CARDIOMETABOLIC RISK: INDEPENDENT ROLE OF VISCERAL AND LIVER FAT

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ABSTRACT

It is known that visceral adiposity is closely related to cardiometabolic abnormalities and visceral fat accumulation leads to drainage of free fatty acids (FFA) to liver via portal vein. This in turn leads to hepatic insulin resistance, increased intra-cellular triglyceride (TG) content, and increased synthesis and secretion of atherogenic lipoproteins. Studies have shown that only 15% of FFA delivered to the liver comes from visceral adipose tissue, while remainder comes from larger subcutaneous fat depot. It is also reported that subcutaneous fat has minimal association with cardiometabolic risks. Independent association of visceral fat and liver fat with cardiometabolic risks (CMR) is not yet clear. This review summarizes all available evidences obtained in clinical studies using computed tomography (CT) and magnetic resonance imaging (MRI) indicating independent association of visceral and liver fat with CMR. Currently, MRI is considered to be the 'gold standard' technique for determining abdominal fat measures non-invasively. Observations from the studies using two different imaging techniques yields contradictory results by far; with MRI based studies showing liver fat to be stronger predictor of CMR than visceral fat as against the results from CT based studies. Further, the review highlights on the dearth of similar evidences with respect to Indian population considering ethnic differences in abdominal fat accumulation and concludes with the gap in existing research.

KEYWORDS: Visceral fat, subcutaneous fat, cardiometabolic risk, computed tomography, magnetic resonance imaging.

INTRODUCTION

For management of low-density lipoprotein cholesterol (LDL-C), blood pressure (BP) and glycaemia, standard treatment methodology is available. However, in predisposed patients, the "residual risk" of vascular events still persists. Statin use has impressively reduced the levels of LDL-C but has shown moderate reduction in total mortality,[1] Cardiometabolic risk (CMR) is the overall risk of cardiovascular disease (CVD) and diabetes resulting from the presence of traditional and non-traditional risk factors. Traditional risk factors involved are age, race, gender, smoking, hypertension, high cholesterol and family history whereas non-traditional risk factors are obesity, insulin resistance, dyslipidemia, dysglycemia and hypertension.[2] The pathophysiology underlying CMR is complex and has only been partially revealed.[3] There are considerable evidences supporting the notion that excess abdominal fat is more closely related to cardiometabolic abnormalities such as insulin resistance, atherogenic dyslipidemia, type 2 diabetes and CVD than measures of general obesity like body mass index (BMI).[4] Further, introduction of imaging techniques like computed tomography (CT) & magnetic resonance imaging (MRI) has allowed for more precise and reliable estimation of individual differences in abdominal fat distribution.[5] There are several studies showing visceral fat, which includes omental, mesenteric & reteroperitoneal fat, to be superior determinant of metabolic risk & metabolic syndrome (MS) as compared to subcutaneous fat after adjustment for BMI and waist circumference (WC).[6] Moreover, with advancements in imaging modalities for metabolic risk assessment, liver fat as determined quantitatively by magnetic resonance spectroscopy (MRS) has emerged as a significant correlate of metabolic risk factors. Currently, research is directed towards accounting the independent association of liver fat to CMR factors whilst visceral fat as gold standard for quantifying obesity related CMR.[7] The purpose of the current review is to assess various evidences that explored the independent association of visceral and liver fat independently to CMR factors.

ACCUMULATION OF FAT IN LIVER AND ITS CONSEQUENCES

Adipose tissue serves as a key platform of energy conservation by storing triglycerides as reserve fuel during periods of calorie deprivation. Subcutaneous adipocytes account for around 80% of the total body fat, followed by visceral adipose tissue (around 10%) and non-adipose tissues or ectopic sites (approximately10%) such as liver, skeletal muscles etc.[8,9] Ectopic sites have no capacity to store excess fat without causing harm,[10] which strengthens the fact that distribution of fat considerably accounts for metabolic heterogeneity of

obesity.[11] Liver, one of the major sites of ectopic fat storage, plays a pivotal role in maintaining energy homeostasis during fasting-fed transitions & in buffering carbohydrate load by suppression of hepatic glucose production and promoting liver glycogen deposition.[12] Fat is stored in liver mainly in the form of triglycerides resulting from increased hepatic influx of free fatty acid (FFA). Liver fat can be derived from: (i) adipose tissue lipolysis leading to increased FFA release (ii) dietary chylomicrons (iii) *de novo* lipogenesis in liver. In patients with increased visceral adiposity, adipose tissue lipolysis contributes most to increased liver fat while, in general, dietary chylomicrons are the major source of liver fat.[13]

