群化とは同じ筋線維タイプが群を形成して存在する状態であり、筋線維タイプの分布異常である。これは筋線維の脱神経支配に伴い、代償性に近隣の筋線維の神経筋接合部からの神経終末の分枝が伸張して再神経支配されることで起きると考えられている[11]が、その機構はよく分かっていない。

そこで、老齢マウスの除神経・再神経支配が筋線維タイプに及ぼす影響を調べるために、独自の評価方法によって筋線維タイプの群化を定量的に解析した。興味深いことに老齢マウスの長指伸筋において、顕著な萎縮を示したTypeⅡb筋線維の脱群化や、それに伴うTypeⅡa及びⅡxの群化が確認された(表2)。老齢マウスのひらめ筋においてもTypeⅠ筋線維の群化が確認された(表2)。今後は、脱神経支配と筋萎縮との関連性も含めて筋線維特異的な群化のメカニズムについて解析を行う。

4. Type1 筋線維 特異的なミトコンドリア呼吸酵素活性の低下

エネルギー代謝が盛んに行われている骨格筋において、ミトコンドリア機能の低下は筋機能の低下や筋萎縮を引き起こすと考えられている[12]。実際に高齢者や老齢動物の骨格筋において、ミトコンドリアの活性が低下することは既に知られている[12,13]。しかし、これまでの研究は筋全体についての生化学的な手法によるミトコンドリア機能解析であり、筋線維タイプ単位でミトコンドリア活性に着目した報告は非常に少ない。そこで、まずは速筋と遅筋におけるミトコンドリア機能の加齢変化を調べるために、nicotinamide adenine dinucleotide dehydrogenase (NADH; 呼吸鎖複合体Ⅰ), succinate dehydrogenase (SDH; 呼吸鎖複合体Ⅱ), cytochrome c oxidase (COX; 呼吸鎖複合体Ⅳ)染色によるミトコンドリア呼吸酵素活性の解析を行った。その結果、老齢マウスのひらめ筋におけるSDH活性は維持されたが、NADH及びCOX活性は顕著に低下しておりミトコンドリアの機能が低下していることが確認された(表2)。一方、老齢マウスの長指伸筋におけるミトコンドリア活性は維持された(表2)。

次に、ひらめ筋の連続切片を作製した。そして、TypeⅠとTypeⅡ(a)の筋線維タイプを区別するためにATPase(pH4.7)染色を行い、COX染色及びNADH染色によって筋線維単位でのミトコンドリア呼吸酵素活性を解析した。その結果、老齢マウスのひらめ筋はType1筋線維特異的にCOX活性及びNADH活性の低下を示すことが明らかとなった(表2)。

これまで老化によりひらめ筋全体のミトコンドリア機能が低下すると考えられていたが、我々の結果はTypeⅠ筋線維特異的にミトコンドリア呼吸酵素活性の低下が起きていることを示している。それでは、なぜTypeⅠ筋線維特異的にミトコンドリア活性が低下するのであろうか？ 近年、ミトコンドリアの融合と分裂といった形態変化がミトコンドリアの機能維持に必要であるとの報告がなされているが[14,15]、骨格筋におけるミトコンドリア形態の加齢変化を解析した研究は極めて少ない。興味深いことに、ミトコンドリアの形態は遅筋線維と速筋線維で異なることが示唆されていることから[16]、加齢に伴い筋線維タイプ特異的にミトコンドリアの形態が変化することが予想される。今後は、筋線維タイプ単位のミトコンドリア形態変化と機能変化に着目して、老化による筋萎縮と筋機能低下の因果関係について研究を行いたいと考えている。

5. おわりに

今回の我々の結果は、ミトコンドリア活性の低下と筋萎縮の因果関係について再考を要することを示している(図)。顕著なミトコンドリア活性の低下を示したTypeⅠ筋線維は筋持久力の低下に関連していると考えられるが、筋線維数と筋線維面積は減少していなかった。一方で、ひらめ筋のTypeⅡa筋線維や長指伸筋のTypeⅡb筋線維はミトコンドリア活性が維持されたが、筋線維数の減少や筋線維面積の低下が見られた。これらの結果は筋機能の低下と筋萎縮のメカニズムが複数存在することを示している。今後は、前述した筋線維タイププレベルでのミトコンドリア形態変化に着目した解析に加えて神経筋接合部の加齢変化ついても合わせて詳細に解析したい。

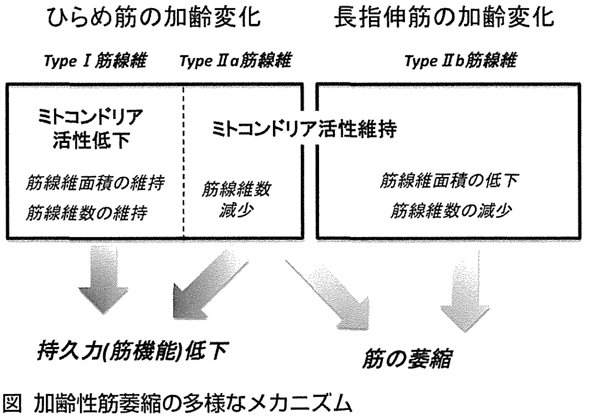

図 加齢性筋萎縮の多様なメカニズム

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筋肉と神経―最新基礎知見を踏まえて

Skeletal muscle and motor neuron: underlying mechanisms in sarcopenia

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Shigemoto Kazuhiro Fukunaga Daichi Mori Syuichi

抄録▶サルコペニアの病因解明には，筋だけでなく運動神経細胞と神経筋シナプス，血管，自律神経を対象として体系的に研究する必要がある．加齢により運動神経細胞数の減少，筋線維の量的・質的変化，神経筋シナプスの形態変化が起きる．また，筋幹細胞の再生能や修復効率も低下する．これらの病理学的変化のメカニズムやサルコペニアの病態との因果関係については，今後の課題として残されている．

Key Words サルコペニア，運動神経細胞，神経筋シナプス，筋線維，サテライト細胞

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はじめに

サルコペニア(加齢性筋肉減少症)は認知症と並んで高齢者のactivity of daily living (ADL)とquality of life (QOL)を損なう主要な原因となることから，その早期診断や予防法などの対策は急務の課題である．サルコペニアの臨床診断は，筋力，筋量と身体能力の3つの因子を測定して評価される[1]．サルコペニアと診断されたケースでは，すでに病態が進んでおり改善させることは困難である．認知症と同様，サルコペニアにおいても早期診断に基づく有効な予防・治療法が必要であるがいまだ確立されておらず，またその原因についてもほとんど解明されていない．サルコペニアは筋力，筋量と身体能力で臨床上評価されるが，それらの指標を対象としたサルコペニアの基礎研究により原因を解明することは困難である．

サルコペニアの基礎研究

筋の機能を維持するためには，運動神経細胞と両者のつなぎ目である神経筋シナプスが重要な役割を果たしている(図1)．サルコペニアの病因を解明するためには，筋だけでなくそれらすべてを対象に体系的に解析しなくてはならない．そのためには，まずサルコペニアの病理学的特徴を明らかにする必要がある．サルコペニアの原因は，さまざまな要因による長時間の相互作用の結果によるものであり，またヒトを対象とした実験は不可能であることから，老化モデル動物はサルコペニア研究の重要なツールとなっている．

加齢による運動神経細胞数の減少

運動神経細胞は老化に伴いどのような変化を示すのであろうか？ この観点の研究報告は極めて少ないが，1977年にイギリスから発表されたデータがある[2]．死亡時に運動機能が正常に

