Atelier: Complications fréquentes de la cirrhose: mode d'emploi

Dr Nicolas Goossens, MD, MSc, PD

Dre Giulia Magini, MD

Service de Gastroentérologie et Hépatologie

Hôpitaux Universitaires de Genève

Journées Romandes d'Hépatologie, Sion

18 Juin 2020

Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE

FACULTÉ DE MÉDECINE

Références

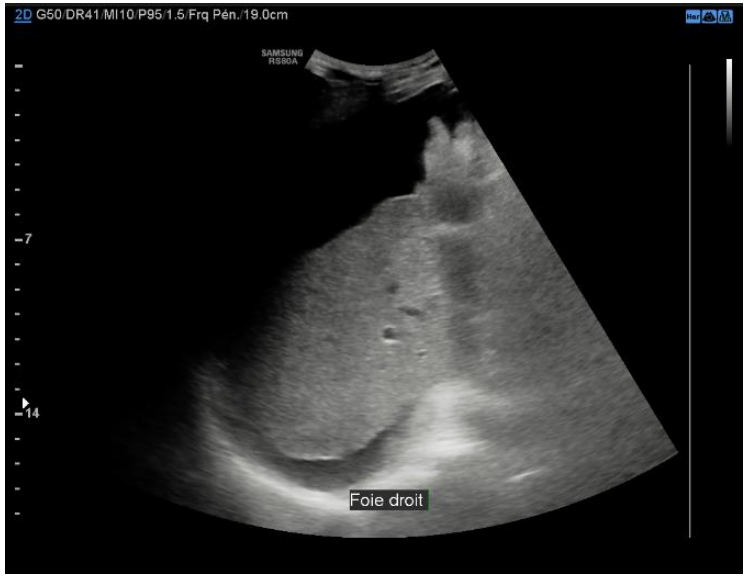
Recommandations EASL:
https://easl.eu/publications/clinical-practice-guidelines/

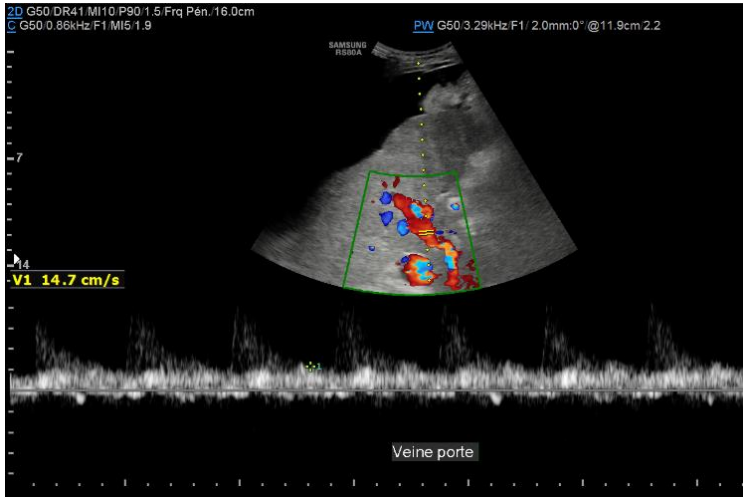
Recommandations SASL:
https://sasl.unibas.ch/6SASLguidelines.php

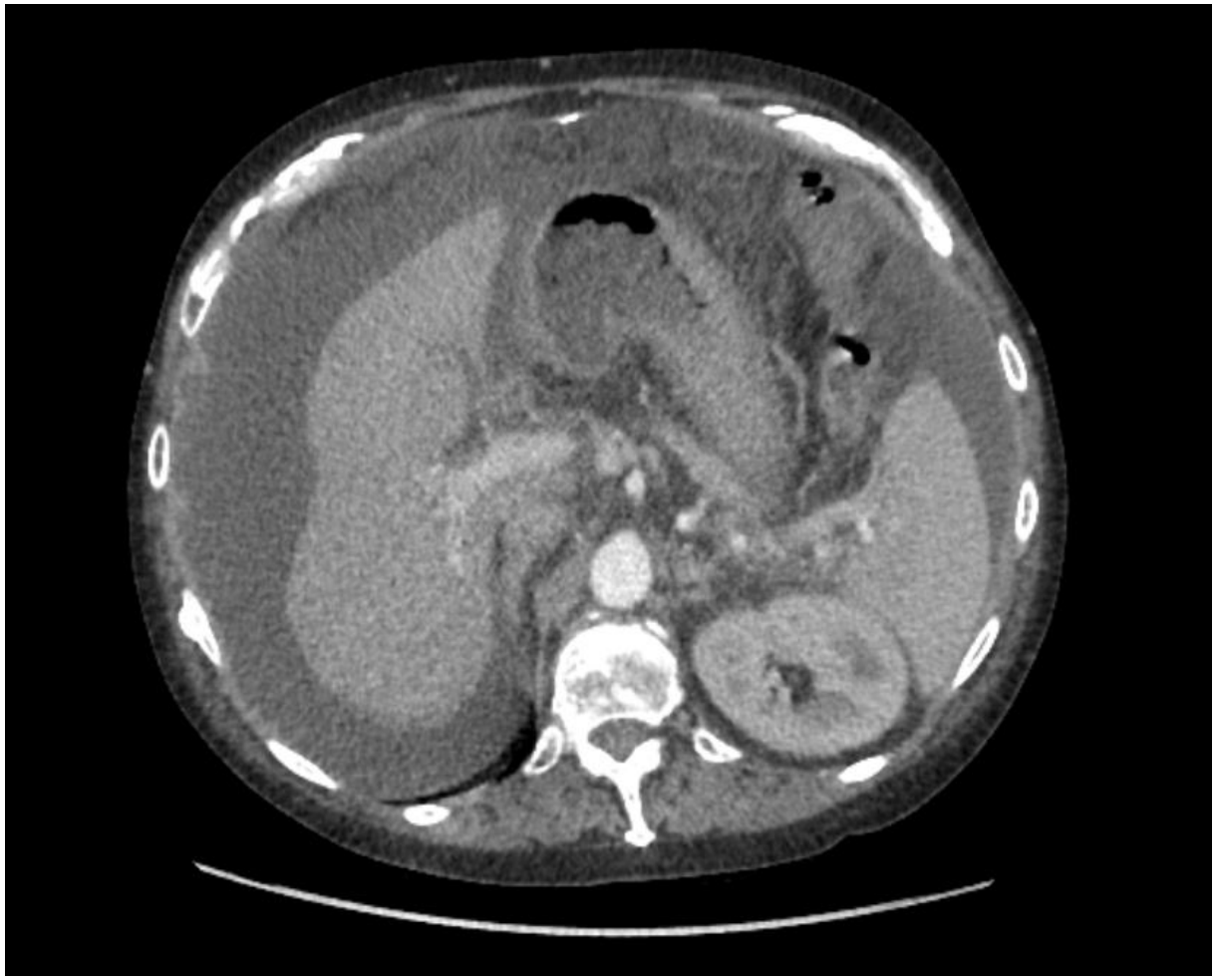
Cas clinique (2017)

