ΠΑΡΟΥΣΙΑΣΗ ΕΝΔΙΑΦΕΡΟΥΣΑΣ ΠΕΡΙΠΤΩΣΗΣ

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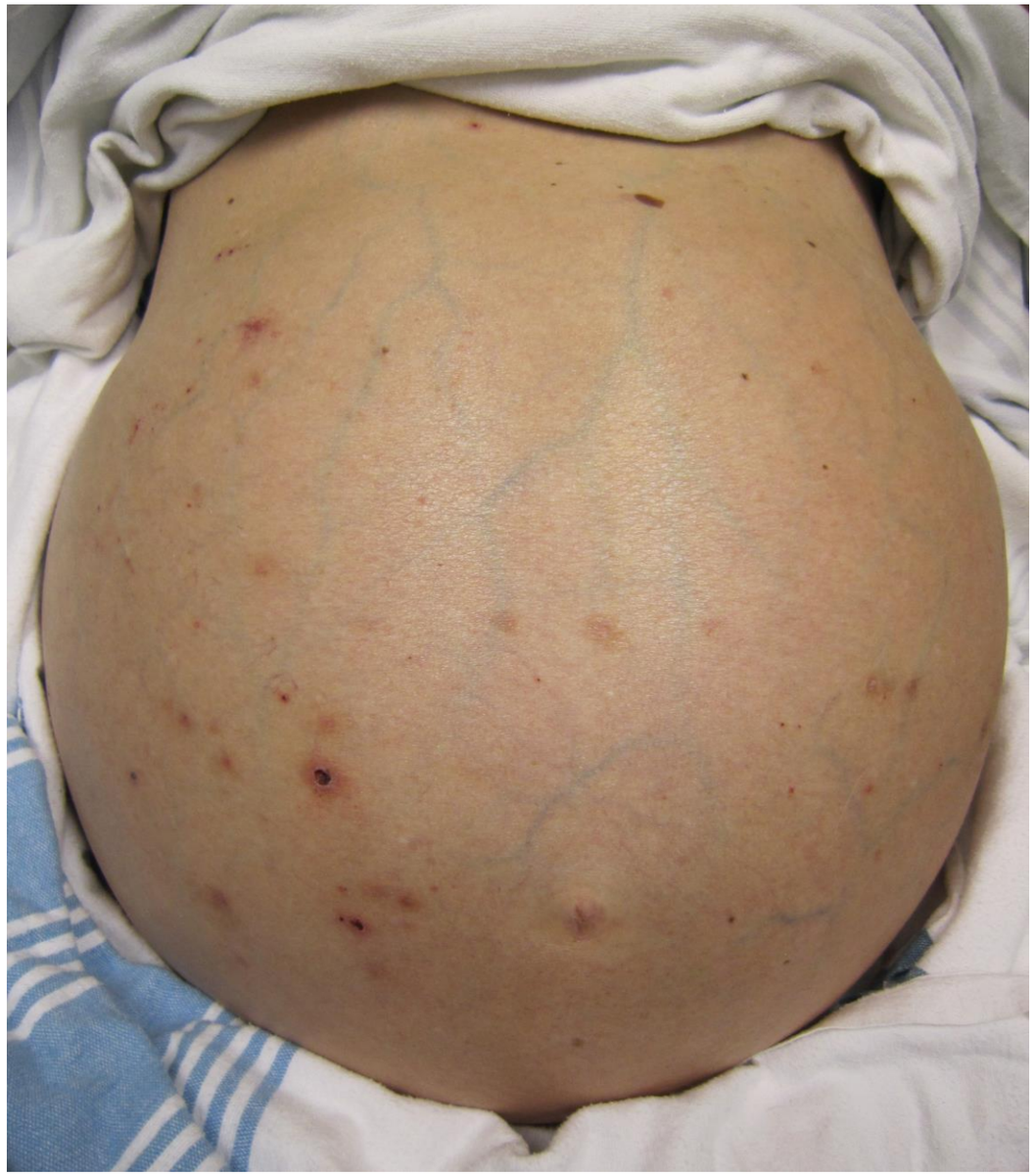
MANAGEMENT OF ASCITES



Goal of therapy

To minimize ascitic fluid volume and decrease peripheral edema, without causing intravascular volume depletion

Benefits

- less abdominal discomfort and shortness of breath
- reduction in the risk of spontaneous bacterial peritonitis through increased ascitic fluid opsonic activity

Ljubicić N1, Bilić A, Kopjar B. Diuretics vs. paracentesis followed by diuretics in cirrhosis: effect on ascites opsonic activity and immunoglobulin and complement concentrations. Hepatology. 1994 Feb;19(2):346-53.

