

COLANGIOCARCINOMA

Numeri, Fattori di Rischio, Classificazione e Diagnosi

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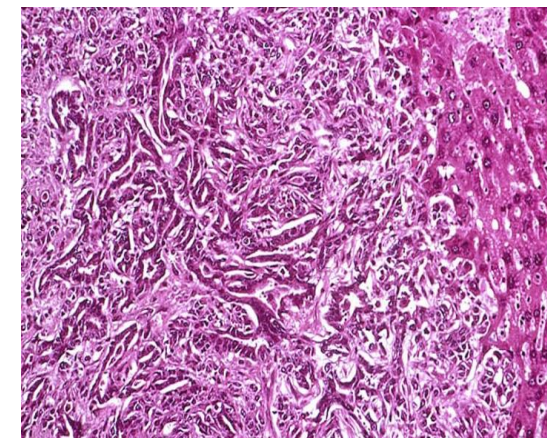
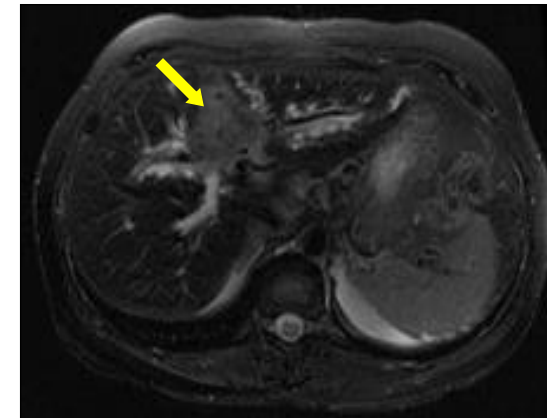
Disclosures: none

Patient Journey

Approccio personalizzato al paziente e esperienze a confronto:
Epatocarcinoma e Colangiocarcinoma

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- Primary liver cancer with features of *cholangiocyte* differentiation
- 3% of GI cancers
- 15-20% of primary liver cancers
- Increasing **incidence** and **mortality** rates in Western countries over the **past 3 decades**
- 3,500 new cases/year in US
- **Late diagnosis** – disease widespread
- Limited therapeutic options
- **Poor prognosis** – 10% survival @ 5yrs

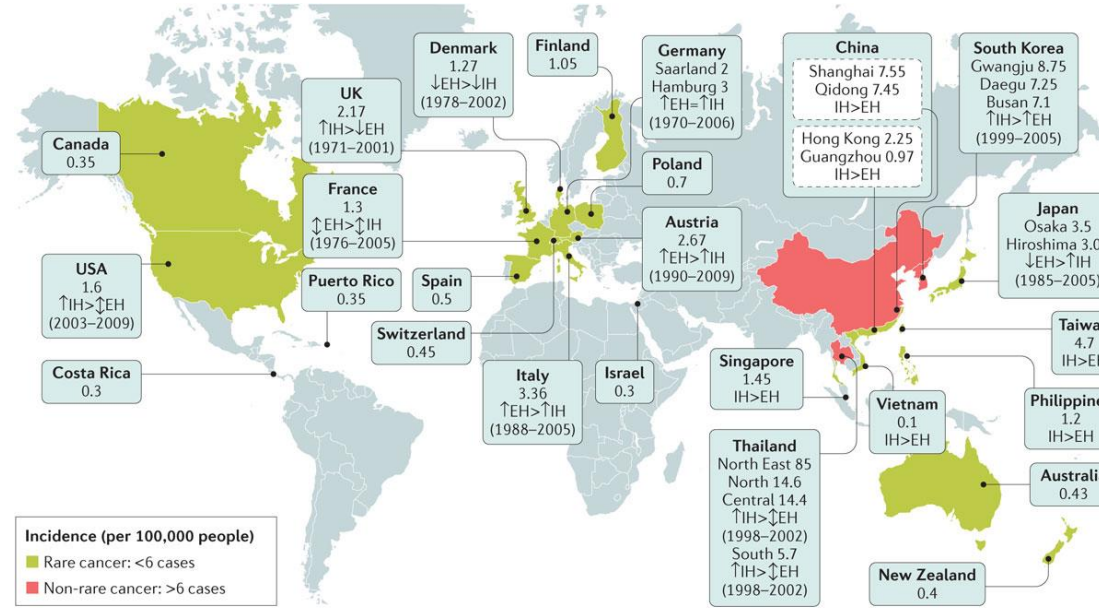


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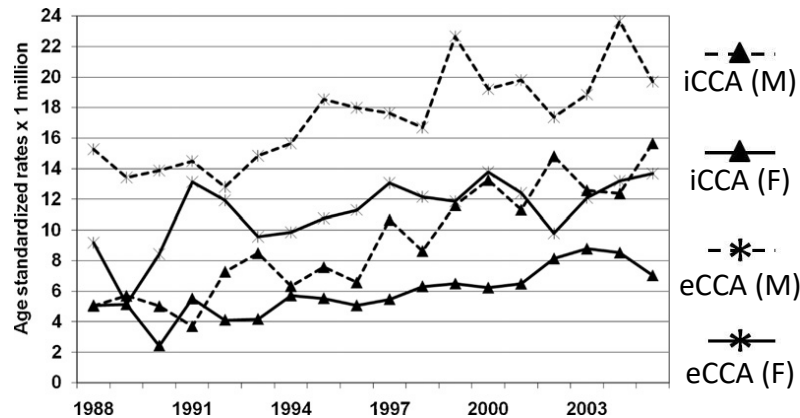
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CCA: a “Rare” Cancer of Increasing Incidence



