

Review Article

The Role of Intermuscular Adipose Tissue in Aging Process: A Future Target Intervention

I Gusti Putu Suka Aryana^{1,2}, Dian Daniella^{3*}

¹Geriatric Division, Department of Internal Medicine, Faculty of Medicine, Udayana University, Bali, Denpasar, Indonesia

²Head of Geriatric Interdiscipline Clinical Team at Ngoerah Hospital, Bali, Denpasar, Indonesia

³Department of Internal Medicine, Faculty of Medicine, Udayana University, Bali, Denpasar, Indonesia

ABSTRACT

It is estimated that the number of elderly people in the world will increase from 1.4 billion in 2030 to 2.1 billion in 2050. With the increasing number of elderly people, it is important to pay attention to the health of the elderly. As age advanced, there was a redistribution of adipose tissue to ectopic sites, such as intermuscular. Intermuscular adipose tissue (IMAT) is adipose tissue located under the muscle fascia, both between muscle fibers and between muscle groups. IMAT proposes harmful impacts in older individuals, involving various organs beyond the musculoskeletal system. The purpose of this study is to discuss the impacts of IMAT in elderly population. We systematically searched Pubmed, Europe PMC and Directory of Open Access Journal (DOAJ). We summarized the data from the searched articles and found that impact of IMAT on the elderly can be grouped into three, namely muscle dysfunction, metabolic, and mobilization. This ectopic deposition of adipose tissue can cause a decrease in muscle mass, quality, and strength. Metabolic disorders occur due to insulin resistance which increases the risk of diabetes mellitus. IMAT also affects the mobilization of the elderly which reduce their quality of life. These three things will increase the morbidity and mortality of the elderly. Handling and prevention of negative impact of IMAT can be done by exercise, medication and modalities such as electrical muscle stimulation.

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*Correspondence

Dian Daniella
 Department of Internal
 Medicine, Faculty of
 Medicine, Udayana
 University, Bali, Denpasar,
 Indonesia

E-mail:
dian.daniella@gmail.com

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1. INTRODUCTION

Based on Indonesian Law No. 13/1994 concerning Elderly Welfare, elderly population is defined as people aged 65 years old and over. In 2019, the global population of elderly reached one billion and expected to reach 1.4 billion by 2030 and 2.1 billion by 2050. Total elderly population is significantly increasing as a consequence of the escalating number of geriatric populations in developing countries. Indonesia is one of those countries. In Indonesia, the percentage of elderly population is increasing from 4.5% in 1971 to 10.7% in 2020. The percentage is estimated to increase by Central Bureau of

Statistics, reaching 19.9% in 2045. Phenomenon of the increasing aging population in number and proportion, makes it crucial to emphasize on the well-being of elderly, especially those which improves the morbidity and mortality of geriatric population.

Adipose tissue plays essential roles in the human body. Besides energy storing, it is further responsible for the secretion of hormones and proinflammatory cytokines in the body. Adipose tissue extends throughout the body with different physiological effects based on its anatomical side. Subcutaneous adipose tissue in the gluteal-femoral region tends to have cardioprotective effects and act as a negative

predictor for metabolic syndrome.¹ However, visceral adipose tissue is associated with glucose intolerance.² Apart from subcutaneous and visceral, adipose cells can be stored in intermuscular, intramuscular, intramyocellular and even bone marrow.³

With advancing age, adipose tissue undergoes significant redistribution, particularly from subcutaneous to other ectopic sites, including intermuscular, creating high IMAT.^{4,5} These adipocyte deposits have several impacts on the elderly population. Visser et al. suggested that these adipocyte deposits are related to lower mobility in geriatric population.⁶ Low mobilization causes immobilization which lead to osteoporosis, muscle atrophy, pulmonary emboli, pressure ulcer, infection and insulin resistance.⁷ Insulin sensitivity index (ISI) was negatively correlated with thigh IMAT ($r = 0.54$).⁸ Bang et al. found that there are association between IMAT and metabolic syndrome.⁹ Adipocyte accumulation in the muscle interfere muscle integrity, hence decreasing muscle strength. Furthermore, IMAT activates some parts of the muscle which secretes inflammatory cytokines, thus give rise to systemic inflammation, like visceral adipose tissue, this in turn reduces muscle strength.⁷ IMAT were negatively correlated with knee extension strength ($r = -0.205$) and gait speed ($r = -0.170$),¹⁰ and changes in it were linked with worse physical performance test.¹¹ Hip IMAT associated with increased gait variability and poorer balance.¹² Bruunsgaard, et al. confirmed that inflammation reduces the beneficial effects of exercise in elderly populations.¹³ Moreover, inflammation increases the risk for other chronic diseases.¹⁴ This indicates the extent of the concerning effects of IMAT, especially in the elderly population.

