Body composition predicts mortality and decompensation in compensated cirrhosis patients: A prospective cohort study

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Graphical abstract

Accurate prognosis in cirrhosis is critical to care planning

Automated evaluation of body composition quantity and quality of muscle and fat is a promising tool

Body composition improves risk prediction

Dense fat denotes high risk

Validated in two cohorts

| Cohort               | Model          | C Statistic | Net Reclassification Improvement | P value |
|----------------------|----------------|-------------|---------------------------------|---------|
| Derivation           | MELD and Morphomics | 0.65 (0.58-0.72) | REF                             | 0.05    |
| Validation Cohort    | MELD and Morphomics | 0.70 (0.65-0.76) | REF                             | 0.04    |
| Child A Cirrhosis Subset | MELD and Morphomics | 0.60 (0.43-0.76) | REF                             | 0.304   |
| Compensated Cirrhosis Subset | MELD and Morphomics | 0.68 (0.43-0.75) | REF                             | 0.304   |

Highlights

- Features of body composition can predict clinical outcomes in patients with cirrhosis awaiting liver transplantation.
- Data are lacking regarding long-term outcomes among patients with compensated disease.
- We show that features of muscle and fat are associated with decompensation and risk of death across the spectrum of cirrhosis.
- CT scans obtained for unrelated clinical purposes can be analyzed as a digital risk biomarker for patients with compensated cirrhosis.

Lay summary

Am I at high risk of getting sicker and dying? This is the key question on the mind of patients with cirrhosis. The problem is that we have very few tools to help guide our patients, particularly if they have early cirrhosis (without symptoms like confusion or fluid in the belly). We found that how much muscle and fat the patient has and what that muscle or fat looks like on a CT scan provide helpful information. This is important because many patients have CT scans and this information is hiding in plain sight.

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Body composition predicts mortality and decompensation in compensated cirrhosis patients: A prospective cohort study

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Background & Aims: Body composition, particularly sarcopenia, is associated with mortality in patients with decompensated cirrhosis undergoing transplant evaluation. Similar data are limited for non-transplant eligible or compensated patients.

Methods: A total of 274 patients with cirrhosis were followed prospectively for ≤5 years after a CT scan. We utilized Analytic Morphomics® to measure body composition (fat, muscle, and bone) which was rendered into relative values (percentiles) in relation to a reference population. The model for end-stage liver disease (MELD) score was used as a reference model for survival prediction. We validated our models in a separate cohort.

Results: Our cohort had a mean Child-Pugh score of 7.0 and a mean MELD of 11.3. The median follow-up time was 5.05 years. The proportion of patients alive at 1, 3 and 5 years was 86.5%, 68.0%, and 54.3%; 13 (4.6%) underwent liver transplantation. Child-Pugh B/C (vs. A) cirrhosis was associated with decreased muscle, subcutaneous, and visceral fat area but increased subcutaneous/visceral fat density. Decreased normal density muscle mass was associated with mortality (hazard ratio [HR] 0.984, p < 0.001) as well as visceral and subcutaneous fat density (HR 1.013 and 1.014, respectively, p < 0.001). Models utilizing these features outperformed MELD alone for mortality discrimination in both the derivation and validation cohort, particularly for those with compensated cirrhosis (C-statistics of 0.74 vs. 0.58). Using competing risk analysis, we found that subcutaneous fat density was most predictive of decompensation (subdistribution HR 1.018, p = 0.0001).

Conclusion: The addition of body composition features to predictive models improves the prospective determination of prognosis in patients with cirrhosis, particularly those with compensated disease. Fat density, a novel feature, is associated with the risk of decompensation.

