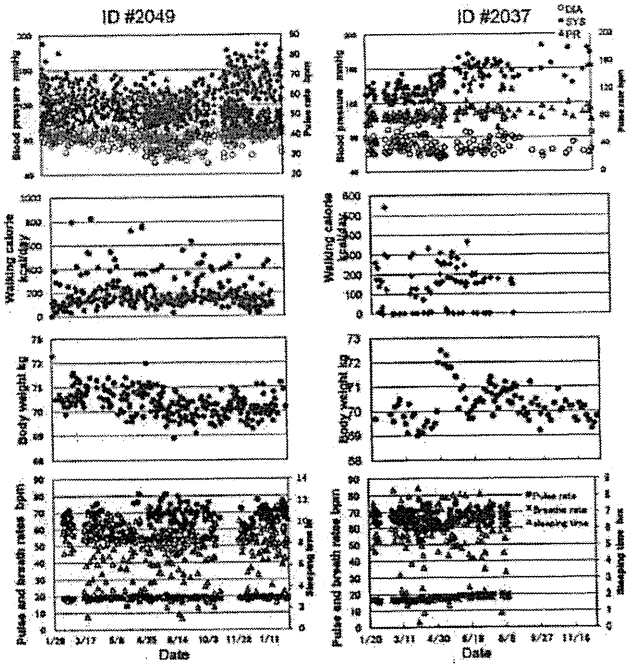

Fig. 4. One-year monitoring of BP, estimated calorie expenditure based on the number of steps walked and exercise training, sleeping conditions, and body weight for the worsened cases, ID#2037 and ID#2049. ID2049 did not get 1 year data for walking calorie and sleeping conditions.

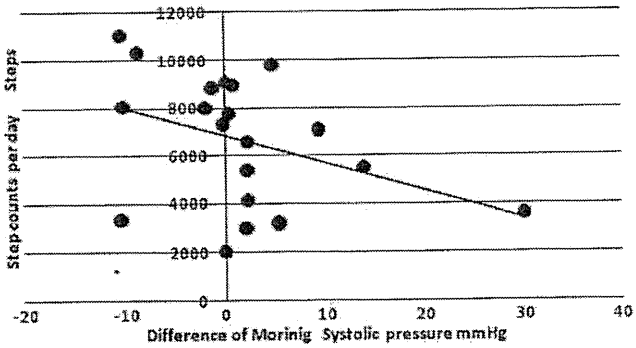

Fig. 5. The relationship between changes in SBP from the first to the last 3 months and steps walked.

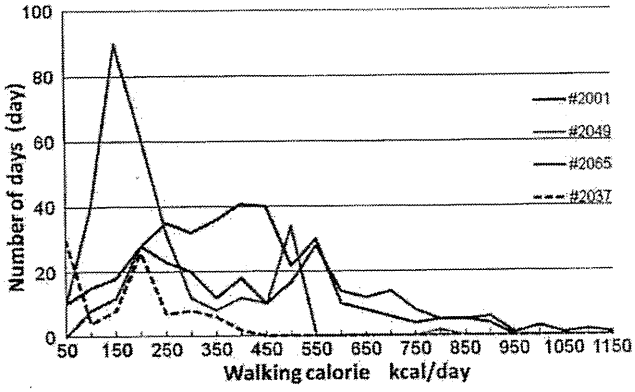

Fig. 6. Distribution of steps walked for the four subjects shown in Figs. 3 and 4.

C. Results of Multivariate Regression Analysis

Two cases that showed improvement and two that showed worsening over the study period were analyzed.

In a case showing SBP improvement, ID#2001, the coefficient of determination (R^2) was 0.47. In this case, SBP was reduced by 4.3 mmHg, with a cumulative total energy expenditure of 10 000 kcal by exercise and walking ($t = -9.04$). However, body weight was not a significant index of changes in SBP. ID#2065 showed a lower coefficient of determination ($R^2 = 0.24$). In this case, sleep influenced the morning SBP. SBP declined by 2.0 mmHg with an increase of 1 h in sleeping time. Furthermore, SBP was reduced by 2.5 mmHg with weight loss of 1 kg.

In the case showing worsening of SBP, ID#2037, the coefficient of determination was $R^2 = 0.57$. In this case, SBP increased by 4.1 mmHg, with a cumulative total energy expenditure of 1000 kcal ($t = 5.65$). This lower accumulated energy expenditure was associated with the elevation of SBP. ID#2049 showed a coefficient of determination of $R^2 = 0.43$. In this case, SBP was also increased by 2 mmHg with total energy expenditure of 1000 kcal ($t = 7.93$) and SBP increased by 9.1 mmHg with an increase of 1 kg in body weight.

D. Evaluation of Walking/Exercise/Energy Expenditure

Subject ID#2001 showed improvement in SBP, with energy expenditure of 333 ± 159 kcal/day (8805 ± 3756 steps/day) over a period of 346 days. ID#2065 showed energy expenditure of 421.8 ± 215.0 kcal/day (10 126 ± 4342 steps/day) over 241 days. On the other hand, subjects ID#2037 and ID#2029 who showed worsening of SBP had energy expenditure levels of 34 ± 115 kcal/day over 86 days and 194 ± 132 kcal/day over 293 days, respectively. The number of steps walked and estimated energy expenditure were determined from the days on which the subject wore the pedometer. Fig. 5 shows the relationship between changes in SBP and steps walked. The intercept for reducing SBP was around 7000 steps per day.

Fig. 6 shows detailed examples of the distribution of the number of steps walked in the improved and worsened cases.

On average, the energy expenditure of subjects who showed improvements in SBP showed a normal distribution, whereas the distribution of steps for those in whom SBP worsened showed higher proportions of low-level energy expenditure.

IV. Discussion

A. Participants

We developed a simple home healthcare system and performed 1-year monitoring for blood pressure control in terms of exercise and sleep. Such 1year monitoring can be troublesome for the subjects, especially the elderly. Our monitoring protocol included a number of restrictions, such as the careful handling of the BP device and monitoring time. Thus, only very limited data were received from the subjects. In fact, only 31 of 61 subjects attempted to measure the physiological parameters more than 150 times. Three of these 31 subjects showed significant

improvement in SBP but two showed significant deterioration of the health condition.

Most previous studies examined the relationship between SBP reduction and exercise, based on data for periods of 6 months. For 1-year monitoring, it is necessary to simplify the handling of medical devices, especially for the elderly.

B. Relationship Between Blood Pressure and Exercise

1) Walking Steps: Our results indicated that higher numbers of walking steps were associated with improved SBP. Paffenbarger *et al.* [11] recommended increasing energy expenditure by 2000 kcal per week to reduce SBP. This is equivalent to 300 kcal per day, which corresponds to the energy expenditure of around 10 000 steps. In previous reports, 12 weeks of walking (average number of walking steps: 13 510 ± 837 steps/day) showed improvements of 10.2 and 8.4 mmHg in SBP and DBP, respectively [12]. Moreau *et al.* reported that resting SBP was reduced by 6 mmHg ($P < 0.005$) after 12 weeks and was further reduced by 5 mmHg at the end of 24 weeks ($P < 0.005$) [10]. In our studies, ID#2001 showed reductions of 10.4 and 7.0 mmHg in morning SBP and DBP after 1 year, respectively. ID#2065 also showed reductions of 8.7 and 5.1 mmHg in morning SBP and DBP, respectively. These results support the findings reported by Moreau *et al.* [10]. Additionally, Fig. 5 shows that a reduction in SBP required that the subject walked for more than 7000 steps per day. This agrees with previous findings [12].

