Benign liver tumours

Stefan Hofmeyr

2023

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THE PROBLEM

- As clinical skills give way to increased reliance on organ imaging, a new clinical problem is identified-the hepatic “incidentaloma.”

July 1990:14(4)

CROSS-SECTIONAL IMAGING

- Incidentalomas reflect its increasing use and widespread availability
- Abdominal pain common
- Defensive medicine
- During investigation of other conditions
- 10% of workload

DOI:10.1111/j.1477-2574.2012.00595.x

HPB

ORIGINAL ARTICLE

HPB 2013, 15, 379–383

Hepatic incidentaloma: the rule of tens

Jonathan B. Koea

10% of lesions referred for resection

10% of cystic lesions malignant

10% of solid lesions malignant

- **Observation: risk of observing a malignancy**
- **Intervention: morbidity of resection if misdiagnosed as malignant**

MDT

Detected lesion

- Cirrhotic or known/suspected liver disease
- Non-cirrhotic

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Benign lesions

Cystic

- Simple cysts - Type 1,2,3
- Hydatids
- Mucinous neoplasms (MCN,IPNB)

Solid

- Haemangioma
- FNH
- Adenomas

- **Adenomas**
- **Mucinous neoplasms**

→ **Malignant potential**

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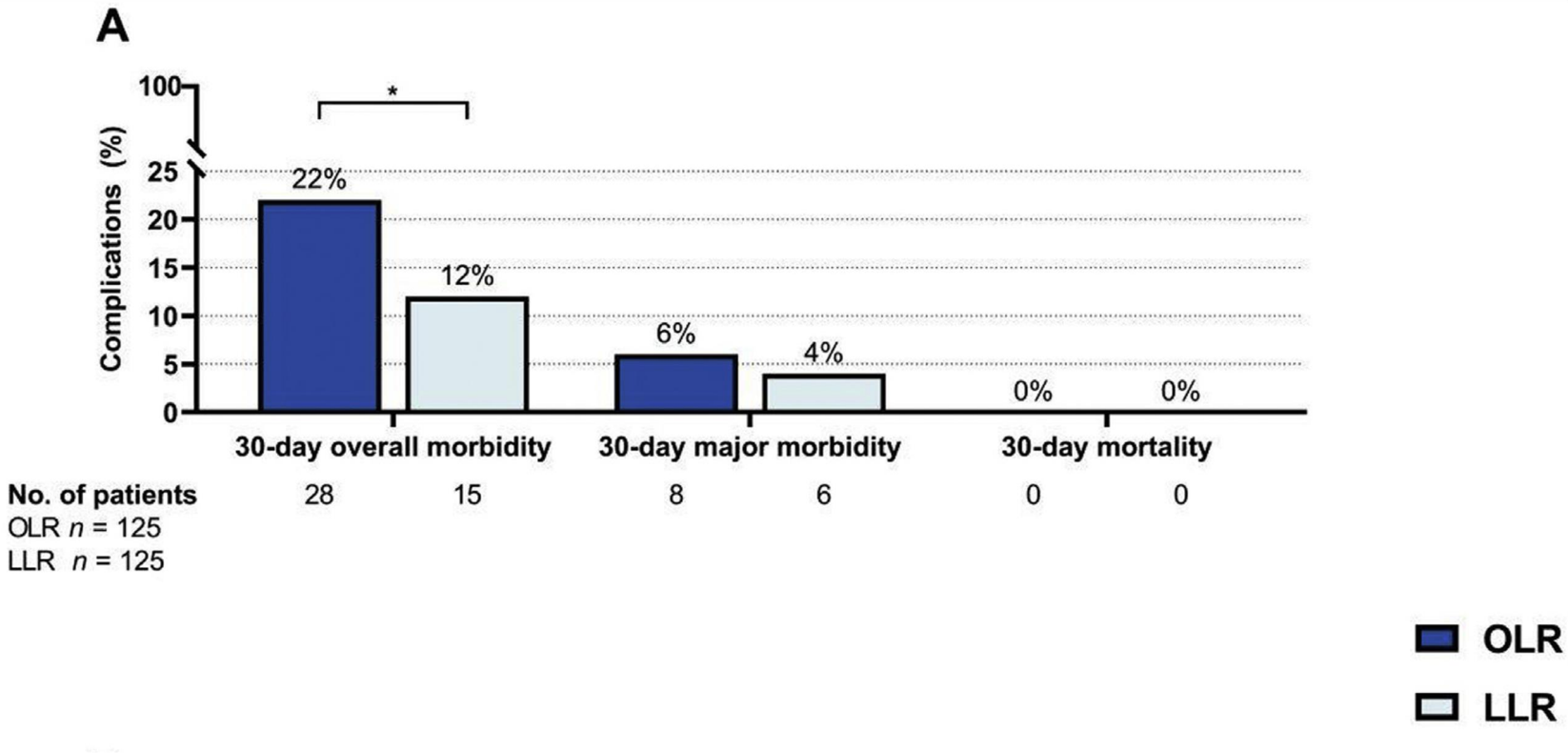
Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines on the management of benign liver tumours☆

European Association for the Study of the Liver (EASL)*

Resection of benign liver tumours



HPB 2021, 23, 1230–1243

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Open access Protocol

BMJ Open

Study protocol for a multicentre nationwide prospective cohort study to investigate the natural course and clinical outcome in benign liver tumours and cysts in the Netherlands: the BELIVER study

- 2021-2026
- BLT eligible for observation or intervention
- Primary outcome = PRO
- Excludes Polycystic, less common tumours

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BLT: observation vs treatment

- Thorough patient education
- Shared decision-making
- Often decision at second or deferred re-consultation

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Treatment?

- Resection
- Ablation
- Embolisation

Haemangiomas

- Most common lesion, (4-20%)
- Other tumours often mistaken for a haemangioma
- Be the biopsy police

Haemangiomas

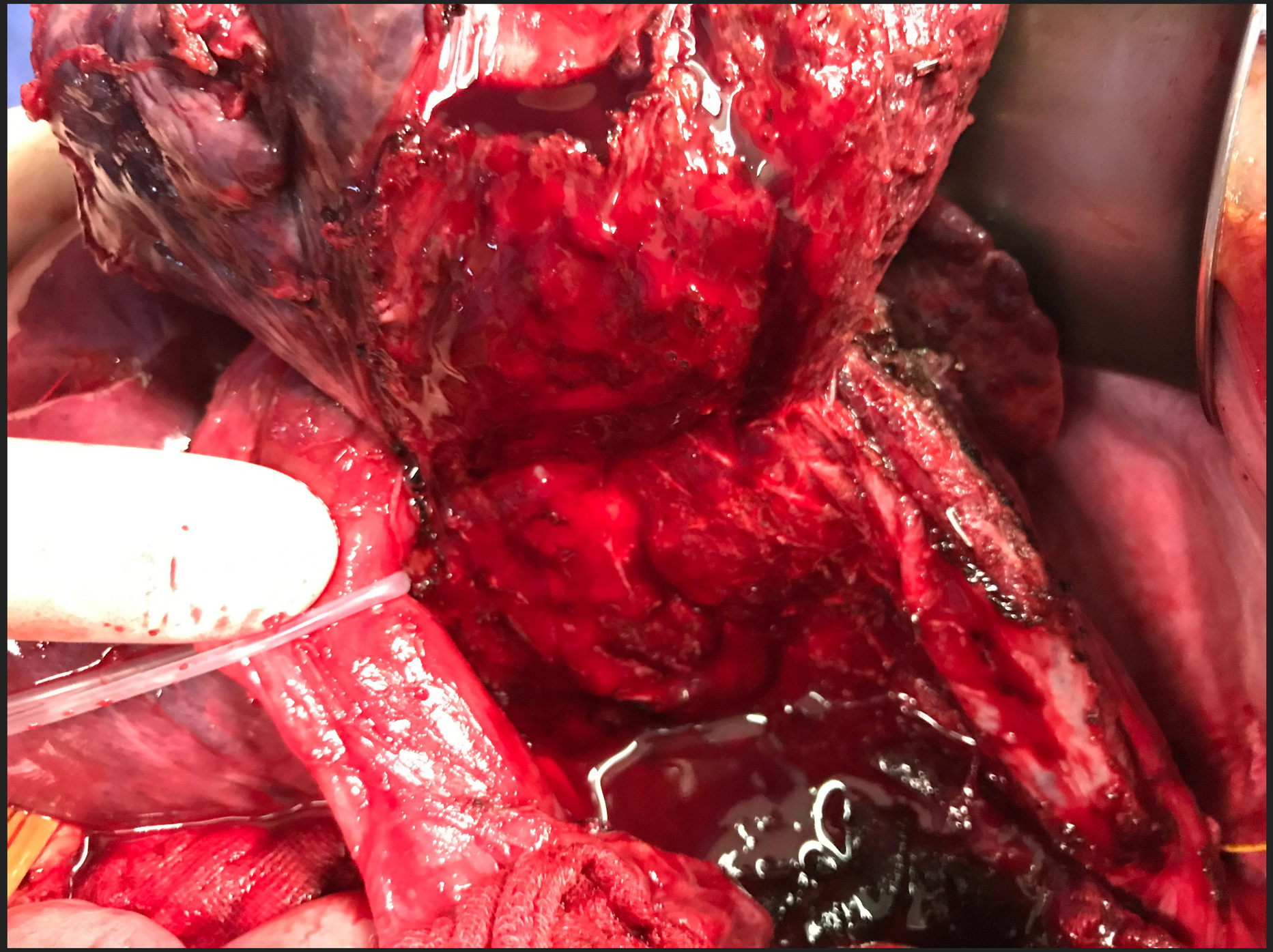
- Small <5cm, large 5-10cm, giant>10cm
- Typical: small, hyperechoic on ultrasound with posterior acoustic enhancement, discrete margin, peripheral and nodular with slow contrast filling to centre
- Atypical - fast/flash-filling (diagnostic danger), giant forms, sclerosing
- Rarely symptomatic - size, Kasabach-Merritt Syndrome