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Introduction

The prevalence of liver disease and cirrhosis has almost doubled in the last decade, resulting in a substantial rise in associated morbidity and mortality.1,2 The end stage of most chronic liver diseases is cirrhosis, which is an important clinical landmark portending increased risk of disability and death.3 Clinical decompensations, such as variceal hemorrhage, ascites and hepatic encephalopathy,4 are the strongest indicators of poor survival (median <2 years).2 By contrast, the median survival of patients with compensated cirrhosis is greater than 12 years, indicating substantial clinical heterogeneity despite similar histology.2 The Child-Pugh and model for end-stage liver disease (MELD) scores leverage features of decompensation to provide excellent short-term survival estimates.3,6 However, these indices poorly discriminate survival in patients who have not decompensated. Risk stratification tools for patients with compensated cirrhosis remain an unmet need.

Owing to the centrality of the liver in metabolic and homeostatic processes, predictive power may be available in measures of body composition.7–9 Loss of core muscle mass (sarcopenia),8,10–13 and other body features such as adiposity and bone density,14–17 have been associated with mortality in transplant-eligible patients with decompensated cirrhosis or liver cancer. Data are limited regarding the prognostic role of body composition in compensated and transplant ineligible patients. Herein, we utilize a novel methodology (Analytic Morphomics®) to examine whether multiple measures of body composition are predictive of survival in patients prospectively followed in a general Hepatology clinic.

Patients and methods

Patient cohorts

Herein, we included the cohort of cirrhosis patients seen at the University of Michigan Hepatology Clinic who were enrolled prospectively in a chronic disease monitoring system (Avitracks, Avicenna Medical Systems, https://www.avicenna-medical.com)18 from March 1, 2010 to July 30, 2015, and who received
an abdominal or chest CT within 365 days of enrollment. Patients were enrolled in the program when they received a diagnosis of cirrhosis based on imaging, laboratory and/or histological parameters from a board-certified gastroenterologist and were followed clinically thereafter (Fig. S1). A validation cohort was constructed using an automated search of our hospital’s clinical data repository for patients evaluated between January 1, 2004 and March 31, 2012, yielding 78 patients who had a CT scan and liver biopsy consistent with cirrhosis within 6 months of each other. All demographic and clinical details were extracted from the chart review; death was confirmed with the national death index and baseline data was obtained within 6 months of the CT date. There were 6 patients who overlapped with the derivation cohort and were excluded (Table S1). In the subset analysis of patients with compensated cirrhosis, decompensation was defined as the development of ascites, hepatic encephalopathy, or variceal bleeding. Those patients who were on diuretics underwent chart review by a hepatologist for the cause for diuretic use. If there was any indication that the diuretics were used for ascites or hydrothorax, this was considered as a decompensating event. For those who received diuretics for edema alone, if the dose was equivalent to less than 40 mg of furosemide, this was considered diuretics as used for other causes. The Institutional Review Board at the University of Michigan Health System approved this study.

Analytic Morphomics®

Body composition features were analyzed in CT studies, using Analytic Morphomics® as previously described.19-21 Briefly, the de-identified imaging files were loaded into the Analytic Morphomics® server. Using semi-automated high-throughput methodology, scan processing and analysis were performed with algorithms programmed in MATLAB® (MathWorks Inc., Natick, MA). The initial processing step was the semi-automated identification of spinal vertebral levels which served as the anatomical reference system for subsequent analyses. This “anatomic indexing” allowed for precise measurements for each individual that could be compared to the remainder of the sample or population-based standards.20 For this study, we examined only measurements that were made from the bottom of the T12 vertebra to maximize the number of clinically available CT images for future studies as T12 was most likely available from scans of both the chest and abdomen. The relational geometries that formed the basis of all morphomic variables were saved in Postgresql and subsequently retrieved to calculate several shape and pixel-based measurements. Descriptions of the analytic morphomic measurements used for this study can be found in the online data dictionary (http://www.med.umich.edu/surgery/morphomics/data_dictionary). For low vs. normal muscle density, we used previously published criteria; between 0-30 Hounsfield units (HU) vs. 31-100 HU, respectively.22 Because age and gender could be confounding factors for body compositions, all direct morphomic measurements were matched to a reference population to generate the age and gender matched percentile for each measurement (Fig. 1). The reference population (Reference Analytic Morphomics Population-RAMP® version 0.0.5) consists of over 6,000 patients who underwent CT scans for trauma indications at the University of Michigan.23

