



Vascular lesions in MASLD pathogenesis: clinical data and implications

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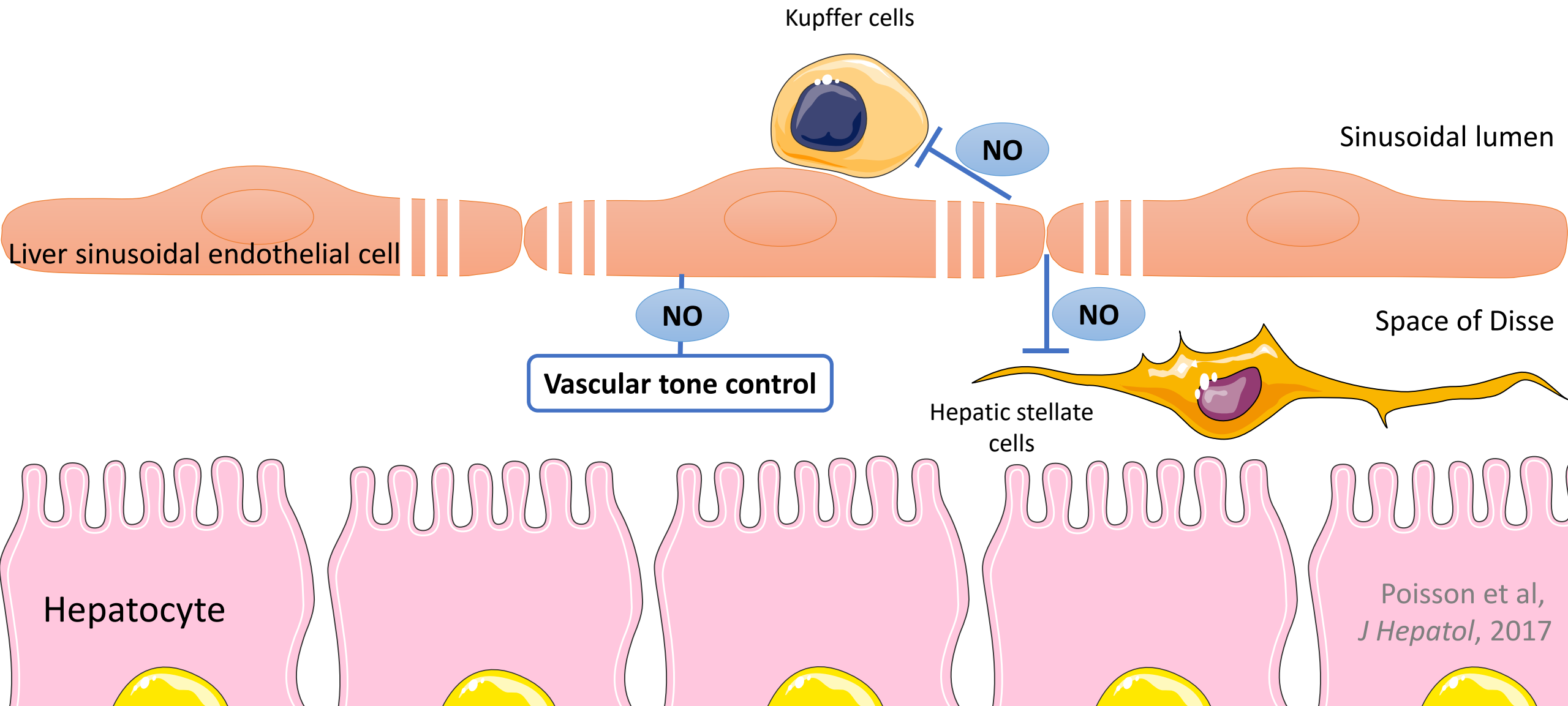
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Vascular lesions in MASLD pathogenesis

- What changes occur in endothelial cells in MASLD?
- What causes those changes?
- What are the consequences?
- MASLD and portal hypertension

Liver sinusoidal endothelial cells (LSECs)



Poisson et al,
J Hepatol, 2017

Liver sinusoidal endothelial cells (LSECs)

