Advanced cirrhosis: physicians role

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Liver transplantation

- Definitive, potentially curative treatment
- Refer early when decompensation occurs
- Should not wait until till patient is moribund or hospitalized in life-threatening condition
- Most transplant centres will accept patients <70 years of age

Liver transplantation: indications

Decompensation

- Child class B/C or MELD score $\geq$ 15
- Index complication such as ascites, variceal bleed
- intractable pruritus, recurrent cholangitis, hepatopulmonary syndrome: lower scores

Hepatocellular carcinoma

- Milan criteria: one lesion ≤5cm or no more than three lesions ≤3 cm each
- No macrovascular invasion or extrahepatic disease

Liver transplantation: contra-indications

Absolute	Severe cardiac and/or pulmonary diseases and severe pulmonary hypertension (mPAP >45 mm Hg)
	Alcohol addiction without motivation for alcohol abstinence and untreated/ongoing substance abuse
	Hepatocellular carcinoma with extrahepatic metastases
	Current extrahepatic malignancies (eventually reevaluation after successful therapy)
	Sepsis
Relative	Untreated alcohol abuse and other drug-related addiction
	Cholangiocellular carcinoma
	Hepatic metastatic neuroendocrine tumors (NET), metastatic hemangioendothelioma
	Morbid obesity
	Persistent non-adherence

Liver transplantation

- Many patients not candidates: clinical & social factors
- Number qualify >> available donor organs
- 14% patients transplant wait-list die annually
- Many de-listed as they become too ill for LT

Evidence based do's and don'ts for some commonly mismanaged complications of advanced liver cirrhosis

Resistant ascites and SBP

- **Diagnostic paracentesis** should be performed regardless of coagulopathy
- Treat SBP aggressively with i.v. antibiotics (third generation cephalosporines)
- Secondary prophylaxis on discharge: quinolones

Resistant ascites

- **Na restriction (2g/day)** combined with diuretics
- Serial, large volume paracentesis (+ i.v. albumin: 8 g/litre of ascites removed) commonly required
- Indwelling peritoneal catheters increase risk of infection
- Drugs that lower BP, including beta blockers (especially carvedilol), ACEI - discontinued
- TIPSS considered if available/no contraindications

Hepatic hydrothorax

- Not infrequent in patients with ascites
- Diagnostic thoracentesis should be performed
- Management: Diuretics and thoracentesis (in patients with dyspnoea)
- Chronic pleural drainage **not** recommended due to frequent complications
- Pleurodesis (talc, tetracycline) in patients with refractory hepatic hydrothorax

Hyponatraemia

- Hyponatremia common in advanced cirrhosis
- **Dilutional** (activation of RAAS and ADH release); not due to excess urinary Na loss
- Routine correction of asymptomatic, mild hyponatremia not recommended
- Indications for correction: neurologic symptoms and /or serum Na <125 mEq/L

Hyponatraemia

- Fluid restriction (1-1.5L/d) mainstay of treatment
- **Sodium restriction** (2 g/d) should be continued (as patients also have ascites)
- Administration of 3% saline considered if Na <110 mEq/L despite fluid restriction
- Rapid correction (>9 mEq/L in 24h) of serum Na may lead to pontine myelinolysis or seizures

Hyponatraemia

- Correction of hypokalemia* and i.v. albumin can raise serum Na and osmolality
- Tol**vaptan**, sata**vaptan**, lixi**vaptan**: oral, selective Vasopressin V_2 receptor blockers, raise serum Na
- **Not currently recommended for routine use in cirrhosis** due to risk of liver damage (FDA, EASL)

*Excess urinary K loss due to increased circulating aldosterone, renal retention of NH_3 in exchange for K, secondary renal tubular acidosis, diuretic therapy

Hepatic encephalopathy

- Correct precipitating factors:
  - Sedatives
  - Constipation
  - Dehydration/electrolyte abnormalities
  - Infection
  - GI bleeding

Hepatic encephalopathy

- Episodic hepatic encephalopathy (No episodes >6m)
  - Metronidazole + lactulose
  - L-Ornithine L-Aspartate i.v.
- Recurrent / persistent HE: Lactulose ± rifaximin
  - Reduces recurrences by 50%
  - May improve refractory HE
  - Improves cognition / co-ordination in minimal HE
- *Faecal microbial transplant: experimental in refractory HE*

Hepatic encephalopathy

- Protein restriction **not** recommended unless severely protein intolerant:
  1.2 to 1.5 g/Kg body wt./day
- Energy: 35-40 KCal/Kg ideal body wt./day

Variceal bleeding

- Acute variceal bleeding should be treated with terlipressin or octretide and Endoscopic Banding Ligation
- Non-selective beta-blockers to prevent recurrent bleeding (when not contraindicated)
  - Carvedilol (NSBB + α1 receptor antagonist)
  - Propranolol

Non-selective beta-blockers

- Mainstay of treatment for portal hypertension (35 years)
- Reduces incidence of first and recurrent variceal bleeds (carvedilol>propranolol)
- Improves survival when portal pressure is reduced (responders: <50%)

Non-selective beta-blockers

- NSSB may cause renal dysfunction / mortality in presence of refractory acsites
  - Dose dependent, manifested by decrease in mean arterial pressure
- Careful dosing / **discontinuation** in presence of
  - Refractory ascites
  - Hypotension (SBP<90mmHg) (carvedilol>propranolol)
  - Acute kidney injury
- Safe to restart upon resolution

