data transfer, and registration was 1.5 to 8 minutes per case, depending on the number, size, and shape of lesions. In contrast, it took about eight hours to enter the gold standard of a visceral space, since the labeling of gold standard data includes that of regions of the diaphragm, liver, spleen, abdominal aorta, kidney, and other regions as well as those of the visceral space.

At the research site, the average time required for data retrieval was 1 to 5 minutes per case (Table 1). We developed CAD applications based on clinical cases registered in CIRCUS DB. The applications were cerebral aneurysm detection in MR angiograms (Fig. 11), lung nodule detection in chest CT images (Fig. 5), skin lesion detection in whole-body FDG-PET/CT images (Fig. 12), virtual straightening of spine in whole-body CT images (Fig. 10), and volumetry of VAT and SAT in whole-body CT images (Fig. 13).

The clinical server with our CAD applications was utilized in our hospital. The time required for the transfer of image files and the processing of CAD applications ranged from 1 to 7 minutes per case, depending on the number of image files and the type of CAD application (Table 2). Table 3 shows the

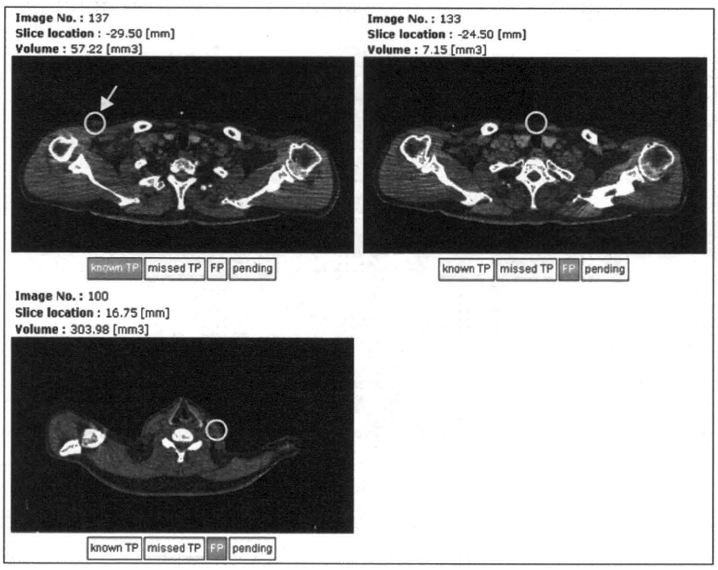

Fig. 12. Result of skin lesion detection in whole-body FDG-PET/CT images. The center slice of the displayed candidate is displayed in a CT image. The circles indicate the location of the lesion candidate, and the circle with an arrow indicates the detected skin lesion.

number of cases processed using CIRCUS CS. At present, the feedback database includes 2,308 cases of cerebral aneurysm detection and 2,311 cases of lung nodule detection. Figure 14 shows an example of a free-response receiver operating

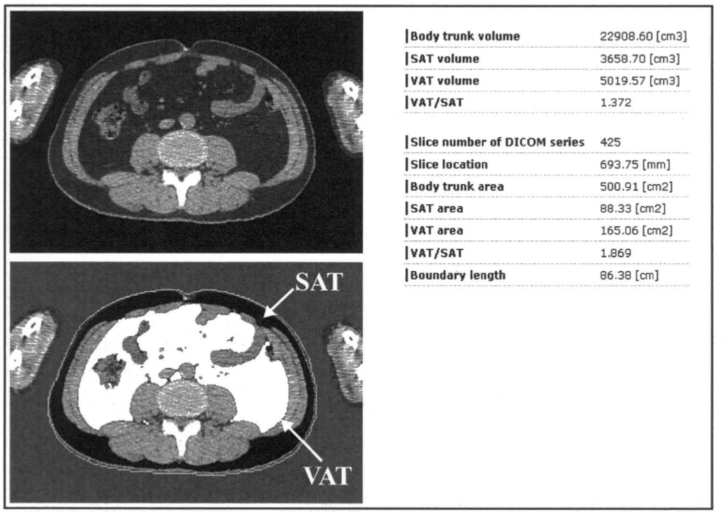

Fig. 13. Result of volumetry of VAT and SAT in whole-body CT images. The upper image shows a CT image in an umbilical slice, and the lower image shows extracted fat regions. The black area represents SAT, and the white area represents VAT. The right table shows measurement results.

Table 3. Number of cases processed using CIRCUS CS (13 Jan. 2009 - 15 Aug. 2010).

CAD application	No. of cases
Cerebral aneurysm detection	2,564
Lung nodule detection	2,682
Skin lesion detection	7*
Vertebral deformity analysis	67*
Volumetry of VAT and SAT	654*

* Retrospective study

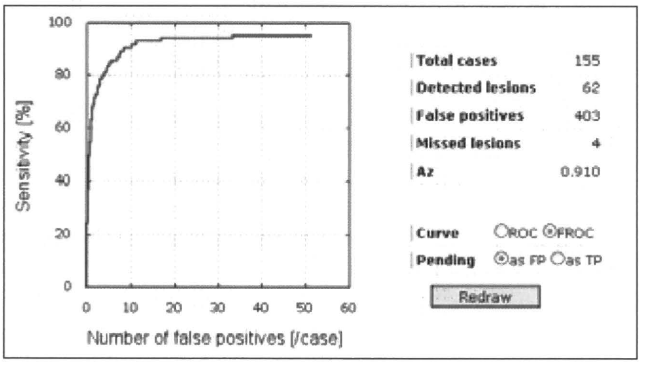

Fig. 14. Example of FROC curve for cerebral aneurysm detection.

characteristic (FROC) curve for cerebral aneurysm detection on the basis of accumulated clinical feedback. The number of FPs was 4.0 per case at 80% sensitivity. Figure 15 shows examples of scatter plots in lung nodule detection. From Fig. 15, individual differences in interpretation characteristics can be observed between two radiologists.

4 Discussion

The results show that CIRCUS DB has the potential to collect and register a sufficient number of clinical cases for CAD software development in a short period. However, the gold standard labeling of a large organ or region is still time-consuming. To reduce the time required for labeling a large organ or region, a labeling interface with interactive segmentation algorithms, such as the level set method [11] and graph cuts [12], is required.

CIRCUS CS makes it possible to use our CAD software in the daily clinical routine and to obtain feedback from radiologists. The method of clinical feedback in our system, which includes the classification of displayed candidates and the locations of FNs, makes it possible not only to evaluate the performance of the CAD software but also to improve the software. A few similar systems can be found in the literature such as in the report by Pietka et al. [13], which includes a workflow of the development, evaluation, and implementation of CAD software including an image database. One of the important original features of our platform is the function for collecting the personal diagnostic decisions of each radiologist, which is realized by the individual login. Collected data enable radiologists to check their own interpretation characteristics. In addition, it is possible to adjust the set of displayed candidates adaptively for each radiologist, such as by changing the criteria for displaying lesion candidates based on the tendency of radiologists to overlook lesions in specific regions. That is, a personalized CAD system optimized for each radiologist's interpretation characteristics can be realized. This aspect is as important as improving the performance of the CAD software.