- Homme de 60 ans hospitalisé pour **douleurs abdominales**
- Antécédents:
  - **Cirrhose OH** (PBF transjugulaire en 2016: cirrhose + stéatohépatite, **gradient 13mmHg**)
  - OGD: **VO** de stade 1, gastropathie d'HTP
  - OH actif (2L vin / jour, plusieurs crises épi sur sevrage)
  - FA non anticoagulée
- Sous curatelle de gestion
- Labo:
  - **CRP 33**, créatinine 56, transas 2N, GGT 458, PhAlc 118, **bilirubine totale/conj 35/20** umol/L, albumine 28g/L
  - **Quick 60%, INR 1.3**
  - Hb 136g/L, leucos 4.3 G/L, **thrombos 78G/L**

Cas clinique (2017) - Imagerie







Cas clinique (2017) - suite

- **Quelle prise en charge pour l'ascite ?**

Ascite non compliquée - diagnostic

- Grading of ascites:
  - Grade 1: mild ascites (US)
  - Grade 2: Moderate ascites (distension abdomen)
  - Grade 3: Large or gross ascites

- **Diagnostic paracentesis** is indicated in:*
  - All patients with new-onset grade 2 or 3 ascites
  - Patients hospitalized for worsening ascites or any complication of cirrhosis

Recommendation
Neutrophil count and culture of ascitic fluid culture† should be performed to exclude **bacterial peritonitis** • Neutrophil count >250 cells/µl denotes SBP
Ascitic total protein concentration (<15 g/L) should be performed to identify patients at higher risk of developing SBP‡
The SAAG should be calculated when the cause of ascites is not immediately evident, and/or when conditions other than cirrhosis are suspected (≥11 g/L = portal HTN)
Cytology should be performed to differentiate malignancy-related from non-malignant ascites

EASL CPG decompensated cirrhosis. J Hepatol 2018

Ascite non compliquée – prise en charge

- Prognosis
  - 1-year mortality: 40%
  - 2-year mortality: 50%
  - Consider referral for LT +++

- **Grade 1 ascites**
  - Unclear if treatment associated with benefit in natural history

- **Grade 2 ascites**
  - Na restriction (4.5 – 7g/d) or no extra salt
  - Spironolactone max 400mg/d
  - Furosemide max 160mg/d
  - Monitor renal function, potassium, weight loss (max 1kg/d if oedema)
  - Avoid nephrotoxic drugs, including NSAIDs and ACEI…

EASL CPG decompensated cirrhosis. J Hepatol 2018

Ascite non compliquée – prise en charge

- **Grade 3** or large ascites
  - LVP, under strict sterile conditions, is the treatment of choice
    - Ascites should be completely removed in a single session*
  - Contraindications to LVP include:
    - Uncooperative patient, abdominal skin infection at puncture sites, pregnancy, severe coagulopathy, severe bowel distention

Recommendation		
LVP should be **followed with plasma volume expansion**	I	1
Plasma volume expansion should be performed by **albumin infusion** (8 g/L ascites) • For >5 L of ascites: more effective than other plasma expanders • For <5 L of ascites (low risk of PPCD): treat with albumin due to concerns about use of alternative plasma expanders	I III	1 1
After LVP, patients should receive the **minimum dose of diuretics** necessary to prevent re-accumulation of ascites	I	1
When needed, LVP should be performed in patients with AKI or SBP	III	1

EASL CPG decompensated cirrhosis. J Hepatol 2018

Cas clinique (2017) - suite

- Ponction d'ascite:
  - 750 PMN, pas de germes à la culture
  - Albumine ascite 9g/L, protéines 12g/L

- Introduction de ceftriaxone 2g/j

- Après 48h:
  - Ponction ascite: 27 PMN
  - Créat 183umol/L
  - Sédiment urinaire: pas de Hb ou de prot
  - Spot urinaire: Na 10 mmol/L

- **Que faire??**

Péritonite Bactérienne Spontanée

- Diagnosis is based on diagnostic paracentesis
- 50% of SBP episodes are present at hospital admission
  - **Signs/symptoms of peritonitis**: abdominal pain, tenderness, vomiting or diarrhoea, ileus
  - **Signs of systemic inflammation**: hyper- or hypothermia, chills, altered WBC count
  - **Worsening liver function**, **HE**, **shock**, **renal failure**, **GI bleeding**

