WHAT IS CHALLENGING IN THE MANAGEMENT OF CHRONIC LIVER DISEASES IN 2020?

HEP Preceptorship

Virtual Meeting
3rd December, 2020

NAFLD/NASH clinical cases

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Interactive question

http://etc.ch/6w2m

INSELGRUPPE

FIRST CLINICAL CASE

Clinical case: 62 years old, M

March 2020 referral to Bern Hepatology outapatient clinic

Elevated transminases

Clinical history:

- Recent journey to India (November 2019-January 2020) where the patient spontaneously stopped statin treatment and part of anti-DM therapy
- Weight 85 kg, height 1.75 m, BMI 27.8 kg/m^2
- Noxae: 15-20 cigarette/day, no alcohol
- Vaccine against HBV and HAV

Clinical history

Medical history:

- ***Metabolic syndrome***
  - → Diabetes mellitus (1996)
  - → Arterial hypertension grade 1(1996)
  - → Overweight (BMI 28 kg/m^2)
  - → Dyslipidaemia
  - → 2013 abdominal ultrasound → hepatic statosis
- ***Schizophrenia***
  - → Clozapin and Aripriprazole

Therapy:

- Clozapin 100 mg 2x ½/d
- Aripriprazole 15 mg 1x/d
- Bisoprolol 5 mg 1x/d
- **Rosuvastatin 5 mg 1x/d** **STOP**
- **Glicazide 60 mg 1x/d** **STOP**
- Insulin Lantus 6 U 8.00 h
- Insulin Novorapid according to individual schedule

Abdominal US: Signs of severe **liver steatosis** with advanced fibrosis. Focal fatty sparing next to the gallbladder.

Fibroscan (device 502, XL probe): Stiffness 12.6 kPa, IQR 2.8 kPa, IQR/MED 20%, **CAP 344 dB/m** IQR 46 dB/m.

Laboratory tests

WBC (x 10.9/L)	8,28
RBC (x 10.12/L)	5,40
Hb (g/dl)	14,5
Hct (%)	44
MCV (fl)	82
PLT (x 10.9/L)	167

ALT/AST (U/L)	108/138
ALP/GGT (U/L)	97/172
Bilirubin (µmol/L)	16
Albumin (g/L)	40
PT (sec) / **INR**	12 / 1,15
Creatinine (µmol/l)	54

Cholesterol (mmol/L)	5,22
HDL (mmol/L)	0,76
LDL (mmol/L)	3,34
Triglycerides (mmol/L)	1,81
Glucose (mmol/L)	15
Hb1Ac (%)	10,3%
M-30 Apopt (U/L)	>1000
Ferritin (µg/L)	149

ANA pos 1:320
AMA, SMA, anti-LKM, pANCA normal

HBV and HCV negative

Rouled out hemochromatosis, Wilson's disease and α-1-antitrypsin deficiency

Interactive question

Do you want to perform a liver biopsy in this patient?

a) Yes

b) No

https://directpoll.com/r?XDbzPBd3ixYqg8ndmvMl7yaKPBQ5bmKqd5jwL1L2

Conclusion and recommendation

MAFLD (Metabolic dysfunction-Associated Fatty Liver Disease)

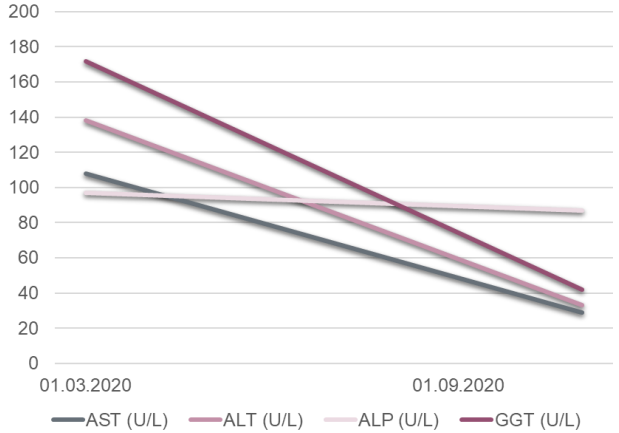
- Lifestyle changing (including weight reduction of 7-10% of actual weight)
- Re-starting statin therapy
- Diabetological evaluation with an endocrinologist
- Follow-up evaluation in our outpatient clinic in 6 months