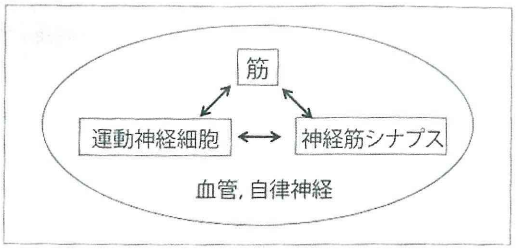

図1　サルコペニアの原因は筋以外にも存在する

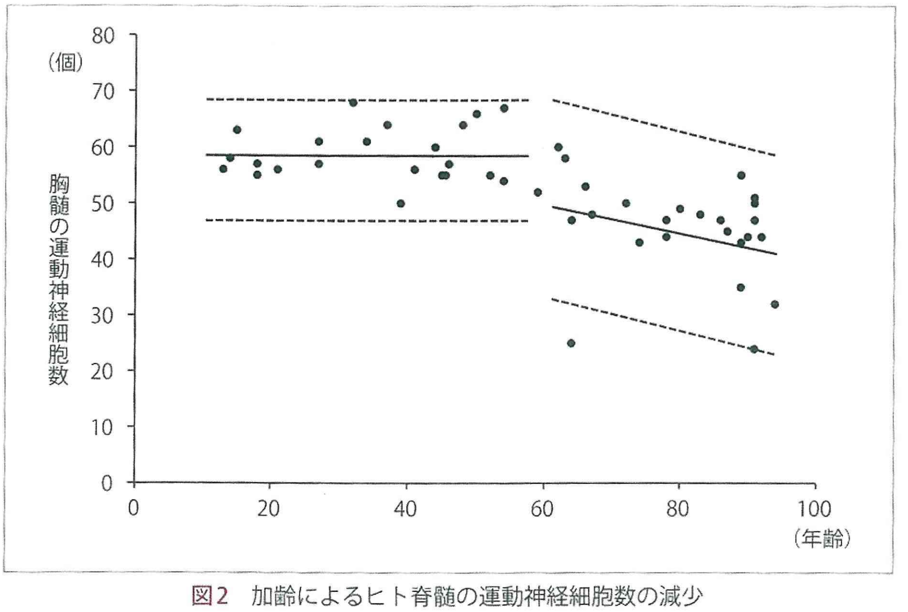

図2　加齢によるヒト脊髄の運動神経細胞数の減少
(J Neuro Sci 1977, Tomlinson et al. の図を改変)

保たれていた13～95歳までの47人の腰仙髄の一定区領域内の運動神経細胞を数えた結果を図2に示す．60歳を境にして急速に運動神経細胞数が減少していることがわかる．老化動物モデルでは，交系ラットの生後20カ月から腓腹筋を支配する運動神経細胞数が減少することが報告されている[3]．ラットの生後20カ月は，死亡率から換算するとヒトの60歳に相当する．加齢による脊髄の運動神経細胞の脱落は，臨床的なサルコペニアの病態と因果関係があると予想される．しかし，筋力低下や筋萎縮など臨床症状の出現と運動神経細胞数との関係(閾値)についてはよくわかっていない．老化モデル動物は，運動神経細胞の減少の原因解明とその病態研究に有用である．

サルコペニアと診断されたヒトの脊髄の病理組織像についての報告は少なく，認知症のように特徴的な組織像を示すかどうかも不明である．興味深いことに，超高齢社会を迎えて運動神経細胞の脱落が主原因とされているALS（筋萎縮性側索硬化症)の患者が増加しているが，一部の非定型のALSはもともと診断が難しく，サルコペニアとの鑑別が問題となりそうである．また，サルコペニアと認知症とは密接な因果関係があることから高齢者の脊髄の病理学的解析が必要である．

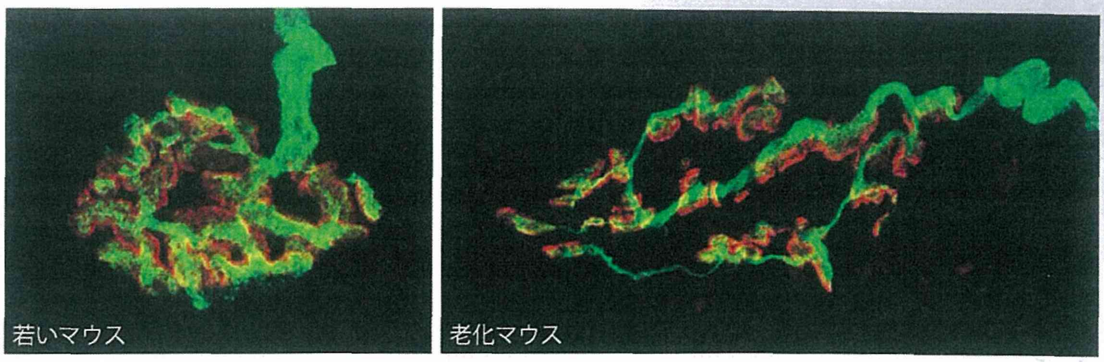

図3　老化による神経筋シナプスの形態変化
緑：運動神経終末，赤：アセチルコリン受容体

加齢による神経筋シナプスの変化

神経筋シナプスは筋と運動神経細胞のつなぎ目として神経伝達の機能を担うだけでなく，筋や運動神経自体の機能を維持するために重要な役割を果たす．加齢によりヒトや老化モデル動物（ラット，マウス）の神経筋シナプスの形態変化が顕著となる[4]．シナプスの形態が断片化，シナプス襞の減少，神経終末の分枝化，部分的あるいは完全な脱神経支配が観察される（図3）．高齢者の神経筋シナプスに関する研究は極めて少ないが，同様に形態が変化するという報告がある[5]．老化マウスの体幹，後肢や頸部の神経筋シナプスは，加齢による形態変化が顕著に観察され，一方，外眼筋や外肛門括約筋では形態が保たれている[6]．興味深いことにALSの進行に伴い患者の運動神経細胞が脱落する一方で，外眼筋を支配する脳幹の動眼神経や外転神経の神経細胞，また外肛門括約筋を支配する仙髄の神経細胞はALSの末期まで保たれることが多いとされる[7]．シナプスの機能・形態の異常は神経伝達の効率を下げて筋力低下や筋萎縮の原因になる．例えば，重症筋無力症では，自己抗体がシナプス形態および機能の維持機構を著しく障害して筋萎縮を誘導する[8~9]．シナプスの機能と形態は，運動神経終末と筋の双方からのシグナルにより保たれており，特に筋で発現するMuSK（muscle-specific kinase）蛋白が，このシナプスの相互維持に重要な役割を果たしていることがわかっている[9]．MuSKの上流および下流の分子機構が加齢により変化することが予想される．

ところで，神経筋シナプスは可塑性があり再生能を有している．そして，シナプス形態の加齢変化をカロリー制限や運動により予防できることが，マウスを使った実験で示された[4]．カロリー制限をすると全身のシナプス形態が若返るのに対して，運動の場合は負荷を受けた筋のシナプスだけが改善した．また，カロリー制限の方が運動負荷よりもシナプス形態の改善度がよかった．マウスのカロリー制限は，生後4カ月から始めて24カ月齢まで連続して行ったが，老年期に開始しても有効かどうかは不明である．運動負荷の場合は，22カ月齢のマウスに対して1カ月間だけでも有効性が確認された．ヒトも同様にシナプス形態が若返るかどうか興味が持たれる．

加齢による筋の質的変化

加齢による筋萎縮に伴う病理学的変化として，筋線維数や面積の減少だけでなく筋線維の質的な変化が起きる．筋収縮を担う筋線維は，収縮特性・代謝特性・疲労耐性などの違いから遅筋線維と速筋線維とそれぞれ性質が全く異な