IMAT proposes harmful impacts in older individuals, involving various organs beyond the musculoskeletal system. Advanced age is prone to fat redistribution, which in turn increases the amount of muscle fat accumulation and decreases subcutaneous adipose tissue. It is estimated that the escalation of IMAT reaches 9 gram/year to 70 gram/year.^{4,15} Older people have highest risk for morbidity dan mortality, therefore it is crucial to identify factors which can increase those risks. The purpose of this study is to discuss the impacts of IMAT in elderly population.

2. METHODS

We systematically searched Pubmed, Europe PMC and DOAJ with the following search terms: "intermuscular" [All Fields] AND ("adipose tissue" [MeSH Terms] OR "adipose" [All Fields]) AND ("tissue" [All Fields] OR "adipose tissue" [All Fields]) AND ("aged" [MeSH Terms] OR "aged" [All Fields] OR "elderly" [All Fields] OR "elderlies" [All Fields] OR "elderlys" [All Fields] OR "elderlys" [All Fields]) in August 11th, 2024. Search results were not limited to

date. After thoroughly read, articles that fulfilled our criteria were included in the study. The final inclusion of studies was merely based on the agreements of all authors.

3. RESULT AND DISCUSSION

3.1. Adipose Tissue

Adipose tissue has historically been classified according to its morphology into white adipose tissue, brown adipose tissue, and beige adipose tissue (Figure 1).¹⁶ White adipose tissue is located at the lower regions of the human body. White adipose tissue has been stored in the subcutaneous region. Subcutaneous adipose tissue, as the name implies, located below the skin. However, in a number of patients, for instance those with obesity, the primary ectopic site for fat accumulation is visceral. Visceral adipose tissue is located in the intra-abdominal region and adheres to internal organs. Visceral adipose tissue surrounds mesenteric, omentum, and visceral organs. Moreover, ectopic adipose tissue further located in epicardial, perivascular, intermuscular, intramuscular, intramyocellular and bone marrow.^{3,16} In addition of being fat storage, white adipose tissues have more lipid and less mitochondria.¹⁷

The role of white adipose tissue is to maintain regulation of energy homeostasis. In positive energy balance, excess fat will be taken and stored in the form of triglyceride. In negative energy balance, this adipose tissue acts as energy sources.¹⁸ In addition, these tissues secrete hormones like adiponectin, leptin and resistin. Subcutaneous adipose tissue primarily produce leptin, whereas visceral adipose tissue predominantly secretes adiponectin.¹⁷

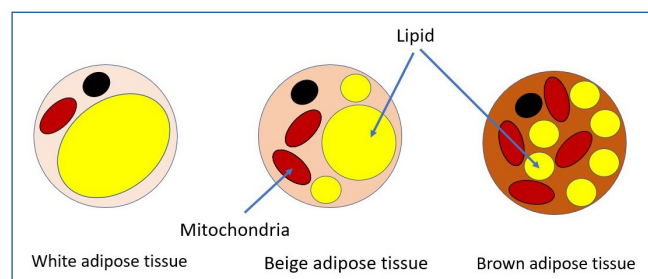
About one third of adipose tissue is composed of adipocytes and the rest are endothelial cells, fibroblasts, macrophage, immune cells, stromal cells, and pre-adipocyte. IMAT is white adipose tissue located in the adipose depot below muscle fascia. Adipose tissue which located between muscle fibers (intramuscular) and between group of muscles (intermuscular) belong to IMAT.¹⁹ Furthermore, there's a fraction of adipose tissue which is located inside myocyte (intramyocellular), however it is not belong to IMAT.²⁰