- reduction in the risk of abdominal wall hernia formation or diaphragmatic rupture (and resulting hepatic hydrothorax) associated with tense ascites

Prognosis

- one and two-year mortality of 40 and 50%, respectively
- independent predictors of mortality: hyponatraemia, low arterial pressure, GFR and low renal sodium excretion

1. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol 2010;53:397–417.

2. Llach J, Gines P, Arroyo V, Rimola A, Tito L, Badalamenti S, et al. Prognostic value of arterial pressure, endogenous vasoactive systems, and renal function in cirrhotic patients admitted to the hospital for the treatment of ascites. Gastroenterology 1988;94:482–487.

Management of ascites

Uncomplicated ascites

Refractory ascites

Grade 1

Grade 2

Grade 3

LVP
±
TIPS
or
Alfapump

no therapy

sodium
restriction
+
diuretics

LVP
+
sodium
restriction
+
diuretics

Management of uncomplicated ascites

Grade 1 or mild ascites

No data on the evolution of grade 1 ascites are available, nor it is known whether its treatment modifies its natural history.

European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018 Aug;69(2):406-460.

Management of uncomplicated ascites

<u>Grade 2 or moderate ascites</u>

- moderate restriction of sodium intake
- diuretics
- patients who develop grade 2 ascites do not require hospitalisation

Grade 2 or moderate ascites

Sodium restriction:

- moderate restriction of sodium intake (80–120 mmol/day, corresponding to 4.6–6.9 g of salt)~no added salt diet with avoidance of pre-prepared meals

- resolution of ascites in about 10% of patients

- extreme sodium restriction (<40 mmol/day) should be avoided

Grade 2 or moderate ascites

Diuretics:

- anti-mineralocorticoid drug alone, starting at 100 mg/day with stepwise increases every 72 h (in 100 mg steps) to a maximum of 400 mg/day

- in case of no response (<2 kg/week weight reduction) or hyperkalemia, addition of furosemide at an increasing stepwise dose from 40 mg/day to a maximum of 160 mg/day

- torasemide can be used in cases of no response to furosemide

Grade 2 or moderate ascites

- a maximum weight loss of 0.5 kg/day in patients without oedema and 1 kg/day in patients with oedema is recommended
- once ascites has largely resolved, the dose of diuretics should be reduced to the lowest effective dose

Discontinuation of diuretic therapy

- severe hyponatraemia (serum sodium concentration <125 mmol/L)
- acute kidney injury
- worsening hepatic encephalopathy
- incapacitating muscle cramps
- severe hypokalaemia (discontinuation of furosemide when serum K^+<3.0 mmol/L)
- severe hyperkalaemia (discontinuation of anti-mineralocorticoid drug when serum K^+>6.0 mmol/L)

Grade 3 or large ascites

- large-volume paracentesis (LVP): first-line therapy
- ascitic fluid should be completely removed in a single session
- when >5 L of ascites is removed, LVP should be followed with plasma volume expansion, using albumin (8 g/L), to prevent PPCD (post-paracentesis circulatory dysfunction)
- diuretics
- sodium restriction

Post-paracentesis circulatory dysfunction

- not fully understood pathophysiology
- fluid shifting, increased cardiac output and arteriolar vasodilation, decreased intra-abdominal pressure
- prolonged activation of the sympathetic nervous system and the renin-angiotensin-aldosterone pathway, resulting in hypovolemia
- clinically silent syndrome
- independent predictor of mortality
- associated with faster reaccumulation of ascites, hyponatremia, renal impairment

Post-paracentesis circulatory dysfunction

- diagnosis: through laboratory results, with increases of more than 50% of baseline plasma renin activity to > 4 ng/mL/h on the 5th to 6th days after paracentesis

- prevention through the use of plasma volume expanders postparacentesis (albumin 8 g/L of ascites removed)

- other strategies include the limitation of the volume of fluid removed to 5 to 6 L at a time

Lindsay AJ, Burton J, Ray CE Jr. Paracentesis-induced circulatory dysfunction: a primer for the interventional radiologist. *Semin Intervent Radiol*. 2014;31(3):276–278. doi:10.1055/s-0034-1382799

Drugs contraindicated in ascites

- non-steroidal anti-inflammatory drugs
- angiotensin-converting-enyzme inhibitors, angiotensin II antagonists, or a1-adrenergic receptor blockers
- aminoglycosides