Several intervention studies used periods of 12 or 24 weeks. In case ID#2001, the averaged SBP and DBP were reduced by 14.1 and 5.1 mmHg, respectively, after 24 weeks. However, after 1 year, the SBP and DBP were reduced by 10.4 and 7.0 mmHg, respectively. On the other hand, ID#2065 showed reductions of 3.6 and 4.5 mmHg in SBP and DBP, respectively, after 24 weeks. After 1 year, the reductions were 8.7 and 5.1 mmHg in SBP and DBP, respectively. The rate of reduction differs among individual subjects as well as by season.

With regard to the intensity of walking, MET (metabolic equivalent task) above 3 is recommended to produce health benefits (ACSM/AHA recommendation) [13]. To promote and maintain health, all healthy adults need to engage in moderate-intensity aerobic physical activities, such as walking for a minimum of 30 min per day 5 days a week, or vigorous intensity aerobic activity for a minimum of 20 min per day 3 days a week. In our pedometer study, we could only estimate exercise, based on the number of walking steps per hour. The data for ID#2001 and ID#2065 shown in Fig. 6 suggested that both subjects walked more than 1000 steps/h. However, this result did not indicate large percentages of high intensity physical activity, above 3 METS, with a walking speed of 4 km/h and around 5300 steps/h. Nevertheless, subjects with more than 7000 walking steps per day showed reductions in SBP.

The estimation is also difficult because of the very large degree of variance in the number of walking steps and because constant walking is typically not possible in the elderly, because of daily changes in physical condition and motivation. For example, subjects may not go outside on days when the weather was bad. Thus, they met the recommendations on only some days during the period of monitoring.

2) Physical Strength, Determined Using an Ergometer: ID#2001 attempted to use the ergometer as an exercise tool and performed to the predetermined intensity of 50 W (about 3 METs) 188 times per year. The average exercise time was 29.6 ± 4.8 min/time and expended 97.1 ± 17.5 kcal/time. One-third of the reduction criterion of 300 kcal was concentrated in the 30-min exercise test. This exercise was good for the winter when the subjects remained at home. That is, the exercise test is safe and applicable for the elderly because it is an indoor activity.

3) Exercise for the Elderly: The ACSM/AHA recommends resistance training at least twice per week to provide a safe and effective means of improving muscular strength and also frequent exercise to improve BP. However, elderly subjects have an increased risk of injury and other adverse events, and therefore exercise must be performed carefully. In a systematic review of studies performed to evaluate the associations between pedometer use and changes in physical activity and health outcomes, Bravata *et al.* [14] reported that the mean intervention duration was 15.2 weeks, and that no evidence was available regarding whether the changes associated with pedometer use were maintained over the long term.

Several conclusions based on the results of this study are as follows:

1) If the subject performed the exercise with a total energy expenditure of 300 kcal, the BP was reduced over a period of 3 months.
2) The number of walking steps showed a large degree of variation and the subjects walked after assessing their conditions.
3) The intensity of exercise is an important factor in maintenance and reduction of SBP. To maintain muscle strength, suitable exercise in the home is required. A simple exercise machine that shows exercise intensity is needed at home.

It is important to develop guidelines that will encourage individuals at highest risk to maintain and reduce their BP. The type, frequency, intensity, and period of exercise are important points for improving the quality of life.

Finally, we have developed a system for monitoring blood pressure and other physiological parameters simultaneously. We tried to monitor a large number of subjects over 1 year, but we could analyze only four subjects precisely. The main reason for the lack of data was subject motivation, as the monitoring proved inconvenient for the subjects. Furthermore, if the subject's data did not differ much from day to day, he or she lost interest in long-term monitoring. Further development of the system should explore two main themes: developing a simple device for blood pressure monitoring and analyzing long-term physiological data in terms of its value in predicting and preventing disease.

V. Conclusion

We have developed a simple home healthcare system with a unique transmission system, with which we performed a 1-

year field trial. The system performed without serious problems, but only 31 of 61 subjects provided sufficient data for statistical analyses. Among these 31 subjects, we carefully analyzed cases that showed both improvements and worsening of BP. The results indicated that subjects with energy expenditure of more and less than 300 kcal showed reduction and elevation of BP, respectively. We conclude that exercise is the most important factor in reducing BP. The improvements and changes in daily activity with or without intervention are important factors, and it is necessary for the subjects to have the motivation to make changes in their daily life. Although we recruited a relatively large number of subjects in the present study, the amount of effective data obtained was relatively low. Further improvements to the home healthcare system are required to enhance the subjects' motivation to monitor their health condition more extensively.

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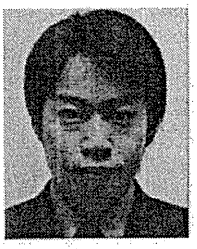

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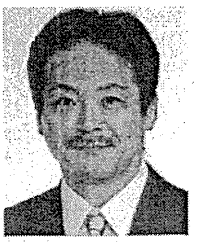

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C. 血管

②PAD：油断できない下肢の痛み

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Introduction

飽食と運動不足により生活習慣病の蔓延をまねいた結果，末梢動脈疾患（peripheral arterial disease；PAD）をとりまく疾病構造は，ここ数10年で大きく様変わりし，かつて多かったBuerger病は減少しその代わりに動脈硬化性の閉塞症が急増し大半を占めるようになった。最近の国際コホート研究REACH（REduction of Atherothrombosis for Continued Health）[1,2]によればPAD患者は心筋梗塞や脳卒中既往患者と比較してより高い心血管死亡率を示し，これを受けてPADの早期診断と適切な早期介入治療においてさらなる改善の必要性が指摘された。

本稿では，PADの適切な早期診断とおおまかな介入指針についてエビデンスに基づいて作成されたガイドラインに沿ってまとめる[3,4]。

1 間歇性跛行の鑑別ポイント

PADの最も多い症状は，歩行時の下腿筋の痛みであり，数分間の休息で痛みは消失し再び歩けるようになれるので間歇性跛行とよぶ。この間歇性跛行症状を訴えて医療機関を受診する患者の約60％は腰部脊柱管狭窄症，20％がPAD，10％は両者の合併といわれている。脊柱管狭窄症とPADとは治療法も予後も大きく異なるため，きちんと鑑別しなければならない。PADの場合，下肢の壊死や最悪の場合下肢の切断に至る場合があり，脊柱管狭窄症の場合悪化すると下肢の麻痺や尿，便失禁などの膀胱直腸障害を呈する場合もある。一方で両疾患とも加齢に伴い有病率は増加するため，一方を治療して症状の改善を認めない場合には両疾患合併を考慮する必要がある。