Banales JM, Nat Rev Gastroenterol Hepatol 2016

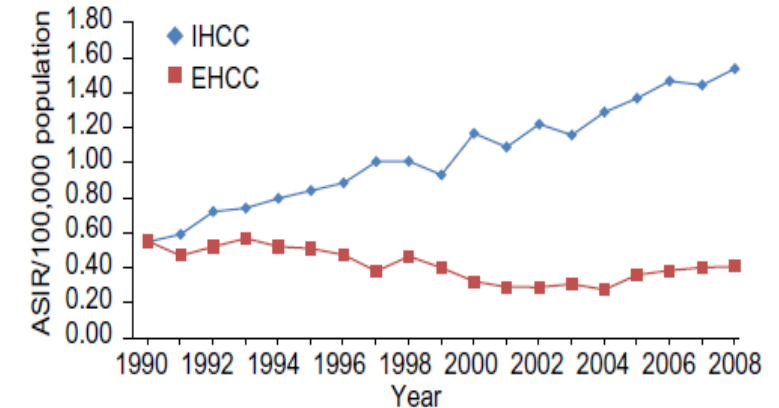
Italy



Alvaro D, Dig Liv Dis 2010

Nature Reviews | Gastroenterology & Hepatology

England + Wales

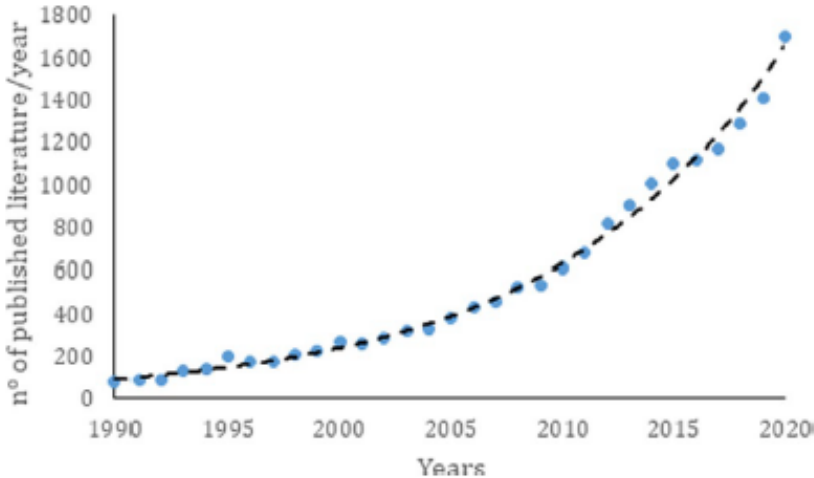


Khan SA, J Hepatol 2012

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Cancer	Incidence (x 100,000)	Articles	2020-23
Breast	30-100	30,326	+ 47.9%
Lung	30-50	26,404	+ 1.8%
CRC	14-40	18,291	+ 5.6%
HCC	4-20	10,701	+ 5.7%
PDAC	8-15	9,858	+ 6.5%
CCA	0.5-10	1,959	+ 15.2%