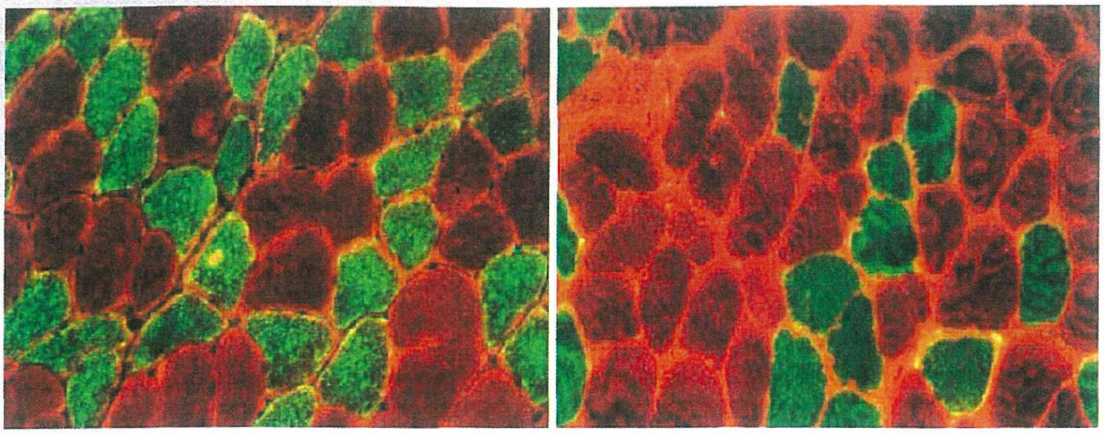

図4　老化により遅筋線維(赤) /速筋線維(緑)の比率が大きくなる(マウスのひらめ筋)

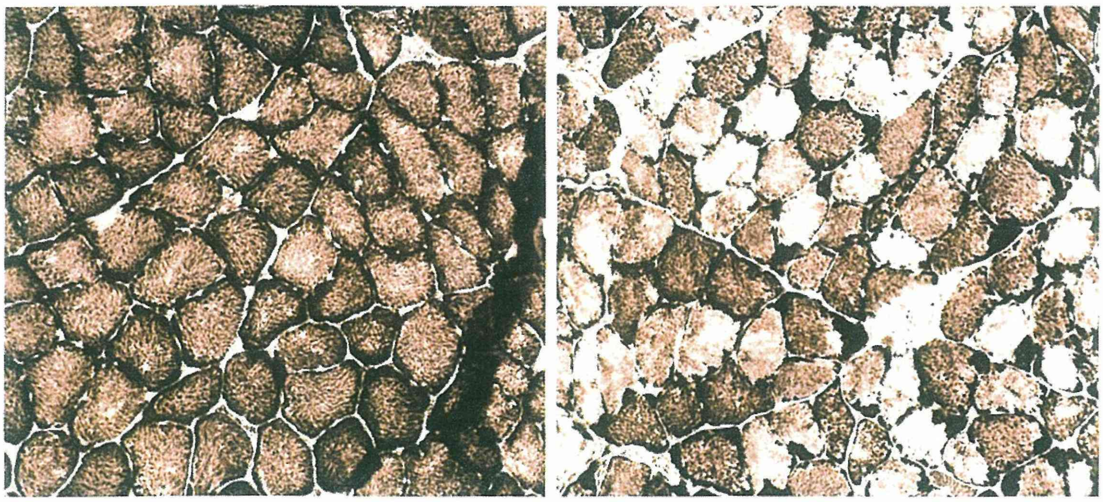

図5　老化による筋線維のミトコンドリア機能低下
シトクロームC酸化酵素活性が低下，筋線維が白く抜けて見える.

る筋線維タイプに分類される．そして，加齢により筋を構成する速筋に比べ遅筋線維の割合が増えることが知られている(図4)[10]．このような，加齢に伴う筋線維タイプの変化は，筋の代謝特性も変化していると予想されるが，実際はよくわかっていない．筋線維タイプ変化は老化動物だけでなくヒトの筋でも起きることが報告されている．

老化マウスでは，筋線維のミトコンドリア呼吸酵素活性が顕著に減少するが，筋全体に均一に起きるのではなく筋の部位そして筋線維ごとに程度が異なる(図5)[10]．ミトコンドリア機能の低下はサルコペニアの原因となると考えられるが，筋線維数と面積の減少とミトコンドリア呼吸酵素活性減少は必ずしも一致しておらず，筋力低下と筋萎縮との因果関係について検討が必要である．サルコペニア患者の筋でも，老化動物と同じ様式でミトコンドリア酵素活性が低下していると予想されるが，詳細な検討が必要である．ミトコンドリア酵素活性が保たれている筋を高齢者から採取することは非常に難しく，老化モデル動物の研究はサルコペニアの原

因を知るうえで今後も重要な手がかりとなるであろう．

筋の再生能

筋組織にはサテライト細胞という幹細胞が筋線維の表面に存在している．サテライト細胞は筋損傷を修復する必要に応じて筋細胞へ分化する．また，サテライト細胞は自己増殖して，筋線維あたり一定数になるよう維持されている．サテライト細胞による筋の修復は，筋組織が破壊されるような筋疾患では顕著に起きているが，健康な筋ではほとんど観察することができない．正常の筋では，サテライト細胞の増殖を伴う再生と修復の頻度は少ないと考えられる．

一方，老化動物では，サテライト細胞の再生能や修復効率が低下することが報告されている．また，サテライト細胞の維持に必要な周辺組織の環境(ニッチ)の老化がサテライト細胞の再生能を低下させるとしている[11]．さらに，老化とともにサテライト細胞の再生能を低下させる血中因子(Wnt蛋白，補体成分のC1qなど)が増加することが報告されている[12,13]．

おわりに

骨格筋は筋線維だけでなく多様な細胞から構成される複雑な組織である．血管や自律神経も，骨格筋の機能と構造維持に重要な役割を果たしている．これらの加齢変化が運動器システム全体の体内環境にどのような病理学的変化と機能的変化をもたらすのか今後の課題として残されている．

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6

Behavioral Treatment for Geriatric Syndrome

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1. Introduction

Geriatric syndrome is a term used to capture complex clinical conditions such as frailty, falls and fractures, urinary incontinence, malnutrition, and declining mental health, which do not fit into discrete disease categories but are serious problems among the elderly population. They are highly prevalent in the elderly, especially in frail adults with low levels of functional capacity. These geriatric syndromes have a large effect on the development of disability, dependence, decrease in quality of life, morbidity, and mortality. Having multiple underlying factors involving impairments in multiple organ systems contribute to the occurrence of geriatric syndromes (Tinetti et al., 1995). Thus, prevention and treatment of geriatric syndromes such as frailty, falls, and urinary incontinence in its early stages are important strategies in maintaining health and independence among the elderly.

This chapter will focus on frailty, falls, and urinary incontinence, as they are the most common geriatric syndromes among community-dwelling elderly people.

1.1 Shared risk factors for distinct geriatric syndrome

A main feature of geriatric syndrome is that multiple risk factors contribute to their etiology. Research has suggested that vision and hearing impairment, anxiety, as well as upper and lower extremity impairments are associated with incontinence, falling, and occurrence of functional dependence.