Brown adipose tissue has a high concentration of mitochondria, this explains its brown shade. Whilst originally believed to be a depot found only in small and hibernated mammals, as well as human babies, recent studies found that human adults have 1%–2% functional brown adipose tissue. These brown adipose tissues are located on the cervical, axilla, and paraspinal region.¹⁶ Brown adipose tissue stores less fat than white adipose tissue, yet high mitochondria and vascularization. Brown adipose tissue has

beneficial roles in thermogenesis and energy balance, blood glucose regulation, reduce insulin resistance and triglyceride.¹⁷ Brown adipose tissue utilizes and distributes energies from lipid to produce fat through uncoupled protein 1 (UCP-1) in the mitochondrial membrane.¹⁸

Beige adipose tissue is similar brown adipose tissues in the white adipose tissue depots.¹⁶ It caused by the alteration of white adipose tissue. This alteration is attributable to sport activity and provide beneficial impact.¹⁶ This particular adipose tissue possesses several characteristics of brown adipose tissues, such as having UCP-1, mitochondria and thermogenesis role.¹⁸

Figure 1. Adipose tissue



3.2. Etiopathology of Intermuscular Adipose Tissue

IMAT derived from different mesenchymal progenitors, typically found in adult skeletal muscle, namely mesenchymal stem cells, muscle-derived stem cells, or muscle satellite cells (SC) (Figure 3). After birth, SC mediates the majority of muscle regeneration. These cells are located close to the myofiber plasma membrane and were first invented in 1961. These cells can to differentiate into various different cells. Generally, these cells are inactive. Nevertheless, they are activated by muscle work and pathological conditions, such as myotrauma. Once activated, SC proliferates, migrates from myofiber, and expresses a specific myogenic marker, thus becoming muscle precursor cells (MPC). Bone marrow progenitor cells contribute to muscle repair by engaging with MPC. Muscle precursor cells, which is advantageous for muscle repair, fuse together forming new multinucleated cells, thus accommodating muscle repair.²¹

There are two types of satellite cells, namely myogenic and non-myogenic satellite cells. After cells are activated, myogenic satellite cells express myogenic transcription factor, such as Myogenic Factor 5 (Myf5), Myogenic differentiation 1 (MyoD), myogenin (MyoG), and Myogenic Regulatory Factor 4 (MRF4) (Figure 2). Myf5 aids in activation and proliferation of muscle precursors, myoD aids in muscle formation and inhibits proliferation, MyoG is useful for the final phase of muscle formation and regeneration. Lastly, MRF4 aids in MPC proliferation. As people age, SC

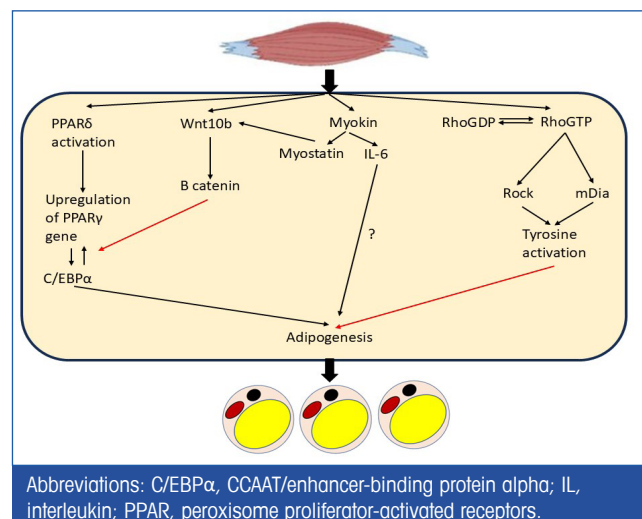
will increase in number, proliferating capacity and differentiation into adipose tissue will change. In addition to that, increased differentiation to adipose tissue will occur. Concurrently, this will simultaneously increase IMAT.²¹