Endothelial *fenestrae*

Kupffer cells

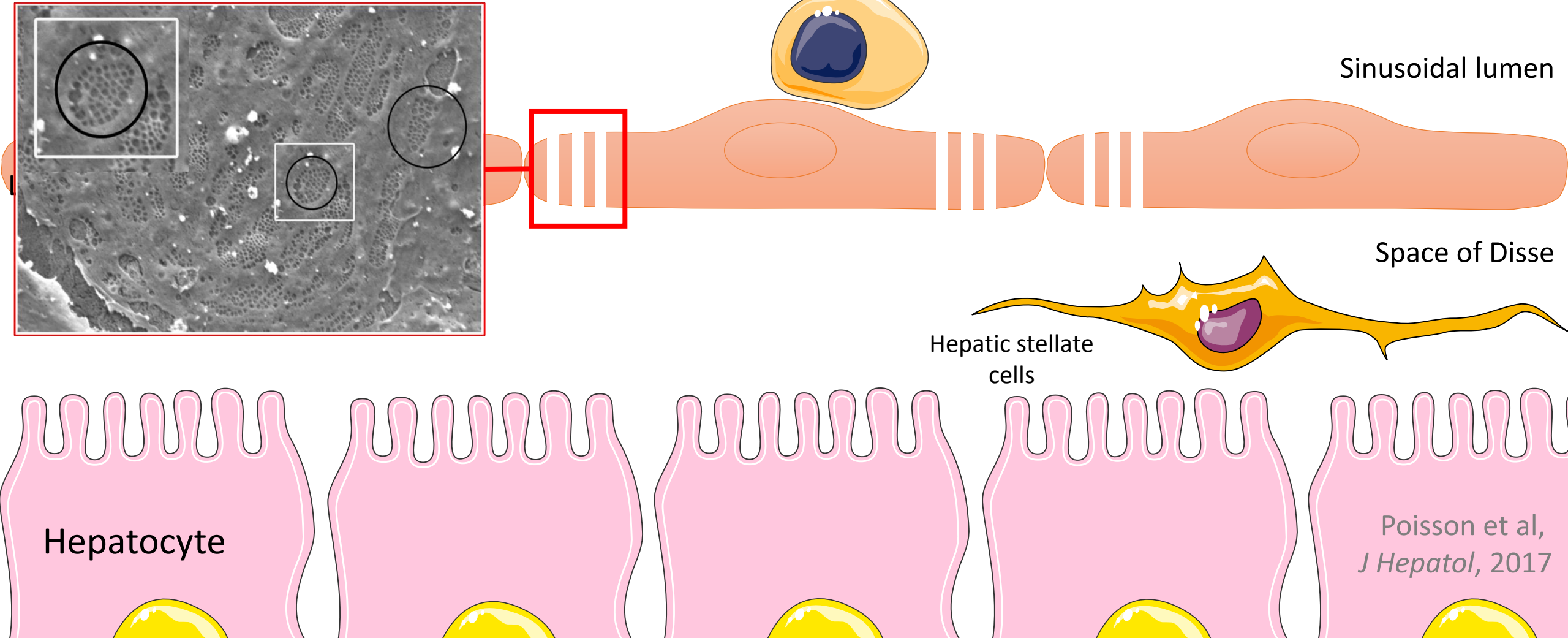
Sinusoidal lumen

Space of Disse

Hepatic stellate cells

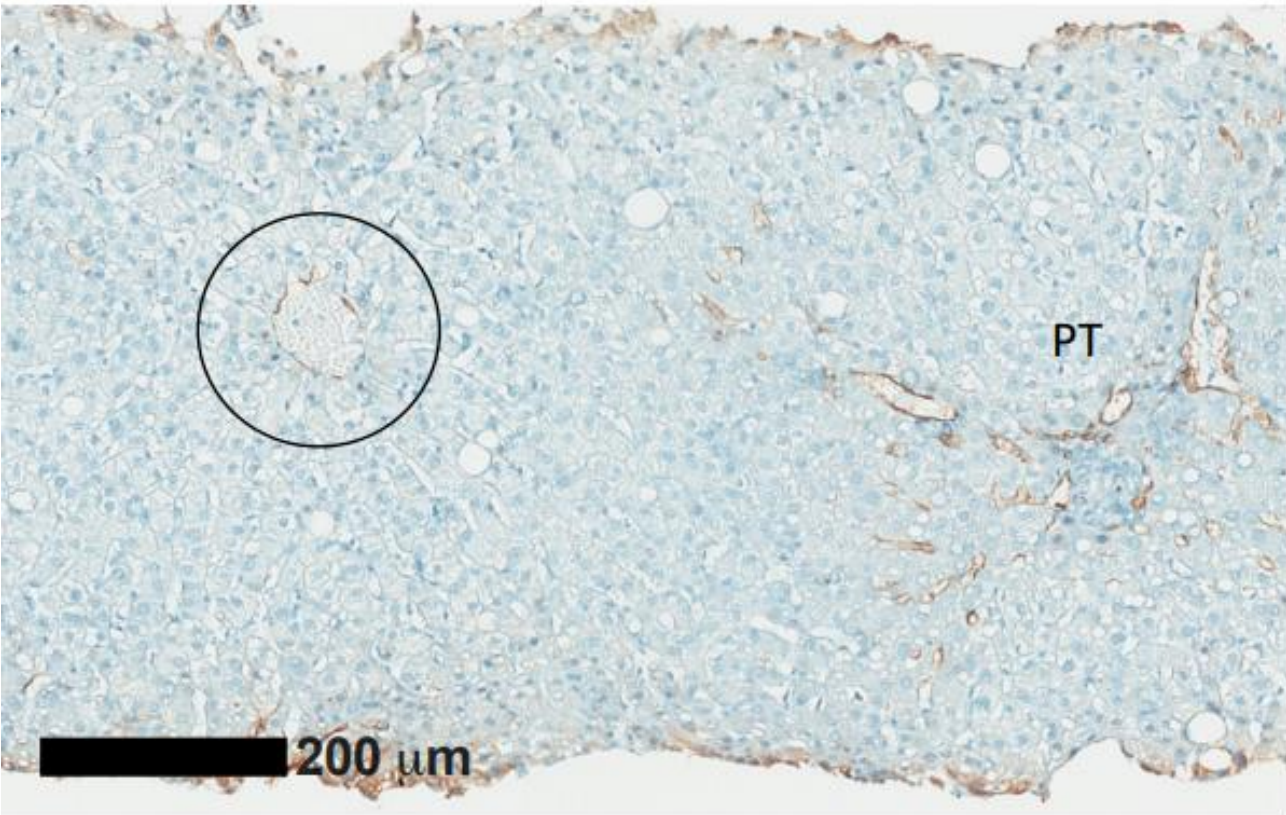
Hepatocyte

Poisson et al,
J Hepatol, 2017



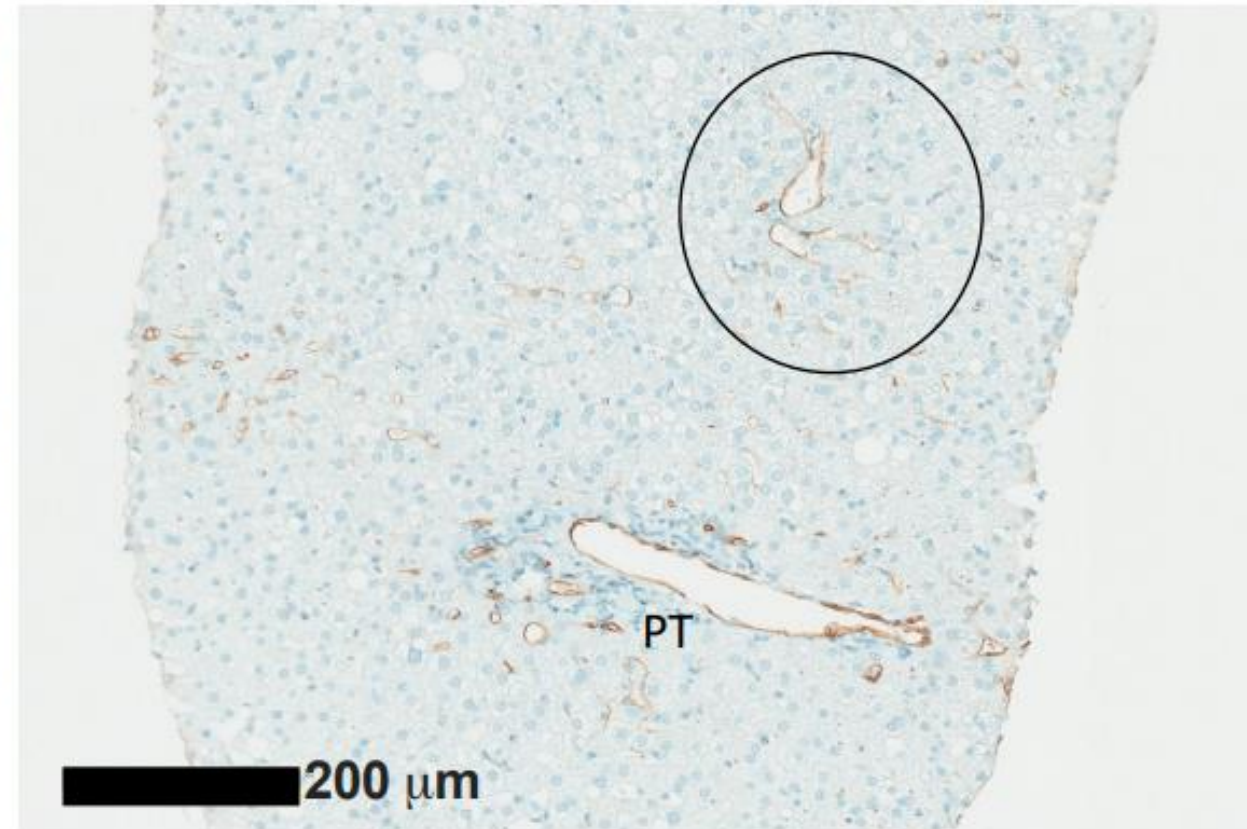
Capillarization precedes MASH: CD34 staining in patients

No SLD



Lobular score: 0/3, Periportal score 1/3

MASLD



Lobular score: 1/3, Periportal score 1/3

38 patients considered for inclusion in the NATIVE trial
CD34 staining

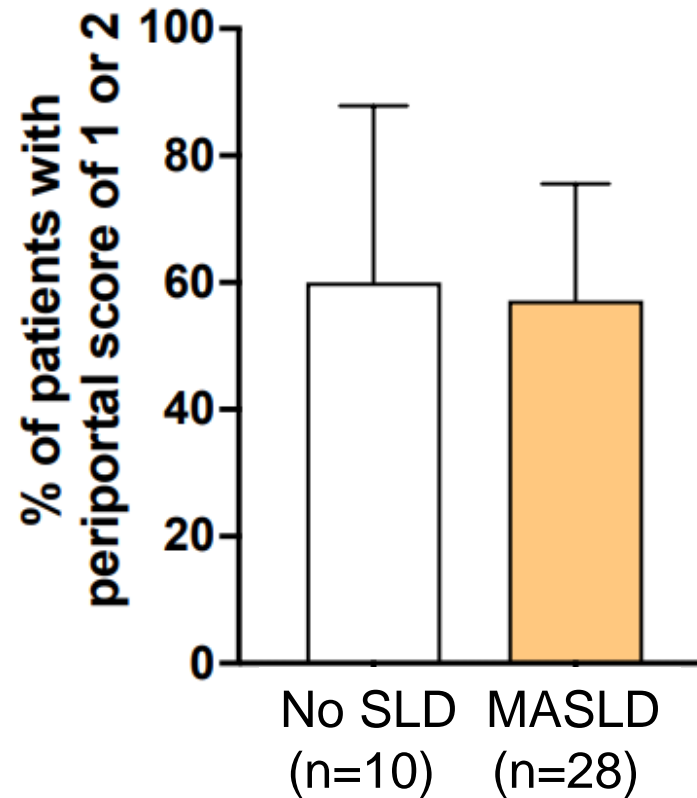
Rautou *et al.*, AASLD 2021
Francque *et al.*, NEJM 2021