Since long it has been considered that non-alcoholic steatohepatitis (NASH), a progressive & more destructive form of fatty liver disease, is strongly associated with metabolic disorders having its outcomes as type 2 diabetes and cardiovascular mortality.[14,15] While fat accumulation in liver appears to be a prerequisite for the development of all forms of nonalcoholic fatty liver disease (NAFLD) including NASH, the imaging tools (Ultrasonography and CT) being utilized routinely fail to detect mild fat in liver. Moreover, ultrasonography (US) provides qualitative information while CT generally involves radiation exposure.[16] It was after the development of MRS technique, quantitative and precise non-invasive measurement is possible. Liver MRS is also found to be well correlated with biopsy results. Utilizing this technique; many studies have reported very strong association between liver fat and CMR factors.[16,17]

Several studies using CT & MRI/MRS tool have reported direct and independent correlation between visceral and liver fat content while subcutaneous adipose tissue has not been related to liver fat content. This can be attributed to unique anatomical location of visceral fat providing free fatty acids & adipokines to the liver through portal blood flow thus contributing to liver fat.[18] reinforcing the prevailing dogma that visceral fat has deleterious metabolic effects.[19] However, if visceral fat was a major contributor to metabolic risk, visceral adipose tissue should be the major source of systemic free fatty acid flux to the liver via portal vein which is not the case. Visceral fat contributes to only 15% of the total systemic free fatty acids whereas majority of free fatty acid is contributed by non-splanchnic adipose tissue. This observation raises the doubt over considering visceral adipose tissue being major contributor of metabolic abnormalities.[20] There is a causal link between liver fat content and metabolic dysfunction. High liver fat content causes hepatic insulin resistance

leading to fasting hyperglycemia, loss of post-prandial suppression of gluconeogensis and dyslipidemia. Increased lipid availability prevents local degradation of apolipoprotein B (ApoB) in hepatocytes leading to overproduction of triglyceride (TG) rich large very low density lipoprotein (VLDL) particles. Thus, a high liver fat content can, by itself, largely explain the hyperinsulinemic, hyperglycemic, hypertriglyceridemic, and elevated apoB dysmetabolic state independent of contribution from visceral adipose tissue. Moreover, liver dysfunction arising from steatosis also releases pro-atherogenic and pro-coagulant proteins such as fibrinogen, c-reactive protein and plasminogen activator inhibitor-1. Collectively, the risk of CVD increases.[9,5]

INDEPENDENT ASSOCIATION OF VISCERAL AND LIVER FAT TO CARDIOMETABOLIC RISK

With a view to explore the pathophysiology of CMR, the research focus is to establish causal link between various ectopic fat depots and cardiometabolic dysfunction. Reports indicate that visceral fat contributes most to the obesity related metabolic abnormalities. Recently it is established that visceral fat correlates directly with liver fat and an increase in liver fat is associated with similar metabolic abnormalities as linked to visceral fat content. Although visceral and liver fat are connected metabolically and both are associated with CMR factors, it is important to know their independent contribution to metabolic disturbances and in turn cardiovascular risk. Table 1 & 2 summarizes the list and results of studies exploring independent association of visceral and liver fat with various metabolic risk factors.

Currently, two techniques viz. CT and MRI are being widely used in research setting for quantifying visceral and liver fat content.[21] CT & MRI give precise estimation of regional fat accumulation and found to be particularly useful in distinguishing fat accumulation in subcutaneous and visceral adipose tissue.[6]

CT estimates liver attenuation in Hounsfield units (HU). Measured liver HU are usually compared to spleen (organ with known low fat content) HU to calculate liver-to-spleen ratio. The major limitation of CT for estimation of liver fat content is its inability to detect low levels of liver fat as observed in patients with non-alcoholic fatty liver disease.[21] CT has reported sensitivity and specificity of 73-100% and 95-100% for the detection of moderate to severe liver fat content (LFC), which is 30% by histological analysis.[22] CT has been used to study the independent association of visceral and liver fat to cardiometabolic traits. Table 1 lists the details of studies carried using CT.

