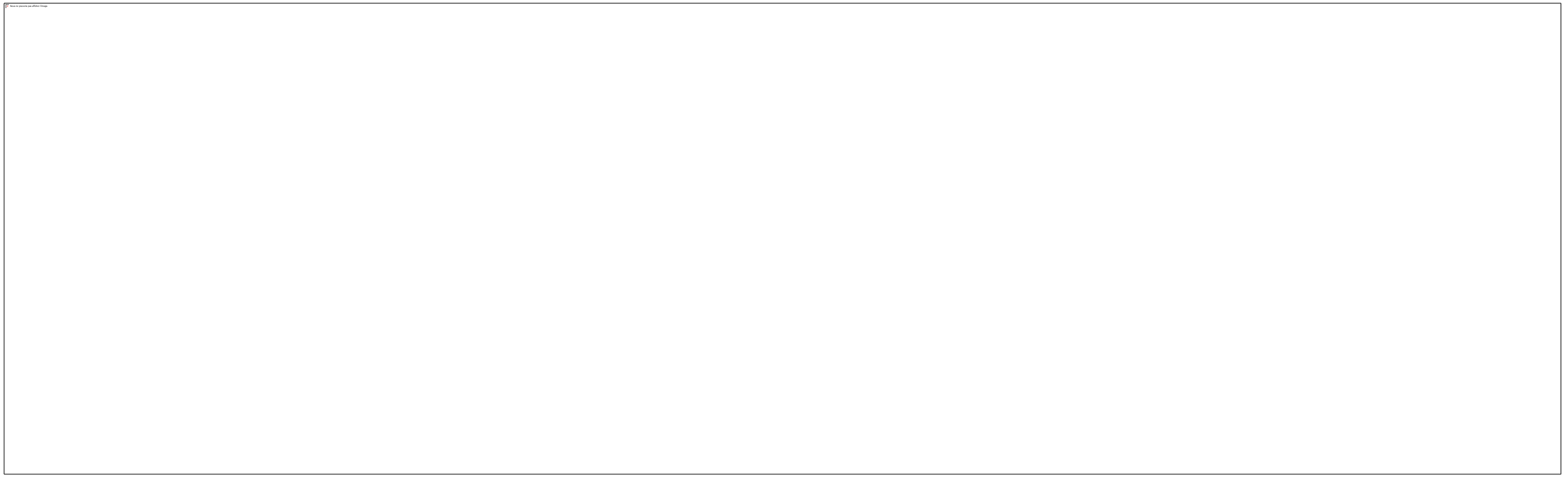
Available Treatment Prior to Immunotherapy = Sorafenib (anti-neoplastic, tyrosine kinase inhibitor)

6 other Tyrosine Kinase Inhibitors Available: limited by resistance development and side effects

Marginal benefit

Oncol., 11 October 2021
Sec. Cancer Molecular Targets and Therapeutics

HEPATOCELLULAR CARCINOMA AND CIRRHOSIS



Cancers 2022, 14, 2018

IMMUNE INHIBITORS

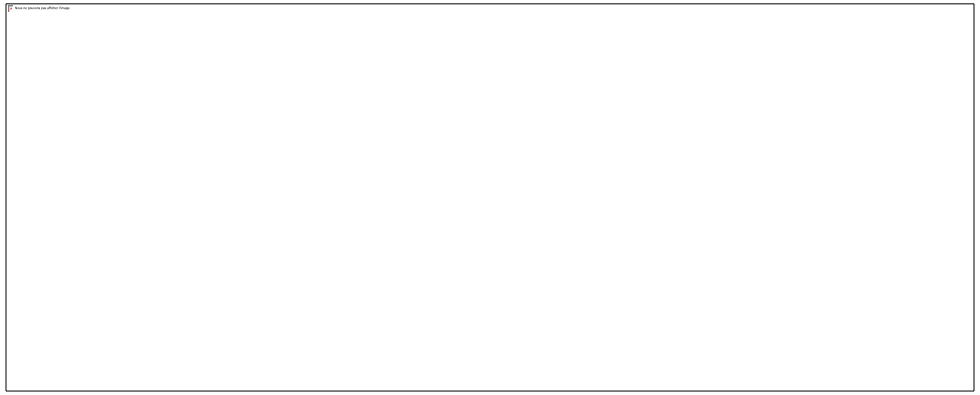
Immunotherapies: Immune checkpoint inhibitors including atezolizumab, nivolumab, and pembrolizumab.