(1)病歴

①動脈硬化危険因子のチェック（糖尿病，喫煙，高血圧，脂質異常症など）：危険因子が多いほどPADの可能性が上がる。

②姿勢による症状の変化：前屈み歩行で跛行が改善すれば，脊柱管狭窄症の可能性が高い。脊柱管狭窄症では下り坂で跛行症状が悪化し，PAD

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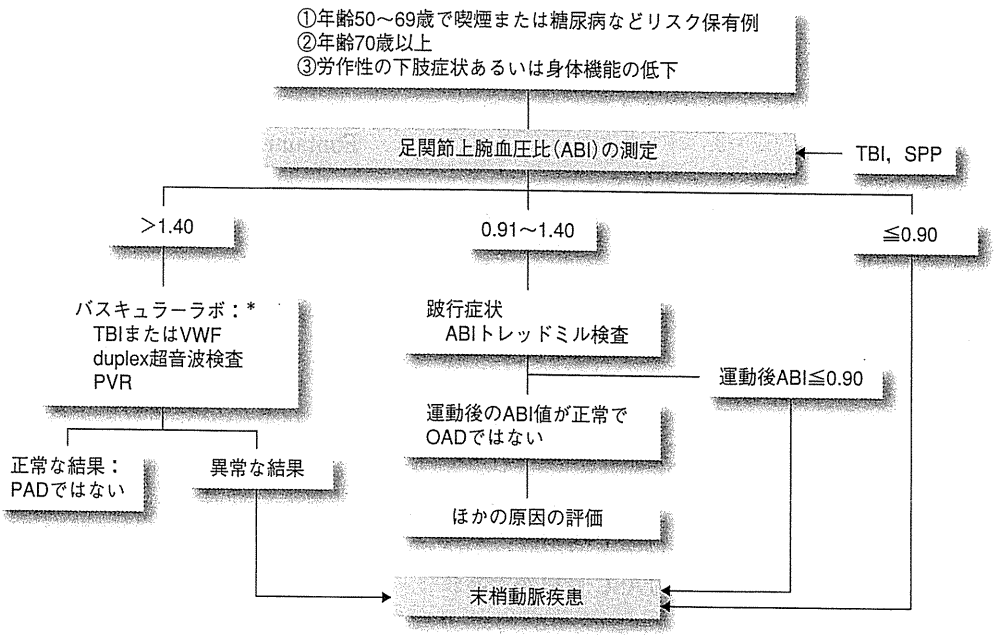

図1 末梢動脈疾患診断のアルゴリズム
(文献3より一部改変引用)
ABIが0.9以下であれば末梢動脈疾患と診断される。糖尿病や慢性腎不全合併例では血管の石灰化が起こり，見かけ上足関節血圧が上昇している可能性があるため，足趾上腕血圧比(toe brachial index；TBI)や皮膚組織灌流圧(skin perfusion pressure；SPP)によりPADを診断することが推奨されている。また，0.91～1.40でも，跛行症状を有する例には，運動負荷後ABI測定により評価を行うことが推奨されている。
*VWF：velocity wave form(速度波形分析)，PVR：pulse volume recording(容積脈波測定)

では昇り坂道で跛行症状が悪化する。理由は下り坂では前屈みになりにくいので脊柱管狭窄症の症状が出やすく，昇り坂道では下肢筋肉の酸素需要が増すからである。

③間歇性跛行の部位：PADでは下腿痛，脊柱管狭窄症では坐骨神経に沿った殿部から大腿裏面痛が多い。

(2)身体所見

①視診：必ず靴下を脱がせて皮膚潰瘍や色調の変化の有無を調べる。

②触診：皮膚温の低下の有無や足背動脈，後脛骨動脈，膝窩動脈の拍動を調べる。

(3)検査

①足関節上腕血圧比(ankle brachial blood pressure index；ABI)を測定し，ABI値が0.9以下であればPADと診断してよい(**図1**)。ABI値0.9以下の下肢動脈に有意狭窄を有する感度と特異度は，それぞれ95%，100%と非常に高く非侵襲的で簡便でどこでも測定可能である。そのため国際ガイドラインinter-society consensus for the management of peripheral arterial disease(TASC Ⅱ)では，ABIをPAD存在診断の最も大切なツールと位置づけている。ABI値が0.9以下であれば，さらに虚血性心疾患や脳血管障害の合併もないかを調べる。またABI＞0.9でも間欠性跛行を呈する場合には，3分間歩行負荷後に再度ABIを測定し0.9以下を示す症例を見逃さないようにする。

②足趾上腕血圧比，皮膚組織灌流圧(skin perfusion pressure；SPP)：足関節よりも中枢側からMönckeberg型中膜硬化により動脈狭窄があるにもかかわらずABI値が正常を示す症例で有用である。

③PADの局所診断法として血管超音波法，CT，MRI，血管造影法がある。血行再建術前に必要である。

治療

(1)心血管系のリスクファクターの管理

TASC ⅡにおけるPADの治療指針(わが国の現状に合わせて一部改変)を**図2**に示す。15のpopulation studyのメタ解析によるとABI≦0.9は，Framinghamリスクスコアとは独立して全死亡に

寄与する。したがって，ABI≦0.9のグループに対して積極的に動脈硬化危険因子の管理をする。

●喫煙

喫煙はPADの危険因子であり，かつ病態を悪化させ下肢切断のリスクを上げ，バイパスグラフトの閉塞率を増加させ，最終的に生命予後を悪化させる。喫煙しているPAD患者に対しては，禁煙外来や禁煙教室を開き，家族の協力を得て禁煙指導を行う。通常の禁煙指導で禁煙できる確率は5%と低く，禁煙補助薬や抗うつ薬を上手に使用すると禁煙率が上昇する。

●肥満

肥満者には減量を，脂質異常症にはLDL100mg/dL以下を目標に食事療法+脂質改善薬を，糖尿病ではHbA1c＜7.0%を目標に血糖をコントロールし，高血圧患者では140/90mmHg未満を目標にコントロールする。

(2)重症下肢虚血や近位部狭窄病変には血行再建術を第一選択

Fontaine Ⅲ，Ⅳの重症虚血肢では，救肢のために迅速な評価と早急な治療(血行再建術)が求められる。血行再建術はカテーテル治療とバイパス治療に大別されるが，その選択基準は血管病変のパターンと合併症や全身状態を考慮して選択する。TASC A病変であれば血管内治療を，TASC D病変であれば外科的血行再建が選択され，BとC病変は各施設の成績と患者の希望を考慮して選択することとなる。詳細はガイドライン[3,4]を参照していただきたい。

(3)重症下肢虚血や近位部病変でない軽～中等症には運動療法+薬物療法を第一選択

Fontaine Ⅰ，Ⅱの軽症から中等症では，運動療法と抗血小板薬の投薬を開始する[3,4]。間欠性跛行を有する末梢動脈疾患患者を対象とした運動療法のメタアナリシス[5]によると，運動療法(主に監視下で1回30～60分間を週2～3日，3～6カ月間トラック歩行，トレッドミル歩行または下肢運動を施行)は，最大歩行距離を通常治療群と比較して約260m延長させた。血行再建術は短期間に最大歩行距離を延長せしめるが1年以上経過すると，積極的運動療法群と比較して差はなくなる[5]。上腕足首血圧比(ABI)は運動療法施行前後で有意な改善をみない。監視下運動療法と

