ASCITES

Ruben De Bosscher
Joke Vliebergh

Prof. Dr. Laleman

Overzicht

- Inleiding
- Etiologie
- Diagnostiek
- Behandeling
- Complicaties

Inleiding

- 'askos'
- Gradaties:
  1. *Milde ascites die enkel te detecteren is met echo*
  2. *Matige ascites met symmetrische distensie van abdomen*
  3. *Belangrijke ascites met grote opzetting van abdomen*

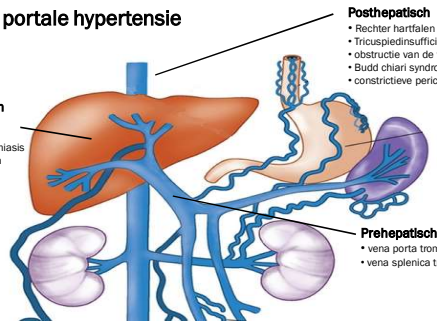
Etiologie

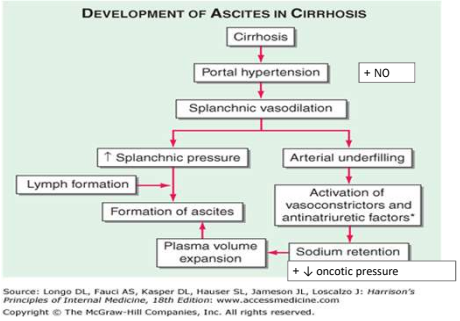
- Oorzaken van ascites
  - Cirrose 81%
  - Maligniteit 10%
  - Hartfalen 3%
  - Tuberculose 2%
  - Dialyse 1%
  - Andere 1%

Etiologie
Indeling volgens pathofysiologie

- Portale hypertensie
- Hypo-albuminemie
  - Nefrotisch syndroom
  - Protein losing enteropathy
  - Ernstige malnutritie
- Peritoneale ziekte:
  - Maligne ascites
  - Infectieus
- Andere

Oorzaak portale hypertensie





Diagnostiek

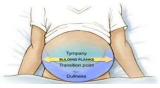
- Anamnese
- Klinisch onderzoek
- Beeldvorming
- Paracentese

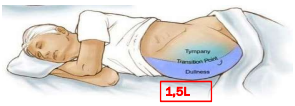
Diagnostiek
Anamnese

- Voorgeschiedenis
  - persoonlijk (maligniteit, virale hepatitis, PSC/PBC, (N)ASH – cirrose,…)
  - familiaal (maligniteit, trombofilie)
- Risicofactoren (bv. ethylabusus, metabool syndroom, recent trauma/heelkunde, zwangerschap, tatoeages)
- Tijdsverloop
- Begeleidende symptomen: koorts? Veranderde mentale status? Gewichtsverlies? Bloeding?

Diagnostiek
Klinisch onderzoek

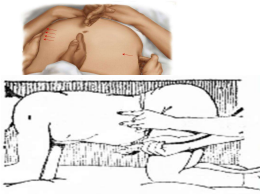
- Inspectie:
  - bolrond opgezet abdomen
  - Verstreken huidplooien
  - Uitpuilende navel
  - Bulging flanks
- Percussie
  - Shifting dullness
    - Sensitiviteit 83%
    - Specificiteit 56%

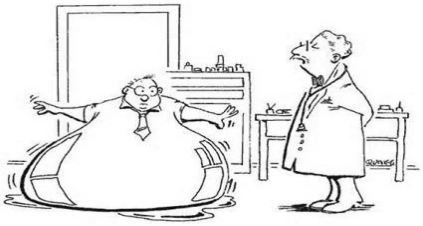




Diagnostiek
Klinisch onderzoek

- Palpatie
  - Fluid wave
- Auscultatie
  - Puddle sign
    - https://www.youtube.com/watch?v=bWxmnwk9iQ





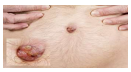
Your tests reveal that you are retaining fluids!

Diagnostiek
Klinisch onderzoek

- Cirrose
  - Palmair erytheem
  - Spider naevi
  - Collateralen abdomen
- Hartfalen
  - Gestuwde CVD
  - Malleolaire oedemen
  - Souffle

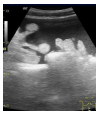
Diagnostiek
Klinisch onderzoek

- Nefrotisch syndroom
  - Anasarc oedeem
- Maligniteit
  - Klieren
  - Sister Mary Joseph's nodule

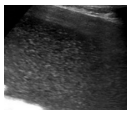


Diagnostiek
Beeldvorming

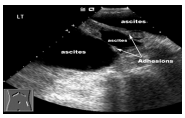
- Echografie



Simple



Debris

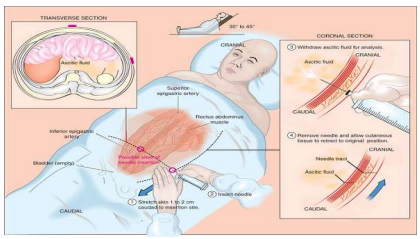


Loculated

Diagnostiek
Beeldvorming

- CT/MRI abdomen
  - Evaluatie hepatische (en andere intra-abdominale) massa

Diagnostiek
Paracentese



Diagnostiek
Paracentese

Transparant, geel, helder	Ongecompliceerde ascites bij cirrose
Troebel	SBP
Melkachtig	Chyleuze ascites met ↑ Tgl (maligniteit, cirrose)
Bloederig	Traumatische punctie, maligniteit, trauma op abdomen
Bruin	Icterus +++, tgv geruptureerde galblaas of duodenaal ulcusruptuur

Diagnostiek
Paracentese

- Biochemie – routine
  - Albumine → SAAG
  - Totaal eiwit
  - Celtelling

SAAG

- Serum albumine min ascites albumine
  = parameter van oncotische druk

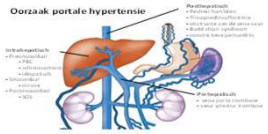
→ *Portale hypertensie of niet?* (97% accuraatheid)

11 g/L < SAAG > 11 g/L

Hypo-albuminemie
- Nefrotisch syndroom
- Protein losing enteropathy
- Severe malnutrition

Peritoneale ziekte:
- Maligne ascites
- Infectieus

Andere



Diagnostiek
Paracentese

- Totaal eiwit concentratie

< 2,5 g/dL (transudaat)	≥2.5 or 3 g/dL (exsudaat)
- Cirrose - Nefrotisch syndroom	-Hartfalen

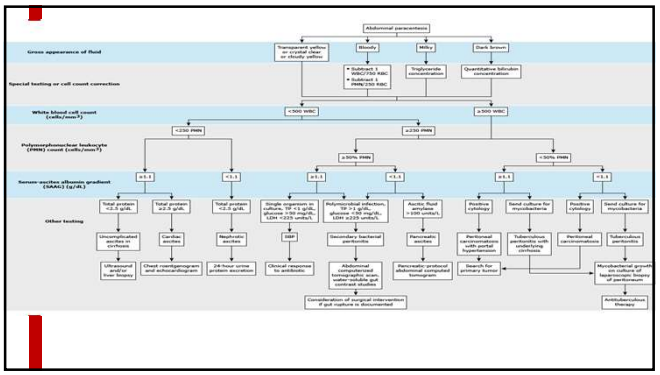
- Celtelling
  - Infectie?
  - Hemorraghische stalen → "gecorrigeerde neutrofielen aantal" (1WBC/750 RBC, 1PMN/ 250RBC)
  - Neutrofielen ≥250/mm³ → overweeg start antibiotica

Diagnostiek
Paracentese

- Biochemie – overig
  - Cultuur/Gramkleuring
    - Bij verdenking van infectie
  - Glucose concentratie
    - Normaal $[glucose]_{serum}$ ~ $[glucose]_{ascites}$
      - Uitzondering: infectie, sommige maligniteiten
  - LDH
    - Bij ongecompliceerde ascites: $LDH_{ascites}$ / LDH_{serum} ~ 0,4
    - > 1: infectie, sommige maligniteiten

Diagnostiek
Paracentese

- Biochemie – overig
  - Amylase concentratie
    - Bij ongecompliceerde ascites: $amylase_{ascites}$ / $amylase_{serum}$ ~ 0,4
    - ↑ bij pancreatitis, darmperforatie
  - Cytologie
    - Slechts 2/3 van de maligne gerelateerde ascites hebben peritoneale carcinomatose (overige: leverM+, chyleuze ascites tgv lymfoom, HDD)
  - CEA
  - Tgl
    - > 200 mg/dL op chylvocht
  - Bilirubine
    - Als $[bilirubine]_{serum}$ < $[bilirubine]_{ascites}$ → biliaire perforatie of duodenumperforatie