Refractory ascites

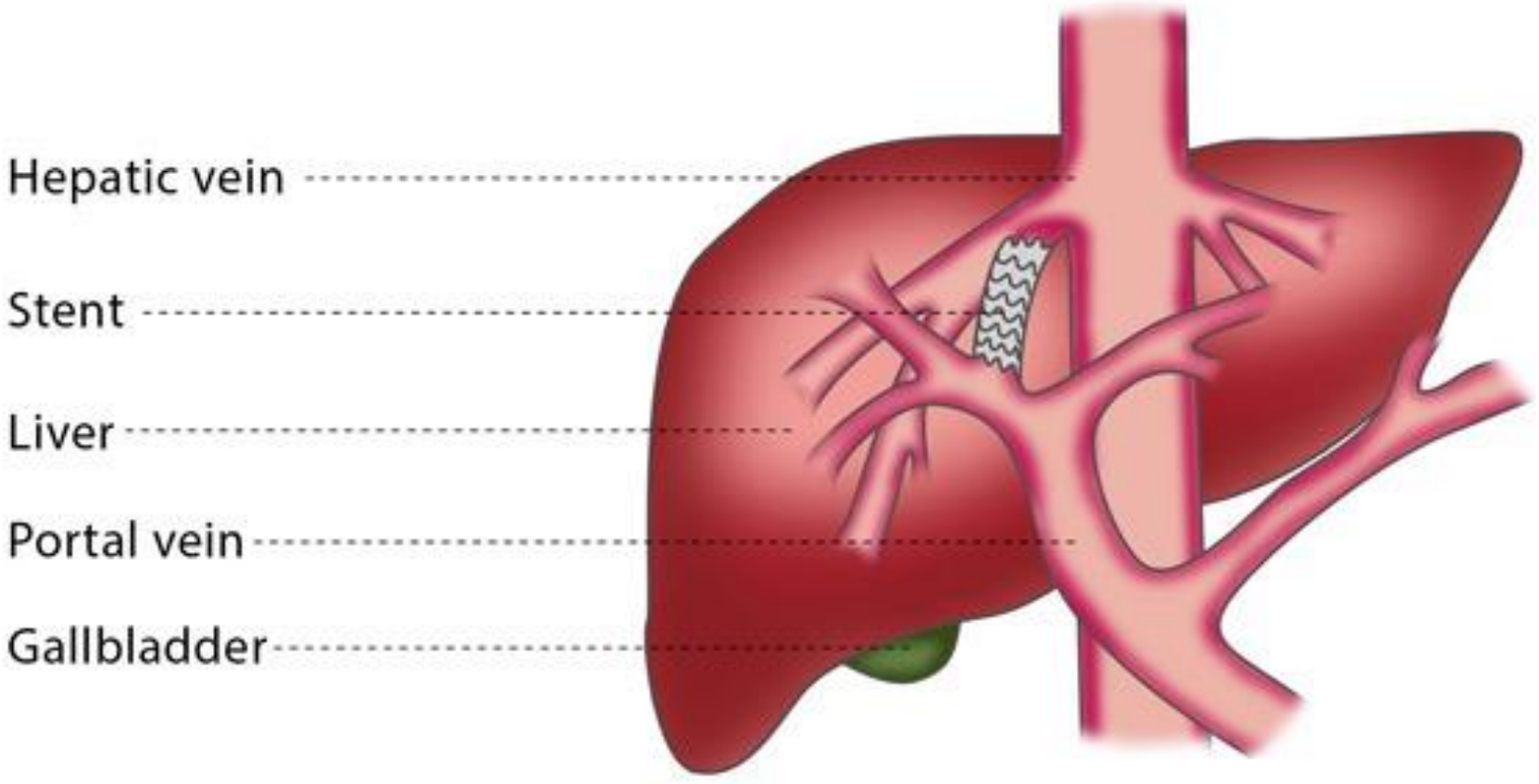
Table 4. Definition and diagnostic criteria for refractory ascites in cirrhosis.