The risk of each geriatric syndrome is greater with increasing number of predisposing factors possessed. Furthermore, incontinence and falling are associated with the occurrence of functional dependence. Geriatric syndromes; therefore, may contribute both indirectly, through shared risk factors, and directly to functional dependence in the elderly. One model unifying the concepts of geriatric syndromes has been proposed by Inouye et al., (2007) demonstrating that shared risk factors may lead to one or more geriatric syndromes, and eventually to frailty. Once frail, this may feedback to the development of more risk factors, which in turn may lead to other geriatric syndromes, further frailness, and ultimately disability, dependence, and even death.

Frailty can be defined as a condition in which three or more of the following criteria are present: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity (Fried et al., 2001). The prevalence of frailty is greater in women than men, and increases which age. Frailty status, or the presence of frailty can predict disability and adverse outcomes, where those who are frail have a significantly higher risk of further debilitation, specifically in mobility, activities of daily living (ADL) and falls, eventually leading to hospitalization and death (Fried et al., 2004) (Table 1).

	Hazard Ratios Estimated Over 3 Years Frail (Versus Not Frail)
Worsening mobility disability	1.50**
Worsening ADL disability	1.98**
Incident Fall	1.29**
First hospitalization	1.29**
Death	2.24**

**$p \leq .05$
ADL= activity of daily living

Table 1. Frailty status predicting disability, falls, hospitalizations, and death over 3 years. (Fried, L.P.; Ferrucci, L.; Darer, J.; Williamson, J.D. & Anderson, G. (2004). Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, Vol.59, No.3, pp. 255-263, by permission of the Gerontological Society of America.)

Falls are an especially serious problem among the elderly, as approximately 30% of community-dwelling older adults over the age of 65 experience falls every year. Falls are the leading cause of unintentional injury, functional decline, hospitalization, institutionalization, and increased healthcare costs. In order to prevent falls, a thorough understanding of the causes and risk factors for falls among the elderly is required for the development of effective preventative strategies.

Urinary incontinence, particularly in the elderly, is considered to be an important determining factor for admission into long-term care and has been associated with loss of independence, reduced quality of life, restricted social activities, increased anxiety and social isolation.

2. Risk factors

Many studies have demonstrated that geriatric syndromes are multifactorial, and shared risk factors including older age, cognitive impairment, functional impairment, and impaired mobility, are often associated with common geriatric syndromes of frailty, falls, and urinary incontinence. The identification and treatment of the risk factors that contribute to geriatric syndromes have been the focus in recent research.

2.1 Frailty

Frailty is highly prevalent in the elderly. Frailty often overlaps with (though is not synonymous with) comorbidity and disability, and is associated with several major chronic diseases such as cardiovascular disease, pulmonary disease and diabetes. Hence, treatments for frail older adults usually require specific care needs (Fried et al., 2004) (Fig. 1). With the presence of comorbid conditions, there may be competition between the treatments. The combinations of medications and treatment regiments may limit the desired effects of the treatments, or have adverse effects. Comorbidities lead to the over-use and mixing of prescription medication which is a risk factor for falls. Frailty, coupled with low bone mass is associated with increased risk of hip fractures which are a major threat to survival in the elderly. Research has shown that 17.4% of people who suffered hip fracture over the age of 65 died within 12 months of a fracture (Magaziner et al., 1989).

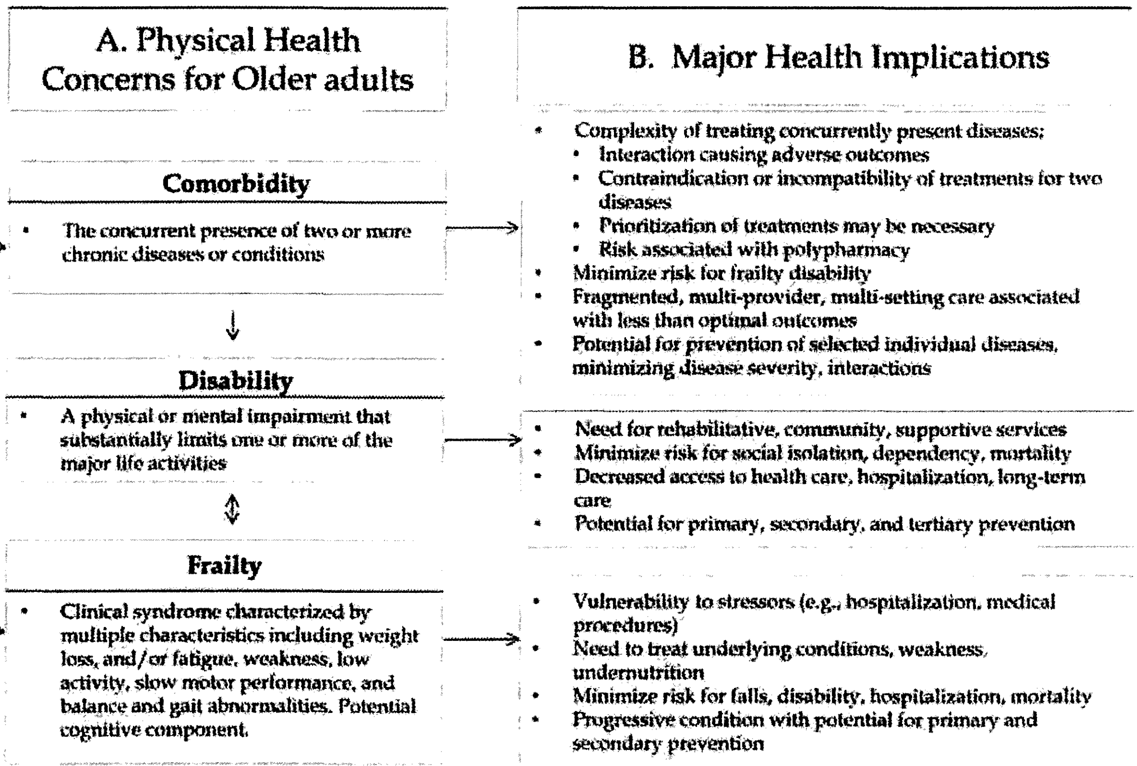


Fig. 1. Comorbidity, disability, and frailty: definitions and major health care implications. (Fried, L.P.; Ferrucci, L.; Darer, J.; Williamson, J.D. & Anderson, G. (2004). Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, Vol.59, No.3, pp. 255-263, by permission of the Gerontological Society of America.)

There are numerous factors that contribute to muscle weakness and loss of muscle mass in aging adults such as chronic disease, a sedentary lifestyle, and under-nutrition, where some factors can be reversed with lifestyle changes, and others need specific medications and cannot be reversed. Xue et al. (2008) hypothesized the cycle of frailty, as many of these factors can theoretically be unified into a cycle associated with decreasing energetics and functional reserve (Fig. 2) The core elements of this cycle, including weight loss, sarcopenia, decrease in strength and walking speed, as well as low activity, are commonly identified as clinical signs and symptoms of frailty.

