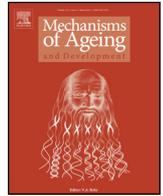




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Adipose tissue, diet and aging

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ABSTRACT

Age related increase in body fat mass, visceral adipose tissue (AT), and ectopic fat deposition are strongly related to worse health conditions in the elderly. Moreover, with aging higher inflammation in adipose tissue may be observed and may contribute to inflammaging. Aging may significantly affect AT function by modifying the profile of adipokines produced by adipose cells, reducing preadipocytes number and their function and increasing AT macrophages infiltration. The initiating events of the inflammatory cascade promoting a greater AT inflammatory profile are not completely understood. Nutrients may determine changes in the amount of body fat, in its distribution as well as in AT function with some nutrients showing a pro-inflammatory effect on AT. Evidences are sparse and quite controversial with only a few studies performed in older subjects. Different dietary patterns are the result of the complex interaction of foods and nutrients, thus more studies are needed to evaluate the association between dietary patterns and changes in adipose tissue structure, distribution and function in the elderly.

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Body fat in humans may be stored in fat mass or in the adipose tissue. Although the two terms are frequently used interchangeably, fat mass and adipose tissue are distinct and different compartments and their separation is important when considering their metabolic characteristics (Shen et al., 2003). Adipose tissue in the tissue–organ body composition level is a connective tissue extensively laden with adipocytes and is an energy storage depot, thermal insulator and mechanical pad. In the reference man it corresponds to 21% of the body mass (Snyder et al., 1975). Usually, percent body fat is higher in women and overweight subjects. On the counterpart, at the molecular body composition level, fat is mainly composed by lipids in form of triglycerides (Wang et al., 1992).

Fat is preeminently but not exclusively stored in adipose tissue, but is present also in non-adipose organs such as muscle, liver, pancreas and heart both in physiologic and pathologic conditions. Fat is the main component of adipose tissue, representing about 80%. The remaining 20% is mainly composed by water, protein and minerals (Wang et al., 1992; Fuller et al., 1999).

Aging influences both fat mass and adipose tissue with a significant age related increase in fat mass, re-distribution of body

fat with increase in visceral adipose tissue and decline in subcutaneous adipose tissue, as well as ectopic fat deposition. Age related increase in body fat mass, visceral adipose tissue, and ectopic fat deposition are strongly related to worse health conditions in the elderly. With aging higher inflammation in adipose tissue may be observed and may contribute to inflammaging (Franceschi et al., 2000).

1. Adipose tissue and aging

Normal aging is associated with a progressive increase in fat mass (FM), which normally peaks at about age 65 years in men and later in women. Increase in total adiposity may be independent of changes in body weight due to concomitant decreases in muscle mass observed with aging, the so-called sarcopenia (Prentice and Jebb, 2001). This has been clearly shown by Hughes et al. (2004), who in a 9-year longitudinal study with a sample of weight-stable men and women aged 60 ± 8 years, observed that FM increased significantly in both genders, and was confirmed by another longitudinal study, performed in Italy in community dwelling elderly men and women, in whom, despite weight stability, a significant increase in total FM was observed (Fantin et al., 2007).

Aging is also associated with redistribution of adipose tissue (AT) still independent of body weight changes. After only 5 years of follow-up, we observed a significant waist circumference increase in a population of elderly, healthy, weight-stable men and women (Fantin et al., 2007).

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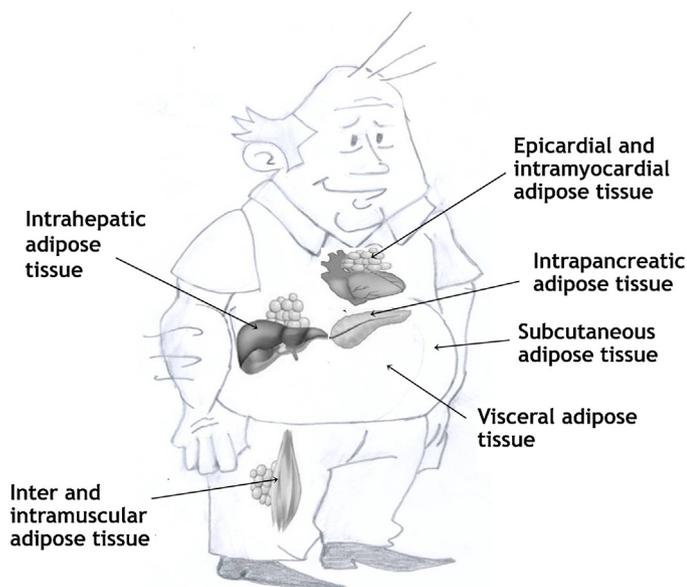


Fig. 1. Ectopic fat deposition in elderly obese. Different sites of ectopic fat deposition in elderly obese.

Years ago, age related body fat distribution changes, as assessed by multi-slice computed tomography (CT), have been evaluated by Kotani et al. (1994), who observed in a study sample with a wide range of age that intra-abdominal AT volume increased with age, while subcutaneous abdominal AT and in particular subcutaneous AT located in thighs and calves decreased.

Moreover in subjects older than 70 years from the Health ABC study it has been recently shown, using CT at the mid-thigh level, that aging also increases the amount of fat inside and around muscle fibers (Goodpaster et al., 2001); in this study fat infiltration inside muscle was directly related to age and BMI.