There are four pathways involving the alteration of SC into adipose tissue. First, peroxisome proliferator activated receptor (PPAR) pathway. Activated PPAR δ will upregulate PPAR γ gene expression. PPAR γ induces expression of C/EBP- α during the terminal stages of adipose differentiation, while C/EBP- α maintains the expression of PPAR- γ , resulting in adipocyte gene expression. The second pathway is the Wnt growth factor. Wnt10b inhibits adipogenesis by inhibiting PPAR γ /C-EBP α , however with advancing age, the expression of Wnt decreases. Third is muscle-derived factors pathway. Muscles secrete numerous proteins called adipokine, like interleukin (IL)-4, and insulin-like growth factor I (IGF-I), myostatin and IL-6. Myostatin inhibit adipogenesis by activating Wnt/ β -catenin pathway, which downregulate PPAR γ . Higher IL-6 as adipokine will disturb insulin action and liver inflammation, that eventually lead to insulin resistance and T2DM, but its role in adipogenic differentiation is still unknown. Fourth, the GEF-GAP-Rho pathway. Guanine nucleotide exchange factors (GEFs) and GTPase-activating proteins (GAPs) activate GTPase-Rho. This will change inactive RhoGDP to active RhoGTP. It is upregulated in during myogenic differentiation and downregulated during adipogenic differentiation.²¹ Through these four pathways, SC differentiates into adipose tissue and magnifies IMAT.

3.3. Measurement of Intermuscular Adipose Tissue

Assessment and calculation of IMAT are estimated by magnetic resonance imaging (MRI) or computed tomography (CT). Despite measurable, the quantification of IMAT is not routinely done in daily practices. CT scan provides fast imaging techniques,

Figure 2. Adipose tissue formation pathway from satellite cells



which utilizes X-ray to indirectly measure IMAT based on the tissue density of a region. Bones are the most dense tissue, fats have lowest density, and muscle mass density without fat is in between both tissues. Muscle tissues visualized by CT imaging are further subdivided into regions with higher and lower density. Higher muscle tissue density is found in regions with less fat infiltration and lower density muscle tissue areas are found in regions with increased level of adipocyte in and between muscle fibers. Presence of adipocytes in this region explains low density muscle tissues seen in CT scan. A person with higher proportion of low density muscle tissues is assumed to have larger portion of IMAT and intramyocellular.⁴ Looijaard et al. measured IMAT using CT scan, and further defined qualitative measurement range of IMAT and subcutaneous adipose tissue from –190 to –30 Hounsfield units (HU). Hounsfield units act as a unit measurement of tissue density using CT scan. Measurement technique regarding for IMAT is from outside inwards in cm^2 .²² The alteration of 1 HU indicates 1% increase of lipid concentration.²³ CT scan expose patient to radiation, high cost and complex post-processing, therefore evaluation is not routinely done.²⁴

Another diagnostic approach besides CT scan is MRI. MRI utilizes the chemical properties of fat and muscle to directly measure the amount of IMAT. Nonetheless, MRI generally requires manual segmentation, which is time consuming. As for identifying premature fat replacement in muscles, MRI has higher sensitivity than CT. Additionally, since it is not density based, it provides better details of soft tissue anatomy than CT.⁴ Marcus et al. did an MRI-based technique to assess IMAT at the inferior extremity region. This study used MRI to visualize one third medial of both thighs and determine the size of IMAT. Four images of one third medial both thighs were obtained and utilized to predict the outer region of IMAT in cm^2 and lean tissue. Subcutaneous fats and bones were manually removed, and region of interest were determined by measuring area under the fascia. Using software, IMAT and lean tissue were measured.²⁵ The technique used to measure IMAT with the medial part of thighs were approved by Ruan et al. Ruan et al. performed MRI scans of the calves, thighs, butts, waists, shoulders, upper arms and forearms on 39 African-American females with body mass index (BMI) of $28.5 \pm 5.4 \text{ kg/m}^2$. Medial thighs were found to be the best place, where middle third area provide the most accurate measurement. This region is thought to be unaffected by menopausal status and BMI, including grading of obesity.²⁶

Compared with both previous modalities, ultrasonography (USG) provides no radiation and low cost. It also could be done bedside, making it a better candidate for primary screening and monitoring.²⁴ Harris-Love et al. conducted research to

compare between USG to CT scan in geriatric male to metabolic parameters, such as two-hour postprandial glucose, low density lipoprotein-cholesterol (LDL-C), and muscle strength. Ultrasonography was performed on the rectus femoris muscle and quantification of echogenicity was carried out with grayscale level (GSL). Measurements of IMAT with CT scans were performed on the medial thigh and IMAT calculation was done. Significant relationship between USG and CT scan measurement was found. Furthermore, both imaging results were related to the amount of fasting blood glucose and LDL-C.²⁷ However, more study analysis for this alternative examination are needed considering subjectivity of USG and the ideal anatomical place to perform USG to identify IMAT has not yet been determined.