Definition	
Diuretic-resistant ascites	Ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of a lack of response to sodium restriction and diuretic treatment
Diuretic-intractable ascites	Ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of the development of diuretic-induced complications that preclude the use of an effective diuretic dosage
Diagnostic criteria	
Treatment duration	Patients must be on intensive diuretic therapy (spironolactone 400 mg/day and furosemide 160 mg/day) for at least one week and on a salt-restricted diet of less than 90 mmol/day
Lack of response	Mean weight loss of <0.8 kg over four days and urinary sodium output less than the sodium intake
Early ascites recurrence	Reappearance of grade 2 or 3 ascites within four weeks of initial mobilisation
Diuretic-induced complications	Diuretic-induced hepatic encephalopathy is the development of encephalopathy in the absence of any other precipitating factor Diuretic-induced renal impairment is an increase of serum creatinine by >100% to a value >2 mg/dl (177 μmol/L) in patients with ascites responding to treatment Diuretic-induced hyponatremia is defined as a decrease of serum sodium by >10 mmol/L to a serum sodium of <125 mmol/L Diuretic-induced hypo- or hyperkalemia is defined as a change in serum potassium to <3 mmol/L or >6 mmol/L despite appropriate measures Invalidating muscle cramps

Refractory ascites

- patients with refractory ascites should be evaluated for liver transplantation (LT)
- first line treatment: LVP associated with albumin administration
- diuretics should be discontinued (except for cases that renal sodium excretion on diuretics exceeds 30 mmol/day)
- non-selective beta-blockers (controversial data)
- transjugular intrahepatic portosystemic shunts (TIPS)

Transjugular intrahepatic portosystemic shunt (TIPS)



Transjugular intrahepatic portosystemic shunts (TIPS)

- shunting an intrahepatic portal branch into a hepatic vein

- indicated in patients with recurrent ascites (improved survival) and in patients with refractory ascites

- improvement in effective volaemia and renal function, ultimately leading to an increase in renal sodium excretion

- technically difficult procedure

- complications: hepatic encephalopathy (50% of patients)

- stent thrombosis and stenosis (80% of all cases)

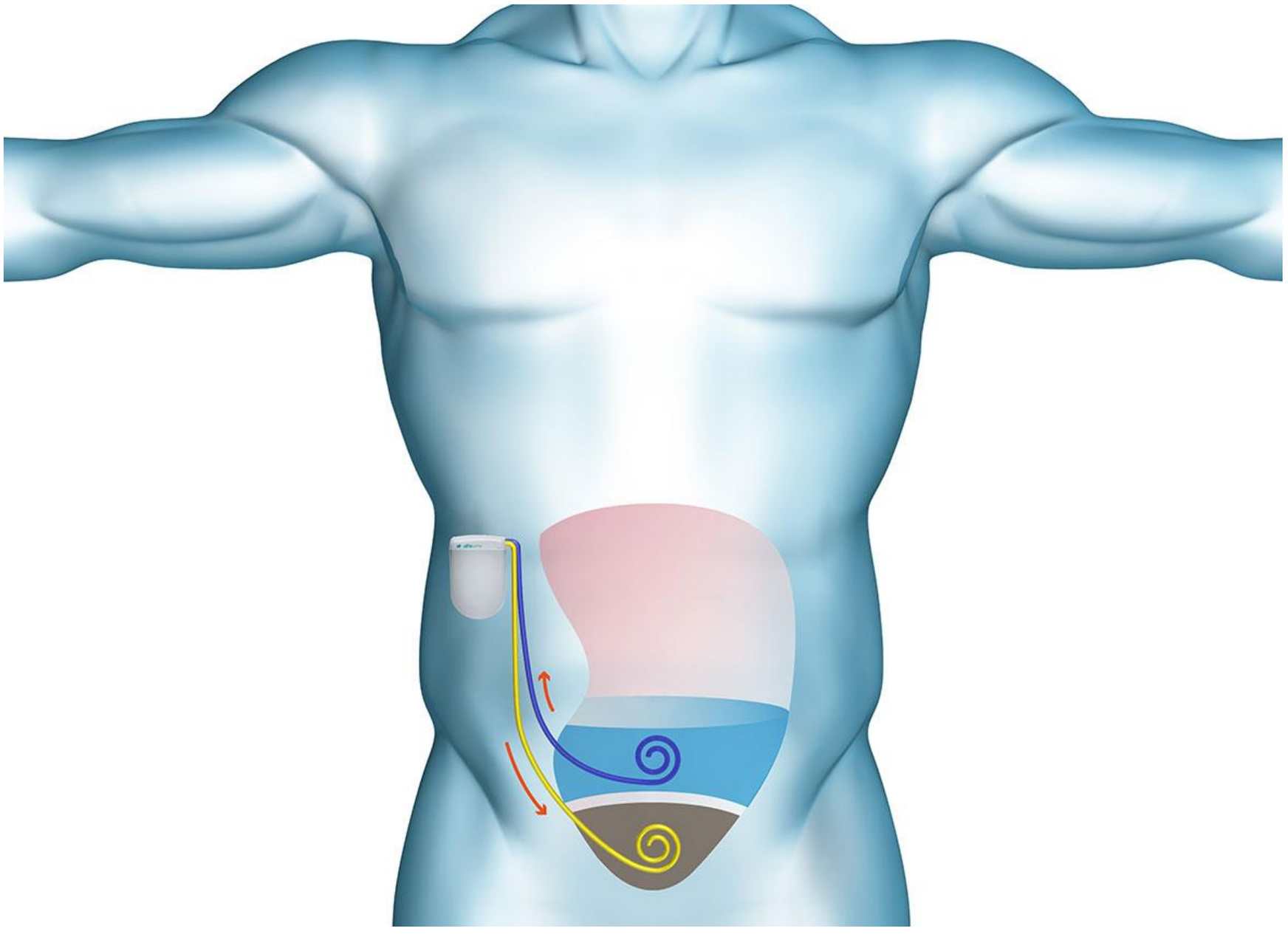
TIPS or LVP?