Thus, aging is associated with a redistribution of AT: visceral fat increases while subcutaneous fat in other regions of the body (abdomen, and in particular thigh, calves) decreases. Accumulation of intra-abdominal fat even without body weight change seems to persist even in elderly stable-weight men and women.

Actually, several factors besides aging may influence body composition changes (Abbasi et al., 1998; Baumgartner et al., 1996; Vermeulen et al., 1999) such as a decline in physical activity (Abbasi et al., 1998; Baumgartner et al., 1996), hormones (Abbasi et al., 1998; Vermeulen et al., 1999) and serum albumin (Baumgartner et al., 1996) and thus should be taken into account.

Age related dys-regulation of lipid metabolism in subcutaneous adipocytes could in part explain not only the increases in visceral adiposity but also fat deposition within non-adipose tissues such as the skeletal and cardiac muscle, liver and pancreas (Després and Lemieux, 2006; Rossi et al., 2011) (Fig. 1). Increased fat free acid (FFA) delivery to other organs, especially when combined with

defective FFA oxidation, leads to ectopic triglycerides storage in these organs, contributing to lipotoxicity and systemic dysfunction (Tchkonina et al., 2006).

Ectopic fat deposition is one of the most important features of body composition in the elderly (Table 1). It could be increased by concurrence of positive energy balance, obesity and diabetes, and may itself be responsible of relevant clinical consequences.

Muscle fat infiltration, the so called myosteatosis, may be distinguished into two different lipid depots: intermuscular adipose tissue, mainly composed by lipid droplets with interspersed adipocytes, located between muscle fibers, also known as extramyocellular lipids, and intramuscular or intramyocellular lipids located within muscle fibers in form of cytosolic triacylglycerols (Gallagher et al., 2005; Rossi et al., 2010). Intramuscular and intermuscular lipid content are related with obesity and in particular visceral fat deposition (Gallagher et al., 2005; Korach-André et al., 2005; Kelley et al., 1999). Both depots are increased with age (Ryan and Nicklas, 1999) and are associated with muscle strength decrease and mobility limitation in elderly men and women independently of age, race and obesity (Goodpaster et al., 2001; Katsiaras et al., 2005).

Although aging itself is related to liver lipid accumulation (Cree et al., 2004), obesity and especially visceral fat, more than aging, are the strongest predictors of liver fat accumulation (Jakobsen et al., 2007; Rossi et al., 2011; Machann et al., 2005).

In the last decade, pancreas fat accumulation raised attention as ectopic fat depot involved in the development of type 2 diabetes (Lee et al., 1994; Nolan et al., 2006). Age related increase in fat deposition inside the pancreas has been observed by Saisho et al. (2007) who performed pancreas computed tomography in 2000 subjects with a wide range of age and showed that over 60 years of age, both total and parenchymal pancreas volumes gradually decline, whereas fat volume in pancreas increases linearly with age in both genders: they (Saisho et al., 2007) also observed in the same subjects that obesity, in particular visceral obesity, determined an increase in both pancreas volume and fat deposition.

Interest has been also focused on fat depots in and around the heart, namely intra-myocardial and epicardial fat respectively. Intra-myocardial fat has important health consequences because associated with left ventricular thickness and heart failure (Szczepaniak et al., 1999; Sharma et al., 2004). Epicardial AT, located between myocardium and pericardium, is reported to be strongly associated with abdominal adiposity and from an anatomical point of view is considered visceral fat inside the thoracic region. In human studies, epicardial fat is positively associated with left ventricular hypertrophy and may be associated with coronary artery disease. Age related increase in epicardial fat independently of obesity has been observed in some (Silaghi et al., 2008) but not all studies (Iacobellis et al., 2003a,b). An increase in intra-myocardial fat with aging, independently of obesity, has been suggested (Silaghi et al., 2008).

Even the amount of fat in the renal sinus gradually increases with age. In lean subjects fat is the largest single constituent of the

Table 1
Ectopic fat depots: effects of obesity, visceral obesity and aging.

	Obesity	Visceral obesity	Aging
Intrahepatic adipose tissue	↑ [Jakobsen 2007]	↑↑ [Jakobsen 2007]	↑ [Machann 2005]
Intrapancreatic adipose tissue	↑ [Saisho 2007]	↑↑ [Rossi 2011]	↑ [Saisho 2007]
Intramyocardial adipose tissue	↑ [Sharma 2004]	↑ [Szczepaniak 1999]	↑ [Szczepaniak 1999]
Epicardial adipose tissue	↑ [Iacobellis 2003]	↑ [Iacobellis 2003]	↑↓ [Silaghi 2008 Iacobellis 2003]
Intramuscular adipose tissue	↑↑ [Kelley 1999]	↑ [Korach-André 2005]	↑↑ [Kelley 1999]
Intermuscular adipose tissue	↑ [Gallagher 2005]	↑ [Gallagher 2005]	↑ [Ryan 1999]
Renal sinus adipose tissue	↑ [Montani 2004]	No data available	↑ [Foster 2011]
Bone marrow adipose tissue	= [Kugel 2001]	= [Kugel 2001]	↑↑ [Liney 2007]
Brown adipose tissue	↓ [Cypess 2009]	↓ [Gómez-Hernández 2012]	↓ [Cypess 2009]

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