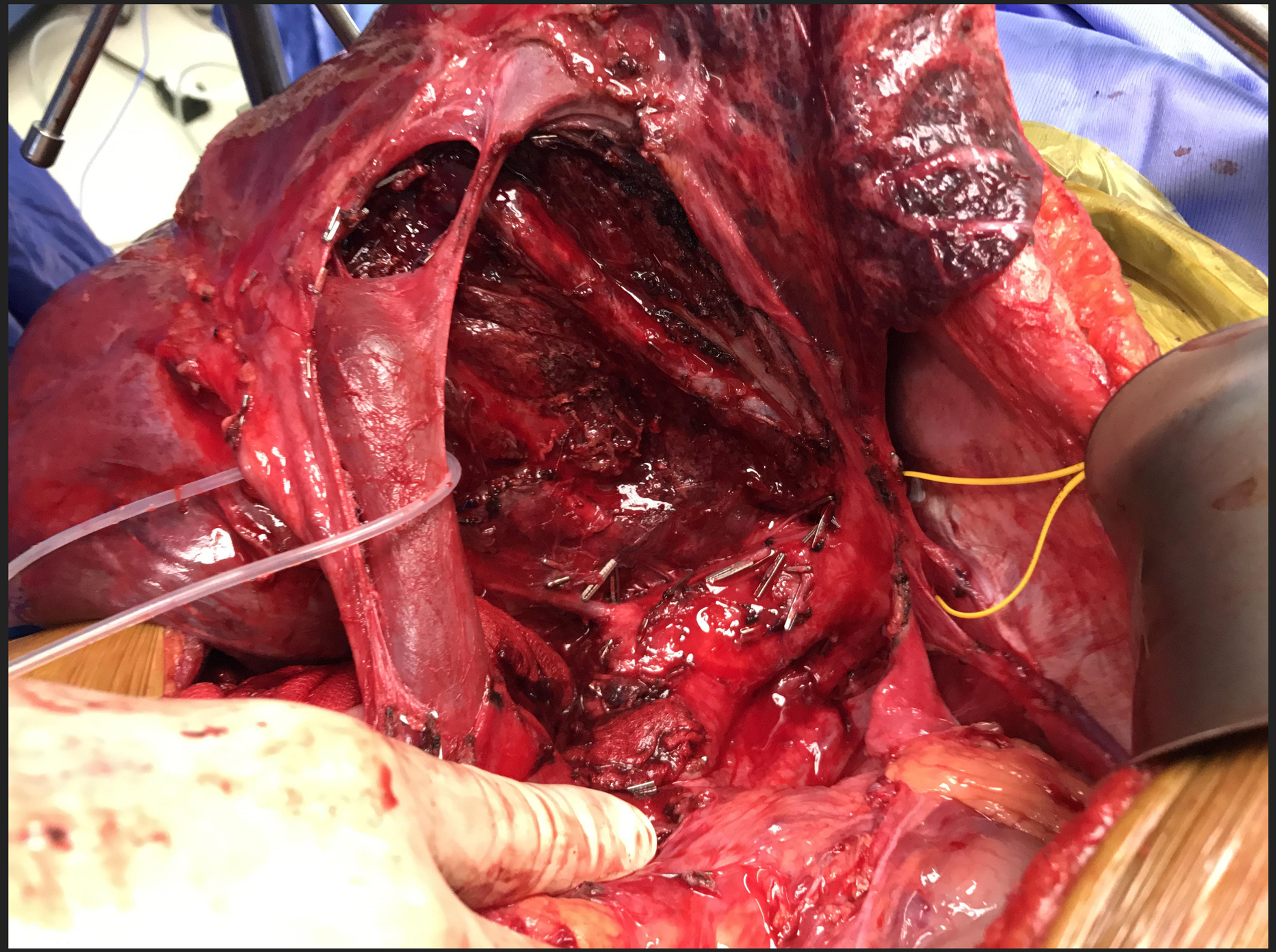
Haemangioma vs HCC: Diagnostic confidence

- Ultrasound < 3cm
- Liver disease, larger, atypical = MRI (CT)

There is a mass lesion situated within the lateral segment of the left lobe of the liver measuring 92 mm TV x 95 mm CC x 59 mm AP. The mass has nodular a

The mass in the lateral segment of the left hepatic lobe is favoured to represent focal nodular hyperplasia or a giant cavernous haemangioma.





Focal nodular hyperplasia

- 0,4-3%
- Response to vascular occlusion
- Rare in men

Box 1
Major criteria on MRI for the diagnosis of focal nodular hyperplasia

- Native contrast close to that of the liver: Not different from the liver before contrast injection, that is, iso- or hypointense on T1-weighted images and iso- or slightly hyperintense on T2-weighted images
- Homogeneity apart from the central scar
- Central stellate area: Presence of a central hypointense area on T1-weighted images and strongly hyperintense on T2-weighted images
- Dynamic enhancement profile: Intense and transient enhancement in the arterial phase without washout
- No capsule
- Lobulated aspect
- Absence of underlying chronic liver disease or clinical history of cancer