In 2003, Nguyen-Duy et al evaluated fasting blood glucose and lipid parameters in 162 overweight/obese male Caucasians. It was found that, both visceral and liver fat carries independent health risk however, visceral fat is a stronger correlate of metabolic risk than liver fat.[23] Results from similar study in 293 overweight/obese male Caucasians was published in 2007, where visceral fat was found to have independent correlation with metabolic markers after adjusting other fat depots whereas liver fat did not.[24] Kuk et al examined mortality as the outcome measure in 291 males (predominantly white) and found that visceral fat was the only fat measure independently predictive of mortality risk.[25] Although, these studies provided a link between visceral fat distribution and CMR, it is noteworthy that these studies had relatively small sample size and included only male participants. Thus, whether these observations can be extended across gender was not evident. Recently, large cohort studies in community-based sample like Framingham Heart Study (sample = 2589) and the AGES-Reykjavik Study (sample = 2495), using CT technology extensively across both genders, generated robust and convincing evidences on metabolic risk associates.

Table 1: Studies using CT to determine independent association of visceral and liver fat with cardiometabolic risk factors

Article	Subjects	Tool	Metabolic parameters	Independent association of Liver fat	Independent association of Visceral fat	Conclusion
(Jackson Heart Study) Liu J et al 2011[25]	**Sample size:** 2882 **Gender:** 35% Males & 65% Females **Condition:** Community based samples **Ethnicity**: African-Americans	CT	Fasting glucose, TG, high density lipoprotein cholesterol (HDL-C), systolic/diastolic BP (SBP/DBP), Metabolic syndrome (MS), diabetes	Significant association with impaired glucose, TG, HDL-C, hypertension, diabetes, MS. Association persisted after adjustment of visceral fat with exception for impaired glucose and hypertension	Visceral fat associated significantly with all cardio metabolic traits (p<0.0001). In regression analysis, association of visceral fat with TG, HDL-C, MS & impaired glucose significantly greater than fatty liver	Fatty liver and visceral fat are independent correlates of CMR but associations are stronger for visceral fat than fatty liver
(AGES-Reykjavik Study) Kim LJ et al 2011[26]	**Sample size:** 2495 **Gender:** 879 Males & 1616 Females **Condition:** Community based samples with no history of coronary artery disease (CAD), Diabetes or liver disease **Ethnicity**: Caucasian	CT	MS	No correlation in normal weight groups. However, significant (p<0.001) independent correlation in overweight/obese groups in women (OR=1.38 & 1.45). And for overweight/obese men OR= 1.38 (p=0.01) & 1.27 (p=0.10)	In women, significant (p<0.01) correlation in normal/overweight/obese groups (OR= 2.78, 1.63, 1.43). However, association diminished with increased BMI. In men, only overweight group showed significant (p<0.01) correlation, OR=1.69.	Visceral & liver fat have independent association with metabolic risk however for visceral fat, association is more significant at lower levels of obesity whereas for liver fat it is more significant at higher levels
(Framingham Heart Study) Speliotes EK et al 2010[27]	**Sample size:** 2589 **Gender:** Male (49%) & female (51%) **Condition:** Community based samples **Ethnicity**: Primarily Caucasian	CT	MS, glucose related parameters (fasting glucose, HOMA-IR, adiponectin); lipid related: TG, HDL-C, total cholesterol (TC), hypertension & BP	Statistically significant (all p<0.001) association of fatty liver with: Diabetes (OR 1.64, 95% CI 1.11-2.41) IGT (OR 1.58, 95% CI 1.21-2.07) IR (OR 2.79, 95% CI 2.14-3.65), MS (OR 1.95, 95% CI 1.48-2.56), TG & HDL. While association with SBP & DBP attenuated (p>0.05) on adjusting for visceral fat	In multivariate analysis, visceral fat remained significantly (p< 0.0001) associated with all metabolic correlates (lipid, glucose traits and SBP/DBP)	After adjustment of visceral fat, fatty liver remained significantly associated with lipid and glucose traits but the association diminished for SBP and DBP
McMillan KP et al 2007[24]	**Sample size:** 293 **Gender:** Males **Condition:** Healthy **Ethnicity**: Caucasian	CT	Glucose, TG, TC, HDL-C	Liver fat was significantly (p < 0.05) associated with TC & TG independent of Subcutaneous fat, age and CRF but not after control for visceral fat.	Visceral fat remained significantly (p< 0.01) associated with all metabolic risk factors after control for liver fat, subcutaneous fat	Visceral fat but not liver fat is associated with metabolic risk independent of other fat depots
Kuk JL et al 2006[28]	**Sample size:** 291 **Gender:** Males **Condition:** (97 decedents & 194 control) **Ethnicity**: Caucasian	CT	All-cause mortality	After adjustment of other fat measures (visceral and subcutaneous fat), liver fat was not found to be significant predictor mortality (OR=0.87; p=0.55)	Visceral fat was the only significant (OR=1.81; p<0.05) predictor of mortality adjusting for other fat measures	Visceral fat was the only fat measure independently predictive of mortality risk.
Nguyen-Duy TB et al 2003[23]	**Sample size:** 162 **Gender:** Male **Condition:** Overweight/Obese **Ethnicity**: Caucasian	CT	Fasting glucose, TG, TC, LDL-C, HDL-C, TC/HDL-C	Liver fat was a significant (p ≤ 0.05) correlate of fasting glucose and TG	Visceral fat was a significant (p ≤ 0.01) correlate of TG, HDL-C & TG/HDL-C after control for liver fat.	Visceral fat is a stronger correlate of metabolic risk in overweight obese men than liver fat

