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Utility of Fully Automated Liver and Spleen Biomarkers for Staging Hepatic Fibrosis in CT

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Introduction/Background

Liver fibrosis can be caused by metabolic disorders (e.g., obesity, Diabetes), alcoholism, or Hepatitis B/C virus. While earlier fibrosis stages are reversible, later stages (advanced fibrosis and cirrhosis) are irreversible. Notably, cirrhosis is the 12th leading cause of death in the US. Biopsies are the gold standard for staging, but they are invasive and prone to sampling error. Consequently, there is a need for non-invasive CT-based biomarkers to distinguish early fibrosis (F0 – F2) from later stages (F3 – F4).

Methods/Intervention

372 patients underwent CT imaging at Institution-A with fibrosis (METAVIR) confirmed through biopsy. An automated deep learning-based model segmented the full liver, 8 liver Couinaud segments, and spleen. Using Couinaud segments 2 and 3, another fully automated technique computed the liver surface nodularity (LSN) score (defined as the smoothness of liver surface). Additionally, CT-based biomarkers, such as volume and attenuation, were also calculated for the full liver, 8 segments, and spleen. Liver Segmental Volume Ratio (LSVR) was also calculated as the sum of the volumes of segments 1 – 3 divided by that of segments 4 – 8. The dataset was divided into 80% training (n = 297) and 20% testing (n = 75) set. Univariate and multivariate logistic regression models were trained to stage fibrosis using the biomarkers and LSN. An AUC below 0.6 was considered clinically ineffective.

Results/Outcome

The best univariate models used spleen volume (Cirrhosis AUC = 0.829, Advanced Fibrosis AUC = 0.805) and LSN (Cirrhosis AUC = 0.766, Advanced Fibrosis = 0.695). The best multivariate model for predicting cirrhosis included LSVR, spleen volume, and segmental volume proportions (AUC = 0.927). For advanced fibrosis, the best multivariate model included LSVR, spleen volume, and automated LSN (AUC = 0.839).

Conclusion

The best multivariate models for staging liver fibrosis included LSVR, spleen volume, segmental volume proportions, and automated LSN. The addition of automated LSN score had the greatest impact for prediction of advanced fibrosis.

Statement of Impact

For population-based studies and opportunistic screening, non-invasive CT-based biomarkers may be clinically useful in differentiating advanced fibrosis and cirrhosis from earlier stages. They play a critical role in early interventions to reverse fibrosis and improve patient care.