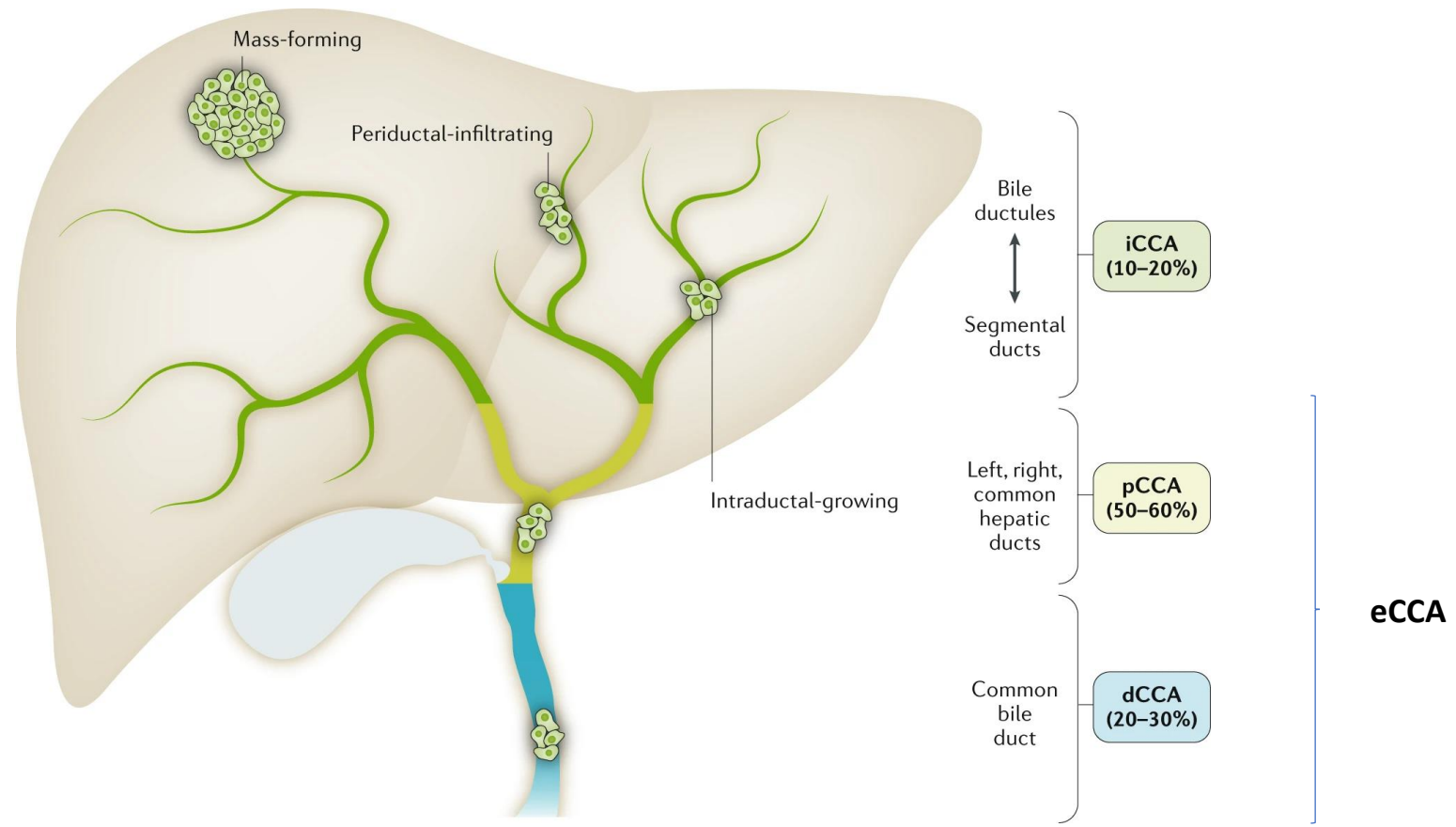
Cadamuro M, LCI 2021

Globocan and PubMed database (updated in 2020 and 2023, respectively)

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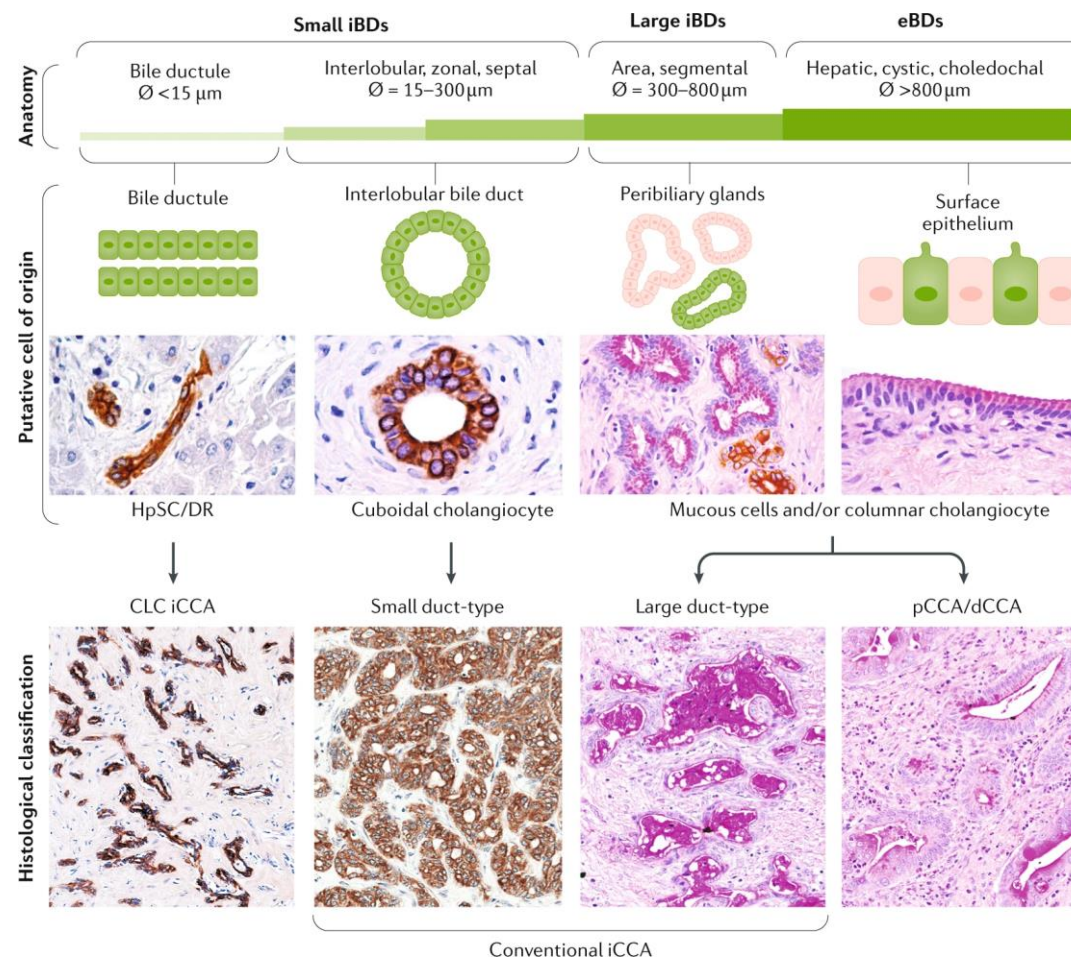
Banales JM ... Gores GJ, Nat Rev Gastroenterol Hepatol 2020