5 Conclusion

We have built an integrated platform for the development and assessment of various types of image analysis software, named CIRCUS. Our current works cover the implementation of an interface for the on-line learning of CAD software, and the tracking of longitudinal changes in performance by the refinement or adaptation of the CAD software in our system. A software toolkit of the web-based clinical server (CIRCUS CS) will be made publicity available after multicenter trials.

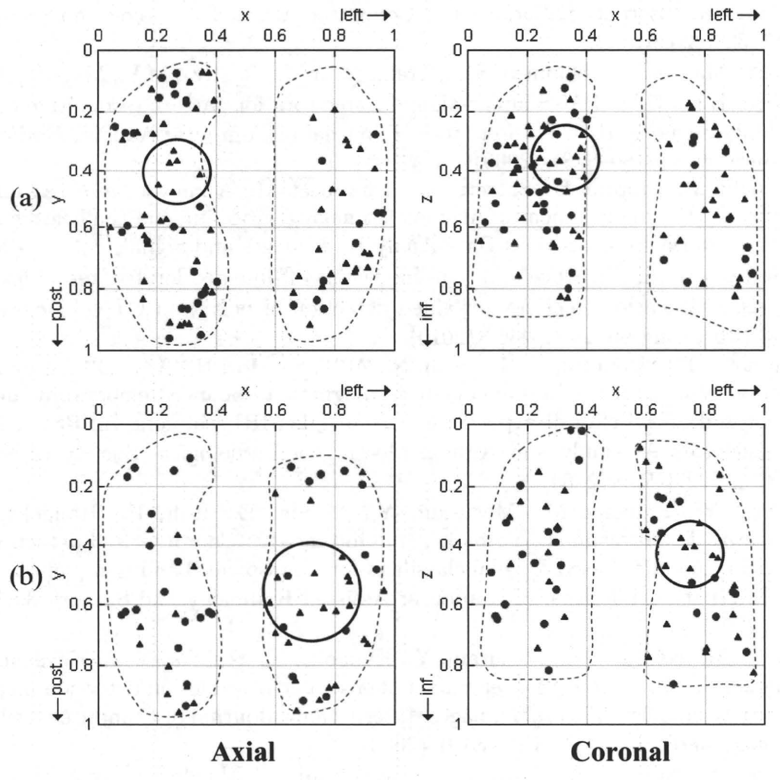

Fig. 15. Example of scatter plots in lung nodule detection. (a) Radiologist A with 14 years of experience; 125 cases, number of lesion candidates: 625. A higher tendency to overlook can be observed in the right pulmonary hilum (circle). (b) Radiologist B with 8 years of experience; 38 cases, number of lesion candidates: 190. A higher tendency to overlook can be observed in the left pulmonary hilum (circle). Dots represent known TPs, and triangles represent missed TPs.

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地域在住高齢者におけるサルコペニア改善のための運動，アミノ酸補充の効果

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Effects of exercise and amino acid supplementation for sarcopenia in community-dwelling elderly people

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はじめに

人間の緒機能は，常に変化する属性を持ち，個体の潜在能力が効率よく発揮できる方向へ変えていくのが一般的である。しかし，中年期を過ぎると様々な組織の機能が十分発揮できなくなり，環境変化への適応能力の低下ないしは機能喪失が徐々に増してくる。その背景要因の一つに，体脂肪やLBM（lean body mass）の変化が挙げられる[1]。中でも，骨格筋量の減少（Sarcopenia）[2]は，筋力の衰え，身体機能の低下をもたらし，身体的障害あるいは老年症候群の発症と密接に関わっていることが多くの疫学調査で指摘されている。骨格筋量の減少には性，年齢，身長，体重，BMI，テストステロン，脂肪量，不活動，ビタミンD，低栄養など様々な要因が複雑に関わっている[3,4]。サルコペニア予防策を構築するためには，多くの危険因子の中で，可変因子の改善を目的とした取組みが有効であり，Fiataroneら（1994）は，骨格筋の不使用と低栄養の改善に焦点を当てた介入が有効であると指摘している[5]。

サルコペニア予防のための戦略

加齢に伴う骨格筋量の減少を予防したり，委縮した骨格筋の機能を回復させるためには，筋に適当な刺激を与えるトレーニングが有効的と考える。しかし，虚弱高齢者を対象とする場合には，筋力発揮に伴うメカニカルストレスの増大や循環器への負担が懸念され，無理のないトレーニングが原則である。運動効果について調べた研究によれば，日常的活動レベルが低く，筋力低下が進んでしまった虚弱高齢者であっても筋力増大の効果が報告されている。虚弱高齢者における著しい筋力増大効果は，筋肥大よりも神経系の機能改善に起因するものと考えられてきた。しかし，最近の研究により高齢者でも筋肥大が起こることが確かめられている[5]。

Fiataroneら（1994）は，72～98歳の長期施設入所者100名を対象に，筋力強化運動，栄養補充効果を検証した。その結果，筋力強化運動群では筋力113%（$P<0.01$），歩行速度11.8%（$P=0.02$），階段昇降機能28.4%（$P=0.01$）と有意に上昇したが，太腿の筋断面積2.7%（$P=0.11$）増加に止まった。一方，240mlの栄養補充（炭水化物60%，脂肪23%，タンパク質17%）の効果は検証されなかったと指摘している[6]。これらの結果は，サルコペニアの改善のためには単なる栄養補充ではなくて，骨格筋量の減少メカニズムを把握した上での処置が必要であることを示唆する試験である。高齢者における骨格筋量の減少（サルコペニア）背景は，高齢者では，筋タンパク質の合成と分解が減弱し，その結果としてサルコペニアが起こるということである。よって，骨格筋量の予防・改善には筋タンパク質合成促進が有効と考える。骨格筋タンパク質合成は血液中のアミノ酸濃度に影響され，血液中のアミノ酸濃度が上昇すると筋タンパク質合成速度が速やかに増加するが，分解速度は変化しないことが指摘されている[7]。特に，高ロイシン含量の必須アミノ酸は比較的少量で筋タンパク質合成が促進されることを検証したことから，その長期摂取による骨格筋量の改善が期待できる[8]。

サルコペニア改善のための運動，アミノ酸補充の効果

1）サルコペニア高齢者の特徴

これらの背景を踏まえて，筆者は，サルコペニアと判定された304名と正常者1,095名の調査項目を比較し，サルコペニア高齢者の特徴を調べた。その結果，サルコペニア群は正常群に比べて，年齢が高く，下腿三頭筋周囲，BMI，筋肉量が有意に低値を示すとともに，健康度自己