Statistical analysis

The primary outcome was mortality (index from the date of the CT), which was censored at the last documented clinical visit or liver transplantation. Only 1 CT was used per patient. Prognostic models of transplant-free survival were developed using Cox proportional hazard regression analysis. Seven morphomic variables (normal density dorsal muscle, low density dorsal muscle, subcutaneous fat area, subcutaneous fat density, visceral fat area, visceral fat density and bone mineral density) were selected a priori as the initial input of the multivariate analysis based on clinical judgement of significance. They also represent measurements from different body composition groups (muscle, fat and bone). The final predictive model was then developed using forward/backward selection under the Cox regression framework with MELD and morphomic variables in considerations, which optimizes the Akaike information criterion (AIC).24 The statistical comparison was conducted between this final predictive model and the MELD model which serves as a reference model. The performance of the models was assessed with C-statistics using the method described by Uno et al., as this methodology was less sensitive to censoring than Harrell’s C-statistics.25 We also assessed whether the addition of morphomic features improved prediction accuracy by using a modification of the continuous net reclassification improvement (NRI) methodology that allowed for the censored data analysis.26 The continuous NRI does not require risk stratification into categories compared with the traditional category-based NRI. We chose to use the continuous NRI since, to our knowledge, there is no consensus categorization of mortality risk in patients with liver diseases. The continuous NRI was obtained using the Hmisc package for the R statistical program.27 To test the generalizability of our model, we examined its performance in an external validation cohort of biopsy proven cirrhosis patients. We also provide the additional measures of the model’s performance in discrimination (Gonen and Heller’s x statistics and Royston and Sauerbrei’s D statistics),28,29 calibration (Calibration Slope),30 and accuracy (Integrated Brier’s Score).31 The Gonen and Heller’s x statistics is a measure of concordance that is robust to censoring and thus may be preferred to Harrell’s C index for survival data.

As a secondary analysis, we also investigated the morphomic predictors of decompenation. The Fine-Grey competing-risk regression analysis was employed to investigate predictors of the cumulative incidences of liver decompensations and non-liver disease-related deaths.24 All statistical analyses were performed using R 3.1.0 with packages glmnet, Hmisc, rms, and survIDINRI.

Results

Cohort characteristics

The baseline characteristics of our study population of 274 patients are detailed in Table 1. In brief, our patients were aged 58 years on average and 56% were male. Overall, 89 (32%) had NAFLD, the mean Child-Pugh score was 7.0 (130 [47%] were Class A), and the mean MELD-Sodium was 12.7 and the average patient was obese (mean body mass index was 30.2). At baseline, 163 (59.4%) had at least 1 decompensation (variceal bleed, ascites or hepatic encephalopathy) episode. Table S1 details the clinical characteristics of our validation cohort.

The median follow-up time was 1,844 days or approximately 5 years in the derivation cohort. Overall, 114 (41.6%) patients died and 13 (4.6%) underwent liver transplantation during the follow-up period. Survival was 86.5% at 1 year, 68.0% at 3 years, and 54.3% at 5 years. Of the 111 patients who were compensated...
at baseline, 23 (20.7%) developed an episode of decompensation during follow-up. In the validation cohort, the median follow-up time was 848 days. Overall, 45 (58%) patients died during follow-up and none were transplanted.

Baseline features of body composition measured with Analytic Morphomics®

Table 2 summarizes the morphomic features of our cohort. Patients with cirrhosis have markedly lower levels of normal density muscle mass than age- and sex-matched controls from the reference population, a distribution which worsens with progressive liver disease (Fig. S2). As liver disease progresses, the quantity of visceral and subcutaneous fat decreases, while their density increases (Fig. S3). Bone density showed a trend towards lower density in Child-Pugh B/C patients which was not significant.