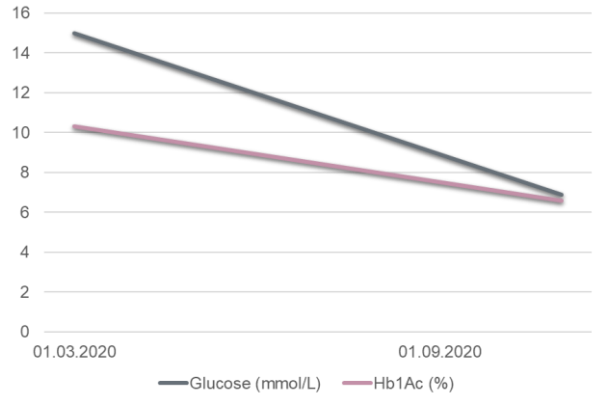
November 2020 Hepatology outpatient clinic

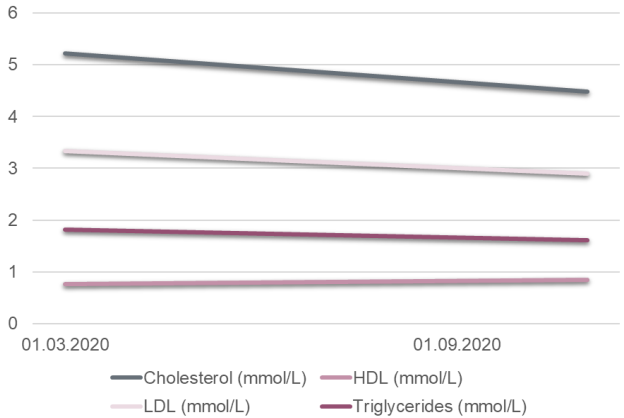
Clinical evolution:

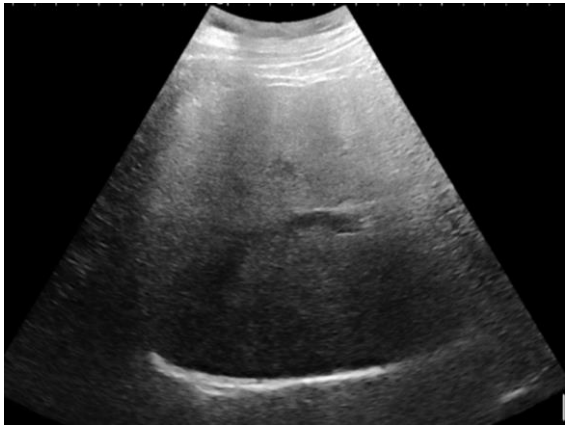
- Diabetological consultation: Optimization of therapy with:
  - → restarting **Glicazide**
  - → introduction of **Metformin + Sitagliptin 1000/50 mg** (Janumet©) 2/d h 8.00-19.00

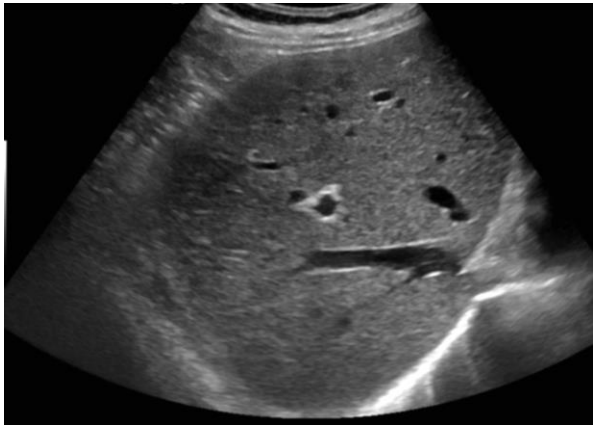
Values	10.03.2020	10.11.2020
Weight (kg)	85	75
BMI (kg/m^2)	27,8	24,5