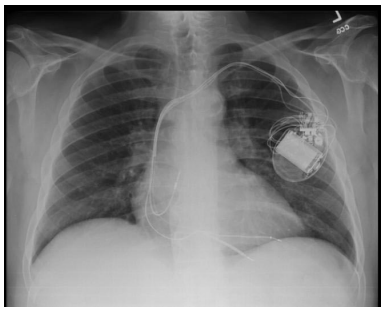


Casus
M, 89 jaar

- Medische voorgeschiedenis
  - 1975: inferior infarct
  - 05/2007: recidief inferior infarct, R/ PCI
  - 03/2011: sustained ventriculaire tachycardie komende vanuit het inferior, blijvend onder cordarone. R/ implantatie AICD (Boston Scientific Teligen 100 tweekamer ICD).
  - 07/2011: opdrijven diuretica tot Burinex 1 mg daags omwille van neigende hyperkaliemie en
  - 20/04/2017: chronische nierinsufficiëntie, vermoedelijk aging kidney
- Usus:
  - Nicotine: rookstop in 1980
  - Ethyl: 3-4 E/dag
- Medicatie: Asaflow, lorazepam, burinex 1mg, movicol, silodyx, cordarone

Casus:
M, 89 jaar

- Anamnese: "AAT", futloos, moe, tevens zwelling van onderste ledematen en opgezet abdomen, dyspnee
- Klinisch onderzoek:
  - Cor: regelmatig ritme, geen souffles
  - Longen: bilateraal VAG
  - Abdomen: soepel, opgezet, shifting dulness +
- Echo abdomen:
  - Normale morfologie van milt, pancreas en beide nieren
  - Geen pyelocaliciële stuwing. Verspreide ascites perisplenisch, perihepatisch en in de Douglas-holte.
  - Globaal hyperechogeen parenchym van de lever met hobbelige contouren.
  - Galblaas in contractie.
  - Matig gevulde blaas met symmetrische wandaflijning. Forse prostaat.



Casus:
M, 89 jaar

- Paracentese:

PUNCTIEVOCHTEN											
Macroscopisch	Lc						oranje, troebel				
Totaal eiwit (punctievocht)	Lc						25.2				g/L
Albumine (punctievocht)	Lc						14.8				g/L
LDH (punctievocht)	Lc						167				IU/L
Cytologie											
RBC (punctievocht)	Lc						5000				/µL
Aantal gekernde cellen	Lc						192				/µL
Witte bloedcellen (Punctievocht)	Lc						172				/µL
Eosinofielen	Lc						0				%
Polymorfonucleairen	Lc						13.0				%
Lymfocyten	Lc						13.0				%
Monocyt./macrofagen	Lc						2.00				%
Mesotheelcellen	Lc						72.0				%
Andere	Lc						0				

- Biochemie

BIOCHEMIE - EIWIT SPECTRUM											
Totaal eiwit	Lc							↓ 52.5		64.0-83.0	g/L
Albumine (colorim.)	Lc							↓ 37.3		38.0-52.0	g/L

  - SAAG: 37,3-16,8 = 20,5
  - Totaal eiwit: 25,2 g/L → > 2,5g/dL

CARDIALE ASCITES

Casus
M, 89 jaar

- TTE:
  - Functie: Linker ventrikel ejectiefractie 35 à 40%.
  - Forse dilatatie van beide atria. Matige dilatatie van het linker ventrikel. Lichte dilatatie van het rechter ventrikel.
  - Ernstige MI. Ernstig TI.
  - Aanwezigheid van pulmonale hypertensie 40 mmHg
  - Gedilateerde vena cava inferior zonder ademhalingsvariatie.
- NT-pro-BNP: 18325 ng/L +++
- R/ diuretica → -16 kg

Casus
M, 56 jaar

- Medische voorgeschiedenis:
  - 1979: Miltruptuur waarvoor heelkunde (geen splenectomie).
  - 09/1996: Varicocoele links waarvoor behandeling.
- Usus:
  - Nicotine: 1 pack/dag
  - Ethyl: 10 E/dag (bier)
- Medicatie: geen

Casus
M, 56 jaar

- Anamnese: zwelling buik en gewichtstoename
- Klinisch onderzoek:
  - Cor: regelmatig ritme, geen souffles
  - Longen: bilateraal VAG
  - Abdomen: soepel, opgezet, shifting dulness +
  - Spider naevi, palmair erytheem
- Echo abdomen:
  - Heterogeen leverparenchym, hobbelige leverrand en afgestompte Li leverlob. Geen duidelijke focale leverletsels.
  - Normale galblaas; geen CCL noch sludge te zien doch postprandiale status met galblaas in contractie. Geen dilatatie van intra-of extrahepatische galwegen.
  - Pancreas niet te beoordelen. Normale milt (miltspan 13 cm). Bilateraal normale nieren.
  - Ascites circumferentieel

Casus
M, 56 jaar

- Paracentese:

	geel		lichtstroomel, oranje		
pH (punctievocht)			7.61		
Totaal eiwit (punctievocht)			22.5		g/L
Albumine (punctievocht)			10.7		g/L
RBC (punctievocht)			4000		/µL
Aantal gekernde cellen			49.0		/µL
Witte bloedcellen (Punctievocht)			32.0		/µL
Eosinofielen			Technisch onuitvoerbaar		%
Polymorfonuclearen			Technisch onuitvoerbaar		%

- Biochemie

BIOCHEMIE					
INWT SPECTRUM					
Totaal eiwit		71.6		64.0-83.0	g/L
Albumine (colorim.)		↑ 32.4		38.0-52.0	g/L

- SAAG: 32,6-10,7 = 20,9
- Totaal eiwit: 22,5 → < 2,5 g/dL

ASCITES TGV LEVERCIRROSE

Ascites
Behandeling & Complicaties

Behandeling
Doelen

- Afname ascites (en perifere oedemen)
- Verbetering van survival, transplant-free-survival en QoL
- Preventie van complicaties
  - Spontane bacteriële peritonitis
  - Hepatorenaal syndroom
  - Hepatische hydrothorax
  - Hernia umbilicalis
- Zonder nevenwerkingen
  - Intravasculair ondervulling
  - Elektrolytstoornissen

Behandeling
Ascites bij cirrose - Causaal

- Ethylisme
  - R/ Abstinentie
  - R/ Baclofen 5mg 3x/d → 10mg 3xd
  - R/ Zoutrestrictie
- Auto-immune hepatitis
  - Corticosteroïden
  - Azathioprine
- Gedecompenseerde hepatitis B cirrose
  - R/ Antivirale therapie
- Post-resuscitatie
  - R/ Stop IV vocht en colloiden

Behandeling
Ascites – Causaal - Baclofen

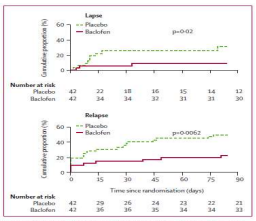


Figure 2: **Kaplan-Meier survival analysis of proportion of lapse and relapse**
Number at risk refers to proportion remaining free of lapse and relapse.

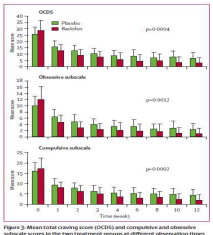


Figure 3: **Mean total craving score (OCDS) and compulsive and obsessive subscale scores in the two treatment groups at different observation times**

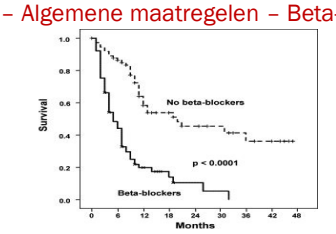
Addolorato G, Leggio L, Ferrulli A, et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis, double-blind controlled study. Lancet. 2007.

Behandeling
Ascites bij cirrose - Algemene maatregelen

Werkzaam bij 90% van ascites obv cirrose

- Te vermijden en/of te stoppen medicatie
  - ACE-I -& Sartanen (hypotensie en verminderde renale perfusie)
  - Propanolol (hypotensie en verminderde survival)
  - NSAID's (verminderde respons op diuretica, ANI, GI-bloeding)
- Zoutrestrictie
  - R/ 2g/d
- Diuretica
  - R/ Spirolactone & Furosemide
    - *Ratio 100/40mg per dag*
    - *Optitreren tot maximaal 400/160mg per dag*
  - Streefdoel: gewichtsverlies 0,5-1kg per dag
- *(Vasopressine receptor antagonisten)*
  - Tolvaptan 3,25-7,5mg/d in combinatie met diuretica
- *(Vochtrestrictie)*
  - Enkel bij hyponatriëmie <120mmol/L

Behandeling
Ascites – Algemene maatregelen – Beta-blokker



Patients at risk : 74 (No beta-blockers) 63 34 21 15 11 8 6 1

Patients at risk : 77 (Beta-blockers) 33 10 5 2 1

Sersté T, Melot C, Francoz C, et al. Deleterious effect of beta-blockers on survival in patients with cirrhosis and refractory ascites. Hepatology 2010; 52:1017.