Table 2: Studies using MRI/MRS to determine independent association of visceral and liver fat with cardiometabolic risk factors

Article	Subjects	Tool	Metabolic parameters	Independent association of Liver fat	Independent association of Visceral fat	Conclusion
Kotronen A et al 2011[4]	**Sample size:** 356 **Gender:** 186 Males & 170 Females **Condition:** No acute or chronic disease other than obesity **Ethnicity:** Caucasian	MRI/ MRS	TG, HDL-C, blood pressure, fasting glucose and insulin, liver enzymes (ALT, AST)	Significant (p<0.001) independent correlation of liver fat with TG, HDL-C, fasting glucose and insulin, liver enzymes	Significant (p≤0.001) independent correlation of visceral fat with TG, HDL-C & Insulin	Both Liver fat and visceral fat had significant independent correlation with metabolic risk parameters. However, Liver fat and NOT visceral fat correlated significantly with fasting glucose and liver enzyme levels
Hoenig MR et al 2010[7]	**Sample size:** 43 **Gender:** 35 Males & 8 Females **Condition:** High risk vascular cohort **Ethnicity:** Caucasian	MRI/ MRS	Metabolic syndrome (MS)	Liver fat independently associated with MS. Odds ratio 1.17. Liver fat of >4.0% identified MS with 84% sensitivity & 82% specificity	Visceral fat did not contribute to MS under logistic regression analysis	Liver fat is associated with metabolic syndrome independent of visceral fat.
Fabbrini E et al 2009[19]	**Sample size:** 31 **Gender:** Males & Females **Condition:** Obese subjects **Ethnicity:** Caucasian	MRI/ MRS	Hepatic, skeletal and adipose tissue insulin sensitivity & hepatic VLDL-TG secretion rate as determined using euglycemic hyperinsulinemic clamp procedure	When matched for visceral fat values, hepatic, skeletal and adipose tissue insulin sensitivity was found to be lower (41, 36 and 13%) while hepatic VLDL-TG secretion rate was double in subjects with higher than normal liver fat content.	When matched for liver fat values, no difference in insulin sensitivity & hepatic VLDL-TG secretion rate observed between normal and higher visceral fat sub groups	Liver fat associated with metabolic derangement independent of visceral fat
Adiels M et al 2006[29]	**Sample size:** 28 **Gender:** Males **Condition:** 10 Diabetic & 18 Non-diabetic = 18 **Ethnicity:** Caucasian	MRI/ MRS	Fasting glucose, Insulin, HOMA-IR, Adiponectin, TG, ApoB	In multiple regression analysis, significant correlation with VLDL, TG and ApoB production rates.	No significant correlation with lipid variables found in multiple regression analysis	Liver fat, and not visceral fat is an independent correlate of lipid variables
Westerbacka J et al 2004[30]	**Sample size:** 132 **Gender:** 66 Males & 66 Females **Condition:** Healthy **Ethnicity:** Caucasian	MRI/ MRS	Fasting Insulin, TG, C-peptide, LDL-C, HDL-C, Adiponectin	Significant (p<0.001) correlation with fasting insulin and TG	Did not correlate significantly with metabolic markers. But has significant (p<0.001) independent correlation with	Liver fat, but not visceral fat independently associated with visceral fat. No gender difference in metabolic markers (insulin, TG, HDL-C & adiponectin) observed for similar amount of visceral and liver fat.
Lindroos AS et al 2002[31]	**Sample size:** 30 **Gender:** Male **Condition:** Healthy **Ethnicity:** Caucasian	MRI/ MRS	Fasting insulin, TG, HDL-C, SBP, in vivo insulin sensitivity of glucose rate of production (Ra), rate of utilization (Rd) & serum FFA	Group with low and high liver fat content showed significant (p<0.05) difference in fasting insulin, TG, HDL-C, SBP. Further, insulin suppression glucose (Ra) and of serum FFA was significantly (p<0.05) impaired in high compared to low liver fat group	Visceral fat correlation with metabolic risk parameters was not studied instead at the same level of visceral fat; subjects were divided into group of High and low liver fat content.	Liver fat independently associated with features of insulin resistance and other metabolic risk