Fibroscan (device 502, XL probe):

Stiffness 12.6 IQR 2.8 kPa, IQR/MED 20%,

CAP 344 IQR 46 dB/m

Fibroscan (device 502, XL probe):

Stiffness 10.8 IQR 0.9 kPa, IQR/MED 8%,

CAP 166 IQR 27 dB/m

PLT (x 10.9/L)	167	141

Interactive question

Do you want to perform a liver biopsy in this patient now?

a) Yes

b) No

https://directpoll.com/r?XDbzPBd3ixYqg8ndmvMl7yaKPBQ5bmKqd5jwL1L2

INSELGRUPPE

MAFLD

METABOLIC

DYSFUNCTION-

ASSOCIATED

FATTY

LIVER

DISEASE

INSELGRUPPE

SECOND CLINICAL CASE

Clinical case: 54 years old, M

October 2019 referral to Bern Hepatology outapatient clinic

Suspected advanced liver disease/cirrhosis during laparoscopic cholecystectomy (05/2019)

Clinical history:

- 05/2019 acute cholecystectomy and liver biopsy for cirrhotic appearance of the liver
- Weight 137 kg, height 1.93 m, BMI 36.8 kg/m^2
- Noxae: 1996-2014 increased alcohol consumption, currently abstinent. Smokes 4-5 pipes per day, no drugs
- No immunity for HAV, HBV and HCV

Clinical history

Medical history:

- ***Metabolic syndrome***
  - → Diabetes mellitus
  - → Arterial hypertension
  - → **Obesity WHO grade II (BMI 36.8 kg/m^2)**
  - → Dyslipidaemia
- ***Severe back pain with leg irradiation***
- ***Cholecystectomy for acute cholecystitis (05/2019)***

Therapy:

- Valsartan/HCT 160/12.5 mg 1x/d
- Rosuvastatin 5 mg 1x/d
- Glicazide 60 mg 2x/d
- Metformin + Sitagliptin 1000/50 mg 2x/d
- Semaglutide 0.25 mg 1x/week
- Insulin degludec 80 U 22.00 h
- Pregabalin 100 mg 3x/d
- Oxycodon/Naltrexon 20/10 mg 3x/d

Laboratory tests

WBC (x 10.9/L)	8,58
RBC (x 10.12/L)	5,13
Hb (g/dl)	15,8
Hct (%)	44
MCV (fl)	85
PLT (x 10.9/L)	176

ALT/ALT (U/L)	20/32
ALP/GGT (U/L)	74/70
Bilirubin (µmol/L)	18
Albumin (g/L)	42
PT (sec)/INR	10,7/1
Creatinine (µmol/l)	86

Cholesterol (mmol/L)	2,65
HDL (mmol/L)	0,85
LDL (mmol/L)	0,98
Triglycerides (mmol/L)	1,81
Glucose (mmol/L)	3,97
Hb1Ac (%)	5,8%
M-30 Apopt (U/L)	188
Ferritin (µg/L)	268

ANA, AMA, SMA, anti-LKM, pANCA
HBV and HCV negative
Rouled out hemocromatosis, Wilson disease and α-1-antitrypsin deficiency

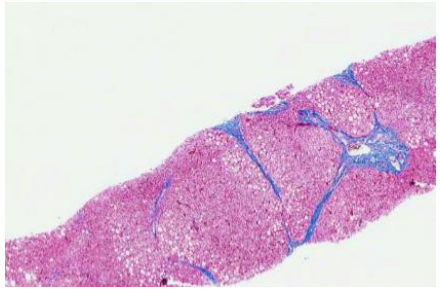
Abdominal MRI

- hepatomegaly and liver dysmorphic
- borderline splenomegaly (13.5 cm)
- portal vein slightly dilated (15.5 mm)