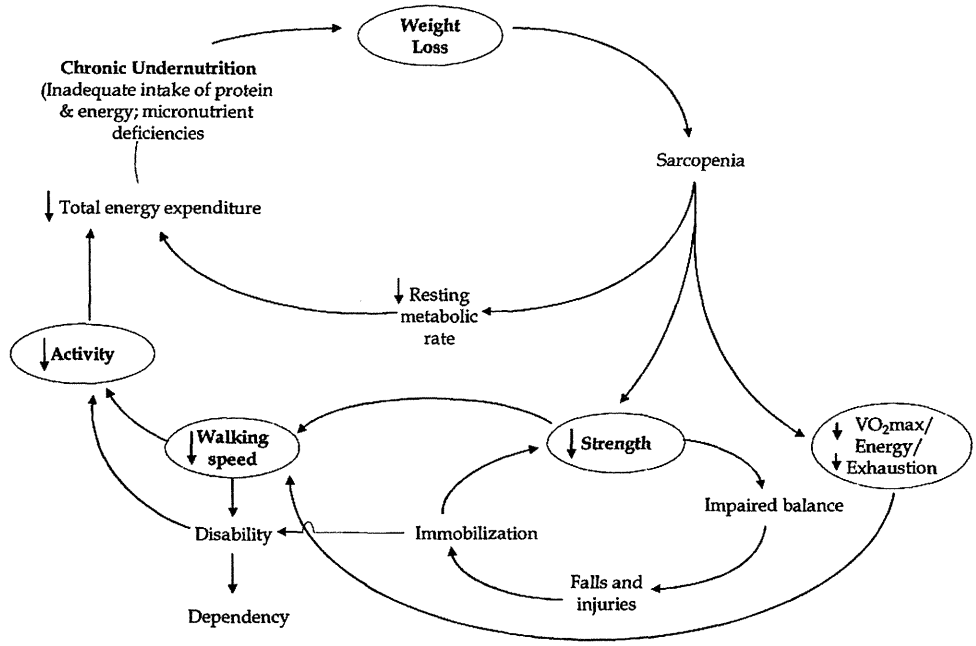


Fig. 2. Cycle of Frailty. (Xue, Q.L.; Bandeen-Roche, K.; Varadhan, R.; Zou, J. & Fried, L.P. (2008). Initial manifestations of frailty criteria and the development of frailty phenotype in the Women's Health and Aging Study II. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences,* Vol.63, No.9, pp. 984-990, by permission of the Gerontological Society of America.)

2.2 Falls

In the recent decade, several epidemiologic studies have identified risk factors for falls. While the classifications of these risk factors have not always been consistent, they are generally classified as intrinsic, extrinsic, and environmental. Intrinsic risk factors include muscle weakness, gait and balance deficits, functional and cognitive impairments, and visual deficits, extrinsic such as the use of four or more prescription medications and bifocals, and environmental factors, which include poor lighting, loose carpets, and lack of bathroom safety equipment (American Geriatric Society et al., 2001). Low vitamin D levels are also significantly associated with a high prevalence of falls in elderly women, as well as low physical performance (Suzuki et al., 2008) (Table 2).

The most common risk factors for falls are muscle weakness, history of falls, gait deficit, balance deficit, use of assistive device, visual deficit, arthritis, impaired ADL, depression, cognitive impairment, and older age (over 80 years old) (American Geriatric Society et al., 2001). The risk of falling increases linearly with the number of risk factors, from 8.0% with none to 78.0% with four or more risk factors (Tinetti et al., 1988). Furthermore, those who experience falls once have a greater chance of recurrent falls, which may lead to a fear of falling. Some older adults may then begin restricting activities both indoors and outdoors. Not only does this lead to a further lack of physical activity, but research has shown that older persons who restrict activity for fear of falling are more physically frail and have greater burden of chronic conditions and depressive symptoms compared with those who do not restrict activity despite their fear of falls (Murphy et al., 2002).

	Male			Female		
Risk Factor	OR	95%CI	*P*	OR	95%CI	*P*
Age (yr)	1.02	0.95-1.10	NS	1.02	0.99-1.06	NS
Normal walking speed (0.1 m/s)	0.87	0.77-0.97	0.015	0.92	0.88-0.97	0.001
Albumin (g/dl)	1.69	0.45-6.33	NS	1.60	0.88-2.90	NS
25(OH)D (mg/ml)	1	0.95-1.06	NS	0.97	0.94-0.99	0.010

Dependent variable was "fall experience over the previous year" (yes=1; no=0).
NS= not significant

Table 2. Multiple logistic regression model of factors associated with fall experience. (Suzuki, T.; Kwon, J.; Kim, H.; Shimada, H.; Yoshida, Y.; Iwasa, H. & Yoshida, H. (2008). Low serum 25-hydroxyvitamin D levels associated with falls among Japanese community-dwelling elderly. *Journal of Bone and Mineral Research*, Vol.23, No.8, pp. 1309-1317, by permission of the American Society for Bone and Mineral Research.)

2.3 Urinary incontinence

There is general agreement on the multifactorial nature of incontinence. Permanent incontinence also is typically the result of neurological damage or, intrinsic bladder or urethral pathology. However, incontinence is associated with several potentially reversible conditions. Lower urinary tract function, environmental factors, physical and cognitive function, psychological distress, mobility, manual dexterity, medical conditions, and medications may all have an effect on urinary incontinence status in the elderly (Landi et al., 2003). The incidence of urinary incontinence is typically higher in women than men, and those who experience incontinence are usually older with lower functional fitness levels for both sexes. Although there is a large amount of information regarding the mechanisms and treatment options for urinary incontinence, little is known about the potentially reversible causes of this condition in community-dwelling elderly people. Several of the known causes that may be reversible include urinary tract infections, as they can cause the urge to void quite frequently, physical restraints and drastic limitations in mobility, and environmental hazards.

Lifestyle and functional fitness are significantly associated with the onset of urinary incontinence in community-dwelling elderly people (Kim et al., 2004) (Table 3).

3. Treatment for geriatric syndrome

Declines in functional fitness such as walking speed, muscle strength and balance ability in the elderly are strongly associated with the development of geriatric syndromes. Hence, exercise focusing on strength, balance, and mobility improvement, even into advanced age, is usually offered as a strategy for the reduction of frailty, falls, and urinary incontinence in the elderly.

Sex	Variable		OR	95%CI
Male	Age (per 1 yr)		1.23	1.11-1.38
	Plasma albumin (per 0.1 g/dl)		0.70	0.54-0.88
	Smoking status	non-smoker	1.00	
		previous smoker	1.53	0.56-4.59
		current smoker	2.33	0.82-7.61
Female	Grip strength (per 1 kg)		0.92	0.86-0.98
	Social role (per 1 point)		1.81	1.19-2.73
	BMI (per 1 kg/m^2)		1.10	1.01-1.20
	Smoking status	non-smoker	1.00	
		current smoker	7.53	1.36-41.63

Table 3. Multiple logistic regression model of risk factors associated with the onset of urinary incontinence

3.1 Frailty

Aging is characterized by a gradual decrease in muscle mass and muscle strength, which contributes to declines in physical function, increased disability, frailty, and loss of independence. Out of many factors associated with the development of frailty, muscle disuse and nutritional deficiencies are the factors that are potentially reversible or preventable through interventions and a more active lifestyle (Fiatarone et al., 1994).

3.1.1 Nutritional supplementation

Declines in muscle mass are related to declines in muscle protein synthesis rates in older adults. In order to resist and reverse the effects of muscle protein synthesis declines, protein or more specifically, amino-acids, have been the focus of research. Investigators have found that leucine enriched essential amino-acid mixtures are primarily responsible for amino-acid-induced muscle protein anabolism in the elderly. Amino-acid supplementation can increase muscle mass in this population; however, an increase in muscle mass is not always accompanied by an increase in muscle strength (Dillon et al., 2009). Essential amino-acid supplementation alone is probably insufficient in increasing muscle strength. Carbohydrate-rich supplements have also been examined for any effects on muscle strength and muscle mass. However, supplements rich in carbohydrates are inadequate for the purpose of increasing muscle mass and strength (Fiatarone et al., 1994). Vitamin D supplementation, which will be discussed further (see section 3.2.1) has also been shown to increase strength.