Baseline features of body composition measured with Analytic Morphomics®

Table 2A,B presents body morphomic features in patients with different clinical characteristics. In Table S2A, we note that at baseline, 23 (20.7%) developed an episode of decompensation during follow-up. In the validation cohort, the median follow-up time was 848 days. Overall, 45 (58%) patients died during follow-up and none were transplanted.
Table 2. Body composition features in Child-Pugh A vs. Child-Pugh B/C patients.

| Body component | Description | Overall | Child A (n = 130) | Child B-C (n = 144) | p value |
|----------------|-------------|---------|------------------|---------------------|---------|
| Low density muscle | Total low density (between 0–30 HU) muscle area | 62.0 ± 27.0 | 59.4 ± 30 | 64.3 ± 24.6 | 0.14 |
| Normal density muscle | Total normal density (between 31–100 HU) muscle area | 33.0 ± 27.2 | 38.3 ± 27.2 | 28.4 ± 26.5 | 0.002 |
| Total muscle area | Total dorsal muscle group area | 39.1 ± 29.2 | 44.6 ± 29.5 | 34.3 ± 28.2 | 0.003 |
| Low density:Normal density muscle Ratio | Ratio of low-density area relative to normal density | 0.46 ± 0.42 | 0.40 ± 0.32 | 0.51 ± 0.48 | 0.04 |
| Visceral fat area | Area of fat within the visceral cavity | 42.8 ± 26.9 | 47.4 ± 27.5 | 38.6 ± 25.8 | 0.007 |
| Visceral fat density | Median pixel HU of fat HU range of pixels inside the visceral cavity. | 68.7 ± 28.4 | 55.6 ± 29.6 | 80.9 ± 21.0 | <0.0001 |
| Subcutaneous fat area | Area of fat between skin and fascia | 51.8 ± 30.6 | 63.1 ± 28.3 | 48.8 ± 31.2 | <0.0001 |
| Subcutaneous fat density | Median pixel HU of fat HU range of pixels in the fat between skin and fascia. | 51.7 ± 32.8 | 37.8 ± 29.1 | 64.2 ± 30.9 | <0.0001 |
| Bone mineral density | Average pixel HU inside a central area of trabecular bone | 42.2 ± 29.0 | 44.8 ± 30.5 | 39.9 ± 27.5 | 0.16 |

All values are mean percentiles (± SD) for age- and sex-matched population-based estimates. The p values are obtained from 2-sample t test. HU, Hounsfield unit.

Table 3. Cox regression to assess predictors of mortality in patients with cirrhosis (n = 274).

| Variable | Cox univariate HR (95% CI) | p value |
|----------|---------------------------|---------|
| MELD     | 1.09 (1.06–1.13)          | 1.06 × 10^-3 |
| Low density muscle | 1.004 (0.997–1.011) | 0.28 |
| Normal density muscle | 0.984 (0.976–0.992) | 0.0002 |
| Visceral fat area | 0.994 (0.987–1.001) | 0.108 |
| Visceral fat density | 1.014 (1.006–1.023) | 0.0005 |
| Subcutaneous fat area | 0.993 (0.986–1.000) | 0.04 |
| Subcutaneous fat density | 1.013 (1.007–1.019) | 3.19 × 10^-3 |
| Bone mineral density | 0.993 (0.987–1.000) | 0.07 |

For all the morphomic features, the HR is represented by each percentile of change. HR, hazard ratio; MELD, model for end-stage liver disease.

Patients with a diagnosis of NAFLD-related cirrhosis had very significant differences in the fat compartments compared to those without NAFLD. In Table S2B, we note that baseline morphomic features of patients with and without a history of decompensation were also markedly different. We found that patients with ascites had significantly less normal density muscle and less fat (visceral and subcutaneous fat), but fat density was increased. Patients with hepatic encephalopathy demonstrated similar declines in high quality muscle, specifically a trend towards decreased normal density muscle and an increase in low density muscle. While hepatic encephalopathy was not associated with diminished abdominal fat area, there was a striking increase in fat density, a consistent feature of worsening liver disease.