Fibroscan

- Stiffness 7.8 kPa, IQR/MED 13%
- CAP 295 dB/m

Liver biopsy



Steatohepatopathy with activity signs (NAS-Score 3 according to Kleiner et al.) & septae and bridging fibrosis (F3 according Brunt); the findings correspond to a SAF score S1A2 (1+1) F3, currently just qualifying for a florid steatohepatitis (NASH)

Conclusion and recommendation

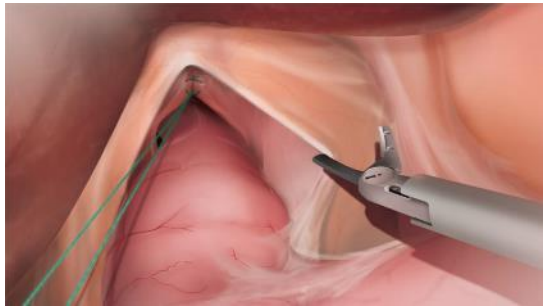
Florid NASH associated to advanced fibrosis in obesity grade II

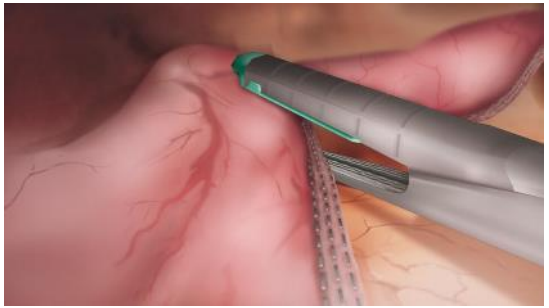
- Bariatric surgery evaluation
- New evaluation in 6 months

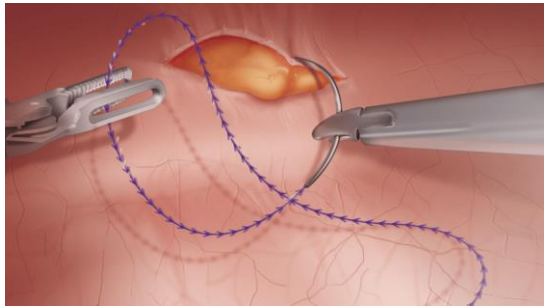
Bariatric surgery

Weight 137.6 kg, BMI 36.9 kg/m^2

On January 21st, 2019, the patient underwent laparoscopic sleeve gastrectomy:







November 2020: Follow-up in Hepatology outapatient clinic

Clinical evolution:

- 42 kg weight loss, weight 96 kg, BMI 28.2 kg/m²
- Resolution of metabolic syndrome, in particular:
  - → no arterial hypertension
  - → no dyslipidemia
  - → controlled DM only with Semaglutide
- Development of chronic diarrhoea

Therapy:

~~Valsartan/HCT 160/12.5 mg 1x/d~~

~~Rosuvastatin 5 mg 1x/d~~

~~Glicazide 60 mg 2x/d~~

~~Metformin + Sitagliptin 1000/50 mg 2x/d~~

Semaglutide 0.25 mg 1x/week

~~Insulin degludec 80 U 22.00 h~~

Pregabalin 100 mg 3x/d

Oxycodon/Naltrexon 20/10 mg 3x/d

Abdominal US: slightly inhomogeneous parenchyma, no sign of liver steatosis or advanced fibrosis. Spleen 12 cm.