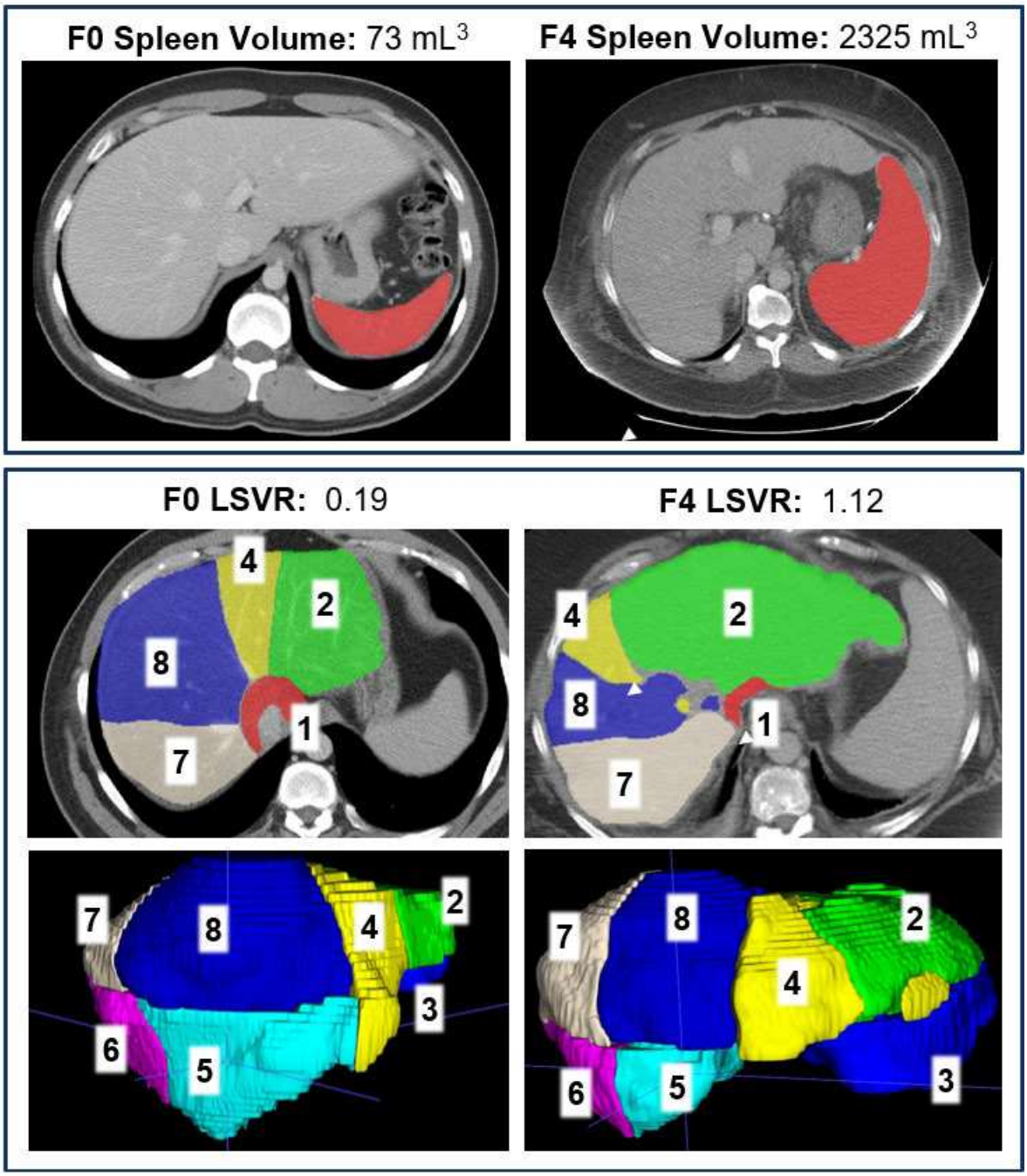

Fig. 1 An internally developed deep learning-based model segmented the spleen (red), liver (not shown), and 8 liver Couinaud segments. Spleen volume (top) and liver segmental volume ratio (LSVR) (bottom) across fibrosis stages. Liver Segmental Volume Ratio (LSVR) was also calculated as the sum of the volumes of segments 1 – 3 divided by that of segments 4 – 8