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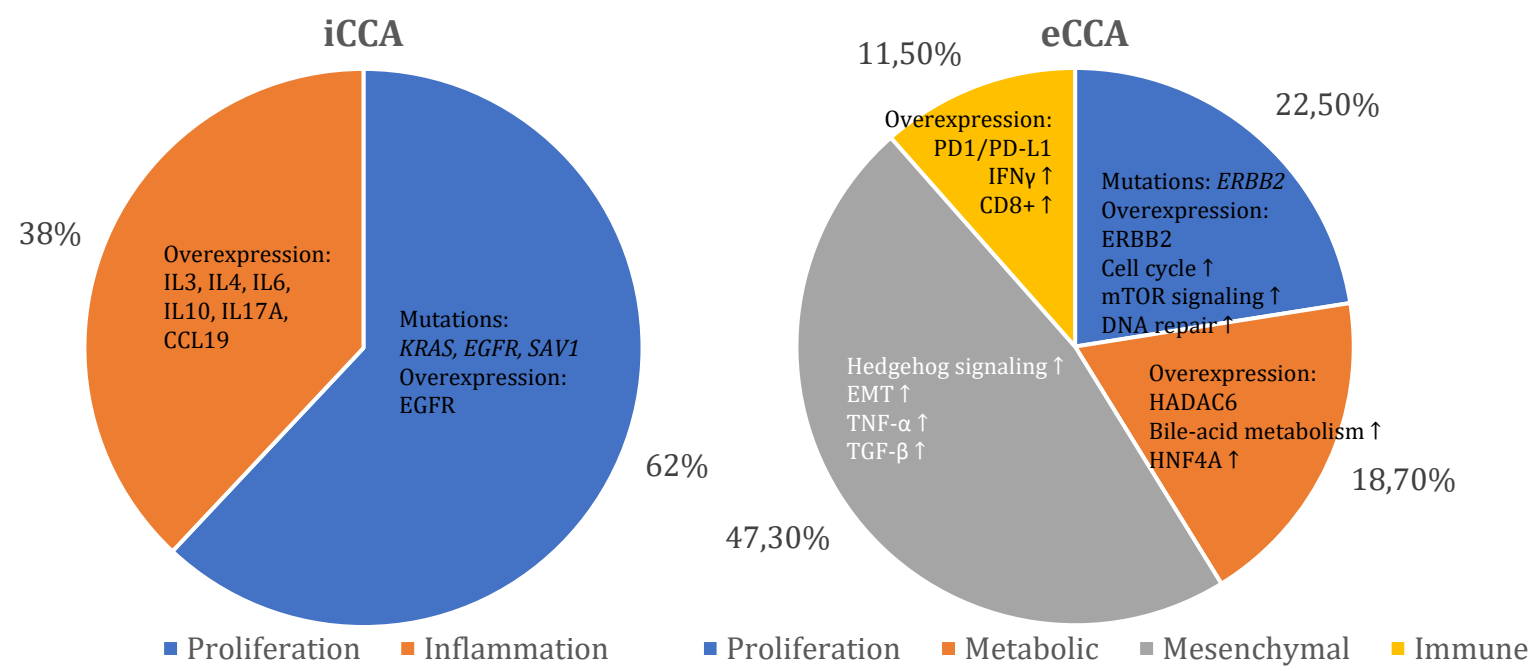


Banales JM ... Gores GJ, Nat Rev Gastroenterol Hepatol 2020

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Cadamuro M, LCI 2021

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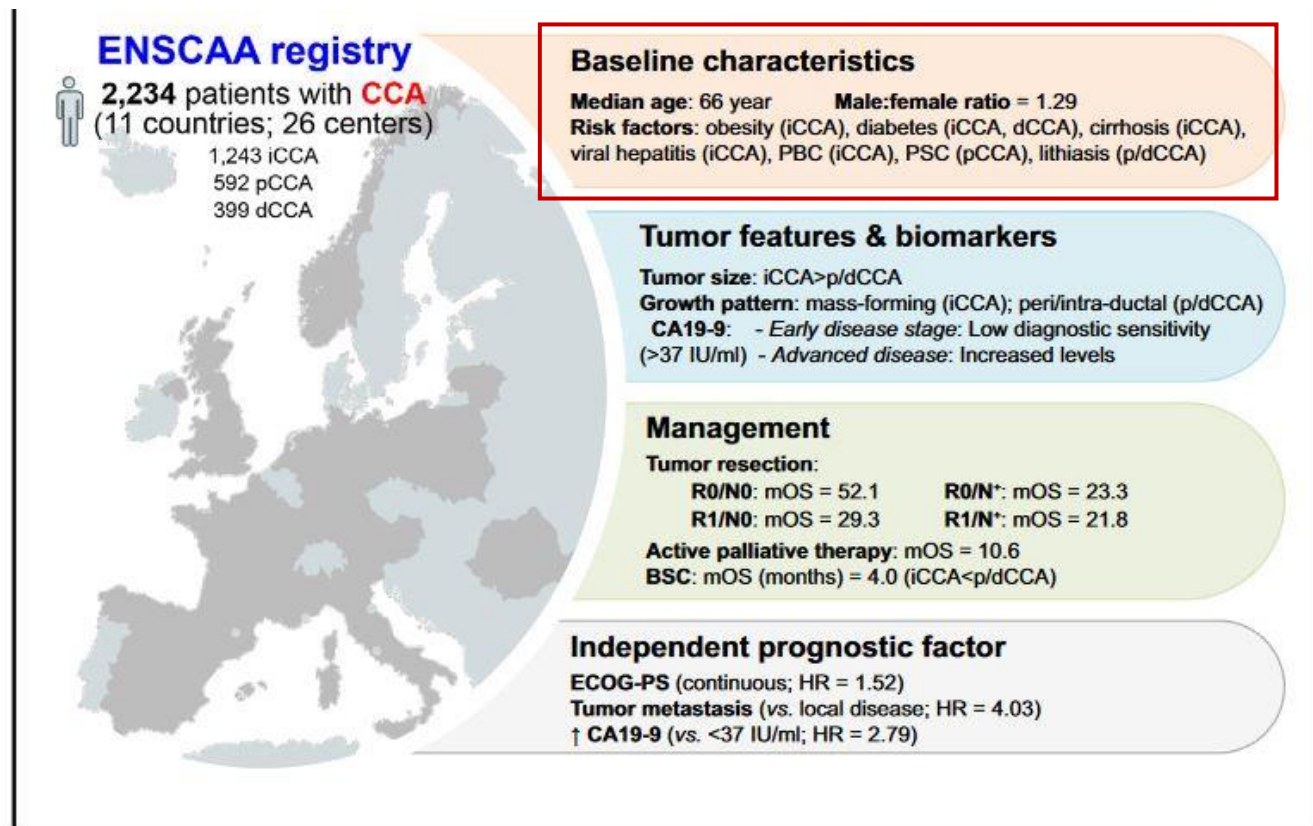
Cholangiocarcinoma landscape in Europe: Diagnostic, prognostic and therapeutic insights from the ENSCCA Registry