Refs.	Refractory/ recidivant ascites (%)	Exclusion criteria	Enrolled patients (N)		Ascites improved (%)		Encephalopathy (%)		Survival (%)	
			TIPS	LVP	TIPS	LVP	TIPS	LVP	TIPS	LVP
Lebrec *et al.* 1995	100/0	Age >70 yr; severe extra-hepatic diseases; HCC; pulmonary hypertension; HE, bacterial infection; severe alcoholic hepatitis; portal or hepatic vein obstruction or thrombosis; obstruction of biliary tract; obstruction of hepatic artery; serum creatinine >1.7 mg/dl	13	12	38	0*	15	6	29	60
Rössle *et al.* 2000	55/45	HE ≥grade 2; serum bilirubin >5 mg/dl, serum creatinine >3 mg/dl; portal-vein thrombosis, hepatic hydrothorax; advanced cancer; failure of LVP (ascites persisting after LVP or need for LVP >once per week)	29	31	84	43*	23	13	58	32
Ginés *et al.* 2002[90]	100/0	Age >18 or >75 yr; serum bilirubin >10 mg/dl; prothrombin time <40% (INR 2.5); platelet count <than 40,000/mm^3; serum creatinine >3 mg/dl, HCC, complete portal vein thrombosis; cardiac or respiratory failure; organic renal failure; bacterial infection; chronic HE	35	35	51	17*	60	34	26	30
Sanyal *et al.* 2003[100]	100/0	Causes of ascites other than cirrhosis; advanced liver failure (serum bilirubin bilirubin >5 mg/dl, PT INR >2); incurable cancers or nonhepatic diseases that were likely to limit life expectancy to 1 yr; congestive heart failure; acute renal failure; parenchymal renal disease; portal vein thrombosis; bacterial infections; HE ≥grade II; florid alcoholic hepatitis, HCC; gastrointestinal hemorrhage within 6 w of randomisation.	52	57	58	16*	38	21	35	33
Salerno *et al.* 2004[99]	68/32	Age > 72 yr; recurrent HE ≥grade 2; serum bilirubin >6 mg/dl; serum creatinine >3 mg/dl; Child-Pugh score >11; complete portal vein thrombosis; HCC; gastrointestinal bleeding within 15 d of randomisation; serious cardiac or pulmonary dysfunctions;bacterial infection; SAAG gradient <11 g/L.	33	33	79	42*	61	39	59	29*
Narahara *et al.* 2011[97]	100/0	Age >70 yr, chronic HE, HCC and other malignancies, complete portal vein thrombosis with cavernomatous transformation, bacterial infection, severe cardiac or pulmonary disease, organic renal disease.	30	30	87	30*	20	5	20	5*

Possible treatment options

- midodrine: not currently recommended
- terlipressin: not currently recommended
- clonidine: not currently recommended
- Alfapump: suggested in patients with refractory ascites not amenable to TIPS insertion, high risk of AKI

Alfapump



Treatment of spontaneous bacterial peritonitis

- Empirical i.v. antibiotics should be started immediately following the diagnosis of SBP