Behandeling
Ascites bij cirrose - Zoutrestrictie

Table 3 *Clinical and biochemical data on 14th day of treatment*

	Salt restricted diet	*Unrestricted diet*	
Patients under treatment	74	61	
Ascites			
Complete disappearance (%)	42	23	NS
Partial disappearance (%)	57	60·6	NS
No disappearance (%)	1	16·4	p<0·01
Loss of weight (kg)	8·1±3	5·4±4	p<0·001
Decrease in abdominal girth (cm)	9·9±6	5·8±4	p<0·001
Edema			
Equal or less (%)	63·5	82	
Improve (%)	36·5	18	p<0·02
% of patients taking maximum spironolactone dose	12	26	p<0·04
Blood urea (mmol/l)	4·7±2·2	5·3±5·7	NS
Difference 14th day – 1st day	*1±1·8	*0·7±1·6	NS
Serum sodium (mmol/l)	132±4	133±4	NS
Difference 14th day – 1st day	14±4·3	†2·4±3·6	S (p=0·025)
Serum potassium (mmol/l)	4·5±0·5	4·3±0·4	NS
Difference 14th day – 1st day	*0·6±0·6	*0·5±0·5	NS
Urine volume (ml/24 h)	*699±674	*521±654	NS
Urine sodium (mmol/24 h)	84·7±117·5	99±129·4	NS
Urine potassium (mmol/24 h)	*29·4±44·9	*17·6±50·5	NS

* representing an increase.
† a decrease from the initial value.

Gauthier A, Levy VG, Quinton A, et al. Salt or no salt in the treatment of cirrhotic ascites: a randomised study. Gut. 1986;27:705–9.

Behandeling
Ascites bij cirrose - Diuretica

Table 2
Effectiveness and safety items in both therapeutic groups[a]

	Group 1: S + F (n = 47)	Group 2: S (n = 47)	P value
Loss of body weight (kg)	7.5 (2–17)	6.6 (2–15)	NS
Time to obtain of response (days)	9.8 (4–35)	10.3 (4–32)	NS
Response or Mobilization of ascites (n/%)	46/98	44/94	NS
Side effects (n/%)	3/7.7	6/13.2	NS
Need to reduce the diuretic dosage (n/%)	32/68	16/34	0.002
Spironolactone (mg)			
Cumulative dose	1934 (400–7700)	2445 (400–7800)	NS
Dose/day	148 (83–233)	170 (100–325)	0.037
Dose/liter of ascites	311 (125–1405)	407 (118–1300)	NS
Cumulative dose of furosemide (mg)	480 (80–3080)	240 and 640[c]	-

[a] Median (range).
[b] In one, furosemide was added.
[c] Only two patients of this group received treatment with furosemide.

Santos J, Planas R, Pardo A, et al. Spironolactone alone or in combination with furosemide in the treatment of moderate ascites in nonazotemic cirrhosis; a randomized comparative study of efficacy and safety. J Hepatol 2003;39:487–92.

Behandeling
Ascites bij cirrose - Diuretica

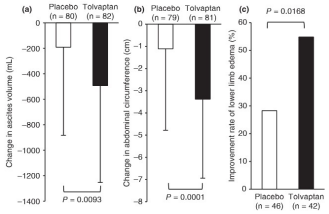
Table 4 Patients who developed adverse effects either prior to or after achieving the effective diuretic step

	Group A (n = 50)	Group B (n = 50)	p Value
Number of patients who developed adverse effects	19 (38%)	10 (20%)	<0.05
Number of patients with hyperkalaemia	9 (18%)	2 (4%)	<0.05
Number of patients with hypokalaemia	1 (2%)	0 (0%)	NS
Number of patients with hyponatraemia	4 (8%)	4 (8%)	NS
Number of patients with renal failure	8 (16%)	6 (12%)	NS

In Group A three patients had two adverse effects simultaneously (renal failure and hyperkalaemia in one patient, and renal failure and hyponatraemia in the remaining two patients). In Group B two patients had two adverse effects simultaneously (renal failure and hyponatraemia in both patients).

Angeli P, Fasolato S, Mazza E, et al. Combined versus sequential diuretic treatment of ascites in non-azotaemic patients with cirrhosis: results of an open randomised clinical trial. Gut. 2010;59:98–104.

Behandeling
Ascites bij cirrose – Vasopressine Receptor Antagonisten



Sakaida I, Kawazoe S, Kajimura K, et al. Tolvaptan for improvement of hepatic edema: a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Hepatol Res. 2014;44:73–82.

Behandeling
Ascites bij cirrose – Vasopressine Receptor Antagonisten

Table 3 Improvement rates of ascites-related clinical symptoms

Symptoms	Placebo %	Tolvaptan %	P-value†
Bloated feeling	37.3 (22/59)	62.5 (35/56)	0.0090
Loss appetite	16.7 (6/36)	38.9 (14/36)	0.0640
Malaise	30.6 (15/49)	58.7 (27/46)	0.0074
Sensation of pressure in decubitus position	26.7 (8/30)	65.8 (25/38)	0.0017
Breathing difficulty	23.8 (5/21)	62.5 (10/16)	0.0233

Data are improvement rates. Improvement rate was calculated by dividing the number of effective case by the number of patients with symptom at baseline.
†Fischer's exact test.

Sakaida I, Kawazoe S, Kajimura K, et al. Tolvaptan for improvement of hepatic edema: a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Hepatol Res. 2014;44:73–82.

Behandeling
Ascites bij cirrose – Vasopressine Receptor Antagonisten

Table 4 Incidence of adverse events

Adverse events	Placebo (n = 80)	Tolvaptan (n = 82)
Total	48 (60.0)	60 (73.2)
Observed in ≥3% of patients		
Thirst	1 (1.3)	11 (13.4)
Constipation	6 (7.5)	6 (7.3)
Renal impairment	6 (7.5)	6 (7.3)
Diarrhea	4 (5.0)	6 (7.3)
Pollakiuria	0 (0.0)	6 (7.3)
Pyrexia	6 (7.5)	4 (4.9)
Hepatic encephalopathy	4 (5.0)	4 (4.9)
Vomiting	2 (2.5)	4 (4.9)
Insomnia	0 (0.0)	4 (4.9)
Stomatitis	1 (1.3)	3 (3.7)
Pruritus	0 (0.0)	3 (3.7)

Data are number of patients (%).

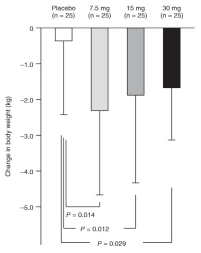
Table 5 Incidence of serious adverse events

Serious adverse events	Placebo (n = 80)	Tolvaptan (n = 82)
Total	10 (12.5)	7 (8.5)
Disseminated intravascular coagulation	0 (0.0)	1 (1.2)
Iron-deficiency anemia	1 (1.3)	0 (0.0)
Esophageal varices hemorrhage	1 (1.3)	0 (0.0)
Liver cirrhosis	0 (0.0)	1 (1.2)
Portal vein thrombosis	0 (0.0)	1 (1.2)
Omphalitis	0 (0.0)	1 (1.2)
Pneumonia	1 (1.3)	0 (0.0)
Femoral neck fracture	2 (2.5)	0 (0.0)
Bile duct cancer	0 (0.0)	1 (1.2)
Liver malignant neoplasm	0 (0.0)	1 (1.2)
Hepatic coma	1 (1.3)	0 (0.0)
Hepatic encephalopathy	3 (3.8)	1 (1.2)
Renal failure	1 (1.3)	0 (0.0)
Renal impairment	1 (1.3)	1 (1.2)
Respiratory failure	0 (0.0)	1 (1.2)
Hemoperitoneum	0 (0.0)	1 (1.2)

Data are number of patients (%).

Sakaida I, Kawazoe S, Kajimura K, et al. Tolvaptan for improvement of hepatic edema: a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Hepatol Res. 2014;44:73–82.

Behandeling
Ascites bij cirrose – Vasopressine Receptor Antagonisten



Ohta K, Kawazoe S, Hasebe C, et al. Dose-finding trial of tolvaptan in liver cirrhosis patients with hepatic edema: a randomized, double-blind, placebo-controlled trial. Hepatol Res.2014;44:83–91.

Behandeling
Ascites bij cirrose – Diureticaresistente ascites

- Persisterende ascites ondanks adherentie aan therapie, of vroegtijdig recidief ascites en/of ontwikkelen van complicaties (azotemie, hepatisch encephalopathie, elektrolytenstoornissen)
  - Secundair aan progressie leverlijden (of complicaties HCC en v. Porta thrombose)
  - Objectivatie: Urinair Na <78meq over 24u zonder gewichtsreductie onder diuretica en zoutrestrictie
  - DD peritoneale carcinomatose, Budd-Chiari, nefrogene ascites

Behandeling
Ascites bij cirrose - Diureticaresistent

- Large volume paracentesis (LVP)
- Albumine IV
- Cell-free concentrated ascites reinfusion therapy (CART)
- Alfa pump
- Peritoneovenous shunt (PVS)
- Transhepatische intrajugulaire portosystemische shunt (TIPS)
- Levertransplantatie

Behandeling
Ascites bij cirrose - Diureticaresistent

- Large volume paracentesis
  - Zo veel als mogelijk (intern maximaal 10L)
  - Bij zoutrestrictie (2g/d) in principe 8L per 2 weken
  - Albumine substitutie 6-8g per 1L ascites
  - Veilig 'ongeacht' INR

Behandeling
Ascites bij cirrose – Large Volume Paracentesis

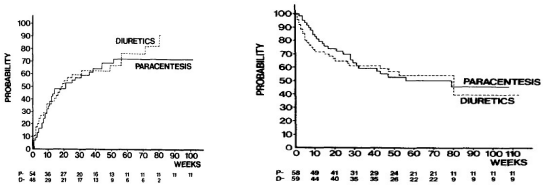
Table 3. Complications During the First Hospital Stay in Patients From Group 1 (Treated With Paracentesis) and Group 2 (Treated With Diuretics)

	Group 1 (n = 58)	Group 2 (n = 59)	p
Patients with complications	10	36	<0.001
Hyponatremia	3	18	<0.001
Encephalopathy	6	17	<0.002
Renal impairment	2	16	<0.001
Hyperkalemia	1	7	NS
GI bleeding	2	6	NS
Peritonitis	0	4	NS
Bacteremia	2	0	NS
Others	0	4[a]	NS

GI, gastrointestinal; NS: not significant. [a] Two patients with possible infections, 1 patient with respiratory failure, and 1 patient with strangulated hernia.