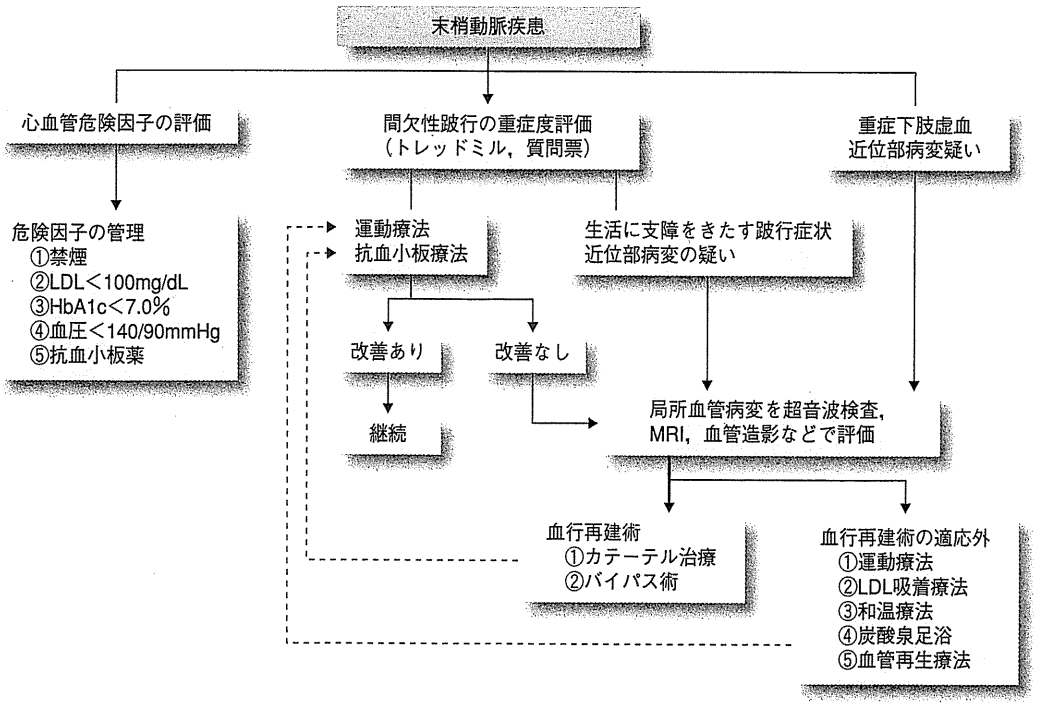

図2 末梢動脈疾患の治療指針
(Hiatt WR: Medical treatment of peripheral arterial disease and claudication. N Engl J Med 344:1608-1621, 2001および文献3より一部改変引用)

非監視下運動療法の無作為化比較試験のメタアナリシスによれば[6]，監視下運動療法は非監視下と比較して3カ月後の最大歩行距離を約150m延長させる。

シロスタゾールは間欠性跛行を有するPAD患者を対象とした8つの二重盲検試験のうち6試験で最大歩行距離の有意な延長を認めたことよりガイドラインで[3,4]，クラスⅠ，グレードA，エビデンスレベルAのPADに対する第一選択薬物療法として記載されている。シロスタゾールは，血小板および血管内皮細胞，血管平滑筋のホスホジエステラーゼ(phosphodiesterase 3；PDE3)を選択的に阻害することにより，細胞内のcAMP濃度を増加させ，抗血小板作用，血管内皮機能改善作用，血管拡張作用，血管平滑筋増殖抑制作用を発揮する。またシロスタゾールは用量依存的に血管内皮細胞において一酸化窒素(nitric oxide；NO)の産生を誘導することも報告されている。シロスタゾールを処方する場合，少量の50mg錠を1日2回投与から開始し，動悸や頭痛などの副作用のないこと確認してから1回100mg錠を1日2回投与に増量することを薦めたい。なお，狭心症や心筋梗塞合併例では抗血小板薬としてアスピリンが第一選択薬となる。

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Recurrent Embolic Stroke Due to Nonbacterial Thrombotic Endocarditis Followed by Transesophageal Echocardiography

A 44-YEAR-OLD MAN with advanced gastric cancer visited our hospital because of a sudden onset of difficulty in speaking. He was diagnosed as having recent embolic strokes of bilateral middle cerebral artery territories (**Figure 1**A and B). Elevated plasma levels of D-dimer indicated ongoing hypercoagulation. Electrocardiography showed normal sinus rhythm. Transesophageal echocardiography revealed a 7-mm mobile isoechoic mass broadly attached to the left and noncoronary cusp of the aortic valve (**Figure 2**A and B). Infective endocarditis was ruled out by negative results in repeated blood cultures and by a normal inflammatory index. The patient developed nonbacterial thrombotic endocarditis (NBTE). Subsequently, anticoagulation was initiated with continuous intravenous infusion of heparin. On day 11, follow-up transesophageal echocardiography demonstrated that the mobile vegetation had shrunk to 5 mm with a decreased whole volume (Figure 2C and D and videos 1, 2, 3, and 4, http://www.archneurol.com). At the same time, recurrent embolic stroke without symptoms was documented by follow-up magnetic resonance imaging (Figure 1C and D).

Video available online at www.archneurol.com

COMMENT

Nonbacterial thrombotic endocarditis, also known as marantic endocarditis associated with malignant or other debilitating systemic diseases, is sometimes difficult to confirm.[1] Most NBTE vegetations are smaller than 3 mm in diameter.[2] Transesophageal echocardiographic images are essential to detect NBTE vegetations because these images are superior to transthoracic echocardiographic images for identification of a cardiac embolic source.[3] The NBTE vegetations are easily dislodged because there is little inflammatory reaction at the site of attachment, and thus the vegetations are a source of multiple organ embolism. Our case strongly suggested that vegetation had dislodged and thus impacted multiple emboli into the cerebral arteries. Magnetic resonance imaging findings of our case were compatible with those of a typical index stroke associated with NBTE, with multiple, widely distributed, small (<10 mm) and large (>30 mm) strokes that are different from those with infective endocarditis.[4] In conclusion, transesophageal echocardiography is useful for the follow-up of NBTE to detect morphological changes in the vegetation as well as for the diagnosis of NBTE.

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Financial Disclosure: None reported.

Online-Only Material: The videos are available at http://www.archneurol.com.

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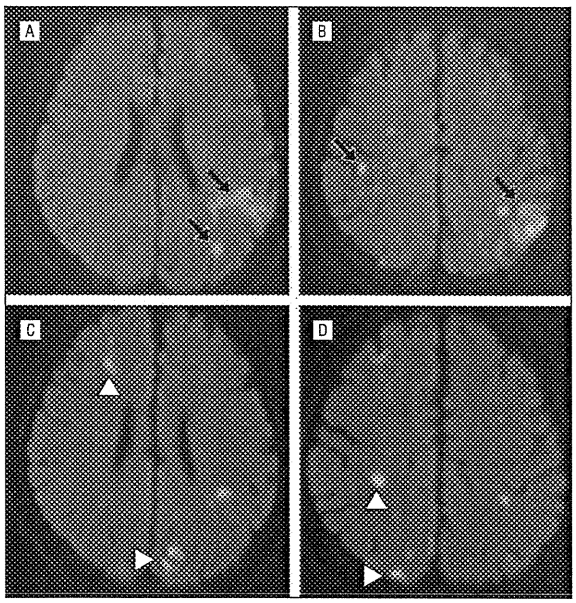

Figure 1. Diffusion-weighted images of the lateral ventricle (A) and the corona radiata (B) on the first day and of the lateral ventricle (C) and the corona radiata (D) 15 days after stroke onset. Multiple recent small and large stroke lesions (arrows on the first day, arrowheads on day 15) increased in bilateral middle cerebral arterial territories despite anticoagulation.