表１．　サルコペニア群と正常群の調査項目の比較

項　目	サルコペニア群	正常群	p値
年齢（歳）	79.49 ± 2.93	78.51 ± 2.77	＜0.001
下腿三頭筋周囲（cm）	30.17 ± 2.03	33.92 ± 2.60	＜0.001
ＢＭＩ（kg/m^2）	18.98 ± 2.01	23.74 ± 2.84	＜0.001
筋肉量（kg）	26.92 ± 2.61	31.73 ± 3.16	＜0.001
健康度自己評価，健康（%）	75.7	85.8	＜0.001
外出頻度, 少ない（%）	4.6	2.5	0.051
運動習慣, 有（%）	27.3	33.5	0.039
既往歴, 有（%）			
高血圧	51.0	58.0	0.029
高脂血症	32.2	40.5	0.009
貧血症	4.6	2.2	0.022
骨粗鬆症	38.2	30.7	0.014
骨折	28.6	22.9	0.038

評価，定期的な運動習慣を持っている者の割合は低かったが，外出頻度低下者の割合は高かった。一方，既往歴においては，貧血症，骨粗鬆症，骨折歴は有意に高かったが, 高血圧症, 高脂血症は正常群より低かった(表１)。

２）運動，アミノ酸補充の効果

サルコペニア改善のための運動，アミノ酸補充の効果を検証するために，介入参加希望者をRCTにより運動群と栄養群に分け，運動群には週２回，１回当たり60分間の筋力強化と歩行機能の改善を目的とした包括的運動指導を，栄養群にはロイシン高配合のアミノ酸３gを１日２回補充する指導を，３ヶ月間実施した。介入前後における身体組成，体力，老年症候群の改善の度合いを検討した。その結果，LBMは運動群で2.4%，栄養群で4.6%の有意な向上が，歩行速度は，運動群で18.6%，栄養群で10.3%の顕著な向上が確認され（図１），地域在住サルコペニアの改善には運動のみならずアミノ酸補充も有効であることが示唆された。しかし，サルコペニア高齢者に多く観察される尿失禁は，運動群で38.9%から

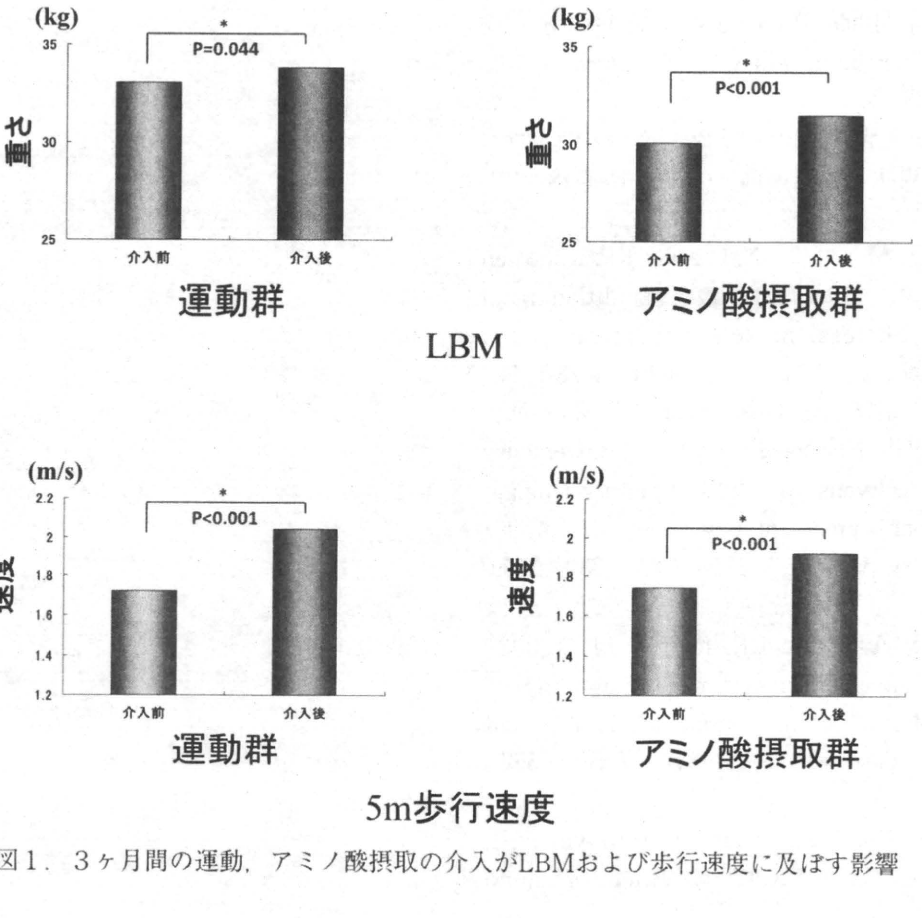

図１．３ヶ月間の運動，アミノ酸摂取の介入がLBMおよび歩行速度に及ぼす影響

19.4%（P=0.021）と有意に改善されたが，栄養群では有意な改善が見られなかった。以上のことから，サルコペニア高齢者のLBMあるいは体力の改善を目的とした場合には，運動指導あるいは栄養補充の両方とも有効な手法であることが確認されたが，サルコペニア高齢者に有症率の高い老年症候群の改善のためには，運動介入の効果が優れる可能性が示唆された。

おわりに

骨格筋量の減少に伴う筋力の衰えを意味するサルコペニアは後期高齢者において有症率が上昇し，身体機能の障害や死亡と強く関連していることが指摘されている。サルコペ二アと関連する要因は様々で複雑であるが，不活動や栄養など可変要因の改善に焦点を当てた予防策の効果を検討したところ，骨格筋量の増加，体力の向上には，運動指導，栄養指導ともに有効であった。しかし，サルコペニア高齢者に多く見られる老年症候群の解消には，運動指導がより有効であることを検証した。

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特集：ロコモティブシンドロームと生活習慣病

3．ロコモティブシンドロームの発症メカニズム

4）サルコペニアとロコモティブシンドローム

Kim Hunkyung
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はじめに

人間の諸機能は，中年期を過ぎると低下ないしは喪失が徐々に増してくる．その背景要因の1つに，体組成の変化が挙げられる．加齢に伴う体組成の変化の中で，最も特徴的なのは脂肪組織量の増加と，骨や骨格筋を含んだ徐脂肪組織量（fat-free mass：FFM）の低下である．加齢に伴うFFMの変化は，男性で0.34 kg/yr，女性で0.22 kg/yr減少することが[1]，筋肉量は，男性で0.19 kg/yr，女性で0.11 kg/yr減少するが，50歳代以降では下肢骨格筋量の減少が顕著であることが指摘されている[2]．加齢に伴って筋肉量や骨格筋量が減少すると，筋の質を表す筋力の衰弱をもたらし，特に下肢筋力の衰えは歩行機能を著しく低下させ，ひいては転倒・骨折の原因となるなど，高齢者の移動能力を制限してしまう重大な要因である．

