Metabolic Outcomes of Aging and Obesity: A Longitudinal Study of the Dallas Heart Study Cohort

Parker Davis, Takeshi Yokoo MD, PhD

Department of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas

Introduction

Sequestration of fat into subcutaneous and intra-abdominal (visceral) compartments influences metabolic outcomes. Visceral fat contains more proinflammatory cytokines, and is more metabolically active, with a greater propensity for lipolysis. It is associated with hypertriglyceridemia, increased VLDL synthesis, liver insulin resistance, and reduced HDL cholesterol, and more strongly predicts mortality (Browning et al., 2004; Chalasani et al., 2018). Additionally, the risk of developing cardiovascular disease, type 2 diabetes, and Non-Alcoholic Fatty Liver Disease (NAFLD) is correlated with visceral adiposity (Lee et al., 2016; Neeland et al., 2013; Iwasa et al., 2011).

Objectives

The purpose of this study is to examine obesity phenotypes in subjects of the Dallas Heart Study (DHS1 1999-2000) and extend the findings in the prospective, longitudinal Dallas Heart Study Phase 3 (DHS3, a.k.a. Dallas Heart and Minds Study, 2020-). This will enable the effects of changes in obesity phenotypes to be tracked over a 20-year period. We hypothesized that visceral adiposity increases with age and predicts the development of cardiovascular disease and the metabolic syndrome.

Cohort Characteristics of Dallas Heart Study Interim Study

N = 135	DHS1 (1999-2000)	DHS3 (2020-)
Gender	F – 71 (52%) M – 65 (48%)	n.a.
Ethnicity	White – 84 (62%) Black – 37 (27%) Hispanic – 14 (10%) Other – 1 (1%)	n.a
Age (years)	43 [37, 50]	63 [57, 70]
BMI (kg/m^2)	28.9 [25.0, 32.8]	29.5 [26.5, 32.7]
Obesity rate (%)	41.9	43.6
HOMA IR	2.1 [1.1, 3.8]	1.1 [0.0, 2.8]
MetS rate (%)	52.6	62.2
SAT @ L2-3 (cm^2)	156.5 [104.8, 216.5]	183.0 [129.9, 241.6]
VAT @ L2-3 (cm^2)	199.0 [132.8, 302.8]	288.94 [199.5, 366.2]

MetS – metabolic syndrome, defined as having ≥3 metabolic risk factors (truncal obesity, hypertension, high cholesterol, high triglyceride, high fasting glucose). SAT – subcutaneous adipose tissue. VAT – visceral adipose tissue. TAT – total adipose tissue

Methods

- In this interim analysis, we included DHS3 subjects who have completed whole-body MRI in DHS3 and also had abdominal MRI in DHS1
- We included subjects who were former DHS1 subjects who had an abdominal MRI in DHS1 and whole-body MRI in DHS3
- In DHS1, contiguous 10mm-thick 2D axial images were acquired on a Philips 1.5T MRI system from diaphragm to pelvis
- In the original DHS1, manual adipose tissue segmentation was performed on a single slice at L2-L3 (Medis Mass software). Subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and total adipose tissue (TAT) cross-sectional areas were measured
- In the current DHS3, contiguous 5mm-thick 3D axial images were acquired from neck to mid-thigh on a Siemens 3T MRI system. SAT, VAT and TAT segmentations were performed on the slice corresponding with each subject's DHS1 segmentation (Horos)
- Changes in SAT, VAT, and TAT areas between DHS and DHMS were calculated to study association with the effects on metabolic syndrome

Risk Factors of Metabolic Syndrome Development*

Variable	Odds Ratio [95% CI]	p-value
Baseline weight	1.04 [1.01, 1.07]	0.0178*
Change in weight	1.11 [1.06, 1.17]	< 0.001**
Baseline BMI	1.10 [1.01, 1.21]	0.040*
Change in BMI	1.34 [1.17, 1.55]	< 0.001**
Baseline HOMA-IR	1.34 [1.03, 1.81]	0.041*
Change in HOMA-IR	1.43 [1.14, 1.89]	0.006**
Baseline SAT @ L2/3	1.00 [0.99, 1.01]	0.215
Change in SAT @ L2/3	1.00 [1.00, 1.01]	0.039*
Baseline VAT @ L2/3	1.01 [1.00, 1.02]	0.029*
Change in VAT @ L2/3	1.02 [1.01, 1.03]	<0.001**
Baseline TAT @ L2/3	1.00 [1.00, 1.01]	0.042*
Change in TAT @ L2/3	1.01 [1.00, 1.01]	<0.001**
Baseline VAT/SAT	1.74 [0.61, 5.40]	0.310
Change in VAT/SAT	1.74 [0.56, 5.88]	0.350