Authors

Laura Izquierdo-Sanchez, Angela Lamarca, Adelaida La Casta, ..., Juan W. Valle, Bas Groot Koerkamp, Jesus M. Banales

Journal of Hepatology 2021 vol. ■ | 1–13



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Risk factors for iCCA and eCCA

	OR > 10	OR 3-10	OR < 3
iCCA	Caroli disease	Liver fluke	Chronic pancreatitis
	Choledocal cyst	CHB, CHC	IBD
	PSC	Cholelithiasis	MASLD, T2DM, MetS
	Cirrhosis	ARLD	Hemocromatosis
	Choledocholithiasis		Cig smoking
	OR > 10	OR 3-10	OR < 3
eCCA	Choledocal cyst	Chronic pancreatitis	MASLD, T2DM, MetS
	Choledocholithiasis	Cholelithiasis	ARLD
	PSC	Liver fluke	IBD
	Caroli disease	Cirrhosis	CHB, CHC
			Cig smoking

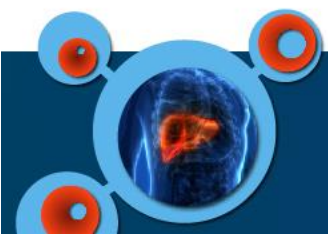
Clements O, ... Khan SA, J Hepatol 2020

Banales JM, ... Gores GJ, Nat Rev Gastroenterol Hepatol 2020

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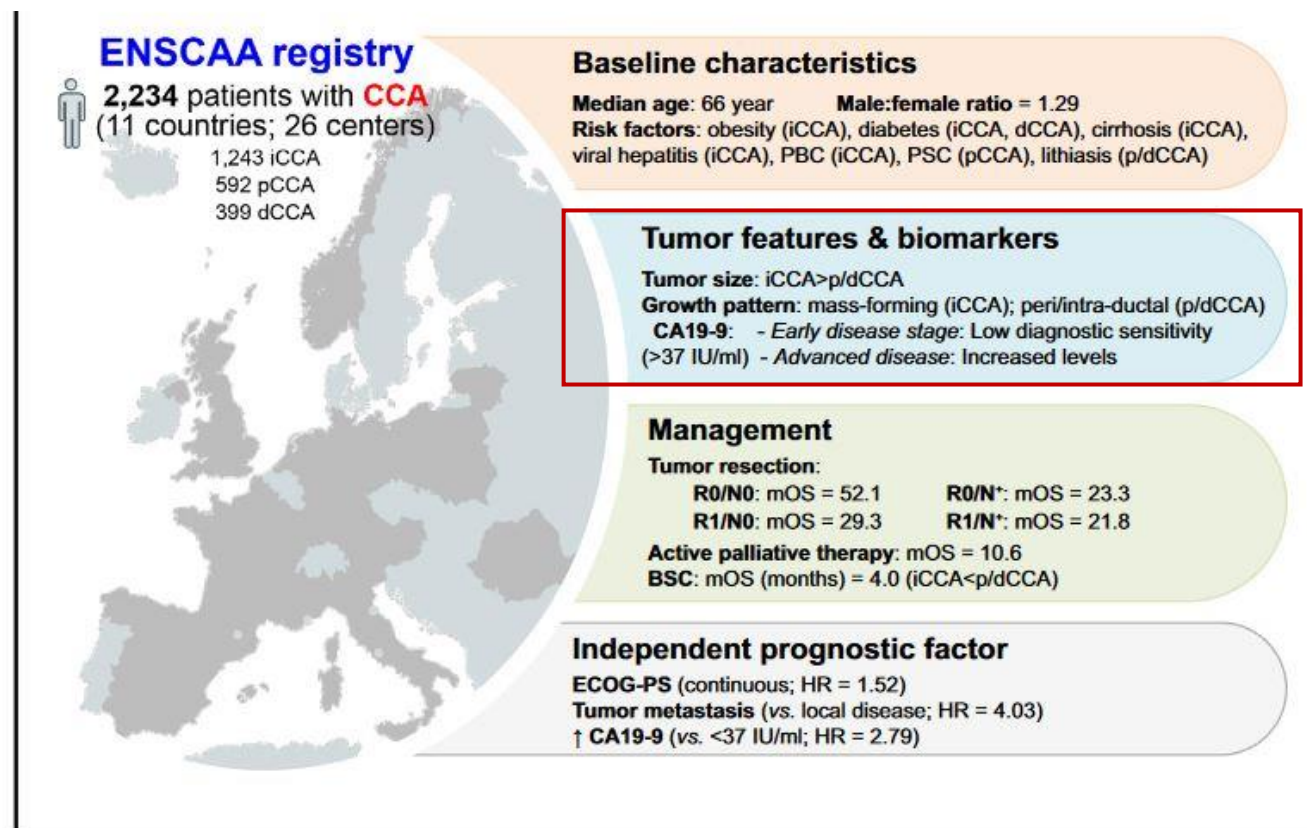
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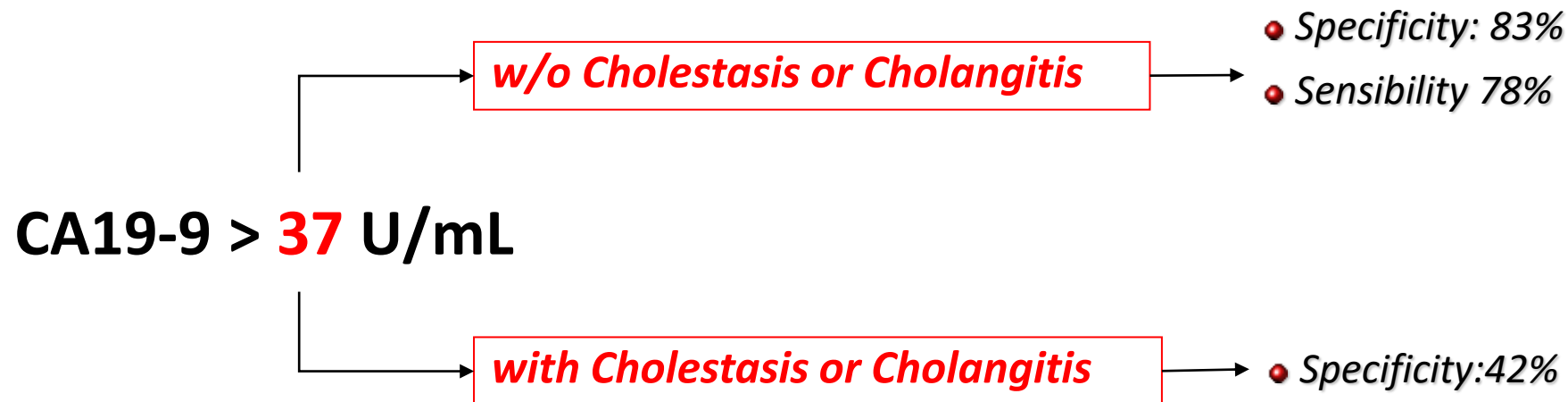
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CA19-9 > **300** U/mL