Fibroscan (device 502, M probe): Stiffness 6.2 kPa, IQR 0.4 kPa, IQR/M 6%,CAP 213 dB/m, CAP IQR 24 dB/m

Interactive question

How do you want to follow-up this patient?

a) Re-biopsy (after 1 year)

b) Starting HCC-screening

c) See the patient early because of risk of malnutrition and progression of liver disease

https://directpoll.com/r?XDbzPBd3ixYqg8ndmvMl7yaKPBQ5bmKqd5jwL1L2

INSELGRUPPE

NAFLD/NASH and Bariatric Surgery

INSELGRUPPE

THIRD CLINICAL CASE

Clinical case: 27 years old, F

November 2009 referral to Bern Liver Unit from another hospital

Severe portal hypertension and splenic vein thrombosis

Clinical examination:

- weight 57 kg, height 1.60 m, BMI 22.3 kg/m^2
- fat distribution disorder with very slim extremities without subcutaneous adipose tissue and fat accumulation on neck and décolleté
- Heart: rhythmic heart activity, no pathological murmur
- Abdomen: hepato- and splenomegaly, umbilical hernia

Medical history

- ***Lipodystrophy (possibly familiar partial form; Dunnigan syndrome, known since 1990)***

  → No detection of lamin A/C gene nor PPARɣ mutation

  → Leptin deficiency (leptin 1.54 ng/ml 09/2004)

  Complications:

  a) Lipoatrophic diabetes mellitus (1990)

  b) Liver disease

  c) Polycystic ovarian syndrome (PCO) and infertility

- ***Liver cirrhosis (Child B)***

  → Liver biopsy 18.05.1990: **liver fibrosis** (etiology not defined)

  → Splenic vein thrombosis (08.06.2005)

  → Gastroscopy (10.06.2005): Portal hypertensive gastropathy, medium-sized esophageal varices

  → Abdominal sonography (10.11.2008): liver cirrhosis with portal hypertension, no liver lesions, no ascites, cholecystolithiasis

Clinical history

Family history:

- Brother (13 yo) and mother with diabetes
- Married, works 80% in office, one son (6 months) adopted

Noxae:

- No nicotine, no alcohol, possible allergy to iron infusion

Therapy:

- Estrogen-based oral contraception 1/d
- Delteparin 7500 IE/4 ml inj. 1x/d
- Propranolol 40 mg 3x/d
- Pantoprazol 20 mg 1x/d
- Pioglitazone 45 mg 1x/d

Laboratory tests

WBC (x 10.9/L)	1,04
RBC (x 10.12/L)	3,38
Hb (g/dl)	9,9
Hct (%)	29
MCV (fl)	86
PLT (x 10.9/L)	32

ALT/ALT (U/L)	42/29
ALP/GGT (U/L)	45/33
Bilirubin (µmol/L)	45
Albumin (g/L)	33
PT (sec) **/ INR**	57/1,31
Creatinine (µmol/l)	37

Cholesterol (mmol/L)	3,49
HDL (mmol/L)	0,98
LDL (mmol/L)	1,91
Triglycerides (mmol/L)	1,91
Glucose (mmol/L)	8,5
Hb1Ac (%)	7,0%

ANA, ANA, SMA, anti-LKM, pANCA normal

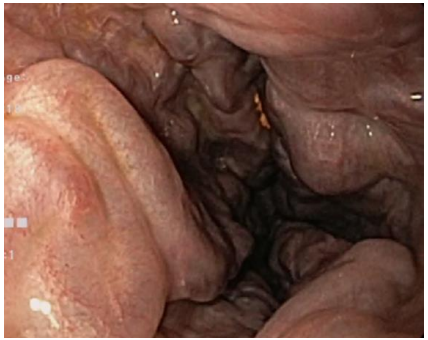
HBV and HCV negative

MELD 13

MELD-Na 15

CHILD PUGH B7

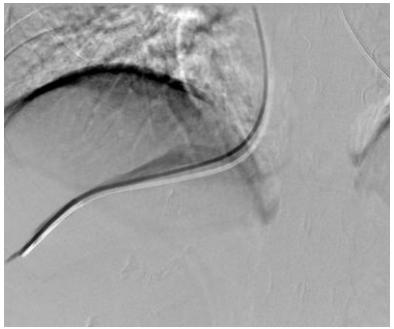
Upper GI endoscopy



- Esophageal varices grade III
- cardia- and duodenal varices
- no ligation of the esophageal varices