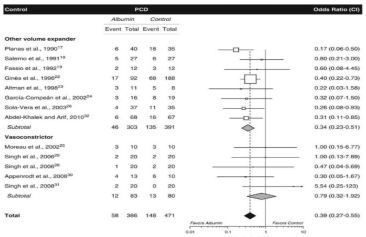
Gines P, Arroyo V, Quintero E, et al. Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites. Results of a randomized study. Gastroenterology. 1987;93:234–41.

Behandeling
Ascites bij cirrose – Large Volume Paracentesis



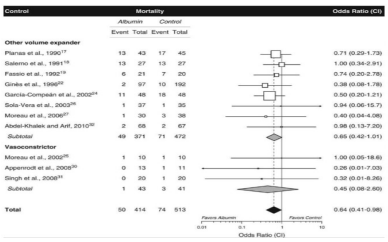
Gines P, Arroyo V, Quintero E, et al. Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites. Results of a randomized study. Gastroenterology. 1987;93:234–41.

Behandeling
Ascites bij cirrose – Albumine



Bernardi M, Caraceni P, Navickis RJ, Wilkes MM. Albumin infusion in patients undergoing large-volume paracentesis: a meta-analysis of randomized trials. Hepatology. 2012;55:1172–81.

Behandeling
Ascites bij cirrose – Albumine



Bernardi M, Caraceni P, Navickis RJ, Wilkes MM. Albumin infusion in patients undergoing large-volume paracentesis: a meta-analysis of randomized trials. Hepatology. 2012;55:1172–81.

Behandeling
Ascites bij cirrose – Albumine

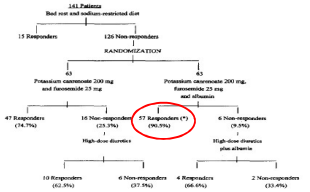
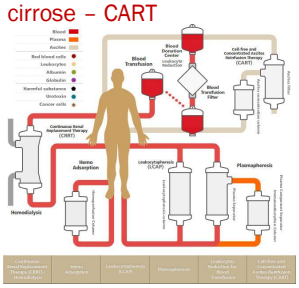


*Fig. 1. Results of the administration of diuretics plus albumin and diuretics to the whole series of cirrhotic patients included in the study (*p<0.05 vs. group A).*

Gentilini P, Casini-Raggi V, Di Fiore G, et al. Albumin improves the response to diuretics in patients with cirrhosis and ascites: results of a randomized, controlled trial. J Hepatol. 1999;30:639–45.

Behandeling
Ascites bij cirrose – CART



Behandeling
Ascites bij cirrose – CART

Table 4. Changes of clinical indices between pre- and post-CART.

Items		Pre-CART	Post-CART	P-value
Patient characteristics				
	Body weight (n = 209) [kg]	56.0 ± 15.1	52.4 ± 14.6	< 0.001
	Abdominal circumference (n = 171) [cm]	89.4 ± 12.6	81.6 ± 13.3	< 0.001
	ECOG PS (n = 317)	2.2 ± 1.0	2.0 ± 1.1	< 0.001
	Dietary intake (n = 296) [%]	48.0 ± 31.5	55.6 ± 32.5	< 0.001
	Daily urine volume (n = 98) [mL]	815 ± 491	1,151 ± 666	< 0.001
Serum biochemistry corrected by Ht changes				
	Total protein (n = 227) [g/dL]	5.9 ± 0.9	6.6 ± 1.2	< 0.001
	Albumin (n = 249) [g/dL]	2.5 ± 0.5	2.9 ± 0.9	< 0.001

ECOG PS: Eastern Cooperative Oncology Group performance status.

Hanada S, Isoai A, Ishihara T et al. Safety and efficacy of cell-free and concentrated ascites reinfusion therapy (CART) in refractory ascites: Post-marketing surveillance results. PLoS One 2017.

Behandeling
Ascites bij cirrose – CART

Table 11. Adverse events associated with reinfusion of filtered and concentrated ascites.

Adverse events (with redundancy)	Patients	Sessions	Time point (sessions)		Severity (sessions)	
			During reinfusion	After reinfusion	Severe	Not severe
Fever	30 (20.5%)	44 (12.4%)	41	3	0	44
Chills	8 (5.5%)	8 (2.3%)	7	1	0	8
Shivering with chills	1 (0.7%)	1 (0.3%)	1	0	0	1
Nausea	1 (0.7%)	1 (0.3%)	1	0	0	1
Hypertension	1 (0.7%)	1 (0.3%)	1	0	0	1
Headache	1 (0.7%)	1 (0.3%)	0	1	0	1
Any adverse events	33 (22.6%)	47 (13.2%)	51	5	0	56

A considerable number of fever/chills cases were observed, but none of them was severe.

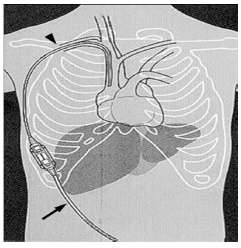
Table 10. Adverse events associated with CART procedures.

Adverse events	Patients	Sessions	Time point (sessions)			Severity (sessions)	
			During ascites drainage	During reinfusion	After reinfusion	Severe	Not severe
Shock	1 (0.7%)	1 (0.3%)	1	0	0	1	0
Hypotension	4 (2.7%)	4 (1.1%)	4	0	0	0	4
Chest pain	1 (0.7%)	1 (0.3%)	1	0	0	0	1
Abdominal pain	1 (0.7%)	1 (0.3%)	1	0	0	0	1
Dyspnea	1 (0.7%)	1 (0.3%)	1	0	0	0	1
Hypoammonemia	1 (0.7%)	1 (0.3%)	0	0	1	0	1
Total	9 (6.2%)	9 (2.5%)	8	0	1	1	8

Most of the adverse events associated with CART procedures were not severe, except one case of hemorrhagic shock at ascites drainage.

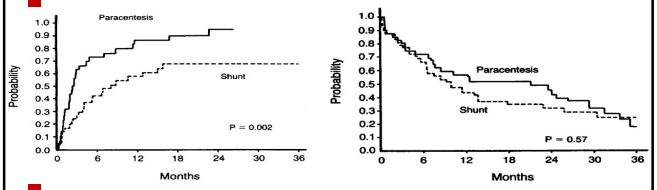
Hanada S, Isoai A, Ishihara T et al. Safety and efficacy of cell-free and concentrated ascites reinfusion therapy (CART) in refractory ascites: Post-marketing surveillance results. PLoS One 2017.

Behandeling
Ascites bij cirrose – PVS



Won JY, Lee DY, Lee KH, Kim SH et al. Percutaneous peritoneovenous shunt for treatement of refractory ascites. J Vasc Interv Radiol. 2008

Behandeling
Ascites bij cirrose – PVS



Gines P, Arroyo V, Vargas V, et al. Paracentesis with intravenous infusion of albumin as compared with peritoneovenous shunting in cirrhosis with refractory ascites. N Engl J Med. 1991;325:829–35.

Behandeling
Ascites bij cirrose – PVS

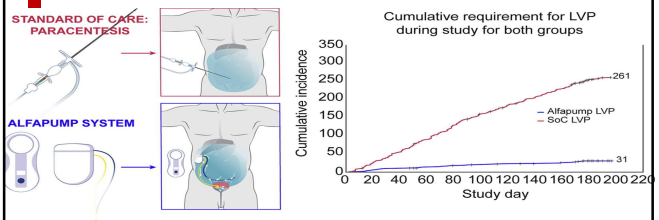
TABLE 6. Efficacy of TIPS or Peritoneovenous (PV) Shunts in Treating Ascites

	1 mo	3 mo	6 mo	12 mo	36 mo	60 mo
TIPS						
Patients alive (no.)	13	12	10	10	7	4
Absent (%)	8	0	0	0	0	0
Controlled (%)	46	67	80	80	86	100
Refractory (%)	46*	33	20	20	14†	0‡
PV shunts						
Patients alive (no.)	15	13	11	9	5	2
Absent (%)	7	0	0	0	0	0
Controlled (%)	73	77	73	56	40	0
Refractory (%)	20	23	27	44	60	100

*Compared to after PV shunts (log-likelihood ratio test, $P = 0.14$).
†Compared to after PV shunts (log-likelihood ratio test, $P = 0.09$).
‡Less than after PV shunts (log-likelihood ratio test, $P = 0.006$).