→ • Specificity

87%

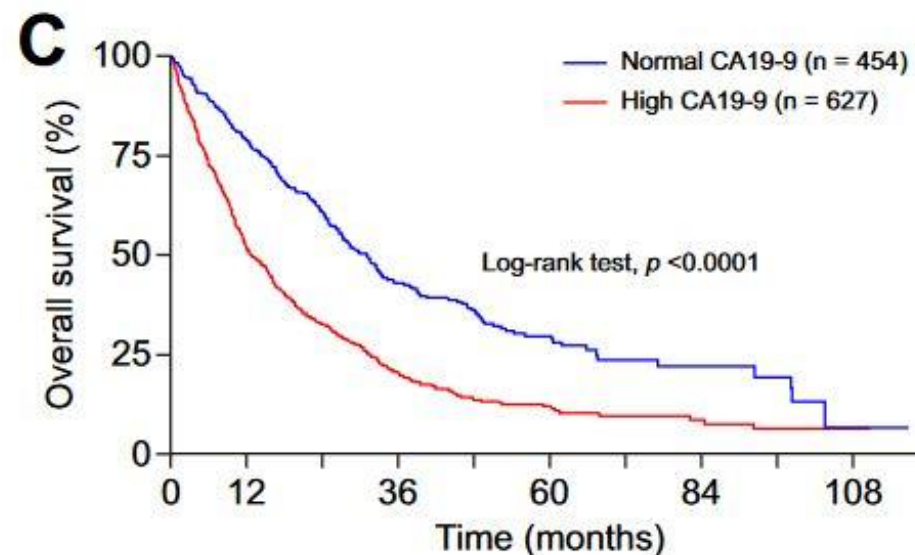
CA19-9 shows low sensitivity in early stages but increased sensitivity in advanced disease.