Transujugular liver biopsy and HVPG mesurements

- Low-grade micro and macro steatosis (approx. 30%)
- small focus of pericellular fibrosis
- findings are compatible with non-alcoholic (NAFLD)
- No evidence for AIH



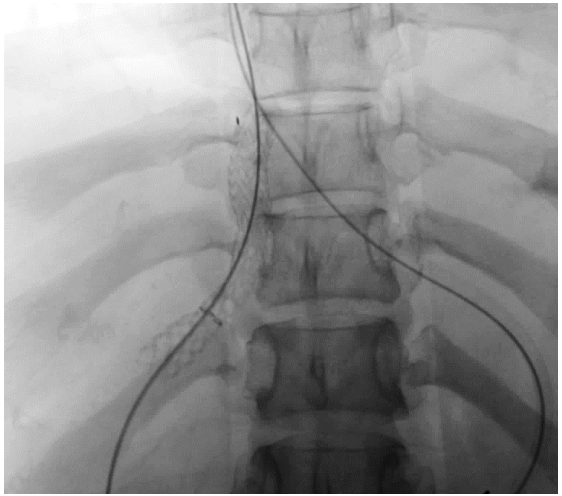
HVPG=30 mmHg

Discharged

NAFLD/NASH cirrhosis (Child B7) with severe portal hypertension and splenic vein thrombosis

December 2009 referral to Bern Liver Unit

Varicel bleeding and hemorragic shock



TIPS placement

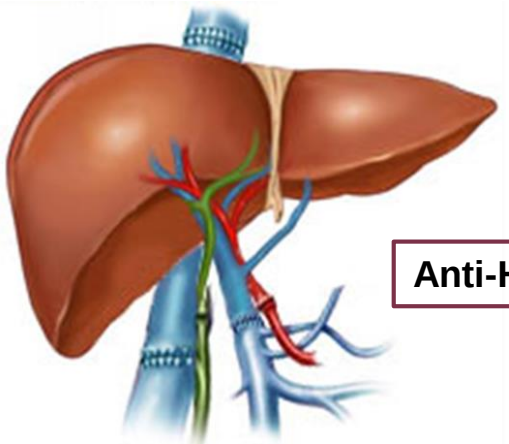
Clinical evolution:

- multiple post-TIPS liver abscesses treated with antibiotic therapy
- worsening of DM and severe DM decompensation
- continuation of anticoagulant therapy
- evaluation for liver transplantation (MELD exception)