Recommendation		
Diagnostic paracentesis should be carried out in: • Patients with cirrhosis and ascites, **at admission**, to rule out SBP • Patients with GI bleeding, shock, fever or other signs of systemic inflammation, worsening liver and/or renal function, and HE	II-2	1
SBP diagnosed by a neutrophil count in ascitic fluid >250/mm^3 • Neutrophil count is determined by microscopy or flow cytometry • **No clear evidence** to support routine use of **reagent strips**	II-2	1
Ascitic fluid culture positivity is not a prerequisite for SBP diagnosis*	II-2	1

EASL CPG decompensated cirrhosis. J Hepatol 2018

Péritonite Bactérienne Spontanée

Recommendation		
Third-generation cephalosporins are recommended as first-line antibiotic treatment for **community-acquired SBP** in countries with **low rates of antibiotic resistance** • In countries with **high rates of antibiotic resistance** piperacillin/tazobactam or carbapenem should be considered	I II-2	1 1
Antibiotic resistance is more likely in **healthcare-associated** and **nosocomial SBP** • Piperacillin/tazobactam: in areas with low prevalence of MDR bacteria • Carbapenem: in areas with high prevalence of ESBL-producing *Enterobacteriaceae* • Carbapenem + glycopeptides, daptomycin linezolid in areas with high prevalence of gram-positive MDR bacteria	I	1

- In patients with SBP treated with a third generation intravenous cephalosporin antibiotic, **albumin** significantly decreased the incidence of type-1 hepatorenal syndrome and reduced mortality[1]

Recommendation		
The administration of albumin is recommended in patients with SBP • 1.5 g/kg at diagnosis and • 1 g/kg on Day 3	I	1

AKI et cirrhose – les définitions

Subject	Definition		
Definition of AKI	• Increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) within 48 hours or • Increase sCr ≥50% within the prior 7 days		
Staging of AKI	• **Stage 1**: increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) or an increase in sCr ≥1.5-2x baseline A: < 130umol/L B: > 130umol/L • **Stage 2**: increase in sCr 2-3x baseline • **Stage 3**: increase of sCr >3x baseline or sCr ≥4.0 mg/dl (353.6 µmol/L) with acute increase ≥0.3 mg/dl (≥26.5 µmol/L) or initiation of renal replacement therapy		
Response to treatment	**No response** No regression of AKI	**Partial response** Regression of AKI stage with a reduction of sCr to ≥0.3 mg/dl (≥26.5 µmol/L) above baseline	**Full response** Return of sCr to a value within 0.3 mg/dl (≥26.5 µmol/L) of baseline

EASL CPG decompensated cirrhosis. J Hepatol 2018

AKI et cirrhose – les définitions

Subject	Definition		
Definition of AKI	• Increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) within 48 hours or • Increase sCr ≥50% within the prior 7 days		
Staging of AKI	• **Stage 1**: increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) or an increase in sCr ≥1.5-2x baseline A: < 130umol/L B: > 130umol/L • **Stage 2**: increase in sCr 2-3x baseline • **Stage 3**: increase of sCr >3x baseline or sCr ≥4.0 mg/dl (353.6 µmol/L) with acute increase ≥0.3 mg/dl (≥26.5 µmol/L) or initiation of renal replacement therapy		
Response to treatment	**No response** No regression of AKI	**Partial response** Regression of AKI stage with a reduction of sCr to ≥0.3 mg/dl (≥26.5 µmol/L) above baseline	**Full response** Return of sCr to a value within 0.3 mg/dl (≥26.5 µmol/L) of baseline

EASL CPG decompensated cirrhosis. J Hepatol 2018

AKI et cirrhose – diagnostic

- All types of AKI can occur in patients with cirrhosis
  - Pre-renal, HRS, intrinsic, particularly ATN, and post-renal
- **Key point is to differentiate HRS-AKI from ATN**
- Classification of HRS was recently revised by the ICA[1]
  - Type 1 HRS now corresponds to HRS-AKI
  - Type 2 HRS includes renal impairment that fulfills the criteria of HRS but not of AKI (non-AKI-HRS or NAKI)