一般的にロコモティブシンドローム（以下，ロコモ）は，運動器の障害のため移動能力の低下を来し要介護状態になっていたり，要介護状態になる危険性の高い状態を指す概念である．身体活動は骨，筋肉，関節，神経などの組織や器官の機能的連合によって産出される結果であり，どれか1つ不具合になっても上手く働かない．

ここでは，ロコモとサルコペニア（sarcopenia）に共通の媒介要因として考えられる筋力の衰えという観点から，ロコモとサルコペニアの関連性や位置づけについて簡単に紹介する．

表1　性・年齢・人種別にみたサルコペニアの有症率

年齢群（歳）	男性		女性	
	ヒスパニック（n＝221）	白人（n＝205）	ヒスパニック（n＝209）	白人（n＝173）
＜70	16.9	13.5	24.1	23.1
70〜74	18.3	19.8	35.1	33.3
75〜80	36.4	26.7	35.3	35.9
＞80	57.6	52.6	60.0	43.2

（文献4より引用）

サルコペニアの定義および有症率

加齢に伴って徐々に起こり得る筋肉量の減少や筋力の衰えを表す言葉として「sarcopenia」が1989年以降使用され[3]，老年症候群の発症と深く関わっていることから注目されるようになっている．

現在サルコペニアの操作的定義として広く用いられているものの1つとしては，Baumgartnerらの定義がある．この定義は，二重エネルギーX線吸収法（dual energy x-ray absorptiometry, DXA）から求めた四肢の筋量（appendicular skeletal muscle mass：ASM）を身長（m^2）で除したskeletal muscle mass index（SMI）を指標としたものである．サルコペニアの定義は，18〜40歳成人のSMI平均より2SD以下の場合とされている．この定義に基づく有症率は，70歳以下の高齢者で13.5〜24.1%の範囲であるが，80歳以上になると43.2〜60.0%に上昇する（**表1**）．さらに，サルコペニアのカットポイントは，SMIが男性で7.26 kh/m^2，5.45 kg/m^2と

表2　サルコペニア選定に用いた骨格筋量のカットポイント

報告者	筋量の測定法	定　義	男　性	女　性
Baumgartner, et al	DEXA	ASM/Ht², 若年成人2SD↓	7.26	5.45
Tanko, et al	DEXA	ASM/Ht², 若年成人2SD↓	*	5.40
Janssen, et al	BI	SMI	8.50	5.75
Chien, et al	BI	SMI, 若年成人2SD↓	8.87	6.42
Sanada, et al	DEXA	ASM/Ht², 若年成人2SD↓	6.87	5.46

ASM(kg) = appendicular skeletal muscle mass estimated by DXA.
SM(kg) = skeletal muscle mass estimated by BI.
SMI = SM/Ht², Ht = height.
（文献4より引用）

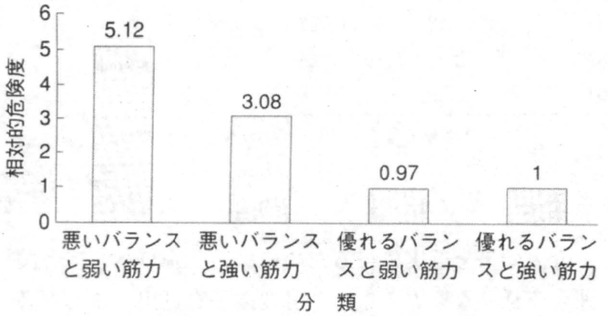

図1　歩行障害の予知因子
（文献5より引用）

提案するとともに，disabilityと密接に関連する（**表2**）ことから，サルコペニアは高齢期の大きな健康問題としてとらえるべきであると強調している[4]．

歩行機能には筋力とバランスが密接に関わっている

歩行機能は，体力全般の代表的な指標である．外出を楽にし，活動範囲を広げ，元気で長生きを実現するためには，歩行機能の維持・向上は不可欠な要素である．高齢者歩行パターンの特徴は，歩行速度の低下，歩幅の短縮，歩隔の増大，両脚支持時間の延長，遊脚期での足の挙上の低下，腕の振りの減少，不安定な方向転換などである．高齢者に多くみられる歩行機能の低下は，死亡率の上昇，転倒率の増加，生活機能の障害など，様々な指標と密接に関わっていることが多くの研究で指摘されている．

Rantanenらが，65歳以上の高齢女性758名を対象に3年間追跡調査し，歩行障害の発生と関連する要因について検討した結果によれば，「筋力の減少とバランス能力の低下」という条件の対象者は「優れる筋力とバランス機能」を有する対象者に比べて，歩行障害発生の危険性の高いことを指摘し（RR = 5.12，95% CI = 2.68–9.80），歩行機能を維持するためには筋力向上とバランス機能の改善が必要であると強調している（**図1**）[5]．

サルコペニアの高齢者の特徴

筆者は，大都市部在住の75歳以上の後期高齢女性1,399名を対象に，「四肢の骨格筋量が少ない」「BMIが低い」「膝伸展力が低い」3つの基準に該当する場合をサルコペニアと定義し，該当者304名（21.7%）を抽出し，特徴を調べている．その結果によれば，サルコペニア高齢者は，年齢が高く，下腿三頭筋周囲，BMI，筋肉量は低値を示すとともに健康度自己評価，定期的な運動習慣をもっている者の割合も低いという傾向である．しかし，外出頻度が少ない者の割合は高値を示し，サルコペニアと判定された高齢者は活動量が少なく，自分の健康に対する自信感を喪失している者が多いと推測できる．一方，既往歴においては，貧血症，骨粗鬆症，骨折歴は有意に高い割合を示しているが，高血圧症，脂質異常症は正常群より低い割合を示していることから，サルコペニア高齢者の場合，骨粗鬆症に伴う骨折危険性が高いことが示唆されている（**表3**）．さらに，サルコペニア高齢者の歩行機能を調べるために，5 mの最大歩行速度を計測し，サルコペニア群と正常群を比較したところ，**図2**に示した通りに，サルコペニア群は1.58 ± 0.34 m/sec，正常群は1.71 ± 0.36 m/secとして，サルコペニア群の歩行速度が有意に低いことが確認されている[6]．

サルコペニアと関連する要因

老化に伴う筋骨格筋量減少の原因としては，加齢，IGF-1の分泌減少，慢性疾患，アンドロゲン・エストロゲン分泌の減少，炎症性サイトカインの増加，身体活

表3　サルコペニア群と正常群の調査項目の比較

項目	サルコペニア群	正常群	p値
年齢(歳)	79.49±2.93	78.51±2.77	＜0.001
下腿三頭筋周囲(cm)	30.17±2.03	33.92±2.60	＜0.001
BMI(kg/m²)	18.98±2.01	23.74±2.84	＜0.001
筋肉量(kg)	26.92±2.61	31.73±3.16	＜0.001
健康度自己評価，健康(%)	75.7	85.8	＜0.001
外出頻度，少ない(%)	4.6	2.5	0.051
運動習慣，有(%)	27.3	33.5	0.039
既往歴，有(%)			
高血圧	51.0	58.0	0.029
高脂血症	32.2	40.5	0.009
貧血症	4.6	2.2	0.022
骨粗鬆症	38.2	30.7	0.014
骨　折	28.6	22.9	0.038