Izquierdo-Sanchez L, ... Banales JM, J Hepatol 2022

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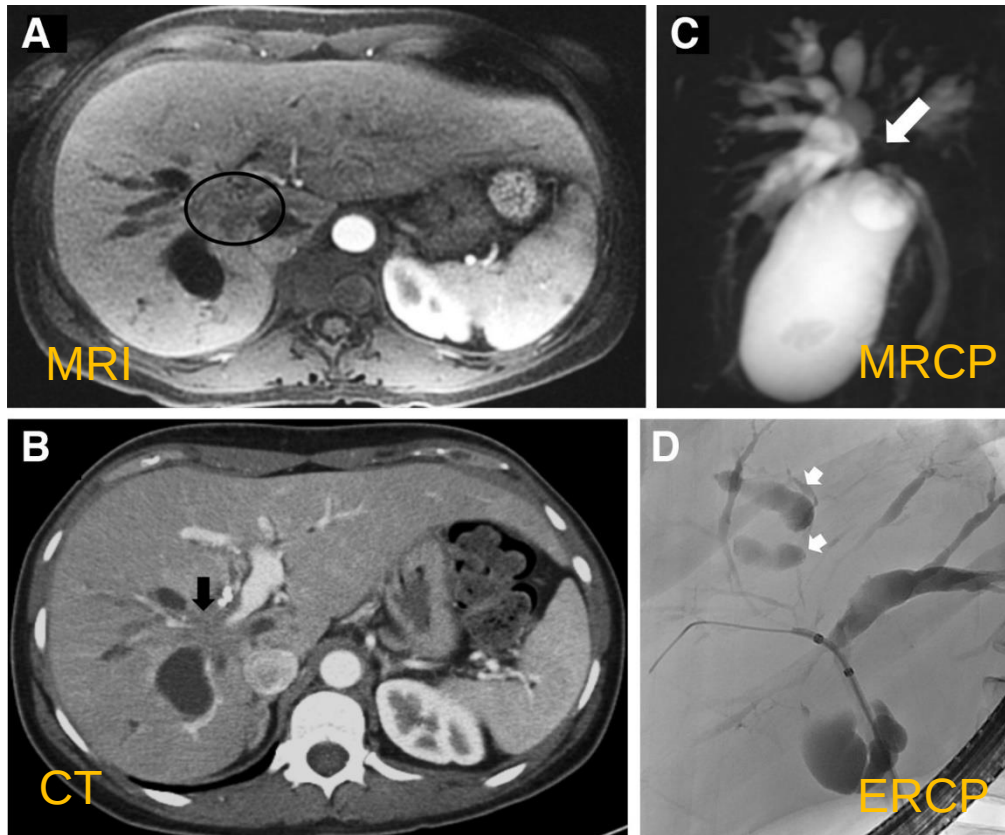


Izquierdo-Sanchez L, ... Banales JM, J Hepatol 2022

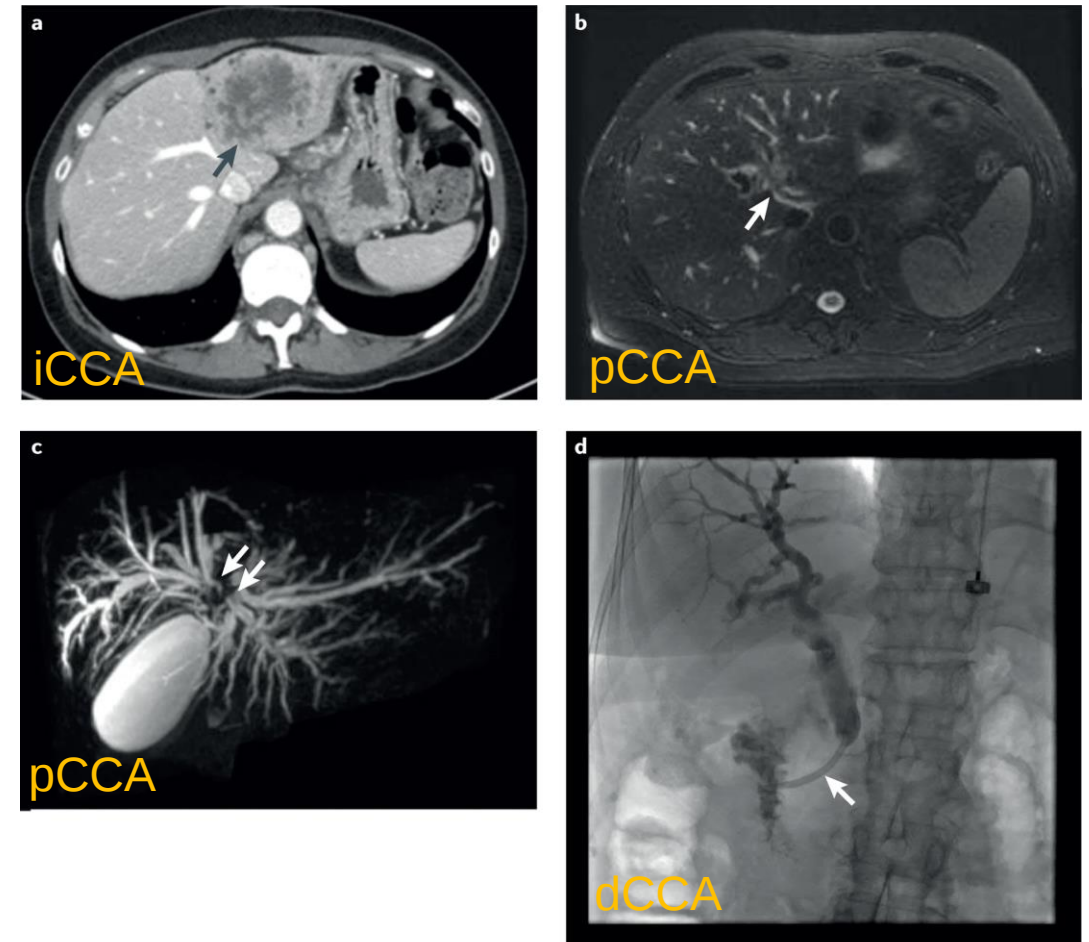
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Rizvi S, Gores GJ, Gastroenterology 2013



Rizvi S, ... Gores GJ, Nat Rev Clin Oncol 2018 Nature Reviews | Clinical Oncology

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Recommendations

- Pathological diagnosis is required for a definitive diagnosis of iCCA
Recommendation A1
- Pathological diagnosis of iCCA is based on the WHO classification for biliary tract cancer. Differentiation of metastatic adenocarcinoma from primary iCCA may require additional clinical and radiological and endoscopic evaluation
Recommendation B1
- Immunostaining to detect markers of hepatocellular carcinoma (e.g., GPC3, HSP70, and glutamine synthetase) or progenitor cell features (e.g., K19, EpCAM) is recommended to distinguish iCCA from mixed hepatocellular-cholangiocarcinoma tumors if this information will change management
Recommendation B1
- A presumed radiographic diagnosis is sufficient in non-cirrhotic patients in whom a decision has been made to proceed with surgical resection
Recommendation B1