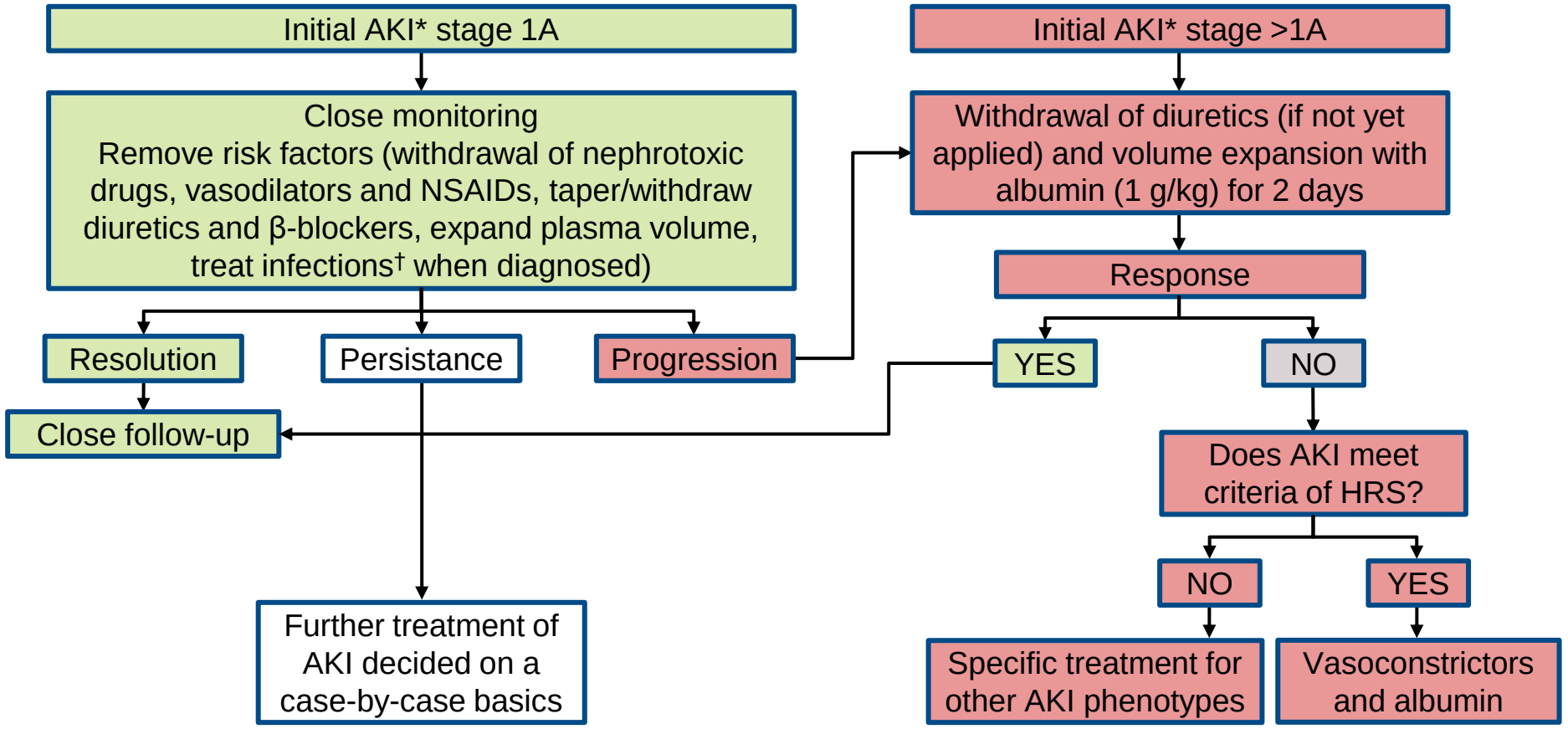
Definition of HRS-AKI (previously type 1 HRS)

- Cirrhosis and ascites
- Diagnosis of AKI according to ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g per kg of body weight
- Absence of shock
- No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc.)
- No macroscopic signs of structural kidney injury,* defined as:
  - Absence of proteinuria (>500 mg/day)
  - Absence of microhaematuria (>50 RBCs per high power field)
  - Normal findings on renal ultrasonography

EASL CPG decompensated cirrhosis. J Hepatol 2018

AKI et cirrhose – prise en charge

- Investigation and management should begin immediately



EASL CPG decompensated cirrhosis. J Hepatol 2018

HRS-AKI– prise en charge

- First-line therapy is terlipressin plus albumin*

Recommendation		
All patients meeting the current definition of **HRS-AKI stage >1A** should be expeditiously treated with **vasoconstrictors and albumin**	III	1
Terlipressin can be administered by IV boluses (1 mg every 4–6 hours) or by continuous IV infusion (2 mg/day)† • In case of **non-response** (decrease in SCr <25% from the peak value) after 2 days, the dose of **terlipressin should be increased** in a stepwise manner to a **maximum of 12 mg/day**	I	1
Albumin solution (20%) should be used at 20–40 g/day • Serial measures assessing central blood volume can help to titrate the dose of albumin to prevent circulatory overload	II-2	1
Noradrenaline can be an alternative to terlipressin‡ • Requires a central venous line often in an ICU Midodrine + octreotide can be an option when terlipressin or noradrenaline are unavailable (but efficacy is much lower)	I I I	2 1 1

EASL CPG decompensated cirrhosis. J Hepatol 2018

Cas clinique (2018) - suite

Finalement apres traitement HRS-AKI induite par la péritonite bactérienne spontanée, le patient RAD.

- Ascite initialement contrôlée par diurétiques.
- Le patient continue à consommer 2L vin / j

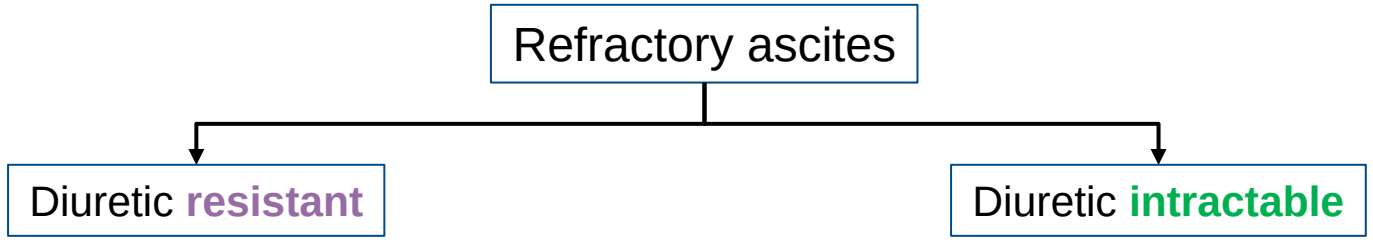
<u>1 an plus tard</u>

- Ponctions d'ascite de 6-7L tous les 10j, plus de PBS sous Norfloxacine prophylactique
- Aggravation fn rénale dès que augmentation Aldactone > 50mg/j et Torasemide > 10mg/j
- Labo: Bilirubine 50umol/L, Quick 50%, INR 1.8, albumine 28g/L, créatinine 100umol/L

Que faire?