（文献6より引用）

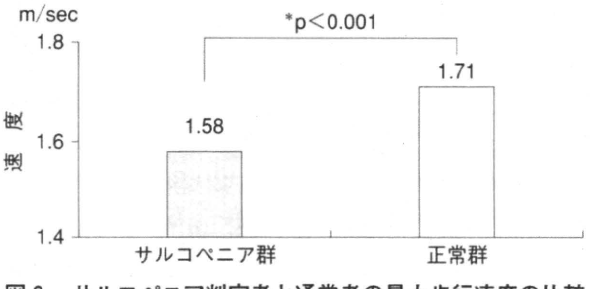

図2　サルコペニア判定者と通常者の最大歩行速度の比較
（文献6より引用）

動量の減少，栄養摂取量の不足が指摘されているが，そのメカニズムは未だ完全には解明されていない．しかし，これらの要因が複合的に作用した結果，筋タンパク質の分解量が合成量を上回ることによって，骨格筋量は徐々に減少するのである．しかし，骨格筋タンパク質合成を促進することができれば，筋量の減少を抑制し，有効なサルコペニア対策として考えられる．

高齢者においても，レジスタンス運動によって，筋肉量や筋力の増大効果が確認されている[7]．さらに，必須アミノ酸の投与によって骨格筋タンパク質の合成促進も認められている[8]ことから，運動と必須アミノ酸補充は有効なサルコペニア対策として注目されている．

サルコペニア改善のための運動，アミノ酸補充の効果

地域在住サルコペニア高齢者の筋力向上や歩行機能の改善には，どのような取り組みが有効であるかに対する答えを得るために行った介入について，簡単に紹介する．

介入効果を確実に得るためには，サルコペニアと関連する様々な要因の中で，可変因子を見出すことが必要である．筆者は，サルコペニアには不活動と筋タンパク質合成能力の低下が密接に関わっているとの先行研究に着目し，不活動を解消するための運動指導，筋タンパク質の合成を促進するための必須アミノ酸補充の効果について調べている．

介入効果を客観的に検証するために，介入参加希望者をRCTにより運動群と栄養群に分け，運動群には週2回，1回当たり60分間の筋力強化と歩行機能の改善を目的とした包括的運動指導を，栄養群にはロイシン高配合のアミノ酸3gを1日2回補充する指導を，3カ月間実施した．介入前後における身体組成，体力，老年症候群の改善の度合いを検討した．その結果，LBMは運動群で2.4%，栄養群で4.6%の有意な向上が，歩行速度は，運動群で18.6%，栄養群で10.3%の顕著な向上が確認され(**図3**)，地域在住サルコペニア高齢者の身体組成や体力を改善するためには，運動指導のみならずアミノ酸補充も有効であることが示唆されている．しかし，サルコペニア高齢者に多く観察される尿失禁は，運動群で38.9%から19.4%(P＝0.021)と有意に改善されたが，栄養群では有意な改善が認められてない．以上のことから，サルコペニア高齢者のLBMあるいは体力の改善を目的とした場合には，運動指導のみならず栄養補充も有効な手法であることが確認されたが，サルコペニア高齢者に有症率の高い老年症候群の改善には，運動介入の効果が優れる可能性が示唆されている．

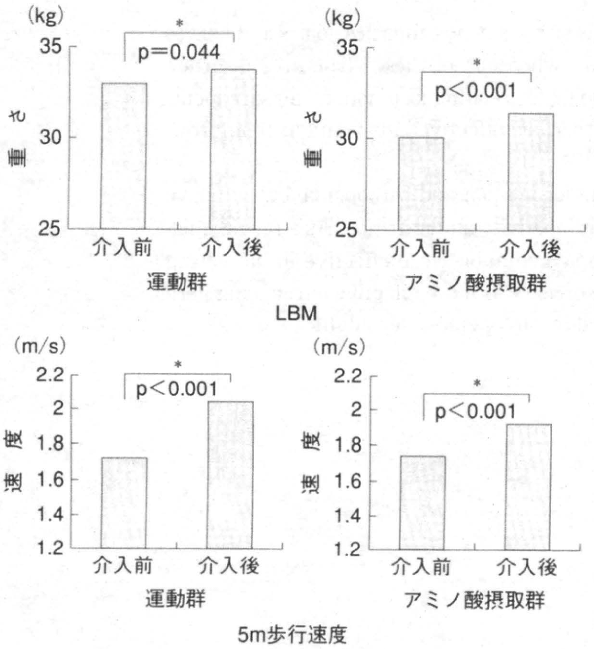

図3　3カ月間の運動，アミノ酸摂取の介入がLBMおよび歩行速度に及ぼす影響

（文献9より引用）

骨格筋量の減少や筋力の衰えと定義されるサルコペニアの改善に効果的な取り組みは，ロコモの改善にも応用できると考えられる．なぜならば，筋力の低下はロコモティブシンドローム出現と強く関わっているからである．

おわりに

骨格筋量の減少に伴う筋力の衰えを意味するサルコペニアは後期高齢者において有症率が上昇し，身体機能の障害や死亡と強く関連していることが指摘されている．サルコペニアと関連する要因は様々で複雑であるが，不活動や栄養など可変要因の改善に焦点を当てた改善策の効果を検討したところ，骨格筋量の増加，体力の向上には，運動指導，栄養指導ともに有効であった．しかし，サルコペニア高齢者に多くみられる老年症候群の解消には，運動指導がより有効であることを検証した．

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The Relationship between Sarcopenia and Locomotive Syndrome in Elderly People

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The prevalence of sarcopenia, which is the loss of skeletal muscle mass and muscle strength, has increased among the elderly and it has been indicated that sarcopenia is strongly related to functional disability, falls, morbidity, and mortality. Locomotive syndrome is a musculoskeletal disorder which decreases mobility and increases the risk of admission to long-term care. Physical activity

is the result of the combination of structures and organs such as bones, muscles, joints and nerves functioning together, and smooth movement is difficult when one of these structures disorder. Here we have assumed that the potentially preventable factor relating locomotion and sarcopenia is the decrease in muscle strength, and we have also described effective interventions to improve walking ability.

Although there are many complex factors related to locomotion and sarcopenia, but we have focused on the examination of reversible factors such as inactivity and nutrition. As a result, guidance and direction in both exercise and nutrition supplementation were effective in increasing skeletal muscle mass and muscle strength. However, exercise was more effective in reducing geriatric syndrome such as urinarg incontinence often seen in sarcopenic older adults.