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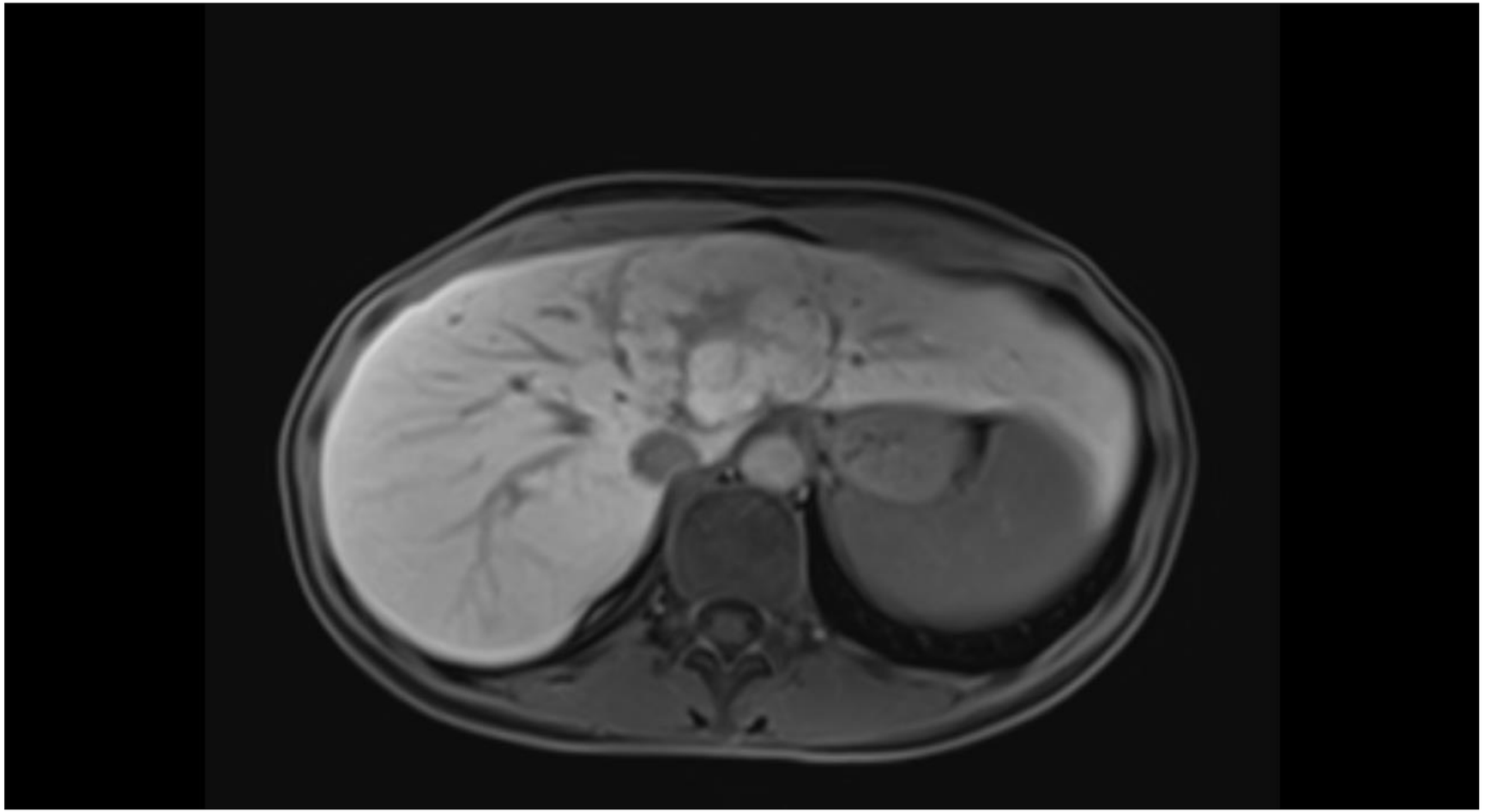
FNH

- Confident diagnosis
- No follow-up required, risk bleeding very low
- No contra-indication to contraceptive use or pregnancy
- Large lesions may cause symptoms



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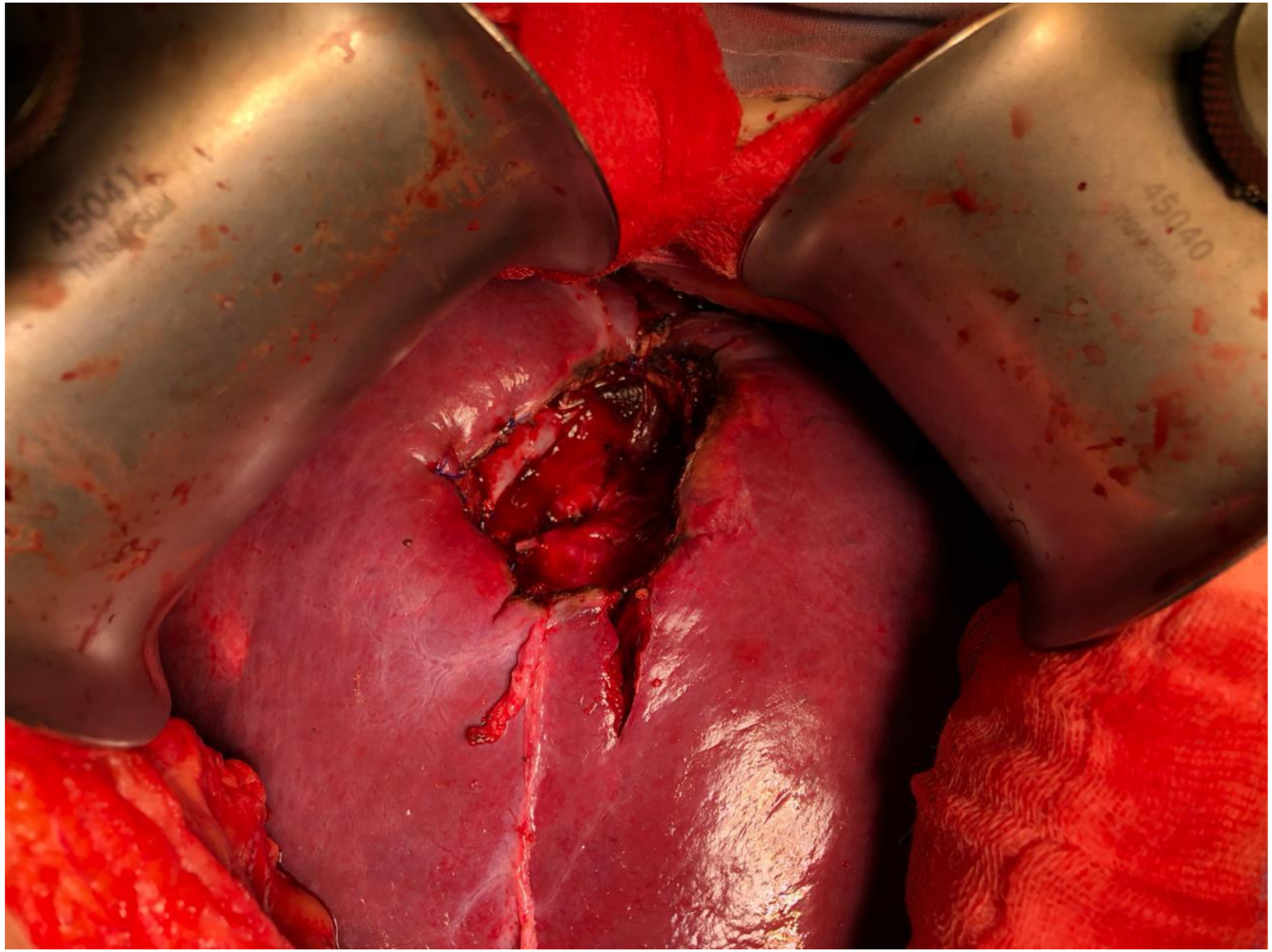

