

# Role of Visceral Adiposity in the Pathogenesis of Non-Alcoholic Fatty Liver Disease in Lean versus Obese Patients: A Comparative Study between Patients at UMHS versus PUHSC

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# Background

- Nonalcoholic fatty liver disease (NAFLD) is a spectrum of liver disease ranging from steatosis to steatohepatitis (NASH) and cirrhosis and is an increasing cause of hepatocellular carcinoma worldwide.
- Global prevalence of NAFLD is increasing rapidly due to the epidemic of obesity and diabetes.
- Prevalence of NAFLD among adults is estimated to be 30% in the United States and 15% in China.
- Major causes of NAFLD are obesity, diabetes and insulin resistance.
- NAFLD may be present in lean persons, particularly Asians.



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# NAFLD in Lean Persons

- Prevalence of NAFLD in lean Chinese reported to be 7-18%.
- ~30% lean NAFLD persons have central obesity and lean NAFLD persons are more likely to have hypertension, diabetes, metabolic syndrome and central obesity than lean persons with no NAFLD.
- Central obesity correlates better with diabetes, metabolic syndrome and NAFLD than overall obesity.
- Central obesity is associated with higher risk of myocardial infarction and all-cause mortality.



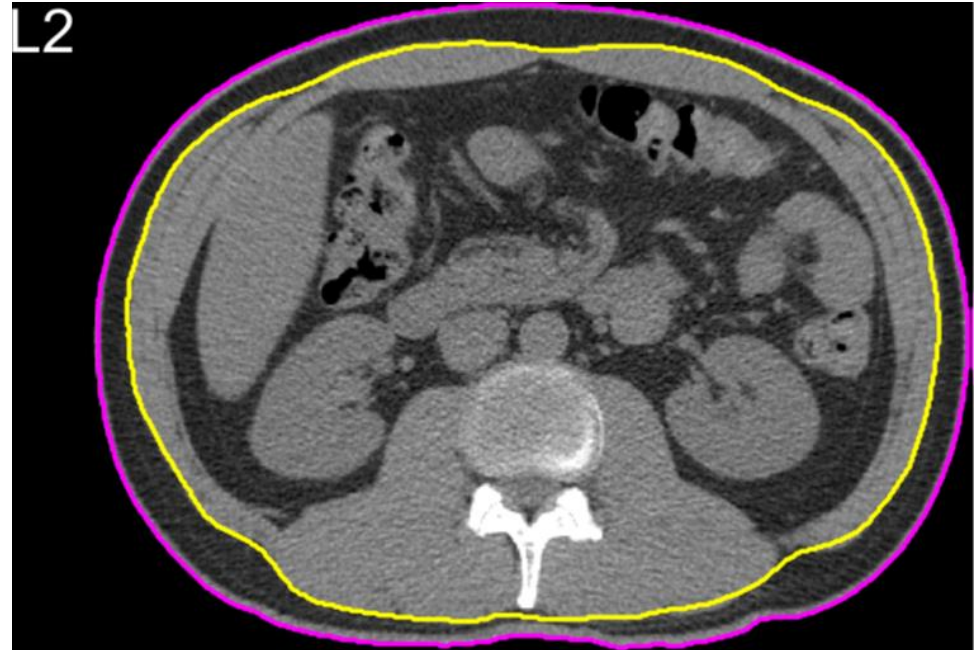
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# Is Waist Measurement an Accurate Measure of Visceral Adiposity?



Waist measurement includes subcutaneous and visceral fat, muscles, bones, abdominal organs, and intestine



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# Aims

- Primary goal – to understand the pathogenesis of NAFLD in lean Chinese
- Aims:
  - Compare quantity and quality of visceral adipose tissue (VAT) and ectopic adipose tissue (EAT) in lean NAFLD vs. lean control vs. obese NAFLD
  - Determine whether quantity and quality of VAT and EAT are better predictors of metabolic abnormalities than BMI
  - Determine whether models that include data on the quantity and quality of VAT and EAT determined by analytic morphomics outperform models that include only routinely available demographics, anthropometrics and laboratory data in predicting risk of NAFLD and metabolic abnormalities



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# Study Design

- Parallel cohorts enrolled at UMHS and PUHSC
- 3 groups at each site: lean and obese NAFLD and lean no NAFLD
- 80 per group at PUHSC and 40 per group at UMHS
- Anthropometrics, metabolic and liver disease assessment: clinical, labs, ultrasound and vibration controlled transient elastography
- Non-contrast limited abdominal CT scan – analytic morphomics to
  - Confirm diagnosis of NAFLD
  - Assess stage of liver disease
  - Measure quantity and quality of fat