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The effects of multidimensional exercise on functional decline, urinary incontinence, and fear of falling in community-dwelling elderly women with multiple symptoms of geriatric syndrome: A randomized controlled and 6-month follow-up trial

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ABSTRACT

This study assessed the effects of multidimensional exercises on functional decline, urinary incontinence, and fear of falling in community-dwelling Japanese elderly women with multiple symptoms of geriatric syndrome (MSGS). Sixty-one participants were randomly assigned either to an intervention ($n = 31$) or to a control group ($n = 30$). For 3-month period, the intervention group received multidimensional exercise, twice a week, aiming to increase the muscle strength, walking ability, and pelvic floor muscle (PFM). Outcome variables were measured at baseline, and after intervention and follow-up. The functional decline of the intervention group decreased from 50.0% at baseline to 16.7% after intervention and follow-up ($Q = 16.67$, $p < 0.001$). For urinary incontinence, the intervention group decreased from 66.7% at baseline to 23.3% after intervention and 40.0% at follow-up ($Q = 13.56$, $p = 0.001$), whereas the control group showed no improvement. Intervention group showed greater and significant decrease in the score of MSGS compared to control group ($F = 12.66$, $p = 0.001$). Within the subjects that showed improvement to normal status of MSGS, a significantly higher proportion demonstrated increased maximum walking speed at follow-up ($Q = 6.50$, $p = 0.039$). These results suggest that multidimensional exercise is an effective strategy for reducing geriatric syndromes in elderly population. An increase in walking ability may contribute to the improvement of MSGS.

1. Introduction

The geriatric syndrome such as functional decline, urinary incontinence, and fear of falling are used to capture those clinical conditions that do not fit into discrete disease categories, and are serious problems among the elderly population (Inouye et al., 2007). Many studies have demonstrated that a decline in walking speed, muscle strength and balance ability of the elderly is strongly associated with the development of geriatric syndrome (Vellas et al., 1997; Ishizaki et al., 2000; Maggi et al., 2001).

It is well documented that as age advances, the proportion of people with more than one symptom of geriatric syndrome increases. In addition, people with MSGS have an increased prevalence of functional disability and mortality compared to people with only one or no symptoms present. Several studies have put emphasis on the fact that multidimensional exercises focusing on strength, balance, and mobility improvement, even into advanced age, was helpful in reducing functional decline, urinary incontinence and fear of falling (Nelson et al., 2004; Gitlin et al., 2006; Kim et al., 2007). These previous studies validated the effectiveness of the multidimensional exercises focusing on the improvement of a single geriatric syndrome such as functional decline or urinary incontinence, but did not provide any information on whether the subjects possessed symptoms other than functional decline or urinary incontinence. One study demonstrated (Tinetti et al., 1995) that falls and urinary incontinence were associated with the occurrence of functional decline, and that the identification of shared risk factors associated with falls and urinary incontinence is the key in establishing effective and efficient interventional strategies. However, few multidimensional exercises studies have been performed in community-dwelling elderly persons with MSGS.

In the present study, we hypothesize that deteriorations in muscle strength, walking and balance ability are common risk factors associated with functional decline, urinary incontinence and fear of falling. We conducted a randomized and controlled trial to evaluate the effects of the multidimensional exercises targeted at reducing the symptoms of functional decline, urinary inconti-

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nence, and fear of falling in community-dwelling Japanese elderly women with MSGS.

2. Methods

2.1. Study sample and procedures

Overall health surveys were conducted at the Tokyo Metropolitan Institute of Gerontology (TMIG), aiming at early screening of geriatric syndromes in elderly persons and at developing intervention strategies, which would reduce those geriatric syndromes. As subjects, 1016 women were chosen randomly from the Basic Resident Register as persons aged 70 or older residing in Itabashi ward of Metropolitan Tokyo.

A letter outlining the study and describing its objective, and the way that the personal data would be used was mailed to the elderly women selected, inviting them to participate in the study. The baseline survey was conducted in November 2004, and 669 women aged 70 years and older participated.

The participants were screened based on three geriatric syndromes: functional decline, urinary incontinence, and fear of falling. A person who was reported as having two or more geriatric syndromes present was defined as having MSGS. Out of the 669 women participated, 102 were classified as having MSGS (Fig. 1). A pamphlet containing information on the "Exercise Classes for the Treatment of Geriatric Syndromes" was mailed to the 102 potential participants. A response was obtained from 74 of them, of whom 61 were willing to participate. There were no statistically significant differences in physical fitness, age, and geriatric syndromes between the 61 willing participants and the 41 unwilling ones including those who did not submit any response. The research protocol was approved by the institutional review board, and informed consent was obtained from each participant.

2.2. Randomization

After baseline assessment, subjects were divided into two groups with an allocation ratio of 1:1 according to computer-generated random numbers. There was no attempt to equalize the sizes of the groups based on characteristics or to recruit subjects with specific characteristics. Thereafter, one group was allocated to the intervention ($n = 31$) and the other group to the control ($n = 30$) (Fig. 1).

2.3. Data collection

Data collected by interview and a physical fitness test at baseline, after 3-month exercise, and were reassessed at 6-month follow-up.

2.3.1. Interview survey

A face-to-face interview was conducted to assess the following variables: The functional decline was measured using the TMIG index of competence (Koyano et al., 1991). For each of the 13 items, "yes" was scored as 1 and "no" as 0 (maximum score: 13). A person with a TMIG index score less than 10 was defined as having functional decline. Urinary incontinence was assessed through the question "Have you ever experienced urine leakage during the last 1 year?" If a subject responded with a "yes", we would then ask concerning the frequency of urinary incontinence. The frequency of urinary incontinence was assessed based on a five-point scale through interview (1: several times per year; 2: once or more per month: 3: once or twice per week; 4: once every 2 days; 5: everyday). A person whose response ranged 2–5 was defined as having urinary incontinence (Burgio et al., 1991). The fear of falling was assessed by asking "At this moment, are you afraid of falling?" and classified as "1. not at all", "2. somewhat", "3. very much", and "4. activity restriction due to fear of falling". Subjects who responded within 2 and 4 were assigned to the fear group (Maki et al., 1991).

The effect of the multidimensional exercises on the geriatric syndromes was assessed based on shifts of the responses from the interview, which was conducted at a baseline, completion of the 3-month exercise, and at the 6-month follow-up. The scores of geriatric syndromes were calculated as follows: functional decline, 0 for TMIG index score more than 11, 1 for 10, 2 for 9, and 3 for less than 8; urinary incontinence, 0 for no urine leakage or several times per year, 1 for once or more per month, 2 for once or twice per week, and 3 for once every 2 days or everyday; fear of falling, 0 for not at all, 1 for somewhat, 2 for very much, and 3 for activity restriction due to afraid of falling. The score of MSGS was calculated as add up three geriatric syndrome score (functional decline, urinary incontinence, and fear of falling). And, a participant with a MSGS score less than 1 was defined as improvement of MSGS.