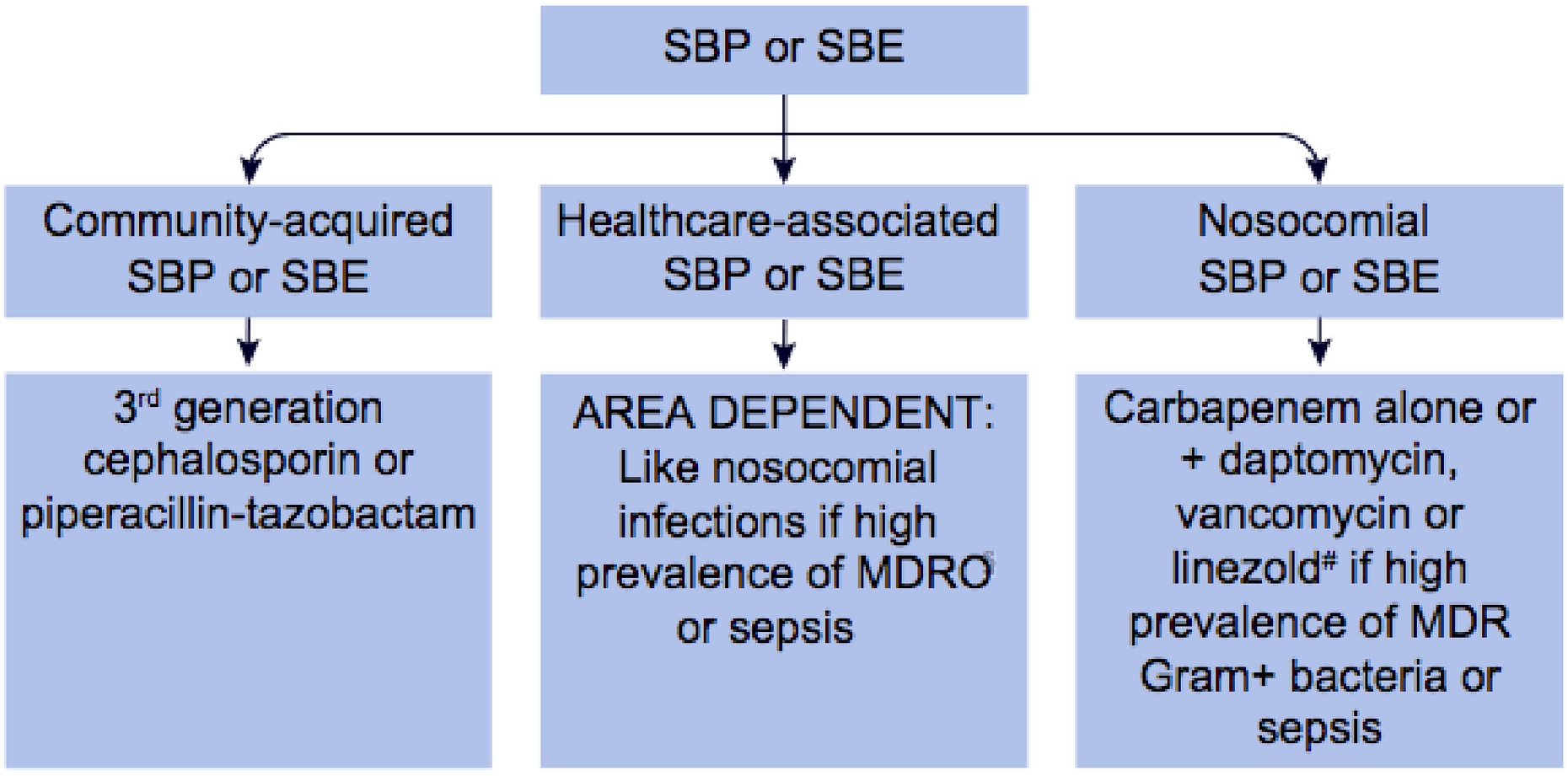
- de-escalation according to bacterial susceptibility based on positive cultures is recommended to minimise resistance selection pressure

- the efficacy of antibiotic therapy should be checked with a second paracentesis at 48 h from starting treatment

- treatment duration of at least 5-7 days

- administration of albumin (1.5 g/kg at diagnosis and 1 g/kg on day 3)

Treatment of spontaneous bacterial peritonitis



European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decomp

Prophylaxis of spontaneous bacterial peritonitis

- Strictly restricted to patients

i) patients with acute GI haemorrhage;

ii) patients with low total protein content in ascitic fluid and no prior history of SBP (primary prophylaxis), and

iii) patients with a previous history of SBP (secondary prophylaxis)

- norfloxacin (400 mg/day)

Ευχαριστώ για την προσοχή σας!