- PET-scan is not accurate for early diagnosis of iCCA; its role as a staging modality remains controversial
Recommendation B2

- Serological tumor markers such as CA19-9 are insensitive for the diagnosis of iCCA and insufficient to establish the diagnosis, but may be of prognostic significance
Recommendation B1

- Assessment of resectability and/or intra- and extrahepatic metastatic disease, as well as venous and arterial invasion, is best accomplished using radiographic studies such as CT and/or MRI
Recommendation A1

Suggestions for future studies

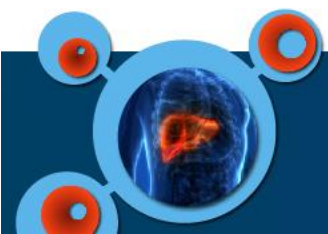
- Screening protocols for early diagnosis of iCCA in PSC and other disease conditions @ risk
- Harnessing potentials of liquid biopsy in CCA

Bridgewater J, ... Gores GJ, J Hepatol 2014 (mod)

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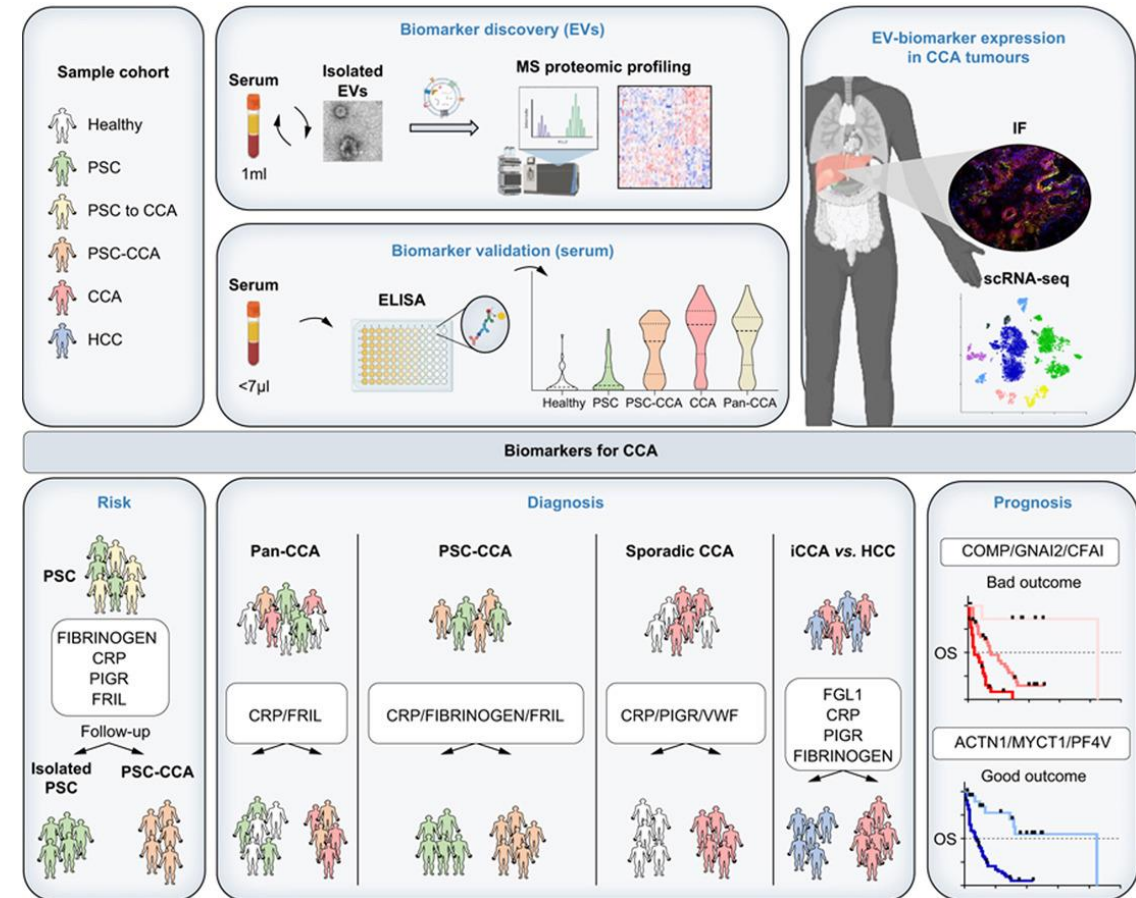
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Liquid biopsy-based protein biomarkers for risk prediction, early diagnosis, and prognostication of CCA

- **Circulating EV-proteins** allow for CCA risk prediction, early and differential (vs. HCC) diagnosis, and prognostication.
- **Serum CRP/FIBRINOGEN/FRIL** levels discriminated patients with early-stage PSC-CCA from those with PSC.
- Most pan-CCA biomarkers are mainly expressed in **malignant cholangiocytes** within human CCA tumours.
- **Serum CRP/FIBRINOGEN/FRIL/PIGR** levels predict CCA development in patients with PSC before radiological tumour evidence.
- The abundance of **EV-proteins** COMP/GNAI2/CFAI and ACTN1/MYCT1/PF4V independently predict **patients' overall survival**.



Lapitz A, ... Banales JM, *J Hepatol* 2023

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H2020 EU
COST action CA18122
COST Action CA22125

PRIN-2022-AHM4AA

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