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Embolisation

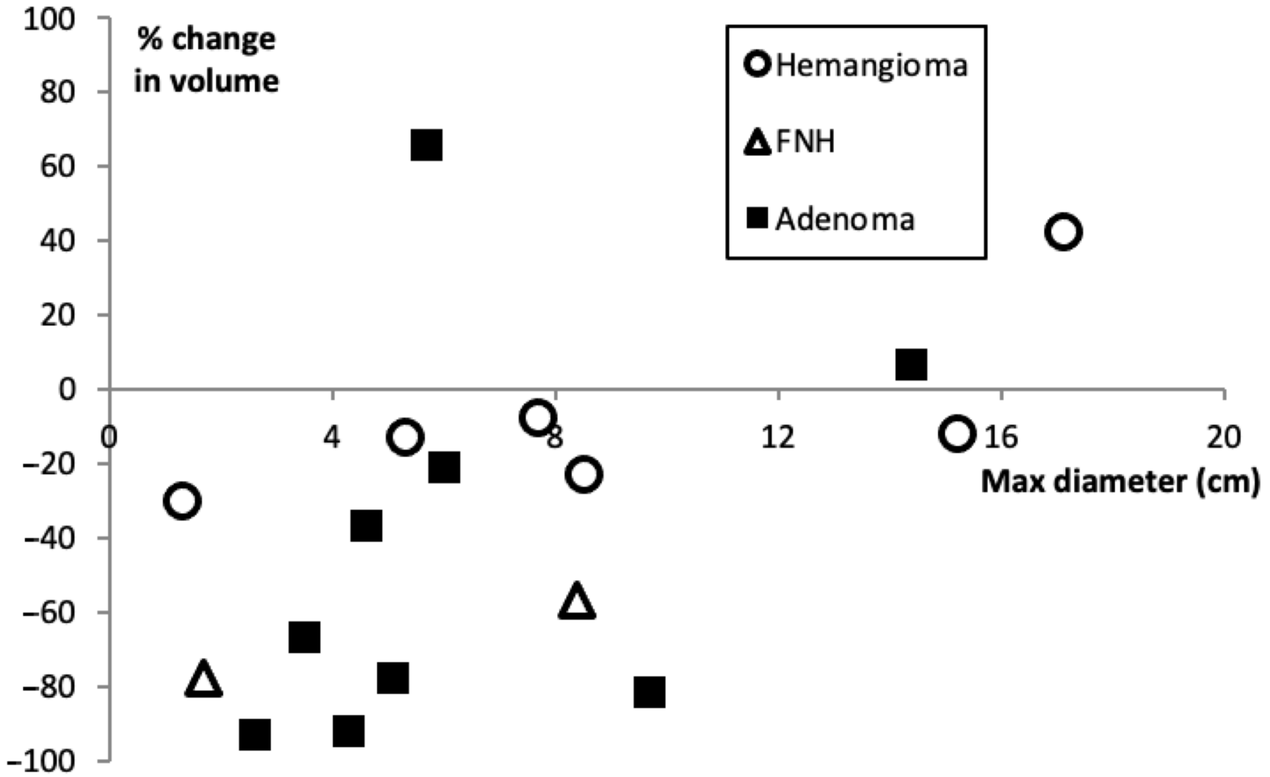

Figure 1. Percent change in lesion volume versus maximum initial diameter for bland transarterial embolization of hepatic hemangiomas, FNH, and adenomas. A negative percent change indicates that the lesion decreased in volume.

Hepatic Adenomas

- Prevalence 0.004% ; least common benign hepatic tumour

- Female:male = 10:1
- Age 35-40yrs

- Hormonal association
  - Oestrogen – promote HNF1a mutations
  - 30-40-fold increased incidence with use of COCs
  - Anabolic steroid use
  - Incidence on low-dose COC unknown

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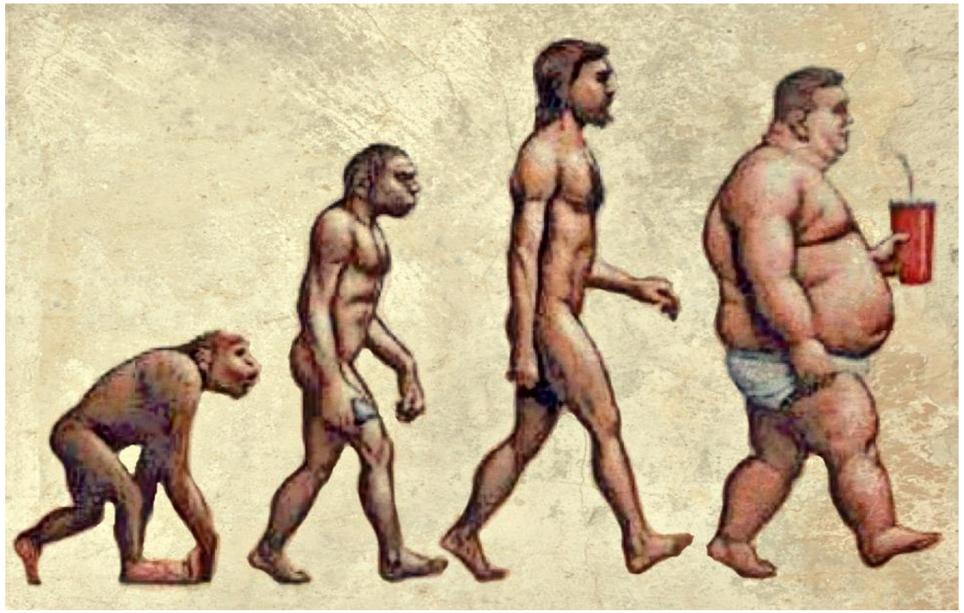
Hepatic Adenomas

- Increasing **obesity** and metabolic syndrome
- Iron overload (Haemochromatosis, Thalassaemia)
- Glycogen storage disorders
- MODY - familial



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Before

- Homogenous entity
- Monoclonal proliferation of well differentiated hepatocytes
- Absence of a portal triad

- Managed with reference to

A. Size (5cm)

B. Symptoms (10-20% have bled at Dx)

C. Family planning

ca. 2006

- 4 Subtypes emerged
- Different molecular and immunohistochemical features
- Phenotype differs as well - risk factors, imaging
- contrasted MRI best
- Rekindled liver biopsy

Bioulac-Sage P, Rebouissou S, Thomas C, et al. Hepatocellular adenoma subtype classification using molecular markers a immunohistochemistry. Hepatology 2007;46:740–748.

Today

- 6 Subtypes
  - Describe
  - Features
  - Risks
  - How this classification affects decision and management?

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Subtypes	HNF1α-Inactivated HCA	Inflammatory HCA	β-Catenin-activated HCA		Sonic Hedgehog HCA	Unclassified
Frequency	35%–40%	35%–45%	15%–20%		5%	<5%
Risk factors	HNF1α germline	Obesity Alcohol use Glycogen storage disease	Androgen Liver vascular disease glycogen storage disease		Obesity	
Specific staining on IHC	LFABP-	CRP++ SAA++	GS +++ β-catenin +	GS+	PTGDS + ASS1+	
Main complications		Hemorrhage	High risk of malignant transformation		Hemorrhage	
Specific MRI features	Diffuse and homogeneous drop of signal on opposed phase	Marked hyperintensity on T2 and persistent enhancement on delayed phase	No specific imaging feature associated with an uptake on the hepatobiliary phase	No specific imaging feature	No specific imaging feature	

Radiol Clin N Am 60 (2022) 755–773

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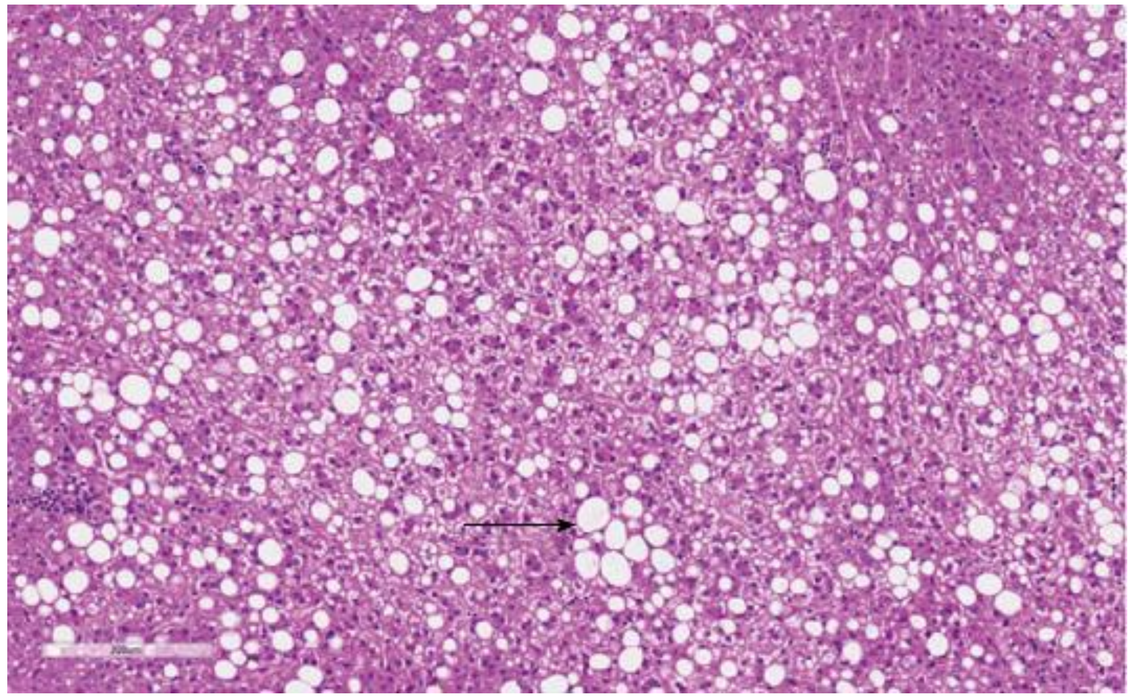
H-HCA (HNF1α inactivated)