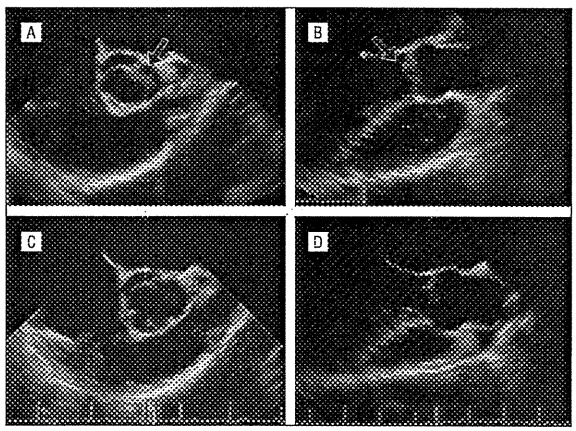

Figure 2. Transverse (A) and longitudinal (B) transesophageal echocardiographic images on the second day after stroke onset, and transverse (C) and longitudinal (D) transesophageal echocardiographic images 11 days after stroke onset. Transesophageal echocardiography revealed that the mobile isoechoic mass (arrows) on the left and noncoronary cusp of the aortic valve had shrunk from 7 to 5 mm.

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Original article

Determinants of progression of aortic valve stenosis and outcome of adverse events in hemodialysis patients

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KEYWORDS
Aortic valve stenosis;
Hemodialysis;
Calcium

Summary
Background: Hemodialysis (HD) is an important risk factor for progression of aortic valve stenosis (AS). However, there are varying degrees of disease progression among patients with AS on HD. The aim of this study was to find determinants of rapid progression of AS in patients on HD.
Methods: We enrolled 30 patients with AS on HD with a mean follow-up period of 4 years. The peak pressure gradient (PPG) between the initial echocardiography and the last echocardiography at least 3 months interval (ΔPPG) was adopted as the indicator of AS progression. We divided the patients into two groups according to ΔPPG per year [rapid progression (ΔPPG > 4.5 mmHg/year), slow progression (ΔPPG < 4.5 mmHg/year)] and compared the clinical characteristics between the two groups.
Results: Overall mean ΔPPG was 4.5 mmHg/year. Systolic blood pressure (SBP), serum calcium, and calcium-phosphate product were significantly higher in rapid progression group compared with slow progression group ($p < 0.05$).
Conclusion: High systolic blood pressure, serum calcium, and calcium-phosphate product were associated with rapid progression of AS in patients on chronic HD.

Introduction

Hemodialysis (HD) is an important risk factor for progression of aortic valve stenosis (AS). Previous reports showed accelerated progression of AS in HD patients compared with

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non-HD patients [1,2]. It has been reported that the progression of AS is associated with the same risk factors as cardiovascular disease including serum low-density lipoprotein level [3–5]. However there are few reports that have investigated whether the rapid progression of AS is associated with a high event-free rate in HD patients during follow-up period. Therefore the aim of this study was to investigate the determinants of progression of AS and identify the high-risk group of rapid AS progression, mortality, or cardiac events in patients with AS on HD.

Methods

Patient inclusion

Follow-up echocardiography recorded at least 3 months later was included. Patients without initial echocardiography data or biochemistry data were excluded. This study was performed with the Helsinki Declaration and approved by the institutional review board. All of the patients had previously granted permission for use of their medical records for research purposes.

Baseline data

Physical examination, medication, and biochemistry data were examined at the time of baseline echocardiography. Serum concentration of calcium was corrected by the concentration of albumin.

Echocardiography

Echocardiography was obtained by using commercially available ultrasound systems (SSA-380A, Toshiba, Tokyo, Japan or SONOS-7500, Phillips, Bothell, WA, USA). Diastolic dimension, systolic dimension, intraventricular septum, posterior wall, and left atrium dimension were measured. Ejection fraction (EF) was calculated by Teichholz method. Peak aortic jet flow was measured on the continuous-wave Doppler echocardiograms.

Long-term data

Follow-up was performed via office visit, letter, or telephone contact. Patients were followed until first events [death or aortic valve replacement (AVR)] or until the study end date (December 31st, 2009). Patients who did not experience an outcome of interest were censored at the last known date of contact. The study endpoints were all-cause death and AVR. The indication of operation was symptomatic (syncope, chest pain, and congestive heart failure) and severe [peak pressure gradient (PPG) over 50 mmHg or aortic valve area (AVA) under 1.0 cm^2] AS with preserved EF (EF > 50%) or moderate (PPG over 36 mmHg or AVA under 1.5 cm^2) AS with reduced EF (EF < 40%).

Statistical analysis

Data are presented as frequencies and percentages for categorical variables and means ± standard deviation for continuous variables. Patient characteristics were compared between the groups divided by the ΔPPG. Data were analyzed with Mann–Whitney *U*-test. Categorical data were compared using Fisher's exact test. Multivariate logistic analysis was applied to investigate whether the two groups of ΔPPG predict adverse events event (death or AVR) after adjusting other variables. In this model, we used mildly significantly different characteristics ($p < 0.10$) between the two groups as the independent variables. All variables were simultaneously adjusted in one step. Hazard ratios and the 95% confidence intervals were calculated. The Kaplan–Meier curves stratified according to the ΔPPG were drawn. A p-value < 0.05 was considered to indicate statistical significance. All analyses were performed using statistical software, SPSS 13.0/Windows (SPSS Inc., Chicago, IL, USA).

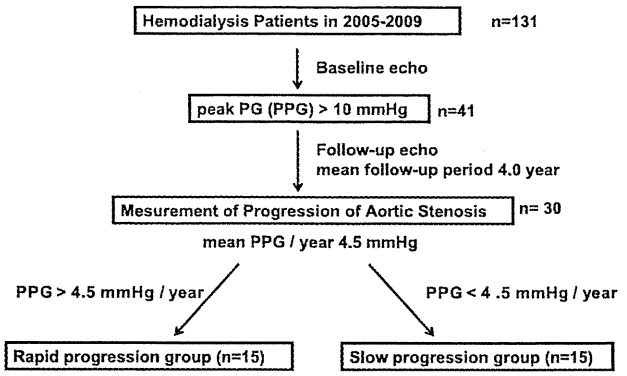

Figure 1 Patients' inclusion flow chart. PG, pressure gradient.

Results

Among 131 HD patients who were admitted to Jichi Medical University Saitama Medical Center between July 2005 and December 2009, echocardiography was performed in all patients (Fig. 1). Among 131 patients, 41 patients had AS with PPG over 10 mmHg. Of the 41 patients, echocardiography was performed at least twice in 30 of them. These 30 patients were divided into two groups according to mean ΔPPG: rapid progression group ($n = 15$, mean ΔPPG per year > 4.5 mmHg), and slow progression group ($n = 15$, mean ΔPPG per year < 4.5 mmHg) (Fig. 1).

Clinical characteristics of the patients are shown in Tables 1 and 2. Although there was a trend toward higher age in the rapid progression group ($p = 0.096$), there was no significant difference between the two groups. Mean baseline PPG of the two groups was not significantly different (Fig. 2). Mean ΔPPG per year was 11.1 ± 6.43 mmHg in the rapid progression group per year versus −2.18 ± 8.25 mmHg per year in the slow progression group ($p < 0.001$). Systolic blood pressure, serum calcium level, and product of calcium–phosphate were significantly higher in the rapid progression group. Corrected calcium level and product of calcium and phosphate were also significantly different between the two groups.

Multivariate Cox regression analysis is shown in Table 3. In this model, the factors with $p < 0.10$ in univariate analysis,

Table 1 Clinical characteristics of aortic stenosis in patients on hemodialysis.