Capillarization precedes MASH: CD34 staining in patients

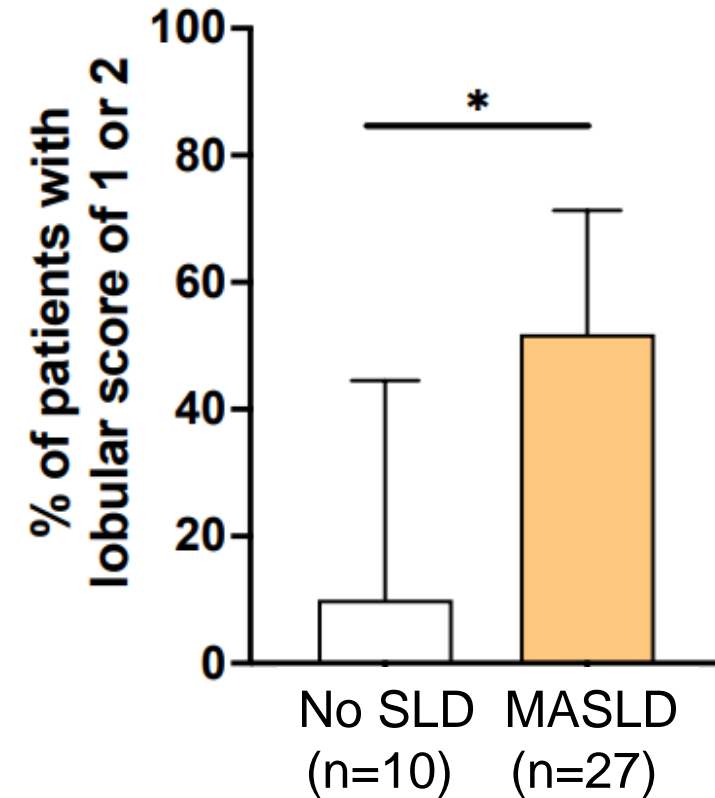
Morphometry



Periportal score



Lobular score

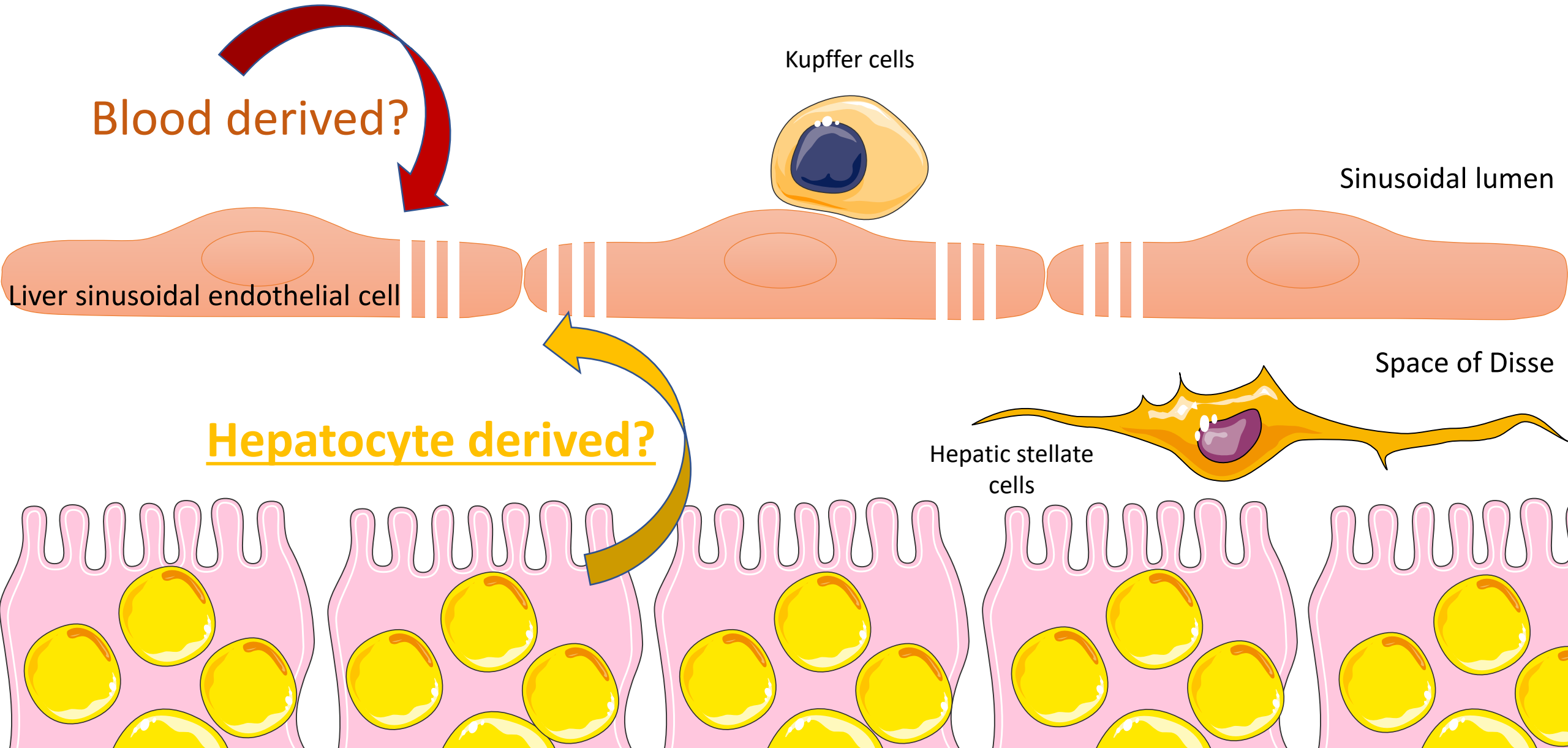


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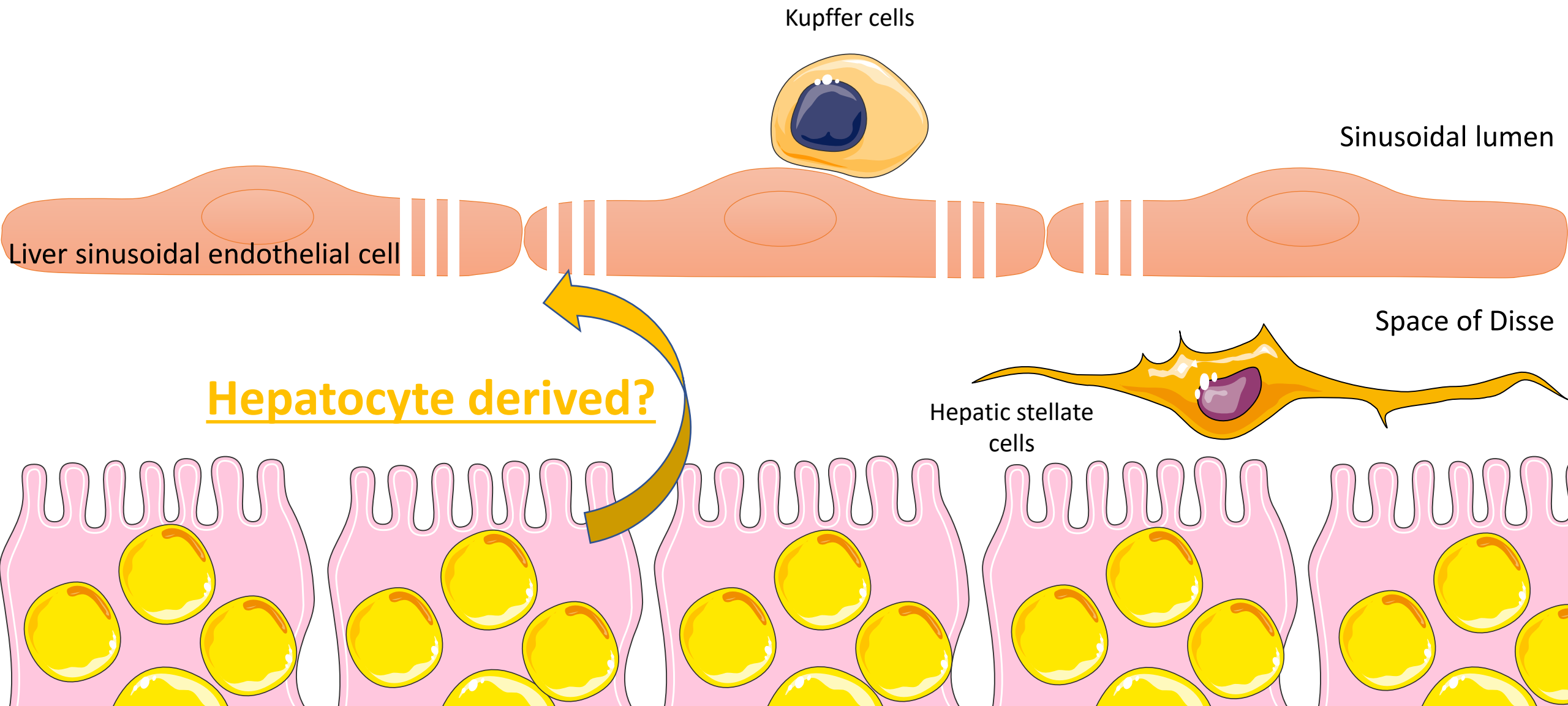
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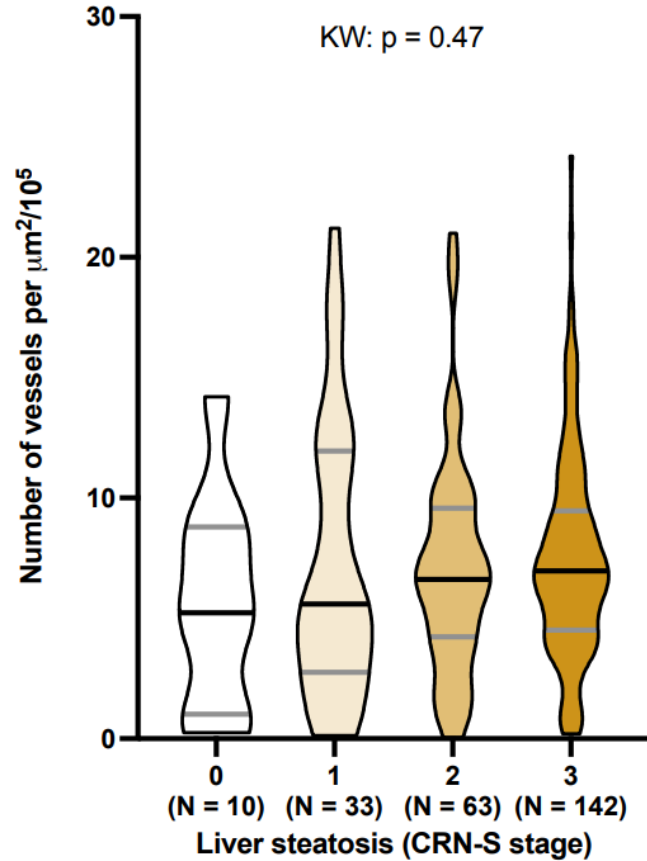


Liver sinusoidal endothelial cells (LSECs)