Rosemurgy AS, Zervos EE, Clark WC, et al. TIPS versus peritoneovenous shunt in the treatment of medically intractable ascites: a prospective randomized trial. Ann Surg 2004;239:883–9; discussion 889-91.

Behandeling
Ascites bij cirrose – Alfa pump



Bureau C, Adebayo D, Cairet de Rieu M, et al. Alfapump system vs. Large volume paracentesis for refractoru ascites: A multicenter randmized controlled study. J Hepatol 2017.

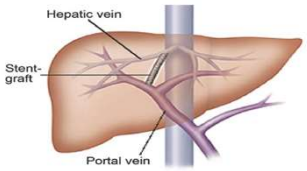
Behandeling
Ascites bij cirrose – Alfa pump

Table 3. Treatment emergent adverse events and treatment emergent serious adverse events.

Treatment emergent adverse events (TEAE)	All			<7 days			>7 days		
	AP N = 27	SoC N = 31	p value	AP	SoC	p value	AP	SoC	p value
Patients with at least one TEAE, n (%)	26 (96.3)	24 (77.4)	0.057	22 (81.5)	9 (29.0)	<0.001	26 (96.3)	24 (77.4)	0.057
Total number of TEAEs, n	199	97		50	10		149	87	
Average number of TEAEs/patient, n	7.4	3.1		1.9	0.3		5.5	2.8	
Patients with at least one serious TEAE, n (%)	23 (85.2)	14 (45.2)	0.002	9 (33.3)	1 (3.2)	0.004	23 (85.2)	13 (41.9)	0.001
Number of serious TEAEs, n	64	27		NA	NA		NA	NA	
Average number of serious TEAEs/patient, n	2.4	0.9		NA	NA		NA	NA	
Summary of patients with treatment emergent SAEs, n (%)	**AP N = 27**	**SoC N = 31**	**p value**	**AP**	**SoC**	**p value**	**AP**	**SoC**	**p value**
Blood and lymphatic system disorders, n (%)	1 (3.7)	0	0.466	0	0	1.0	1 (3.7)	0	0.466
Cardiac disorders, n (%)	0	1 (3.2)	1.0	0	0	1.0	0	1 (3.2)	1.0
Gastrointestinal disorders, n (%)	7 (25.9)	2 (6.5)	0.068	1 (3.7)	0	0.466	6 (22.2)	2 (6.5)	0.129
General disorders and administration site conditions, n (%)	4 (14.8)	1 (3.2)	0.173	0	0	1.0	4 (14.8)	1 (3.2)	0.173
Hepatobiliary disorders, n (%)	4 (14.8)	3 (9.7)	0.694	0	0	1.0	4 (14.8)	3 (9.7)	0.694
Infections and infestations, n (%)	9 (33.3)	8 (25.8)	0.574	2 (7.4)	1 (3.2)	0.593	0	0	1.0
Injury, poisoning and procedural complications, n (%)	3 (11.1)	0	0.095	3 (11.1)	0	0.095	0	0	1.0
Investigations, n (%)	0	1 (3.2)	1.0	0	0	1.0	0	1 (3.2)	1.0
Metabolism and nutrition disorders, n (%)	4 (14.8)	1 (3.2)	0.173	0	0	1.0	4 (14.8)	1 (3.2)	0.173
Nervous system disorders, n (%)	6 (22.2)	1 (3.2)	0.042	0	0	1.0	6 (22.2)	1 (3.2)	0.042
Psychiatric disorders, n (%)	1 (3.7)	0	0.466	1 (3.7)	0	0.466	0	0	1.0
Renal and urinary disorders, n (%)	14 (51.9)	3 (9.7)	<0.001	4 (14.8)	0	0.041	10 (37.0)	3 (9.7)	0.025
Respiratory, thoracic and mediastinal disorders, n (%)	1 (3.7)	0	0.466	0	0	1.0	1 (3.7)	0	0.466

Bureau C, Adebayo D, Cairet de Rieu M, et al. Alfapump system vs. Large volume paracentesis for refractoru ascites: A multicenter randmized controlled study. J Hepatol 2017.

Behandeling
Ascites bij cirrose – TIPS



A stent-graft will be placed to connect your portal vein with your hepatic vein.

Behandeling
Ascites bij cirrose – TIPS

- Indicaties
  - Diureticaresisitent of intolerant
  - Intolerant voor seriële paracentese
- Contra-indicaties
  - Leeftijd >65j
  - Bilirubine totaal >5mg/dL
  - INR >2
  - Child Pugh > C11 – MELD >18
  - Hepatische encephalopathie graad 2
  - Ejectiefractie <60% - Harfalen
  - Aantasting CZS

Behandeling
Ascites bij cirrose – TIPS

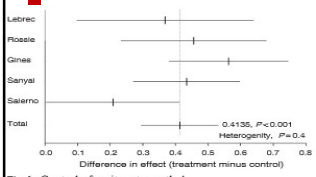


Fig. 1. Control of ascites at month 4.

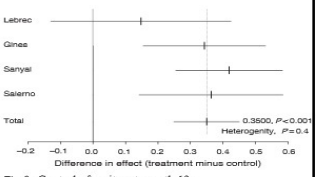


Fig. 2. Control of ascites at month 12.

Deltenre P, Mathurin P, Dharancy S, et al. Transjugular intrahepatic portosystemic shunt in refractory ascites: a meta-analysis. Liver Int. 2005;25:349–56.

Behandeling
Ascites bij cirrose – TIPS

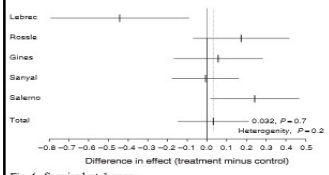


Fig. 4. Survival at 1 year.

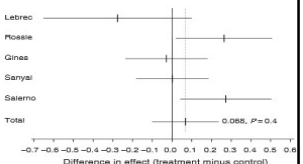


Fig. 5. Survival at 2 years.

Deltenre P, Mathurin P, Dharancy S, et al. Transjugular intrahepatic portosystemic shunt in refractory ascites: a meta-analysis. Liver Int. 2005;25:349–56.

Behandeling
Ascites bij cirrose – TIPS

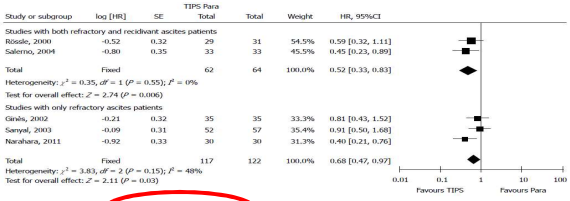


Figure 3 Subgroup analyses of liver transplantation-free survival in trials compared transjugular intrahepatic portosystemic shunt with paracentesis. Forest plots represent HR and 95%CI. TIPS: transjugular intrahepatic portosystemic shunt.

Bai M, Qi XS, Yang ZP, et al. TIPS improves liver transplantation- free survival in cirrhotic patients with refractory ascites: an updated meta-analysis. World J Gastroenterol. 2014;20:2704–14.

Behandeling
Ascites bij cirrose – TIPS

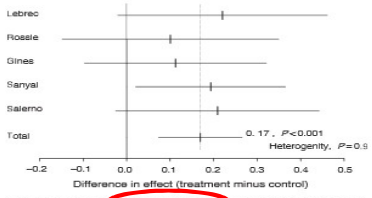


Fig. 3. Incidence of encephalopathy after transjugular intrahepatic portosystemic shunt.

Deltenre P, Mathurin P, Dharancy S, et al. Transjugular intrahepatic portosystemic shunt in refractory ascites: a meta-analysis. Liver Int. 2005;25:349–56.

Behandeling
Ascites bij cirrose – TIPS

Table 3 | Procedure-related complications

Type of complication (*n* = 43)	*n* (%)
Infectious complications	15 (3.9)
Septicaemia	5 (1.3)
Fever	10 (2.6)
Intra-abdominal bleeding and liver haematoma	8 (2.1)
Iatrogenic dissection of the inferior vena cava	1 (0.3)
Biliovenous fistula with biliary bleeding	4 (1.0)
Renal failure	7 (1.8)
Pulmonary embolism with bucrylate	1 (0.3)
Lung embolisation of balloon fragment	1 (0.3)
Liver infarction	1 (0.3)
Severe hypotonia requiring medication	2 (0.5)
Nausea and vomiting	3 (0.8)

Forty-three patients (11.1%) developed procedure-related complications after TIPSS implantation.

Table 4 | Predominant shunt-related and other nonprocedure-related complications

Type of complication	*n* (%)
Post-TIPSS hepatic encephalopathy	113 (29.0)
Grade I	72 (18.5)
Grade II	30 (7.7)
Grade III	7 (1.8)
Grade IV	4 (1.0)
Acute hepatic decompensation	16 (4.1)
Incarcerated stent-graft or shunt	1 (0.3)
Infectious complications (nonprocedural)	20 (5.1)
Spontaneous bacterial peritonitis	3 (0.8)
Urinary tract infection	8 (2.0)
Pneumonia	5 (1.3)
Others (sinusitis, bursitis, erysipelas, phlegmone)	4 (1.0)
Deep vein thrombosis	2 (0.5)

Bettinger D, Schultheiss M, Boettler T, et al. Procedural and shunt-related complications and mortality of the transjugular intrahepatic portosystemic shunt (TIPSS). Aliment Pharmacol Ther. 2016.