In the Framingham heart study, both visceral and liver fat were significantly associated independently with lipid-glucose traits.[27] In the AGES-Reykjavik study, independent association of visceral and liver fat estimates with metabolic syndrome differed across the levels of obesity (BMI <25, 25-29.9 and ≥30 kg/m^2). For visceral fat, significant (p<0.01) correlation was found in females across all obesity levels but association diminished with increased BMI. In males, only overweight group showed significant (p<0.01) correlation. For liver fat, no correlation was found in normal weight group, however significant (p<0.001) independent correlation observed in overweight & obese groups in females (odds ratio 1.38 & 1.45) and for overweight & obese males odds ratio of 1.38 (p=0.01) and 1.27 (p=0.10) was observed.[26] Jackson heart study enrolled over 2000 African-Americans who underwent CT to examine the independent correlation of visceral and liver fat with cardiometabolic risk. It was found that both liver fat and visceral fat were independent correlates of cardiometabolic risk, but associations were stronger for visceral than for liver fat.[25]

Results from studies using CT are consistent with respect to demonstrating strong correlation between visceral fat and various metabolic markers while not so assertive for liver fat. However, with the availability of MRS, various studies have been carried out in the same line showing very strong association between liver fat content and cardiometabolic risk profile predicting type 2 diabetes mellitus and CVD. MRS determines observed signal into a frequency spectrum, providing biochemical information.[32] Overall, the main benefit of MR (MRI & MRS) over other imaging techniques is its capability to detect low levels of liver fat as compared to CT and US. In the histological range of liver fat content of 5-10%, sensitivities of greater than 85% and specificity of almost 100% have been reported.

Table 2 illustrates the outcomes of the studies done using MR technique. These studies estimated visceral fat using MRI while for liver fat content, MRS was used. Despite the relative superior performance, which is achieved without the use of ionizing radiation, MRI is not as widely used as one would expect. The main reasons are high costs per examination, the dependence on full patient cooperation, and some contraindications for the examinations such as a pacemaker implant or patient claustrophobia.

As early as in 2002, Lindross et al. studied the differences in insulin sensitivity using euglycemic insulin clamp technique within the low and high liver fat groups having same level of visceral fat. Study was carried out in 30 Caucasian males and it was found that fat accumulation in liver is, independent of visceral obesity, characterized by several features of

insulin resistance in normal weight and moderately overweight subjects.[31] A similar study including both male and females carried out in 2009 supported these results. In addition, when groups were matched for liver fat values, no difference in insulin sensitivity was observed between normal and high visceral fat subgroups.[19] Further, these studies showed a strong independent association between liver fat content and metabolic markers that included lipid parameters, whereas visceral fat did not correlate independently.[29,7] In 2011, results from a study in relatively larger sample size of 356 including both genders were published. Key metabolic parameters under study were TG, HDL-C, fasting blood glucose & insulin. Both visceral and liver fat found to have significant independent correlation with these parameters except for association between visceral fat & fasting blood glucose.[4]

Thus, irrespective of the radio-diagnostic tool employed (whether MRI or CT), most of the studies clearly demonstrate strong metabolic connection between these fat depots (visceral & liver fat). However, while exploring individual contribution of these fat depots to cardiometabolic risk, those studies which employed CT as the radio-diagnostic tool for fat estimation showed strong independent correlation between visceral fat and the metabolic markers. Whereas studies employing MR technique provided contrasting results i.e. liver fat having significant independent association with various metabolic markers. Indeed, MRI technique is considered to be far more precise for estimating liver and visceral fat content but the studies done so far using MRI method had relatively small sample size than those employing CT technique. Further, it is worth noting that the results of studies using CT technique enrolling large sample size (AGES-Reykjavik study and Framingham heart study) showed results in line with MRI based study results, i.e. liver fat being stronger correlate of cardiometabolic risk.