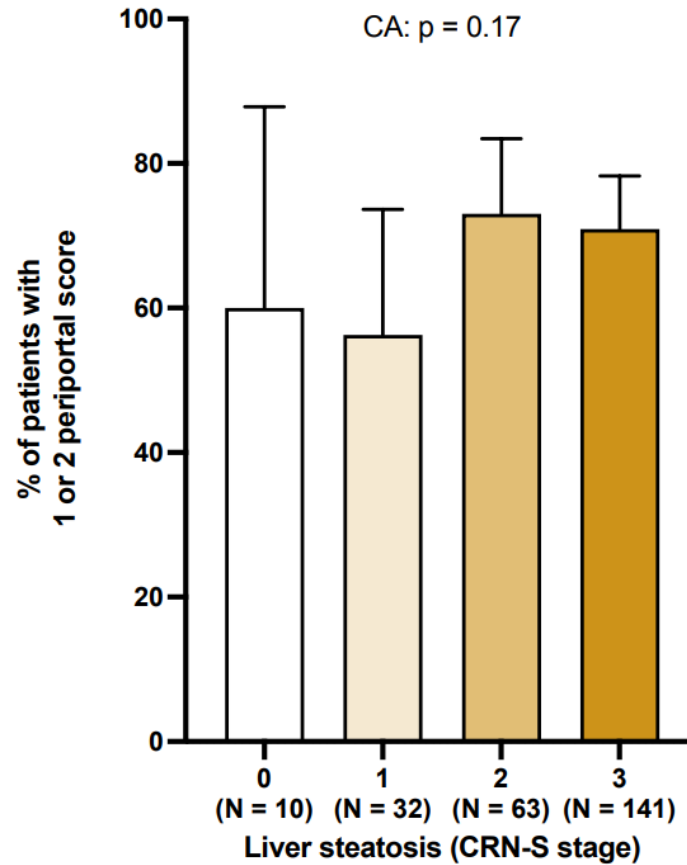


Capillarisation and steatosis: no link in patients

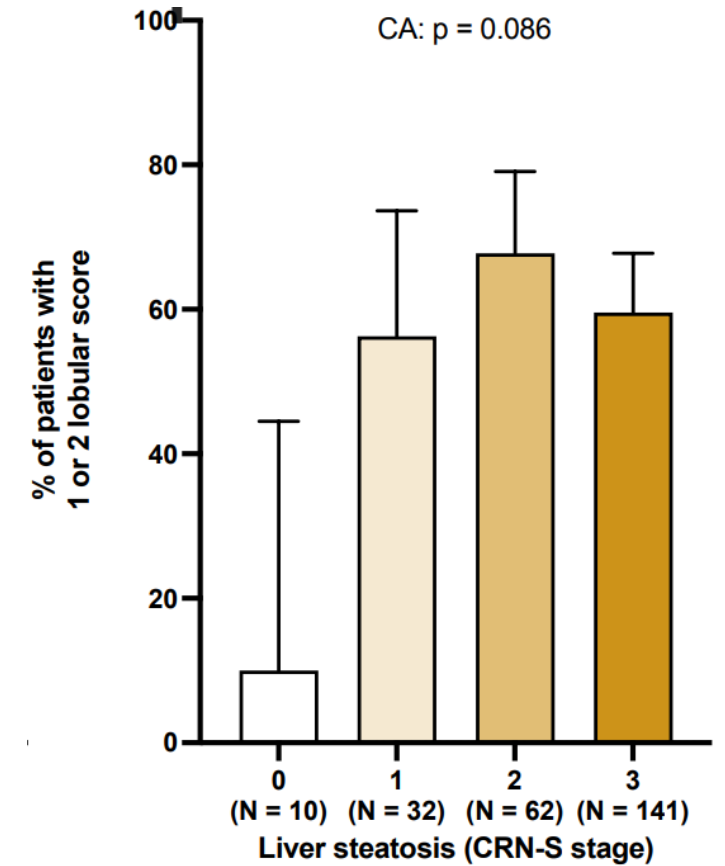
Morphometry



Periportal score



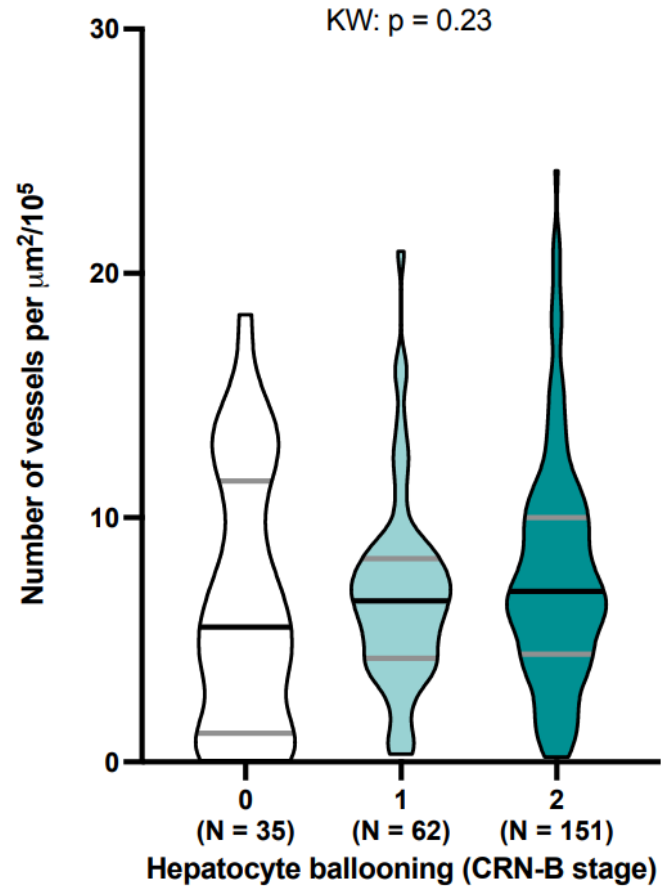
Lobular score



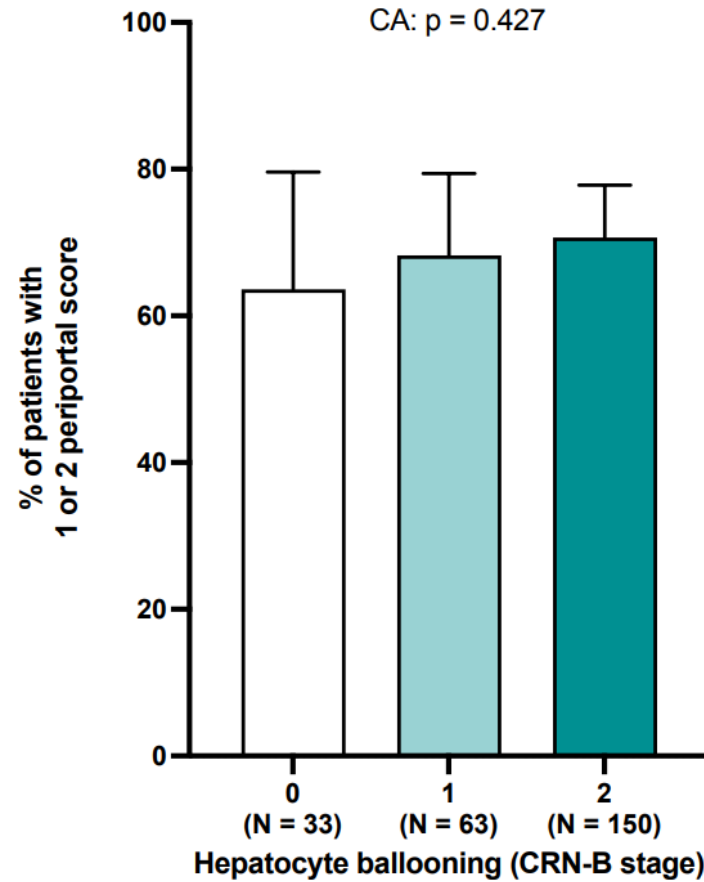
248 patients considered for inclusion in the NATIVE trial