Casus
V, 90 jaar

- Anamnese: Epigastrische pijn, opgezet, sinds enkele weken. Systeemanamnese is verder negatief.
- KO: licht opgezet, soepel, geen drukpijn, geen peritoneale prikkeling, geen shifting dulness. Cor en long normaal. Euvoleem.
- Parameters : HD stabiel

Casus
V, 90 jaar

- Labo: Normale hematologie, nierfunctie, ionogram, leverset, INR en Albumine (38,6). LDH 507. CRP 38.
- Echo abdomen:
  - Lever: Normale grootte en reflectiviteit. Geen verdachte focale leverletsels. Normale hepatopetale portale flow.
  - Matige hoeveelheid vrij vocht intra-abdominaal

Casus
V, 90 jaar

- Ascites punctie

WBC telling	0.997	10**9/L
RBC telling automaat	0.005	10**12/L
Totaal eiwit	49	g/L
Albumine colorimetrisch	31.5	g/L
LDH	1411	U/L
Amylasen	32	U/L

Casus
V, 90 jaar

- APO:

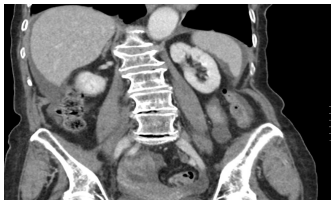
MICROSCOPISCH ONDERZOEK
De cytologie bevat talrijke ronde glandulaire groepjes, bestaande uit cellen met sterk atypische, vergrote,hyperchromatische kern, en vaak een ruime hoeveelheid mucusinhoud. We zien ook talrijke losliggende atypische cellen. Verschillende cellen bevatten een mitosespoel.

BIJKOMENDE TECHNIEKEN
PAX 8
positief

BESLUIT
Ascitesvocht: Maligne: aanwezigheid van een adenocarcinoom. Morfologisch en immunohistochemisch voorkeur voor ovariele origine.

Casus
V, 90 jaar

- CT abdomen:



MALIGNE ASCITES

Behandeling
Maligne ascites vs Maligne gerelateerde ascites

Maligne ascites (zonder PHT, SAAG <11g/L, chyleuze maligne ascites en peritoneale carcinomatose	Maligne gerelateerde ascites (met PHT, SAAG >11g/L, levermetastase, HCC)
Geen diuretica	Diuretica
LVP zonder albumine	LVP met albumine
Permanente catheters zonder albumine	Permanente catheters met albumine
PVS	PVS
CART	CART
Anti-tumorale therapie	Anti-tumorale therapie

Behandeling
Ascites bij maligniteit

Hepatology. 1988 Sep-Oct;8(5):1104-9.

Ascitic fluid analysis in malignancy-related ascites.

Runyon BA[1], Hoefs JC, Morgan TR

Author information

Abstract

A prospective study identified 45 patients with malignancy-related ascites among 448 ascites patients (10% of the total). Patients were categorized into five subgroups based on the pathophysiology of ascites formation. Each subgroup had a distinctive ascitic fluid analysis. Patients with peritoneal carcinomatosis but without massive liver metastases (53.3% of the series) with malignancy-related ascites) had a uniform pattern of ascitic fluid cytology, high ascitic fluid protein concentration and low serum-ascites albumin gradient. Patients with massive liver metastases and no other cause for ascites formation (13.3% of the series) had a negative cytology, low ascitic fluid protein concentration, high serum-ascites albumin gradient and markedly elevated serum alkaline phosphatase. Those with peritoneal carcinomatosis and massive liver metastases (13.3% of the series) had a nearly uniformly positive ascitic fluid cytology, variable protein concentration, high serum-ascites albumin gradient and markedly elevated serum alkaline phosphatase. Chylous ascites (6.7% of the series) was characterized by a milky appearance, negative cytology and an elevated ascitic fluid triglyceride concentration. Patients with hepatocellular carcinoma superimposed on cirrhosis (13.3%) had negative ascitic fluid cytology, low ascitic fluid protein concentration, high serum-ascites albumin gradient and elevated serum and ascitic fluid alpha-fetoprotein concentration. Two-thirds of patients with malignancy-related ascites had peritoneal carcinomatosis; 96.7% of patients with peritoneal carcinomatosis had positive ascitic fluid cytology. Ascitic fluid analysis is helpful in identifying and distinguishing the subgroups of malignancy-related ascites.

Behandeling
Ascites geassocieerd aan maligniteit - Diuretica

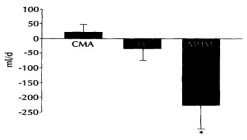


Figure 2. Mean ± SE rate of change in ascites volume (mL/day) in patients with CMA, PC, and MHM during therapy with oral diuretics (*P < 0.01 for MHM vs. PC; P − 0.05 for MHM vs. CMA).

Pockros PJ, Esrason KT, Nguyen C et al (1992) Mobilization of malignant ascites with diuretics is dependent on ascitic fluid characteristics. Gastroenterology 103(4):1302-1306

Behandeling
Ascites geassocieerd aan maligniteit – Permanente catheters

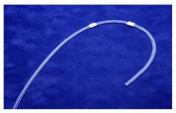


Fig. 1 Tenckhoff® peritoneal dialysis catheter (Cook Medical Inc., Bloomington, IN, USA)

Fig. 2 PleurX® catheter (Denver Biomedical, Golden, CO, USA)

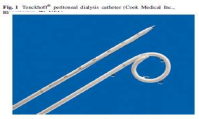
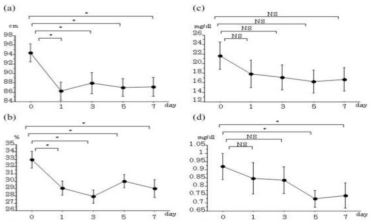


Fig. 3 Cope-type loop catheter (Cook Medical Inc., Bloomington, IN, USA)

Fig. 4 Peritoneal Port-a-Cath® (Bard Medical, C. R. Bard Inc., Covington, GA, USA)

Behandeling
Ascites geassocieerd aan maligniteit – PVS



Saiki M, Kitatani I, Sakai Y. Treatment of malignant ascites in patients with advanced cancer: peritoneovenous shunt versus paracentesis. J Gastroenterol Hepatol 2007.

Behandeling
Ascites geassocieerd aan maligniteit – CART

	Before		After		*p* value
	Mean (SD)	*n*	Mean (SD)	*n*	
Laboratory data					
Total protein—g/dL	6.1 (0.8)	104	6.3 (1.1)	104	0.016
Albumin—g/dL	3.1 (0.5)	104	3.3 (0.7)	104	< 0.0001
Total bilirubin—mg/dL	1.0 (1.5)	104	1.2 (1.6)	104	< 0.0001
Cholinesterase—IU/L	143.6 (63.7)	99	121.3 (54.8)	104	< 0.0001
Creatinine—mg/dL	0.94 (0.54)	104	0.88 (0.56)	104	< 0.0001
eGFR—mL/min/1.73 m^2	66.0 (29.0)	104	75.8 (35.6)	104	< 0.0001
C-reactive protein—mg/dL	4.6 (4.6)	104	4.7 (4.4)	104	0.42
White blood cell—$\times 10^3/\mu L$	8.0 (4.7)	104	8.5 (5.5)	104	0.16
Lymphocytes—%	13.0 (7.8)	104	10.5 (7.5)	104	< 0.0001
Hemoglobin—g/dL	10.2 (2.3)	104	9.0 (2.1)	104	< 0.0001
Platelet count—$\times 10^4/\mu L$	32.0 (14.6)	104	27.6 (12.4)	104	< 0.0001
Physical findings					
Systolic blood pressure—mmHg	109.3 (15.7)	104	108.3 (16.8)	104	0.43
Diastolic blood pressure—mmHg	68.3 (10.9)	104	64.0 (11.1)	104	< 0.0001
Heart rate—bpm	85.3 (14.1)	104	80.0 (13.3)	104	0.0006
Body temperature—°C	36.6 (0.4)	104	36.7 (0.5)	102	0.71
Body weight—kg	53.1 (12.1)	94	49.8 (15.5)	96	0.015
Abdominal circumference—cm	92.2 (9.3)	101	82.8 (12.4)	101	< 0.0001
Femur circumference—cm	37.8 (6.5)	61	36.2 (7.9)	63	< 0.0001
Lower leg circumference—cm	33.0 (5.5)	64	31.9 (5.3)	64	< 0.0001

SD standard deviation, *eGFR* estimated glomerular filtration rate

Hanada R, Yokomichi N, Kato C, et al. Efficacy and safety of reinfusion of concentrated ascitic fluid for malignant ascites: a concept-proof study. Support Care Cancer 2017.