3.1.2 Exercise

Exercise in elderly individuals may potentially modify risk factors for age-associated reductions in muscle mass (Liu & Latham, 2009). Research has shown that high intensity resistance training is effective in counteracting muscle weakness and physical frailty in elderly people. More specifically, exercise interventions focused on the major muscle groups that are crucial for performing functional activities, are especially important for the reversal of muscle weakness.

Extensive research has confirmed that doing resistance training two to three times a week can improve physical function and functional limitations, and also reduce disability and muscle weakness in older people. Resistance training in elderly people produces increases in strength from 9 to 15% (Borst, 2004), and about 1.1 kg in lean body mass (Peterson et al., 2011). While more improvements are seen with high intensity and volume resistance training, moderate intensity exercises are also beneficial, and are much safer for aging adults. Exercise prescriptions must be of a safe intensity, duration and frequency to avoid further injury and complications (Taaffe, 2006) (Table 4).

Combinations of both exercise and nutritional supplementation have also been studied by researchers. Amino-acid supplementations alone have beneficial effects such as increasing walking speed, and exercise itself also has beneficial effects of improving physical function. Exercise and amino-acid supplementation together have significant effects in enhancing muscle mass, strength and functional fitness. The combination of high resistance exercise and a high carbohydrate mixture containing small amounts of soy protein is effective in the enhancement of muscle strength. High resistance exercise alone increases both muscle mass and strength, while the carbohydrate supplementation alone does not (Fiatarone et al., 1994). Further research is still needed to investigate which supplementations coupled with exercise, or alone, are most effective.

Resistance training program recommendations	
Exercises	8-10 that target the major muscle groups
Repetitions	8-12 per set. When able to achieve 12 repetitions, increase resistance so that 8 repetitions are possible
Sets	Minimum of 1, preferable 2-3 per exercise with 1-2 minutes rest between sets
Frequency	1-3 days per week with at least 48 hours between sessions
Velocity	2-3 seconds concentric and 2-3 seconds eccentric. Some sets of rapid concentric movements can also be included
Breathing	Normal breathing on each repetition (no breath holding)
Duration	Less than 1 hour

Table 4. Resistance training program recommendations. (Taaffe, DR. (2006). Sarcopenia—exercise as a treatment strategy. *Australian Family Physician*, Vol.35, No.3, pp. 130-134. ©2011 *Australian Family Physician*. Reproduced with permission from The Royal Australian College of General Practitioners. Text and images copyright of *Australian Family Physician*. Permission to reproduce must be sought from the publisher, The Royal Australian College of General Practitioners).

3.2 Falls

The development of effective preventative strategies to reduce the fall rate in community-dwelling elderly people who are at risk of falling require a better understanding of the modifiable risk factors for falling. Among the numerous risk factors for falling, those that are considered modifiable include muscle weakness, impairments in balance and gait, and the use of multiple prescription medications. These risk factors can be modifiable through behavioral strategies such as muscle strengthening exercises, balance and gait training, and education about nonpharmacologic treatments to reduce the number of prescription medications used (Tinetti et al., 1994). Furthermore, the occurrence of falling rises with increasing number of risk factors present; therefore, strategies targeted to reduce these modifiable risk factors may be effective in the prevention of falls.

3.2.1 Vitamin D supplementation

In several trials of older individuals at risk for vitamin D deficiencies, vitamin D supplementation improved strength, function, and balance in a dose-related pattern. A high daily vitamin D supplementation dose (about 700-1000 IU) can reduce the risk of falls by approximately 20%; although small doses (less than 400 or 700 IU) may not be sufficient to reduce falls (Bischoff-Ferrari et al., 2009).

3.2.2 Exercise

Falls in older people are not purely random events but can be predicted by assessing a number of risk factors. Some of these risk factors such as decreased muscle strength, impaired balance, and gait deficit can be modified using exercise, whereas poor vision, and psychoactive medications require different strategies. Exercise can be used as a fall prevention intervention on its own or as a component of a multifaceted program. The pooled estimate of the effects of exercise was that it reduced the rate of falling by 17.0% (Sherrington et al., 2008). Home-based and tailored group exercise classes seem to be effective in reducing falls by improving balance and muscular strength. Also, while home hazard management (e.g. removing tripping hazards) and vision screening are not markedly effective in reducing falls when used alone, they add value when combined with an exercise program (Day et al., 2002).

3.2.3 An exercise-based falls prevention program

Exercise programs designed for fall prevention in elderly people should address three major areas - strength, balance and gait. People at high risk of falling due to muscle weakness, balance impairment, and gait deficit should be instructed to perform low or moderate intensity exercise containing safe and simple movements at entry level.

Strength training

A moderate-intensity strength training program aimed to reduce falls should target the major muscles such as the tibialis anterior, soleus, quadriceps femoris, iliopsoas, tensor fasciae latae, and sartorius (Fig. 3). Tripping is a leading cause of falls in community-dwelling elderly people, responsible for up to 53% of falls in this population (Blake et al., 1988). Trips may be associated with weakness of the tibialis anterior muscle, which would cause low toe-clearance or walking in a "shuffling" manner where the toes do not lift off the ground sufficiently to avoid small obstacles that may cause trips.

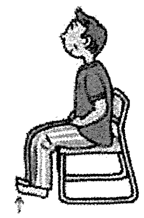
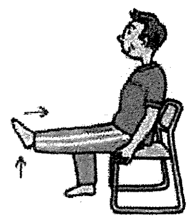
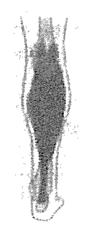
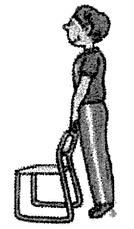
Target Muscle	Exercise	Exercise Description
Tibialis Anterior 	Seated Toe Raises 	Place hands in comfortable position while seated. Lift toes of both feet as high as possible with the heels still on the floor. Hold for 3-5 seconds, breath normally, and slowly lower toes to the floor. Perform 8-10 repetitions. Remind participants to not rock the body back when raising toes.
Quadriceps 	Seated Knee Extension 	Lift one leg still bent at the knee while inhaling, and extend the leg without "locking" the knee (keep knee slightly bent) while exhaling. Bend the knee again, with the hip still flexed, and place the foot on the floor. Perform 8-12 repetitions, and repeat on the other side. Remind participants to not lean back while lifting the leg, or extending the knee.
Soleus and Gastrocnemius 	Heel Raises 	Stand tall with feet flat, shoulder-width apart. Hold on to back of a chair for support. Slowly lift both heels off the floor while exhaling. Hold for 5-10 seconds, breath normally, and slowly lower the heels to the floor. Repeat 10 times.

Fig. 3. Examples of lower extremity strength training exercises.

Balance and gait training

Training is crucial for the improvement of balance in the elderly, and static as well as dynamic and lateral balance exercise have been recommended for reducing falls. Balance exercises progress from holding on to a stable supporting structure such as a chair, to performing the exercises independent of support. Not all elderly people will necessarily start at the first level of each exercise or be prescribed all the balance exercise such as one-leg standing, tandem stance, tandem walking, and side step (Fig. 4).

The results of a large scale study, known as the Frailty and Injuries: Cooperative Studies of Intervention Techniques (FICSIT) trials, suggest that exercise interventions (flexibility, resistance, balance) and Tai Chi for elderly people reduce the risk of falls (Province et al., 1995). To evaluate the effect of Tai Chi on functional fitness and falls, it is necessary to analyze the characteristic movements of Tai Chi. Tai Chi consists of a series of smooth movements linked together in a continuous sequence of whole body weight-shifting, with a low center of gravity. Also, Tai Chi movements involves shifting the weight forward and standing on one foot while lifting the other foot an inch off the floor, which contributes to the improvement of static balance. Moreover, the safe completion of the steps requires an adequate amount of dynamic balance, postural strength, and lateral stability (Li et al., 2004). Participants in the FICSIT trial were instructed on correct foot placement and posture, standing in a semi-squat position, which requires substantial lower extremity strength. These movements are directly or indirectly related to improvement of functional fitness.

