

Clinicopathological characterization of steatohepatic variant of hepatocellular carcinoma (SH-HCC)

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Introduction

Hepatocellular carcinoma of steatohepatitis variant (SH-HCC), described in 2010, is thought to account for 5-20% of HCCs and to occur more frequently in patients with metabolic syndrome and/or hepatitis C virus (HCV). There is currently no consensus definition of SH-HCC and its prognosis remains discussed.

The aims of this study were (1) to propose a consensual morphologic definition of SH-HCC and (2) to clarify its prevalence and prognosis in a retrospective cohort of surgically resected HCC.

Method

We conducted a monocentric retrospective study including 297 patients with **surgically resected** HCC between 2012 and 2019. Clinical characteristics and follow-up data were collected. Macroscopic and microscopic characteristics of the tumor and non-tumoral liver were reassessed by two pathologists for each case.

CHC-SH retained if: $\geq 4/5$ criteria* + SH contingent $> 50\%$.

*Microscopic criteria: steatosis, ballooning, Mallory-Denk bodies, fibrosis, inflammation

Results

Our cohort included 13% (n=39) of SH-HCC. SH-HCC were significantly associated with a higher age (mean age 66 vs 61 years, $p=0.004$), **metabolic syndrome** (56% vs 26%, $p < 0.001$) and **chronic alcohol intake** (28% vs 15%, $p=0.039$). These were **smaller tumors** (mean size: 4 cm vs. 6.9 cm, $p < 0.001$). There was no significant difference with other HCC in terms of histo-prognostic factors, recurrence-free survival and overall survival. **Ballooning, fibrosis and inflammation were found in all SH-HCC** (n = 39, 100%), steatosis in 36 cases (92%) and Mallory-Denk bodies in 29 cases (74%). Fibrosis was mixed (pericellular and septal) in 30 cases (77% vs 3% of other HCC, $p < 0.001$), and was moderate or extensive in 51% of SH-HCC (vs 22%, $p < 0.001$). Inflammation was moderate or intense in 31% of SH-HCC (vs 17%, $p=0.05$).