- 35-40%
- HNF1α regulates gluconeogenesis and fatty acid metabolism
- Lipid accumulation
- Exclusive of other mutations



WJG July 2013

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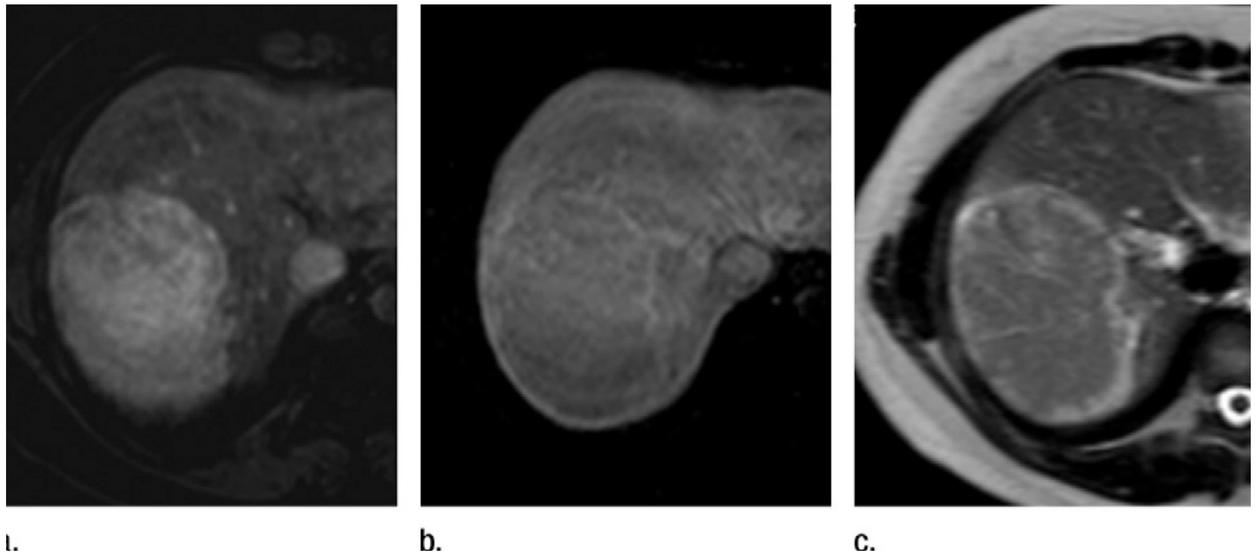
I-HCA (Inflammatory)

Radiology: Volume 261: Number 1—October 2011 ▪ *radiology.rsna.org*

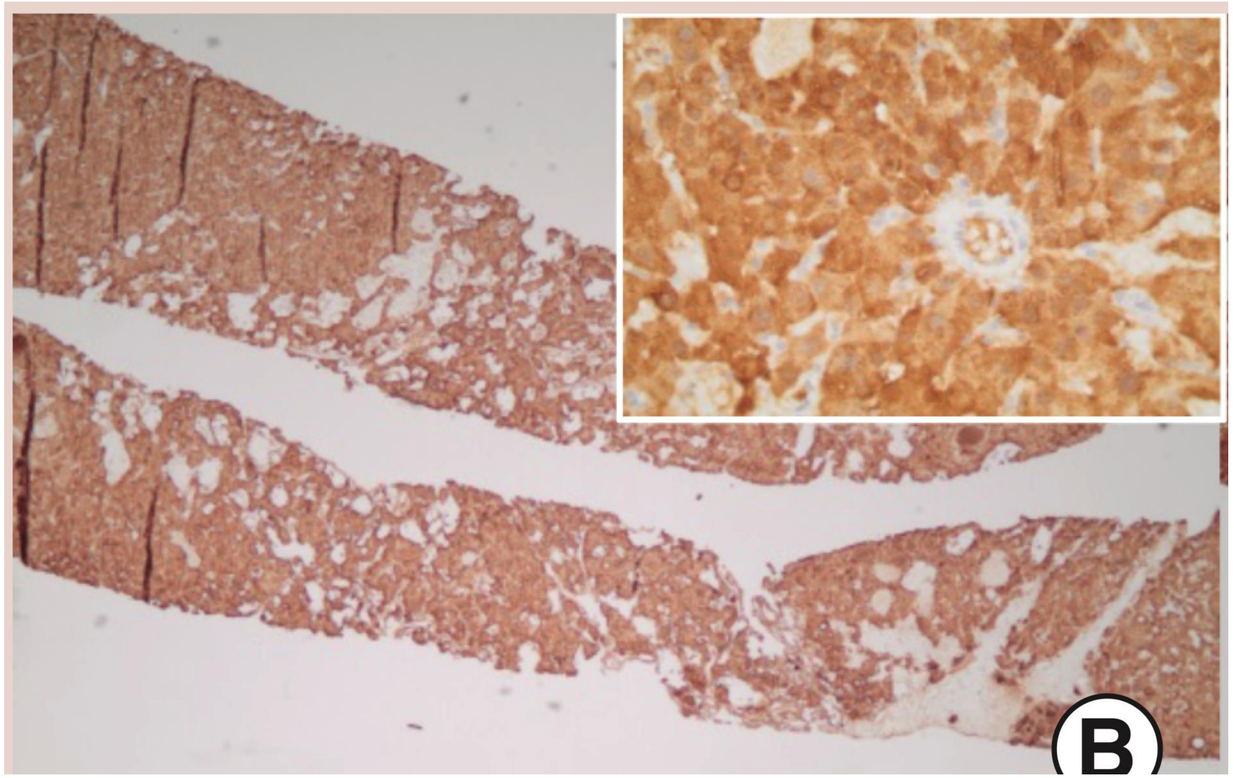
- 40%
- Uncontrolled activation of inflammatory pathway (IL6/JAK/STAT)
- inflammatory infiltrates/sinusoidal dilation(telangiectasia)
- Strong arterial and PV enhancement
- Atoll sign



a. b. c.

B_{exon3} HCS (β-catenin mutated)

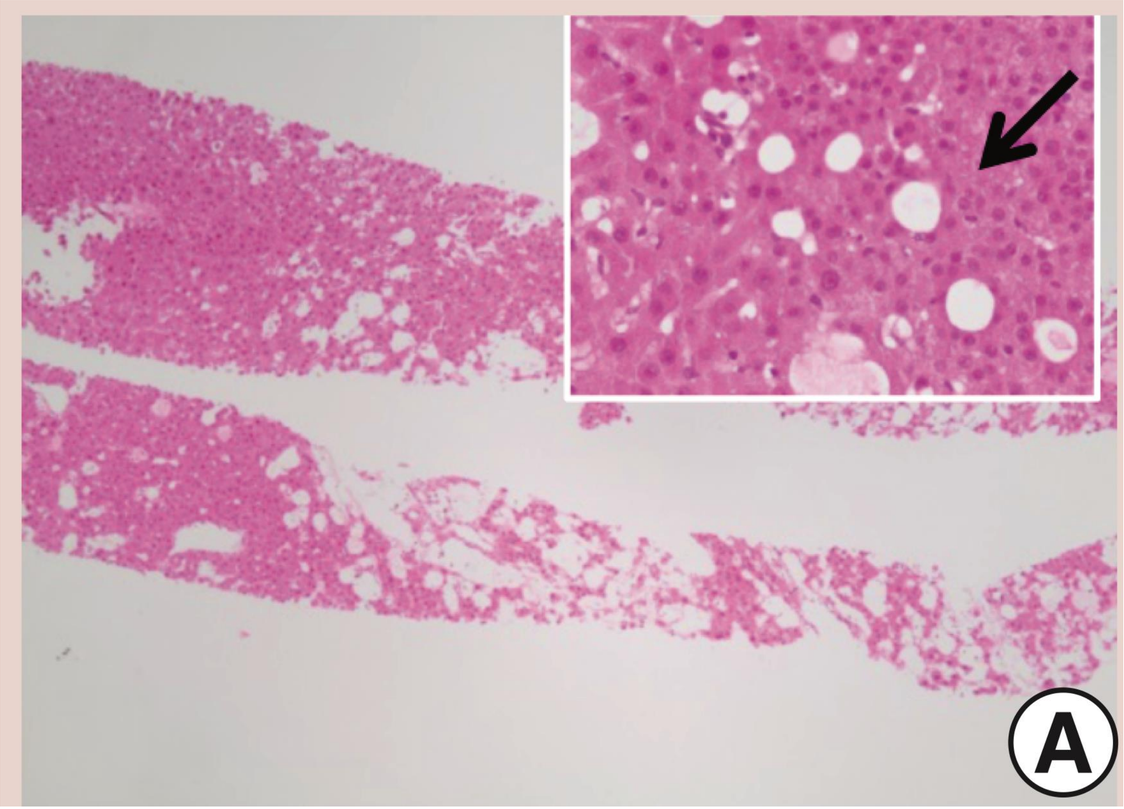
- 10%
- Male predominance
- Pathway involved in embryogenesis and hepatic regeneration
- 50% have an inflammatory pathway activation
- highest risk of HCC