3.4. Adverse Effect of Intermuscular Adipose Tissue on Elderly

3.4.1. Metabolic problem

Various factors play an important role in increasing IMAT, including obesity, inactivity, injury and aging. The percentage increase of IMAT/muscle tissue is approximately 2.9% per year. As aging continues, muscle tissues undergo atrophy, thus part of those missing tissues are replaced into adipose tissue.²⁸ Goodpaster et al. stated that, IMAT is correlated with insulin resistance and risk of type 2 diabetes mellitus (T2DM).² Further research regarding the exact mechanism of metabolic disturbance affected by IMAT is needed. One possible underlying mechanism is explained by the relationship between IMAT and BMI, since increased IMAT will definitely be followed by increased BMI. Increased BMI accompanied by metabolic syndrome will further increase the risk of developing T2DM and cardiovascular disease.^{29,30}

In geriatric population, IMAT could be a predictor for fasting blood glucose and insulin. Goodpaster et al. conducted research on 2,964 elderly with mean age 73.6 years old. This research found higher IMAT in elderly with T2DM and glucose intolerance. Even in elderly with normal BMI, IMAT was correlated with higher fasting blood glucose. Higher IMAT were associated with impaired glucose tolerance resulting in higher fasting insulin in men ($r = 0.24$ for intermuscular fat, $p < 0.0001$) and women ($r = 0.20$ for intermuscular fat, $p < 0.0001$).² Ectopic adipose tissue possess high lipolytic activity, which in turn responsible for the formation of free fatty acid (FFA). Excess amount of FFA interferes with insulin action, resulting in insulin resistance.³¹

This can also be explained by other negative impacts of IMAT, particularly its ability to secrete proinflammatory cytokine, causing inflammation both locally and systemic, such as IL-1 β . This cytokine will recruit various other pro-inflammatory mediators

after binding with its receptor IL-1RI and through involvement of MYD88 and Nuclear factor kappa-B cells (NF- κ B). It will impaired insulin secretion by inducing apoptosis and fibrosis in β - cells of pancreatic islets. In peripheral tissue, it will cause systemic inflammation that cause impaired insulin signaling, hence insulin resistance. IL-6 activates the suppressor of cytokine signalling proteins which block signal transducer and activator of transcription of insulin receptor (STAT5B). Other pro-inflammatory mediators, such as tumor necrosis factor (TNF)- α also linked to insulin resistance and T2DM. TNF- α binds with its receptor and triggers a broad-spectrum signaling cascade that results in the activation of various transcriptional pathways such as NF- κ B and Jun NH2-terminal kinase (JNK). Once, they are activated, they phosphorylate serine 307 in Insulin Receptor Substrate-1 (IRS-1) which result in the insulin resistance.³²

Besley et al. measure inflammatory markers, such as IL-6, C-reactive protein (CRP) and TNF- α . High IMAT correlated with high inflammatory marker and inversely correlated to subcutaneous fat. Abdominal visceral adiposity was most associated with significantly higher IL-6 and CRP concentrations in all race/gender groups ($p < 0.05$).³³ High proinflammatory cytokines in turn increases lipolysis rate in skeletal muscle, which as well increases glucose concentration in skeletal muscle and further causes insulin resistance. This ends up with T2DM.⁴

IMAT responsible for the decreasing of insulin resistance through local inflammatory reaction and increasing concentration of local FFA.³⁴ The muscle primarily expresses glucose transporter (Glut)-1 and Glut-4. Glut-4 is responsible for transporting glucose in muscle fibers. Muscles have two domains of plasma membrane, namely sarcolemma and transverse tubules (t-tubules). Insulin stimulates the increasing density of Glut4, both in sarcolemma and t-tubule, in such a way that glucose transport occurs smoothly. However, in severe inflammatory conditions, Glu4 decreases. This will in turn affects glucose transport, considering that insulin influences glucose transport in the muscle through Glut4.³⁵