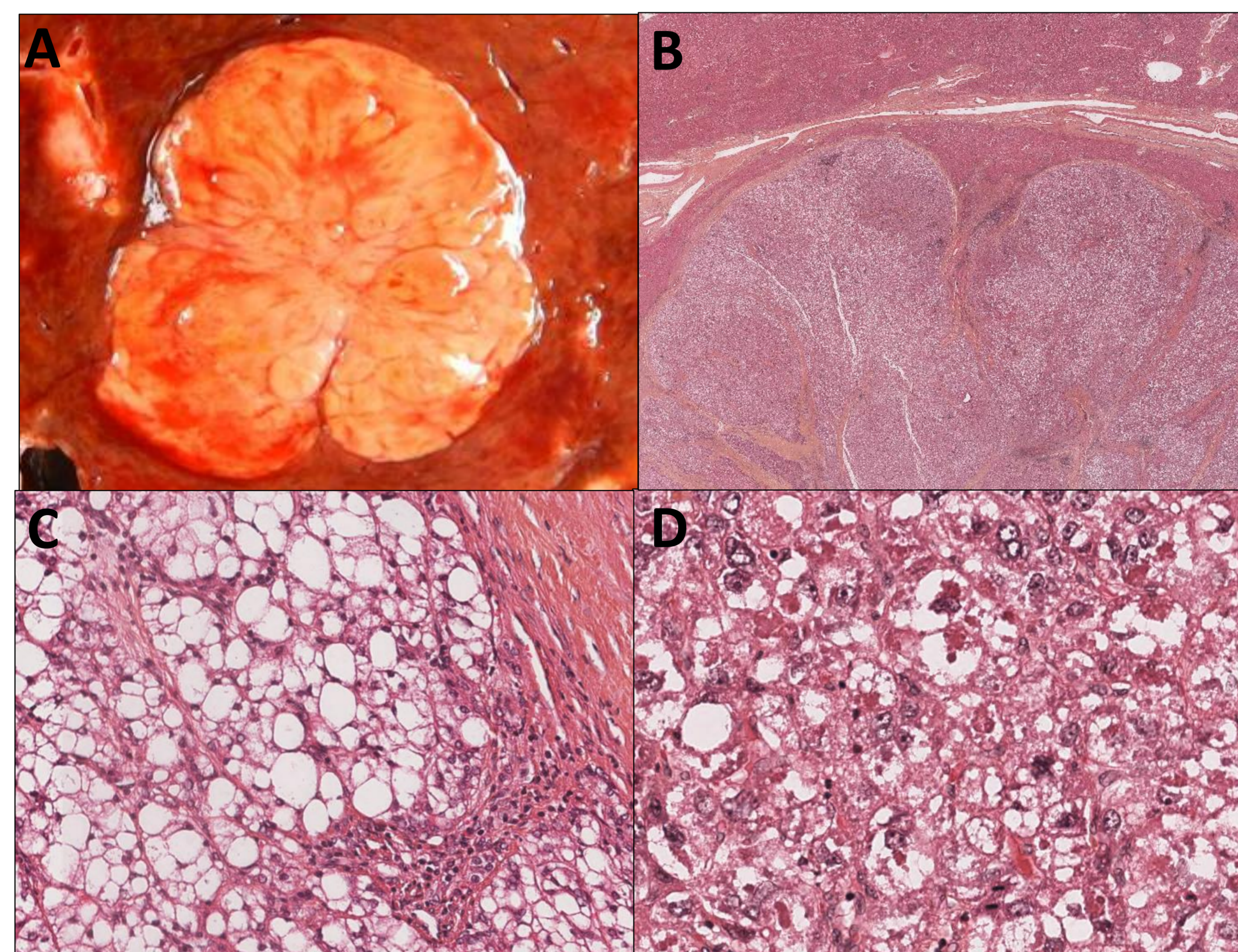


Figure 1. Macroscopic and microscopic features of steatohepatic hepatocellular carcinoma (SH-HCC).

A. On gross examination, SH-HCC is well demarcated, unencapsulated of yellowish color
B. At low magnification, demarcation, steatosis and fibrosis are already apparent
D. High magnification showing steatosis, inflammation and fibrosis (pericellular type)
E. High magnification showing tumor cells ballooning and Mallory-Denk bodies