2022 guidelines: combination of atezolizumab with bevacizumab (monoclonal antibody) is currently the first-line treatment for patients with HCC (survival benefit versus sorafenib)

Adverse effects: skin rash, fatigue, and diarrhea, thyroid dysfunction, liver function

Survival may not be improved in patients with non-viral HCC

OTHER COMPLICATIONS OF CIRRHOSIS

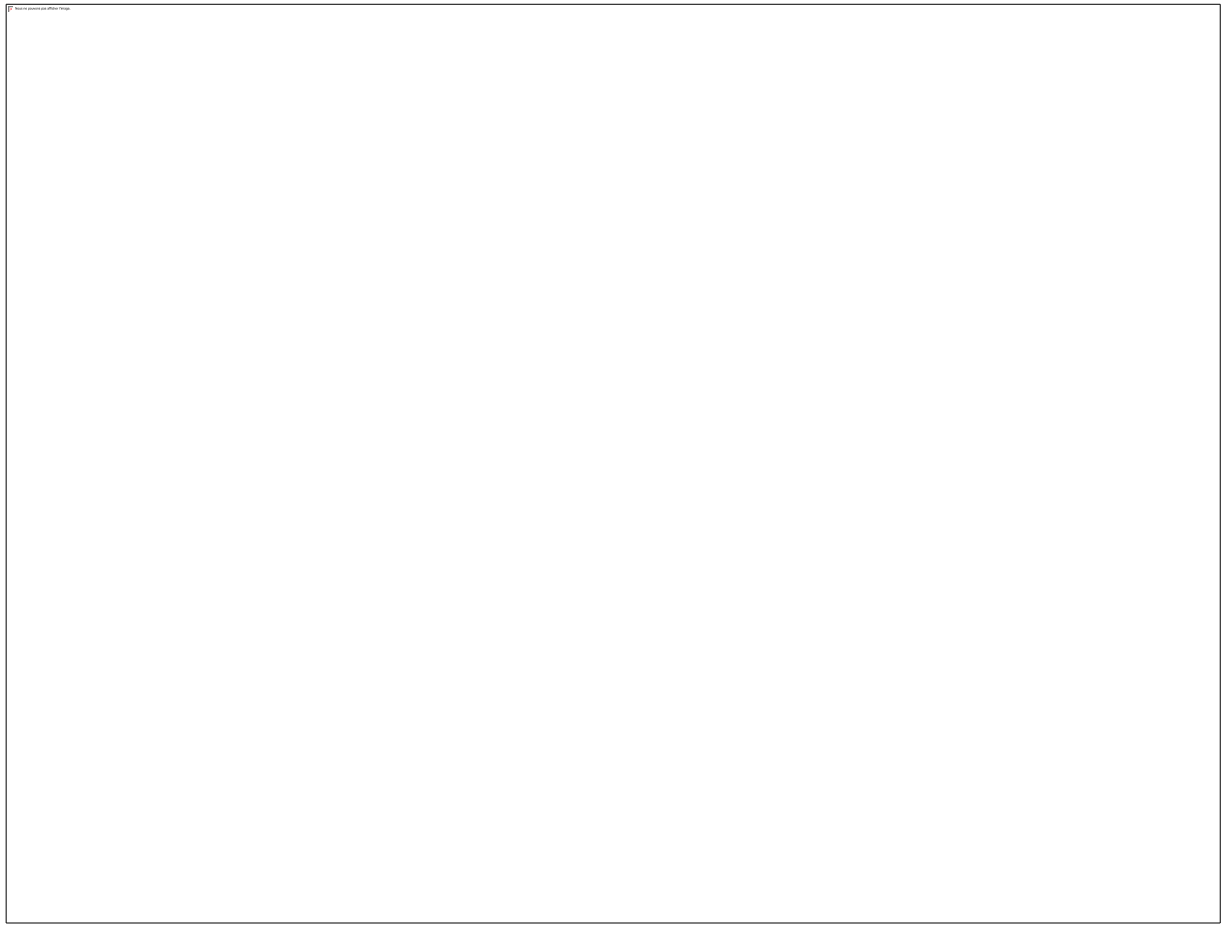


COAGULOPATHY, ANAEMIA, THROMBOCYTPENIA

- Nutritional correction and education
- Minimal modifications possible
- Transfusion not recommended, if no bleeding present

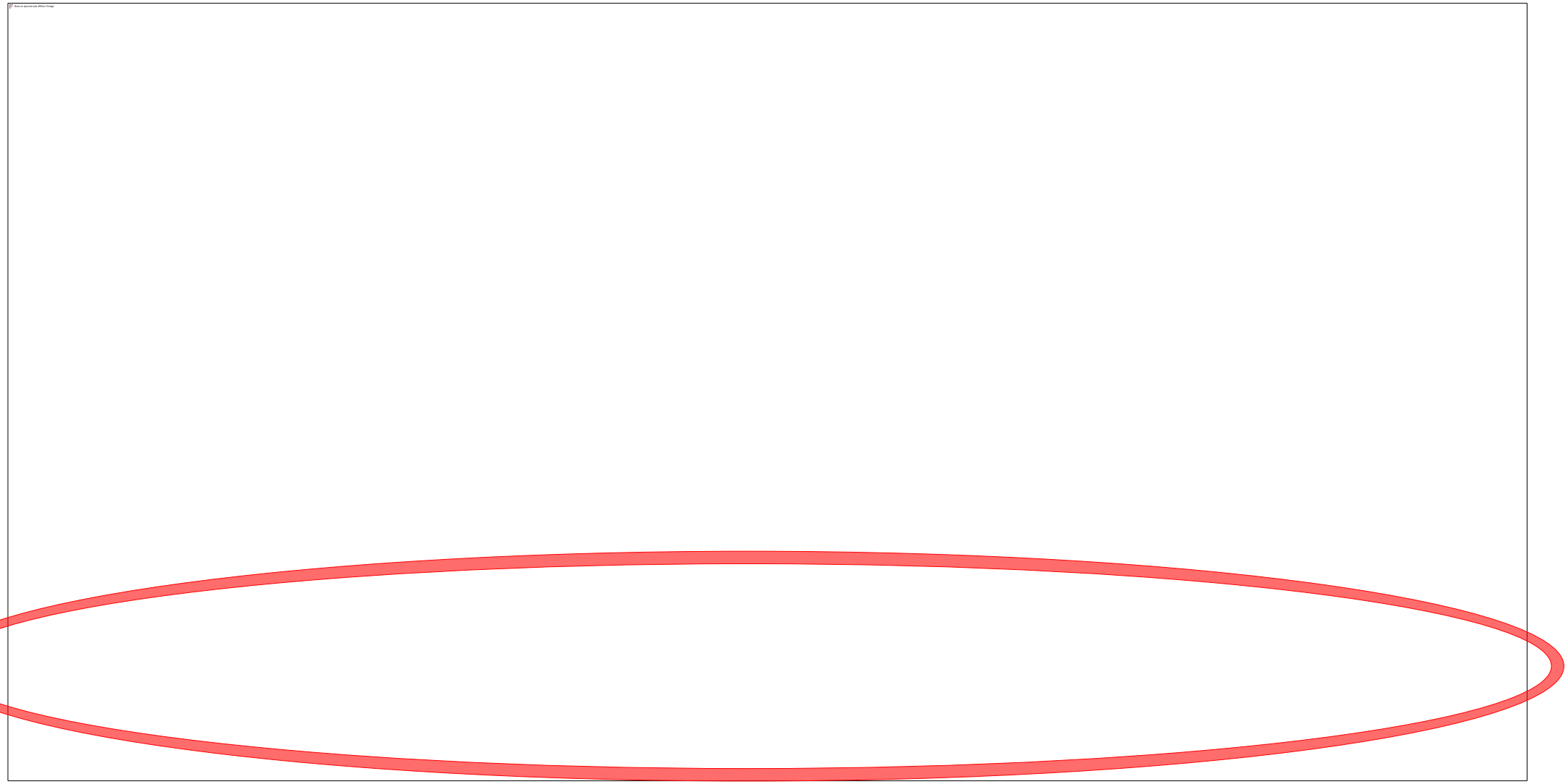
HEPATIC HYDROTHORAX (HH)