Chemokines such as monocyte chemoattractant protein-1 is produced by macrophage in obese people. These macrophages maintain recruit M1 macrophages in obese adipocytes and producing various pro-inflammatory mediators such as TNF- α , IL-6, and IL-1 β in conjunction with other infiltrated immune cells and adipokines.³²

Apart from the amount of blood sugar, IMAT additionally affects cholesterol level. Despite the fact that visceral adipose tissue serves as fat storage, this tissue also becomes a storage for ectopic adipose which correlated with the disturbance of

fat oxidation, thus disturbing its ability to oxidize fat and loss its capacity to store the remaining energy.³⁶ Yim et al. stated that, IMAT had a correlation with total cholesterol, in which higher IMAT lead to the increasing amount of total cholesterol. IMAT was associated with level of glucose ($p < 0.001$) and total cholesterol ($p < 0.05$).³¹ These will increase the risk of morbidity and mortality in elderly.

3.4.2. Muscle problem

In elderly, sarcopenia often occur as part of aging process and affects quality of life. Aging process itself will decrease in muscle mass, occurring mostly at age 40 years old and gradually increases 1% per age year. Generally, muscle strength decreases earlier, with approximately 3%–4% per year in male and 2.5%–3% per year in female. This reduction is influenced by several factors, such as genetic, hormonal changes, comorbidity, unhealthy lifestyle, and malnutrition.³⁷ Reduce muscle strength and mass are caused by IMAT, as a consequence of fat infiltration to muscle tissues.¹⁵ Increased IMAT causes the reduction of muscle strength from 4%–6%. As aging process occur, muscle strength and mass will tend to decrease, especially in geriatric population (Figure 3). However, reduced muscle strength in aging is not comparable to decreased muscle mass, thereby IMAT has been considered to impact muscle strength.⁴ A study conducted by Goodpaster et al. on elderly revealed the relationship between IMAT and reduced muscle strength, as well as muscle quality. Midthigh muscle were negatively associated with total body fat ($r = -0.53$, $P < 0.01$).³⁸ Perkisas et al. conducted a research on 303 patients with mean age of 83.0 ± 6.4 years old and found negative correlation between IMAT and muscle strength, along with muscle mass. IMAT was negatively correlated with hand grip strength in left hand ($p = 0.001$, PCC -0.251), the right hand ($p = 0.001$, PCC -0.331) or the best measurement of both hands was selected ($p < 0.001$, PCC -0.323). In fact, higher death risk is also found to have correlation with IMAT.³⁹ Decreased muscle quality will interfere daily activities. In elderly with comorbid diseases, such as chronic obstructive pulmonary disease, stroke, osteoarthritis, renal insufficiency, and cognitive decline, reduced muscle quality will be exaggerated.

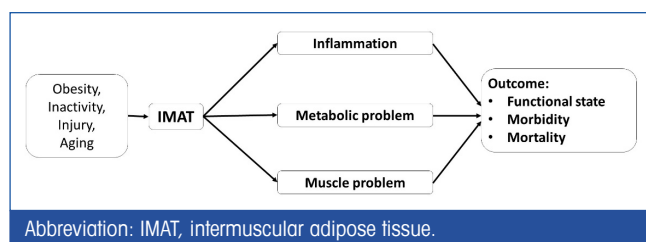
Moreover, IMAT further decreases the beneficial effects of sport exercise in elderly. Beneficial effects of sport exercise in elderly usually obtained after 12 weeks of exercise three times per week. Nevertheless, increased muscle quality will only occur in elderly with low IMAT. Even after 12 weeks of sport exercise, no significant change of muscle quality in elderly with high IMAT.⁴⁰