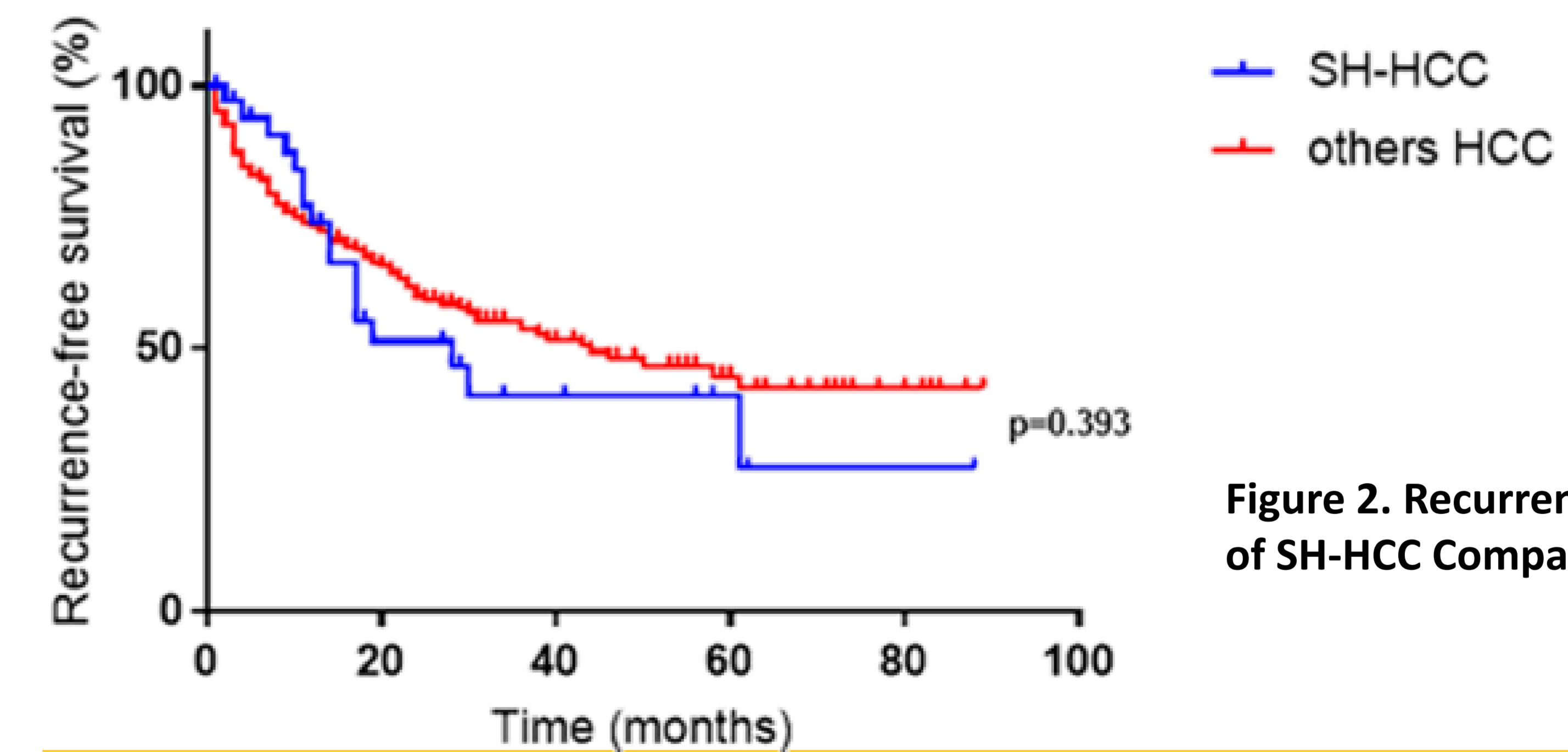


Figure 2. Recurrence-free survival curves of SH-HCC Compared to other HCCs

	SH-HCC n=39 (%)	Other HCC n=228 (%)	P
Age (median)	66 [38-79]	61 [21-99]	0,004
Gender (male)	34 (87)	174 (76)	0,121
Etiologies			
Metabolic syndrome	22 (56)	60 (26)	<0,001
Chronic alcohol intake	11 (28)	34 (15)	0,039
HCV	9 (23)	64 (29)	0,527
HBV	5 (13)	68 (30)	0,029
Non neoplastic liver			
Cirrhosis	19 (49)	74 (32)	0,048
NASH	13 (33)	25 (11)	< 0,001
Macroscopic features			
Tumor size (cm)	4 [0.6-25]	6.9 [0.5-25]	< 0,001
White	18 (46)	29 (13)	<0,001
Microscopic features			
Steatosis (>5%)	36 (92)	18 (8)	<0,001
Ballooning	39 (100)	25 (11)	<0,001
Mallory-Denk bodies	29 (74)	8 (3)	<0,001
Fibrosis	39 (100)	185 (81)	0,003
- Moderate/extensive	20 (51)	50 (22)	<0,001
- Mixed	30 (77)	8 (3)	<0,001
Inflammation	39 (100)	152 (67)	<0,001
- Moderate/intense	12 (31)	40 (17)	0,05
Well differentiation	16 (41)	72 (31)	0,239
Moderate differentiation	23 (59)	135 (59)	0,978
Poor differentiation	0	21 (9)	0,052
Microscopic vascular invasion	15 (39)	108 (47)	0,189
Satellite nodule	5 (13)	55 (24)	0,118
Follow-up/Prognosis			
Overall survival (median)	23	24	0,430
Recurrence-free survival (median)	14	13	0,393

Table. Comparison of clinico-pathological characteristics of SH-HCC and other HCC.

Conclusion

SH-HCC represent **13% of HCC** in our cohort. Diagnosis of SH subtype can be based on **3 major criteria: ballooning, fibrosis and inflammation** (especially moderate or intense). Steatosis and Mallory-Denk bodies are minor criteria, supporting the diagnosis of SH-HCC, particularly if the inflammation and fibrosis are mild. Although, this subtype presents specific macroscopic and microscopic features, there is **no prognostic impact compared to other HCC**. The study of this subtype would be interesting for imaging.