Liver transplantation

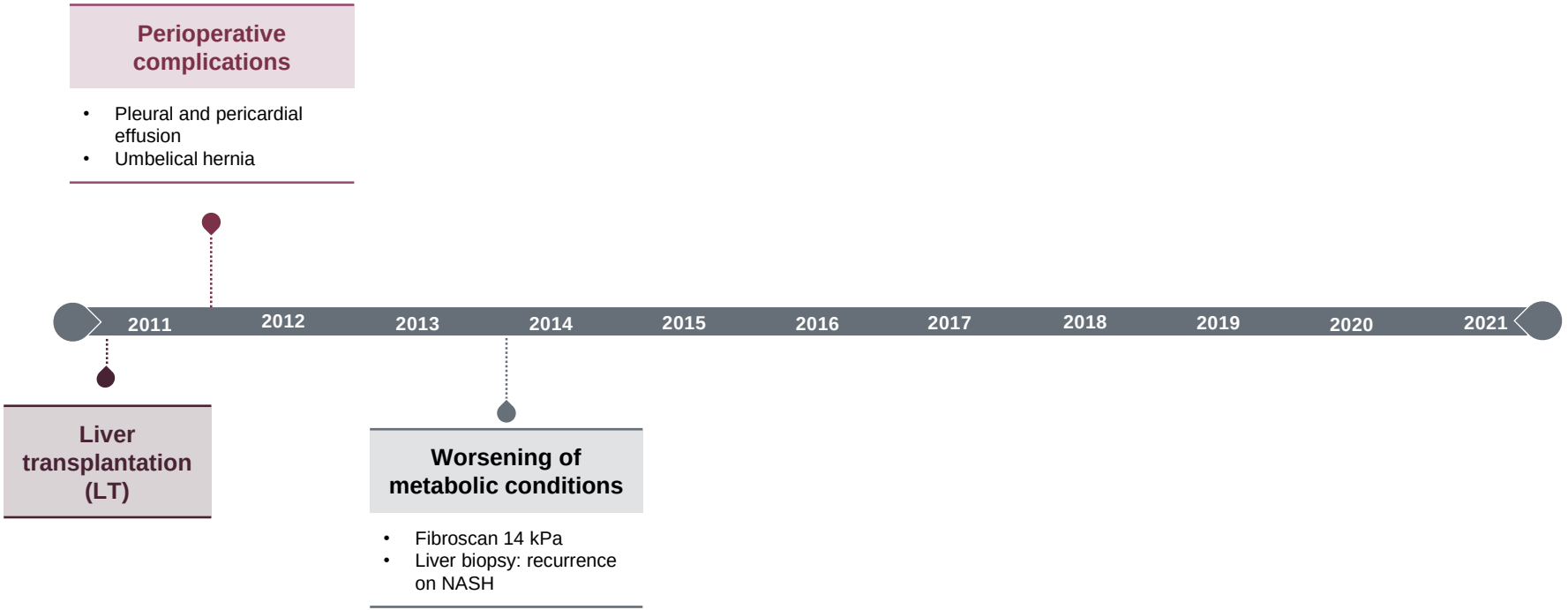
On October 30, 2011, the patient underwent liver transplantation

Child C 13, MELD score 18 and severe encephalopathy



Anti-HBc Donor

Standard immunossuppression was started with rapid steroids withdrawal plus TAC and MMF; HBV reactivation prophylaxis with Lamivudine


Perioperative complications
• Pleural and pericardial effusion
• Umbelical hernia
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
Liver transplantation (LT)
Worsening of metabolic conditions
• Fibroscan 14 kPa
• Liver biopsy: recurrence on NASH

Interactive question

What do you want to do in order to improve the metabolic condition?