Behandeling
Ascites bij Budd-Chiari

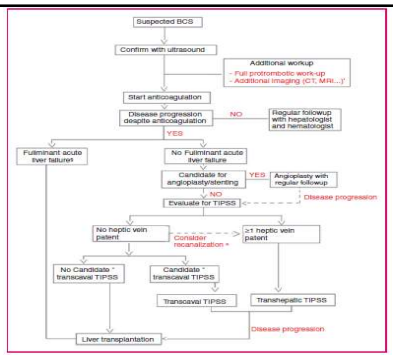
- Anticoagulatie
- Overweeg thrombolyse
- Zoek naar uitlokkende factor (myeloproliferatieve aandoeningen, thrombofilie, maligniteit)
- Angioplastie en stenting
- TIPS
- Levertransplantatie

Table 1. Distribution prothrombotic risk factors according to ENVIE Cohort.

Risk factor	EN-Vie cohort *n/n* (%)[3]
Myeloproliferative disorder	56/143 (39%)
Inherited thrombophilia	32/154 (21%)
- Factor V Leiden	18/147 (12%)
- *G20210A* prothrombin	5/144 (3%)
- Protein C deficiency	5/117 (4%)
- Protein S deficiency	3/108 (3%)
- Antithrombin deficiency	3/112 (3%)
Acquired conditions	
- Antiphospholipid antibodies	37/150 (25%)
- Hyperhomocysteinemia	28/129 (22%)
- PNH	15/77 (19%)
- Behçet	4/163 (2.5%)
- Sarcoïdosis	2/163 (1%)
- Oral contraceptives	31/93 (33%)
- Pregnancy	6/93 (6%)
Combinations	
- Single risk factor	135/160 (84%)
- Multiple risk factors	74/160 (46%)

PNH: paroxysmal nocturnal hemoglobinuria.

Martinelli I, Stevens F. Budd-Chiari syndrome. United European Gastroenterol J 2015.



Martens P, Stevens F. Budd-Chiari syndrome. United European Gastroenterol J 2015.

Complicaties
Spontane Bacteriële Peritonitis

- Surinfectie van het ascitesvocht zonder een aantoonbare bron noch heelkunde behandeling
- Meest frequente infectie bij gehospitaliseerde cirrose patiënten
- Mortaliteit 10-50%
- Kliniek: paucisymptomatisch tot koorts, abdominale pijn, diarree, suf, hepatische encephalopathie, sepsis en shock
- Pathogenese: translocatie van gram negatieve kiemen (E. Coli, Klebsiella Pneumoniae, Enterobacteriacae)
- Diagnose: ascites punctie

Complicaties
Spontane Bacteriële Peritonitis

Analyse ascitesvocht	Spontane bacteriële peritonitis	Secundaire bacteriële peritonitis
Cytose	> 250/mm³ PMN	> 250/mm³ PMN
Totaal eiwit	< 1g/dL	> 1g/dL
LDH	> ULN	> ULN
Glucose	> 50mg/dL	> 50mg/dL
Amylase	< 50% serumwaarde, normaal	> 50% serumwaarde (pancreatitis, darmperforatie)
Bilirubine	< serumwaarde, normaal	> serumwaarde, >6mg/dL (galblaasperforatie)
Gramkleuring en cultuuur	monobacterieel	multibacterieel

Complicaties
Spontane Bacteriële Peritonitis

- Behandeling
  - Breedspectrum AB:
    - 3de generatie cefalosporine
    - Cefotaxime 2g 3x/d gedurende 5 dagen
  - Albumine:
    - Bij creatinine >1mg/dL, ureum > 30mg/dL of totaal bilirubine > 4mg/dL
    - 1,5g/kg op dag 1 en nadien 1g/kg op dag 3

Complicaties
Spontane Bacteriële Peritonitis

- Profylaxis
  - Bij hoge GI bloeding
  - Secundair profylaxis
  - Te overwegen bij totaal protein in ascites < 1,5g/dL (lager gehalte van opsonines)
  - Norfloxacine 400mg/d of Ciprofloxacine 500mg/d of Sulfamethoxazol/Trimetoprim 800/160mg /d

Complicaties
Spontane Bacteriële Peritonitis

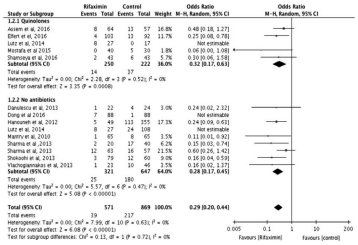
Table 7. Antibiotic therapy for prophylaxis of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis.*

Reference	Type of prophylaxis	Treatments	Number of patients	Number of GNB[b] infections	*p*-value	Incidence of SBP n (%)	*p*-value
Ginès, 1990 [158]	Enrolled only patients with prior SBP[c]	Norfloxacin versus placebo	40 40	1 10	–	5 (12) 14 (35)	0.02
Soriano, 1991 [153]	Enrolled patients without prior SBP and patients with prior SBP[d]	Norfloxacin versus no treatment	32 31	0 9	<0.001	0 (0) 7 (22.5)	<0.02
Singh, 1995 [161]	Enrolled patients without prior SBP and patients with prior SBP[d]	Trimethoprim–sulfamethoxazole versus no treatment	30 30	9 0	–	1 (3) 8 (27)[e]	0.03
Rolachon, 1995 [160]	Enrolled patients without prior SBP and patients with prior SBP[c]	Ciprofloxacin versus placebo	28 32	1 0	–	1 (4) 7 (22)	<0.05
Novella, 1997 [154]	Enrolled only patients without prior SBP[d]	Continuous norfloxacin versus in patient-only prophylaxis	56 53	11 13	–	1 (1.8) 9 (16.9)	<0.01
Grangé, 1998 [155]	Enrolled only patients without prior SBP[c]	Norfloxacin versus placebo	53 54	0 6	<0.04	0 (0) 5 (9)	NA
Fernández, 2007 [156]	Enrolled only patients without prior SBP[c]	Norfloxacin versus placebo	35 33	13 6	–	2 (6) 10 (30)	0.02
Terg, 2008 [157]	Enrolled only patients without prior SBP[c]	Ciprofloxacin versus placebo	50 50	–	–	2 (4) 7 (14)	0.076

NA, not available.
[a] Studies appear in chronological order.
[b] GNB means Gram-negative bacteria.
[c] Randomized, double-blind, placebo-controlled trial.
[d] Randomized, unblinded trial.
[e] Including one patient with spontaneous bacteremia due to *Klebsiella pneumonia*.

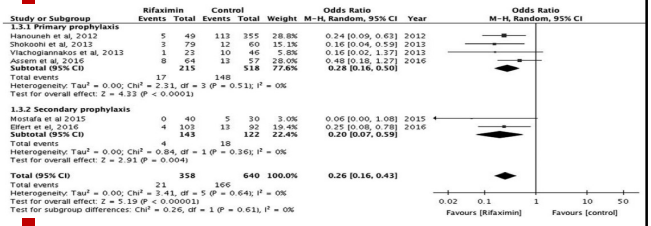
Pires et al. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. Journal of Hepatology 2010.

Complicaties
Spontane Bacteriële Peritonitis



Kamal K, Khan MA, Khan Z, et al. Rifaximin for the prevention of spontaneous bacterial peritonitis and hepatorenal syndrome in cirrhosis: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2017.

Complicaties
Spontane Bacteriële Peritonitis



Kamal K, Khan MA, Khan Z, et al. Rifaximin for the prevention of spontaneous bacterial peritonitis and hepatorenal syndrome in cirrhosis: a systemisch review and meta-analysis. Eur J Gastroenterol Hepatol 2017.

Complicaties
Hepatorenaal syndroom

Criteria for diagnosis of hepatorenal syndrome in cirrhosis.

Cirrhosis with ascites

Serum creatinine >1.5 mg/dl (133 µmol/L)

Absence of shock

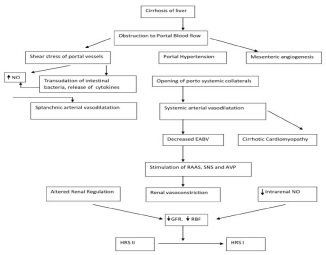
Absence of hypovolemia as defined by no sustained improvement of renal function (creatinine decreasing to <133 µmol/L) following at least 2 days of diuretic withdrawal (if on diuretics), and volume expansion with albumin at 1 g/kg/day up to a maximum of 100 g/day

No current or recent treatment with nephrotoxic drugs

Absence of parenchymal renal disease as defined by proteinuria <0.5 g/day, no microhaematuria (<50 red cells/high powered field), and normal renal ultrasonography

Pires et al. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. Journal of Hepatology 2010

Complicaties
Hepatorenaal syndroom

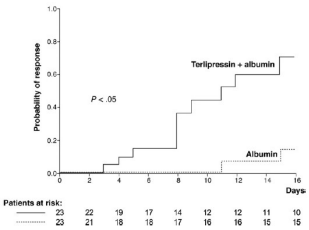


Pratshu MP, Sukanya B, Santosh Pai BH et al. The hepatorenal syndrome-a review. G Ital Nfrol2014.