Hepatocellular Ca

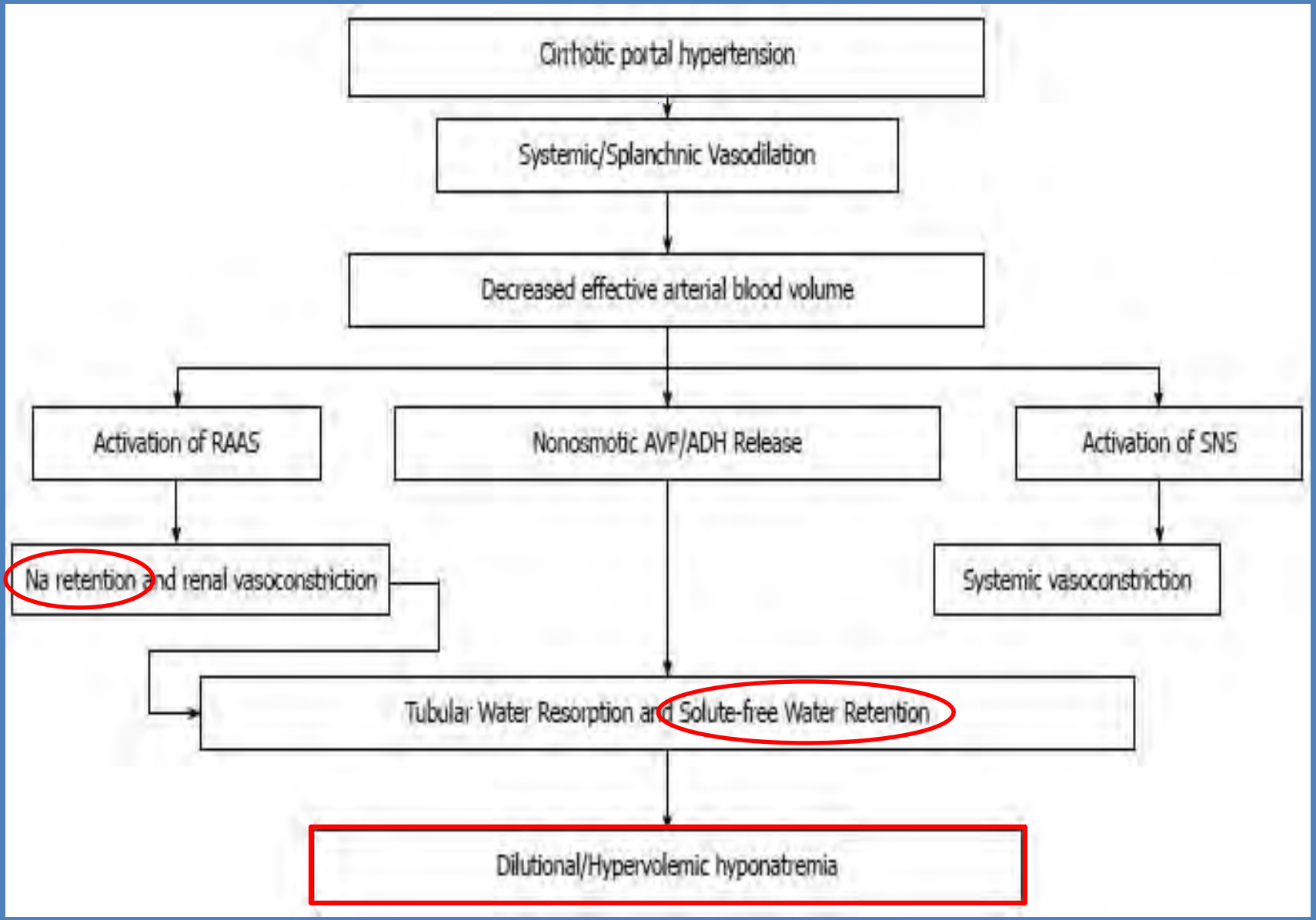
- Patients with cirrhosis increased risk for HCC
- **Screening: U/S liver (±AFP) every 6 months**
- Surveillance:
  - early stage diagnosis
  - higher rates of curative treatment
  - improved survival
- **Diagnosis confirmed by multiphase CT/MRI** (rarely FNAC/Biopsy)

Hepatocellular Ca

- TACE, RFA, Microwave ablation, alcohol injection most effective for lesions <3cm
- Kinase inhibitors (sorafenib) palliative treatment for advanced lesions
- Patient tolerance of treatment depends on liver function

Summary

- Liver transplant only potentially curative treatment for advanced cirrhosis
- Current medical management – physicians role:
  - Regular monitoring
  - (Evidence based) treatment of complications
  - Refer for liver transplantation when indicated


Cirrhotic portal hypertension
Systemic/Splanchnic Vasodilation
Decreased effective arterial blood volume
Activation of RAAS
Nonosmotic AVP/ADH Release
Activation of SNS
Na retention and renal vasoconstriction
Systemic vasoconstriction
Tubular Water Resorption and Solute-free Water Retention
Dilutional/Hypervolemic hyponatremia

General health maintenance

- Pain: paracetamol (2g/d) safe; avoid NSAIDs
- Muscle cramps: Vitamin E, Baclofen, HCQS
- Pruritus:
  - **anti-histamines not effective**
  - Moisturizers for dry skin
  - colestyramine, naltrexone (opiate antagonist), sertraline, UDCA

General health maintenance

- Screen for alcohol use in all patients
- **Vaccination**: influenza, pneumococcal, HAV/HBV
- Refer early to dietitians: **do not restrict protein**
- Sleep dysfunction: treat HE (for inversion), melatonin
- Sexual dysfunction: sildenafil can be used