SAT – subcutaneous adipose tissue. VAT – visceral adipose tissue. TAT – total adipose tissue. Odds ratio (and 95% confidence interval) have been adjusted for the presence of metabolic syndrome at baseline and gender.

Results

135 DHS3 subjects have been included in this interim analysis. Subjects had an average weight gain of +1.245kg over 20 years, BMI increased by +0.792kg/m^2, SAT increased +67cm^2, and VAT increased by +31 cm^2. The change in body weight was significantly correlated with changes in SAT (Pearson r=0.74, p=0) and VAT (Pearson r=0.59, p=0). Changes in SAT and VAT were correlated (Pearson r=0.23, p=0.006). DHMS subjects with HOMA-IR >2.73 during DHS1/2 had significant percent decreases in weight (p=0.003), subcutaneous adiposity (p<0.001), and visceral adiposity (p<0.001), in contrast to the trends described above.

Logistic regression analysis was conducted to predict the development of metabolic syndrome in DHS3, adjusted for gender and baseline metabolic syndrome in DHS1. Though all obesity phenotypes had statistically significant association with metabolic syndrome, gain in weight, Body Mass Index (BMI) and HOMA-IR had larger effect sizes (Odds Ratio 1.1 – 1.4) than the abdominal adipose tissue compartments (Odds Ratio 1.0 – 1.1). No statistically significant association with metabolic syndrome was found for visceral-to-subcutaneous adipose tissue ratio.

Conclusion

In this interim analysis of DHS3 (a.k.a. Dallas Heart and Minds Study), worsening of obesity is associated with increased risk of metabolic syndrome, independent of having metabolic syndrome at the baseline 20 years prior. Gain in abdominal adipose tissue was associated with metabolic syndrome, but its effect size was small, and specific compartments (visceral vs. subcutaneous) of fat deposition may not be important. These analyses will be repeated with the full cohort of DHS3 (~2000 subjects planned).

References

1. Abate, N., A. Garg, R. Coleman, S. M. Grundy, and R. M. Peshock. 1997. 'Prediction of total subcutaneous abdominal, intraperitoneal, and retroperitoneal adipose tissue masses in men by a single axial magnetic resonance imaging slice', *Am J Clin Nutr*, 65: 403-8.
2. Browning, J. D., L. S. Szczepaniak, R. Dobbins, P. Nuremberg, J. D. Horton, J. C. Cohen, S. M. Grundy, and H. H. Hobbs. 2004. 'Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity', *Hepatology*, 40: 1387-95
3. Chalasani, N., Z. Younossi, J. E. Lavine, M. Charlton, K. Cusi, M. Rinella, S. A. Harrison, E. M. Brunt, and A. J. Sanyal. 2018. 'The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases', *Hepatology*, 67: 328-57.
4. Iwasa, M., R. Mifuji-Moroka, N. Hara, M. Ishidome, K. Iwata, R. Sugimoto, H. Tanaka, N. Fujita, Y. Kobayashi, and Y. Takei. 2011. 'Visceral fat volume predicts new-onset type 2 diabetes in patients with chronic hepatitis C', *Diabetes Res Clin Pract*, 94: 468-70.
5. Lee, J. J., A. Pedley, U. Hoffmann, J. M. Massaro, and C. S. Fox. 2016. 'Association of Changes in Abdominal Fat Quantity and Quality With Incident Cardiovascular Disease Risk Factors', *J Am Coll Cardiol*, 68: 1509-21.
6. Neeland, I. J., C. R. Ayers, A. K. Rohatgi, A. T. Turer, J. D. Berry, S. R. Das, G. L. Vega, A. Khera, D. K. McGuire, S. M. Grundy, and J. A. de Lemos. 2013. 'Associations of visceral and abdominal subcutaneous adipose tissue with markers of cardiac and metabolic risk in obese adults', *Obesity (Silver Spring)*, 21: E439-47.