	Rapid progression ($n=15$)	Slow progression ($n=15$)	p-Value
Age (years)	73.6±6.1	69.8±7.5	0.096
Male sex, no. (%)	6 (40%)	8 (53%)	0.72
Height (m)	1.58±0.08	1.57±0.08	0.84
Weight (kg)	57.8±7.56	53.9±11.2	0.36
Diabetes mellitus, no. (%)	7 (67%)	10 (47%)	0.46
Hypertension, no. (%)	15 (100%)	15 (100%)	1.00
Dyslipidemia, no. (%)	3 (20%)	7 (47%)	0.25
Current smoker, no. (%)	8 (53%)	6 (40%)	0.72
Atrial fibrillation, no. (%)	2 (13%)	2 (13%)	1.00
Lipid			
Total cholesterol (mg/dl)	111±78	138±64	0.98
Triglyceride (mg/dl)	116±81	138±64	0.18
HDL-cholesterol (mg/dl)	41±8	43±13	0.50
Medication, no. (%)			
Angiotensin-converting enzyme inhibitor	5 (33%)	5 (33%)	1.00
Angiotensin receptor blocker	12 (%)	10 (%)	0.68
Calcium antagonists	11 (73%)	10 (67%)	1.00
β-Blockers	3 (20%)	5 (33%)	0.34
α-Blockers	2 (13%)	4 (27%)	0.65
Diuretics	5 (33%)	4 (27%)	1.00
Statin	1 (7%)	2 (13%)	1.00
Phosphate adsorbent	9 (60%)	6 (40%)	0.47
Vitamin D3	6 (40%)	5 (33%)	1.00
Etiology of hemodialysis, no. (%)			
Diabetic nephropathy	7 (47%)	8 (53%)	
Chronic glomerulonephritis	4 (27%)	2 (13%)	
Hypertensive nephropathy	1 (7%)	3 (20%)	
Chronic nephritis	1 (7%)	1 (7%)	0.74
IgA nephropathy	1 (7%)	1 (7%)	
Chronic nephropathy	1 (7%)	1 (7%)	
Rapid progressive glomerulonephritis	1 (7%)	0 (0%)	
Etiology of AS, no. (%)			
Degenerative	14 (46.7%)	15 (100%)	
Rheumatic	0 (0%)	0 (0%)	1.00
Bicuspid	1 (3.33%)	0 (0%)	

HDL, high-density lipoprotein; AS, aortic valve stenosis.

age, systolic blood pressure, and serum calcium were adopted as independent variables. Systolic blood pressure and serum calcium were strong predictors of adverse events even after adjusting for these factors (Table 3).

The relationship between the progression of AS and death or AVR is shown in Fig. 2. There were 15 events (4 deaths and 6 AVR in rapid progression group, 2 deaths and 3 AVR in slow progression group) during a mean period of 4.0 years ($p=0.07$, Table 2, and Fig. 2).

Discussion

Our study showed that the overall change in mean PPG per year in AS patients on HD was 4.5 mmHg. Systolic blood pressure and serum calcium concentration were strongly associated with rapid progression in HD patients. Moreover our study also showed that the clinical event rate was higher in the rapid progression group than in the slow progression group.

Previous reports showed that the mean ΔPPG per year of AS in HD patients was 3.9 mmHg [6] and the mean PPG per year in non-HD patients was 1.0 mmHg [7]. Our results, 4.5 mmHg, are similar to AS in HD in the previous study [6]. These results also confirmed that the progression of AS in HD is more rapid compared with non-HD patients.

Earlier studies identified male gender, history of atherosclerosis, and impaired renal function as the determinants of AS progression in non-HD patients [2,8,9]. Hypercholesterolemia is reported to be a risk factor for the development and progression of calcific AS [3,10], although recent studies throw doubt on this hypothesis [4]. It is reported that aortic valve calcification is also accelerated in HD patients [11]. Increased calcium–phosphate product, secondary hyperparathyroidism, and excess vitamin D are thought to be responsible for calcium deposition [12–15]. Accelerated calcium deposition not only in the coronary arteries but also on the aortic valves may comprise a morbid problem in HD patients [12,15–17]. Owens and Otto [18] reported that the conventional atherosclerotic factors

Table 2 Univariate analysis of determinants of the progression of aortic stenosis.

	Rapid progression ($n=15$)	Slow progression ($n=15$)	p-Value
Follow-up (year)	4.02 ± 2.11	4.05 ± 2.84	0.82
Hemodialysis (year)	9.53 ± 4.27	9.80 ± 4.96	0.72
ΔPeak pressure gradient (mmHg/year)	11.1 ± 6.43	−2.18 ± 8.25	<0.001
Ejection fraction (%)	59.7 ± 10.8	65.1 ± 9.7	0.19
Systolic blood pressure (mmHg)	161 ± 21.5	142 ± 24.4	0.04
Diastolic blood pressure (mmHg)	80.2 ± 13.7	71.4 ± 14.2	0.12
Heart rate (/min)	74.9 ± 12.0	74.8 ± 16.1	0.76
LDL-cholesterol (mg/dl)	97.4 ± 40.2	93.2 ± 34.5	0.65
Hemoglobin A1C (%)	5.3 ± 0.8	5.6 ± 0.8	0.38
C-reactive protein (mg/dl)	0.32 ± 0.21	0.28 ± 0.45	0.11
Serum Ca (mg/dl)	9.66 ± 1.05	8.87 ± 0.91	0.02
Serum albumin (mg/dl)	3.80 ± 0.53	3.80 ± 0.55	0.88
Corrected serum Ca (mg/dl)	10.0 ± 0.89	8.87 ± 1.34	0.01
Serum P (mg/dl)	5.66 ± 1.00	5.47 ± 1.17	0.90
Ca × P	54.5 ± 9.94	48.2 ± 10.1	0.10
Corrected Ca × P	56.5 ± 10.5	48.3 ± 11.6	0.11
Death	4 (26%)	2 (13%)	0.33
Aortic valve replacement	6 (40%)	3 (20%)	0.21
Heart failure re-hospitalization	2 (13%)	1 (7%)	0.50
Death and aortic valve replacement	10 (67%)	5 (33%)	0.07

LDL, low-density lipoprotein.

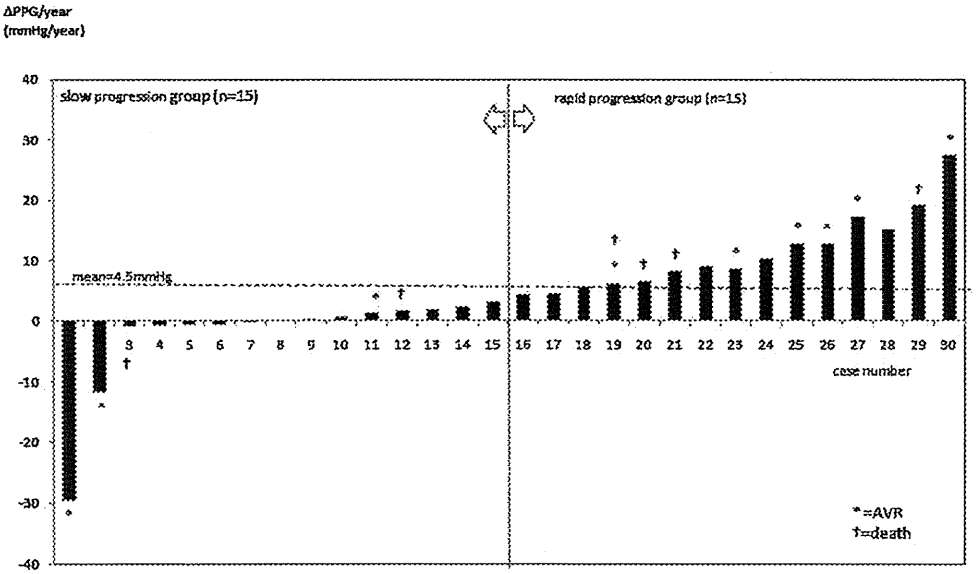

Figure 2 The relationship between the progression of aortic stenosis and death or aortic valve replacement. AVR, aortic valve replacement; PPG, peak pressure gradient.