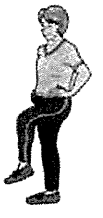
Target Balance Type	Exercise	Exercise Description
Static Balance	One-Leg Stand 	Stand tall with feet flat, shoulder-width apart. Lightly hold on to back of a chair for support or place hands on the hips. Slowly lift one foot off the floor while exhaling. Hold position for 10 seconds, breath normally, and slowly lower the foot to the floor. Repeat by lifting the other leg. Perform 2-3 sets per day.
Dynamic Balance	Tandem Walk 	Stand tall with feet flat on the floor, near a wall or railing for safety. Place one foot directly in front of the other foot, allowing the heel of the front foot to touch the toes of the back foot. Repeat with the other foot. Continue for 10 steps.
Lateral Balance	Cross Step 	Place a piece of tape or draw a line (refrain from anything that may cause trips) on the floor. Begin by standing with both feet together on one side of the tape. Lift the foot farther from the tape, and place it forward (diagonal) on the other side of the tape in a cross-fashion. Shift weight to the front foot, cross the other foot and place on the other side of tape. Note: Both feet do not come together. Continue for 10 steps.

Fig. 4. Examples of balance and gait exercises.

3.3 Urinary incontinence

The common treatments for urinary incontinence include surgery, drug therapies, and behavioral treatments. Behavioral treatments such as pelvic floor muscle (PFM) exercises and bladder training are recommended as a first line of treatment in the management of urinary incontinence, because of the potential benefits with few risks and no side effects. Urinary incontinence is usually classified into three different types: stress, urge, and mixed. Stress incontinence is urine leakage associated with increased abdominal pressure such as coughing, sneezing, laughing, heavy lifting, standing, running, or other types of physical activity. Urge incontinence is leakage associated with running water, or an urge to void and not being able to reach the toilet in time. Mixed urinary incontinence is when characteristics of both stress and urge incontinence types are present.

3.3.1 Pelvic floor muscle exercise

PFM exercises (Fig. 5), initiated by Kegal in 1948, is hypothesized to enhance urethral resistance by increasing the strength and endurance of the periurethral and perivaginal muscles and by improving the anatomic support to the bladder neck and proximal urethra (Kegel, 1948). These exercises are the preferred treatment for stress incontinence but have recently been recommended for urge or mixed incontinence because of reflex bladder inhibition associated with pelvic floor muscle contraction. The efficacy of PFM exercises in improving urine leakage has been validated by many investigators, and the improvement rate has been reported to range widely from 17 to 84% (Bo, 1995).

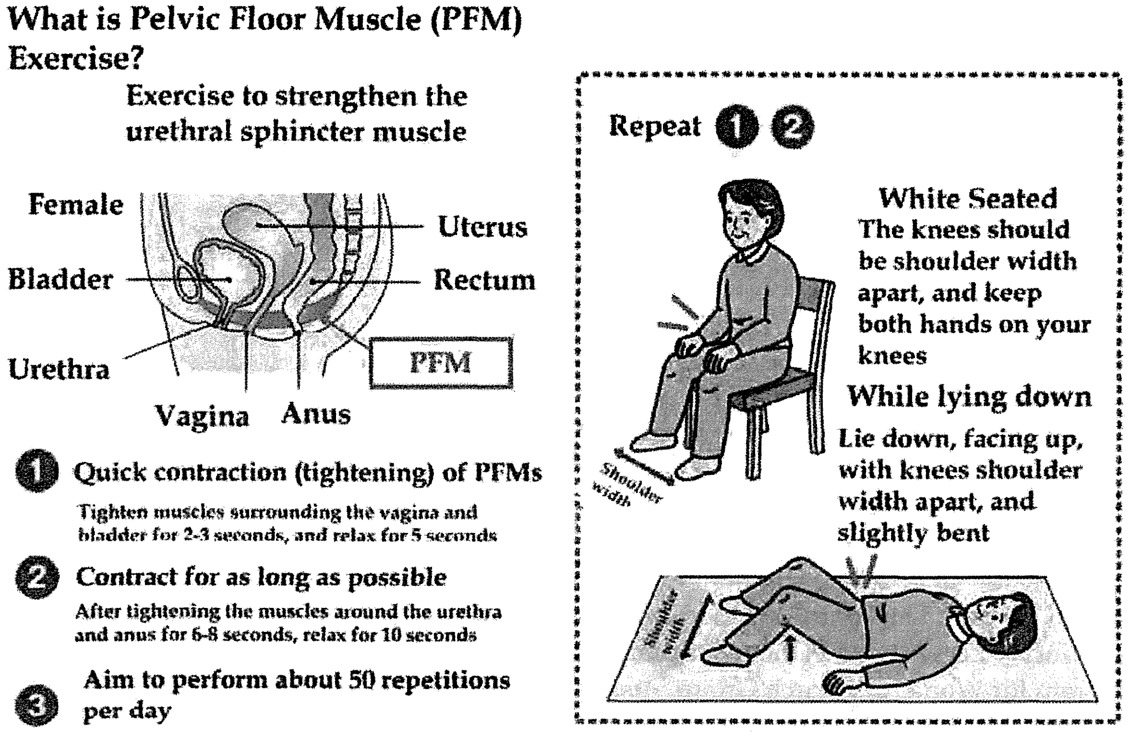


Fig. 5. Pelvic floor muscle exercise for the prevention of urinary incontinence.

At the beginning of PFM training, it is important to teach the elderly people participating in a training program, the structure of the PFM in order to gain awareness of these muscles. The participants should be taught that straining the abdomen would increase the abdominal pressure and would exert load on the PFM. Training should focus on how to exert force on the PFM without excessively straining the abdomen. Most exercise regimens are designed to strengthen the fast and slow-twitch fibers located at the pelvic floor. PFM exercise programs often incorporate alternations of fast contractions, usually held only for about three seconds, sustained contractions, where the participants would hold the contraction for about six to eight seconds, and ten-second relaxation periods between the contractions. The PFM exercises are usually performed in the seated, lying, and standing positions with the legs apart, and the emphasis placed on training of the PFM and relaxing of the other muscles.

The durations of the exercise training periods vary between 3 weeks and 6 months. Bladder training appears to have its greatest efficacy at 6 weeks; PFM exercise appears to be best between 11 to 12 weeks; and combined bladder training and PFM exercise seems to be most effective between 8 to 12 weeks of training (Wyman et al., 1998) (Fig. 6).