Complicaties
Hepatorenaal syndroom

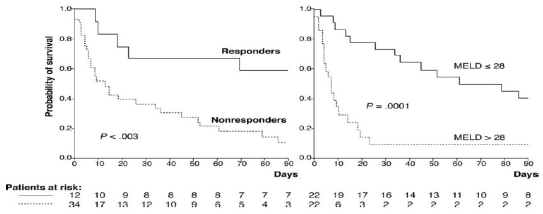
- Behandeling:
  - Monitoring
  - Stop diuretica
  - Albumine 1mg/kg op dag 1 gevolgd door 40mg/d
  - Terlipressine 0,5-1mg om de 4-6u, opdrijven tot 2mg om de 4-6u zo geen 25% verbetering van het creatinine op dag 3
  - Gemiddelde behandelingsduur van 14 dagen
  - TIPS
  - Nierdialyse
  - Levertransplantatie

Complicaties
Hepatorenaal syndroom



Martin-Llahi M, Pépin MN, Guevara M, et al. Terlipressin and albumin vs albumin in patients with cirrhosis and hepatorenal syndrome: a randomized study. Gastroenterology 2008.

Complicaties
Hepatorenaal syndroom



Martin-Llahi M, Pépin MN, Guevara M, et al. Terlipressin and albumin vs albumin in patients with cirrhosis and hepatorenal syndrome: a randomized study. *Gastroenterology* 2008.

Complicaties
Hepatorenaal syndroom

TABLE 2. Details of Assigned Treatment in Responders (Complete and Partial)

	TERLI-INF Group (n = 26)	TERLI-BOL Group (n = 24)	P
Length of treatment, days	9.31 ± 4.06	8.52 ± 3.86	0.4705
Cumulative dose of albumin, g	189.20 ± 91.78	164.38 ± 89.36	0.3311
End of treatment sCr, μmol/L	120.00 ± 33.34	121.25 ± 38.53	1.0000
Maximum daily dose of terlipressin, mg	2.62 ± 1.06	4.50 ± 3.06	0.0001
Mean daily dose of terlipressin, mg	2.23 ± 0.65	3.51 ± 1.77	0.0001
Delta CTP	−0.62 ± 0.65	−0.52 ± 0.79	0.8014
Delta MELD	−7.31 ± 3.70	−6.88 ± 3.48	0.6048
Delta MELD-Na	−7.69 ± 4.27	−5.46 ± 6.88	0.2712
Delta MAP			
Day 3 of treatment versus baseline	9.10 ± 11.32	5.35 ± 12.53	0.5957
Middle of treatment versus baseline	15.04 ± 18.04	10.75 ± 12.54	0.5164
End of treatment versus baseline	12.11 ± 19.34	9.20 ± 12.90	1.0000

Abbreviations: CTP, Child-Turcotte-Pugh; MAP, mean arterial pressure; MELD, Model for End-Stage Liver Disease; MELD-Na, MELD including sodium; TERLI-BOL, terlipressin by intravenous boluses; TERLI-INF, terlipressin by intravenous infusion.

Cavallin M, Piano S, Romano A, et al. Terlipressin given by continuous intravenous infusion versus intravenous boluses in the treatment of hepatorenal syndrome: A randomized controlled study. *Hepatology* 2016 .

Complicaties
Hepatorenaal syndroom

TABLE 3. Severe Treatment-Related Adverse Events (Defined as Needed to Withdraw Terlipressin)

	TERLI-INF Group (n = 34)	TERLI-BOL Group (n = 37)	P
Patients, no. (%)	7 (20.59)	16 (43.24)	<0.05
Suspected intestinal ischemia	—	3	—
Peripheral ischemia	1	—	—
Circulatory overload	2	5	—
Angina pectoris	3	3	—
Arrhythmia	—	1	—
Arterial hypertension	1	—	—
Persistent diarrhea	—	2	—
Others	—	2	—

Abbreviations: TERLI-BOL, terlipressin by intravenous boluses; TERLI-INF, terlipressin by intravenous infusion.

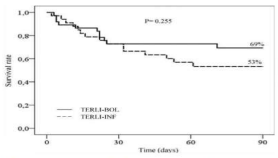


FIG. 2. Ninety-day transplant-free survival according to assigned group.

Cavallin M, Piano S, Romano A, et al. Terlipressin given by continuous intravenous infusion versus intravenous boluses in the treatment of hepatorenal syndrome: A randomized controlled study. *Hepatology* 2016 .

Complicaties
Hepatorenaal syndroom

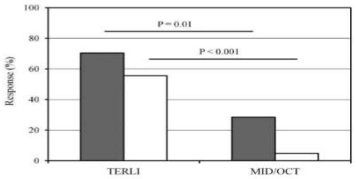


Fig. 2. Rates of response in patients who were randomized to terlipressin plus albumin (TERLI) or to midodrine and octreotide plus albumin (MID/OCT). Gray bars represent patients with complete or partial response; white bars represent patients with complete response.

Cavallin M, Kamath PS, Merli M, et al. Terlipressin plus albumin versus midodrine and octreotide plus albumin in the treatment of hepatorenal syndrome: A randomized trial. *Hepatology* 2015

Complicaties
Hepatorenaal syndroom

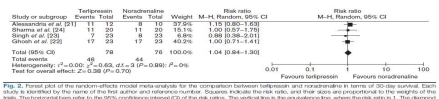


Fig. 2. Forest plot of the random-effects model meta-analysis for the comparison between terlipressin and noradrenaline in terms of 30-day survival. Each study is identified by the name of the first author and reference number. Squares indicate the risk ratio, and their sizes are proportional to the weights of the trials. The horizontal bars refer to the 95% confidence interval (CI) of the risk ratios. The vertical line is the equivalence line, where the risk ratio is 1. The diamond represents the 95% CI of the pooled risk ratio. M-H, Mantel-Haenszel method.

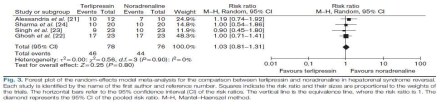
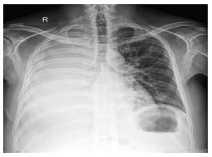


Fig. 3. Forest plot of the random-effects model meta-analysis for the comparison between terlipressin and noradrenaline in hepatorenal syndrome reversal. Each study is identified by the name of the first author and reference number. Squares indicate the risk ratio and their sizes are proportional to the weights of the trials. The horizontal bars refer to the 95% confidence interval (CI) of the risk ratios. The vertical line is the equivalence line, where the risk ratio is 1. The diamond represents the 95% CI of the pooled risk ratio. M-H, Mantel-Haenszel method.

Mattos AA, Mattos AA, Ribeiro RA. Terlipressine versus noradrenaline in the treatment of hepatorenal syndrome: systemati review with meta-analysis and full economic evaluation. Eur. J Gastroenterol Hepatol 2016.

Complicaties
Hepatisch hydrothorax



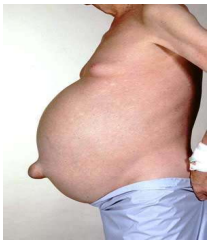
Complicaties
Hepatisch hydrothorax

Table 5. Advantages and disadvantages of the different treatment modalities for HH

Treatment	Advantages	Disadvantages
Medical management	– Cheap – Noninvasive	– High noncompliance rate – Risk of acute kidney injury and renal failure – Ineffective in refractory HH
Thoracentesis	– Relief of symptoms – Allows pleural fluid analysis to rule out other diagnoses like SBEM	– Frequent requirement – Complications like pneumothorax, hemothorax, reexpansion pulmonary edema
TIPS	– Bridge to liver transplant – Success rate of 70–80%	– Post-TIPS hepatic encephalopathy – Shunt occlusion and thrombosis – Poor survival in MELD >15, CTP class C and high pre-TIPS creatinine of >2 mg/dl
Pleurodesis	– Repair of diaphragmatic defects can be performed – Success can be increased with CPAP, somatostatin – Considered in patients when TIPS is contraindicated	– Repeated procedures are needed – General anesthesia needed for VATS – Complications like empyema, sepsis, septic shock – Increase bleeding risk with mechanical pleurodesis – Cannot be performed in trapped lung
Surgical repair of diaphragmatic defects	– Increase success of pleurodesis	– Not always visualized – Invasive
Liver transplant	– Most effective management option	– Long waiting time

Singh K, Rawa A, Shujaat A. Evidence based review of the management of hepatic hydrothorax. Respiration 2013.

Complicaties
Hernia Umbilicalis



Complicaties
Umbilicale hernia

- Behandeling
  - Urgente heelkunde bij inklemming/strangulatie
  - Electieve heelkunde bij verdunnen van de huid of eschar met verlies van ascitesvocht
  - Herstel bij levertransplantatie zo ongecompliceerd

Take Home Messages

- Ascites is niet onschuldig
- Cirrose is de belangrijke oorzaak
- Steeds ascitespunctie, SAAG is je vriend
- Diuretica en zoutrestrictie zijn de hoeksteen van de behandeling
- SBP voornaamste verwikkeling, bepaal ook cytose en kweek in HC-flessen. R/Cefalosporines
- Levertranplantatie

Overige referenties

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