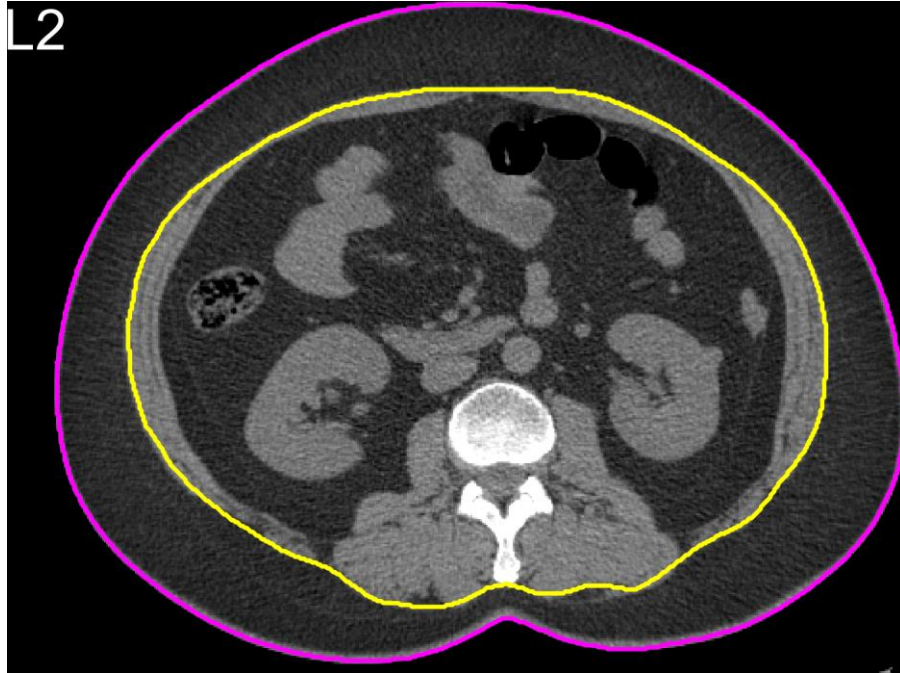


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# CT Scan of Lean NAFLD and Lean Control



Lean NAFLD



Lean Control

Lean NAFLD have more visceral fat than lean control with no NAFLD

# Enrollment 6/2016-8/2017

No. enrolled	UM	PKU
Lean Control	0	36
Lean NAFLD	3	61
Obese NAFLD	43	60

Target – 40 in each group at UM and 80 in each group at PKU

NAFLD – diagnosed by biopsy or imaging

Controls = no history of DM or liver disease, HBsAg-, anti-HCV-,  
no hepatic steatosis on ultrasound



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# Barriers to Implementation of Protocol

- Difficulty finding lean NAFLD that meet enrollment criteria at UM site, protocol had to be revised to allow NAFLD patients with any BMI to be enrolled and abandonment of lean controls
- Difficulty having UM Radiology Department follow CT scan protocol for this study despite clear instructions
- PKU server having intermittent problems preventing timely entry of data into database (REDCap)



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# Characteristics of UM vs. PKU NAFLD Patients

	UM (n=43)	PKU (n=106)
Sex, % men	41.9	51.9
Mean age, years	49.7 ± 12.4	46.0 ± 11.5
BMI, kg/m <sup>2</sup>	35.3 ± 5.5	27.2 ± 4.6
% Truncal obesity	88.4	62.3
% Diabetes	44.2	25.5
% Metabolic syndrome	81.4	42.5



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# Characteristics of PKU Patients

	Lean Control (n=31)	Lean NAFLD (n=49)	Obese NAFLD (n=57)
Age, years	45 (35-53)	48 (40-58)	44 (34-54)
Sex, men	14 (45.2)	22 (44.9)	33(57.9)
BMI, kg/m <sup>2</sup>	22.0 (20.6-23.1)	22.9 (21.9-23.7)	30.4 (29.2-32.9)
Waist circumference, cm	75.0 (69.0-83.0)	80.0 (76.0-83.5)	98.0 (93.5-104.5)
Truncal obesity	3 (9.7)	10 (20.4)	56 (98.2)
Diabetes	0	11 (22.4)	16 (28)
Metabolic syndrome	1 (3.2)	6 (12.2)	39 (68.4)

Data expressed as no. (%) or median (IQR)



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# Fat Deposition in PKU Patients

	Lean Control (n=31)	Lean NAFLD (n=49)	Obese NAFLD (n=57)
Liver HU	61.9 ± 3.2	48.5 ± 11.4	40.3 ± 12.1
Liver/spleen HU ratio	1.3 ± 0.1	1.0 ± 0.2	0.9 ± 0.3
Subcutaneous Fat area, cm <sup>2</sup>	99.2 ± 38.6	108.1 ± 37.8	204.5 ± 55.3
Visceral Fat area, cm <sup>2</sup>	77.6 ± 42.4	127.1 ± 45.8	213.1 ± 79.2
Visceral Fat HU	-99.5 ± 6.3	-106.3 ± 2.4	-108.3 ± 3.1
Muscle HU	33.7 ± 7.9	33.1 ± 6.7	52.9 ± 13.4
Low density / total muscle area (%)	27.8 ± 8.1	30.5 ± 6.8	35.4 ± 7.7

Data expressed as mean±SD

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# Summary

- Pure lean NAFLD uncommon in the US
- Chinese lean NAFLD
  - More metabolic abnormalities and visceral (but not subcutaneous) fat than lean controls
  - Similar prevalence of diabetes and other metabolic abnormalities as obese NAFLD
  - Less fat (liver, subcutaneous, visceral, and muscle) than obese NAFLD

See poster showing comparisons between patients with and without metabolic syndrome



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# Visceral Fat and Myosteatorsis in PKU Lean vs. Obese NAFLD