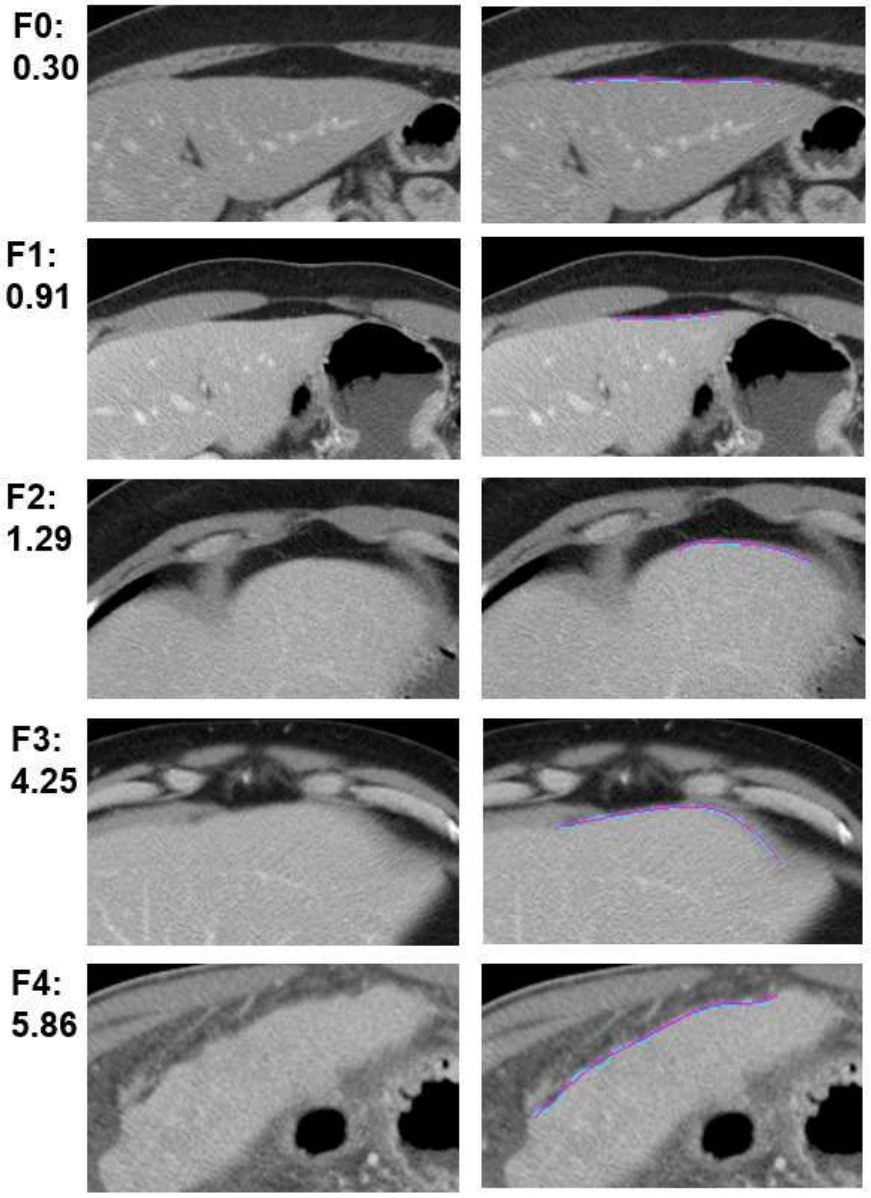

Fig. 2 Liver surface nodularity (LSN) scores depicted for each fibrosis stage. A fully automated pipeline for measuring the liver surface nodularity (LSN) was developed. An internally developed deep learning-based model segmented the full liver (not shown) and 8 Couinaud segments. The extent of the Couinaud segments 2 and 3 were determined, its centroid was found, and projected to the first row of each slice that contained that liver segment. Stemming from this point, radial lines of a length of 512 pixels were cast in the angular range [0, 180] degrees to intersect with the full binary liver segmentation and find the liver surface. Any points detected along the liver surface that fell outside the extent of the Couinaud segments were discarded. The remaining points were stitched together to form a curve (cyan) that ran along the liver edge. A 4^{th} order spline (magenta) that was fit to this surface. The LSN score is the mean distance between the detected and fit surfaces. Note that as the fibrosis stage increases, there is a corresponding increase in the liver surface nodularity.

		Cirrhosis			Advanced Fibrosis		
		AUC	**Sensitivity**	**Specificity**	**AUC**	**Sensitivity**	**Specificity**
Univariate Models	Liver Volume Only	0.506	0.683	0.400	0.613	1.000	0.233
	Liver Attenuation SD Only	0.581	0.883	0.333	0.512	0.311	0.500
	LSN Only	0.766	0.800	0.600	0.695	0.578	0.767
	LSVR Only	0.757	0.800	0.733	0.696	0.800	0.600
	Volume Proportions Only	0.759	0.733	0.733	0.649	0.778	0.533
	Spleen Volume Only	**0.829**	**0.817**	**0.733**	**0.805**	**0.911**	**0.600**
Multivariate Models	LSVR and Spleen Volume	0.900	0.850	0.867	0.831	0.933	0.633
	LSVR, Spleen Volume, and LSN	0.898	0.850	0.867	**0.839**	**0.933**	**0.667**
	LSVR, Spleen Volume, and Volume Proportions	**0.927**	**0.867**	**0.933**	0.810	0.956	0.600
	LSVR, Spleen Volume, Volume Proportions, and LSN	0.926	0.833	0.933	0.805	0.933	0.600
	LSVR, Spleen Volume, Volume Proportions, and Liver Attenuation SD	0.924	0.833	0.933	0.810	0.956	0.600
	LSVR, Spleen Volume, Volume Proportions, Liver Attenuation SD, and LSN	0.923	0.833	0.933	0.804	0.933	0.600

Table 1 Results of predicting cirrhosis and advanced fibrosis using univariate and multivariate models. Area under the receiver operating characteristics curve (AUC), sensitivity, and specificity are determined. Bold font indicates the best results. Of the 372 patients, there were 43 patients in the F0 stage, 52 patients in the F1 stage, 82 patients in the F2 stage, 56 patients in the F3 stage, and 139 patients in the F4 stage. Among the 75 patients in the testing set, there were 15 patients in each fibrosis stage.

Keywords

CT; Liver Fibrosis; Cirrhosis; Liver Segmental Volume Ratio; Liver Surface Nodularity