Body composition is predictive of mortality in patients with cirrhosis

In addition to MELD (HR 1.07), features of body composition were also associated with mortality using univariate Cox proportional hazards regression (Table 3). These included normal density muscle mass (HR 0.984), visceral fat density (HR 1.014) and subcutaneous fat density (HR 1.013). To determine if these morphomic features might be incrementally helpful to MELD in discriminating survival in cirrhosis patients, we used backward and forward selection to develop the best predictive model (Table 4). A priori, we utilized 7 morphomic features (normal density dorsal muscle, low density dorsal muscle, subcutaneous fat area, subcutaneous fat density, visceral fat area, visceral fat density and bone mineral density) as input variables because they represented features which might have clinical significance and represent different body composition groups. As shown in Table 4, the final model included MELD, normal density muscle, subcutaneous fat density and bone density (c-statistic 0.70). MELD-alone yielded a c-statistic of 0.65. To assess model performance, we calculated the net reclassification improvement (NRI) and found that addition of morphomic measures outperformed MELD alone in accuracy (NRI 0.305, p <0.0001). We then externally validated this model in a different cohort of patients with biopsy-proven cirrhosis and found similar improvements. To further assess the models, we utilized Conen and Heller’s k statistics and Royston and Sauerbrei’s D statistics to measure discrimination and calculated the calibration slope on both the derivation and validation cohorts. Overall prediction accuracy was evaluated using the integrated Brier score. In all cases, the models with morphomic features performed favorably compared to MELD alone (Table S3).

Body composition predicts survival in patients with Child-Pugh A cirrhosis

We then examined the subset of patients within our cohort who had Child-Pugh A cirrhosis (Table S4). Our best multivariate model did not include MELD. In the best multivariate models selected, features that were selected included normal density muscle, visceral fat density and subcutaneous fat area. We evaluated model discrimination for mortality and the models which had morphomic features markedly outperformed MELD (Table 4). Because not all patients with Child-Pugh A cirrhosis are considered compensated (i.e. never developed variceal bleed, hepatic encephalopathy, or ascites), we further analyzed the subset of patients in our cohort who did not have a history of decompensation at the index CT. We found 111 patients who were compensated; 99 patients were Child-Pugh A and 12 patients were Child-Pugh B. Similar to the Child-Pugh A patients, prediction models which included morphomic features significantly outperformed MELD (Table 4).

Predictors of decomposition

Recognizing that predicting the likelihood of decomposition in the cohort of patients who are compensated would be an important clinical tool, we examined the risk of decomposition in the subset of patients with compensated cirrhosis. The median follow-up time for the cohort of compensated cirrhosis patients was 1,921 days. At 1,921 days, 11.4% of patients had died and 23.3% of patients had decompenated. To account for
the competitive risk of death, we utilized competing risk regression. Only subcutaneous fat density was significantly associated with mortality, subdistribution HR 1.018 (1.07–1.34) (Table S5). MELD was not associated with the risk of decompensation. Fig. 2 presents a cumulative incidence curve for both outcomes, demonstrating a significant association with fat density.

**Discussion**

Risk assessment is a fundamental part of clinical practice and patient counselling. We have excellent tools such as MELD to predict short-term mortality in patients who present for transplant evaluation. In contrast, tools for patients with compensated cirrhosis are limited. In this study, we show that information on body composition derived using Analytic Morphomics® from incidental CT scans ordered for other clinical purposes, muscle features are an attractive target for refinement. These data extend the literature on the prognosis of cirrhosis and the impact of body composition in several important ways.