Ascite refractaire – définition et pronostic

- **International Ascites Club**:
  - "Ascites that cannot be mobilized or the early recurrence of which (after LVP) cannot be satisfactorily prevented by medical therapy"



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**

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**

NB: Refractory ascites is associated with a poor prognosis (Median survival around 6 months)

EASL CPG decompensated cirrhosis. J Hepatol 2018

Ascite refractaire – prise en charge

- Consider **liver transplantation** +++++
- Repeat LVP is safe and effective
- Consider reducing / discontinuing NSBB
- Consider TIPS in selected patients
  - Contraindications include high MELD, HE, heart failure, age, HCC…
  - Small-diameter PTFE stent
- Other therapies in selected patients:
  - PleurX
  - Alfapump

EASL CPG decompensated cirrhosis. J Hepatol 2018

Cas clinique (2018) - suite

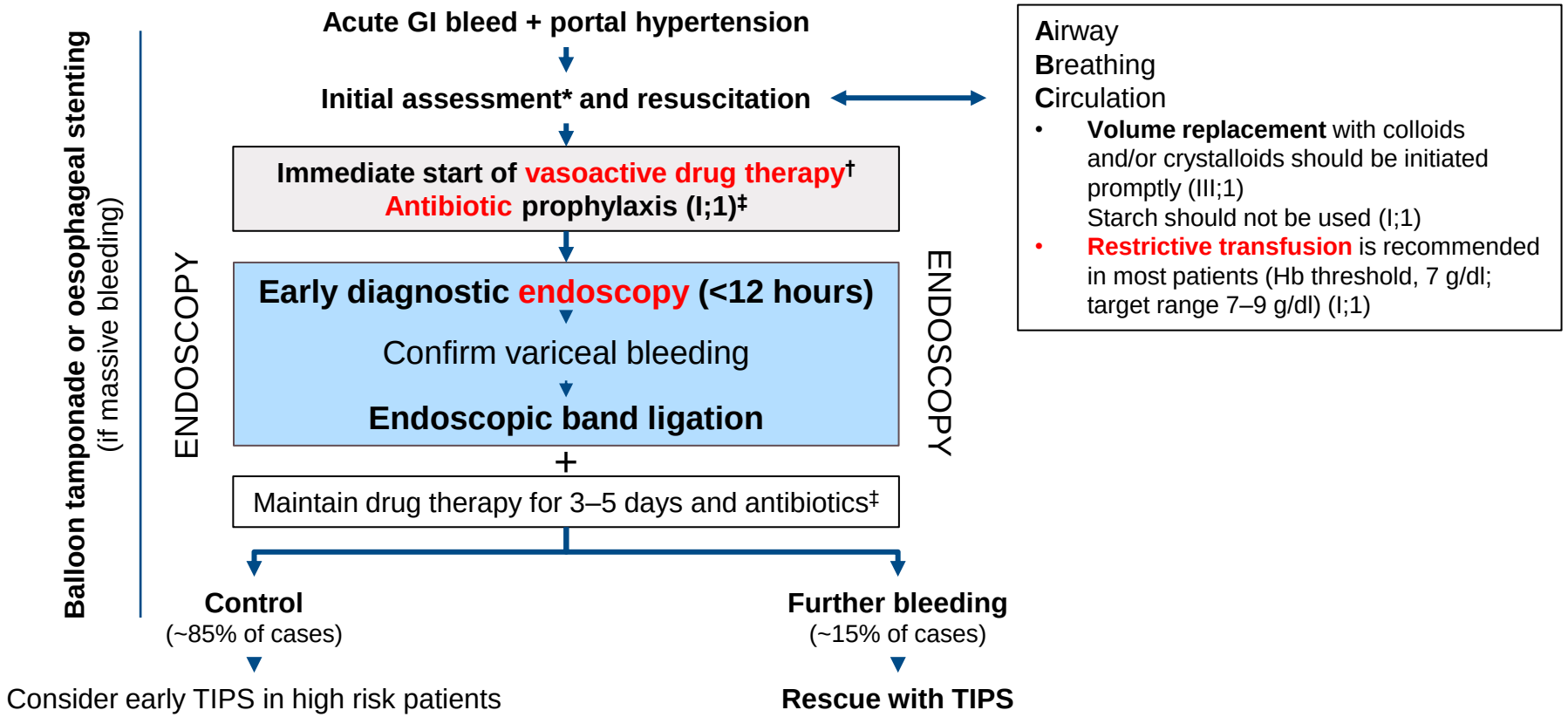
- Ascite refractaire prise en charge par ponction évacuatrices itératives

- Admis aux urgences 5 mois plus tard pour **hématémèse:**
- Hb 77g/L, bilirubine 67umol/L, INR 2.3, albumine 25g/L.
- Patient confus et somnolent
- OGD: 3 cordons de VO avec signes rouges mais sans saignement actif, gastropathie d'HTP. Pose de 10 ligatures sur les VO.

Que faire?

Hémorragie sur hypertension portale – prise en charge

- **Medical emergency**: high rate of complications and mortality in DC
  - Requires immediate treatment and close monitoring



EASL CPG decompensated cirrhosis. J Hepatol 2018

Hémorragie récurrent sur hypertension portale – prise en charge

- Up to 10–15% of patients have persistent bleeding or early re-bleeding
  - Despite treatment with vasoactive drugs and EBL, and prophylactic antibiotics

Recommendation		
TIPS should be used as the **rescue therapy** of choice in cases of persistent bleeding or early re-bleeding	I	1
With the pre-requisite of expertise, **balloon tamponade** should be used in case of **uncontrolled bleeding** as a temporary "bridge" (max 24 hours) until definitive treatment can be instituted	III	1
• Removable, covered and self-expanding oesophageal stents can be used as an alternative to balloon tamponade	I	2
In the context of bleeding, where encephalopathy is commonly encountered, prophylactic lactulose may be used to prevent encephalopathy, but further studies are needed	I	2