2.3.2. Physical fitness test

Body mass index (BMI) was calculated from body weight (kg) divided by height (m) squared. Physical fitness tests were used for the assessment of muscle strength, walking speed, and balance ability. The following standardized tests were performed: grip strength (Suzuki et al., 2004); adductor muscle strength (Kim et al., 2007); usual and maximum walking speed (Suzuki et al., 2004); one leg standing time with eyes open (Suzuki et al., 2004); tandem walking (Speers et al., 1998); functional reach (Duncan et al., 1990). The staff members who performed the assessments did not know the subjects' group assignments.

2.4. Interventions

2.4.1. Exercise group

The exercise group participated in an intervention comprised of 60-min exercise sessions held at the TMIG Health Promotion Classes, twice per week for 3-month. Weight-bearing exercise: strength training of the thigh, abdominal, and back muscles was performed and included bending the knees, and other similar exercises.

PFM exercise: The exercise regimen was designed to strengthen the fast- and slow-twitch muscle fibers located at the pelvic floor. Participants were initially instructed to perform 10 fast contractions (3-s) with a 5-s relaxation period and 10 sustained contractions (6–8 s) with a 10-s relaxation period in between the contractions. The PFM exercise was performed in sitting, lying, and standing positions with legs apart, emphasizing training of the PFM and relaxation of the other muscles.

Chair exercises: Used in the early stage of the program. The exercises included seated toe and heel raises, seated lift foot and point/flex toes, and others.

Resistance band exercise: Focused on increasing the strength of the muscles of the upper extremities, abdomen, and lower extremities in frail elderly people (arm pull back, leg extension, and others).

Ball exercise: Exercises with a training ball were conducted using a small (diameter: 21 cm) and a large ball (diameter: 45–55 cm), aiming to increment the muscle strength and balance (sitting on the ball and extending legs, and others).

Walking ability training: Focused on maintenance of stability during walking and on the improvement of responses to postural changes during walking (walking with directional changes, gait pattern variations and enhancement, and others).

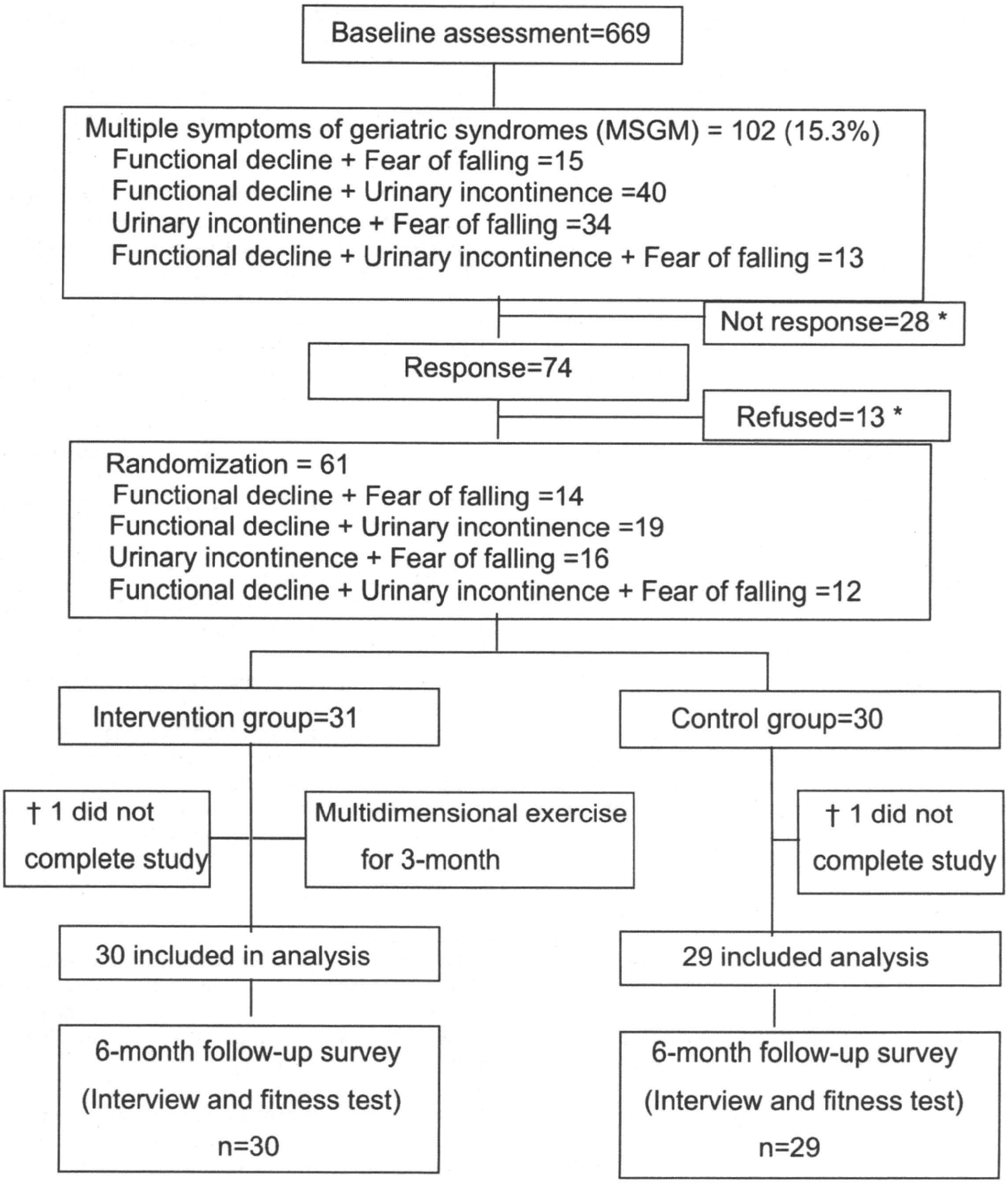

Fig. 1. Flow chart of participants through the randomized controlled trial of the exercise program and analysis. (*) Forty-one of MSGM ($n = 102$) were excluded due to the not response ($n = 28$) and refusal ($n = 13$). (†) Two subjects could not complete the study because of hospitalization ($n = 1$), and fracture ($n = 1$).

Balance training: Focused on the improvement of the static, dynamic, and lateral balancing ability (multidirectional weight shifts, tandem walking, and others).

2.4.2. Control group

The control group attended a general health education class (albumin, osteoporosis, and prevention of malnutrition) held at the TMIG once a month for a 3-month period.

2.5. Follow-up and compliance

During the 6-month follow-up period, subjects of the intervention group attended group exercise classes (60 min) once per month in addition to receiving a home-based exercise program. The home-based exercise program consisted of two to three sets of the 15 exercises and PFM exercise that they had learned during the group exercise session. They were also advised to do the home-based exercises at least three times or more per week for about 30-min per day. In order to accurately monitor the exercise times and the number of sets performed at home during the follow-up period, a pamphlet illustrating the PFM and strengthening exercises and a recording sheet were distributed to the participants, who were instructed to record the time and sets of exercises performed at home everyday. The record sheets were collected once a month at the group exercise class and analyzed in order to calculate the mean exercise frequency per week, and the mean exercise time per day.