**Body composition enhances prognostication in compensated cirrhosis**

First, by providing associations with decompensation and outperforming MELD, these data indicate that body composition data derived from Analytic Morphomics® represent a promising solution for risk prediction in patients with compensated cirrhosis. Several strategies have emerged for compensated patients, albeit with limited outcomes data available for comparison. Portal pressure measurements, for example, accurately predict mortality for compensated patients.34 However, they are invasive, costly, and largely unavailable. Similarly, costly and specialized direct measures of liver metabolic function such as Indocyanine Green clearance are predictive of short-term (i.e. after liver resection) and long-term outcomes in selected cohorts.8,39 It is increasingly recognized that sarcopenia (loss of muscle mass) may have a significant influence on overall mortality.4,30 Given the widespread use of CT scans for clinical purposes, muscle features are an attractive target for refining cirrhosis prognosis. The presence of sarcopenia, adjusting for MELD, has been linked with worsening pre- and post-transplant outcomes in patients with decompensated cirrhosis.6,10 In this prospective cohort study, we confirm that sarcopenia is common in patients with cirrhosis and that progression of liver disease is associated with greater muscle loss, particularly of normal density muscle. However, we also show that other features of body composition are associated with progression of liver disease, including loss of fat and increased fat density. In comparing predictive models, we found that models which included both muscle and fat features showed greater risk-discrimination than MELD alone. We further validated our models in a separate cohort, highlighting the incremental value of body composition measures over liver-specific indices in predicting survival in patients with cirrhosis. As hypothesized, in the subset of patients with Child-Pugh A cirrhosis, the best multivariable model did not select MELD. Furthermore, Analytic Morphomics®, particularly subcutaneous fat density, identified patients at risk of first decompensation.

**Body measurements need not be taken at L3-L4**

Second, our validated body composition features were obtained from the T12 level. Whereas nearly all studies of body composition in cirrhosis utilize measures obtained at L3-L4,8,37,39–42 by using features from a higher vertebral level we expand the number of CT scans (i.e. chest or abdominal-alone vs. abdominopelvic) that can be utilized for prognostic purposes. Previous

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Table 4. Summary statistics for mortality risk prediction in all patients with cirrhosis.

| Cohort                        | Model                  | C-statistics  | Net reclassification improvement | p value |
|-------------------------------|------------------------|---------------|----------------------------------|---------|
| Derivation                    | MELD                   | 0.65 (0.58–0.72) | Ref.                             | <0.0001 |
|                               | MELD and Morphomics    | 0.70 (0.65–0.76) | 0.305                            |         |
| Validation cohort             | MELD                   | 0.67 (0.57–0.76) | Ref.                             |         |
|                               | MELD and Morphomics    | 0.69 (0.58–0.79) | 0.219                            | 0.04    |
| Child-Pugh A cirrhosis subset | MELD                   | 0.60 (0.43–0.76) | Ref.                             |         |
|                               | MELD and Morphomics    | 0.75 (0.59–0.92) | 0.346                            | 0.0004  |
| Compensated cirrhosis subset  | MELD                   | 0.58 (0.42–0.75) | Ref.                             |         |
|                               | MELD and Morphomics    | 0.63 (0.58–0.75) | 0.346                            | 0.0001  |

The derivation cohort represents all patients who were prospectively followed in general hepatology clinic as described in Table 1. The validation cohort represents all patients in a separate cohort of patients with biopsy proven cirrhosis identified retrospectively using an automated search of the medical record as described in Table S1. MELD, model for end-stage liver disease.

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Fig. 2. Subcutaneous fat density is associated with first decompensation. In this cumulative incidence curve, individuals with a subcutaneous fat density greater than the median (68.3 Hounsfield units) had a higher risk of decompensation or death. The y-axis represents the proportion of patients experiencing a decompensation.
studies have shown that multiple muscle areas such as psoas muscle at L4 and skeletal muscle at L3 were predictive of survival in cirrhotic patients undergoing liver transplantation.4,42 We have previously shown a high correlation in muscle measurements from healthy kidney donors between T12 and L3-L4.43,44 We also note that there is strong correlation between body composition measurements between T12 and L3 in our cohort (data not included). Thus it is perhaps not surprising that measurements at T12 could also predict mortality in liver transplantation40 and in this paper we further expand on this body of data that morphomic features at T12 can be predictive of survival and decomposition in patients with compensated cirrhosis.