a) **Optimizing DM therapy**

b) **Changing immunosuppressive therapy**

c) **Leptin substitution**

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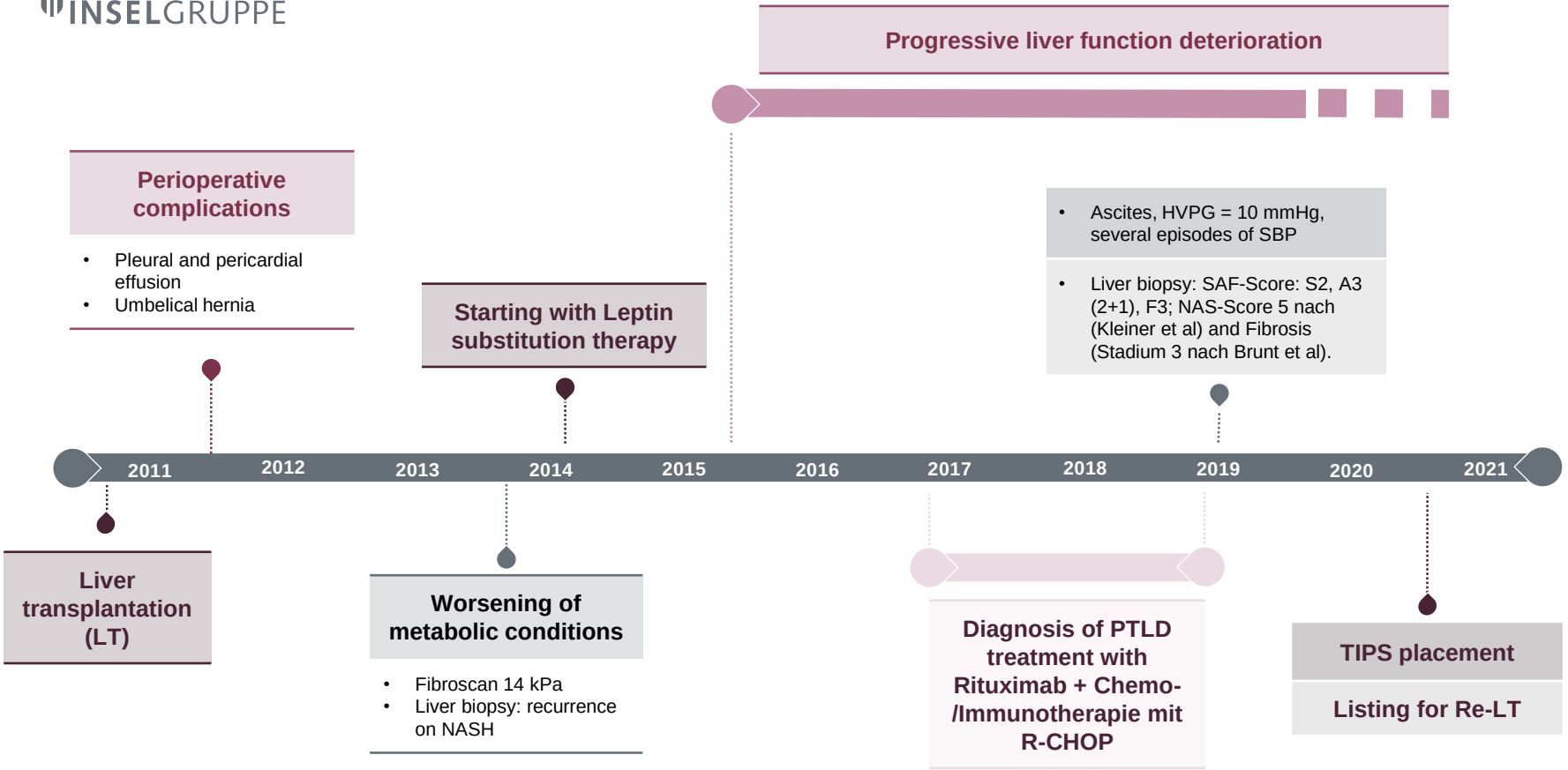
Progressive liver function deterioration
Perioperative complications
• Pleural and pericardial effusion
• Umbelical hernia
Starting with Leptin substitution therapy
• Ascites, HVPG = 10 mmHg, several episodes of SBP
• Liver biopsy: SAF-Score: S2, A3 (2+1), F3; NAS-Score 5 nach (Kleiner et al) and Fibrosis (Stadium 3 nach Brunt et al).
2011
2012
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2020
2021
Liver transplantation (LT)
Worsening of metabolic conditions
• Fibroscan 14 kPa
• Liver biopsy: recurrence on NASH
Diagnosis of PTLD treatment with Rituximab + Chemo-/Immunotherapie mit R-CHOP
TIPS placement
Listing for Re-LT

INSELGRUPPE

NASH/NAFLD

AND RARE MONOGENIC DISORDERS

WHAT IS CHALLENGING IN THE MANAGEMENT OF CHRONIC LIVER DISEASES IN 2020?

Dr. med. Guido Stirnimann, Hepatologie, Inselspital *(senior)*

Dr. med. Chiara Becchetti, Hepatologie, Inselsptial *(junior)*

Thank you for your attention