Table 3 Results of multivariate logistic regression analysis.

Variables	Odds ratio	95%CI	p-Value
Age (+1 year)	1.27	1.00–1.61	0.05
Systolic blood pressure (+10 mmHg)	1.06	1.00–1.11	0.04
Serum Ca (+1 mg/dl)	6.08	1.28–28.8	0.02

CI, confidence interval.

promote the 'sclerosis of the aortic valve' [19], and the stenosis of aortic valve progresses in the later phase [18]. Our results showed that low-density lipoprotein cholesterol, C-reactive protein [20], and age were not significant determinants for the progression of AS, while systolic blood pressure, serum calcium level, and products of calcium and phosphate were strong determinants of rapid progression in HD patients. The patients on HD are considered to be already in the later phase of the cascade of AS. These results suggest that calcium plays an important role in the progression of AS in patients on HD.

The present study also showed the event-free rate of the rapid progression group was lower than in the slow progression group. The event-free rate in the rapid progression group of AS in HD is 40% while the event-free rate of the slow progression group is 67% during 4 years of follow-up (Table 2). A previous report from Japan has shown that the mean 4-year survival rate of HD patients is 80% [21]. Our results show that the freedom from death or AVR in AS patients on HD is worse than non-AS patients on HD.

Study limitations

A retrospective study design with a relatively small sample size in a single center may pose a risk for patient selection bias. The interval between baseline and follow-up echocardiography was different among patients. The data of serum concentration and blood pressure were collected at the start of follow-up, which may not reflect the data of the whole clinical course.

Severe calcification of aortic valve often makes acoustic shadow in echocardiography and interrupts accurate measurement and AVA is not always measured exactly in all cases of AS with severe calcification in HD patients. In this study, 20 cases were interrupted to measure accurate AVA with severe calcification. For these reasons, PPG was adopted as a parameter of progression of AS in HD, instead of AVA, however the weak point of PPG was its dependence on cardiac function and some cases with deteriorating EF in the rapid progression group may be included in the slow progression group.

In this study, parathyroid hormone was checked only in 10 cases, because the measurement of serum parathyroid hormone was limited only to the patients whose serum calcium and phosphate level was treated by standard therapy and decreased to the adequate cut-off level by the Japanese guidelines about the treatment of the patients with secondary hyperparathyroidism in HD patients in 2006. The hyperparathyroidism was treated by vitamin D3 and phosphate absorbent according to the guidelines.

Conclusions

Our study showed that high systolic blood pressure and serum calcium level were associated with rapid progression of AS in patients on chronic HD. It is an open question whether the careful clinical follow-up of AS and the control of blood pressure and serum calcium may lower the event rate of AS patients on HD.

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当院心臓血管外科術後におけるリハビリテーションの現状
～ICU担当理学療法士の立場から～

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Ⅰ．はじめに

鹿児島医療センター（以下，当院）の心臓リハビリテーション（以下，心リハ）は，2007年の開設時からリハビリテーション科専門医（以下，リハ医）・専従看護師（以下，専従Ns）・専従理学療法士を中心に実施されてきた[1)2)]。リハ科のスタッフの充実や，心臓・がん・脳卒中部門のリハスタッフの経験がつまれてきた事で，2010年10月より病棟担当制へと体制を整備することが可能となった。ICUにおいても，担当理学療法士を配置し，理学療法士のより早期からのリハ介入が可能な体制となった。今回，ICU担当理学療法士の立場から，当院での心臓血管外科術後リハの現状について調査したので，冠動脈バイパス術（以下，CABG）後の症例紹介も交えて，現状と課題を報告する。

Ⅱ．当院の術後心リハの概要

心臓血管外科術後患者のリハは，術後３日目にリハ医による診察・リハ処方がなされ，ICU内で理学療法士によるリハ介入が開始される（図１）。術後４日目に一般病棟へ転棟後，病棟での歩行拡大を行い，術後７日目に専従Nsが集団リハオリエンテーションを実施し，リハ室での集団運動療法へと移行する。2010年10月からは理学療法士もICUでの離床訓練から，自転車エルゴメータ（以下，エルゴ）による集団運動療法まで一貫して関わることができる体制となった。

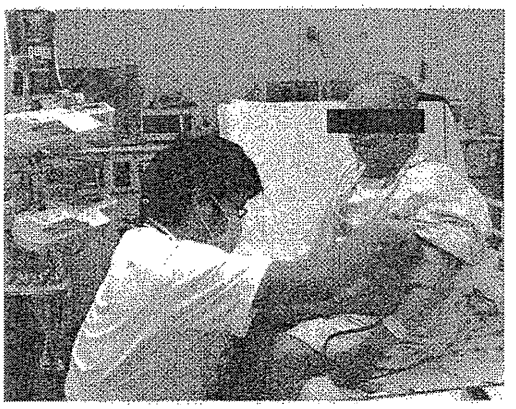


図１　ICU内におけるリハ実施

Ⅲ．対象・調査内容

2010年10月１日から2011年１月31日までの４ヵ月間に心臓血管外科にて心・大血管手術が施行された86例を対象に，①手術内容とリハ介入の有無，②ICUにおける理学療法士介入率，③ICU在室日数，④リハ介入期間，⑤集団運動療法移行率について調査した。

Ⅳ．結果

手術内容はCABG　30例，弁膜症手術22例，血管系（末梢血管含む）手術31例，その他３例，で

表１　手術内容とリハ介入症例の内訳

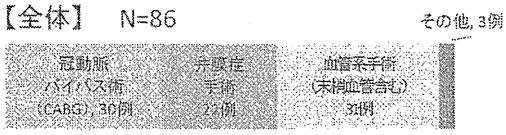
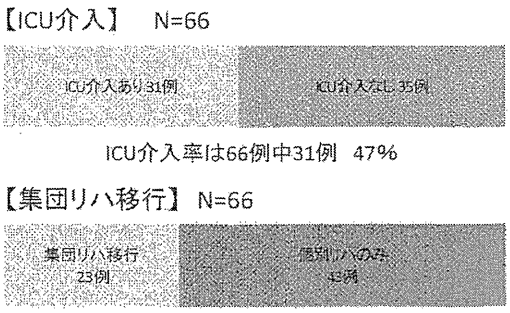


表２　ICU 介入と集団リハ移行



あった。86例のうちリハ介入となった症例は66例で CABG・弁膜症術後はクリティカルパスを使用し，術後早期死亡例１例を除く全症例にリハ介入した。なお当院では腹部大動脈瘤の術後症例は原則病棟看護師での対応としているためにリハは実施されず，血管系術後症例のリハ介入数は減少している（表１）。

この66例においては，ICU 在室日数は平均5.4日，リハ介入期間は平均18日であったが，実際にICU でリハ介入症例は66例中31例（47.0%）であった。集団運動療法に移行した症例は66例中23例（34.8%）であり（表２），そのうち ICU からのリハ介入症例は23例中15例（65.2%）であった。