Hepat. Oncol. (2018) 5(1)

$B_{exon7/8}$ HCS (β-catenin mutated)

- 10%
- Milder activation
- Exclusive of exon3
- 50% inflammatory as well
- Less risk of malignant transformation



Hepat. Oncol. (2018) 5(1)

sh HCA (Sonic hedgehog)

- 4%
- Fusion of 2 promoter genes
- Not unique to adenoma
- Obesity
- Tendency to bleeding
- No current IHC markers
- No characteristic imaging

U HCA (Unclassified)

- Less than 7%

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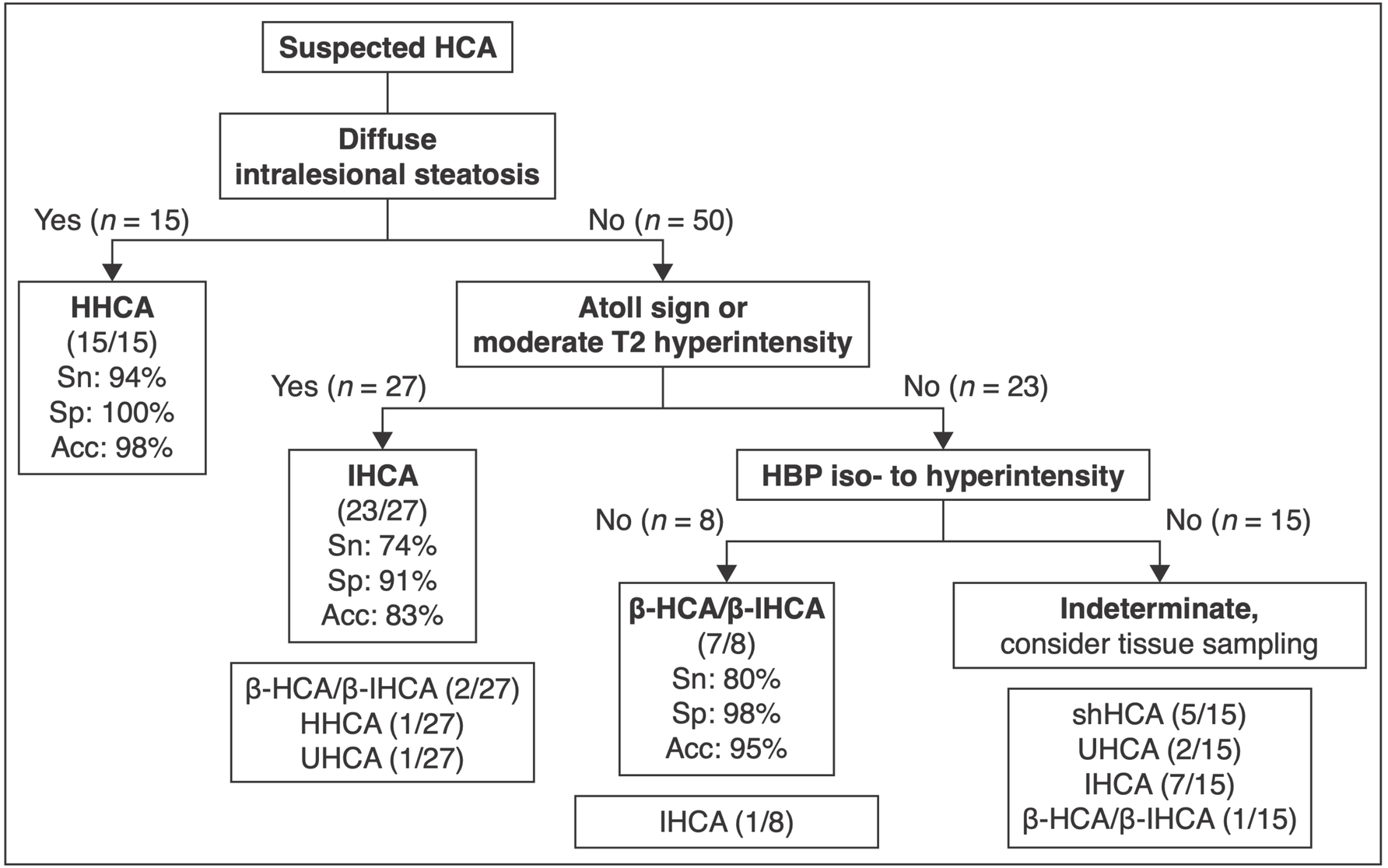
Pathological assessment

- Still some cases: Adenoma vs well diff HCC vs FNH
- Four key IHC markers (SAA, FABP1, glutamine synthase and β-catenin)
- IHC is unable to detect β-catenin-mutated HCA on exons 7–8 and sonic hedgehog HCA
- 70% of patients with multiple adenomas: same molecular subclass.
- Different subclasses: exon 3 mutation was primarily observed in the largest nodule

Imaging

- Contrasted MRI
- Differentiates HHCA and IHCA
- IHCA: unable to exclude BHCA subgroups with high risk

	Imaging (MRI)
HHCA	T1 chemical shift sequence: signal dropout on opposed Phase I
IHCA	Hyperintense signal on T2, arterial enhancement persisting in delayed phases