This ectopic adipose tissue can further affect the ability to mobilize in elderly. Increased IMAT is correlated with reduced six-minute walk distance,

walking speed, physical performance, difficulty getting up from chair, and lower walking speeds of elderly people on walking down the stairs.⁴ In a research conducted on 3075 elderly aged 70–79 years old, found that patients with higher IMAT were at higher risk of developing mobility disturbance compare to those with lower level of IMAT.⁶ IMAT alters the structure of muscle, which in turn causing the loss of muscle elasticity. This will further lower the available strength formed in muscle contraction.⁴¹ Furthermore, IMAT is also related to lower bone density and increases the risk of pelvic fracture. An increase of one standard deviation of muscle density in the thigh is associated with a 50% increase in the risk of hip fracture.⁴² A study demonstrated by Cawthon et al. on 3000 elderly aged 70–80 years old found that reduced muscle density increased the risk of hospitalization. Weakest grip strength were at greater risk of hospitalization (IRR = 1.52, 95% CI = 1.30–1.78, Q1 vs. Q4). All of this deleterious effect of high IMAT affects quality of life of elderly.⁴³

Inflammation, metabolic problem and muscle problem will affect various outcomes, such as functional state, morbidity and mortality.

Figure 3. Adverse effect of IMAT on elderly



3.5. Management and Prevention

Aerobic exercise and resistance are both useful to lower IMAT. Sport exercise will increase muscle-work, thus IMAT can be useful for energy sources. Recommended duration for exercise sport to reduce IMAT is minimum 12 weeks exercise protocol.⁴ Randomized controlled trial to 160 obese older adults, found that combination exercise for 26 weeks decrease IMAT 41%, with increased ISI (86%) and improvement of knee strength. Exercise was done three times per week, lasting 60–90 minutes. Aerobic exercise was performed on a treadmill, bike, or elliptical trainer at approximately 65% of their peak heart rate, which was gradually increased to 70%–85% of peak heart rate. Resistance exercise was performed on weight-lifting machines consisting of 9 upper-body and lower-body exercises. The initial sessions were 1–2 sets of 8–12 repetitions at 65% of the one-repetition maximum (1-RM), which was increased progressively to 2–3 sets at approximately 85% of the 1-RM.¹¹

Studies stated that IMAT has the ability decrease the advantageous effects of sport exercise on

muscles. Disruption of muscle contraction will decrease the muscle's ability to utilize IMAT as an energy source. This shows that, besides sport exercise, other modalities such as electrical muscle stimulation (EMS) are needed. This modality will increase muscle contraction and possibility of increasing muscle ability to utilize IMAT as energy sources, which further decreases the amount of IMAT.⁴

Pharmacologic treatment can act as another modality which can be used to reduce the harmful effects of IMAT on metabolism. Basically, IMAT is an ectopic adipose tissue located at an abnormal site, which further causes metabolic disturbance, such as insulin resistance. This condition is similar to fat deposition in the liver. Tiazolidinediones (TZD), frequently used for the pharmacologic management of nonalcoholic steatohepatitis, could potentially contribute in the management of IMAT.⁴⁴ Meta-analysis conducted to study the use of TZD in nonalcoholic steatohepatitis showed significant lower fasting blood glucose compared to placebo. This is due to the ability of TZD to improve insulin sensitivity.⁴⁵ This suggests that TZD may play a role in patients with high IMAT.

Other antidiabetic drug that is being proposed for adipose tissue is Sodium-glucose cotransporter 2 (SGLT2) inhibitors and Glucagon-like peptide 1 (GLP-1) analogs. Total of 551 patients were included in 10 articles. Meta-analysis results showed that compared with the control group, the visceral adipose tissue (MD = -16.29 cm^2 , 95% CI = $-25.07 \sim -7.50$, $P < 0.00001$) and subcutaneous adipose tissue (MD = -19.34 cm^2 , 95% CI = $-36.27 \sim -2.41$, $P < 0.00001$) of the trial group significantly reduced.⁴⁶ Forty five studies was included in the systematic review analyzing usage of GLP-1 analogs to adipose tissue. GLP-1 analog reduces adipose tissue, body weight and even improve non-alcoholic steatohepatitis.⁴⁷

4. CONCLUSION

With increasing age, the IMAT build up in the muscle increases. IMAT poses several deleterious effects, specifically metabolic dysfunction, muscle dysfunction, and mobility dysfunction. With its harmful effects, geriatric population will undergo the impacts. Practicable management and prevention for elderly patients with high IMAT, include exercise, pharmacology, and other modality, such as EMS. Further studies regarding management and prevention for IMAT are needed, considering its deleterious impact.

CONFLICTS OF INTEREST

There is no conflict of interest.

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