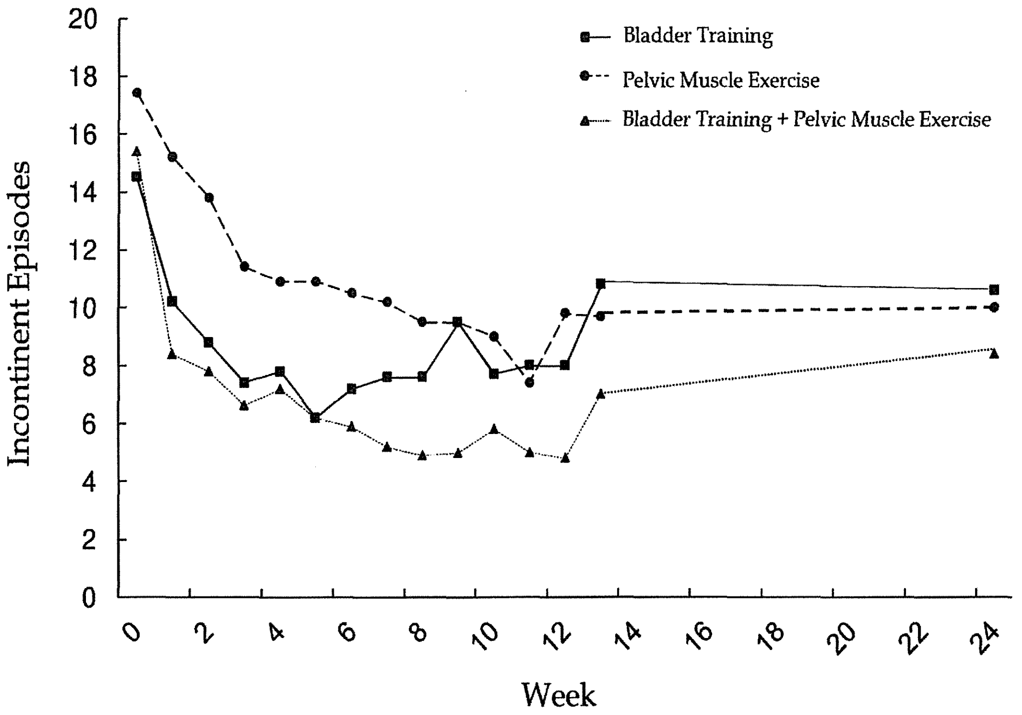


Fig. 6. Change in mean weekly number of incontinent episodes over time by treatment group. (Wyman, J.F.; Fantl, J.A.; McClish, D.K. & Bump, R.C. (1998). Comparative efficacy of behavioral interventions in the management of female urinary incontinence. Continence Program for Women Research Group. *American Journal of Obstetrics and Gynecology*, Vol.179, No.4, pp. 999-1007, with permission from Elsevier).

3.3.2 Fitness exercise

Several studies have reported that obesity and high body mass index (BMI) are associated with urinary incontinence. Presumably, increases in body weight causes increases in abdominal-wall weight, hence increasing intra-abdominal pressure and intra-vesicular pressure (Bo, 2004). Therefore, reductions in abdominal fat from exercise may contribute to decreasing intra-abdominal pressure, causes improvements in urethral sphincter contraction, and therefore decreased risk of urinary incontinence (Fig. 7; Fig. 8). Weight reduction is desirable for women complaining of urinary incontinence (Subak et al., 2009). Bump et al. (1992) found that surgically induced weight loss in obese women significantly reduces weekly incontinence episodes.

Although a direct cause-effect relationship between obesity and incontinence has not yet been established, there is evidence that weight reduction or decrease in BMI may be beneficial for treatment of incontinence. Kim et al. (2007) investigated the distribution of subjects cured from urinary incontinence according to tertiles of BMI, maximum walking speed, and adductor muscle strength, found that a significantly higher proportion among those who were cured of incontinence episodes, demonstrated improvements in BMI and walking speeds (Kim et al., 2007). Therefore, weight reduction, decrease in BMI, and increase in walking ability are desirable qualities for the treatment of urinary incontinence (Table 5).

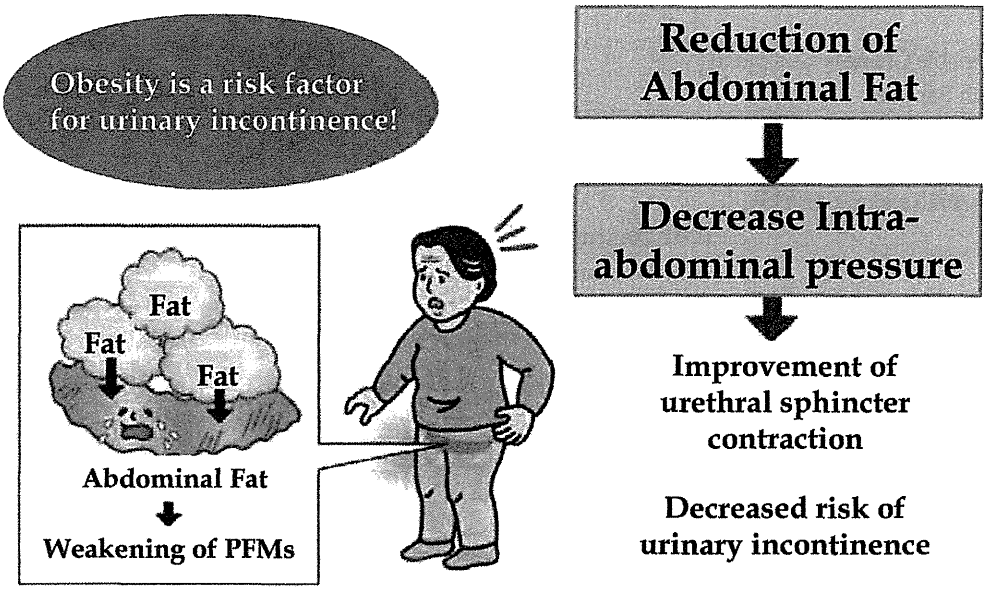


Fig. 7. Strengthening exercises to reduce abdominal fat prevents urinary incontinence

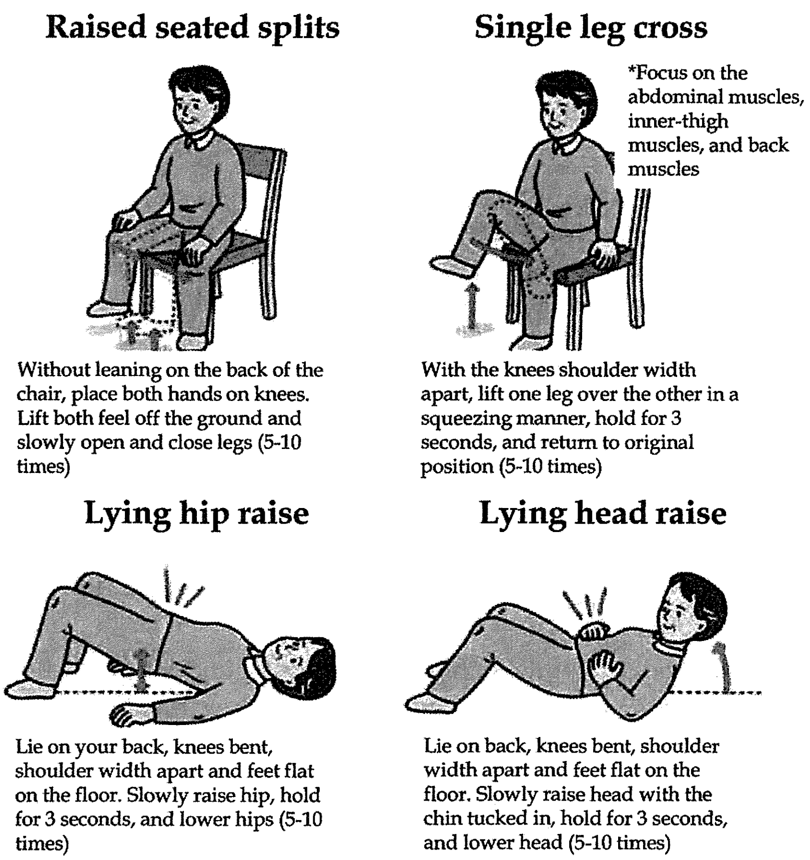


Fig. 8. Examples of exercises aimed to reduce abdominal fat.