HCA Subtype Diagnosis on Gadoxetate Disodium–Enhanced MRI

AJR:220, April 2023

European Radiology (2019) 29:2436–2447
https://doi.org/10.1007/s00330-018-5784-5

HEPATOBILIARY-PANCREAS

New MRI features improve subtype classification of hepatocellular adenoma

Difficult to type when >50% of the lesion consists of haemorhagic areas

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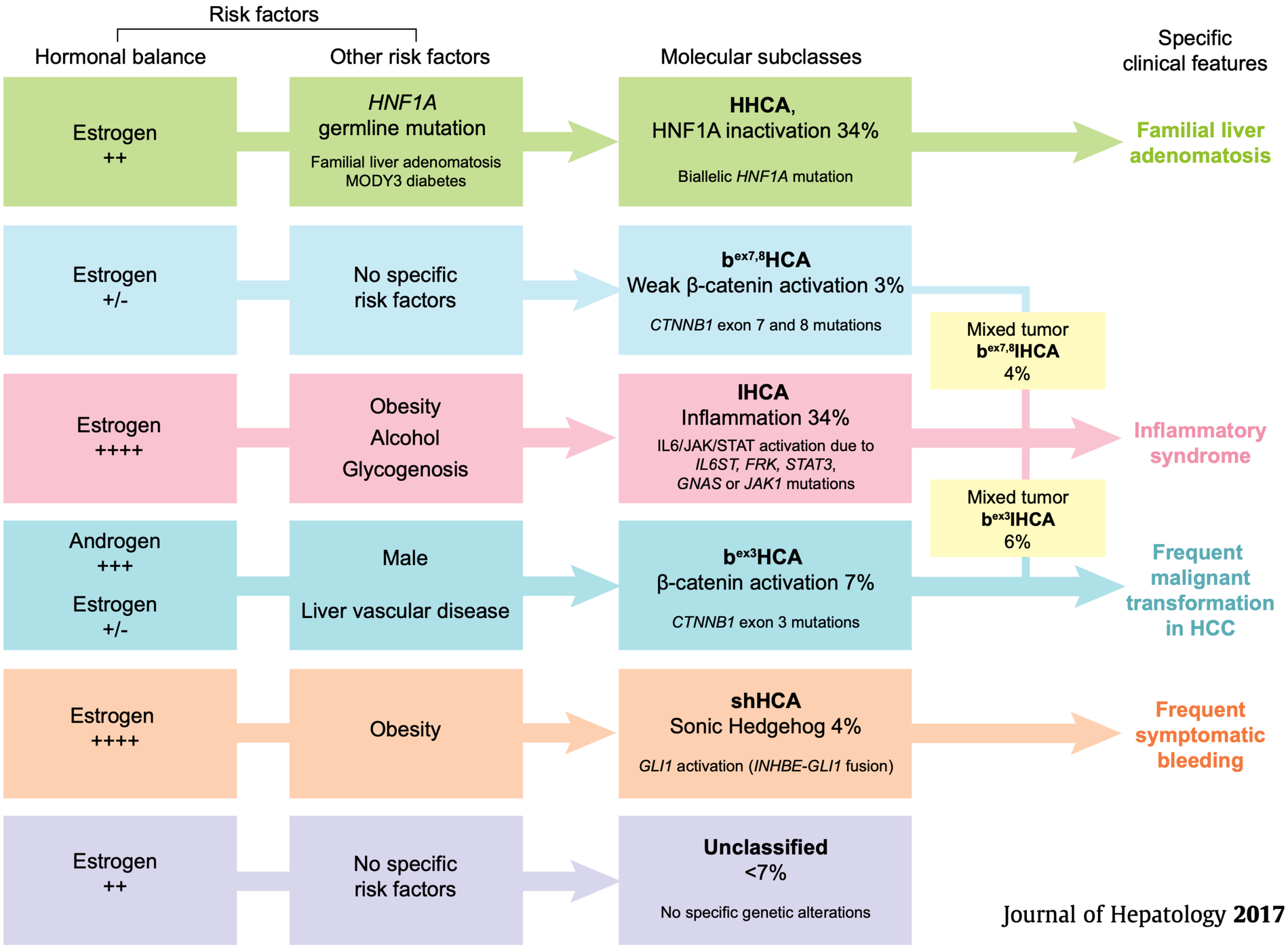

Journal of Hepatology **2017** vol. 67 | 1074–1083

Presentation

- ASx/Imaging
- Pain, mass
- 50% normal liver enzymes
- Normal tumour markers
- Paraneoplastic syndrome with IHCA: inflammation, anaemia

Risk factors and screening

- Oral contraception and androgen intake must be discontinued;
- Weight reduction is a key point in IHCA and sonic hedgehog HCA. Reduction in size has been described after weight loss following bariatric surgery;
- Screening for the *HNF1A* germline mutation and familial adenomatosis in *HNF1A*-inactivated adenomatosis is recommended;
- Screening of HCA in glycogenosis (50% of patients with glycogenesis type IA have adenomatosis at adulthood, sometimes associated with malignant transformation) should be performed.

Management

- Sex
- Size
- MRI
- Location - exophytic protrusion
- Subtype

- Strong systematic evidence lacking

- Biopsy
- Molecular capability lacking

?

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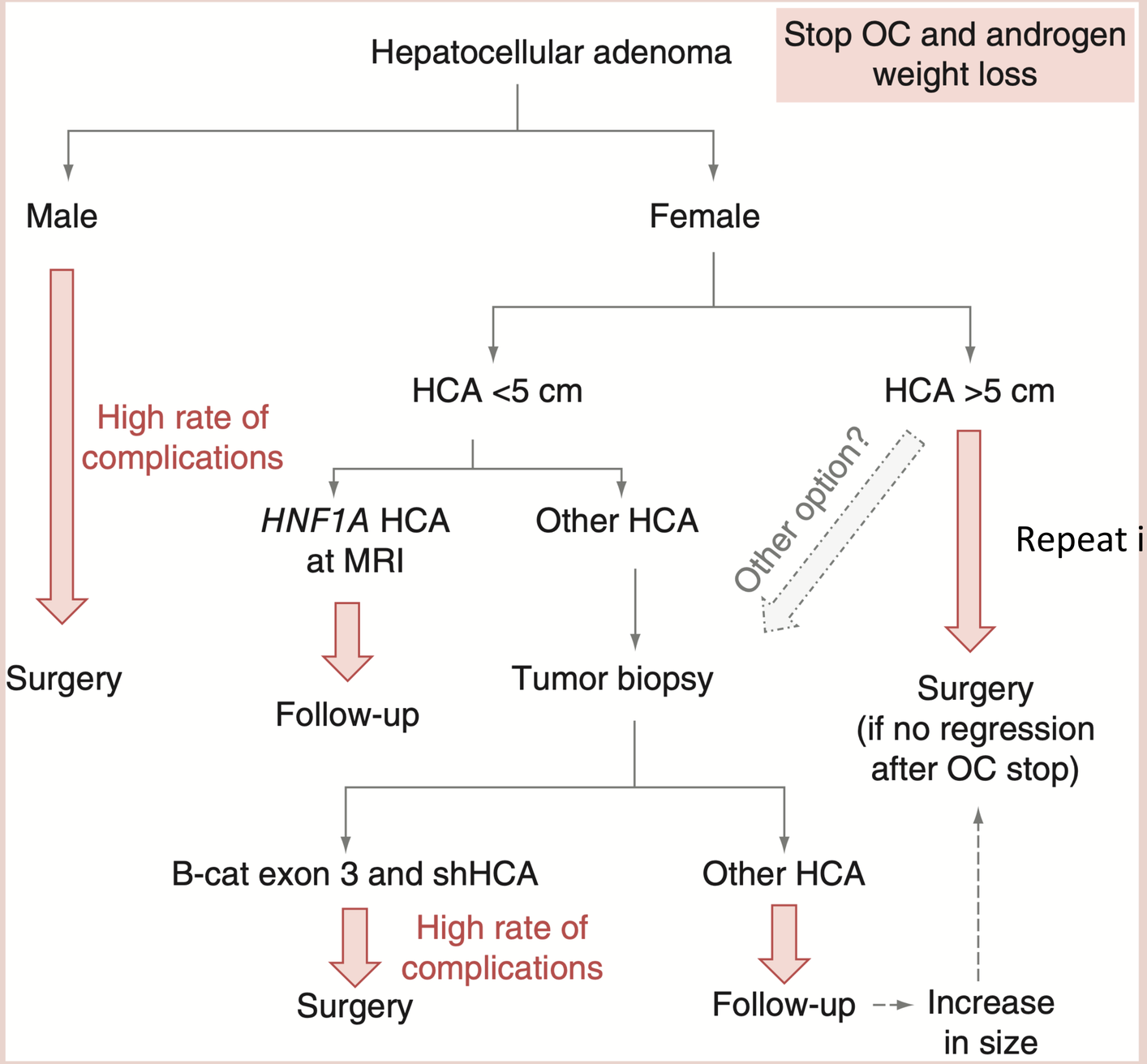
Expected complications

- *Risks exist irrespective of size*
- Bleeding
  - Inflammatory type HCA
  - Tumour > 5cm
  - Grade 1 lesion, 2 liver, 3 peritoneum

- Malignant transformation
  - Risk 4-8%
  - Male
  - B-catenin mutation
  - Size >5cm
  - 5% specimens have malignancy



Hepat. Oncol. (2018) 5(1)

Present with significant bleed

Submit a Manuscript: http://www.f6publishing.com

World J Gastroenterol 2017 July 7; 23(25): 4579-4586

DOI: 10.3748/wjg.v23.i25.4579

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

Management and outcome of hepatocellular adenoma with massive bleeding at presentation

Anne J Klompenhouwer, Robert A de Man, Maarten GJ Thomeer, Jan NM Ijzermans

https://doi.org/10.1016/j.hpb.2018.06.1796 HPB

ORIGINAL ARTICLE

Hemorrhage of hepatocellular adenoma: a complication that can be treated by conservative management without surgery

Safi Dokmak[1], Béatrice Aussilhou[1], Fanjandrainy Rasoaherinomenjanahary[1], Maxime Ronot[2], Rafik Dahdouh[1], Fadhel S. Ftériche[1], François Cauchy[1], Valérie Paradis[3], Jacques Belghiti[1] & Olivier Soubrane[1]