The importance of muscle and fat quality (in addition to quantity)

Third, we expand the concept of body composition’s relationship with risk to include tissue quality. We show that fat density and muscle density are associated with specific cirrhotic complications and mortality. For example, given the metabolic functions of muscle in ammonia homeostasis,46 hepatic encephalopathy (HE) should be associated with sarcopenia. However, rather than total muscle area, we find that HE is associated with predominant lower quality (low-density) muscle. We also report novel data regarding density as a predictor for mortality. Previous retrospective studies have associated fat quantity with clinical outcomes by measuring adipose tissue area in imaging studies.45,47 We show that in addition to area, the density of both visceral and subcutaneous fat was associated with complications such as ascites and encephalopathy. Increased subcutaneous fat density was the single best predictor for decomposition. These data suggest that changes in the adipose compartment, which may not be otherwise appreciated, occur with progression of liver disease. Increased density may reflect edema. Since fat is less dense than water, edema within this compartment would increase the density of fat. Alternatively, increased inflammatory burden would appear the same way. Although, the mechanism for fat density’s association with risk requires further study, both edema (vis-a-vis portal hypertension) and inflammation are plausible candidates. These data also confirm similar findings from our study of patients with hepatocellular carcinoma undergoing transarterial chemoembolization,42 as well as a study linking mortality with increased fat density both in the visceral and subcutaneous compartments of elderly (non-cirrhotic) patients.40 Taken together, these findings suggest that fat density may be an important radiographic biomarker that warrants investigation.

Contextual factors

These data must be interpreted in the context of the study design. First, the use of CT scan with contrast restricts the cohort to one with relatively preserved renal function which may influence outcomes. Second, in contrast to other studies of CT-defined sarcopenia, our morphomic features can be both handled as continuous variables and in reference to population norms. Many studies have examined the prognostic importance of psoas muscle area and used specific cut-offs to define sarcopenia.35 Statistically optimal cut-offs for sarcopenia derived from single center studies are fundamentally confounded, reflecting the local demographics, management decisions, and secular trends that drive clinical outcomes.39 Conversely, our study renders all morphomic features into percentiles from generalizable population norms taken from a repository of over 4,000 CT scans obtained from a random population of patients. Third, all values evaluated are taken at baseline. Further study is underway to determine the role of longitudinal assessment of Analytic Morphomics®.

Conclusion

Body composition features derived with Analytic Morphomics® are predictive of clinical outcome in a prospective cohort that adjusts for conventional predictors. For patients with chronic liver disease who have received CT scans for clinical purposes, our findings clearly indicate that important prognostic information is waiting for extraction.

Abbreviations

HE, hepatic encephalopathy; HR, hazard ratio; HU, Hounsfield units; INR, international normalized ratio; MELD, model for end-stage liver disease; NRI, net reclassification improvement.

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Conflict of interest

The University of Michigan has 2 patents relating to the process of analytic morphomics. GLS is a co-inventor on one of these patents. Elliot Tapper has served as consultant to Norvartis and Allergan, has served on advisory boards for Mallinckrodt and Bausch Health, and has received unrestricted research grants from Gilead and Valeant. No other author has any conflicts of interest. Please refer to the accompanying ICMJE disclosure forms for further details.

Authors’ contributions

Dr Su is the guarantor of this article. Concept: Su, Tapper. Analysis: Tapper, Su, Zhang. Data acquisition: Su, Tapper, Nault, Garg, Leary, Krishnamurthy. Writing: Tapper, Su. Critical revision: Zhang, Nault, Garg, Leary, Krishnamurthy.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhepr.2019.11.005.

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