2.6. Statistical analysis

Both the mean and standard deviation were calculated for each variable. The differences in the baseline data between the

Table 1
Selected variable characteristics of participants at baseline by study group, mean ± S.D.

Variables	Intervention group	Control group	$p^{\dagger}$
Number	31	30	
Age (year)	79.0 ± 3.9	78.1 ± 4.4	0.424
Height (cm)	146.9 ± 5.4	147.0 ± 5.8	0.940
Body weight (kg)	47.4 ± 6.4	50.7 ± 9.1	0.108
BMI (kg/m^2)	22.0 ± 2.6	23.4 ± 3.6	0.084
One leg standing time (s)	29.2 ± 23.5	34.6 ± 22.8	0.367
Tandem walking (step)	7.2 ± 4.7	7.8 ± 4.7	0.631
Functional reach (cm)	31.0 ± 7.1	33.2 ± 4.9	0.167
Grip strength (kg)	16.5 ± 4.3	17.9 ± 4.7	0.239
Adductor muscle strength (kg)	17.3 ± 4.0	18.0 ± 5.1	0.740
Usual walking speed (m/s)	1.1 ± 0.3	1.2 ± 0.2	0.685
Maximal walking speed (m/s)	1.7 ± 0.4	1.7 ± 0.4	0.979
TMIG index score (point)	10.6 ± 1.6	10.4 ± 1.5	0.654
Urinary incontinence, yes (%)	64.5	50.0	0.252
Functional decline, yes (%)	51.6	43.3	0.517
Fear of falling, yes (%)	67.7	76.7	0.390
Chronic medical conditions, yes (%)			
Hypertension	58.1	60.0	0.902
Stroke	13.2	13.3	0.988
Diabetes	19.4	20.0	0.948

† Two group *t*-test for continuous variables and the χ^2-test for categorical variables.

exercise and control group were analyzed using *t*-test for the continuous variables and Chi-square test for the categorical variables. The changes in dependent variables pre-intervention, post-intervention and follow-up in the exercise and control group were analyzed using an analysis of variance (ANOVA) with repeated measures. Significant interactions were analyzed to determine whether or not the effects were greater in the intervention than the control group. Cochran's *Q*-test was used to evaluate within-group differences of the effect of the exercise on the categorical variables for pre-intervention, post-intervention, and follow-up data. In the case of items which were showing significant differences, a post hoc analysis was performed using McNumar's test. One-way ANOVA was performed to evaluate the within-subgroup effect of the intervention on multiple geriatric syndrome scores at baseline, after the 3-month exercise, and at 6-month follow-up. For the subgroup showing significant differences, a post hoc analysis was performed using Scheffe's method. The percentage improvement in physical fitness was calculated using the following formula: % improvement = {(after 3-month exercise or at 6-month follow-up values − baseline value)/baseline value × 100}. The percentage improvement was divided into tertiles. The power of the current study was calculated at 80% to demonstrate a difference in the outcome variable of at least 20% at a significance level of alpha = 0.05. All the analyses were performed using the SPSS software package for Windows version 15.0 (SPSS, Inc., Tokyo, Japan).

3. Results

There were no significant differences between the groups in any of the baseline characteristics such as age, BMI, walking speed, adductor muscle strength, functional decline, urinary incontinence, fear of falling, and chronic medical conditions (Table 1).

Attendance 15 (62.5%) or more than of the exercise sessions (24) was defined as trial completion. Two participants (3.3%) could not complete the trial after the randomization because of hospitalization (n = 1) and fracture (n = 1) (Fig. 1). The mean attendance rate was 77.4% (61.3–90.3%) during the intervention period and 74.2% during the follow-up. In the exercise group, 32.3% of the subjects attended the exercise sessions 24 times, 22.6% attended 20–23 times, 35.5% attended 16–19 times, 6.5% attended 15 times, and 3.3% attended 14 or less of the exercise sessions. During the follow-up, the mean frequency of performing the

Table 2
Comparison of physical fitness and geriatric syndrome variables between intervention = I (n = 30) and control = C (n = 29) groups after 3-month exercise and at 6-month follow-up, mean ± S.D.

Variables	Gr	Baseline	3-Month exercise	6-Month follow-up	ANOVA F=	p=
Body weight (kg)	I	46.6 ± 5.4	47.4 ± 5.4	47.1 ± 5.4	(1,57) = 2.74	0.105
	C	51.0 ± 9.5	51.0 ± 9.4	50.6 ± 9.1		
BMI (kg/m^2)	I	21.5 ± 2.2	21.9 ± 2.2	21.8 ± 2.2	(1,57) = 2.82	0.100
	C	23.4 ± 3.9	23.4 ± 3.8	23.3 ± 3.6		
One leg standing time (s)	I	34.0 ± 24.2	28.2 ± 20.4	32.4 ± 22.6	(1,57) = 0.01	0.920
	C	33.4 ± 23.4	28.8 ± 23.5	32.4 ± 24.6		
Tandem walking (step)	I	7.2 ± 4.7	6.1 ± 4.5	5.9 ± 3.3	(1,57) = 4.70	0.036
	C	7.8 ± 4.7	5.2 ± 3.8	3.5 ± 2.0		
Functional reach (cm)	I	31.7 ± 6.8	33.5 ± 5.13	3.5 ± 4.4	(1,56) = 4.18	0.046
	C	33.7 ± 4.7	32.7 ± 5.3	31.6 ± 8.8		
Grip strength (kg)	I	17.2 ± 4.0	20.9 ± 5.2	17.9 ± 4.7	(1,57) = 0.02	0.874
	C	18.0 ± 4.6	21.5 ± 5.1	18.6 ± 4.8		
Adductor muscle strength (kg)	I	17.2 ± 4.0	18.9 ± 5.1	19.3 ± 4.7	(1,57) = 4.18	0.045
	C	17.9 ± 5.0	18.2 ± 4.01	17.8 ± 3.7		
Usual walking speed (m/s)	I	1.1 ± 0.3	1.1 ± 0.2	1.2 ± 0.2	(1,57) = 13.03	0.001
	C	1.2 ± 0.2	1.1 ± 0.3	1.1 ± 0.3		
Maximal walking speed (m/s)	I	1.7 ± 0.4	1.8 ± 0.5	1.8 ± 0.4	(1,56) = 4.24	0.044
	C	1.7 ± 0.4	1.6 ± 0.4	1.6 ± 0.4		
Functional decline, yes (%)	I	50.0	16.7	16.7	16.67[a]	<0.001
	C	41.4	31.0	27.6	4.10[a]	0.109
Urinary incontinence, yes (%)	I	66.7	23.3	40.0	13.56[a]	0.001
	C	51.7	44.8	44.8	4.00[a]	0.135
Fear of falling, yes (%)	I	66.7	70.0	70.0	0.17[a]	0.920
	C	75.9	62.1	75.9	2.91[a]	0.234

[a] Cochran's *Q*-value.