- Size 7-8 cm
- Conservative if stable
- Embolise +/- pack if unstable
- High morbidity with resection
- 25% may totally regress
- Most become smaller
- Individualise management

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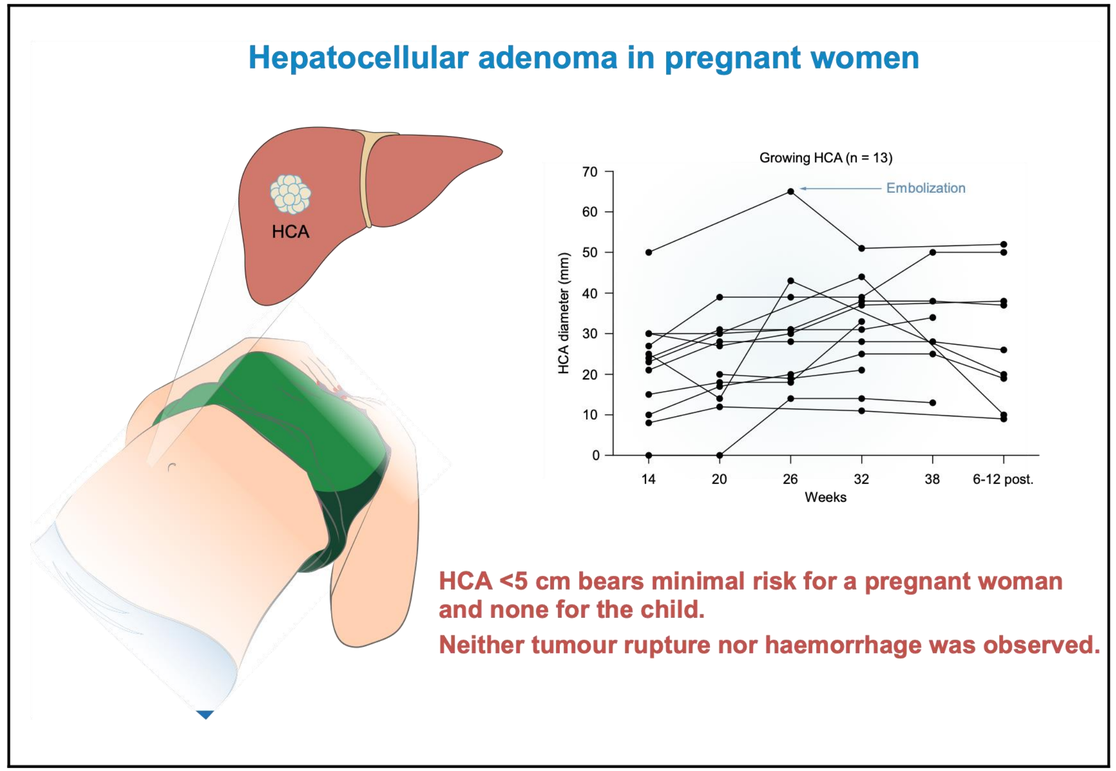
Wish to become pregnant

- 40% historic mortality risk with rupture
- Minimal evidence to recommend avoidance - major impact
- Adenoma not a contra-indication
- Factors: insight, distance from hospital, accept risk of intervention if growth
- Treat: >5cm, HCA complication during previous pregnancy

Growth of hepatocellular adenoma during pregnancy: A prospective study

Journal of Hepatology **2020** vol. 72 | 119–124



- **13 of 51 pregnancies = growth**
- **Median = 14mm**
- **One pt reached 70mm, success with embolisation**

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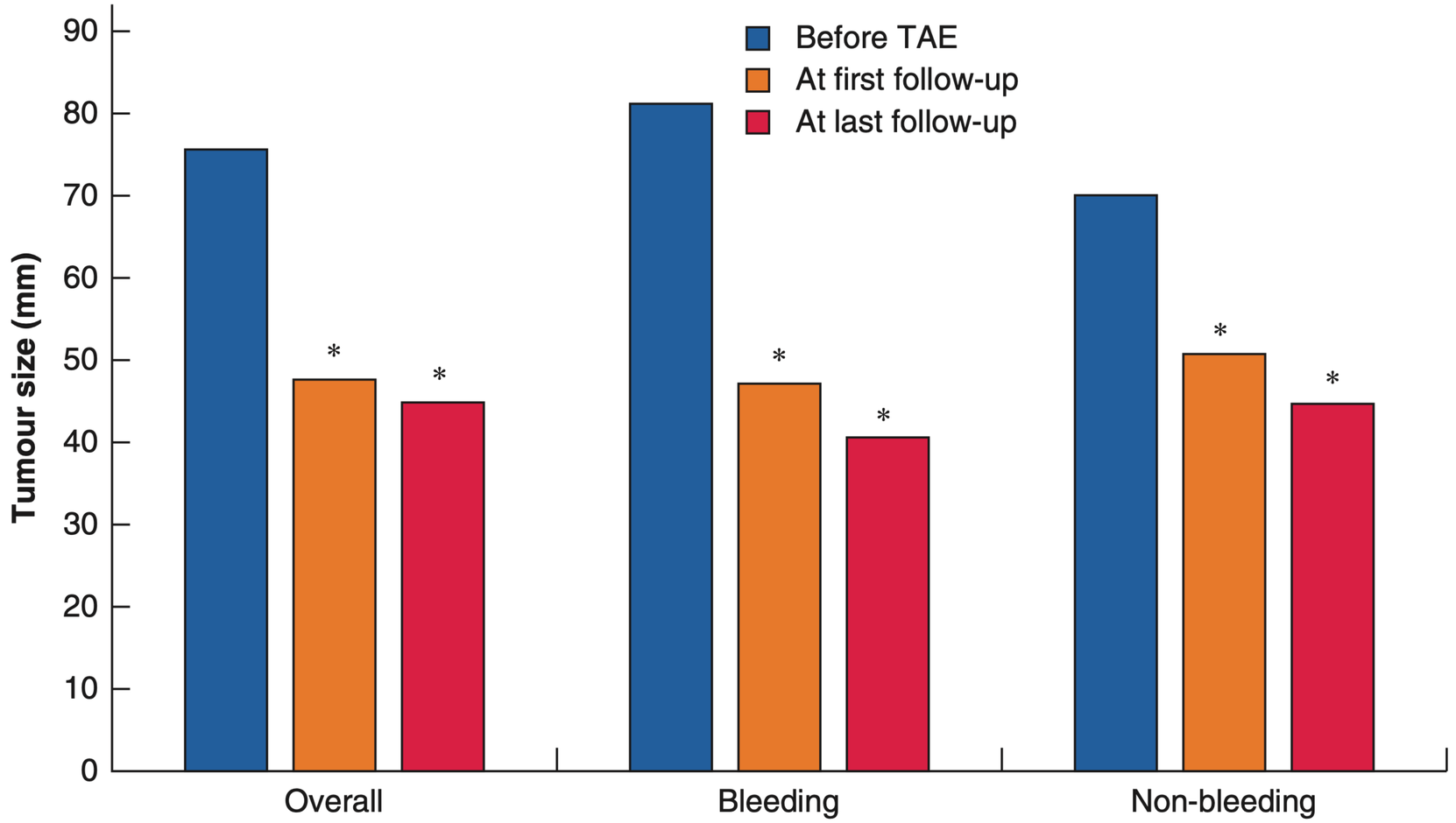
Diagnosed in Pregnancy

- Close U/S follow-up (6/52)
- Size, location
- Type less important
- Vaginal delivery: Not exophytic, less than 5cm
- Growing: embolisation considered
- Growing: prior to 24/40 an option if anteriorly situated and not major

TA Embolisation

Fig. 1 Median tumour size before and after transarterial embolization



TA Embolisation

- 10% complication rate
- One third median reduction in size

- Acceptable alternative for selected patients

Thermal ablation

- Effective ablation zones of 4.5-5cm
- Biopsy before recommended
- Effective
- Natural history of ablated lesions? Short f/up

- Q: How does biology change in decreased size?

- Am I sure this a ….?
- What is the risk of observation vs intervention
- Solid understanding of each entity to inform practice, as direct comparison evidence lacking

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