- Transudative effusion in a patient with portal hypertension without other underlying cardiopulmonary cause
- Asymptomatic ➔ respiratory distress
- 20% of patients do not have ascites
- 70% right sided, 18% left sided, 12% bilateral

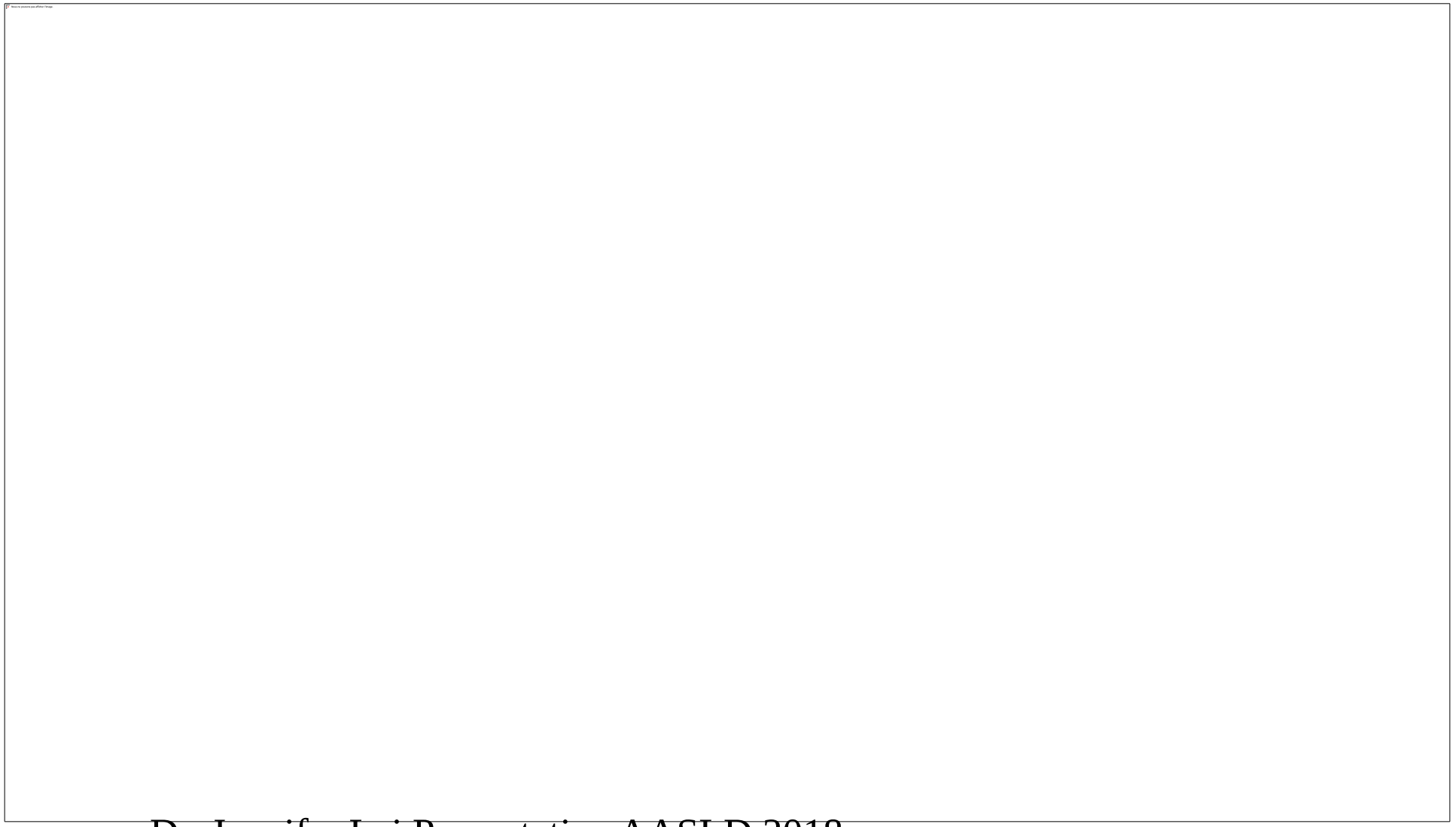


Machicao et al. Hepatology 2014

Malnutrition in ESLD

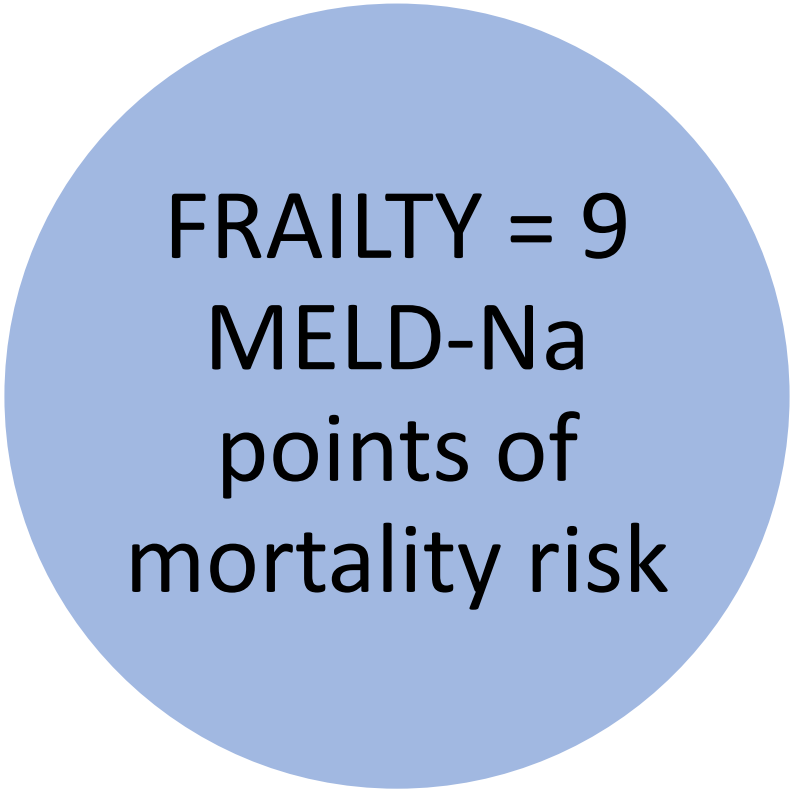


Frailty and Cirrhosis



Dr. Jennifer Lai Presentation AASLD 2018

Frailty Index Predicts Mortality Better than MELD-Na Alone



Dr. Jennifer Lai Presentation AASLD 2018

https://cirrhosiscare.ca/wp-content/uploads/2021/03/CC-Cirrhosis-discharge-orders-March-24.pdf

https://cirrhosiscare.ca/wp-content/uploads/2021/11/Cirrhosis_Admission_Order_set.pdf

ASK ME YOUR QUESTIONS

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