All these studies give an important insight over the metabolic heterogeneity of obesity and its related cardiovascular risk. It also reemphasizes on the gender difference in visceral adipose tissue and ectopic fat accumulation predisposing males to higher cardiometabolic risk. Data from other metabolic studies have clearly established that males have overall less favorable plasma lipid profile, which includes high fasting TG and low HDL-C concentrations compared with females. Both genders show marked differences in indices of plasma glucose-insulin homeostasis. These differences have been for long attributed to increased visceral adipose tissue (AT) accumulation in males compared with females. Westerbacka et al in their MR imaging study done in 132 apparently healthy (66 males and 66 females) subjects to

explore the gender difference in markers of cardiovascular risk found that despite twice as much subcutaneous fat in women, amount of visceral and liver fat were comparable to that in males. No gender difference in metabolic markers (TG, HDL-C, Insulin and adiponectin) was observed for similar amounts of visceral and liver fat. Further, multiple linear regression analysis revealed that visceral fat was significantly associated with liver fat independent of subcutaneous fat. Liver fat and not visceral fat independently is predictive of variation in fasting serum insulin levels.[30]

ETHNIC DIFFERENCES – RESEARCH GAP IN INDIAN PERSPECTIVE

Irrespective of the tool employed (MR or CT); most studies described above were carried out in Caucasians, Whites or Western population. Thus, it is not reasonable to generalize result of these studies across different ethnicities and races.

Various evidences have shown that metabolic consequences of obesity manifest at relatively lower absolute amount of total body fat in south Asians than in Whites. Indeed these differences are so large that BMI-based definition of obesity is now much lower for South Asians than in Whites.[33] The World Health Organization has recognized the need for defining obesity specific to individual population & thereby revised (rather lowered) obesity cutoff in Asians from BMI >30 kg/m^2 to >25 kg/m^2.[34] Thus, it is certain that ethnicity and race are associated with differences in susceptibility to the selective deposition of visceral adipose tissues and further ectopic fat.[35] There are considerable evidences, which suggest that unlike Blacks, Asians are more prone to visceral fat deposition.[6] At similar BMI, South Asians have increased visceral fat and greater insulin resistance compared to European population. Further, both diabetes and CAD occur about 10 years earlier among South Asians than in any other population.[34,36] Over the past decade, many studies have been carried out in Indians to evaluate body fat distribution & CMR factors. Asian Indians are now recognized to have a unique phenotype called as the "Asian Indian Phenotype" characterized by greater degree of central body obesity, increased visceral fat, higher plasma insulin levels, insulin resistance and lower adiponectin levels.[37] In recent past, several studies have estimated subcutaneous/visceral fat amount in Asian Indians to understand obesity related metabolic and cardiovascular complications in them. Most of the studies have been carried out using CT (not MRI) only. In 2010, Sandeep et al published results of their study carried out in 120 (49 males and 71 females) non-diabetic Asian Indians. They found visceral, but not subcutaneous fat (as estimated using CT) having strong association with metabolic syndrome (OR: 1.013,

95% CI: 1.001- 1.025; P=0.041) even after adjusting for age, gender and BMI. Although the results of this study gave insight on early identification of at-risk individuals, the cause/effect inferences cannot be drawn from such cross sectional study.[38]

CONCLUSIONS

Various epidemiological evidences reemphasize predominance of metabolic heterogeneity in obesity and its cardiometabolic consequences. All the studies irrespective of the tool employed for estimation of fat depots (CT or MRI/MRS) showed strong correlation between visceral and liver fat. Results from studies done using CT represented visceral fat to be a stronger independent correlate of cardiometabolic risk. While studies utilizing MRS, considered to be gold standard for non-invasive estimation of liver fat content, showed significant correlation between liver fat and metabolic markers independent of visceral fat measure. With the advancement in imaging tools (MRS), the imaging studies reinforced the causal link between liver fat content and the risk of type 2 diabetes and CAD surpassing earlier notion of visceral fat being the primary target to treat obesity related metabolic dysfunction and CV risk. However, most studies were carried out in relatively small sample size representative of western population; the results cannot be generalized across different ethnicities. While it is known that Asian Indians tend to have high visceral adiposity than whites at relatively similar levels of BMI and are more predisposed to CV risk, there are no published reports that provide quantitative estimates (as obtained by MRS) of liver fat content in Indian population. Thus, there is a strong unmet need for extensive research in this direction to come out with a plausible target to treat cardiometabolic risk.

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