Ⅴ．症例紹介

ここで順調に心リハを実施できた症例の紹介を行う。

【症例】40歳代前半，男性。

【診断名】狭心症，陳旧性心筋梗塞，高脂血症，高尿酸血症。

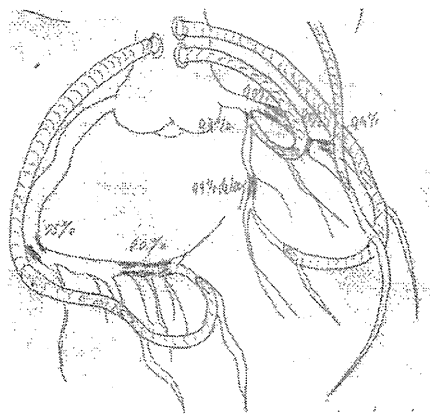
【生活習慣】運動習慣なし，偏食（外食中心の生活），喫煙。

【現病歴】Ｘ年Ｙ月下旬の夕食中に胸痛を自覚し，近医へ救急搬送された。急性心筋梗塞が疑われ，緊急で冠動脈造影検査が施行され，３枝病変を認めた。保存的加療を行い，一時退院後のＹ＋１月に当院心臓血管外科を紹介され，手術目的で入院となった。

【入院時検査所見】

胸部レントゲン：肺胸郭比46%，胸水・肺うっ血所見なし。心臓超音波検査：左室駆出率53%，有意な弁膜症なし。壁運動は後壁の基部～中部と側壁の基部～中部が重度に低下していた。冠動脈造影検査（前医施行）：

#2）75%，#4PL）90%，#6）90%，#7）70%，#9）90%，#11）99%，#13）99%delay。



CABG6枝

LITA-#7、Ao-SVG-#4PD-#4PL、

Ao-SVG-#9-#14 、Ao-SVG-#12（HL position）

図２　冠動脈バイパス術

【手術】CABG 6枝（図2）

LITA - #7, Ao - SVG - #4PD-#4PL, Ao - SVG - #9-#14, Ao - SVG - #12 (HL position)。

【術後リハ経過】

①ICU～一般病棟でのリハ介入

術後3日目：リハ医診察後にICU内で理学療法士介入し，端座位・起立・1m歩行を実施。

術後4日目：一般病棟転棟後，歩行練習開始（午前30m・午後100m）。

術後5日目：午前病棟歩行200～300m，午後病棟歩行300～400m。

術後6日目午前：病棟歩行500m＋階段昇降訓練。

病棟リハ期間は，原則午前・午後の1日2回介入し，歩行距離の拡大・創部や呼吸状態等の確認を中心にリハを実施した。

②リハ室での集団運動療法・教育指導

術後6日目午後：エルゴ；20ワット／10分×2セット。集団教育指導の場面では，積極的な発言を認めた。

術後7日目：午前歩行練習10分，午後エルゴ20～30ワット／20分。

術後10日目：心肺運動負荷試験が実施され，運動処方（エルゴ；35ワット／30分・目標心拍数120拍／分，歩行：100m／1分30秒＝3METS）が決定された。

術後11日目：午前15分間歩行，午後エルゴ：35ワット／30分。

術後12日目：午前屋外歩行，午後エルゴ：35ワット／30分，退院時リハ指導実施。

術後13日目：自宅退院。

エルゴによる運動を歩行へ定着するために，理学療法士は，午前中に歩行練習，午後は集団運動療法にてエルゴトレーニングの管理を行い，1日2回の介入を継続した。

③外来心リハへの移行

退院1週間後に初回外来心リハ実施となった。専従Nsによる問診（図3）と集団運動療法を実施

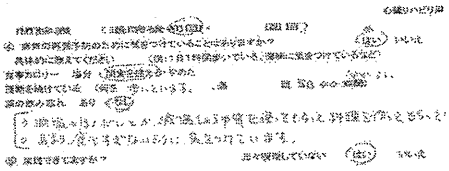


図3　専従Nsによる問診票

し，退院時リハ指導の「禁煙・運動の継続・食事への注意」が守れていることを確認した。以降，月2回の外来心リハを継続し，術後2カ月目に復職を果たした。

VI. 考察

2010年10月以降はICUでの早期リハ介入を開始したが，術後介入66例のうち，ICUより介入できたのは31例と約半数にとどまっていた。ICUから全例に対してリハ介入できていない要因として，①術後経過が極めて良好でありリハ介入前に一般病棟へ転棟する，②循環動態が安定するまでに期間を要し，結果として一般病棟転棟後からリハが開始される，③リハ実施のない土日に転棟すること，が挙げられる。今回提示した症例は，当院で最も術後リハ介入数の多いCABG後29例の中で，ICUで早期リハ介入を開始して集団リハまで移行した。結果的に平均リハ介入期間18日の現状の中で，リハ介入期間10日間という非常に短期間で入院心リハを終えて，外来心リハへの移行まで達成できた症例である。順調に外来心リハまで移行できた要因として，①ICUから介入したことで早期より患者との信頼関係が築けたこと，②離床訓練～集団運動療法まで理学療法士が一貫して関わることができたこと，③集団運動療法でのエルゴトレーニングの管理だけではなく運動療法を今後の日常生活へ定着させるために歩行練習を繰り返し実施したこと，が挙げられる。前述の調査結果のように術後平均リハ介入期間は約18日間と決して長くはなく，その間に外来心リハへ順調に

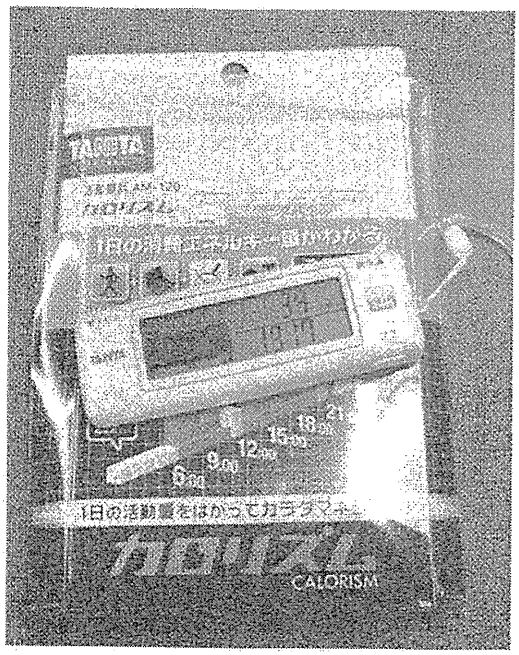


図４　消費カロリー等が測定可能な歩数計

移行させていくために，理学療法士もICUにおける術後早期離床訓練から退院時リハ指導までリハ医・専従Nsと同様に一貫して関わり，信頼関係を築くことは重要である。さらに集団運動療法（エルゴトレーニング）と並行して個別運動療法（歩行訓練）を入院中継続して行うことは培った運動習慣を日常生活へ定着させるために有効な方法と考えられた。

課題は，理学療法士による歩行練習を中心とした個別運動療法を実施していくうえで，まだ客観的な要素が不足している点である。今後は消費カロリー等が測定可能な歩数計（図４）や脈拍測定器等を使用して客観的な指標を示し，より運動が定着しやすい方法の指導と歩行練習の質の向上が必要であると考える。また，現在は人員的な要因により理学療法士の業務は入院中の術後リハが中心であり，術前リハ・退院後の外来心リハは基本的にリハ医・専従Nsが行っているので，当院におけるこの領域への理学療法士の関わりを今後は検討していきたい。

Ⅶ．文献

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