EASL CPG decompensated cirrhosis. J Hepatol 2018

Prévention primaire de l'hémorragie sur HTP

OGD	Prise en charge	Rythme surveillance
Pas de VO	Tt étiologique Pas de BB	2-3 ans
VO de petite taille (gd 1)	Tt étiologique +/- BB (surtout si signes rouges ou Child C)	1-2 ans
VO de grande taille (gd 2-3)	Tt étiologique BB ou ligature	-
Varices gastriques	Tt étiologique BB ou tt endoscopique	-

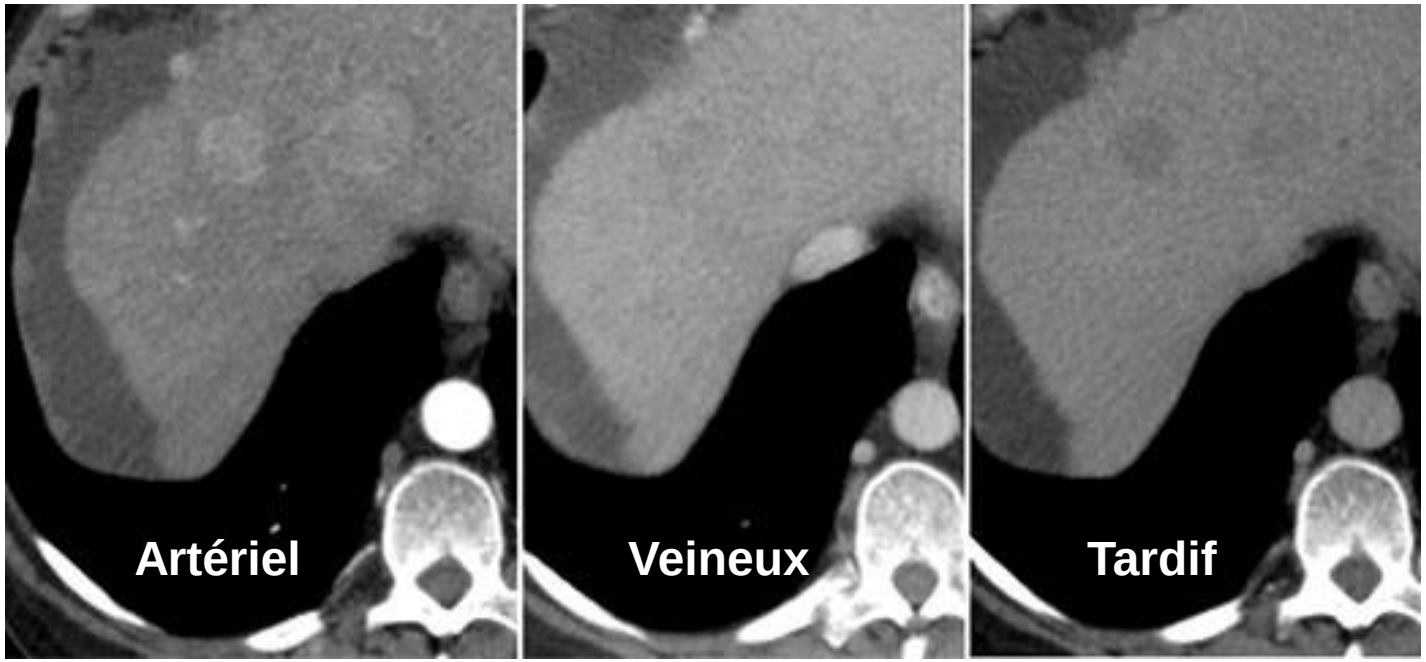
EASL CPG decompensated cirrhosis. J Hepatol 2018
Conférence de consensus BAVENO 6, 2015

Cas clinique (2018) - suite

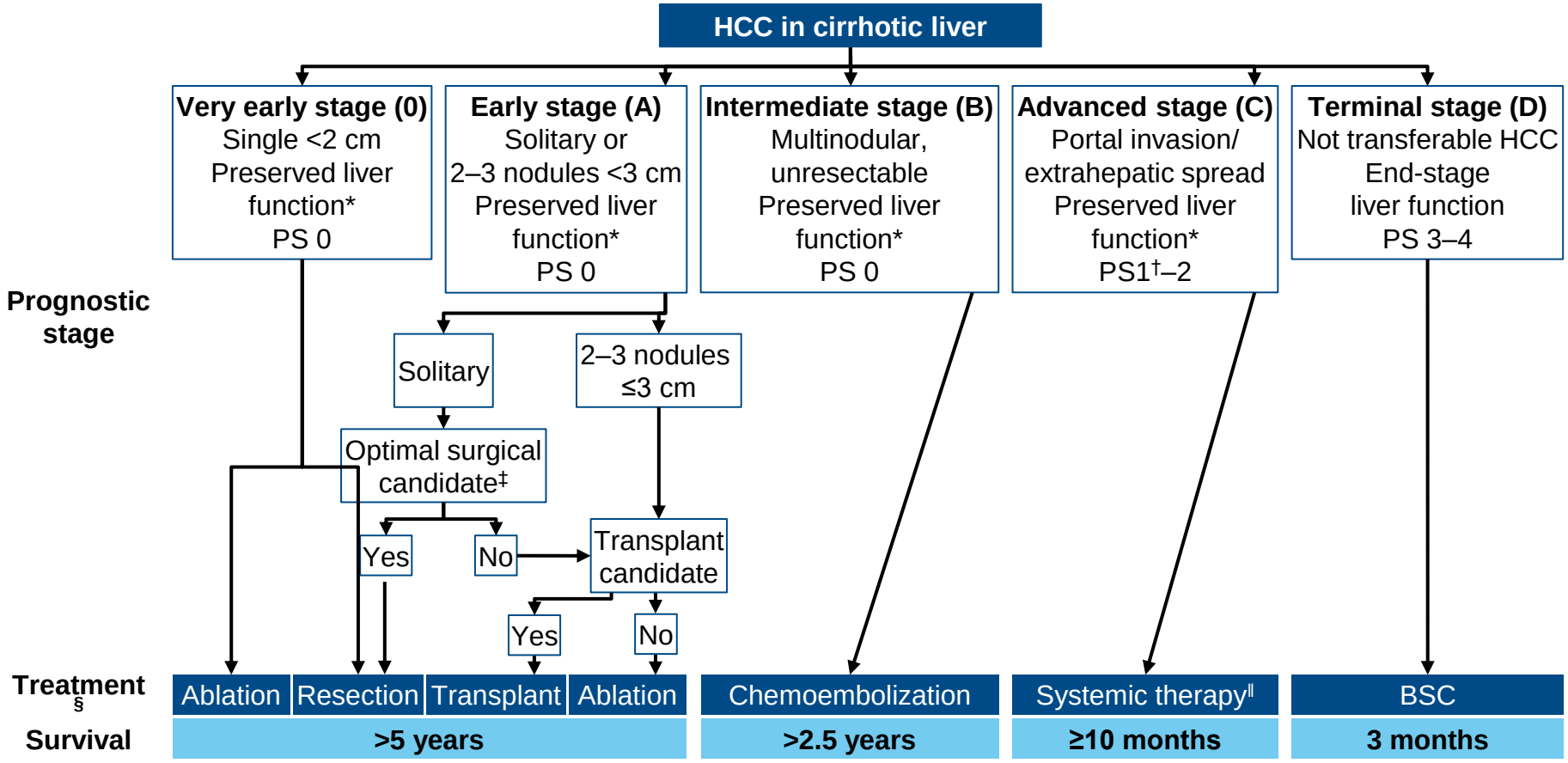
- Patient stabilisé après prise en charge de l'hémorragie sur VO

