

Table 2. Machine learning algorithms applied to hepatocytic ballooning in NASH.

Author/Year	Number of Liver Pathologists	Dataset	Image Analysis Method	Deep Learning	Quantitative or Qualitative Analysis	Histological Structures	Classification Results of Hepatocytic Ballooning
Vanderbeck et al., 2015	Two	Digital images of 59 slide (20×)	Image Preprocessing Classifier learning	No	Semi-quantitative analysis	Ballooning Lobular Inflammation	Recall ≤54% Precision ≤91% Accuracy ≤98.9% AUC ≤98.3% Spearman ≤46%
Heinemann et al., 2019	One	Digital images of 258 slide (high magnification tiles, 0.44 μm/px)	Image Preprocessing CNN	Yes	Semi-quantitative analysis	Ballooning Steatosis Inflammation Fibrosis score	Classification accuracy: Train (94%), Validation (93%) MAE (best = 0): Train (16%), Test (30%) Cohen's κ (best = 1): Train (70%), Test (42%) (Pathologist scores=the ground truth)
Arjmand et al., 2020	Not mentioned	Digital images of 64 slide (20×)	Image Preprocessing Training Testing MLP-ANN, CNN _{Adam}	Yes	Quantitative analysis	Ballooning Fat Sinusoid Vein	Accuracy: 100% (CNN _{Adam} models), 95% (CNN _{SGDM} models) Accuracy ≤95% [†] Precision ≤ 95% [†] Recall ≤ 95% [†] F-score ≤ 95% [†] Specificity ≤ 98% [†]

CNN _{SGDM} classifications							
Teramoto et al., 2020	One	Digital images of 79 slide	Forming persistence images Preprocessing topological data Analysis methodology combined with linear machine learning techniques	No	Qualitative analysis	Ballooning	AUC: 94.6% [‡]
Liu et al., 2020	Three	Digital images of 219 slide (20×)	Image Establishment of the Models Training Validation	No	Semi-quantitative analysis	Ballooning Fibrosis Inflammation Steatosis	AUC: 81.3%
Forlano et al., 2021	Two	Digital images of 246 slide	Image preprocessing Quantification features engaged machine learning	No	Quantitative analysis	Ballooning Steatosis Inflammation Fibrosis score	Image analysis: Inter-observer agreement 96% Intra-observer agreement: 95% ICC: 94.6% The Spearman correlation between percentage of ballooning and ballooning score was significant

			techniques with conventional image processing methods				($\rho = 0.52$; $P < 0.001$) and the relation was linear (JTT test $z = 4.4$; $P < 0.001$).
			Validation of Image Analysis in the Validation Cohort				
Taylor- Weiner et al., 2021	Three	Digital images of 4510 slide (WSI) 45,081 annotations	Image Training and deploying models model predictions (optimizer train a deep CNN with stochastic minibatch gradient descent)	Yes	Quantitative analysis	Ballooning Steatosis Inflammation Fibrosis score	Cohen's κ values: 66.6% Consensus NAS grades by the pathologists were significantly correlated with the ML model's scores (HB, $\rho = 0.62$; $P < 0.001$) C- index [95% CI] of ML: 0.55 [0.51-0.60] C- index [95% CI] of CP: 0.53 [0.50-0.56]
Brunt et al., 2021	Nine	digital images of 22 slide	Image Preprocessing Training q-Ballooning2 algorithm	No	Quantitative analysis	Ballooning	Fleiss κ statistic for overall inter-observer agreement: 19.7% (95%CI 0.094-0.300), rising to 36.2% (0.258-0.465) Intra-class correlation coefficient for consistency: 71.8% (0.511-0.900)

							AI-pathologist pairwise concordance 19-42%, comparable to inter-pathologist pairwise concordance of between 8-75%
Qu et al., 2021	One	digital images of 87 slide (5×, 10×, 20×, WSI)	Image Preprocessing Training Testing CNN base on ResNet18	Yes	Semi- quantitative analysis	Ballooning Steatosis Fibrosis score	AUC: 81.1% (10x)

Abbreviations: ML: machine learning; NASH: nonalcoholic steatohepatitis; WSI: whole-slide image; CNN: convolutional neural network; CP: central pathologist; ICC: interclass correlation coefficient.

† Statistical data for all histological structures related to ballooning in NASH (ballooning, fat, sinusoid, vein).

‡ The classification of NASH (type 3 and type 4 of Matteoni classification) and NAFL (type 2 of Matteoni classification) where the main difference is ballooning. Matteoni classification is as follows: type 1 is fatty liver alone; type 2 is fat accumulation and lobular inflammation; type 3 is fat accumulation and ballooning degeneration; type 4 is fat accumulation, ballooning degeneration and either Mallory-Denk bodies or fibrosis.