CD34 staining

Capillarisation and ballooning: no link in patients

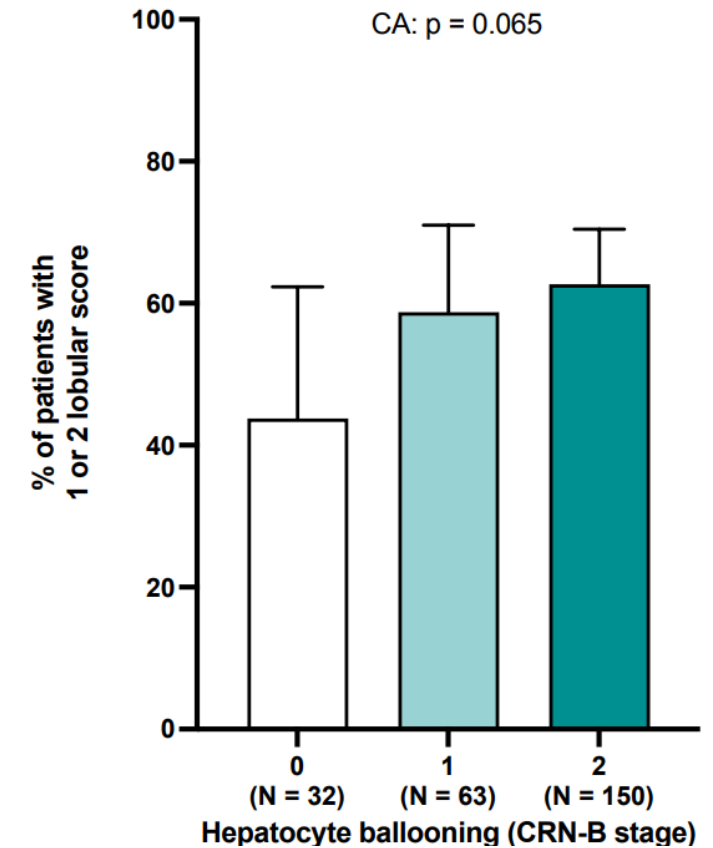
Morphometry



Periportal score

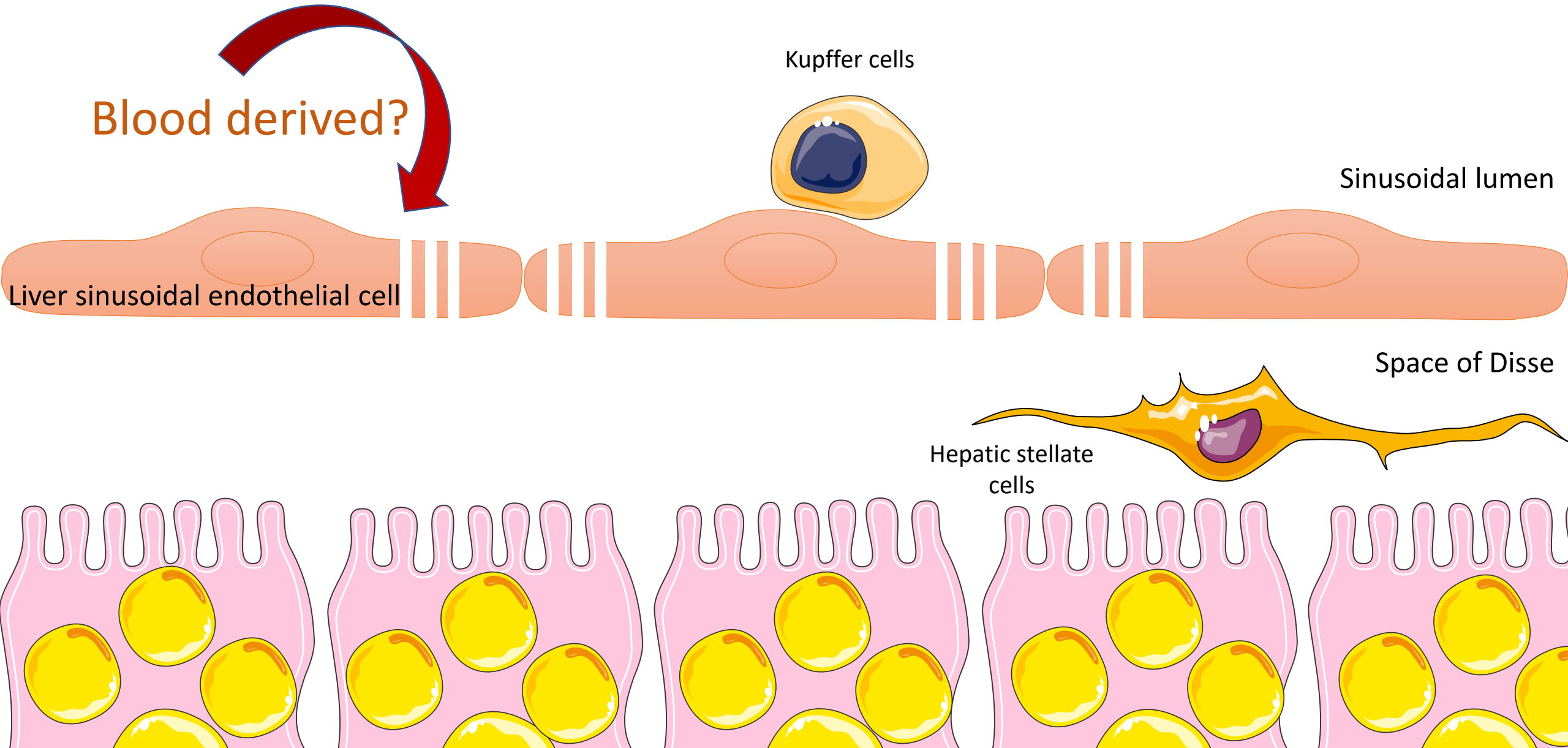


Lobular score



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CD34 staining

Liver sinusoidal endothelial cells (LSECs)



Portal blood contains elevated IL-6 concentrations in obese patients

Adipokine	Sample site	
	Radial artery	Portal vein
IL-6 (pg/ml)	28.5 ± 27.6	42.1 ± 41.8*
TNF-α (pg/ml)	1.87 ± 0.8	1.93 ± 0.8
MCP-1 (pg/ml)	205 ± 88	190 ± 99
Resistin (pg/ml)	18.5 ± 11	18.1 ± 11
Leptin (ng/ml)	101 ± 51	81 ± 42†
Total adiponectin (μg/ml)	14.3 ± 10	14.7 ± 11

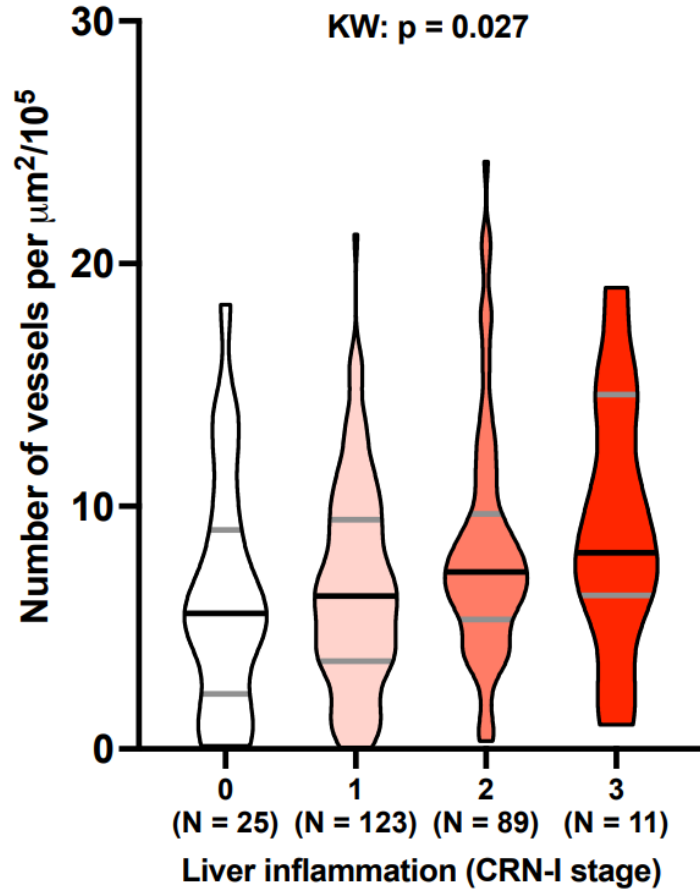
N=25; by-pass surgery

Vascular lesions in MASLD pathogenesis

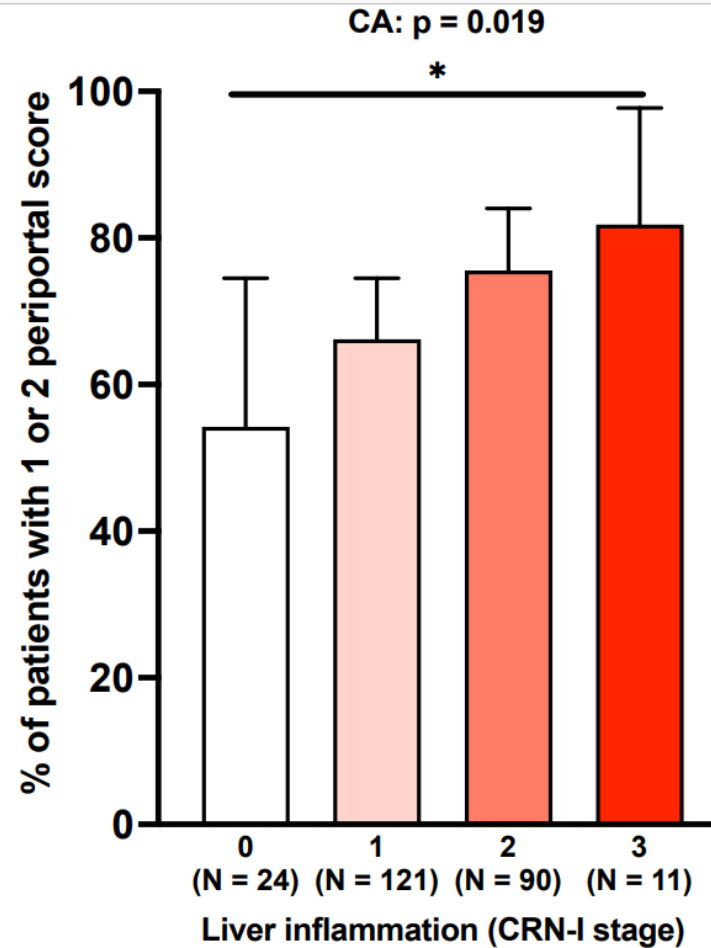
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LSEC capillarization and liver inflammation in patients with MASLD

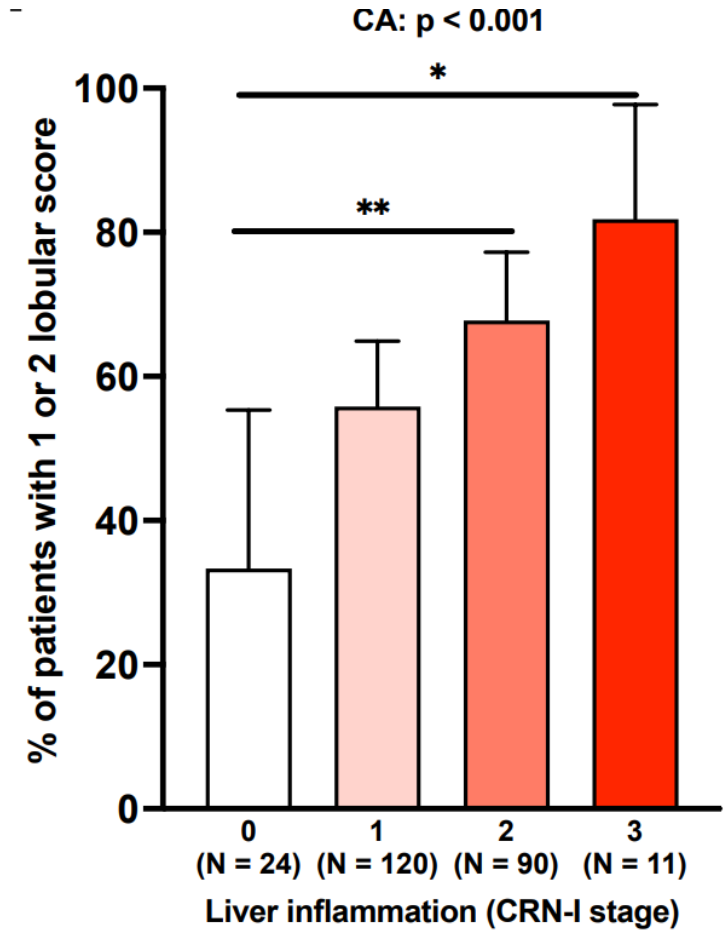
Morphometry



Periportal score



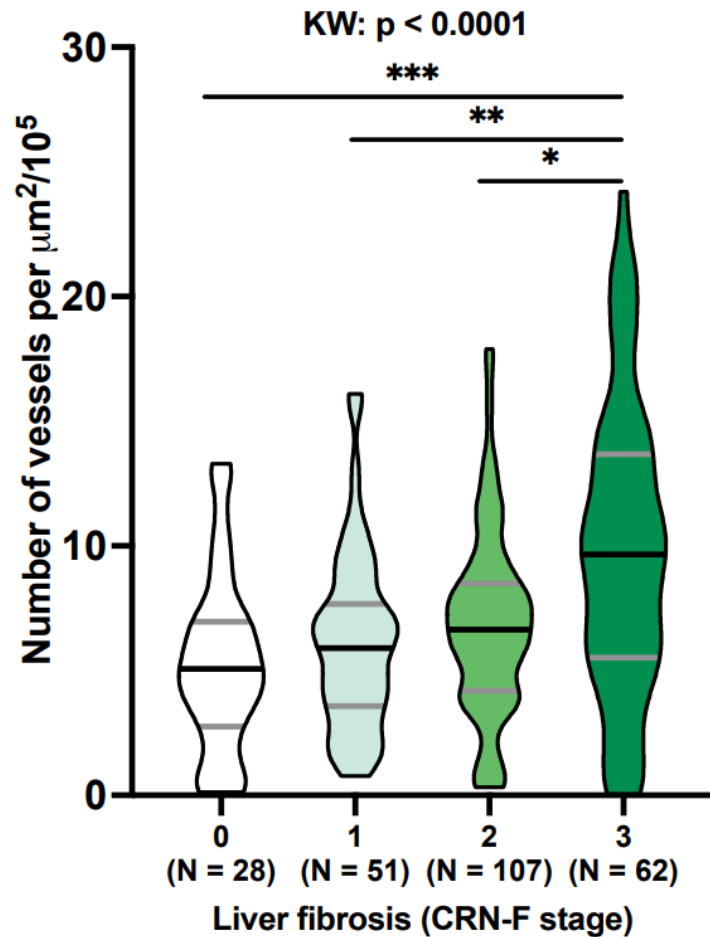
Lobular score



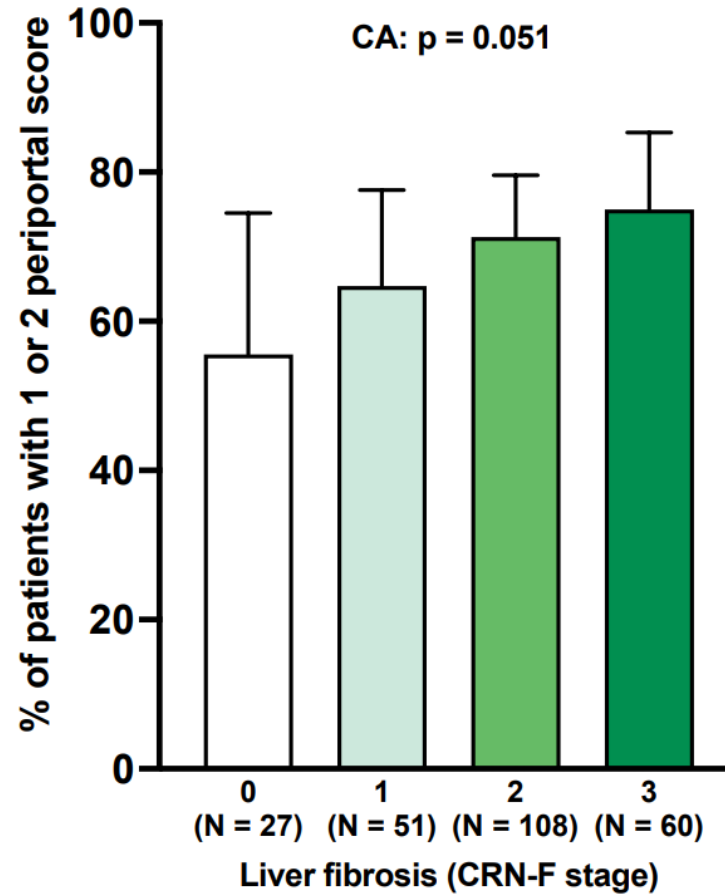
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LSEC capillarisation and liver fibrosis in patients with MASLD

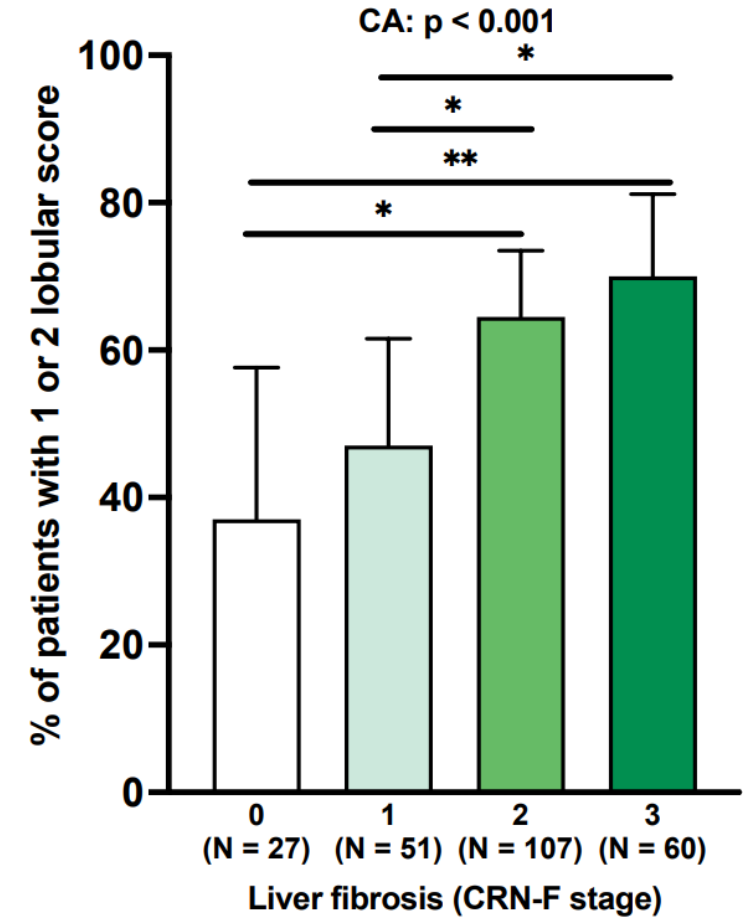
Morphometry



Periportal score



Lobular score

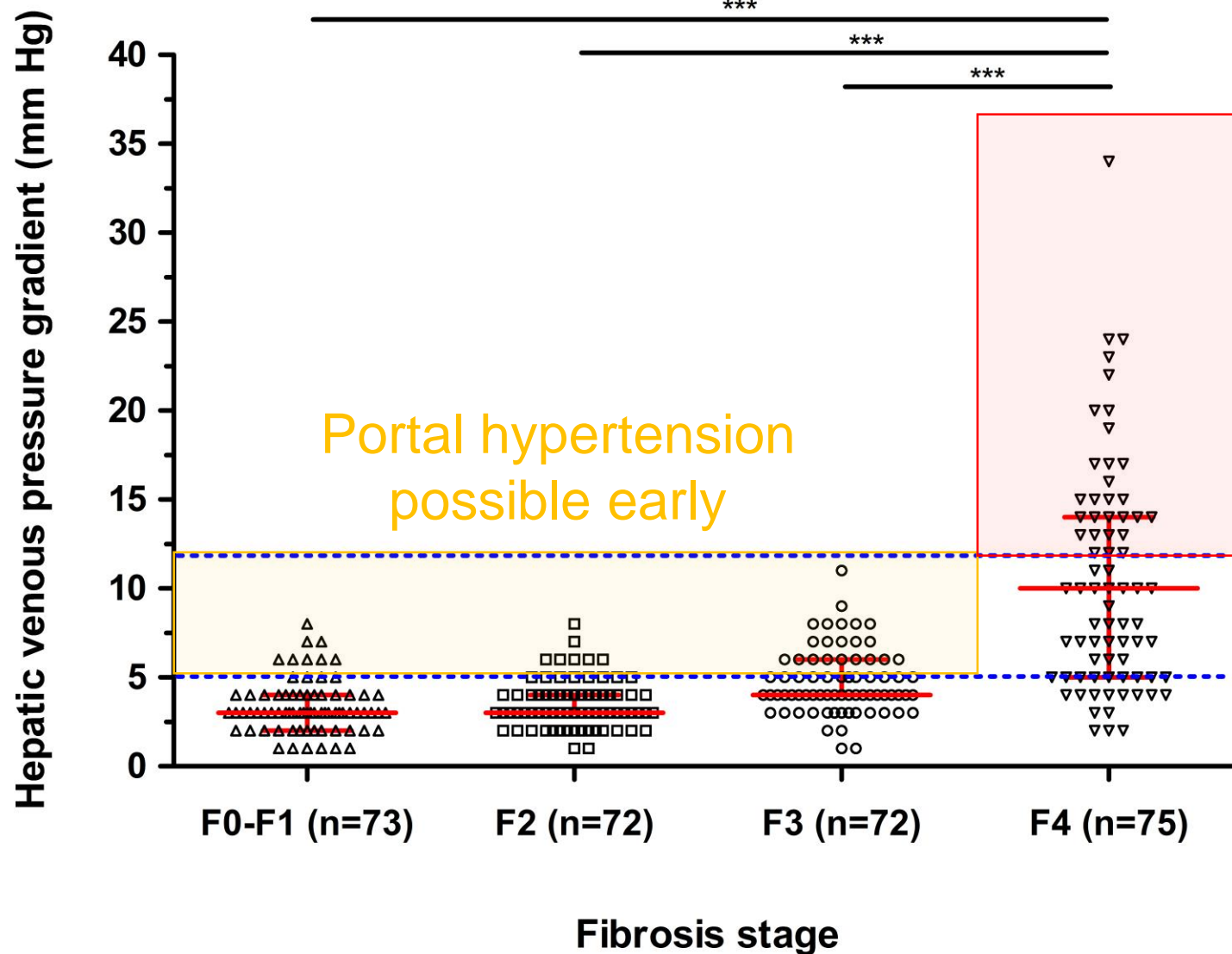


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Patients with MASLD do not have severe portal hypertension in the absence of cirrhosis

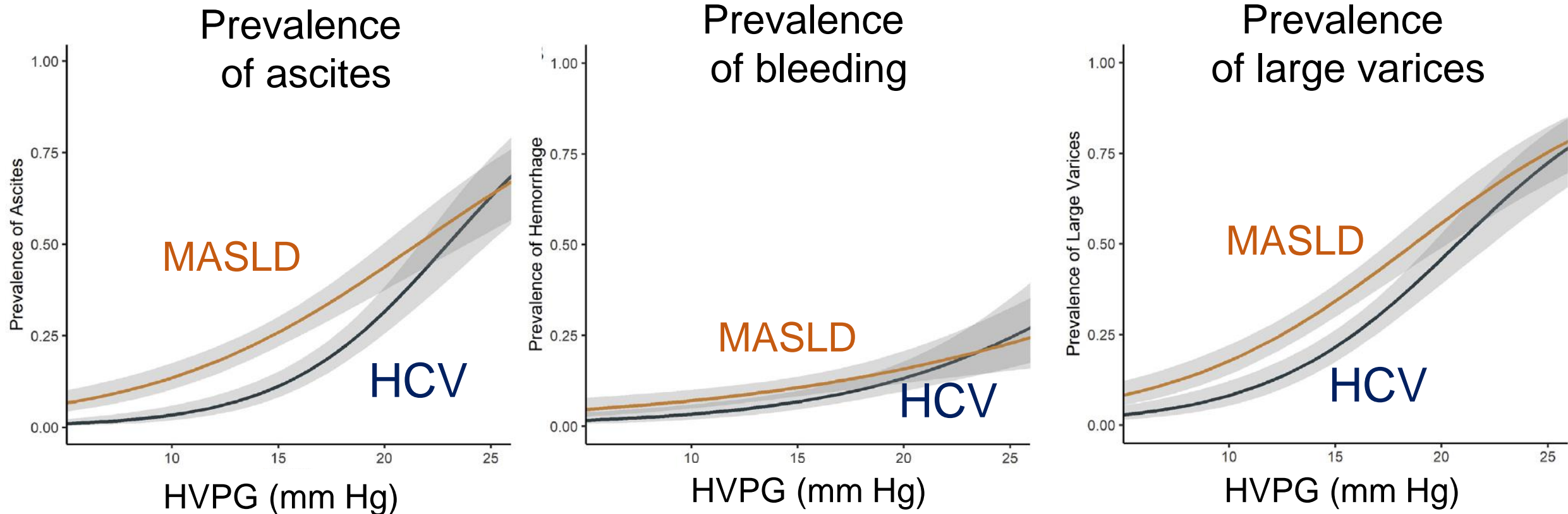


HVPG in 292 patients with NAFLD

Severe portal hypertension only in cirrhosis

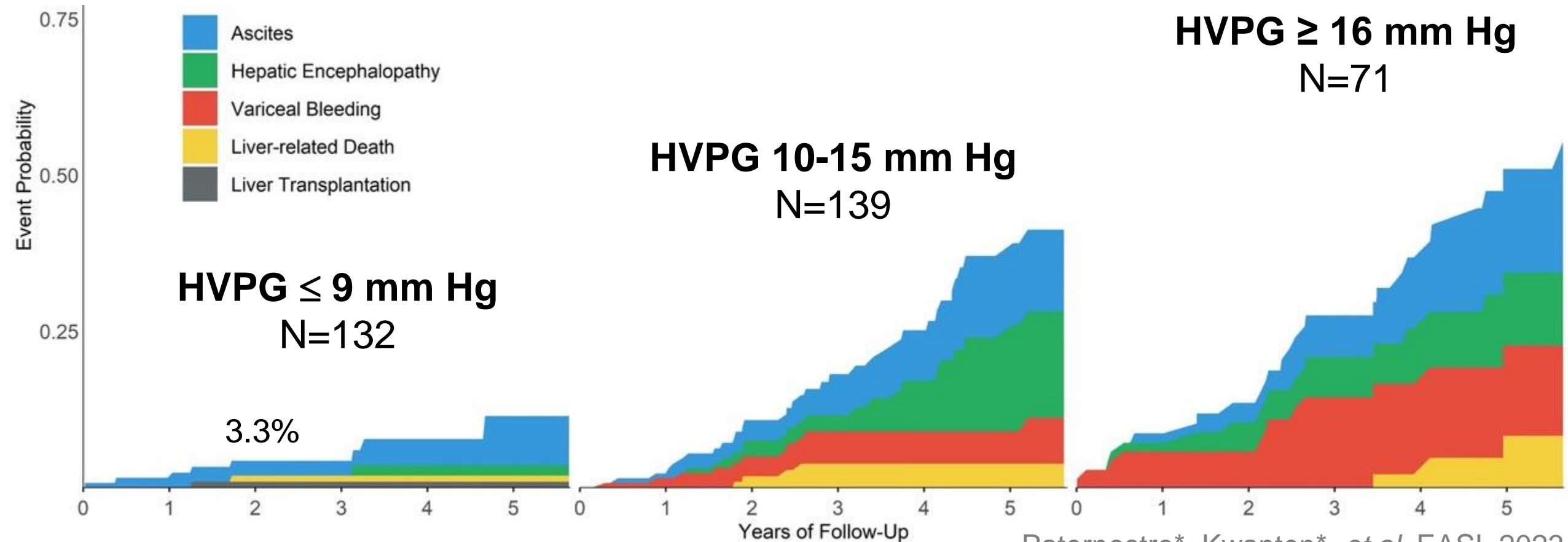
Decompensation in MASLD may occur at lower HVPG

548 patients with NAFLD and 444 with HCV (F3-F4)



HVPG predicts liver related complications in MASLD

342 patients with MASLD related cirrhosis
20 European centers
Median follow-up of 41.5



Conclusion

- **Sinusoid Capillarisation in MASLD:**
 - ✓ Occurs before MASH
 - ✓ Does not seem to favor steatosis nor ballooning
 - ✓ Increases with inflammation and fibrosis
- **Portal hypertension in MASLD:**
 - ✓ May occur at F1-F2 fibrosis
 - ✓ Is only severe in patients with cirrhosis
 - ✓ May lead to decompensation at lower HVPG level



Hepatology unit, Beaujon Hospital
Reference center for vascular liver diseases



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