- US puis CT effectués pendant l'hospitalisation
- 2 nodules hypervasculaires avec wash-out de 16 et 28mm du foie droit
- AFP 47

Quel diagnostic?
Que faire?

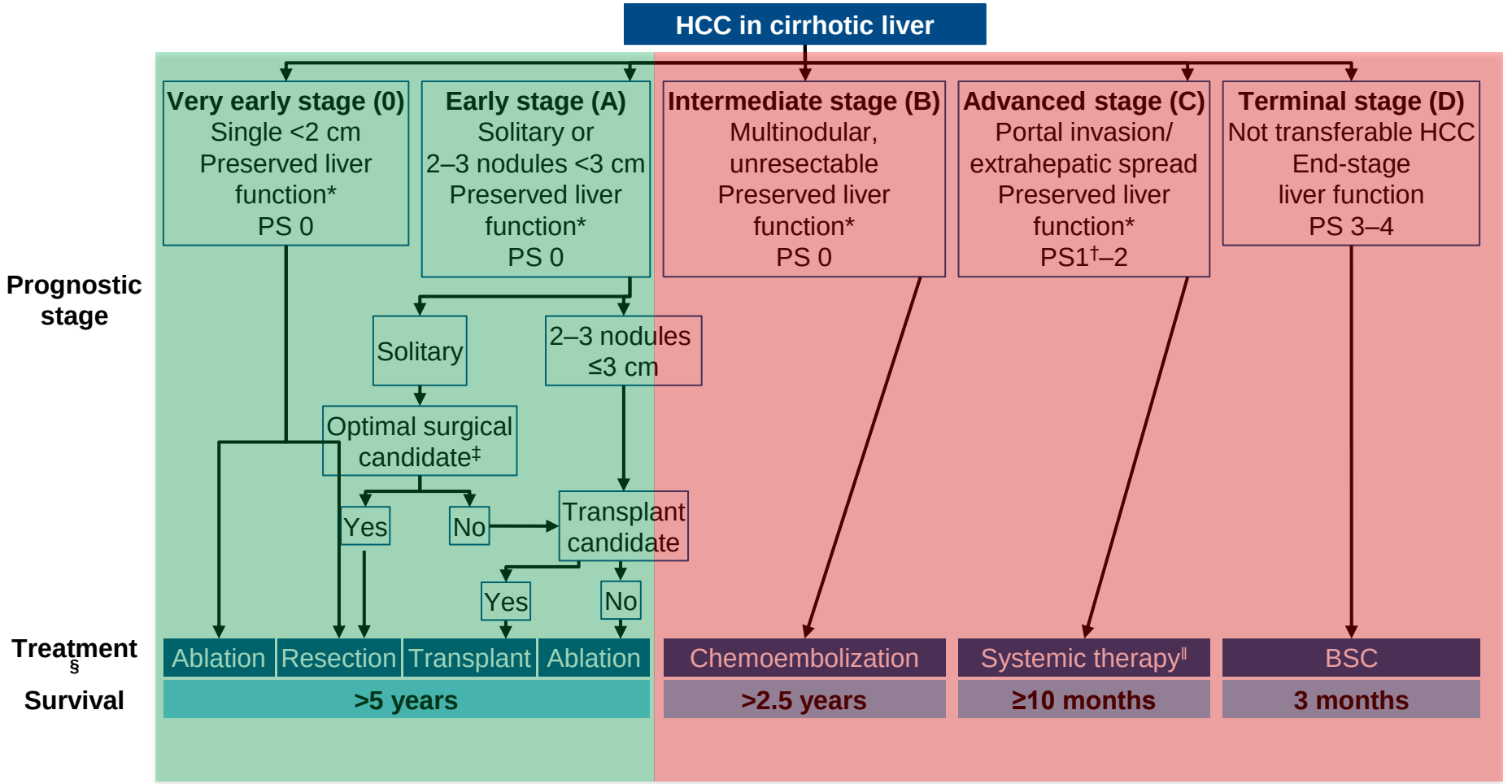


Carcinome hépatocellulaire – prise en charge



EASL CPG HCC. J Hepatol 2018

Carcinome hépatocellulaire – prise en charge



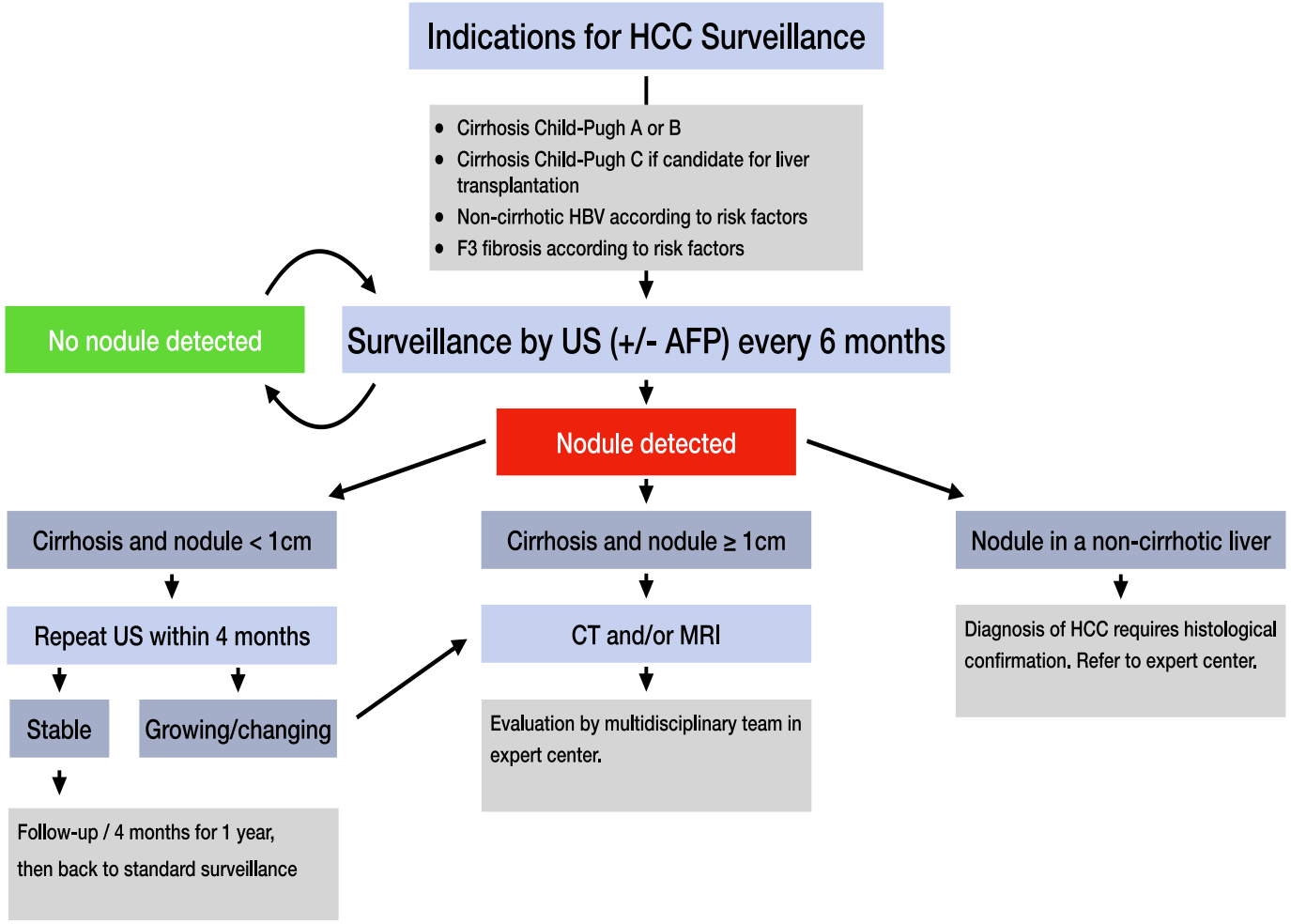
EASL CPG HCC. J Hepatol 2018

Carcinome hépatocellulaire –qui dépister?

Société	Qui dépister?	Comment dépister?
EASL 2018 	• **Cirrhose** (Child A, B et Child C si candidat pour TH) • **HBV**: si non-cirrhotique à risque interméd-haut • **F3**: individualisé selon facteurs de risque	Echographie 1x / 6 mois
AASLD 2011 et 2018 	• **Cirrhose** (Child A, B et Child C si candidat pour TH) • **HBV**: Selon origine ethnique, âge et antécédents familiaux de CHC • HCV F3 et NAFLD sans cirrhose le **bénéfice est incertain**	US +/- AFP 1x / 6 mois

Seuil de coût-efficacité: incidence de CHC > 0.8-2.3% / année

Carcinome hépatocellulaire –qui dépister?



Goossens, Heim, Toso (SASL), SMW in press, 2020

Cas clinique (2018) – suite et fin

- Au vu de la fonction hépatique (Child-Pugh C) et la consommation éthylique active le CHC du patient a été classé BCLC-D

- Il est décédé 5 semaines plus tard à domicile avec l'aide des soins palliatifs ambulatoires.

Messages clés

- Considérer la transplantation hépatique après la 1ère complication de la cirrhose
- Eviter la iatrogénie (en particulier pour la fn rénale)
- Penser au dépistage du CHC
- Ne pas hésiter à consulter le spécialiste ou un centre expert en cas de questions / doutes

Merci pour votre attention

Hôpitaux Universitaires Genève

HÉPATOLOGIE
GASTRO-ENTÉROLOGIE
GENÈVE

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE